Between May 2008 and October 2015, 143 patients were randomised to infliximab or laparoscopic ileocecal resection. Follow-up. Furthermore, the mean direct costs per individual patient were proportionally calculated. A multicenter randomized controlled, open-label trial was performed in 33 centers in the Netherlands and the United Kingdom. Adult patients with CD of the terminal ileum who failed > 3 months of thiopurine treatment or steroids without signs of a critical stricture were randomised to infliximab or laparoscopic ileocecal resection. Patients with a prior ileocecal resection, a disease length > 40 cm, abdominal abscesses or fluid collections or an American Society of Anesthesiologists (ASA) score of III or IV were excluded. The primary endpoint was QoL measured by the Inflammatory Bowel Disease Questionnaire (IBDQ) at one year follow-up. Furthermore, the mean direct costs per individual patient were prospectively documented and analysed according to intention-to-treat until one year after start of treatment. Dutch Trial Registry NTR1150.

Results: Between May 2008 and October 2015, 143 patients were randomised (32.9% male) with a median age of 27.0 years (interquartile range (IQR) 22.0–40.0). Eventually, 65 patients started with infliximab treatment and 70 patients were operated. On April 28th 2016, 96.5% of the patients have completed follow-up. At baseline, the mean difference (MD) in IBDQ score was 4.9 points in favour of the resection group. After correction for the baseline difference, the MD at one year follow-up was 5.8 points in favour of resection (95% confidence interval (CI) = 4.3 to 16.3, p=0.28). The mean direct total costs per patient at one year were €14,589 in the infliximab group and €10,318 in the resection group (MD 0.47, 95% CI 0.125 to 0.716, p=0.005). Infliximab was stopped in 21 patients (30.0%) due to intolerance or insufficient response, 13 of whom underwent an ileocecal resection after a median time of 27.0 weeks (IQR 11.0–33.5) after start of infliximab treatment. CD related serious adverse events in the infliximab group occurred in 3 patients (4.2%) compared with both C57BL/6J (1.0 ± 0.01 g, n = 5) and non-transplanted nNOS−/− mice (0.31 ± 0.06 g, n = 5; P = 0.0016). In transplanted colonic segments, addition of the nitric oxide synthase blocker L-NAME resulted in significant reductions in the observed EFS-induced relaxation (0.13 ± 0.006 g, n = 5) compared with either non-transplanted nNOS−/− mice (0.31 ± 0.06 g, n = 5; P = 0.0093) and non-transplanted nNOS−/− mice (0.05 ± 0.008 g, n = 5; P = 0.0025). These high-amplitude contractions were not affected by application of tetrodotoxin, suggesting that transplantation of ENSC can also lead to changes in underlying myogenic motility patterns. To assess the mechanisms involved in these non-cell autonomous phenomena we sought to investigate potential changes in gut morphology. No significant change was observed in the diameter of the distal colon between transplanted nNOS−/− mice (1.04 ± 0.135 mm; n = 3) compared to either non-transplanted nNOS−/− mice (1.1 ± 0.09 mm; n = 3; P = 0.069) or sham-operated nNOS−/− mice (1.05 ± 0.02 mm; n = 3; P = 0.947). In addition, no change in muscle thickness was observed between transplanted nNOS−/− mice (35.33 ± 8.67 μm; n = 3) compared to either non-transplanted nNOS−/− mice (34.0 ± 0.90 μm; n = 3; P = 0.915) or sham-operated nNOS−/− mice (35.33 ± 2.96 μm; n = 3; P = 0.918). Ongoing work is targeting other potential processes such as modification of cell types involved in neurotransmitter signaling, including interstitial cells of Cajal within the transplanted microenvironment.

Conclusion: Here we demonstrate, for the first time, that transplanted ENSC integrate and effect restoration of function, at the organ level, in a pathological GI disease model potentially via both ENSC-specific and non-ENSC-specific processes.
Introduction: Dietary interventions may be recommended to IBS patients yet effects on gut microbiota and factors predicting response are largely unknown.

Aims & Methods: We aimed to determine how two different diets affect gut microbiota and if bacterial profiles and modelling thereof can be used to predict patient intervention response in a secondary analysis of a previously published interventional study (Böhm et al.2015). After a 10 day screening period 61 IBS patients with at least moderately severe IBS symptoms according to IBS Symptom Severity Score (IBS-SSS) followed either a traditional IBS (n=30) or low-FODMAP (n=31) diet for 4 weeks. Faecal samples were collected and IBS-SSS were completed before and after the intervention. Food intake was recorded in 4-days food diaries before (baseline) and during the interventions. Responders were defined as having a reduction of IBS-SSS > 30 after the intervention. Faecal bacterial composition was evaluated by GA-map™ Dysbiosis Test which measures probe signal intensity (PSI) of 54 DNA probes targeting ≥300 bacteria on different taxonomic levels. A bacterial profile was generated for each patient by multivariate analysis discrimination and graded from 1–5, relative to a healthy reference group. A dysbiosis index (DI) ≤ 2 signifies normal microbiota composition, ≥ 6 signifies altered microbiota composition (dysbiosis). For all models, both strong and moderate outliers were sequentially excluded.

Results: At baseline, 45 patients (25 randomized to traditional diet and 20 to low-FODMAP) had a DI ≥ 3, i.e. dysbiosis; of these, 10 patients following the traditional diet and 4 patients following the low-FODMAP diet experienced an improvement in DI, while 6 following the traditional diet and 11 on the low-FODMAP diet had worsening of their dysbiosis; the rest experienced no change. In the low-FODMAP group not all traditional diet group responders (n=90) had more severe dysbiosis than responders (n=12) (3 (3–4) DI; 2 (2–3) DI; p=0.007) at baseline. Although patients on a traditional diet consumed significantly less protein, fat, and alcohol, they experienced no change in overall bacterial composition after the intervention. Patients on a low-FODMAP diet ate significantly less carbohydrates, fibre, monosaccharides, fructose and total FODMAPs, and had significant reduction in potentially beneficial Bifidobacterium after the intervention (23 (25.4–122.8) PSI) compared to before (152 (45.7–70) PSI, p=0.0005) which was even more prominent in non-responders. An OPLS-DA model of before the low-FODMAP intervention demonstrated satisfactory model performance with the low-FODMAP group randomized to low-FODMAP diet (R2Ycum = 0.652; Q2 cum = 0.541), showing that bacterial profiles differed between responders and non-responders. An OPLS-DA model of the traditional diet group was inadequate, showing good model fit but poor predictive abilities (R2Ycum 0.652, Q2 cum 0.541), demonstrating that bacterial profiles did not differ between responders.

Conclusion: Faecal bacterial profiles predict patient responsiveness to a low-FODMAP dietary intervention. Thus, before considering dietary interventions, bacterial profiles need to be determined in order to identify patients whom are likely to respond favourably.

Disclosure of Interest: L Öhman: Unrestricted research grants from AstraZeneca; Co-founder of Enterogenex, member for Genetic Analysis; Speaker for Genetic Analysis, Takeda and Abbot.

All other authors have declared no conflicts of interest.
C. Gasink: Employee of Janssen Research & Development, LLC
D. Jacobsen: Employee of Janssen Research & Development, LLC
L.L. Gao: Employee of Janssen Research & Development, LLC
J. Johanns: Employee of Janssen Research & Development, LLC
P. Szapary: Employee of Janssen Research & Development, LLC
J. Colombel: Investigator for Janssen Research & Development, LLC
S. Targan: Investigator for Janssen Research & Development, LLC
S. Ghosh: Investigator for Janssen Research & Development, LLC

Conclusion: This is the first real-life experience with VDZ that shows substantial variability in exposure to VDZ between patients. A clear exposure-response correlation was observed as early as w2 and w6, with significant impact of higher VDZ TC on meaningful outcomes as biological response, remission and endoscopic healing. Our data support a potentially important role for early therapeutic drug monitoring also with VDZ.

Disclosure of Interest: A. Gils: Lecture fee(s) MSD, Janssen Biologics, Abbvie, Pfizer, Takeda. Consultancy: UCB. Conflict: with: license of infiximab, anti-infliximab and adalimumab ELISA from Institution to apDia and with lateral flow infiximab to Biopharm-A
S. Vermeire: Grant/research support Takeda, MSD, Abbvie Consultancy/speakers’ fees from Abbvie, MSD, Takeda, Pfizer. Guapagos, Genentech/Roche, Mundipharma, Celgene, Hospira, Second Genome
All other authors have declared no conflicts of interest.

OP006 VEDOLIZUMAB EXPOSURE CORRELATES WITH CLINICAL, BIOLOGICAL AND ENDOSCOPIC OUTCOME IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE
A. Gilis1, E. Dreesen1, G. Compernolle1, M. Peeters1, E. Brouwers1, V. Ballet2, M. Noman2, M. Ferrante2, G. Van Assche2, S. Vermeire2

Contact Email Address: severeine.vermeire@uzleuven.be

Introduction: Vedolizumab (VDZ) specifically targets the a4β7 integrin on gut-homing lymphocytes and has been approved for the treatment of patients with moderate to severe Crohn’s disease (CD) and ulcerative colitis (UC). We studied the relation between serum VDZ trough concentrations (TC) and clinical, biological and endoscopic outcomes in real-life practice.

Aims & Methods: The first 75 patients (49 CD, 26 UC) who initiated VDZ therapy (300 mg IV administered) in our tertiary referral center were sampled at trough during induction (w2 and w6) and early maintenance (w10, w14 and w22) treatment. Clinical response (clinical symptoms and physical global assessment) was correlated to VDZ TC. All patients with UC received simethicone at baseline and w10 and mucosal healing was defined as a Mayo endoscopic subscore of 0 or 1. Biological response (CRP decrease ≥50% from baseline) and remission (CRP<5 mg/L) were assessed at w6 and w22 in patients with CD. An ELISA for measuring serum VDZ TC was developed in house. TC are shown as median [IQR].

Table 1: Vedolizumab trough concentrations, in µg/mL, median [IQR] (n), during induction (w2 and w6) and early maintenance (w10, w14 and w22) treatment correlated with biological remission (CRP <5 mg/L at w22) in patients with CD.

<table>
<thead>
<tr>
<th>Week</th>
<th>Median [IQR] (n)</th>
<th>Biological response</th>
<th>Remission</th>
</tr>
</thead>
<tbody>
<tr>
<td>w2</td>
<td>31.8 [23.9–38.9] (23)</td>
<td>23.6 [18.4–31.9] (17)</td>
<td>14.0 [9.7–18.6] (17)</td>
</tr>
<tr>
<td>w10</td>
<td>37.9 [24.4–45.1] (15)</td>
<td>12.8 [7.5–19.3] (10)</td>
<td>14.0 [9.7–18.6] (17)</td>
</tr>
<tr>
<td>w22</td>
<td>16.1 [9.5–25.2] (23)</td>
<td>6.3 [2.8–11.2] (17)</td>
<td>14.0 [9.7–18.6] (17)</td>
</tr>
</tbody>
</table>

*p < 0.05; ** p < 0.01; *** p < 0.001

Clinical response was achieved in 65% (47/72) of patients with UC. Patients with endoscopic healing had significantly higher VDZ TC at w6 (30.5 µg/mL [18.6–30.0]), compared to patients who did not achieve endoscopic healing (16.6 µg/mL [11.0–29.3]) (p = 0.02). Clinical response was achieved in 69% (47/68) of the patients. Only in patients with UC, clinical response was associated with higher VDZ TC at w2 (27.8 µg/mL [22.3–37.3], n = 16) and w6 (32.0 µg/mL [17.8–37.7], n = 16) compared to absence of clinical response (2.16 µg/mL [10.0–25.2] and 16.6 µg/mL [11.0–20.6], resp., n = 7) (p = 0.03 and p = 0.02).

Contact Email Address: bellgeysh@gmail.com

Introduction: Vedolizumab is an anti-α4β7 monoclonal antibody effective in ulcerative colitis (UC) and Crohn’s disease (CD). Data regarding pharmacokinetics/pharmacodynamics of vedolizumab are still scarce.

Aims & Methods: Aim: To assess whether early vedolizumab trough levels (weeks 2, 6) correlate with response to vedolizumab induction therapy. Methods: A novel ELISA-based assay was developed, for measuring Vedolizumab Zaera, and employed in prospectively-followed IBD patients receiving vedolizumab induction therapy. Drug levels were assessed for association with clinical remission defined by HBI and CRP normalization.

Results: Seventy-two patients were included (47 CD, 25 UC), of whom 14 (30%) and 15 (32%) of CD patients and 6(25%) and 8 (32%) of UC patients reached clinical remission by weeks 6 and 14, respectively. The median level of vedolizumab at week 6 was not different between patients who achieved remission by week 6 and those who did not (37.3 vs. 29.4 µg/mL respectively, p = 0.085). Clinical remission rates at week 6 were also not associated with drug level quartiles at week 6. Similarly, neither week 2 or 6 levels were predictive of clinical remission at week 14 (35.4 vs. 44.8 µg/mL, p = 0.75, 33.9 vs. 25.5 µg/mL, p = 1, respectively). Vedolizumab levels were also not associated with steroid free remission (p = 0.57) or with CRP normalization (p = 0.26, p = 0.73) at weeks 6 and 14, respectively. Among UC patients separately analyzed, week 2 levels were associated with clinical remission at week 14 (p = 0.04). However, statistical significance for this difference was not retained after Bonferroni correction for multiple testing. Finally, multivariable analysis for clinical remission at week 6 has been performed including baseline albumin level and patient weight. When adjusting for these co-variates, week 6 vedolizumab levels were not associated with clinical remission at week 6 (p = 0.56).

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S. Ben-Horin: Prof. Ben-Horin has received consulting and/or advisory board fees from Janssen, Takeda, Celltron, Abbvie, & Schering-Plough and research support from Celltron and Abbvie.
All other authors have declared no conflicts of interest.
OP008 PREDICTORS OF NON-RESPONSE OR LOSS OF RESPONSE TO TUMOUR NECROSIS FACTOR ANTAGONIST THERAPIES IN INFLAMMATORY BOWEL DISEASE

L. Peyrin-Biroulet1, A. Armuzzi2, J. P. Gisbert3, G.C. Nguyen4, B. Bokemeyer5, J. Lindsay6, M. Smyth7, M. Munsaka8, S. Ramagopalan9, J.M. Khalid10

1Department Of Gastroenterology, Nanyang University Hospital, Yanduanve les-Nancy/France
2Complejo Integrato Columbus, Internal Medicine and Gastroenterology - Complejo Integrato Columbus Catholic University, Rome/Italy
3Digestive Services, Hospital Universitario de La Princesa, Instituto de Investigacion Sanitaria Princesa (IP) and Centro, Madrid/Spain
4Mount Sinai Hospital Toronto, Toronto/Canada
5Gastroenterology Practice Minden, Minden/Germany
6Dept. Of Digestive Diseases, Digestive Disorders Clinical Academic Unit, Barts & The London School of Medicine & Dentistry, London/United Kingdom
7Global Medical Affairs, Takeda Pharmaceutical Global Medical Affairs, London/United Kingdom
8Safety Statistics & Observational Research Analytics, Takeda Development Center Americas, Deerfield/United States of America/IL
9Investigación Sanitaria Princesa (IP) and Centro, Madrid/Spain
10Evidera Real-world Evidence, London/United Kingdom
11Global Outcomes Research, Takeda Development Centre Europe Ltd, London, United Kingdom

Contact E-mail Address: peyrinbiroulet@gmail.com

Introduction: Tumour necrosis factor antagonists (anti-TNFs) are effective at inducing and maintaining disease remission in patients with moderate to severe ulcerative colitis (UC) or Crohn’s disease (CD). However, considerable proportions of patients do not respond to therapy or lose response over time. This study uses real-world data to identify predictors of non- or loss of response to anti-TNF therapy. The study recruited UC and CD patients from 6 countries [Canada, France, Germany, Italy, Spain, and the United Kingdom (UK)] aged ≥18 years who initiated anti-TNFs (infliximab/adalimumab or certolizumab during Jun 2009 to June 2011 (CD) or Jun 2009 to June 2013 (UC)]. Data were collected on patient demographics, clinical characteristics and healthcare resource use. Patients were classified as having non- or loss of response if they: were hospitalized or required UC/CD surgery whilst on therapy, discontinued due to UC or CD flare, required dose-escalation or augmentation with steroids, or immunosuppressants 4 months after therapy initiation, or disease severity became worse after therapy initiation. Multilevel multivariable logistic regression was used to identify predictors of non- or loss of response.

Results: The study included 1195 patients (45% UC, 55% CD; 9.6% Canada, 13% France, 22% Germany, 23% Italy, 19% Spain and 14% UK). Mean age: 40.3 (SD = 13.7); 51%: male. Most patients had a Charlson comorbidity index (CCI) score of 0–1 (83%), 16% were current smokers, mean BMI was 24.8 (SD = 7.18) and mean disease duration was 8 years (SD = 8.07). Most patients had a physician global assessment of moderate (45%) at study entry. Mean follow up was 3.4 years (UC) and 4.4 years (CD). Overall, 22% of patients had a primary non-response and 71% were classified as having non- or loss of response to anti-TNF therapy in the maintenance period (4 months after initiating anti-TNF) over a mean follow up period of 32 months (SD = 20.4). Significant predictors of non-/loss of response are shown in the Table 1. Soft stools per day. These predictors should be considered when evaluating treatment options for patients.

Disclosure of Interest: L. Peyrin-Biroulet: Consulting fees from Merck, Abbvie, Janssen, Genentech, Mitsubishi, Ferring, Norgine, Tillots, Vifor, Therakos, BMS, UCB-pharma, Hospira, Celltrion, Takeda, Biogaran, Boehringer-Ingelheim, Lilly, Pfizer, Amgen, Sanden, Celgene, Biogen, Janssen. A. Armuzzi: Grant/research support from: MSD, Consultant for: Abbvie, Celltrion, Hospira, Janssen, Lilly, MSD, Mundipharma, Pfizer, Sofar, Samsung, Takeda, Speaker bureau with: Abbvie, Astra-Zeneaca, Chiesi, Ferring, Hospira, MSD, Mundipharma, Otsuka, Takeda, Zambon. J.P. Gisbert: Grant/research support from and is on speaker bureau with MSD, Abbvie, Hospira, Kern Pharma, Takeda, Janssen, Pfizer, Ferring, Faes Farma, Shire Pharmaceuticals, Dr. Falk Pharma, Chiesi, Casen Fleet, Gebro Pharma, Osuka Pharmaceutical, Vifor Pharma. G.C. Nguyen: Consultant for: Janssen, Abbvie, and Takeda. B. Bokemeyer: Grant/research support from: Abbvie, Ferring, UC3T, Consultant for: Abbvie, MSD, Shire, Ferring, UC3T, Hospira, Takeda, Movets, Speaker bureau with: Abbvie, Ferring, MSD, Merckle, Falk, HLJ, UCB. J. Lindsay: Grant/research support from and is on speaker bureau with: MSD, Abbvie, Hospira, Takeda, Janssen, Ferring, Shire Pharmaceuticals, Vifor Pharma, Atlantic Health care, Actavis (Warner Chilcott), and Tillots. M. Smyth: Employee of Takeda Development Centre Europe Ltd, London, United Kingdom. S. Ramagopulan: Employee of Evidera and was commissioned by Takeda Development Centre Europe Ltd. to conduct the study. J.M. Khalid: Employee of Takeda Development Centre Europe Ltd, London, United Kingdom.

Table 1: Predictors of non-response or loss of response among patients with ulcerative colitis and Crohn’s disease

<table>
<thead>
<tr>
<th>Baseline Variables</th>
<th>Odds Ratio (95% Confidence Interval)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients with Ulcerative Colitis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rectal Bleeding (Reference: None)</td>
<td>0.04</td>
<td></td>
</tr>
<tr>
<td>-Passing blood alone</td>
<td>0.24 (0.06–0.97)</td>
<td></td>
</tr>
<tr>
<td>-Passing blood with stool ≥50% of time</td>
<td>0.35 (0.19–1.9)</td>
<td></td>
</tr>
<tr>
<td>-Passing blood with stool &lt;50% of time</td>
<td>0.17 (0.05–0.62)</td>
<td></td>
</tr>
<tr>
<td>Endoscopic Findings (Reference: Inactive; Mild)</td>
<td>0.02</td>
<td></td>
</tr>
<tr>
<td>-Moderate</td>
<td>3.19 (1.14–8.97)</td>
<td></td>
</tr>
<tr>
<td>-Severe</td>
<td>4.86 (1.61–14.7)</td>
<td></td>
</tr>
<tr>
<td>Patients with Crohn’s Disease</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Number of Liquid or Soft Stools per Day</td>
<td>1.12 (1.00–1.24)</td>
<td>0.04</td>
</tr>
<tr>
<td>C-reactive Protein (CRP)</td>
<td>1.02 (1.00–1.03)</td>
<td>0.03</td>
</tr>
</tbody>
</table>

Note: Only the significant predictors are included in the table above. Other non-significant variables included age, gender, body mass index, disease duration, Charlson comorbidity index score, and use of corticosteroids or immunomodulators. Both were analyzed as continuous variables. Highest CRP values during the baseline period were used.

Conclusion: In this cohort the majority of patients did not respond or lost response to anti-TNF therapy over time. Predictors for patients with UC included the absence of rectal bleeding and moderate/severe endoscopic scores, and for patients with CD included higher CRP and higher number of liquid or

OP009 INFLAMMATORY BOWEL DISEASE COURSE AND THERAPEUTIC MANAGEMENT IN REAL LIFE PRACTICE IN THE CURRENT ERA OF ANTI-TNFs: ANALYSIS OF THE FRENCH ADMINISTRATIVE HEALTH DATABASES 2009–2014

J. Kirchgesner1, 2, M. Lemaître3, A. Racine4, M. Zurik5, F. Carbonnel6, R. Drayer2

1Institut Pierre Louis D’Épidémiologie Et De Santé Publique (unité Miste De Recherche En Santé 1136), INSERM, Paris/France
2Department Of Epidemiology Of Health Products, French National Agency for Medicines and Health Products Safety (ANSM), Saint-Denis/France
3Gastroenterology Unit, CHU de Bicêtre, APHP-Université Paris Sud, Le Kremlin Bicêtre/Paris

Contact E-mail Address: julien.kirchgesner@gmx.com

Introduction: Management of inflammatory bowel disease (IBD) has evolved in the last decade. Clinical trials have shown that the combination of anti-TNFs and thiopurines is more efficient than monotherapy with either of these. The impact of these results in real-life practice is unknown. Moreover, the frequency of treatment withdrawal has never been assessed in population-based cohort studies.

Aims & Methods: Our aim was to assess IBD course and therapeutic management including treatment withdrawal, surgery rates and hospital stays in the current era of anti-TNFs. Every patient affiliated to the French national health insurance with a diagnosis of IBD based on listed long-term diseases and/or hospital discharge diagnosis was included from 2009 to 2013, and followed up until 31 December 2014. Cumulative incidence rates were used to estimate the cumulative probabilities of medication use, surgery and hospitalization among prevalent and incident patients. Treatment sequences including treatment withdrawal after introduction of thiopurines, anti-TNFs and comotherapy were assessed for incident patients included between 2009 and 2012.

Results: 195,834 individuals were diagnosed with IBD (Crohn’s disease (CD), 106 436 (31,353 incident patients); ulcerative colitis (UC), 89,398 (27,578 incident patients)). Among incident patients treated with thiopurines or anti-TNFs (17 566 CD and 8035 UC patients), the first treatment was thiopurines, anti-TNFs monotherapy, and comotherapy in 69.1%, 24.8% and 6.1% of CD patients and 78.5%, 17.7% and 4.1% of UC patients, respectively. Subsequently, 36.8% and 20% of CD patients were exposed to anti-TNFs monotherapy and comotherapy, respectively, 5 years after diagnosis. More than 25% of CD and UC incident patients included between 2009 and 2012 withdrew thiopurines or anti-TNFs, during more than three months after a first treatment course. Drug withdrawal was related to hospitalization or surgical procedures in less than 30% of these patients. Nearly 50% of CD patients and 40% of UC patients went back to their initial treatment after withdrawal. Around 5% of CD patients and 4% of UC patients stopped all IBD therapy during follow-up. Five years after diagnosis, the cumulative risks of first intestinal resection in CD, and colectomy in UC were 12.8% and 3.5%, respectively.

Conclusion: The step-up approach remains the dominant strategy in IBD, where exposure to anti-TNFs is high and surgery rates are low. Treatment withdrawal in IBD is more common than expected. This study emphasizes the growing need of studying de-escalation strategy in IBD.

Disclosure of Interest: F. Carbonnel: Franck Carbonnel had consulting fees for Genentech, Otsuka, Vifor, and Leo Pharma. All other authors have declared no conflicts of interest.
The identification of children at risk for failure to reach sustained remission despite exposure to anti-TNF remains challenging in Crohn’s disease. Aims & Methods: Aims: of paediatric CD) were analysed after 5 yrs follow-up. Disease severity was scored at diagnosis and yearly thereafter as inactive, mild and moderate-to-severe on a 3- point scale based on PDAI/PGA scores. Sustained remission was defined as inactive disease for ≥ 2 yrs follow-up. Univariate analyses were performed between anti-TNF exposed patients with or without sustained remission and correlations assessed between variables and the outcomes average disease activity score and remission at diagnosis and yearly thereafter as inactive, mild and moderate-to-severe. Differences between groups were assessed by the 2-sample t test or the sign test. Results: Of 66 anti-TNF exposed patients (median (IQR) age 13.1 (11.5-15.2) yrs, 50% male), 17% failed to reach sustained remission. Disease location was similar in both groups and mild disease at diagnosis (45%/ vs. 16%; p = .03) more frequent in the patient groups. There were no differences between age, gender, WBC or CRP at diagnosis and treatment between both groups. Percentages of infliximab and adalimumab use were similar in both groups, including drug switching and dose or interval adjustments. When stratified by follow-up clinic, infliximab in paediatric follow-up was less frequently associated with failure to reach sustained remission compared to sustained remission.

Univariate analyses of the type of follow-up clinic and anti-TNF treatment between patients with or without sustained remission (more than one anti-TNF possible).

<table>
<thead>
<tr>
<th>Variable, number (%)</th>
<th>No sustained remission (n = 11)</th>
<th>Sustained remission (n = 5)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Paediatric follow-up and infliximab</td>
<td>3 (27)</td>
<td>7 (67)</td>
<td>.01</td>
</tr>
<tr>
<td>Paediatric follow-up and adalimumab</td>
<td>1 (9)</td>
<td>8 (15)</td>
<td>.63</td>
</tr>
<tr>
<td>Adult clinic follow-up and infliximab</td>
<td>6 (55)</td>
<td>14 (25)</td>
<td>.05</td>
</tr>
<tr>
<td>Adult clinic follow-up and adalimumab</td>
<td>2 (18)</td>
<td>4 (7)</td>
<td>.25</td>
</tr>
<tr>
<td>Paediatric follow-up and adjustments</td>
<td>1 (9)</td>
<td>8 (15)</td>
<td>.63</td>
</tr>
<tr>
<td>Adult follow-up and adjustments</td>
<td>1 (9)</td>
<td>3 (11)</td>
<td>.65</td>
</tr>
</tbody>
</table>

Higher average disease severity (2.1 (2.0-2.3) vs. 1.6 (1.3-1.8); p < .001), adult clinic follow-up (73% vs. 27%; p < .01), surgery for CD (1 (0-3) vs. 0 (0-3); p < .01) and MISO (median 5 yrs (91% vs. 24%; p < .05) were associated with failure to reach sustained remission. Both colonic disease and adult follow-up (AUC = .66; both p = .04) correlated with average disease severity (no correction for multiple testing). No other correlations were found.

Conclusion: Patient phenotype at diagnosis does not predict failure to reach sustained remission despite anti-TNF exposure. Mild disease may not trigger appropriate drug dosing and lead to active and complicated disease course. Sustained remission occurred most with infliximab in paediatric follow-up. Information on serum levels is lacking.


Disclosure of Interest: All authors have declared no conflicts of interest.
Conclusion: Kaplan–Meier curves showed that higher APLN expression was significantly related to an oncogenic role in promoting liver tumor growth via activation of PI3K-AKT pathway. Higher expression of APLN is correlated with a more advanced clinical stage and worse prognosis in HCC patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP014 TUMORS SKW THE CCR2-DEPENDENT ANTI-TUMOR IMMUNE RESPONSE INITIATED BY ONCOGENIC CELLS AND REDUCE SENSING TOARDS TUMOR GROWTH PROMOTION

T. Eggert, M. Heikenwild, X. W. Wang, L. Z. Zender, T. Greten
1Thoracic and Gastrointestinal Oncology Branch, National Cancer Institute, Bethesda/United States of America/MD
2Chronic Inflammation and Cancer, German Cancer Research Center, Heidelberg/Germany
3Laboratory Of Human Carcinogenesis, National Cancer Institute, Bethesda/United States of America/MD
4Dept. Of Internal Medicine J, University Hospital Tuebingen, Tuebingen/Germany
5Thoracic and Gastrointestinal Oncology Branch, National Cancer Institute, Bethesda/United States of America

Contact E-mail Address: eggert.tobias@nih-hannover.de

Introduction: Oncogen-induced senescence induces the immune-mediated clearance of these precancerous senescent hepatocytes, preventing malignant transformation and tumor initiation; a process termed ‘senescence surveillance’ (1). However, senescent hepatocytes can give rise to hepatocellular carcinoma (HCC), if the senescence program is abrogated and/or senescent cells are not cleared (1). We set out to identify the mechanism of recruitment of senescent cells and clearing macrophages. Furthermore, we studied the effect of senescence-associated immune responses in tumor-bearing full-blown tumor cells in the liver.

Aims & Methods: To induce senescence in mouse livers, either oncogenic Nras (NrasG12V) or an effecter loop mutant (NrasG12V/D38A), which is incapable of downstream signaling and senescence induction, were hydrodynamically delivered into C57BL/6, CC2R KO and p19 KO mice. To achieve tumor development in senescent livers, luciferase-expressing hepatocellular carcinoma cells were intrasplenically injected into mice after hydrodynamic gene delivery. Tumor growth was assessed using weight and bioluminescence measurements as well as quantification of macroscopic tumors. Senescent livers with or without tumors were analyzed using flow cytometry and immunohistochemistry. Furthermore, peritumoral tissue of 226 HCC patients was hierarchical clustered based on the expression of 35 senescence-associated genes (2). Senescence-associated gene signature expression was then compared with chemokine expression and survival. In addition, human peritumoral tissue was analyzed by immunohistochemistry for the presence of senescence and myeloid cell markers.

Results: In tumor-free livers, senescent hepatocytes induced CC2R+ immature myeloid cell (iMC) accumulation, followed by iMC maturation into macrophages, which clear senescent hepatocytes. In CCR2 KO mice, iMC recruitment and macropage accumulation was impaired, causing persistence of oncogenic Nras-expressing hepatocytes and ultimately HCC development. In contrast, however, tumor cells in senescent livers blocked the maturation of CC2R+ iMC into macrophages, which lead to an accumulation of iMC. These iMC inhibited NK cell cytotoxicity against tumor cells, as demonstrated by reduced NK cell degranulation upon hepatocellular carcinoma cells or hepatocellular carcinoma cells through senescence-induced iMC, leading to accelerated tumor growth. Accordingly, in CC2R KO mice or C57BL/6 wild type mice depleted of iMC, senescence-induced tumor growth promotion was abrogated. Finally, gene expression and immunohistochemistry analyses in peritumoral tissue of patients with hepatocellular carcinoma confirmed the association of senescence-induced CC2R expression, myeloid cell accumulation, NK cell inhibition and poor prognosis.

Conclusion: Senescence-induced CCL2-CCR2 signaling and the ensuing myeloid cell accumulation harbor context dependent functions in preventing HCC initiation, but also promoting progression of established HCC. These findings hold important translational significance for clinical practice. 1. CC2R antagonists may fuel liver cancer growth in patients with chronic liver disease, in which senescent hepatocytes accumulate. 2. In patients with HCC, CC2R antagonists may reduce senescence-associated immunosuppression induced by liver tumors. Disclosure of Interest: All authors have declared no conflicts of interest.

References
Introduction: Non-lifting (NL) large laterally spreading and colorectal lesions (NL-LSL) are challenging to resect endoscopically and often necessitate surgery. Previously attempted endoscopic resection, pre-resection biopsy and sub-lesion carbon particle suspension are common reasons for NL. Conventional endoscopic mucosal resection (EMR) techniques are often ineffective due to extensive submucosal fibrosis. Simple methods for safe and effective endoscopic management of NL-LSL have not been described.

Aims & Methods: The study aimed to evaluate the characteristics of NL-LSL and the safety and efficacy of endoscopic treatment by Cold Forcescopes Avulsion (CFA) followed by thermal ablation of the avulsion site by Snare Tip Soft Coagulation (STSC). Amongst a prospective observational study of patients referred for wide field EMR of LSL >20mm, LSLs which could not be completely resected by snare due to NL were labelled NL-LSL and naïve, non-lifting LSLs (NNL-LSL). [MBI] Such lesions had completion of resection using a standardized approach with CFA and STSC. The NL area was isolated by circumferential snare excision of all adjacent tissue including adenoma and/or normal mucosa to free the lateral margins. This then allowed effective CFA of NL adenoma. Systematic CFA was then performed to remove all visible NL adenoma. The exposed submucosa of the avulsion site and its margins were treated with controlled thermal ablation using STSC (ERIE effect 4, 80W). Scheduled surveillance colonoscopy was performed at 5 months (SC1) and 18 months (SC2) post the index procedure. The primary outcome was endoscopic and histological evidence of adenoma clearance. The secondary outcome was safety. Statistical analyses were performed to compare standard LSL with NL-LSL.

Results: From January 2012 to April 2016, 677 patients (mean age 69 years, 50.6% male) with 780 lesions (median size 35 mm (IQR 25–45mm), 65.4% proximal colon) were referred for WF-EMR. 33 lesions were excluded due to suspicion for submucosal invasive cancer and the patients referred for surgery. EMR was performed on 83 NL-LSL and 664 standard LSL. 14 lesions were exposed submucosa of the avulsion site and its margins were treated with controlled thermal ablation using STSC (ERIE effect 4, 80W). Scheduled surveillance colonoscopy was performed at 5 months (SC1) and 18 months (SC2) post the index procedure. The primary outcome was endoscopic and histological evidence of adenoma clearance. The secondary outcome was safety. Statistical analyses were performed to compare standard LSL with NL-LSL.

Conclusions: CFA and adjunct STSC is a safe, effective and surgery-sparing therapy for the majority of NL-LSL. It is easy to use, inexpensive and does not require additional equipment. Early recurrence rates at SC1 are comparable between PANL-LSL and standard LSL. NL-LSL recur more frequently. Non-granular LSLs were over-represented in both groups. They may be more susceptible to developing fibrosis after biopsy and therefore care should be taken to avoid significant tampering with these lesions prior to referral for definitive endoscopic treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP005 COLD FORCESPES AVULSION (CFA) WITH ADJUVANT SNARE TIP SOFT COAGULATION (STSC) IS AN EFFECTIVE AND SAFE STRATEGY FOR THE MANAGEMENT OF NON-LIFTING LARGE LATERALLY SPREADING COLORECTAL LESIONS (NL-LSLS)

D. J. Tate, F. Bahin, L. Desomer, V. Gupta, M. Sidhu, M. J. Bourke
Gastroenterology and Hepatology, Westmead Hospital, Sydney/Australia

Contact E-mail Address: djtate@gmail.com

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Disclosure of Interest: All authors have declared no conflicts of interest.

Abstract No: OP005

Table 1: lesions where cold forcescopes avulsion and snare tip soft coagulation (CFA and STSC) was used in the resection of PANL or NNL, p values represent comparison to LSL. Two stage procedures were excluded. SD – standard deviation, IQR – interquartile range, SC1 – surveillance colonoscopy 1, IVC – ileocaecal valve, PANL – previously attempted non lifting lesion, NNL – naïve non lifting lesion.

<table>
<thead>
<tr>
<th>Patient</th>
<th>PANL n = 33</th>
<th>p</th>
<th>NNL n = 50</th>
<th>p</th>
<th>LSL n = 650</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, mean (SD)</td>
<td>70.2 (8.6)</td>
<td>.121</td>
<td>73.0 (9.5)</td>
<td>&lt;.001</td>
<td>66.9 (12.1)</td>
</tr>
<tr>
<td>Male, (%)</td>
<td>18 (54.5)</td>
<td>.598</td>
<td>29 (88.0)</td>
<td>.266</td>
<td>324 (49.8)</td>
</tr>
<tr>
<td>Lesion</td>
<td>Median size (IQR)</td>
<td>25 (20–30)</td>
<td>&lt;.001</td>
<td>37.5 (25–50)</td>
<td>.424</td>
</tr>
<tr>
<td>Morphology (%)</td>
<td>Granular</td>
<td>8 (25.0)</td>
<td>.003</td>
<td>22 (44.0)</td>
<td>.012</td>
</tr>
<tr>
<td></td>
<td>Non granular</td>
<td>20 (62.5)</td>
<td></td>
<td>23 (46.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Unclassified</td>
<td>4 (12.5)</td>
<td></td>
<td>5 (10.0)</td>
<td></td>
</tr>
<tr>
<td>Location (%)</td>
<td>Rectum</td>
<td>11 (34.4)</td>
<td>.121</td>
<td>6 (13.0)</td>
<td>.091</td>
</tr>
<tr>
<td></td>
<td>Sigmoid to sigmoid</td>
<td>6 (18.8)</td>
<td></td>
<td>11 (23.9)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Transverse</td>
<td>5 (15.6)</td>
<td></td>
<td>14 (30.4)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Ascending and caecum (±ICV)</td>
<td>10 (31.3)</td>
<td></td>
<td>15 (32.6)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Submucosal fibrosis</td>
<td>33 (100)</td>
<td>&lt;.001</td>
<td>50 (100)</td>
<td>&lt;.001</td>
</tr>
<tr>
<td></td>
<td>Previous attempt at resection (%)</td>
<td>33 (100)</td>
<td>&lt;.001</td>
<td>0 (0)</td>
<td>&lt;.030</td>
</tr>
<tr>
<td></td>
<td>Previous biopsy (%)</td>
<td>naïve</td>
<td>16 (32.0)</td>
<td>.001</td>
<td>90 (13.8)</td>
</tr>
<tr>
<td></td>
<td>SPOT mark within 10 mm of lesion (%)</td>
<td>naïve</td>
<td>13 (26)</td>
<td>&lt;.001</td>
<td>25 (3.8)</td>
</tr>
<tr>
<td></td>
<td>Histopathology (%)</td>
<td>Conventional adenoma</td>
<td>25 (92.6)</td>
<td>.324</td>
<td>44 (90.0)</td>
</tr>
<tr>
<td></td>
<td>Serrated adenoma</td>
<td>2 (7.4)</td>
<td></td>
<td>4 (10.0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Cancer</td>
<td>0 (0)</td>
<td></td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td></td>
<td>Other</td>
<td>0 (0)</td>
<td></td>
<td>0 (0)</td>
<td></td>
</tr>
<tr>
<td>Procedure</td>
<td>Duration, minutes, median (IQR range)</td>
<td>35 (18–45)</td>
<td>.004</td>
<td>25 (15–40)</td>
<td>.003</td>
</tr>
<tr>
<td></td>
<td>Intraprocedural bleeding requiring endoscopic control (%)</td>
<td>2 (7.7)</td>
<td>.078</td>
<td>11 (22.4)</td>
<td>.966</td>
</tr>
<tr>
<td></td>
<td>Deep injury</td>
<td>6 (18.2)</td>
<td>.181</td>
<td>1 (2.0)</td>
<td>.049</td>
</tr>
<tr>
<td></td>
<td>Outcomes</td>
<td>Endoscopic Recurrence at SC1 (%)</td>
<td>4 (16.0)</td>
<td>.578</td>
<td>11 (28.2)</td>
</tr>
</tbody>
</table>
Aims & Methods:  A total of forty patients (20 female, median age 69 years) underwent TEMS and TAR, it will play an increasingly significant role in the management of RPDLs. As KAR is a viable alternative to full ESD, demonstrates that for Western endoscopists, KAR is a very safe and effective technique in the treatment of RPDLs. As KAR is a viable alternative to full ESD, and careful inspection of the defect to ensure no residual adenoma, mucosal defects were randomized 1:1 to either thermal ablation of the margin of the post EMR mucosal defect with STSC, results in significantly lower adenoma recurrence rates at first surveillance colonoscopy (SC1). Endoscopic, and histologic recurrence in patients randomised to null versus active arm of the SCAR study. Relative risk (RR); Confidence interval (CI)

Table 1: Endoscopic and histological recurrence in patients randomised to null versus active arm of the SCAR study. Relative risk (RR); Confidence interval (CI)

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<tr>
<td>Morphology, n (%)</td>
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Conclusion: This is the largest reported series of KAR for RPDLs. Our data demonstrates that for Western endoscopists, KAR is a very safe and effective technique in the treatment of RPDLs. As KAR is a viable alternative to full ESD, TEMS and TAR, it will play an increasingly significant role in the management of RPDLs.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP008 THERMAL ABLATION OF THE MARGIN OF THE POST ENDOSCOPIC MUCOSAL RESECTION (EMR) MUCOSAL DEFECT TO REDUCE ADENOMA RECURRENCE FOLLOWING EMR. THE “SCAR” STUDY

A. Klein1, V. Jayasekeran1, L. Hourigan2, D. J. Tate3, R. Singh3, G. Brown4, F. Bahin5, N. Burgess5, S. J. Williams1, E. Lee5, M. J. Bourke6
1Gastroenterology and Hepatology, Westmead Hospital, Sydney/Australia/NSW
2Gastroenterology, Princess Alexandra Hospital, Brisbane/Australia/QLD
3Gastroenterology, Lyell McEwin hospital, Adelaide/Australia/SA
4Adfred Hospital, Melbourne/Australia/VIC
5Gastroenterology and Hepatology, Westmead Hospital, Westmead/Australia/NSW

Contact E-mail Address: djate@gmail.com

Introduction: Endoscopic mucosal resection (EMR) of large sessile and lateral spreading colonic lesions ≥20 mm (LSLS) is safe and effective. The main limitation is adenoma recurrence, which occurs in up to 20% at first surveillance colonoscopy (SC1), mandating a structured surveillance program. Surveillance procedures create compliance burdens, additional costs and potential patient morbidity. Endoscopically invisible micro-adenoma present at the margin of the resected LSL may account for adenoma recurrence. Adjuvant thermal ablation of the EMR defect margin may reduce adenoma recurrence rates.

Aims & Methods: A prospective multi-center randomized control study was performed (NCT01789749). The primary end-point was endoscopic and histological recurrence at SC1. Standard inject and resect EMR technique was used for all lesions. Exclusion criteria included previously attempted lesions, incomplete snare excision or involvement of the ileocecal valve. After successful complete LSL excision by EMR and careful inspection of the defect to ensure no residual adenoma, mucosal defects were randomized 1:1 to either thermal ablation of the margin of the post EMR mucosal defect with STSC, results in significantly lower adenoma recurrence rates at first surveillance colonoscopy (SC1). Endoscopic, and histologic recurrence at SC1 were significantly lower in the active arm (8/138 (5.8%) versus 6/124 (20.2%), p = .001), relative risk (RR) = 0.29 (95% CI 0.14–0.61) and no difference in delayed perforation (0/124 (0%) versus 1/136 (0.7%), p = .957) and no difference in delayed perforation (0/124 (0%) versus 1/136 (0.7%), p = .341).

null arm n = 178, active arm n = 181). Patient, procedure and lesion characteristics were similar between the two groups. 267 (74.3%) patients have completed SC1. Endoscopic, and histologic recurrences at SC1 were significantly lower in the active arm (8/138 (5.8%) versus 6/124 (20.2%), p = .001), relative risk (RR) = 0.29 (95% CI 0.14–0.61) and no difference in delayed perforation (0/124 (0%) versus 1/136 (0.7%), p = .341).

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Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: We aimed to evaluate the feasibility and long-term outcomes of ESD performed with an SB knife Jr for treating early colorectal neoplasms. ESD was performed for 227 lesions in 211 patients (male:female ratio = 116:95; mean age = 69.1 ± 13.1 years) between October 2010 and March 2016. We counted the number of hemoclips used per case to assess the cost and efficacy of the procedure.

Results: The neoplasms were as follows: right colon, 94 lesions (41.4%); left colon, 58 (25.6%), and rectum, 75 (33.0%). Regarding the macroscopic type of the resected tumors was 32.0 mm (range, 1–1,000 mm), and 78 (34.4%) were tubular adenomas. The mean size of the resected tumors was 32.0 ± 14.9 mm, and the median procedure time was 76.5 minutes (range, 10–420 minutes). The rates of on block resection, histological complete resection, and R0 resection were 98.2% (227/232 lesions), 93.8% (213/227), and 85.0% (193/227), respectively. All lesions were treated easily and safely without an unexpected incision, and no perforations occurred during the procedure. Delayed bleeding, delayed perforation, and rectal stricture occurred in 3.8% (6/227), 0.4% (1/227), and 0.4% (1/227) of the lesions, respectively, and all of these complications were cured conservatively. The median follow-up time was 48 months (range, 18–1,976 days). Local recurrence was observed in only 0.8% of the lesions (2/227). One patient (0.5%) died of colorectal cancer, and 5 patients (2.3%) died of other diseases. The 5-year overall survival rate and disease-specific survival rate were 94.8% and 98.7%, respectively.

Conclusion: ESD performed with an SB knife Jr is a technically efficient and safe method that is associated with favorable long-term outcomes in cases of early colorectal neoplasms.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
It is important highlight that only one session of Spyglass + EHL was performed in each patient of our protocol. Better success rates can be achieved with two or more sessions and increase up to 90%. Cross-over of the failure cases in both groups is bringing us a very interesting result and suggests that in some cases the methods can be complementary. There was no statistical difference between the groups, although spyglass group had numerically a little higher success rate. The study provides us an evidence-based algorithm of difficult stones endoscopic treatments. In addition, we observed potential advantages when we associate the methods, providing one step more before declaring endoscopic failure in treating a difficult biliary stone.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

MORNING, OCTOBER 17, 2016 10:30–12:00 PREVENTION OF GI CANCERS: NUTRITION AND CHEMOPREVENTION – ROOM 1.E1.1

OP023 CD24 INDUCES THE ACTIVATION OF B-CATENIN IN INTESTINAL TUMORIGENESIS

A. Fokra1, S. Shapira2, D. Kazanov3, F. Bedny4, E. Brazowski5, C. Varol6, S. Kraus7, N. Arber8 1Faculty Of Medicine, Tel Aviv University, Tel Aviv/Israel 2The Integrated Cancer Prevention Center, Tel Aviv Sourasky Medical Center, Tel Aviv/Israel 3Pathology Institute, Tel Aviv Sourasky Medical Center, Tel Aviv/Israel 4Research Center For Digestive Tract and Liver Diseases, Tel Aviv Sourasky Medical Center, Tel Aviv/Israel

Contact E-mail Address: afokra@gmail.com

Introduction: CD24 is a GPI-linked protein that functions as an adhesion molecule and is overexpressed at an early stage of CRC. The Wnt/b-catenin signaling pathway plays an important role in CRC carcinogenesis process. We had shown that CD24 could affect the tumorigenesis process in Apc Min mice. Aims & Methods: Aim to study the cellular interactions between CD24 and β-catenin, and their effects on intestinal tumorigenesis Methods CD24-inducible 293T-Req cells previously developed in our lab and SW480 CRC cells stably transduced with CD24 were used to study this interaction in vitro. Apc Min and Cdc24 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 previous treatments in refractory patients were 4 (3–9). All patients reached normal Hb levels after 6 months. The mean difference between prehybrid-APC (5.98 ± 1.49 gr/dl) and 6m after hybrid-APC (7.74 gr/dl) (p < 0.0001) was 1.74 gr/dl and 7.74 gr/dl, respectively. Conclusion: Based on these preliminary results, Hybrid-APC is safe and effective for the treatment of GAVE (naïve or refractory) with the advantage of needing only 1 or maximum 2 applications and with excellent results at medium term.

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using mice colonoscopy. Histology confirmed by an experienced pathologist was used to study this interaction in vitro.

Results: In vitro Western blotting analyses showed that expression of CD24 in 293T-Res cells induced the activation of β-catenin and co-immunoprecipitation studies demonstrated that these two proteins were co-activating, while down-regulation of CD24 in SW480 cells caused a decrease in the levels of active β-catenin and cytoplasmic/nuclear fractionation showed that more active β-catenin enters the nucleus in cells thatexpressed CD24 (clone 1) compared to control cells (clone 4). In addition, in both cell lines, TOP-Firefly reporter assay showed a significant increase in Luciferase activity upon CD24 expression induction Depletion of CD24 alleles in Apc Min mice led to a significant reduction in the number of polyps in the intestine C37BL/6J mice carrying the Apc Min mutation developed 2.4±3.7 adenomas and several carcinomas in the smallintestine by the age of 16 weeks. The ApcMin/CD24-/- mice developed 8.3±1 polypos and ApcMin/CD24+/- (control) mice developed 7.1±1 polypos (p=0.006). Colonoscopy showed a significant reduction in the number and size of polyps upon depletion of CD24 alleles. The ApcMin displayed severe spondylopathy (353.3±68 mgcompared to 205±51 mg) in ApcMin/CD24-/- mice and (14±49 mg) in double KO mice similar to WT mice (p=0.006). Hb level was 3.8±2.5 in the ApcMin significantly lower than in the double KO mice (8.2±0.9) and the WT (p=0.0009).

Conclusion: Down regulation of CD24 may an important aim in the therapy of CRC.

Disclosure of Interest: N. Arber: Consultancy Fee: Bio-View, Check-Cap, Bayer Stock Shareholder: Micromedic, Gi-VieW
All other authors have declared no conflicts of interest.

OP025 LOSS OF PTPN2 IN MACROPHAGES AGGRAVATES COLITIS BUT PROTECTS FROM COLORECTAL TUMOUR FORMATION

M. R. Spalinger1, S. H. Kasper1, S. Bengs1, C. Götter1, K. Arrot1, T. Raselli1, G. Rögler1, M. Schafr1
1Gastroenterology and Hepatology, University Hospital Zurich, Zurich/Switzerland
2Department Of Gastroenterology and Hepatology, USz, Zurich/Switzerland
3Division Of Gastroenterology and Hepatology, University Hospital Zurich, Zurich/Switzerland
4Klinik Für Gastroenterologie Und Hepatologie, Universitätsklinikum Zurich, Zurich/Switzerland

Contact E-mail Address: Marianne.Spalinger@usz.ch

Introduction: Variants in the gene locus encoding protein tyrosine phosphatase non-receptor type 2 (PTPN2) are associated with Crohn’s disease (CD) and ulcerative colitis (UC). We have previously shown that loss of PTPN2 in T cells results in enhanced colitis and signs of autoimmunity. Inflammasomes form upon cytosolic presence of danger molecules and induce the cleavage of pro-IL-1β and pro-IL-18 into their active forms. Secretion of IL-1β is an important activator of sterile inflammatory responses, and adaptive immune functions, while IL-18 is involved in epithelial cell protection.

Aims & Methods: In this study, we aimed to address whether loss of PTPN2 in macrophages affects inflammasome activation and cytokine expression/secretion. In acute colitis, PTPN2-LysMCre mice did not differ from that observed in WT mice (p=0.006). Hb level was 3.8±2.5 in the ApcMin significantly lower than in the double KO mice (8.2±0.9) and the WT (p=0.0009).

Conclusion: Down regulation of CD24 may an important aim in the therapy of CRC.

Disclosure of Interest: N. Arber: Consultancy Fee: Bio-View, Check-Cap, Bayer Stock Shareholder: Micromedic, Gi-VieW
All other authors have declared no conflicts of interest.

Aims & Methods: To test the validity of this recommendation we performed a prospective multicenter study aimed at evaluating the technical feasibility, procurement yield, and diagnostic accuracy of this newly developed 19-gauge nitrol flexible needle in patients with solid lesions or enlarged lymph nodes that could be punctured only from the duodenum. Consecutive patients with solid lesions who needed to undergo EUS sampling from the duodenum were prospectively enrolled in 6 tertiary care referral centers. Puncture of the lesion was performed with the 19-gauge flexible needle (ExpektM 19 Flex and Slimline ExpectM 19 F) and at least 3 needle passes were performed in each case. The feasibility, procurement yield and diagnostic accuracy were evaluated.

Results: 246 patients (144 males, mean age 65.1±12.7 years) with solid lesions (203 cases, 82.5%) or enlarged lymph nodes (43 cases, 17.5%) were enrolled. The mean size of the target lesion was 32.6±12.2 mm. The procedure was technically feasible in 228 (92.7%) patients, with an overall procurement yield of 76.8%.

Conclusion: The findings of our study, with a procurement yield and diagnostic accuracy of only 76.8% and 73.6%, respectively, redefine the role of the 19-gauge fine needle biopsy (EUS-FNB) can result in a greater chance to reach a diagnosis than a typical EUS-FNA sample. Based on a previous study (2), which reported a 19-gauge flexible needle to be able to sample transduodenal lesions and be diagnostic of all 32 included patients, an algorithm for EUS-tissue acquisition (EUS-TA) of solid lesions from the duodenum depending on the availability of ROSE has been proposed. Thus, in institutions with no availability of ROSE, for lesions located from the duodenum, which represent the most difficult sampling position because of the stiffness induced by the needle assembly on the echoendoscope shaft, the authors recommended the use of a 19-gauge needle made of nitinol with increased flexibility (1).

Disclosure of Interest: N. Arber: Consultancy Fee: Bio-View, Check-Cap, Bayer Stock Shareholder: Micromedic, Gi-VieW
All other authors have declared no conflicts of interest.

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### Analysis of Procedure Outcomes

<table>
<thead>
<tr>
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<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>ROSE-Diagnostic adequacy:</strong> n (%)</td>
<td>88 (100)</td>
<td>86 (97.7)</td>
<td>85 (100)</td>
<td>91 (100)</td>
<td>0.182</td>
</tr>
<tr>
<td><strong>Total no. of passes for onsite diagnostic adequacy</strong></td>
<td>Mean (SD)</td>
<td>1.8 (1.9)</td>
<td>2.8 (2.7)</td>
<td>1.7 (1.5)</td>
<td>2.0 (2.2)</td>
</tr>
<tr>
<td><strong>Specimen bloodiness:</strong> n (%)</td>
<td>Mild</td>
<td>1 (1-2)</td>
<td>2 (1-3)</td>
<td>1 (1-1)</td>
<td>1 (1-2)</td>
</tr>
<tr>
<td><strong>Adverse events:</strong> n (%)</td>
<td>Moderate</td>
<td>20 (22.7)</td>
<td>34 (38.6)</td>
<td>20 (23.5)</td>
<td>30 (33.0)</td>
</tr>
<tr>
<td><strong>Technical failure:</strong> n (%)</td>
<td>Severe</td>
<td>16 (18.2)</td>
<td>22 (25.0)</td>
<td>10 (11.8)</td>
<td>18 (19.8)</td>
</tr>
</tbody>
</table>

**ROSE-Diagnostic performance:** % (95% CI)

- **Accuracy:** 98.9 (93.8–100) vs. 93.2 (85.7–97.5) vs. 97.6 (91.8–99.7) vs. 97.8 (92.3–99.7) (p = 0.230)
- **Specificity:** 93.3 (68.1–99.9) vs. 95.0 (75.1–99.9) vs. 100 (79.4–100) vs. 100 (95.8–99.8) (p = 0.011)
- **PPV:** 98.6 (92.7–100) vs. 98.4 (91.6–100) vs. 100 (94.6–100) vs. 98.8 (93.2–100) (p = 0.008)
- **NPV:** 70 (80.7) vs. 79.2 (72–87.9) vs. 88.9 (65.3–98.6) vs. 90.9 (58.7–99.8) (p = 0.177)

**EUS-FNA-Diagnostic performance:** % (95% CI)

- **Accuracy:** 98.9 (93.8–100) vs. 93.2 (85.7–97.5) vs. 98.8 (93.4–100) vs. 98.9 (94.0–100) (p = 0.060)
- **Specificity:** 98.6 (92.6–100) vs. 92.6 (83.7–97.6) vs. 98.6 (92.2–100) vs. 98.8 (93.2–100) (p = 0.177)
- **PPV:** 100 (78.2–100) vs. 95.0 (75.1–99.9) vs. 100 (79.4–100) vs. 100 (71.5–99.8) (p = 0.177)
- **NPV:** 93.8 (69.9–99.8) vs. 97.2 (78.9–92.4) vs. 94.1 (71.3–99.9) vs. 91.7 (61.5–99.8) (p = 0.179)

**Technical failure:** n (%) | 0 | 4 (4.5) | 3 (3.4) | 7 (25.0) | 10 (11.0) | 0.179

**Adverse events:** n (%) | 4 (4.5) | 4 (5.7) | 5 (1.2) | 7 (7.7) | 10 (11.0) |

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**References**


Endoscopic enteral stenting (ES) in malignant gastric outlet obstruction (GOO) is limited by high rates of stent obstruction. EUS-guided gastroenterostomy (EUS-GE) is a novel procedure that potentially offers sustained patency without tumor ingrowth/overgrowth. The aim of this study is to compare EUS-GE with ES in terms of technical feasibility and success with low rates of complications.

Aims & Methods: This was a prospective, non-randomised, single-centre study. Patients presenting with malignant GOO were either EUS-GE at 4 centers between 2013 and 2015 or ES at one center. The main outcome measures studied were technical success, clinical success, adverse events and the need for various endoscopic reinterventions, using step-up approach.

Results: A total of 205 patients (mean age 34.8±12.5 years, 181 males) underwent EUS-GE or ES. Technical success was achieved in 203 patients (99%). Per-procedure adverse events occurred in 8 (3.9%) patients (bleeding in 6 and perforation in 2). WON resolved with BFMS in 158 (77.1%) patients, required in 49 (23.9%) patients, for persistent or new onset symptoms, was approached in step-up manner. At first, de-bugging of BFMS alone succeeded in 10 out of 21. Second step of naco-cystic placement by BFMS followed by irrigation with saline and hydrogen peroxide improved 16 out of 23 (73.9%). At final step, DEN improved outcome in 19 out of 23. BFMS migrated in 5 (2.9%) patients (2 internal, 3 external). Four patients failed to achieve clinical success, requiring surgery (n=2) or additional percutaneous drainage (n=2). Overall, clinical success was achieved in 198 (96.5%) patients.

Discussion: EUS-guided drainage with BFMS is safe and effective in WON. BFMS substantially reduces the requirement of DEN. Success rate incrementally improves with endoscopic step-up approach.

Disclosure of Interest: All authors have declared no conflicts of interest.

Bile calprotectin in relation to variables of PSC activity


Disclosure of Interest: All authors have declared no conflicts of interest.

References

1. Introduction: Primary sclerosing cholangitis (PSC) is a chronic inflammatory disease of biliary epithelium leading to strictures intra- and extrabiliary bile ducts and finally to cholestasis and secondary biliary cirrhosis (1). The chronic inflammation is associated with increased proliferation of biliary epithelial cells and a markedly increased risk of biliary dysplasia and cholangiocarcinoma (2). SIR ranging from 55 to 973 (3–4). The lifetime risk of CCA is around 10% (5). CCA is the most common reason for death among PSC patients (6–7). CCA is thought to develop through metaplasia, low-grade dysplasia, and high-grade dysplasia (8). Chronic inflammation has been regarded as risk factor for dysplasia and malignancy. Because CCA is generally a contraindication for liver transplantation (LT) and the prognosis of CCA is dismal, it would be feasible to screen the dysplastic changes of the biliary epithelium to treat patients with LT before development of advanced malignancy, detected based on imaging methods or symptoms.

Aims & Methods: We aimed to evaluate the grade of bile duct inflammation as a risk factor for dysplasia and cholangiocarcinoma in PSC patients. In total, 210 patients with confirmed PSC referred for ERC for disease surveillance were included (1 female, 199 males). Biliary examination of the common bile duct bile sample was aspirated using balloon catheter and immersed immediately in liquid nitrogen (−196°C) and then stored in −20°C. Brush cytology (BC) was collected both from extra- and intrahepatic bile ducts for Papanicolaou 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). Bile concentrations of calprotectin were analyzed using ELISA method. Liver function tests were taken at the time of ERC. ERC findings were scored according to modified Amsterdam score, [Helsinki score] (9).

Results: Bile duct inflammation assessed by biliary calprotectin correlated significantly with neutrophils in BC, with S-CA19-9, S-ALP and S-AST levels and S-Ca19–9, S-ALP and S-AST levels and significantly with S-IgG. Patients with dysplasia or CCA had markedly elevated B-calprotectin, as compared to those without dysplasia (34.7 vs 4.0 mg/l, respectively, see table). The risk of dysplasia was associated with advanced biliary duct disease, (mERCC score > 8 vs < 4, OR 15.2 [95% 1.8–127.6], p = 0.012), increased bile duct inflammation based on BC-neutrophils (BC-Neutrophil 1-2 vs 0, OR 8.2 [95% 1.1–64.0], p = 0.044), B-calprotectin higher than 45 mg/l (OR 3.3 [95% 1.2–9.9], p = 0.0032) and S-CA19-9 > 26 kU/l vs ≤ 26 kU/l (OR 7.4 [95% 2.0–27.6], P = 0.003).

Bile calprotectin in relation to variables of PSC activity

<table>
<thead>
<tr>
<th>Variable</th>
<th>N</th>
<th>B-calpro, mg/l, median [25%–75%]</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>ERC-score ≤ 4</td>
<td>94</td>
<td>0.4 [0–1.3–9]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>ERC score &gt; 4</td>
<td>116</td>
<td>13.8 [1.6–96.3]</td>
<td>&lt;0.00001</td>
</tr>
<tr>
<td>Bili-Neutrophils</td>
<td>- 70</td>
<td>0.2 [0–1.1]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>- 100</td>
<td>5.3 [0.9–22.9]</td>
<td>&lt;0.0001</td>
<td></td>
</tr>
<tr>
<td>- 2</td>
<td>36</td>
<td>172.8 [39.1–286.8]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Dysplasia</td>
<td>- No</td>
<td>203</td>
<td>4.0 [0.2–41.0]</td>
</tr>
<tr>
<td>- Yes</td>
<td>14</td>
<td>34.7 [4.8–99.5]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>S-CA19-9 &lt; 26 kU/l</td>
<td>198</td>
<td>2.7 [0.2–28.5]</td>
<td>0.003</td>
</tr>
<tr>
<td>≥ 26 kU/l</td>
<td>12</td>
<td>57.4 [19.4–179.3]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>S-ALP, U/l</td>
<td>- &lt; 105 (UNL)</td>
<td>101</td>
<td>1.2 [0.2–9.6]</td>
</tr>
<tr>
<td>≥ 105 (UNL)</td>
<td>109</td>
<td>6.1 [0.5–81.9]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>S-AST, U/l</td>
<td>- &lt; 40 (UNL)</td>
<td>142</td>
<td>1.4 [0.0–21.0]</td>
</tr>
<tr>
<td>≥ 40 (UNL)</td>
<td>69</td>
<td>8.3 [1.0–89.6]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>S-IgG, g/l</td>
<td>- &lt; 15 (UNL)</td>
<td>177</td>
<td>2.8 [0.2–27.0]</td>
</tr>
<tr>
<td>≥ 15 (UNL)</td>
<td>33</td>
<td>19.5 [1.3–112.1]</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Results and Discussion

Conclusion: S-ALP, AST and IgG seem to be good surrogate markers for bile duct inflammation compared to biliary calprotectin levels. Risk of dysplasia is associated with bile duct inflammation assessed by brush cytology neutrophils, B-calprotectin and S-CA19-9 levels > 26 kU/l. These variables seem be useful for individual risk stratification for PSC patients for disease progression and dysplasia.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


Contact E-mail Address: martti.farkkila@hus.fi

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP035 GUT BARRIER FAILURE BIOMARKERS ARE ASSOCIATED WITH POOR DISEASE OUTCOME IN PATIENTS WITH PRIMARY SCLEROSING CHOLANGITIS

T. Tornai1, G. Kovacs1, Z. Vitalis1, I. Tornai1, K. Fechner2, D. Roggenbuck3, D. Tornai4, G. Kovacs4, Z. Vitalis4, I. Tornai4, K. Fechner5, D. Roggenbuck5

Aims & Methods: Gut-liver interaction is a pathogenic feature of primary sclerosing cholangitis (PSC), however the extent of this cross-talk on the disease course has not been fully elucidated. A panel of serological markers that reflect either mucosal or gut barrier dysfunctions were assessed in a cohort of patients with PSC. Association of these markers with disease specific characteristics and the long-term disease course was evaluated.

Results: In PSC, median I-FABP level was similar to that in HCONT (216 vs. 244 μg/ml) but higher than in UC (176 μg/ml, p < 0.05). sIgA level (95.7 ± 27 μg/ml) was twofold higher compared to either the HCONT or the UC (p < 0.001, for both). 28%, 9% and 20% of PSC patients were positive for AAA IgA, AGA and AGA IgG, respectively. Frequencies of AAA IgA (p < 0.001, for both) and AAA IgG (p = 0.01, for both) were not higher than in the UC but not AGA IgG were significantly higher compared to either the HCONT or the UC or the UC (p < 0.001, for both). 15.7% of PSC patients were positive for AGA IgM and 6.5% for AGA IgG, whereas no patients were positive for AGA IgA. Combination of markers further enhanced their predicative potential (HR[95%CI]: 11.3[3.2–44.9] for ≥ 2 marker positivity).

Conclusion: In a multivariate study, gut-derived type IgA antibodies identified patients with progressive disease, further highlighting the importance of the gut-liver interaction in PSC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

Contact E-mail Address: hugobritol1@gmail.com

Introduction: Farnesoid X receptor (FXR), a bile acid (BA)-activated nuclear receptor, plays a critical role in maintaining lipid, glucose and BA homeostasis. FXR expression is significantly decreased in livers of non-alcoholic fatty liver disease (NAFLD) patients and genetic ablation leads to hepatic steatosis and hyperlipidemia. The FXR gene expresses four biologically active variants (FXRα1–4), which regulate hepatic and lipid metabolism in an isotype-dependent manner.

Aims & Methods: Our aim was to screen potential BA-derived FXR agonists for their ability to selectively activate different FXR isoforms and protect liver cells against free fatty acid (FFA)-induced steatosis and cytotoxicity. Nineteen novel BA derivatives, synthesized based on the cholic (CA), deoxycholic (DCA), chenodeoxycholic (CDCA) and ursodeoxycholic (UDCA) acid scaffolds were incubated in HepG2 cells (3h) with FA-induced lipid accumulation. The expression ratio plasmids for FXRα1–4 isoforms were then co-incubated in HepG2 cells treated with 200 and 500 μM oleic and palmitic acid (2:1 ratio), for assessment of cellular cytotoxicity using the MTS, Lactate dehydrogenase (LDH) and ToxilightTM assays, as well as intracellular lipid accumulation, by Oil Red O (ORO) staining. Additionally, mRNA levels of both direct and indirect key FXR-targets, namely SREBP1-c, PPARα, CYP7a1 and VLDLR, were assessed after incubation of primary mouse hepatocytes with the select BA derivatives.

Results: As a result of the diverse structural modifications, BA derivatives showed differential activation of the FXRα1–4 isoforms, when compared to their precursor BAs. From the precursor BAs, only CDCA, a natural FXR ligand, significantly activated FXRα1 and u2 isoforms, with CA and UDCA displaying a modest activation of FXRα1 isoform only. Interestingly, 2 novel CA-, 1 DCA- and 4 UDCA-derivatives were stronger activators of both FXRα1 and u2, comparing with their corresponding precursors. Further, 3 novel CA-, 2 DCA-, 3 CDCA- and 4 UDCA-derivatives specifically and significantly activated FXRα1 and u4. Incubation of HepG2 cells with the FFAs mixture led to a 30–50% increase in cell death and a 15–35% increase in cell death, comcomitantly with a dose-dependent accumulation of lipid droplets. Pre-incubation of cells with CA-derivatives preferentially activating FXRα2 over u1 isoform, were the most of the FFAs-induced cell death and lipid accumulation. Of note, these derivatives were among the strongest inducers of SHP, VLDLR and PPARα mRNA expression in primary mouse hepatocytes.

Conclusion: Altogether, we have developed a novel strategy to screen for selective agonists of FXRα1–4 isoforms and have identified new selective BA-derived FXRα1–4 agonists. In particular, derivatives with a higher FXRα2 over u1 bias might be more effective in affording cytoprotection against lipotoxicity in liver cells. The differential functional effect of these new molecules will undoubtedly contribute for a better understanding of pharmacological targeting and therapeutic efficacy of FXR agonists in liver diseases such as NASH, NAFLD. Supported by: FCT, UID/LNCC/00994/2013, SFRH/BD/80975/2011, SFRH/BD/110672/2015 and SFRH/BD/80975/2011 FCT, Portugal.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
The PNPLA3 rs738409 C>G allele is associated with increased triglyceride synthesis and accumulation in liver (1). The conversion of isoleucine to methionine at position 148 (I148M) causes a loss of function for carbohydrate-regulated lipogenic and/or lipolytic enzymes in liver. The mutation is also associated with inflammatory bowel disease and markedly increased risk of cholangiocarcinoma (3,4). PLPN3 variant has been associated with elevations of liver enzymes in IBD (5) and in increased risk of bile duct stenosis in male PSC patients (6). Survival free of liver transplantation is reduced in male PSC patients with dominant strictures in carriers of PNPLA3 I148M variant (5).

Aims & Methods: To evaluate the allele dose effect of PNPLA3 variant on the clinical manifestations, disease severity, progression and prognosis of PSC in a large patient population from single center.

Results: Of the 563 patients (349.3%) had the wild type (CC), 197 (35.7%) were heterozygous (CG) and 32 (5.7%) were homozygous for the mutation (GG). A concomitant IBD was diagnosed in 80% of the males and 60% of the females. Summary of the results are presented in the table.

<table>
<thead>
<tr>
<th>Variable, mean(SD)</th>
<th>CC, n = 334</th>
<th>CG, n = 197</th>
<th>GG, n = 32</th>
<th>p for linearity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Males, n (%)</td>
<td>195(38)</td>
<td>124(63)</td>
<td>17(53)</td>
<td>0.75</td>
</tr>
<tr>
<td>Age at diagnosis, y</td>
<td>38(14)</td>
<td>36(13)</td>
<td>35(13)</td>
<td>0.10</td>
</tr>
<tr>
<td>Weight, kg, males</td>
<td>82(14)</td>
<td>80(15)</td>
<td>81(14)</td>
<td>0.37</td>
</tr>
<tr>
<td>Weight, kg, females</td>
<td>69(7)</td>
<td>70(17)</td>
<td>71(13)</td>
<td>0.62</td>
</tr>
<tr>
<td>IBD, n (%)</td>
<td>263(71)</td>
<td>152(77)</td>
<td>21(65)</td>
<td>0.49</td>
</tr>
<tr>
<td>Age at diagnosis IBD</td>
<td>26(11)</td>
<td>26(11)</td>
<td>29(12)</td>
<td>0.74</td>
</tr>
<tr>
<td>ERC-score (0–16)</td>
<td>5.8(3.5)</td>
<td>5.4(3.3)</td>
<td>5.7(3.7)</td>
<td>0.88</td>
</tr>
<tr>
<td>Dominant strictures, n (%)</td>
<td>128(31)</td>
<td>63(31)</td>
<td>9(28)</td>
<td>0.061</td>
</tr>
<tr>
<td>Progression of ERC score/month*</td>
<td>0.014</td>
<td>0.002</td>
<td>0.004</td>
<td>0.44</td>
</tr>
<tr>
<td>Advanced fibrosis F3/4, %*</td>
<td>8.5</td>
<td>15.12</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>S-ALP, U/l &lt;105</td>
<td>183(148)</td>
<td>194(170)</td>
<td>194(170)</td>
<td>1.00</td>
</tr>
<tr>
<td>S-GT, U/l &lt;40</td>
<td>191(249)</td>
<td>236(269)</td>
<td>189(154)</td>
<td>0.94</td>
</tr>
<tr>
<td>S-ALT, U/l &lt;50</td>
<td>74(125)</td>
<td>78(96)</td>
<td>61(50)</td>
<td>0.35</td>
</tr>
<tr>
<td>S-AST, U/l &lt;45</td>
<td>55(37)</td>
<td>54(63)</td>
<td>59(41)</td>
<td>0.68</td>
</tr>
</tbody>
</table>

*Adjusted for sex, age and IBD. Cholangiocarcinoma was diagnosed in 12 (3.6%) patients with CC, in 6 (3.3%) of CG an in none of GG, (p for linearity=0.42; adjusted for sex, age and IBD). 49 patients underwent liver transplantation during 5 years mean follow up: 2.5% (95% CI: 1.2 to 5.1) in CC, 3.1% (95% CI: 1.3 to 7.3) in CG and 7.1% (95% CI: 1.8 to 24.4) in GG, (p for linearity=0.12, adjusted for sex, age and IBD).

Conclusion: The PNPLA3 I148M variant did not have any significant impact on clinical manifestation, disease progression, development of dominant strictures, on risk of cholangiocarcinoma or liver transplantation in PSC.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Aims & Methods: To investigate the role of calcineurin and NFAT in intestinal tumor development, we generated mice with intestinal epithelial cell-specific deletion of the regulatory B1 subunit of calcineurin and analyzed these mice in the Apcfl/wt and ApcMin/+ model. Antibiotic treatment of mice as well as backcrossing to a Myd88-deficient background revealed that the activation of oncogenic epithelial cells and their abnormal microenvironment plays an important role in CRC development.

Results: We demonstrated that systemic inhibition of calcineurin with cyclosporine leads to increased intestinal tumor growth in Apcfl/wt mice, which is consistent with an increased CRC incidence observed in patients receiving calcineurin inhibitors. In contrast, intestinal epithelial cell-specific deletion of calcineurin is associated with reduced intestinal tumor formation and growth in the Apcfl/wt and ApcMin/+ model. Antibiotic treatment of mice as well as backcrossing to a Myd88-deficient background revealed that the activation of oncogenic epithelial cells is dependent on the intestinal microbiota and results from tumor-associated alterations in microbial composition and stratification as well as from increased tumor-associated toll-like receptor expression. Tumor-promoting effects of epithelial calcineurin are elicited through NFAT-dependent transcriptional regulation of Lgr5-positive tumor stem cells as shown by chromatin immuno-precipitation (ChIP), gene expression analysis and functional studies together leading to control of tumor stem cell apoptosis and proliferation as shown by FACS and immunofluorescence staining. Moreover, somatic mutations identified in human CRC are associated with constitutive activation of calcineurin, while nuclear translocation of NFAT correlates with reduced survival in a large cohort of CRC patients.

Conclusion: These results support the concept of cell-specific roles of calcineurin in the regulation of colorectal carcinogenesis and reveal novel potential targets for the prevention and treatment of CRC.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP040 NHERF2 REGULATES COLON CANCER PROGRESS VIA STAT3
S. Umemura1, Y. Fujita1, M. Natsume1, A. Kato1, H. Ohara3, T. Joh1
1Gastroenterology and Metabolism, Nagoya City University Graduate School of Medical Sciences, Nagoya/Japan
2Division Of Digestive Diseases, Emyo University School of Medicine, Atlanta/ United States of America/GA
3Community-based Medical Education, Nagoya City University Graduate School of Medical Sciences, Nagoya/Japan

Contact E-mail Address: mityoshi@med.nagoya-u.ac.jp

Introduction: scaffold proteins mediate protein-protein interactions to bring together key members of signaling pathways that drive cell division and growth. The N-terminus exchanger regulatory factor (NHERF) family of proteins is a scaffold that orchestrates interaction of signaling proteins with downstream signaling pathways. Among the NHERF proteins, NHERF1 and NHERF2 share most similarities with transient PDZ domains and an ERM interacting motif in the carboxyl domain that enables anchoring to the actin cytoskeleton. One major function of NHERF1/2 is to recruit and spatially organize signaling proteins that either alters protein functions or downstream signaling pathways originating from receptor. NHERF1 is reported to be a tumor suppressor. However, the role of NHERF2 in cancer progression has not been reported.

Aims & Methods: We investigated the role of NHERF2 in colon tumor progression. We first determined NHERF2 expression in human colorectal cancer (CRC) using a tissue microarray. Next, the role of NHERF2 on colon cancer growth and invasion was assessed by a loss-of-function approach (shRNA) and a small peptide which blocked the PDZ domain of NHERF2 to bind using colon cancer cell lines (HCT116, SW480, and HT-29). We validated tumor growth change by xenograft model. Moreover, we used ApcMin/+ mouse model to investigate the tumorigenesis in intestine with NHERF2 homozygous deletion mice. To investigate the molecular mechanism of NHERF2 in tumor growth, we performed the transcriptom analysis.

Results: We found that NHERF2 expression is elevated in advanced-stage CRC. Knockdown of NHERF2 decreased cancer cell proliferation and invasion in vitro, and tumor growth in a mouse xenograft tumor model. Histologic analysis confirmed the reduction of cell proliferation by Ki67 immunostaining. In addition, deletion of NHERF2 in APCMin/+ (ApcMin+/-;Nherf2-/-) mice resulted in decreased tumor growth in APCMin+/- mice and increased lifespan. Blocking NHERF2 interaction with a small peptide designed to bind the second PDZ domain of NHERF2 attenuated cancer cell proliferation. Although NHERF2 is known to facilitate the effects of lysophosphaticid acid receptor 2 (LPAR2) and STAT3 phosphorylation and CD24 expression, LPA2-regulated genes largely differ from LPA2-regulated genes. Moreover, ApcMin+/+ mice model to investigate the tumorigenesis in intestine with NHERF2 homozygous deletion mice. To investigate the molecular mechanism of NHERF2 in tumor growth, we performed the transcriptom analysis.

Conclusions: We demonstrated that NHERF2 stimulates colon cancer growth by interacting with multiple signaling nodes. NHERF2 potentiates the oncogenic effects in part by regulation of STAT3 and CD24. This study provides NHERF2 as a new potential target for cancer treatment.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP041 THE EXTRACELLULAR MATRIX PROTEIN EMILIN2 AS A REGULATOR OF THE MYELOID RESPONSE AND ALTERATION OF IMMUNFLAMMATION-INDUCED COLON CARCINOGENESIS
E. Andreuzzi1, A. Paulitti1, G. Taricchino1, E. Di Carlò1, R. Pellicani2, A. Colombatti1, R. Cannizzaro3, M. Mongiat1
1Translational Research, Experimental Oncology I, CRO-IRCCS, Aviano/Italy
2Department Of Oncology and Experimental Medicine, University of Chieti- Pescara, Chieti/Italy
3Oncological Gastroenterology, Centro di Riferimento Oncologico di Aviano S.O.C. di Gastroenterologia, Aviano/Italy

Contact E-mail Address: andrauzzi@cro.it

Introduction: EMILIN2 is an extracellular matrix molecule belonging to the EMI Domain ENAdowed (EDEN) protein family that exerts pleiotropic effects in the tumor microenvironment including functioning as a tumor suppressor (mouse EMILIN2-/-;Nherf2-/-) and tumor promoter (human EMILIN2+;Nherf2-/-). EMILIN2 affects tumor cell viability and proliferation by activating apoptosis and functioning as a negative regulator of the Wnt/β-catenin axis. Interestingly EMILIN2 expression is down-modulated by methylation in a number of tumors including breast and colorectal cancer (4). Our preliminary results highlight a possible new function for E2 in the control of CRC incidence. In particular these findings indicate that E2 seems to modulate the myeloid response and to profoundly affect the inflammatory microenvironment associated with CRC.

Aims & Methods: Given its involvement in the regulation of Wnt signaling, a crucial pathway in colon carcinogenesis, and its altered expression in colorectal cancer, we took advantage of the EMILIN2 null mouse model to assess its role in colorectal cancer (CRC) development, subjecting the mice to the inflammation-related AOM/DSS protocol. Colorectal tumors were induced subjecting the mice to a 2-week AOM/DSS treatment. Tumor development was assessed by colonoscopy. Histopathological and IHC analyses were performed on colon samples from treated mice. β-catenin activation was assessed by Western blot and qPCR. Multiplex serum cytokine analyses from the two mouse models were performed through Luminex screening and peripheral blood cells were counted. The inflammatory infiltrate was analysed by flow cytometry.

Results: The EMILIN2 KO mice developed a significantly higher number of tumors compared to WT mice. Tumors from EMILIN2 KO mice were more undifferentiated and at an advanced stage compared to the tumors from control mice. Surprisingly, and contrary to our expectations, tumors from EMILIN2 KO mice did not display any changes in the activation of the Wnt/β-catenin pathway compared to the controls. Accordingly, the β-catenin target genes cyclin D1 and c-Myc were not altered in the tumors and in the normal mucosa of the two mouse models (tumor vs. normal mucosa). Histopathological and IHC analyses were performed on colon samples from treated mice. β-catenin activation was assessed by Western blot and qPCR. Multiplex serum cytokine analyses from the two mouse models were performed through Luminex screening and peripheral blood cells were counted. The inflammatory infiltrate was analysed by flow cytometry. EMILIN2 KO mice were more undifferentiated and at an advanced stage compared to the tumors from control mice. Surprisingly, and contrary to our expectations, tumors from EMILIN2 KO mice did not display any changes in the activation of the Wnt/β-catenin pathway compared to the controls. Accordingly, the β-catenin target genes cyclin D1 and c-Myc were not altered in the tumors and in the normal mucosa of the two mouse models (tumor vs. normal mucosa). Histopathological and IHC analyses were performed on colon samples from treated mice. β-catenin activation was assessed by Western blot and qPCR. Multiplex serum cytokine analyses from the two mouse models were performed through Luminex screening and peripheral blood cells were counted. The inflammatory infiltrate was analysed by flow cytometry.

Conclusions: Our results let us suggest that EMILIN2 may affect colon carcinogenesis by impinging on the recruitment and/or the activation of myeloid cells. By altering the inflammatory microenvironment, EMILIN2 may significantly influence colon cancer development.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Disclosure of Interest:
renewal of colon spheres and differentiation ability of HCT116 colon spheres.
Conclusion: spheres overexpressing miR-145 (p
of Internal Medicine Dept. of Gastroenterology, Rome/Italy
this context, we hypothesise that miR-145 may play a role in the ability of colon CSCs (CCSCs) to self-renew and differentiate.

Introduction: H. pylori infection and treatment (31 countries and 280
regimens were 79.9% (341/427) and 85.3% (318/373) respectively. VPZ has a rapid, sustained, and possibly more potent
effective agents are unstable and degraded in the stomach. Esomeprazole (EPZ) is a
cell line, and examined their ability to form colon spheres in ultralow-
empty vector control cells using HCT116, HT29, SW480 and SW620 colon
cancer cell lines, and examined their ability to form colon spheres in ultralow-
attachment plates and specific CSCS media. Colon spheres were dissociated to single cells and reseeded to yield the second and third generation of colon spheres. The number of spheres and cells per sphere were counted over 3 gen-
eration. miRNA expression levels of stemness markers were evaluated by SYBR Real-Time PCR. CD44 and CD133 expression levels and aldehyde dehydrogenase 1 (ALDH1) activity were evaluated by flow cytometry. Results: We showed that forced miR-145 overexpression reduced colon sphere diameter and number of cells per sphere in HCT116, HT29, SW480 and SW620 cells. Moreover, miR-145 overexpression had an impact on HT29 and SW620 sphere growth, reducing the number of colon cancer spheres. Similar results were observed with the second and third generation of cell line-derived colon spheres. miRNA expression levels of the stemness markers KLF4 and BM11, were sig-
ificantly reduced in HCT116 colon spheres overexpressing miR-145 (p < 0.01). In addi-
tion, HT29 and SW480 cell line-derived colon spheres overexpressing miR-145 displayed reduced OCT4 mRNA levels. Furthermore, miR-145 overexpression significantly decreased the production of CD44/CD133 cells and ALDH1 activity (p < 0.05). The mature colorectal marker, CK20, was increased in HCT116 spheres overexpressing miR-145 (p = 0.01).
Conclusion: miR-145 appears to be involved in colon sphere formation, self-
renewal of colon sphere and differentiation ability of HCT116 colon spheres, miR-145 may contribute to the induction of CSCC differentiation to cells that are sensitive to chemotherapy and targeted agents.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016 10:30-12:00
GASTRODUODENAL DAMAGE: H. PYLORI, ACID AND BILE – ROOM 1.86

OP043 PAN-EUROPEAN REGISTRY ON H. PYLORI MANAGEMENT (HP-EUREG): INTERIM ANALYSIS OF THE TREATMENT WITH BISMUTH, LEVOFLOXACIN AND AMCINOLIN
1Digestive Services, Centro de Investigación Biomédica en Red de Enfermedades Hepáticas y Digestivas (CIBERehd), Madrid/Spain
2Inserm U853, Hopital Pellegrin, Laboratoire de Bacteriologie, Bordeaux Cedex, France
3Gastroenterology, Abakus Medicina d.o.o., Rovugak Stitnna,Slovenia
4Department Of Gastroenterology and Infectious Diseases, Otto-von-Guericke University Magdeburg, Magdeburg/Germany
5Department of Gastroenterology and Liver Diseases, Gemelli Hospital Dept. of Internal Medicine Dept. of Gastroenterology, Rome/Italy
6Department Of Pancreatic, Biliary and Upper GI Diseases, Moscow Clinical Scientific Center, Moscow/Russian Federation
7Gastroenterology Unit, Hospital Nuestra Señora de Valme, Sevilla/Spain
8Hospital Universitario de La Fe, Valencia/Spain
9Dept. De Gastroenterología, Hospital San Pedro de Alcantara, Cáceres/Spain
10Central Asutrias University Hospital, Osileo/Spain
11Hospital Universitario de la Princesa, Madrid/Spain
12Digestive Services, Hospital Universitario de La Princesa, Madrid/Spain
13Faculty Of Health Sciences, Trinity College Dublin, Dublin/Ireland
14Hospitale a 4-I, 1,Mondor University Service de Gastroentérologie, Crétial/France
15Digestive Services, Hospital Universitario La Princesa, Madrid/Spain
16Astrazeneca, Casen Recordati, Nycomed.
All other authors have declared no conflicts of interest.

Introduction: A proton pump inhibitor (PPI)-based triple regimen containing two antibiotics (amoxicillin, PAMC, and clarithromycin, CAM) was considered the gold standard for the eradication of Helicobacter pylori for more than a decade. However, low eradication rates have been reported worldwide in the last decade because of increased prevalence of clarithromycin-resistant H. pylori. Insufficient acid inhibi-
tion during treatment also causes eradication failure. This is because the anti-
cibal agents are unstable and degraded in the stomach. Esomeprazole (EPZ) is a
new PPI available since September 2011. EPZ has an improved pharmacokinetic profile as regards CYP2C19 genotype; therefore, it shows less individual variability. Vonoprazan (VPZ) is a potassium-competitive acid blocker (P-CAB). P-CABs are a new class of gastric acid suppressants available since
February 2015 in Japan. VPZ has a potent and long-lasting anti-secretory effect on H+K+/ATPase due to its high accumulation in, and slow clearance from, the parietal cells. Therefore, VPZ shows improved efficacy rates compared with conventional PPIs. The aim of this study was to compare H. pylori eradica-
tion rates with EPZ-based and VPZ-based triple therapies with CAM and AMPC.

Aims & Methods: A total of 807 patients who had undergone upper gastrointestinal endoscopy and diagnosis with H. pylori infection from November 2013 to March 2016 were enrolled. From December 2013 to September 2014, 431 patients were treated with EPZ-based triple therapy, while 376 patients were treated with VPZ-based triple therapy from April 2015 to March 2016. At baseline, demo-
 graphical and clinical characteristics including gender, age, body mass index (BMI), smoking status, and consumption of alcohol were checked. The first-
line eradication regimens were CAM 200 mg, AMPC 750 mg, and either EPZ 20 mg or VPZ 20 mg, each twice daily for 7 days. The second-line eradication regimen was metronidazole 250 mg, AMPC 750 mg, and either EPZ 20 mg or VPZ 20 mg, each twice daily for 7 days. The eradication of H. pylori infection was diagnosed using 13C-urea breath test 4-8 weeks after each of therapy.

Results: The overall first-line eradication rate was 79.1% (341/431) for the EPZ regimen and 84.6% (318/376) for the VPZ regimen based on Intention to treat (ITT) analysis. The eradication rate assessed by PP protocol was 79.6% (341/431) and 85.3% (318/373) respectively. Significant differences were found between both ITT analysis (p = 0.045) and in PP analysis (p = 0.046). The overall second-line eradication rate was 72.6% (45/62) for the EPZ regimen and 85.3% (29/34) for the VPZ regimen based on ITT analysis. Using PP analysis, the eradication rate was 88.2% (45/51) for the EPZ regimen and 87.9% (29/33) for the VPZ regimen. There were no statistically significant differences in the infection eradication rates for both in both groups, as judged by the ITT and PP analyses.

Conclusion: In conclusion, VPZ has a rapid, sustained, and possibly more potent acid-inhibitory effect than EPZ, irrespective of CYP2C19 genotype. The rate of H. pylori eradication obtained using the first-line VPZ regimen was significantly recruiting investigators). A local coordinator was selected from each country. Each coordinator selected a representative group of recruiting investigators from his/her country. An electronic clinical research file (e-CRF) was created on AEG-REDCAP to systematically register all adult patients infected with H. pylori. In total, over 200 participants were randomized in 32 sites. This study assessed the safety and effectiveness of the second-line eradication regimens, adverse events, and outcomes (cure rates, compliance, follow up, etc.). Patients with both eradication confir-
matory test and with less than one year follow-up have been considered ongoing and were excluded from the analysis.

Results: Up to now, 16,025 patients have been included, and 12,921 have finished follow up (95% females, 87% Caucasian). Mean age was 55 years. The bismuth-
levofoxacin quadruple therapy was prescribed to 327 patients (2% of patients) of whom 131 (40%) patients were prescribed to 67 patients (20%) with comorbidities, and 32 (9%) patients were prescribed to 16 patients (5%) with comorbidities. Significant differences found between the eradication rates in both groups, from 75–93%) by ITT and 92 and 99% (89–94%) by PP. Treatment was generally prescribed with esomeprazole (95%) and as a 14 day regimen (98%). Compliance with treatment was 99%. Adverse events were reported in 38% of cases and caused treatment discontinuation in 7 (2.1%) patients.

Conclusion: A 14-day regimen combining bismuth salts with levofloxacin triple therapy as second-line treatment for H. pylori eradication achieves near 90%
treatment, there were no significant differences between the eradication rates from EPZ and VPZ regimens.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Aims & Methods: Using gastric tissue from humans, rats treated with proton pump inhibitors and/or a cholesterol type B receptor (Cox-2) inhibitor, we examined the expression pattern and gastrin-mediated regulation of secretory CLU in vitro. Parallel reaction monitoring mass spectrometry, in situ hybridization and immuno- histochemistry. Human gastric cancer cell lines were used to study the gastrin- mediated regulation and biological function of secretory CLU in vitro.

Result: CLU was highly expressed in normoxic mucosal tissue of humans and normoxic mucosa of human cells, rats and mice. In response to hypergastrinemia, expression of CLU was significantly increased and localization shifted from neuroendocrine cells to basal groups of proliferating gastric glands. In response to hypergastrinemia, expression of CLU was significantly increased and localization shifted from neuroendocrine cells to basal groups of proliferating gastric glands. The osmotic mucosa of H K-KO mice contained distinct areas with CLU-positive mucous cell hyperplasia, possi- bly representing SPEM. In vitro, gastrin increased the secretion of CLU, and both gastrin and secretory CLU promoted survival of gastric cells following starvaton- and chemotheraphy-induced stress.

Conclusion: Our findings suggest that gastrin and CLU participate in premalignant remodeling of the oxyntic mucosa by influencing the balance between sur- vival and apoptosis in gastric epithelial cells.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Conclusion: The majority of H. pylori-infected subjects have reduced intragastric acidity compared to the uninfected population and this is most marked close to the gastroesophageal junction. The density of parietal cells and chief cells is reduced in H. pylori infected subjects throughout the gastric mucosa. These findings may be strongly associated between H. pylori infection and both gastroesophageal reflux disease and oesophageal adenocarcinoma.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Disclosure of Interest: All authors have declared no conflicts of interest.
Disclosure of Interest: A.J. Bredenoord: Received research funding from Endostim, Medical Measurement Systems, Danone and Given and received speaker and/or consulting fees from MMS, Astellas, AstraZeneca and Almirall. All other authors have declared no conflicts of interest.

OP051 LARYNGOPHARYNGEAL SYMPTOMS IN PRIMARY CARE: USEFULNESS OF SALIVARY PEPsin MEASUREMENT IN PREDICTING GERD

A. Bozzani1, R. De Bastiani2, M. Della Coletta3, E. Savarinò4, L. Grattagliano5
1Primary Care, Carugate Brianza/Italy 2Primary Care, Feltrio/Italy 3Division Of Gastroenterology, Department Of Surgery, Oncology and Gastroenterology, University of Padua, Padua/Italy 4Department Of Surgery, Oncology and Gastroenterology, University of Padua, Padua/Italy 5Primary Care, Monopoli/Italy

Contact E-mail Address: marcodelacotta@gmail.com

Introduction: Incidence of chronic laryngeal symptoms in primary care is about 2% per year and, gastroesophageal reflux disease (GERD) is considered by far the main disorder associated to them, leading to a specific syndrome called Laryngopharyngeal Reflux (LPR). Several studies demonstrated that pepsin monosodium imipramine can be used as a distinct marker of GERD in the patients. Recently, a low-cost, non-invasive salivary pepsin test (PeptestTM, RD Biomed Limited, UK) was found to measure pepsin in the saliva/sputum and to discriminate with good sensitivity and specificity between patients with GERD (i.e. with heartburn and regurgitation), confirmed at impedance-pH monitoring, from those without reflux disease (i.e. functional heartburn).

Thus, it has been hypothesized about the utility of using this novel device to diagnose LPR in primary care setting.

Aims & Methods: We aimed to investigate the usefulness of PeptestTM in primary care patients presenting with chronic laryngeal symptoms suggestive of LPR. In a prospective multicenter, controlled, pilot study, consecutive patients presenting with chronic laryngeal symptoms were enrolled by primary care physicians. Uninvestigated individuals with no gastrointestinal symptoms or disease (including GERD or dyspepsia) or history of surgery served as healthy controls (HCs). All subjects completed the validated reflux index (RSI) questionnaire and in case of a score >13, a symptom-based diagnosis of LPR was made. Also the gastrointestinal symptom scale (GIS) questionnaire was completed to investigate reflux symptoms and Quality of Life. All individuals were asked to provide 2 samples of sputum collected one hour after lunch and dinner. A positive PeptestTM was considered in case of a concentration of pepsin higher than 25 mg/mL.

Results: Between February and April 2014 and during August 2015, 86 patients with LPR (37 Male/49 Female, age 54 ± 14, RSI=13, mean RSI 22 ± 6, mean GSI 22 ± 6.4) and 59 healthy controls (30 Male/29 Female, age 41 ± 15, RSI<5, mean GSI 33 ± 6) were tested. In total 256 samples were examined, whereas 34 samples were discarded because of technical problems (i.e. unclear storage, poor/excessive quantity). At least one positive result was found in 64/86 (74%) LPR patients and in 54/59 (92%) HCs (p < 0.005), whereas two positive results were observed in 34/70 (49%) LPR patients and 26/46 (57%) HCs (p = 0.4505). One (in case of a single test) or two negative tests were registered in 22/86 (26%) LPR patients vs 4/59 (7%) of HCs (p = 0.0030). PeptestTM had an accuracy of 47% (IC95 39%-55%) a specificity of 74% (IC95 65%-84%) and a positive predictive value of 54% (IC95 45%-63%) and a negative predictive value of 2% (IC95 0%–8%) in identifying LPR as diagnosed by RSI.

Conclusion: In this pilot study, PeptestTM was not able to discriminate among primary care patients with LPR from those without and therefore cannot be suggested as preliminary tool to select patients requiring pH monitoring. Further studies including investigated healthy controls are mandatory to elucidate the diagnostic utility of salivary pepsin measurement in primary care setting.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP052 INADEQUATE SYMPTOM CONTROL ON LONG-TERM PPI THERAPY IN GERD – FACT OR FICTION? (LOPA II STUDY)

J. Labenz1, G. Labenz2, D. Stephan3, E. Willeke4
1Abt. Für Innere Medizin, Diakonie Klinikum Abt. für Innere Medizin, Siegen/Germany 2Praxis für Ernährungsmedizin und Prävention, Barbach/Germany 3St. Marienkrankenhaus Siegen, Siegen/Germany

Contact E-mail Address: j.labenz@t-online.de

Introduction: Randomized controlled trials report about 30% of GERD patients complain of bothersome remaining symptoms (heartburn, regurgitation) despite PPI therapy. The LOPA (Lost Patients) I Study of 333 GERD patients seen in primary care practice revealed 46% of patients experienced heartburn or regurgitation symptoms at least twice per week despite PPI. A total of 20% were dissatisfied with their treatment. Few patients had received specific GERD diagnoses or recommended other options (<10%).

Aims & Methods: The LOPA II study is a prospective, multicenter, observational study conducted in 7 general practice clinics. Patients with chronic GERD, taking PPI therapy for at least 1 year, and not satisfied with their treatment were asked to complete a questionnaire. Patients were asked the duration of their PPI therapy, satisfaction with their current condition, frequency of symptoms in the last week, whether they had previously received diagnostic evaluation or surgical consultation related to GERD, whether they plan to consult a reflux specialist for further diagnostics, and reasons for dissatisfaction with their current treatment. “Lost Patients” were defined as those with a satisfaction score of 1 or 2 on a 5-point Likert scale (1: very dissatisfied; 2: dissatisfied, GerdQ score at least 8, and have not previously received specialized GERD diagnostics.

Results: 300 consecutive patient responses were collected within one year. Patients suffered from GERD an average of 9.7 years and prescribed PPI therapy for an average duration of 8.2 years. 74% were dissatisfied or very dissatisfied on their current PPI therapy (score of 1 or 2), 89% reported heartburn or regurgitation at least 2 days in the prior week (57% 4-7 days). 53% reported using additional medication other than their prescribed PPI at least 2 days per week (10% 4-7 days). In patients dissatisfied on PPI, most cited insufficient symptom control (91%) as a reason for dissatisfaction. In addition, 26% cited concern with long-term use of drugs and 23% the need for daily medication. 92% of patients had received an upper endoscopy, 8% had a prior pH-metry, 5% manometry, and 7% received prior surgical consult for GERD. The rate of “Lost Patients” in this study was 63%.

Conclusion: Chronic GERD patients who are dissatisfied with their PPI therapy are rarely offered specialized GERD diagnostic procedures or treatment alternatives. Half of the patients took medication in addition to PPI to control their reflux. In addition to persistent symptoms, concerns of long-term PPI use and burden of daily medication play a role in patient dissatisfaction with PPI therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP053 EFFICACY OF ACOTIAMIDE IN PATIENTS WITH GASTROESOPHAGEAL REFLUX DISEASE UNRESPONSIVE TO PROTON PUMP INHIBITOR THERAPY

H. Yamashita1, A. Kanamori2, A. Okada2
1Gastroenterology, Osakafu Saiseikai Nakatsu Hospital, Osaka/Japan 2Gastroenterological Medicine, Osakafu Saiseikai Nakatsu Hospital, Osaka/Japan

Contact E-mail Address: onakaryoko0310@gmail.com

Introduction: Acid suppression is the mainstay of gastroesophageal reflux disease (GERD) therapy, and proton pump inhibitors (PPIs) are the first choice of drug therapy. Few patients are offered specialized GERD diagnostic procedures or treatment alternatives. Half of the patients took medication in addition to PPI to control their reflux. In addition to persistent symptoms, concerns of long-term PPI use and burden of daily medication play a role in patient dissatisfaction with PPI therapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: This study design was a randomized, placebo-controlled, double-blind, parallel-group trial conducted in 7 general practice clinics. Patients who had used PPI therapy for at least 1 year and not satisfied with their PPI therapy were randomized to receive either acotiamide (10 mg thrice daily) or a matching dose of placebo for 2 weeks. The medication was administered 30 min before each meal. In addition, patients continued their PPI treatment regime (maintenance dose and type) during the 2 week study period. Symptoms were assessed at baseline and weeks 1 and 2 using questionnaires, and graded as 1 (much improved) to 7 (severely worsened). Grade 1 or 2 (improved) was indicative of treatment efficacy. If possible, 24-h multichannel intraluminal impedance-pH (24-H MI-pH) monitoring was performed at baseline and week 2.

Results: In total, 22 patients were enrolled in this study. The acotiamide and placebo groups consisted of 12 and 10 patients (6 and 7 women; mean age, 56 and 68 years, mean body mass index [BMI], 21 and 23, respectively). There were no significant differences in patient characteristics between both groups. The effective rate was 25 and 10% for acotiamide and the placebo after 2 weeks, respectively, and no statistical significance was observed (p = 0.368). Fifteen patients consented to the 24-H MI-pH monitoring at baseline and after 2 weeks. The acotiamide group showed a significant decrease in the number of total reflux events, acid and liquid reflux events (39.6 vs. 25.5, p = 0.028; 14.7 vs. 5.4, p = 0.009, respectively). The placebo group...
showed no significant change. In patients with a symptom index >30% or total reflux events >40, the effective rate was significantly different (p=0.038) at 60 and 33% for the acitamidine and placebo groups, respectively. These results suggest that acitamidine may be effective in patients with associated reflux events. Co-administration of acitamidine and PPIs may be a new strategy for PPI-refractory GERD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
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mines the occurrence of transient lower esophageal sphincter relaxations and reflux events in patients with gastro-esophageal reflux disease. 

OP054 A RANDOMIZED CONTROLLED TRIAL TO ASSESS THE CLINICAL EFFICACY OF EPZ 20 mg FOR RESOLUTION OF GASTRO-ESOPHAGEAL REFLUX DISEASE SYMPTOMS IN NEWLY DIAGNOSED PATIENTS
S. Ishihara
Internalmedicine, Ishihara Gastroenterology Clinic, Zenzsai/Japan
Contact E-mail Address: cuy63898@yahoo.co.jp
Introduction: Esomeprazole (EPZ) and lansoprazole (VPZ) are proton pump inhibitors. The aim of this study was to assess the clinical efficacy of EPZ 20 mg and VPZ 20 mg once daily for the resolution of symptoms in newly diagnosed patients.
Methods: Newly diagnosed patients with GORD symptoms were randomized to treatment with EPZ or VPZ. All patients provided informed consent before enrolment in the trial. The primary outcome was the proportion of patients with sufficient relief of symptoms after 4 weeks of treatment. Secondary endpoints were the proportion of patients with complete overall symptom resolution (score 0) on the 4-point Likert scale and the proportion of patients with at leastmoderate severity of symptoms at baseline. All patients were assessed for adverse events and their quality of life was assessed using the QOLGastroesophageal reflux disease (QOLGERD) questionnaire.
Results: 88 patients were included in the study (44 in the EPZ group and 44 in the VPZ group). After 4 weeks, a significantly greater proportion of patients treated with EPZ achieved sufficient relief of symptoms compared to those treated with VPZ (88.6% vs. 60.0%, p<0.01). In the EPZ group, 57.1% of patients achieved complete symptom resolution compared to 27.3% in the VPZ group (p<0.01). Adverse events were reported in 38.6% of patients in the EPZ group and 34.1% in the VPZ group. No serious adverse events were reported.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP055 EFFICACY AND SAFETY OF THE ENDOLUMINAL MANAGEMENT OF REFRACTORY GASTROESOPHAGEAL REFLUX WITH BAND LIGATION
W. M. Seleem, A. S. Hanafy
Internal Medicine, Zagazig University, Zagazig/Egypt
Contact E-mail Address: amrhanafy@zua.edu.eg
Introduction: Gastroesophageal reflux disease is characterized by reflux of the gastric contents causing troublesome esophageal and extraesophageal symptoms that could affect adversely the quality of life. About 10-40% of patients with GERD fail to show adequate symptomatic response to the standard dose of PPI. severe mechanisms could explain refractory GERD as improper PPI dosing, patient non-compliance, esophageal hypersensitivity, residual acid reflux, alkaline or bile reflux, nocturnal acid breakthrough. Alternative therapeutic options included laparoscopic fundoplication, lower esophageal magnetic band, patients are expensive, and about 10% of patients experience persistence of heart burn, or develop dysphagia
Aims & Methods: We aimed to evaluate the safety and efficacy of endoluminal rubber band ligation in the management of refractory GERD. 20 patients were enrolled in the study after informed consent was taken. They were treated with rubber band ligation and the cap used for ligation had a diameter of 11 mm and loaded with 6 rings. The main outcome is reduction of reflux symptoms measured by GERD health related quality of life Questionnaire. Patients were included if they were 18 years of age or older with typical symptoms of heartburn or regurgitation refractory or less responsive to maximally optimized dose of PPI therapy (given twice, 30 min before food) and even after adding H2 receptor blocker before bedtime and bacoften 10 mg twice daily to the unresponsive patients. Patients excluded if they had lower esophageal ulcers, pregnancy, red flag signals as loss of weight, fever, dyspnea, odynophagia, bleeding. Large hiatal hernia more than 2 cm, paraesophageal hernia, active Helicobacter pylori infection, eosinophilic esophagitis were also excluded. Band ligation was performed in the four quadrants 5 mm distal to the Z-line which is measured before and after the sessions were completed.
Results: 13 males and 7 females were enrolled in the study. Their mean age 39.5 ± 6.2 with a range (31-49 years). The pre-endoscopic intervention character-

References
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OP056 ENDOSTIM® LES STIMULATION THERAPY IMPROVES GERD IN PATIENTS WITH LAPAROSCOPIC SLEEVE GASTRECTOMY (LSG)  
  
Introduction: LSG is the most commonly performed bariatric procedure in the US and Canada and the Asia-Pacific region. However, LSG can result in new GERD and may worsen preexisting GERD.1 LSG patients with GERD not well controlled with PPI do not have good treatment options except for more invasive, anatomy-altering gastric bypass surgery. LES electrical stimulation therapy has shown to improve outcomes in GERD patients.ii-iii 

Aims & Methods: To evaluate the safety and efficacy of LES stimulation in LSG patients with GERD not controlled with maximum dose PPI therapy. Patients with follows-up 12 months after bariatric surgery who demonstrated symptoms on maximum dose PPI therapy were evaluated. Underwent LES stimulator implant procedure and were enrolled in an international patient registry prospectively tracking outcomes in GERD patients treated with LES electrical stimulation. LES stimulation was delivered at 5mA, 220usec pulse in 12, 30 minute sessions daily. GERD outcomes pre and post-stimulation were evaluated.

Results: 12 patients, 66% (8/12) women at 8 centers have been treated. Median age was 46 (IQR 34–56). 72% (9/12) had more than double-dose PPIs. All 12 (100%) were on double-dose PPIs at their last follow-up (median = 12 months), 75% (6/8) were off-PPIs and one each was using PPIs on < 50% of days and standard dose one a day. The latest pH test results were for chronic steroid therapy for kidney transplants and not GERD symptoms. Median esophageal pH at baseline was 16.4% (IQR 8.5–22.4), which improved to 1.3% (IQR 4.0–2.2) at last follow-up at least 6 months post-implant (n = 6; p = 0.01). Most patients showed improvement in esophageal acid exposure and GERD symptoms. All patients were off-PPIs postoperatively. At their last follow-up (median 34–55 years), all patients had normalized acid exposure and 16% patients had >40% improvement in distal esophageal acid exposure. Median GERD-HRQL scores at baseline was 25 (IQR 8–31) which improved to 4 (IQR 3–10) at last follow-up (n = 6; p = 0.01). SAEs related to the device or procedure were reported. No dysphagia or other GI side effects were reported.

Conclusion: Preliminary results on patients with LSG and GERD with bothersome symptoms on maximal medical therapy is promising, revealed that LES stimulation is safe and results in a significant improvement in GERD symptoms and esophageal acid exposure. Most patients were off their PPI therapy with remaining taking PPI at a reduced dose. Data from a larger patient experience for this indication is being collected using the international registry trial.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
4. EST reported. Median GERD-HRQL score had improved from 12.8(5.2,30.5) to 6.8(3.0,8.0). There was an improvement >50% in PPI-exposure showing median esophageal pH at baseline of 25.75(10.2, 54.5) that improved to 9.0(8.4, 25.1). 4/5 patients (80%) were either free of PPI or with a reduced those compared to pre-op. Those patients with good response, 2 of 5 were also on chronic immunosuppressant drugs for their lung transplant and not for reflux symptoms. Interestingly, one of the lung transplanted patients improved his FEVI from 49 to 77 after the procedure while the second one remained stable at ~47 under chronic rejection.
5. Our preliminary case-series represents the first report of successful use of LES-EST in patients with GERD associated with severe esophageal dysmotility or lung transplant. Our early results suggest that LES-EST maybe a safe and effective treatment in these patients without the risk of new-onset dysphagia. A longer follow-up in a larger group of patients is required to fully establish the role of LES-EST in this difficult group of patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016
14:00–15:30 IMPROVING THE ADENOMA DETECTION RATE – ROOM E1

OP058 ENDOCUFF-ASSISTED COLONOSCOPY OUTPERFORMS CONVENTIONAL COLONOSCOPY TO DETECT MISSED-ADENOMAS: EUROPEAN MULTICENTER, RANDOMIZED, BACK-TO-BACK STUDY


Introduction: Colonoscopy reduces adenoma miss-rate by more than three times, even when targeted and focused on the proximal colon. However, index colonoscopy does not reveal missed advanced adenomas overall or in the proximal colon. Colonoscopy is a device that mounted on the tip of the scope promises inspection of greater surface of the colonic mucosa as the endoscope is gradually withdrawn by pushing backwards, flattening and stretching the colonic folds. We aimed to compare adenoma miss-rates of Endocuff-assisted colonoscopy (EC) with that of the conventional one (CC).

Aims & Methods: Our study population underwent same-day, back-to-back, (EC as the first procedure followed by CC or vice versa, randomized to the second procedure) for the two procedures was the study’s primary end-point. Secondary endpoints included among others, measurement of missed-advanced adenoma rate, modification of the surveillance schedule according to the second exam, true negative index colonoscopies and early adverse events rate.

Disclosure of Interest: All authors have declared no conflicts of interest.

Results: We randomized 200 patients (aged 61±10 years; 86.4% CRC screening-surveillance cases). There were 7 EC and 1 CC incomplete exams. Scope insertion times were similar for EC and CC (5.44±3.13 min vs. 5.37±0.32 min, p=0.6); however, there was a trend for longer EC withdrawal times (7.15±2.52 min vs. 6.50±1.52 min, p=0.06). Overall, we detected one cancer and 194 EC-CC adenomas; 84 in the proximal colon. By per lesion-analysis (table), EC showed significant lower overall and proximal colon adenoma miss-rates compared with CC (14.7 [8–21]% vs. 37.6 [27–48]%; p=0.0004 and 10.4 [1.8–19]% vs. 39 [23–55]%; p=0.004, respectively). A similar superiority for EC was not revealed regarding adenomas overall or in the proximal colon. Index colonoscopy did not miss the cancer. By per-patient analysis, the second exam indicated modification of the surveillance schedule, according to the ASGE guidelines, in 17 and 5 patients under CC and EC index exams (OR=3.8 [95%CI:1.4–9.9]; p=0.01), respectively; however no difference in the modification of the surveillance schedule was detected when European guidelines were taken into account. The CC index arm had significantly more false negative (no adenoma) first examinations compared to EC (14 of 100 vs. 3 of 94; p=0.01). There were no adverse events related to EC or CC.

Disclosure: In comparison with conventional colonoscopy, Endocuff-assisted colonoscopy reduces adenoma miss-rate by more than three times, even when highly efficient endoscopists perform the procedures.

Disclosure of Interest: All authors have declared no conflicts of interest.
Abstract No: OP058


M. Misawa1, S. Kudo1, Y. Mori2, K. Takeda1, Y. Maeda1, S. Kataoka1, H. Nakamura1, T. Kudo1, K. Wakamatsu2, T. Hayashi1, H. Miyachi1, A. Katagiri1, T. Baba1, F. Ishida1, H. Inoue3, M. Oda4, K. Mori5

1Digestive Disease Center, Showa University Northern Yokohama Hospital, Yokohama/Japan
2Digestive Disease Center, Showa University Northern Yokohama Hospital
3Diagnostic Disease Center, Yokohama/Japan
4Digestive Disease Center, Showa University Koto Toyosu Hospital, Tokyo/Japan
5Graduate School Of Information Science, Nagoya University, Nagoya/Japan
6Information and Communications, Nagoya University, Nagoya/Japan

Contact E-mail Address: misawanny@gmail.com

Introduction: Endoscopy-scopic (EC) can be used to evaluate not only cell nuclei but also microvessels in vivo. We reported the efficacy of observing the endoscopic vascular (ECV) pattern by using EC with narrow-band imaging for diagnosing colorectal lesions (Kudo S, et al. GIE 2015.1). As the interpretation of the ECV pattern is difficult for novice endoscopists and requires substantial training, we have developed a tentative model of a computer-aided diagnosis (CAD) system for the ECV pattern (ECV-CAD) (Misawa M, et al. Gastroenterology, in press.). However, in our previous study, we did not compare the performance of ECV-CAD with that of human endoscopists. Therefore, it is uncertain whether ECV-CAD can achieve a diagnostic ability as high as that of expert endoscopists.

Aims & Methods: The aim of this study was to compare the diagnostic ability of ECV-CAD with that of human endoscopists in characterization of colorectal lesion. The algorithm of ECV-CAD is based on texture analysis, which can quantify the pattern of endoscopic images, and vessel features. ECV-CAD provides a 2-class (neoplasm or non-neoplasm) including its probability value. To validate the diagnostic ability of ECV-CAD, 173 randomly selected EC images (non-neoplasm, 49; neoplasm, 124) were not used for training. To compare diagnostic ability between ECV-CAD and manual endoscopy, we selected 4 expert endoscopists (with an experience of ≥500 cases of IC) and 3 novices (with an experience of <200 cases of IC). The EC images used for the evaluation were used with ECV-CAD were randomly allocated to the assessors. The assessors recorded their diagnosis (non-neoplasm or neoplasm) with its confidence level (high or low). For ECV-CAD, a high-confidence diagnosis ratio of ECV-CAD was 72.0% (124 of 172). The NPV for neoplasms with a high confidence was 94.4%, 84.6%, and 46.3% for ECV-CAD, experts, and novices, respectively. The details of the diagnostic abilities are shown in the Table.

Table: Diagnostic Abilities

<table>
<thead>
<tr>
<th>Found at Index</th>
<th>Missed and found by EC</th>
<th>Missed and found by CC</th>
<th>OR (95%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>CC Index</td>
<td>53</td>
<td>32</td>
<td>3.5 (1.8–7)</td>
</tr>
<tr>
<td>EC Index</td>
<td>93</td>
<td>16</td>
<td>5.5 (1.7–17)</td>
</tr>
</tbody>
</table>

Conclusion: The overall accuracy of ECV-CAD was comparable to that of experts and significantly better than that of novices. Thus, ECV-CAD could be a powerful decision-making tool for endoscopists.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

MONDAY, OCTOBER 17, 2016

LONG-TERM MANAGEMENT OF IBD – ROOM G

OP060 LYMPHOMA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A FRENCH NATIONWIDE OBSERVATIONAL COHORT STUDY

M. Lemaître1, J. Kirchengesser2, A. Rudnichi1, F. Carrat2, A. Racine1, M. Zureik1, R. Dray-Spira1, F. Carbonnel1

1Department Of Epidemiology Of Health Products, French National Agency for Medicines and Health Products Safety (ANSM), Saint-Denis/France
2Institut Pierre Louis D’Epidemiologie Et De Santé Publique (unite Mixte De Recherche En Santé 1136), INSERM, Paris/France

Contact E-mail Address: Magali.LEMAITRE@ansm.sante.fr

Introduction: Thiopurines are associated with an increased risk of lymphoma. The risk of lymphoma associated with anti-TNFs is uncertain.

Aims & Methods: The aim of this study was to assess the risk of lymphoma in patients with inflammatory bowel disease (IBD) treated with thiopurines, anti-TNFs or the combination of both treatments (combotherapy). Every patient affiliated to the French national health insurance with a diagnosis of IBD, based on listed long-term diseases and/or hospital discharge diagnosis, was included from 1st July 2009 through 31st December 2013, and followed up until December 31st, 2014. A propensity score was built, using a multinomial logistic regression model to control for baseline differences between patients exposed to thiopurines or anti-TNFs and those exposed to both treatments. The risk of lymphoma was estimated using Cox proportional hazards regression in which each treatment was introduced as a time-dependent covariate.

Results: The cohort included 173,190 patients with IBD, followed for a median time of 4.9 years, accounting for 522,487 persons-years of observation. A total of 166,56, and 31 patients developed lymphoma, respectively. Patients exposed to combotherapy had a more than four-fold higher risk of lymphoma compared to those exposed to thiopurines or anti-TNFs. Patients exposed to combotherapy had a more than four-fold increased risk of lymphoma associated with anti-TNFs or combotherapy at baseline. Hazard ratios for lymphoma were calculated using Cox proportional hazards regression in which each treatment was introduced as a time-dependent covariate.

Conclusion: The risk of lymphoma associated with combotherapy is more than two-fold higher than that associated with thiopurines and anti-TNFs monotherapy. This risk should be taken into consideration and weighed against potential benefits of combotherapy.

Disclosure of Interest: F. Carbonnel: Franck Carbonnel had consulting fees from Genentech, Otsuka, Vifor, and lecture fees from Hospira. All other authors have declared no conflicts of interest.
In a long-term multicentre study, clinical characteristics of IBD (UC extent, penetrating CD, perianal CD) were risk factors for incident cancer. CRC was more frequent in UC and extracolonic cancers in CD.

Disclosure of Interest: L. Biancone: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, Astra Zeneca, Chiesi, Ferring, MSD, Otsuka, Takeda, Zambon, and served as consultant for Abbvie, Hospira, Lilly, MSD, Sofar.

M.L. Scibano: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study.

A. Orlando: No conflicts of interest specifically related to the study. Lecture fees from Abbvie, Takeda, MSD, Takeda, Zambon, and served as consultant for Abbvie, Hospira, Lilly, MSD, Sofar.

M. Daperno: No conflicts of interest specifically related to the study. Financial support for research not related to the present study from MSD, lecture fees from Abbvie, MSD, Hospira, Mundipharma, Takeda, Sofar, Chiesi, Ferring.

C. Papí: The study was not sponsored by any pharmaceutical company.

A. Kohn: Financial support for research not related to the present study: MSD, Takeda, Zambon, and served as consultant for Abbvie, Hospira, Lilly, MSD, Sofar.

L. Guidi: No conflicts of interest related to the study. Lecture fees from Abbvie, MSD, Sofar, Giuliani.

S. Ardizzone: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, Chiesi, MSD, Otsuka, Takeda, Sofar, Zambon, Mundipharma and served as consultant for Abbvie, Hospira, Lilly, MSD, Sofar.

F. Pallone: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, MSD, Hospira, Ferring.

G. Riegler: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study. Lecture fees from Abbvie, MSD, Hospira, Ferring.

M. Scribano: The study was not sponsored by any pharmaceutical company.

A. Armuzzi: The author declares no conflicts of interest specifically related to the study.

L. Biancone: The study was not sponsored by any pharmaceutical company. The author declares no conflicts of interest specifically related to the study.

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A. Armuzzi: The author declares no conflicts of interest specifically related to the study.
OP062 USE OF IMMUNOSUPPRESSANTS AND BIOLOGICAL AGENTS IN IBD PATIENTS WITH A PAST HISTORY OF CANCER: A MULTICENTRE STUDY OF THE GETECCU


1Gastroenterology, Hospital Universitari Germans Trias i Pujol, Badalona/Spain
2Gastroenterology, Hospital Universitari de Bellvitge, Barcelona/Spain
3Gastroenterology, H Clinic, Barcelona/Spain
4Gastroenterology Unit, Hospital Clínico Universitario de Valencia, Valencia/Spain
5Hospital Clínico de Valladolid, Valladolid/Spain
6Gastroenterology, University Hospital Reina Sofia, Córdoba/Spain
7Hospital Ramón y Cajal, Madrid/Spain
8Gastroenterology, Hospital Universitario de La Princesa, Madrid/Spain
9Hospital Universitario de Burgos, Burgos/Spain
10Gastroenterology, Hospital Universitari Mutua Terrassa, Terrassa/Spain
11Hospital de Sabadell, Institut Universitari Parc Taulí, Sabadell/Spain
12Hosp. General Ciudad Real, Ciudad real/Spain
13Hospital 12 de octubre, Madrid/Spain
14Hospital de Domostia, san sebastian/Spain
15Gastroenterology, H Mar, Barcelona/Spain
16Río Hortega University Hospital, Valladolid/Spain
17Hospital Terrassa, Barcelona/Spain
18U G E Elbe, Eke/Spain
19CH Navarra, Navarra/Spain
20Hospital La Fe, Valencia/Spain
21H San Jorge, Huesca/Spain
22H Basurto, Basurto/Spain
23Hosp.de La Candelaria, Santa Cruz de Tenerife/Spain
24Hospital Universitario La Paz, Madrid/Spain
25HU Salamanca, Salamanca/Spain
26Gastroenterology, Hospital de Torrejón, Madrid/Spain
27Gastroenterology, Marqués de Valdecilla University Hospital, Santander/Spain
28Hospital Universitario de Canarias, Santa Cruz de Tenerife/Spain
29Gastroenterología, Hospital Clínico, Universidad de Zaragoza, IIS Aragón, Zaragoza/Spain
30Gastroenterología, H Santa Lucia, Caraguata/Spain
31Gastroenterology Unit, Hospital Universitario Miguel Servet, Zaragoza/Spain
32H Royo Villanova, Zaragoza/Spain
33Digestive Services, Hospital Universitario de la Princesa, Instituto de Investigación Sanitaria Princesa (IP) and Centro, Madrid/Spain
34Gastroenterology Unit, Hospital Germans Trias i Pujol, Badalona, Barcelona/Spain

Contact E-mail Address: mmaluena.germanstrias@gencat.cat

Introduction: Conventional immunosuppressants (thiopurines or methotrexate) are relative contraindications for their use in inflammatory bowel disease (IBD). However, anti-TNFs monotherapy and the combination of both treatments (combi) are treatment options in IBD patients with a past history of cancer (aged 18–64 years) and HRQoL scores exceeding ½ standard deviation (SD) as clinically relevant. Serious and opportunistic infections were classified according to infection sites and pathogens, respectively.

Results: We aimed to describe the risk of incident cancers (recurrent or new) in patients with IBD and a past history of malignancy treated with IMMs, compared to unexposed patients. The risk of serious and opportunistic infections was higher with anti-TNFs monotherapy and combiotherapy compared to thiopurines and combi (HR95%: 1.31 (1.14–1.51), HR95%: 2.12 (1.49–3.00), respectively), while exposure to anti-TNFs was associated with an increased risk of serious infections compared to thiopurines in patients aged 18–64 years and ≥ 65 years: HR95%; 1.82 (1.67–1.99) and 1.83 (1.43–2.23), respectively. Exposure to thiopurines was associated with an increased risk of viral infections compared to anti-TNFs' monotherapy in patients aged 18–64 years (HR95%; 1.74 (1.20–2.52)). Similar results were observed in a sensitivity analysis conducted in incident patients.

Conclusion: Thiopurines, anti-TNFs monotherapy and combiotherapy are all associated with an increased risk of serious infections in IBD patients compared to unexposed patients. However, the risk of serious infections is higher with anti-TNFs than with thiopurines and the risk of serious and opportunistic infections is increased with anti-TNFs compared to anti-TNFs. The risk of serious and opportunistic infections should be taken into consideration and weighed against potential benefits of anti-TNFs.

Disclosure of Interest: F. Carbonnel had consulting fees from Tenebentec, Osuka, Vifor, and lecture fees from Hospira. All other authors have declared no conflicts of interest.

OP063 RISK OF SERIOUS AND OPPORTUNISTIC INFECTIONS IN IBD PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A NATIONWIDE FRENCH COHORT STUDY

J. Kirchgesner1, M. Lemaître2, M. Zureik2, F. Carbonnel3, R. Dray-Spira2
1Institut Pierre Louis D’Epidémiologie Et De Sante Publique (unité Mixte De Recherche En Santé 1136), ANSPRM, Paris/France
2Department Of Epidemiology Of Health Products, French National Agency for Medicines and Health Products Safety (ANSM), Saint-Denis/Paris
3Gastroenterology Unit, CHU de Békeeper, APHP-Université Paris Sud, Le Kremlin Bicêtre, France

Contact E-mail Address: julien.kirchgesner@gmx.com

Introduction: Serious and opportunistic infections are a major concern in patients with inflammatory bowel disease (IBD) treated with immunosuppressive agents and biologics.

Aims & Methods: The aim of this study was to assess the risk of serious and opportunistic infections associated with thiopurines monotherapy, anti-TNFs monotherapy and the combination of both treatments (combi). Every patient affiliated to the French national health insurance with a diagnosis of IBD based on listed long-term diseases and/or hospital discharge diagnosis was included from 2009 to 2013, and followed up until 31 December 2014. Kaplan-Meier curves were used to describe the cumulative incidence of the different endpoints, and the Cox proportional hazards model was used to estimate the relative risks.

Results: The aim of this study was to assess the risk of serious and opportunistic infections associated with thiopurines monotherapy, anti-TNFs monotherapy and the combination of both treatments (combi). Every patient affiliated to the French national health insurance with a diagnosis of IBD based on listed long-term diseases and/or hospital discharge diagnosis was included from 2009 to 2013, and followed up until 31 December 2014. Kaplan-Meier curves were used to describe the cumulative incidence of the different endpoints, and the Cox proportional hazards model was used to estimate the relative risks.

Disclosure of Interest: We aimed to describe the risk of incident cancers (recurrent or new) in patients with IBD and a past history of malignancy treated with IMMs, and to identify risk factors.

Results: We identified 947 patients with previous cancer of whom 526 did not receive IMMs before the diagnosis of cancer. Of these, 385 were controls and 141 were subsequently treated with IMMs after a median of 60 (23–130) months from cancer diagnosis. After a median follow-up of 60 months (27–126), 52 patients(10%) developed incident cancers (50% recurrent and 50% new). The most frequent recurrent ones were breast (35%) and prostate (20%) cancers. Incident cancers occurred similarly in patients further treated with IMMs and controls (9% vs. 12% p = 0.33), as did regarding the type of the index cancer. However, cancer-related deaths were more frequent among controls (4% vs. 0% p < 0.031). Cancer-free survival was 99%, 98% and 97% at 1, 2, and 5 years in patients further treated with IMMs and controls, 97%, 96% and 92% at 1, 2 and 5 years in controls, respectively (p = 0.003).

Conclusion: In this large, retrospective cohort, treatment with conventional immunosuppressants or anti-TNF agents in patients with IBD and a past history of cancer was not associated with an increased risk of new or recurrent cancers.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP064 THE COURSE OF HEALTH-RELATED QUALITY OF LIFE IN IBD PATIENTS WITH A PAST HISTORY OF CANCER: A 20 YEARS AFTER DIAGNOSIS - DATA FROM THE IBSEN STUDY

G. Huppertz-Hauss1, B. Moom2, T. Berkle3
1Dept. Of Gastroenterology, Oslo University Hospital Ullevål, Oslo/Norway
2Research and Development, Vestfold Hospital, Tonsberg/Norway
3Dept. Of Gastroenterology, Telenorke Hospital, Skien/Norway

Contact E-mail Address: Gert.Huppertz-Hauss@sths.no

Introduction: Previous population-based cross-sectional studies have shown that health-related quality of life (HRQoL) in patients with the inflammatory bowel disease (IBD) is significantly lower than that in the general population, especially in association with disease activity. Data describing the course of HRQoL in IBD are scarce.

Aims & Methods: The aim of the present study was to assess the course of HRQoL at three prescheduled time-points during 20 years of follow-up in an inception cohort with IBD patients. IBD patients included in a population-based inception cohort from 1990–93 (Inflammatory Bowel Disease in South-East Norway – IBSEN) were invited to follow-up visits five, ten and 20 years after diagnosis. In addition to structured interviews and clinical examinations at inclusion and follow-up visits, the Short Form 36 (SF-36) and the Norwegian version of the Inflammatory Bowel Disease Questionnaire (N-IBDQ) were completed by the patients at all follow-up visits. The mean N-IBDQ total scores and the mean SF-36 dimensional scores were calculated. In this abstract, we present the total N-IBDQ scores and the dimensional SF-36 scores for general health (GH), physical functioning (PH), role limitations due to physical problems (RP), role limitations due to emotional problems (RE), energy/fatigue (EF), pain (PA), social functioning (SF) and mental health (MH).

Results: Of the initially 756 included patients with confirmed IBD, 599 (79%) were alive and followed up until at least 20 years after diagnosis. HRQoL questionnaires were answered by 522, 327
and 438 patients at the five, ten and 20 years follow up, respectively. Of these patients, 199 (139 UC, 60 CD) and 191 (133 UC, 58 CD) answered the N-IBDQ and the SF-36 at every follow up visit, respectively. We could not register clinically relevant changes between the mean N-IBDQ total scores and the mean GH dimensional scores during the different follow up visits (Table 1). Of 139 UC patients and 60 CD patients, who answered the N-IBDQ at all follow up visits, 54 (38.9%) and 17 (28.3%) had stable scores. Of 133 UC patients and 58 CD patients, who answered the SF-36 at all follow up visits, 31 (23.3%) and 13 (22.4%) had stable scores.

Table 1: N-IBDQ total scores and General Health dimensional scores

<table>
<thead>
<tr>
<th>N-IBDQ</th>
<th>UC</th>
<th>Women</th>
<th>5</th>
<th>10</th>
<th>20</th>
<th>5</th>
<th>10</th>
<th>20</th>
<th>5</th>
<th>10</th>
<th>20</th>
<th>5</th>
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<th>5</th>
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<td>IBDO</td>
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<td>140</td>
<td>168</td>
<td>113</td>
<td>154</td>
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<tr>
<td></td>
<td>mean</td>
<td>190</td>
<td>187</td>
<td>181</td>
<td>179</td>
<td>186</td>
<td>186</td>
<td>174</td>
<td>180</td>
<td>172</td>
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<tr>
<td></td>
<td>SD</td>
<td>25</td>
<td>29</td>
<td>29</td>
<td>33</td>
<td>28</td>
<td>31</td>
<td>26</td>
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<td>SF-36</td>
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<td>178</td>
<td>104</td>
<td>165</td>
<td>110</td>
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<td>21</td>
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</table>

Table: Hazard ratios for any serious or opportunistic infections according to medication exposure

<table>
<thead>
<tr>
<th>Medication</th>
<th>Hazard Ratio (95% CI)</th>
<th>Hazard Ratio (95% CI)</th>
<th>Hazard Ratio (95% CI)</th>
<th>Hazard Ratio (95% CI)</th>
<th>Hazard Ratio (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>None</td>
<td>1.29 (1.20–1.39)</td>
<td>1.27 (1.15–1.39)</td>
<td>2.40 (2.23–2.58)</td>
<td>2.31 (2.10–2.53)</td>
<td>3.82 (2.65–5.34)</td>
</tr>
<tr>
<td>Thiopurines</td>
<td>0.94 (0.81–1.10)</td>
<td>1.39 (0.97–1.47)</td>
<td>1.76 (1.43–2.16)</td>
<td>2.18 (1.73–2.76)</td>
<td>1.82 (1.03–3.22)</td>
</tr>
</tbody>
</table>

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
1. Norman GR, Sloan JA and Wyrwich KW. Interpretation of changes in health-related quality of life: the remarkable universality of half a standard deviation. Medical Care 2003; 41: 582-592.

OP006 PROGNOSTIC FACTORS FOR LONG-TERM INFlixIMAB TREATMENT IN CROHN’S DISEASE PATIENTS: A 20-YEAR SINGLE CENTER EXPERIENCE

T. Billiet 1, C. Leynen 1, V. Ballet 1, M. Ferrante 2, G. Van Assche 2, A. Gils 3, S. Vermeire 4

1KU Leuven TARGID, Leuven/Belgium
2Department Of Gastroenterology and Hepatology, University Hospitals Leuven, Leuven/Belgium
3Laboratory for Therapeutic and Diagnostic Antibodies, Department of Pharmaceutical and Pharmacological Sciences, KU Leuven, Leuven/Belgium

Introduction: The long-term efficacy of infliximab (IFX) in Crohn’s disease (CD) patients is substantial and prognostic factors for real-life long-term efficacy are insufficiently studied.

Aims & Methods: The aim of this study was to identify patient- and disease-related factors influencing the real-life long-term response of infliximab in CD at Kings College London - ISS on November 25, 2016ueg.sagepub.comDownloaded from
week 14 were available in 199 (76.2%) patients, and in this subgroup of patients, IFX concentration at week 14 was also a significant predictor of IFX failure-free survival (HR 0.87 (0.80-0.94), p = 0.001).

Conclusion: This study identified several predictors of clinically relevant IFX failure. Stratifying patients according to the amount of risk factors can identify patients at high risk for IFX failure. Initiating IFX sooner rather than later and using TDM in this group to proactively strive for adequate drug concentrations may ensure optimal disease outcome.

Disclosure of Interest: T. Billiet: Lecture Fee: Ferring
M. Ferrante: - Research grant: Takeda - Speakers fee: Abbvie, Boehringer-Ingelheim, Chiesi, Falk, Ferring, Jansen, Mitsubishi Tanabe, MSD, Takeda, Tillots, Zeria - Consultancy: Abbvie, Boehringer-Ingelheim, Ferring, Jansen, MSD
G. Van Assche: - Financial support for research: Abbvie, MSD - Lecture fees: Abbvie, Ferring, MSD, Janssen - Consultancy: Abbvie, MSD - Takeda, Ferring, Falk Pharma, Hospira, Tillots - Consultancy: Abbvie, MSD, Takeda, Ferring, Genentech/Roche, Shire, Pfizer, Galapagos, Mundipharma, Hospira, Celgene - Goncourt, Japan, MSD - All other authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016
14:00-15:30
MICROBIOTA AND DIET: FROM BENCH TO BEDSIDE – ROOM K

OP066 CIRCULAR ENTERAL NUTRITION FOR THE MAINTENANCE OF REMISSION IN PEDIATRIC CROHN’S DISEASE PATIENTS
B. Pigneur1, S. Nobrega2, F. Ruemmele3
1Pediatric Gastroenterology Unit, Necker Enfants Malades Hospital, PARIS/France
2Hospital Dom Desteñía, Lisbon/Portugal
3Paris-cité Hospital, Université Sorbonne, Paris/Paris
Contact E-mail Address: benedict.pigneur@aphp.fr

Introduction: Enteral nutrition (EN) is a well-established treatment in pediatric Crohn’s disease (CD) for induction and maintenance of remission. Cyclic EN consists of a 6 weeks phase of normal feeding and a remission phase lasting 2 months. This study aimed to test feasibility and efficacy of cyclic EN as sole maintenance therapy.

Aims & Methods: Nine patients with active luminal paediatric Crohn’s disease, L1 (n = 2) or L3 (n = 7), followed at Necker Hospital between 2012 and 2014 were included in this prospective pilot study. After 8 weeks of exclusive enteral nutrition with Modulen IBID, patients who came into complete CRP-negative remission were proposed to continue on cyclic EN therapy as sole treatment in an open manner. Cyclic EN consists of a 6 weeks phase of normal feeding followed by a 2 weeks phase of exclusive enteral nutrition, without any concomitant CD-related medication. Patients were followed on a fixed scheme (3 months visits) with collection of anthropometric, clinical and biological data.

Results: At inclusion, all patients were in deep remission (CRP-negative). At month 6 and 12 follow-up visit, 8 of the 9 patients (89%) (wPCDAI 8.4 ± 9.2) and 5 of 6 patients (wPCDAI 5.7 ± 3.2), respectively were in clinical remission. Concomitant to the clinical response, biological scores markedly improved with mean CRP 21.8 ± 4.2 mg/L at M0, 9.8 ± 11.7 mg/L at M6 (p < 0.05) and 5.4 ± 2.7 at M12 (n = 6) (p < 0.05) and albumin normalization with 33.8 ± 3.8 g/L at M0, 39.3 ± 4.1 g/L at M6 (p = 0.00) and 42.8 ± 2.9 at M12 (n = 6) (p < 0.05). 3 patients relapsed before M12. Patients presented catch up growth with net improvement of their anthropometric measurements at M2 and stabilisation thereafter (Table 1).

<table>
<thead>
<tr>
<th>M0 (n = 9)</th>
<th>M2 (n = 9)</th>
<th>M6 (n = 9)</th>
<th>M12 (n = 6)</th>
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<tbody>
<tr>
<td>Z score weight</td>
<td>-0.96 ± 1.13</td>
<td>-0.37 ± 0.97</td>
<td>0.07 ± 0.81</td>
</tr>
<tr>
<td>Z score height</td>
<td>-0.18 ± 0.84</td>
<td>-0.11 ± 0.80</td>
<td>0.09 ± 1.14</td>
</tr>
<tr>
<td>Z score BMI</td>
<td>-1.37 ± 1.07</td>
<td>-0.38 ± 0.89</td>
<td>-0.82 ± 1.15</td>
</tr>
</tbody>
</table>

Conclusion: This study demonstrates for the first time prolonged clinical, biological remission and improved growth in pediatric CD patients treated only with cyclic enteral nutrition. Cyclic EN can be an efficacious non pharmacological treatment of Crohn’s disease potentially acting ahead of the inflammatory cascade in the intestinal mucosa. A sufficiently powered randomized controlled trials is currently conducted by the GETAID pédiatrique to confirm these pilot data.

Disclosure of Interest: F. Ruemmele: Nestle Nutrition Institute, Nestlé Health Science
All other authors have declared no conflicts of interest.

OP067 CHANGES IN MUCOSAL-ASSOCIATED INTESTINAL MICROBIOTA AND FECAL BACTERIA IN INFILTRATING BOWEL DISEASE PATIENTS AND HEALTHY SUBJECTS: A PILOT STUDY
M. P.L. Guarino1, L. Putignani2, A. Altomare3, F. Del Chierico2, S. Cocca1, S. Emerenziani4, B. Dalla Piccola5, M. Cicala5
1Gastroenterology Unit, Campus Bio Medico University, Rome/Italy
2Parasitology and Metagenomics Unit, Bambino Gesù Children’s Hospital and Research Institute, Rome/Italy
Contact E-mail Address: a.altomare@unicampus.it

Introduction: The existing literature on intestinal microbiota in inflammatory bowel diseases (IBD) reveals conflicting changes in microbiota composition in all patients, having most of studies been conducted only on fecal microbiota. Microbiota adhesion to the gut mucosa might affect epithelial and mucosal function to a greater degree than fecal bacteria.

Aims & Methods: The aim of the present study was to evaluate the mucosal and fecal microbiota composition in healthy controls (CTRLs) and IBD patients, in a case-control study exploited by 16s rRNA targeted metagenomics-based approach (phylootyping, PH). Fecal specimens were collected from 14 IBD patients [10 Crohn’s disease (CD), 4 ulcerative colitis (UC)], and from 11 healthy subjects. Mucosal samples were obtained during colonoscopy from the terminal ileum, and descending colon. PH was assessed by pyrosequencing as follows. All patients were in wash-out from antibiotics, probiotics and corticosteroids. Genomic DNA was isolated from the entire set of samples. The V1-V3 region of 16s rRNA amplicon was amplified on a 454-Junior Genome Sequencer. Reads were analyzed by Quantitative Insights into Microbial Ecology (QIME, v.1.8.0), grouped into operational taxonomic units (OTUs) at a sequence similarity level of 97% by PyNAST for taxonomic assignment, and aligned under UCLUST for OTUs matching against Greengenes database (v. 13.8).

Results: In adult IBD patients colonic biopsies showed a statistically significant increase of Proteobacteria and decrease of Firmicutes and Actinobacteria, compared to CTRLs. The microbiota analysis of stool samples from IBD patient showed an increment of Proteobacteria and decrease of Bacteroidetes, the difference was not significant compared to CTRLs. Particularly, a predominant presence of Enterobacteriaceae in IBD and a predominant presence of Ruminococcaceae, Rikenellaceae and Prevotellaceae in CTRLs were prevalent (P < 0.05). Patient specific findings, according to intestinal sampling site, of the analysis revealed that only Ruminococcaceae resulted statistically increased in the colon. Tackling in account only colon biopsy samples, a significant reduction of Enterobacteriaceae, predominate Rikenellaceae, Roseburia, Ruminococcaceae was observed in patients and an increment of Enterobacteriaceae was observed in CTRLs. Finally, stratifying patients according to the status of disease activity a decrease of Ruminococcaceae, Peptostreptococcus and Paraprevotella and an increase in Enterococcus was associated to active disease status (P < 0.05).

Conclusion: The present study shows that in the mucosal microbiota of IBD patients, irrespective of disease localization and activity, phylum Proteobacteria was significantly more represented, while phylum Firmicutes and Actinobacteria were reduced. The profiles of fecal microbiota partially replicate those of the mucosal microbiota being not able to differentiate from controls. It appears that microbiota adhesion to the gut mucosa better discriminates patients from controls especially when considering family species. Our data suggest the high diagnostic potential of microbiota profiling with special reference to mucosal biosystem.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP068 BACTERIOPHAGE THERAPY: A NEW STRATEGY TO TARGET ADHERENT-INVASIVE ESCHERICHIA COLI BACTERIA IN THE GI TRACT OF CROHN’S DISEASE PATIENTS
M. Galitter1, L. De Sordi2, A. Sivignon3, A. De Valle3, D. Maura4, C. Neut3, O. Rahmouni4, K. Wannerberger5, P. Desreumaux6, N. Barnich2, I. De Barbrieux2
1Dpt Of Microbiology, Institut Pasteur, Molecular Biology of the Gene in Extremophiles Unit, Paris/ France
2Universite d’Auvergne Inserm U 1071, Clermont-Ferrand/France
3Aix Marseille University, Inserm U1040, INSERM U919, INSERM U1076; CHU Purpan, Toulouse/France
4Univ. Lille, Inserm, LIRIC, UM9895, Lille/ France
5Ferring Pharmaceuticals, Saint-Prey/Switzerland
6Univ. Lille, Inserm, CHU Lille, LIRIC-UM9895; Claude Huriez hospital, Lille/ France
Contact E-mail Address: adeline.sivignon@u-clermont1.fr

Introduction: Adherent-invasive Escherichia coli (AIEC) are abnormally predominant on Crohn’s disease (CD) ileal mucosa. AIEC are pathobiont bacteria able to cause inflammatory responses that could initiate or perpetuate the chronic gut inflammation. Antibacterial treatments, such as bacteriophages (viruses infecting bacteria) represent a way to eliminate these bacteria from the GI tract without disturbing the mucosa-hormonal homeostasis. Here, we report improvement of bacteriophages to reduce AIEC colonization associated to intestinal mucosa.

Aims & Methods: Three bacteriophages were selected to efficiently target AIEC isolated from CD patient. Efficacy of this bacteriophage cocktail was investigated using two in vivo experimental models: transgenic mice expressing CEACAM6 colonized by AIEC strain LF82 and the DSS chemically-induced colitis model infected with AIEC strain LF82.

Results: In LF82-colonized CEACAM6-expressing mice, 24h after the oral administration of a cocktail of three bacteriophages, the fecal...
concentration of LF82 bacteria has significantly dropped by two log in the bacteriophage group and stays significantly lower than in control group four days post-treatment, without any additional bacteriophage administration demonstrating the benefit of self-amplification of bacteriophages over time. Furthermore, we found that administration of the cocktail during the first day reduces progressively over a period of five days the colonization level of LF82 bacteria through the entire gut. In addition, bacteriophage treatment reduced colitis symptoms in the DSS-induced model, with a reduction of LF82 bacteria levels in feces, compared to the control group. Then, we showed that bacteriophages were driving a long-term digestive tract decolonization of AIEC LF82 bacteria which in turns reduces colitis symptoms.

Disclosures of Interest: All authors have declared no conflicts of interest.

References

and 8, open label mid and end of treatment (if applicable), and 8 weeks after FMT, colonic biopsies were collected at week 0 and 8, and end of open label treatment (if applicable). Faecal samples were also collected from individual donors and donor batches. DNA was extracted from faecal samples and 16S ribosomal RNA sequencing performed using 2x300 bp Illumina MiSeq chemistry (F27 & 519R). Raw sequences were analysed using MOTHUR, and statistical tests performed on counts and relative abundances.

Results: Faecal and colonic samples were collected from 70 study patients. 14 donors contributed to 21 donor batches. 314 patient and 113 donor (individual + batch) faecal samples along with 160 patient colonic samples were analysed. 26976 ± 540 clean sequences per faecal sample and 26993 ± 881 per colonic biopsy were obtained with rarefaction curves suggesting sampling had reached saturation. In both faecal and colonic samples α-diversity significantly increased at all FMT treatment time points relative to baseline (p < 0.005); this persisted 8 weeks after FMT in the faecal samples. On PCA, Cluster, and PERMANOVA analyses FMT significantly influenced patient microbial profiles, with the shift towards healthy donor microbiota most notable at the genus and OTU levels. LEfSe analysis of both faecal and colonic samples showed a decrease in patient Bacteroides and an increase in donor Prevotella with FMT, independent of clinical outcome. A range of other microbial taxa were identified as transplanted or displaced with FMT across all taxonomic levels. Patients receiving FMT who achieved remission had greater baseline faecal and colonic mucosal α-diversity than those who did not achieve remission, and also had greater resultant diversity with and after FMT treatment. Specific taxa were consistently significantly associated with FMT remission across both faecal and colonic samples: taxa within Barnesiella were associated with remission, while OTUs within Fusobacterium and Sutterella were associated with lack of remission.

Conclusion: Baseline patient microbial diversity in UC appears to be predictive of therapeutic response to FMT. Intensive FMT is associated with increased microbial diversity, with the greatest diversity noted in patients achieving remission. Increased diversity persists 8 weeks after cessation of therapy. Specific bacterial taxa associated with FMT outcome of which are associated with FMT treatment outcome. A high level of concordance was observed between the faecal and colonic mucosal microbiota. These findings may be important in both understand and predicting the pathophysiology of the microbiota in UC and shaping future bacterial therapy.

Disclosure of Interest: T.J. Borody: Thomas J. Borody has an interest in the Centre for Digestive Diseases, where faecal microbiota transplantation is a treatment option for patients and has filed patents in this field.

All other authors have declared no conflicts of interest.


MONDAY, OCTOBER 17, 2016
14:00–15:30
FREE PAPER SESSION: THE FUTURE OF DIAGNOSIS IN HBP AND UPPER GI – ROOM N1

OP073 A QUANTITATIVE IMAGING PLATFORM TO REAL-TIME MEASURE SPECIFIC ROS LEVELS IN LIVER DISEASES
H. Wang1, X. Liang1, X. Liu1, R. Zhang2, M. Roberts1
1 School Of Medicine, The University of Queensland, Brisbane/Australia
2 Australian Institute For Bioengineering and Nanotechnology, The University of Queensland, Brisbane/Australia

Contact E-mail Address: h.wang21@uq.edu.au

Introduction: Reactive oxygen species (ROS) are chemically reactive molecules containing oxygen, including the peroxide (H2O2), hypochlorous acid (HOCl), singlet oxygen (O2·), and superoxide (O2−). ROS have been reported to play an important role in the development of liver diseases. For example, H2O2 can activate hepatic stellate cells in liver fibrogenesis. During hepatic ischemia-reperfusion injury, HOCl is generated by neutrophils and diffuses into hepatocytes, causing oxidant stress-mediated injury. O2· can react with nitric oxide to form peroxynitrite to modify the cell structure and function of proteins in diseased liver. Various methods have been developed to monitor ROS generation in the liver, but the presence of different cellular sources for ROS as well as the distinct chemical properties of specific ROS may lead to conflicting results. Most developed ROS-detection probes were difficult to be distinguished from endogenous fluorophores and only can be employed under one-photon microscopy. Thus, an optimal strategy for precise real-time ROS detection is highly required to rapidly and accurately reveal the cellular microenvironment in liver diseases in clinic.

Aims & Methods: Four different two-photon fluorescent probes were designed and synthesized for selective detection of chemically reactive molecules of H2O2, HOCl, and ROS including glutathione (GSH), H2O2, HOCl, and O2−. Mouse models of hepatic steatosis, fibrosis and ischemia-reperfusion injury were developed to mimic human liver diseases. After sacrificing the animals, unfixed liver tissues were collected and incubated with each probe at the final concentration of 50 to 100 µmol for 10 min, and then imaged using multiphoton microscopy (JanLab GmbH, Jena, Germany).

Results: Each probe exhibited a strong positive fluorescent response only in the presence of specific chemically reactive molecule, whereas negligible fluorescent signals were observed upon the additions of other reactive oxygen/nitrogen species and metal ions. There was a good linear relationship between the probe response fluorescent intensity and the concentration of specific ROS. In the liver with ischemia-reperfusion injury, reduced autofluorescence was detected, indicating the hepatocyte necrosis. Remarkable enhancement of red fluorescence was observed in hepatocytes with decreased autofluorescence, indicating the reaction of with endogenous HOCl. The cellular concentration of GSH decreased and H2O2 increased in the liver with fibrosis and steatosis compared to the control. The concentration of each specific ROS was first calculated based on the intensity of images at the cellular level.

Conclusion: We developed a quantitative imaging platform to real-time measure specific ROS changes in liver diseases at the cellular level. This technique can be used to investigate ROS-mediated liver injury and predict treatment response in human liver biopsy, and can be readily extended to examination of diseases and injury of other organs. We anticipate that in the near future this quantitative imaging platform will be evaluated from bench to bedside, leading to real-time monitoring of cellular microenvironment in human diseases.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
**Aims & Methods:** In a RCT, our primary aim was to compare 30-day rebleed rates of index lesions for patients treated with Standard vs. DEP guided endoscopic hemostasis. In a 2-center study, patients were resuscitated & consented. They & managing medical-surgical teams were blinded to endoscopic treatments. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic hemostasis. In a 2-center study, patients were resuscitated & consented. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic signs of rebleeding, & repeat endoscopy with more hemostasis as needed. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic signs of rebleeding, & repeat endoscopy with more hemostasis as needed. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic signs of rebleeding, & repeat endoscopy with more hemostasis as needed. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic signs of rebleeding, & repeat endoscopy with more hemostasis as needed. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic signs of rebleeding, & repeat endoscopy with more hemostasis as needed. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic signs of rebleeding, & repeat endoscopy with more hemostasis as needed. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic signs of rebleeding, & repeat endoscopy with more hemostasis as needed. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic signs of rebleeding, & repeat endoscopy with more hemostasis as needed. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic signs of rebleeding, & repeat endoscopy with more hemostasis as needed. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic signs of rebleeding, & repeat endoscopy with more hemostasis as needed. Patients with severe inpatient or outpatient start of UGIH (clinical signs, hemodynamic signs of rebleeding, & repeat endoscopy with more hemostasis as needed.

**Conclusion:** In a RCT of patients with severe NVUGIH, use of Doppler probe as a guide to endoscopic hemostasis significantly reduced 30 day rebleed & surgery rates compared to Standard, visually guided hemostasis. We now recommend DEP (along with SRH) as a new guide for risk stratification & definitive endoscopic hemostasis in patients with severe NVUGIH. RCT was supported by a VA Merit Review Research Grant & in part by NIH-NIDDK AM 41301.

**OP005 ESOPHAGEAL HIGH RESOLUTION MANOMETRY WITH A SOLID TEST MEAL IMPROVES DETERMINATION OF CLINICALLY RELEVANT ESOPHAGEAL DYSFUNCTION AND SYMPTOM REPRODUCIBILITY: A VALIDATION STUDY IN A MULTIRACIAL ASIAN COHORT**

D. Ang1, M. Lee1, T. Tan1, M. Zhang1, M. Fox2

1Gastroenterology, Changi General Hospital, Singapore/Singapore

2Department Of Gastroenterology, St. Ciaracapital, Basel/Switzerland

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References:**

1. Fox et al., DDW 2014.


**Disclosure of Interest:** All authors have declared no conflicts of interest.
Summary of Manometry Findings with Single Water Swallows (SWS) and Solid Test Meal (STM)

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<tr>
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Contact E-mail Address: yoshirok@md.okayama-u.ac.jp

Introduction: A value of the combination of magnifying endoscopy of and image enhancement endoscopy (IEE) technology (e.g. NBI, BLI) is reported in a diagnosis for the early gastric neoplasm. This combination is effective, but it is necessary to speculate in real histology from the pattern of a two-dimensional monotone. Therefore, this diagnostic method is still more difficult for general endoscopists. Linked Color Imaging (LCI) was recently developed using a laser endoscopic system (Fujifilm Co., Tokyo, Japan). LCI acquires images by simultaneously using narrow-band short wavelength light and white light in an appropriate balance. This combination of light provides more information about the vasculature and architecture on the mucosal surface than that obtained with typical white-light imaging. When we use acetic acid indigocarmine mixture (AIM) with LCI mode, we discovered that the magnifying images of early gastric cancer are very clear, three-dimensional and near to real histology. So, we examined the utility of this method.

Aims & Methods: This was a prospective observational study performed at a single tertiary referral center. The subjects are 72 lesions of 67 patients with gastric neoplasm. We are indicated of the endoscopic submucosal dissection (ESD), and were given pre-ESD endoscopy in our hospital from September 2014 to February 2016. Firstly we observed the lesions by magnifying endoscopy with LCI method and diagnosed using VS classification system. Furthermore, we classified the visualization ability of the surface fine structure, proliferation, migration, invasion and increased apoptosis, and the same phenomenon was seen when transfect miR-21 inhibitor into the exosomes from GC cells and co-culture the transfected exosomes with GC cells. Moreover, exosomal miR-21 markedly enhanced sNAT and vimentin expression in GC cells, while significantly decreasing E-cadherin levels, suggesting that exosomal miR-21 might play a role in epithelial-to-mesenchymal transition (EMT) process. Finally, circulating exosomal miR-21 levels were closely associated with TNM stage, and lymph node metastasis in GC patients and could be used as a useful diagnostic marker. In this study, we used miRNA microarray technology to identify exosomal miRNAs that were differentially expressed in GC patients and controls. We further examined the biological function of exosomal miR-21 on cell viability, apoptotic death and metastasis in human GC cells and explored the possible downstream mechanism. We also included another 100 GC patients and 100 controls to study whether exosomal miR-21 could be used as a potential biomarker.

Results: By the pathology results, 60 lesions were gastric cancer and 12 lesions were gastric adenoma. The differentiation ability of a cancer and the non-cancer (adenoma) did not have the significant difference between the BLI mode and the LCI+AIM methods. In the classification of visualization ability, 12 lesions were Clear, 22 lesions were Visible, 38 lesions were Invisible by BLI mode. On the other hand, 33 lesions were Clear, 34 lesions were Visible, 5 lesions were Invisible by LCI+AIM method. In the visualization ability of the surface fine structure, LCI+AIM method is significantly clearer than BLI mode (p < 0.05). Conclusion: When we use AIM, indigocarmine accumulates in pit of the duct, and duct structures become clear by the acetic acid. By LCI mode, we can observe the vascular pattern of the lesion clearly. So by the combination of AIM and LCI, we can observe the lesion three-dimensionally. By this method, we can compare histopathology with an endoscopic image intuitively, so we believe that we can magnifying endoscopy diagnosis of the gastric cancer is enabled even if we do not use various confusing classifications.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
Introduction: Modern medical technology and diet can cause many problems that can contribute to gastric cancer (GC). Accurate diagnosis is thus needed to choose an optimal treatment for GC; however, the current imaging diagnosis is not reliable enough to identify incurable factors including peritoneal metastasis and local invasion. We have previously reported the usefulness of urinary biomarkers for diagnosis of GC. With the goal of discovering non-invasive biomarkers for progression and incurability of GC, we conducted this study using urine samples from patients with GC and healthy controls. Aims: To study gene expression patterns to identify potential candidate biomarkers, and three proteins were found to be elevated in the urine of advanced GC patients compared to early GC patients. Among them, urinary kallikrein-10 (uKLK10) and proteinase 3 were positively associated with tumor stage progression. Moreover, urinary kallikrein-10 (uKLK10) was significantly elevated in the urine of inoperable GC patients compared to operable GC patients (uKLK10: median, 35.5 ng/ml vs. 10.8 ng/ml; P < 0.0001), and disease-free survival (DFS) was significantly lower for GC patients with high uKLK10 compared to low uKLK10 (HR: 2.53 (95%CI, 1.23–5.21), P = 0.007). Urinary KKL10 distinguished operability of GC with an area under the curve (AUC) of 0.710 and the combination of uKLK10 with tumor size showed an AUC of 0.835. Immunohistochemical analyses also demonstrated a positive correlation between tumor stage and uKLK10 expression in GC tissues. In addition, GC patients with high expression of pathological KLK10 (pKLK10) significantly showed a shorter DFS compared to those with low pKLK10 levels. Conclusion: uKLK10 is a promising non-invasive biomarker for incurable GC.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016

14:00–15:30
FROM SYMPTOMS TO DIAGNOSIS IN IBS – ROOM N2

OP079 POPULATION PREVALENCE OF ROME III AND ROME IV IRRITABLE BOWEL SYNDROME (IBS) IN THE UNITED STATES, CANADA AND THE UNITED KINGDOM (UK)

O.S. S. Palsson1, M. Van Tilburg2, M. Simrén3, A. D. Sperber4, W. E. Whitehead5

1Dept. Of Medicine, University of North Carolina, Chapel Hill, NC/United States of America
2Dept. Of Medicine, University of North Carolina, Chapel Hill/United States of America
3Dept Of Internal Medicine, Sahlgrenska University Hospital, Gothenburg/Sweden
4Ren-Gurion Univ. of the Negev, Tel Aviv/Israel
5Dept of Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC/United States of America

Contact E-Mail Address: opałsson@med.unc.edu

Introduction: IBS criteria have undergone several adjustments in diagnostic requirements for IBS compared to Rome III. It is unknown how this will affect the prevalence and demographic distribution of IBS.

Aims & Methods: We used data from a large internet survey of the general population in 3 countries to measure and compare Rome IV vs. Rome III IBS rates and the demographics of the disorder. A community sample of 6,300 individuals were included. Quota-based sampling was used to ensure equal proportion of sex (50%/50%) and age groups (40% aged 18–39, 40% aged 40–64, 20% aged 65+) across countries, and to control education distributions (30% maximum with college degree or equivalent). The survey included the Rome 4 Diagnostic Questionnaire for Adults, Rome III diagnostic modules for IBS, and demographic questions. Latest national census figures were used to calculate correction weights for age (in 5 year bands) and gender proportions and obtain comparable IBS prevalence estimates for each country.

Results: Of the 6,300 survey completers, 5,931 were retained for analysis (49.2% male; mean age = 47.4, range 18–92; 1,949 US, 1,994 UK, 1,988 Canada) after 369 inconsistent respondents were eliminated. Due to the quota-based sampling, sex or age group proportions did not differ between countries. Rome IV vs. Rome III IBS prevalence rates (census-corrected estimates in parentheses) were consistent for both countries. However, the Rome IV IBS prevalence rate was significantly higher in all countries (p < 0.0001) than with Rome III (16.6% IBS-C, 20.6% IBS-D, 60.1% IBS-M and 2.1% IBS-U).

Table: Table 1 shows the Rome IV and Rome III IBS rates (%) by sex and age groups in the US, UK and Canada survey samples (without census weighting).

Rome III IBS

Age 18–34 Age 35–49 Age 50–64 Age 65+

US Females (n = 962) 15.6 16.6 13.7 9.9 14.2
US Males (n = 987) 7.2 9.3 8.4 5.6 7.6
UK Females (n = 976) 14.2 15.4 15.1 8.9 13.9
UK Males (n = 1018) 4.9 7.2 9.5 3.6 6.5
Canada Females (n = 980) 14.6 16.8 15.4 12.9 15.1
Canada Males (n = 1008) 6.3 10.3 8.2 5.9 7.6

Rome IV IBS

Age 18–34 Age 35–49 Age 50–64 Age 65+

US Females (n = 962) 6.6 10.6 6.9 3.7 7.1
US Males (n = 987) 8.8 3.6 4.2 1.9 5.1
UK Females (n = 976) 6.7 10.2 8.6 3.2 7.5
UK Males (n = 1018) 1.8 5.1 5.5 1.6 3.6
Canada Females (n = 980) 7.1 9.8 8.1 5.3 7.8
Canada Males (n = 1008) 2.5 5.4 5.0 2.1 3.7

Conclusion: These first-ever national population prevalence estimates for Rome IV IBS show that IBS prevalence and demographic distribution is equivalent in the US, UK and Canada, and confirm that the disorder is female-predominant and less common in the elderly. IBS prevalence is significantly lower when Rome IV criteria are used than with Rome III, and the new criteria also change IBS subtype distribution, markedly reducing the IBS-M proportion. [Support: National Institute of Diabetes and Digestive and Kidney Diseases (NIDDK), National Cancer Institute (NCI).]


OP080 FUNCTIONAL HEARTBURN OVERLAPS WITH IRRITABLE BOWEL SYNDROME MORE OFTEN THAN GERD - DEVELOPMENT OF A PREDICTIVE MODEL FOR CLINICAL PRACTICE


1Dept. Of Gastroenterology, University of Pisa, Pisa/Italy
2Gastroenterology Unit, University of Pisa, Pisa/Italy
3Gastroenterology, University of Verona, Verona/Italy
4Department Of Surgery, Second University of Naples, Naples/Italy
5Department Of Medicine, University of North Carolina, Chapel Hill, NC/United States of America
6Dept Internal Medicine, Università di Genova, Genova/Italy
7Dept. Of Gastroenterology, University of Pisa, Pisa/Italy
8Gastroenterology Unit, University of Pisa, Pisa/Italy
9Division Of Gastroenterology, Department Of Internal Medicine, University of Genoa, Genoa/Italy
10Dept. Of Gastroenterology, University of Pisa, Pisa/Italy
11Department Of Medical and Surgical Sciences, University of Bologna, Bologna/Italy

Contact E-Mail Address: salvatore.tolone@unina2.it

Introduction: Gastroesophageal reflux disease (GERD) and irritable bowel syndrome (IBS) are gastrointestinal (GI) disorders affecting a large part of the general population, with relevant impact on quality of life and health care costs. To date, population- and clinical-based studies have reported a certain degree of overlap between GERD and IBS, which cannot be explained solely by chance.1 By means of multichannel intraluminal impedance and pH (MII-pH) monitoring, patients with proton pump inhibitor (PPI)-refractory heartburn can be distinguished into PPI-refractory GERD and functional heartburn (FH), the latter to be considered a functional GI disorder separate from GERD. Symptoms of IBS have not yet been assessed in patients with reflux symptoms as distinct from GERD and FH. Recently, it has been reported that patients with GERD as well as patients with IBS have increased levels of anxiety, in turn associated with increased perception of symptoms and reduced quality of life. Again, the prevalence of anxiety in patients with reflux symptoms as clearly been captured in GERD and FH has not yet been assessed.
Aims & Methods: Our aim was to assess the prevalence of IBS as well as anxiety and depression in adult IBS patients with typical reflux symptoms subdivided into GERD and FH by means of upper GI endoscopy and MII-pH monitoring. We also aimed to assess the prevalence of various clinical and endoscopic characteristics in IBS and FH patients in order to develop a predictive model for distinguishing FH from GERD in patients presenting with typical reflux symptoms, potentially useful in clinical practice. Patients underwent a structured interview based on questionnaires for GERD (GERDQ), IBS (RIIQA), anxiety and depression (HADS). Upper GI endoscopy and 24h MII-pH oesophageal monitoring were performed in all cases. In patients with IBS, faecal calprotectin was measured and colonooscopy was scheduled for values $>100 \mu g$/kg to exclude organic disease. Multivariate logistic regression analysis was performed to identify independent risk factors for FH. A predictive model for FH diagnosis based on clinical and endoscopic findings was developed by applying the purposeful selection of covariates. The coefficients estimated in the multivariate logistic regression analysis were used to predict FH diagnosis. The performance of the predictive model was then assessed by examining measures of discrimination and calibration. Discrimination was considered as the ability of the predictive model to differentiate between patients with FH diagnosis and patients with GERD diagnosis and was quantified by calculating the area under the ROC curve (AUC). A calculator to help clinicians in automatically computing the predicted probability of FH versus GERD in patients presenting with heartburn was built. 

Table 1: Probabilities for IBS-related symptoms to persist or subside over a five-year period.

<table>
<thead>
<tr>
<th>Symptom persists</th>
<th>Probability</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Depression</td>
<td>22%</td>
<td>18-26%</td>
</tr>
<tr>
<td>Sense of coherence</td>
<td>21%</td>
<td>18-24%</td>
</tr>
<tr>
<td>Coping resources</td>
<td>19%</td>
<td>18-21%</td>
</tr>
<tr>
<td>GI-specific anxiety</td>
<td>16%</td>
<td>14-18%</td>
</tr>
<tr>
<td>Quality of life</td>
<td>16%</td>
<td>14-18%</td>
</tr>
<tr>
<td>GI symptom severity</td>
<td>12%</td>
<td>10-14%</td>
</tr>
</tbody>
</table>

Conclusion: For the first time, we show that IBS-related symptoms develop differentially over time. GI symptoms had a high likelihood of subsiding over time, in contrast to depression, sense of coherence, and coping resources. We suggest more attention needs to be paid to the management of depression, and to providing tools for better coping resources in IBS patients.
Conclusion: Symptoms compatible with functional bowel disorders in general, and not only IBS, are common in patients with UC in deep remission. However, the overall disease burden seems to be greater in patients with symptoms compatible with IBS than with the other FBDS. These observations are of great importance when managing patients with IBD to avoid escalating anti-inflammatory treatment, and instead focus on other treatment options to help these patients to manage their symptoms.

Disclosure of Interest: M. Simren: Unrestricted research grants from Danone, and Ferrung Pharmaceuticals; Consultant/Advisory Board member for AstraZeneca, Danone, Nestlé, Chr Hansen, Almirall, Allergan, Albireo, Glycom and Shire; Speaker for Tillotts, Takeda, Shire and Almirall; B. Jonéfält: Speaker for Abbvie, MSD and MEDA; O. Palsson: Salary support from research grants from Salix Pharmaceuticals, Takeda Pharmaceuticals and Ironwood pharmaceuticals, as well as honoraria for participation in educational programs supported by these companies. W.E. Whitehead: Unrestricted research grants from Takeda Pharmaceuticals; Unrestricted educational grants from Takeda and Ferrung Pharmaceuticals; Consultant/Advisory Board member for Ono and Ferrung Pharmaceuticals and from Americare USA; H. Törnblom: Consultant/Advisory Board member for Almirall, Danone and Shire.

Disclosure of Interest: A. Steiner: Consultant/Advisory Board member for AstraZeneca; Consultant/Advisory Board member for Genetic Analysis; Speaker for Takeda and Abbvie. M. Simren: Unrestricted research grant from AstraZeneca; Consultant/Advisory Board member for Genetic Analysis; Speaker for Takeda and Abbvie. H. Strid: Consultant/Advisory Board member for Takeda, Abbvie, Ferrung Pharmaceuticals, Tillotts, MSD; Speaker for Takeda, Abbvie, Ferrung Pharmaceuticals, Tillotts, MSD and Shire.

Contact E-mail Address: ruchitsood@gmail.com

Introduction: Symptom-based criteria to diagnose irritable bowel syndrome (IBS) positively perform only modestly. Our aim was to assess whether including other items from the clinical history and diagnostic workup improves their performance.

Aims & Methods: We collected complete symptom, colonoscopy, and history data from 318 consecutive, unselected adult patients with lower gastrointestinal (GI) symptoms in secondary care. The reference standard used to define presence of true IBS was patient-reported lower abdominal pain or discomfort associated with a change in bowel habit, in the absence of organic GI disease. Sensitivity, specificity, and positive and negative likelihood ratios (LRs), with 95% confidence intervals, were calculated for Rome III criteria, as well as for modifications, incorporating nocturnal symptoms, results of simple blood tests and from biopsies. The predictive values were calculated for Rome III criteria, as well as for modifications.

Results: Sensitivity and specificity of Rome III criteria for identifying IBS was 69.6%, and 82.0%, respectively, with positive and negative LRs of 3.87 and 0.37. Clinically useful enhancements in positive LRs when combining Rome III criteria with items from the clinical history, and blood tests, are shown in the table. Conclusion: Incorporating nocturnal symptoms, somatisation, and affect from the clinical history, and haemoglobin and CRP measurements, enhances performance of symptom-based criteria for IBS. Our findings suggest a different approach to the development of future diagnostic criteria should be used.

Disclosure of Interest: All authors have declared no conflicts of interest.

Abstract No: OP083

<table>
<thead>
<tr>
<th>Rome III Criteria and normal Hb and CRP</th>
<th>Sensitivity (95% CI)</th>
<th>Specificity (95% CI)</th>
<th>Positive LR (95% CI)</th>
<th>Negative LR (95% CI)</th>
</tr>
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<tbody>
<tr>
<td>Rome III criteria and normal Hb and CRP</td>
<td>49.0% (34.4%–63.4%)</td>
<td>89.2% (83.2%–93.6%)</td>
<td>4.37 (2.76–6.76)</td>
<td>0.59 (0.46–0.72)</td>
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<tr>
<td>Rome III criteria and normal Hb and CRP ≥8</td>
<td>47.2% (35.3%–59.9%)</td>
<td>89.1% (84.2%–92.9%)</td>
<td>4.32 (2.76–6.76)</td>
<td>0.59 (0.46–0.72)</td>
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<tr>
<td>Rome III criteria and normal Hb and CRP ≥8</td>
<td>37.9% (26.2%–50.7%)</td>
<td>94.8% (89.0%–97.5%)</td>
<td>7.27 (3.74–14.2)</td>
<td>0.66 (0.53–0.77)</td>
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<tr>
<td>Rome III criteria, normal Hb and CRP, and HADS score ≥8</td>
<td>34.0% (20.0%–49.3%)</td>
<td>93.2% (87.9%–96.7%)</td>
<td>5.04 (2.48–10.2)</td>
<td>0.71 (0.55–0.84)</td>
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<tr>
<td>Rome III criteria, normal Hb and CRP, and high somatisation</td>
<td>24.4% (12.4%–40.3%)</td>
<td>96.8% (92.0%–99.1%)</td>
<td>7.56 (2.63–21.7)</td>
<td>0.78 (0.63–0.90)</td>
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<td>Rome III criteria, no nocturnal passage of stool, and HADS score ≥8</td>
<td>22.2% (13.3%–33.6%)</td>
<td>95.4% (91.7%–97.8%)</td>
<td>4.84 (2.33–10.0)</td>
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<tr>
<td>Rome III criteria, no nocturnal passage of stool, and high somatisation</td>
<td>18.2% (9.8%–29.6%)</td>
<td>99.0% (86.3%–99.9%)</td>
<td>17.3 (4.45–67.6)</td>
<td>0.83 (0.72–0.90)</td>
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**Abstract No: OP084**

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<th>Adjusted mean number in past 6 months (SE)</th>
<th>Diagnosed IBS-D (n = 859)</th>
<th>Undiagnosed IBS-D (n = 370)</th>
<th>Controls (n = 56,932)</th>
<th>p-value: Diagnosed vs. controls</th>
<th>p-value: Undiagnosed vs. controls</th>
<th>p-value: Diagnosed vs. undiagnosed</th>
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<td>5.17 (0.35)</td>
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<td>Emergency room visits</td>
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**Disclosure of Interest:**

All authors have declared no conflicts of interest.

**Table**

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<td>61</td>
<td>81</td>
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<td>92</td>
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**MORO**

**LONG-TERM OUTCOMES OF ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) – ROOM 17**

**OP085**

**WHAT IS NEW IN GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION (ESD) – ROOM 17**

**OP086**

**PREDICTING CLINICAL OUTCOMES OF GASTRIC ENDOSCOPIC SUBMUCOSAL DISSECTION USING A BAYESIAN APPROACH**

**Disclosure of Interest:**

All authors have declared no conflicts of interest.

**Reference**

Long-term outcomes of gastric endoscopic submucosal dissection: focus on metachronous and non-curative resection management

D. Libin1, P. Pimentel-Nunes1, L. Afonso2, R. Henrique2, M. Dinis-Ribeiro1
1Gastroenterology Department, Portuguese Oncology Institute of Porto, Porto/Portugal
2Pathology Department, Portuguese Oncology Institute of Porto, Porto/Portugal

Contact Email Address: dioliberin@hotmail.com

Introduction: Endoscopic submucosal dissection (ESD) is an effective treatment for gastric superficial neoplasms, being curative in 80–85% Identification of risk factors for a non-curative resection is of paramount importance to improve patient selection. Furthermore, it is important to evaluate the management after an unsuccessful treatment in order to assess the clinical outcomes of each option: observation and surgical treatment. Moreover, patients with an early neoplastic lesion are at risk of developing metachronous lesions and endoscopic surveillance will still be needed after endoscopic resection. The identification of risk factors for metachronous development is also important to adequate surveillance.

Aims & Methods: The aims of this study were to identify risk factors for non-curative resection and metachronous development and to evaluate management and outcomes after non-curative resection. Methods: Single centre assessment of a cohort of consecutive patients submitted to gastric ESD, with a minimum follow-up of 18 months. The Japanese Gastric Cancer Treatment Guidelines criteria were used in clinical practice; resections were also classified with the recently published European Society of Gastrointestinal Endoscopy univariate analysis (independent samples t-test, Mann-Whitney U test or chi-square test as appropriate) and multivariate logistic regression were performed to identify risk factors. Odds ratios (OR) were computed with 95% confidence intervals (CI). Survival was analyzed with Kaplan-Meyer curves and log-rank test. Significance level was defined as p < 0.05.

Results: A total of 1,064 gastric ESDs were performed during the study period. Patients with an early neoplastic lesion were at risk of developing metachronous lesions and endoscopic surveillance will still be needed after endoscopic resection. The identification of risk factors for metachronous development is also important to adequate surveillance.

Disclosure of Interest: All authors have declared no conflicts of interest.

Endoscopic full-thickness resection with defect closing in the stomach by using a novel GRASP-AND-LOOP (GAL) CLOSURE METHOD: WITH VIDEOS

J. Hu, P. Zhou, M. Xu, Q. Li, T. Chen
Endoscopy Center and Endoscopy Research Institute, Endoscopy Center and Endoscopy Research Institute, Zhongshan Hospital, Fudan University, Shanghai/China

Contact Email Address: hu.jiarwei@zs-hospital.sh.cn

Introduction: Endoscopic full-thickness resection (EFR) is a minimally invasive method for en bloc resection of GI lesions originating from the muscularis propria layer. Successful closure of the wall defect is a critical step. We aimed to evaluate efficacy and safety of a novel and simplified endoscopic GRASP-AND-LOOP (GAL) closure method using an endoloop assistant with a grasping forceps for defect closure. From January 2012 to March 2015, 25 patients were enrolled in this study. Success of the muscularis propria layer under endoloop ENTR were enrolled in this study. After successful tumor resection, an endoloop was anchored onto the circumference of the defect with grasping forceps and tightened gently (with videos). Patient characteristics, tumor size, en bloc resection, and post-operative complications were evaluated.

Results: Of the 13 lesions in the stomach, 2 were located in the greater curvature (three on the anterior wall and two on the posterior wall), 2 on the lesser curvature, 6 were on the greater curvature (one on the anterior wall and five on the posterior wall), 2 on the fundus, and 1 on the mid-octal body. The endoscopic GAL closure method was successfully performed after EFR in all 13 patients without laparoscopic assistance. The median procedural time was 43.5 min (range 35–70 min), while the GAL closure procedure took a median of 9 min (range 3–18 min). Pathological diagnosis of these lesions was 11 gastrointestinal stromal tumors (GISTs) and 2 leiomyomas. No major adverse events occurred during or after the procedure. All lesions were discharged after a median post-procedural time of 2.4 days. No residual lesion or tumor recurrence was found during the follow-up period (median, 5 months; range 1–15 months).

Conclusion: The endoloop closure method is feasible, effective, and safe for closing the gastric defect after EFR in patients. Disclosure of Interest: All authors have declared no conflicts of interest.

References:
K. Kawaura1, T. Kosaka2

Reference


Contact E-mail Address: xxmeyergerspach@gmail.com

Introduction: Activation of gastrointestinal (GI) smooth muscle by taste receptors by caloric sweeteners such as glucose or fructose induces the secretion of GI peptides to regulate food intake. The effect of non-caloric sweeteners on GI peptide secretion and satiety is controversial. We have recently shown that motilin-induced gastric phase III contractions of the migrating motor complex (MMC) signal hunger feelings. The mechanism underlying interruption of the MMC by specific sweet tastants has not yet been studied. It is conceivable that this requires sweet taste receptor activation and accompanying changes in the release of GI peptides.

Aims & Methods: The aim was to determine the effect of caloric and non-caloric sweeteners on GI motility and GI peptide secretion as well as on hunger feelings by using animal and satiety feelings. The parameters were analyzed using mixed model analysis. Post-hoc analyses were corrected using Bonferroni.

Results: Antral motility was significantly reduced in response to the caloric sweeteners glucose: p = 0.004 and fructose: p = 0.026, respectively. The change over time of plasma glucose concentrations was significantly increased after glucose and fructose administration compared to placebo (fructose: p = 0.006; ace-K: p = 0.032, respectively). The change over time of plasma motilin concentrations was significantly decreased after fructose (p = 0.001) administration; ace-K administration induced a no difference compared to placebo. Plasma motilin levels were significantly decreased after the caloric sweeteners compared to the non-caloric sweetener ace-K (glucose: p = 0.005 and fructose: p = 0.008, respectively). The time course of satiation scores differed significantly between glucose and ace-K (p = 0.041) with a slower decrease in satiation scores after glucose compared to ace-K administration.

Conclusion: Caloric and non-caloric sweeteners have dissociable effects on antral but not duodenal motility; the reduction in antral motility after glucose and fructose administration parallels changes in motilin secretion. These findings provide an important contribution to the current discussion about possible physiological effects of non-caloric sweeteners on appetite metabolism.

Disclosure of Interest: All authors have declared no conflicts of interest.

Contact E-mail Address: ac.meyergerspach@gmail.com

Introduction: With the increasing prevalence of obesity and its possible association with increasing sucrose consumption, non-nutritive sweeteners are gaining popularity. Artificial sweeteners might have adverse effects and alternative solutions are sought. Polyols such as xylitol and erythritol have been known for a long time and their beneficial effects on caries prevention and potential health benefits in diabetic patients have been demonstrated in several studies. Ingredients such as glucagon-like peptide-1 (GLP-1) and gastrointestinal peptides such as cholecystokinin (CCK) are released from the gut in response to food intake, promote satiation, reduce gastric emptying (GE) and modulate hormone release. While glucose ingestion stimulates sweet taste receptors in the gut, and leads to incretin and gastrointestinal peptide release, the effect of xylitol and erythritol has not been studied.

Aims & Methods: The aim was to study gastrointestinal peptide and incretin release in healthy humans.


1Inst. Für Biomedizin, University Hospital Basel, Basel/Switzerland
2Department Of Surgery, St. Claren’s Hospital Basel, Basel/Switzerland
3Diabetes Complications Research Centre, Conway Institute University College Dublin, Dublin/Ireland
4Department Of Clinical Biochemistry, Rigshospitalet, University of Copenhagen, Copenhagen/Denmark

Contact E-mail Address: ac.meyergerspach@gmail.com

Disclosure of Interest: All authors have declared no conflicts of interest.

OP092 XYLOLIT AND ERYTHRITOL INDUCE SATIATION PEPTIDE RELEASE AND RETARDATION IN GASTRIC EMPTYING IN HEALTHY HUMANS


1Inst. Für Biomedizin, University Hospital Basel, Basel/Switzerland
2Department Of Surgery, St. Claren’s Hospital Basel, Basel/Switzerland
3Diabetes Complications Research Centre, Conway Institute University College Dublin, Dublin/Ireland
4Department Of Clinical Biochemistry, Rigshospitalet, University of Copenhagen, Copenhagen/Denmark

Contact E-mail Address: ac.meyergerspach@gmail.com

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016
14:00–15:30

OP099 CALORIC AND NON-CALORIC ARTIFICIAL SWEETENERS HAVE DISSOCIATIVE EFFECTS ON ANTRAL MOTILITY AND PLASMA MOTILIN LEVELS IN HEALTHY VOLUNTEERS

A.C. Meyer-Gerspach, E. Deloose, J. Biesiekierski, I. Depoortere, L. Van Oudenahme, J. Tack

Targi, KE, Leuven, Leuven/Belgium

Contact E-mail Address: ac.meyergerspach@gmail.com

Disclosure of Interest: All authors have declared no conflicts of interest.

Contact E-mail Address: xxmeyergerspach@gmail.com

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

ML tap water were control treatments. Solutions were enriched with L-Cysteine (0.04% of dry mass, equivalent to sodium cysteinate) and sodium gluconate. The sodium salt of MeS has been reported to improve CCK, as well as plasma insulin and glucose levels. GE was measured by L-Cysteine acetate breath test.

Results: CCK and xylitol led to a marked increase in CCK (p < 0.001, respectively) and GLP-1 (p = 0.001 and p < 0.001, respectively); ii) plasma insulin and glucose were not (xylitol) or minimally (xylitol) affected; iii) xylitol and xylitol ethvlidtute antral and duodenal phase III contraction during the hindgut period was evaluated.

Results of the study were as follows: the phase III period was longer in the control group (15.6 ± 2.0 vs. 12.2 ± 3.1 hours, p = 0.005) and the phase III occurrence was higher in the control group (18.4 ± 0.005 vs. 13.6 ± 0.001, p = 0.005) (Table). In the control group, phase III occurrence and origin (p = 0.05 for both). In DF the mean postprandial levels of TNF were significantly higher than in HV (p < 0.05). As far as the antioxidant response is concerned, postprandial levels of UA were significantly higher in HV (52.94 ± 6.08 μM) than in DF patients. However, the between-group differences between patients with HV and DF were not significant (p = 0.05 for all).

Conclusion: A prospective study of LG for systemic inflammatory response in patients with PDS is needed. Furthermore, PDS patients had significantly higher levels of both inflammatory and antioxidant markers in comparison with HV.

References:

OP068 INFLAMMATORY AND ANTIOXIDANT RESPONSE FOLLOWING STANDARD MEAL CONSUMPTION IN PATIENTS WITH FUNCTIONAL DYSPEPSIA AND HEALTHY VOLUNTEERS

M. Di Stefano 1, B. Valvo 1, M. Bergonzi 2, I. Benedetti 1, M. De Amici 2, C. Torre 2, G. Testa 2, E. Pagani 2, G. Maresgila 2, G.R. Corazza 2
1Department Of Internal Medicine, IRCCS S. Matteo Hospital Foundation, University of Pavia, Pavia/Italy
2Pediatrics, IRCCS S. Matteo Hospital Foundation, University of Pavia, Pavia/Italy

Contact Email Address: beatricevalvo@gmail.com

Introduction: The Rome Committee on Functional Dyspepsia (FD) and the epigastric pain syndrome (EPS). The underlying pathophysiological mechanisms of these syndromes are partially known. Recently, the worsening of hypersensitivity in the postprandial period was shown in patients (p = 0.001, respectively) in comparison with HV (0.26 ± 0.15, 0.13 ± 0.11 and 7.45 ± 0.68, p < 0.05 for all).

Table:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>placebo</th>
<th>LG</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average IGP drop 30 min from the drink (mMHg)</td>
<td>7.7 ± 1</td>
<td>6.6 ± 0.6</td>
<td>0.6</td>
</tr>
<tr>
<td>GE t½ (min)</td>
<td>69.6 ± 5.1</td>
<td>119.4 ± 18.4</td>
<td>0.005</td>
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</tbody>
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Conclusion: Acutely administered LG decreases both antral and duodenal motility during the interdigestive state and delays gastric emptying after a standard liquid meal. However, at this dose it does not seem to influence gastric accommodation or hunger and satiety feelings.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP091 A DOUBLE-BLEND, PLACEBO-COEROLLATED, CROSS-OVER STUDY USING BACLOFEN IN THE TREATMENT OF RUMINATION SYNDROME

A. Pauwels 1, C. Broers 1, B. Van Houtte 1, N. Rommel 2, T. Vanuytsel 2, J. Tack 2
1Clinical and Experimental Medicine, Translational Research Center For Gastrointestinal Disorders (tagrid), KU Leuven, Leuven/Belgium
2Experimental Oto-rhino-laryngology, KU Leuven, Leuven/Belgium

Contact Email Address: ans.pauwels@med.kuleuven.be

Introduction: Ruminating syndrome and supra-gastric belching are two conditions with limited treatment options. Baclofen, a gamma-aminobutyric acid agonist, increases lower oesophageal sphincter (LOS) pressure. We previously demonstrated, in an open-label study, that baclofen reduces reflux episodes in patients with clinically suspected rumination and/or supra-gastric belching.

Aims & Methods: To study the effect of baclofen in a placebo-controlled, double-blind, cross-over study in patients with clinically suspected rumination and/or supra-gastric belching. Continuous patients with clinically suspected rumination and supra-gastric belching were randomized in a double-blind fashion to receive baclofen (10 mg, 3 t.i.d) or placebo for 2 weeks with cross-over to the alternative intervention after 1 week wash-out. At the end of each treatment period, patients underwent a solid state high resolution impedance manometry (HRM) measurement. After positioning of the probe, 10 wet swallows were performed to assess oesophageal function. After 30 min recording, patients received a 1000 kcal solid meal and recordings continued for 1 hour. Patients filled in daily diaries, questionnaires at the end of each treatment period, completed the overall treatment evaluation (OTE) on -3 to +3 scale) and registered symptoms during the HRM using an event marker. The number of symptoms registered and number and type of flow events during the HRM were compared between placebo and baclofen.
Disclosure of Interest:

Conclusion:

The vomiting score ranging from 0 (daily vomiting) to 4 (no vomiting) and the percentage of straining episodes was significantly lower in the baclofen arm (14.6 ± 8.1 vs. 23.4 ± 12.6, p = 0.0003). The number of postprandial regurgitation symptoms marked by the vomiting score was significantly lower in the baclofen arm compared to the placebo arm (17.8 ± 4.1 vs. 28.2 ± 14.9 mmHg, p = 0.001). The number of transient LOS relaxations was lower (6 ± 1 vs. 8 ± 2, p = 0.05) and the integrated relaxation pressure was significantly higher (11.8 ± 1.0 vs. 8.1 ± 1.2 mmHg, p = 0.003) after baclofen compared to placebo. The number of reflux events did not differ between both arms (4 ± 1 vs. 3 ± 1, NS). The number of rumination episodes was significantly lower in the baclofen arm (4.3 ± 3 ± 1, NS). In the baclofen arm, distribution was similar, with 66% being primary rumination, 11% secondary rumination and 23% supra-gastric belch associated rumination. In the baclofen arm, distribution was similar, with 66% being primary rumination, 11% secondary rumination and 23% supra-gastric belch associated rumination. No difference in straining episodes between placebo and baclofen arm, but the percentage of straining episodes associated with rumination was significantly lower in the baclofen arm (14.6 ± 3.8 vs. 31.2 ± 5.96, p = 0.0005). The number of postprandial regurgitation symptoms marked by the vomiting score was significantly lower in the baclofen arm compared to the placebo arm (17.8 ± 4.1 vs. 28.2 ± 14.9 mmHg, p = 0.001). The number of transient LOS relaxations was lower (6 ± 1 vs. 8 ± 2, p = 0.05) and the integrated relaxation pressure was significantly higher (11.8 ± 1.0 vs. 8.1 ± 1.2 mmHg, p = 0.003) after baclofen compared to placebo. The number of reflux events did not differ between both arms (4 ± 1 vs. 3 ± 1, NS).

Results:

Disclosure of Interest:

Conclusion:

Contact E-mail Address: jiaoyuai@163.com

Introduction: Despite numerous efforts to develop novel therapies, pancreatic ductal adenocarcinoma (PDAC) has remained one of the most devastating and lethal malignancies worldwide. There is an urgent need to identify novel targets that can mitigate the aggressive behavior of PDAC. Bcl-3 (cereblon) is an atypical member of the ankyrin-repeat containing IB family of NF-κB inhibitors that was first identified as a candidate proto-oncogene in chronic lymphocytic leukemia. A recent study has evidenced that the Bcl-3 expression results in increased cell proliferation, cell survival and malignant potential. However, the functional role of Bcl-3 in pancreatic cancer has not been elucidated so far. In this study, we aim to identify whether Bcl-3 impacts pancreatic cancer development and progression in humans and mice.

Aims & Methods: PDAC tissues and cell lines obtained from humans and a KrasG12D mouse model (KC) of pancreatic cancer were investigated for Bcl-3 expression. The overall survival of human PDACs expressing high and low levels of Bcl-3 was compared. Further, Bcl-3 was deleted in a KrasG12D mouse model (KC) and tumor incidence, metastases as well as proliferation, and apoptosis in tumor cells and primary tumor cells in vivo were studied. Pancreatic Intraepithelial Neoplasia (PanIN) in KC and KCB mice at 13 and 24 weeks was analyzed.

Results: We show that Bcl-3 is highly expressed in human PDACs and in a KC mouse model of pancreatic cancer correlating with progression and overall survival. Bcl-3 promotes cell growth and cell survival in vivo and in vitro. Further, Bcl-3 leads to acceleration in PanIN progression, tumor development and metastasis in the KC mouse model of pancreatic cancer.

Conclusion: In summary, our data provide the first insights into the function of Bcl-3 in pancreatic cancer, and indicate that Bcl-3 has an important pro-tumorigenic role in pancreatic cancer development and progression.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016

14:00-15:30

BASIC MECHANISMS IN PANCREATIC CANCER – ROOM 1.86

OP097 BCL-3 ACTS AS A PROTO-ONCOGENE IN PANCREATIC CANCER IN HUMANS AND ANIMAL MODELS


Bi: Medizinische Klinik, Klinikum rechts der Isar, München/Germany

Disclosure of Interest:

Disclosure of Interest:

Contact E-mail Address: jiaoyuai@163.com

Introduction: Despite numerous efforts to develop novel therapies, pancreatic ductal adenocarcinoma (PDAC) has remained one of the most devastating and lethal malignancies worldwide. There is an urgent need to identify novel targets that can mitigate the aggressive behavior of PDAC. Bcl-3 (cereblon) is an atypical member of the ankyrin-repeat containing IB family of NF-κB inhibitors that was first identified as a candidate proto-oncogene in chronic lymphocytic leukemia. A recent study has evidenced that the Bcl-3 expression results in increased cell proliferation, cell survival and malignant potential. However, the functional role of Bcl-3 in pancreatic cancer has not been elucidated so far. In this study, we aim to identify whether Bcl-3 impacts pancreatic cancer development and progression in humans and mice.

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Results: We show that Bcl-3 is highly expressed in human PDACs and in a KC mouse model of pancreatic cancer correlating with progression and overall survival. Bcl-3 promotes cell growth and cell survival in vivo and in vitro. Further, Bcl-3 leads to acceleration in PanIN progression, tumor development and metastasis in the KC mouse model of pancreatic cancer.

Conclusion: In summary, our data provide the first insights into the function of Bcl-3 in pancreatic cancer, and indicate that Bcl-3 has an important pro-tumorigenic role in pancreatic cancer development and progression.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP098 INTEGRIN ALPHAS AS A NOVEL PROGNOSTIC AND THERAPEUTIC TARGET IN PANCREATIC TUMOR STRUMA

P. Kuninty1, S. W. De Geus2, R. Bansal3, P. J. Kuppen4, A. Vahrmeijer5, A. Ostman6, C. F. Sier5, J. Prakash6

1University of Twente, Enschede/Netherlands

2Leiden University Medical Centre, Enschede/Netherlands

3Maastricht University, Enschede, Netherlands

4Leiden University Medical Centre, Leiden/Netherlands

5Surgery, Leiden University Medical Centre, Leiden/Netherlands

6Oncology-pathology, Karolinska Institutet, Stockholm/Sweden

Contact E-mail Address: j.prakash@utwente.nl

Introduction: Pancreatic cancer is the deadliest tumor type with less than 5% survival rate, characterized by the presence of abundant stroma. Pancreatic stellate cells (PSCs) are the main precursor of myofibroblasts (cancer-associated fibroblasts, CAFs) in tumor stroma and therefore become key target in pancreatic tumor stroma (1). CAFs secrete growth factors, exosomes and matrix (ECM) and thereby aggravate tumor growth and metastasis (2). This is of paramount importance to find out new targets in stromal myofibroblasts which can be used for developing novel prognostic, diagnostic and therapeutic strategies.

Aims & Methods: In this study, we investigated integrin α5 (ITGA5), a receptor for ECM protein fibronectin, which is expressed in pancreatic tumor stroma. The ITGA5 expression was investigated using immunohistochemical staining on tissue microarray consist of 137 patient samples of pancreatic tumors. In vivo, Panc-1 and PSCs were co-injected subcutaneously into the flank of SCID mice and investigated the expression of ITGA5 versus Panc-1 tumor alone. To elucidate the role of ITGA5, we knocked down the expression of ITGA5 in PSCs using siRNA-ITGA5. We investigated the phenotypic changes in ITGA5-KD PSCs after TGFβ activation, using immunostainings, quantitative PCR and RT2 profiler human fibroblast array. We also examined the paracrine effect of TGFβ-activated ITGA5-KD PSCs on the proliferation of pancreatic tumor cells (Panc-1).

Results: In human patient tumor samples, a total of 85% and 66% of patients were positive for stromal α-SMA and ITGA5, respectively and well co-localized, shown with double immunostaining. The ITGA5 expression was positively correlated with α-SMA in 72% patients. Overall, clinical data analysis reveals that the overexpression of ITGA5 (log-rank p = 0.022) and α-SMA (log-rank p = 0.006) are linked to significant decreased overall survival. In vivo, mice co-injected with Panc-1 and α-SMA showed a significant increase of tumor growth and a higher ITGA5 expression compared to Panc-1 tumors. Next, we studied the effect of ITGA5 knockdown in PSCs on their phenotypic characteristics.

Knockdown (60%) of ITGA5 led to a dramatic reduction of several ECM molecules and integrin receptors, shown with RT2 human profiler array. ITGA5-KD PSCs had morphological changes, as they became flattened and lost FAK, Rac, Cdc4 signaling, indicating the loss of lamelopodia and filopodia formation. Furthermore, functional assay showed a decrease in cell adhesion, migration (wound healing assay), proliferation and 3D spheroid formation compared to control siRNA-PSCs. Also, knockdown of ITGA5 abolished the tumor cell proliferation induced by TGF-β1 activated ITGA5-KD PSCs. These data indicated that ITGA5 induces differentiation and phenotypic changes in PSCs and thus, it is a potential therapeutic target for pancreatic cancer.
Conclusion: In conclusion, the present study reveals ITGA5 as a novel prognostic and therapeutic target in pancreatic tumor stroma. These data make a strong base to utilize this target for developing novel diagnostic and therapeutic strategies against pancreatic tumor.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP099 MICRONA-622 INHIBITS EPITHELIAL-MESENCHYMAL TRANSITION BY TARGETING LONG NON-CODING RNA HULC IN HUMAN PanCREATIC CANCER
K. Takahashi, Y. Ota, Y. Suzuki, H. Iwamoto, K. Yamakita, Y. Kitano, Y. Makino
Division Of Metabolism and Biosystemic Science, Department Of Internal Medicine, Asahikawa Medical University, Asahikawa;Japan

Contact E-mail Address: k-tkenji@asahikawa-med.ac.jp

Introduction: Transforming growth factor (TGF-β)-induced epithelial-mesenchymal transition (EMT) is a trigger of invasion and metastasis in pancreatic cancer. Although long non-coding RNAs (lncRNAs), which are defined as non-coding RNAs (ncRNAs) more than 200 nucleotides in length, have been implicated in disease pathogenesis, their contributions to pancreatic cancer are not well understood. Recently, the inter-relationship between two classes of ncRNA, microRNAs (miRNAs) and lncRNAs, has been reported to contribute to the epigenetic regulation of gene expression in several cancers.

Aims & Methods: Our aims were to investigate the involvement and functional roles of TGF-β-induced lncRNA during EMT and reveal contributions of the inter-relationship between the TGF-β-induced lncRNA and miRNA to the regulatory mechanisms of EMT in human pancreatic cancer. We used human pancreatic cancer (Panc-1, BxPC-3, MiaPaCa-2, QGP-1 and KP-3) and non-malignant pancreatic ductal epithelial (hTERT-HPNE) cells. Expression profiling of 90 IncRNAs and 2565 miRNAs were performed using qPCR and miRNA microarray. miRNA targets were predicted by miRanda. Cells were treated with 10 ng/ml of TGF-β for 72 hours to induce EMT. siRNA or miRNA mimics were used to modulate RNA expression. Cell viability was assessed by MTS assay and trypan blue. Cell invasion and migration were examined by transwell and wound healing assay. Expression of RNA was assessed by qPCR and of protein by Western blot.

Results: LncRNA expression profiling identified 22 IncRNAs that were induced by TGF-β in Panc-1 cells by >1.4-fold. Of these, HULC was amongst the top most significantly up-regulated. HULC expression was induced by TGF-β by 1.5 to 2.7-fold in a panel of pancreatic cancer cells and up-regulated by 2.4 to 8.9-fold in pancreatic cancer cells compared to hTERT-HPNE cells. In Panc-1 cells, knockdown of HULC by siRNA significantly increased expression of E-cadherin and decreased expression of N-cadherin, Snail and Vimentin (p<0.05). Moreover, siRNA to HULC decreased cell viability, invasion and migration. Furthermore, to identify miRNAs that can target HULC and suppress EMT, miRNA microarray and bioinformatics analysis were performed. Microarray identified 187 miRNAs that were decreased by <0.87 fold in Panc-1 cells treated with TGF-β compared to control. Of these, miR-622 was predicted to target HULC by miRanda. miR-622 expression was reduced by TGF-β by 0.5 to 0.9-fold in a panel of pancreatic cancer cells. Overexpression of miR-622 using miRNA mimics significantly decreased expression of HULC, increased expression of E-cadherin and decreased expression of Snail, N-cadherin and Vimentin (p<0.05). In addition, miR-622 overexpression significantly reduced cell invasion and migration.

Conclusion: These findings provide mechanistic insights into EMT in pancreatic cancer by (a) identifying HULC as a highly induced lncRNA by TGF-β, (b) demonstrating that HULC promotes EMT, (c) identifying that miR-622, as a down-regulated and miRNA by TGF-β, can target HULC, and (d) showing a functional role for miR-622 in EMT via targeting HULC. These observations imply that miR-622 would suppress invasion and metastasis by inhibiting EMT signaling through targeting HULC and suggest potential strategies to inhibit invasion and metastasis in human pancreatic cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP100 ESSENTIAL ROLE OF THE NON-RECEPTOR Tyrosine-phosphatase PTPN1/SHP-2 IN ORGAN DEVELOPMENT AND HOMEOSTASIS OF THE MURINE EXOCRINE PanCREAS
D. Ruess, H. Algül
Ii. Med. Klinik, TU Munich, Klinikum rechts der Isar, Munich;Germany

Contact E-mail Address: dietrich.ruess@uniklinik-freiburg.de

Introduction: The Src-homology-2 (SH2) domain containing protein tyrosine phosphatase SHP-2 is expressed ubiquitously and is involved in an array of intracellular signal transduction processes (Ras-Raf-MAPK, JAK-STAT, PI3K-Akt-mTOR, NF...). Thus, for instance, SHP-2 plays a role in cellular proliferation, survival, differentiation, migration and metabolism. The role of SHP-2 in organ development and homeostasis of the murine exocrine pancreas has so far not been explored.

Aims & Methods: Mouse models with pancreas specific deletion of SHP-2 (Ptf1a-CreE(LSL-KrasG12D)Ptpn11fl/fl) with or without mutated Kras (LSL-KrasG12D) and/or lineage tracing allele (ACTB-TdTomato-EGFP) were used for analysis.

Results: Early embryologic Deletion of SHP-2 in the pancreas via Ptf1a-CreE(LSL-KrasG12D)Ptpn11fl/fl and lineage tracing allele (ACTB-TdTomato-EGFP) revealed no significant differences in organ structures compared to wildtype mice. These findings provide mechanistic insights into EMT in pancreatic cancer.

Contact E-mail Address: t-kenji@asahikawa-med.ac.jp

Disclosure of Interest: All authors have declared no conflicts of interest.
Aims & Methods: Here we describe several applicable tools, using live cell and tissue imaging, co-culture assays of cancer cells with immortalized PDAC xenograft tissues with freshly isolated dorsal root ganglia (DRG), primary DRG neurons and F11 hybridoma neurons to investigate the reciprocal interaction at the tumor cell-nerve interface.

Results: To study the invasion of tumour cells along neurites we have combined 3D co-culture assays of dorsal root ganglia (DRG) and tumour cells with time-lapse microscopy and specifically track the unidirectional movement of individual tumour cells along neurites extending from DRGs. Quantification of the dynamic process revealed that neuronal scaffolds provide the infrastructure for an accelerated and consistent migration of tumour cells towards the DRG as the source of chemotactic gradients. In another approach, using explanted PDAC xenograft tissues instead of tumour cell colonies, it occurred that neurite outgrowth from DRG pathway lured towards the tissue. Thus, neurites facing the tumour were more elongated than neurites at the opposite site of the DRG, suggesting that tumour gradients stimulate and/or attract neurite outgrowth and elongation. In support of a tumour-derived chemotactic effect, supernatants from organotypic immortal tumour cell cultures varied in their ability to induce neurite outgrowth of freshly isolated primary neurons in transwell assays. In order to gain a more dynamic representation on how neurites explore a chemoattractant gradient, F11 hybridoma neurons were co-cultured with PDAC cell lines in separate patches divided by a 500μm gap. These assays use time-lapse imaging and endpoint analysis in order to track the locomotion of individual neurite extensions, monitor their outgrowth from neurites and elongation towards the tumour cell front, and allow to quantitate length, velocity, forward migration index, and directness of each protruding trajectory in response to different PDAC cell lines. Moreover, the extent of growth cone formation and collapse can be scored by determining dynamic changes in circumferential size and area of protrusions.

Conclusion: These in vitro and ex vivo models emulate several important aspects of nerve-tumour interactions and allow pharmacological and gain-and loss-of-function manipulations. In addition, semi- to fully-automated quantification for high-throughput screening can be offered. We offer investigators reliable tools to test their candidate target genes or drugs.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
was observed in the primary randomized maintenance population, but small sample sizes (UST n = 46; PBO n = 24) precluded definitive conclusions. In the larger post-hoc pooled maintenance population (Table 1b), consistent trends in support of UST maintenance, especially UST 90 mg q8w, were observed across endoscopic endpoints at Wk44.

**Conclusion:** The endoscopic substudy primary endpoint was met; a single IV dose of UST induced significantly greater reduction in endoscopic disease activity vs PBO, despite a relatively early evaluation at Wk8. Results in the small primary randomized maintenance population were supported by the larger post-hoc pooled maintenance population; greater proportions of subjects receiving UST maintenance, especially UST 90 mg q8w, achieved maintenance end-points vs PBO. Together, these data support the efficacy of UST in inducing & maintaining endoscopic healing of the mucosa in CD.


**References**


1. *University of Leuven, Leuven/Belgium*
2. *Janssen Research and Development, LLC, Spring House/United States of America*
3. *Janssen Research and Development, LLC, Spring House/United States of America*
4. *Feinberg School of Medicine, Chicago/United States of America*
5. *Atlanta Gastroenterology Associates, Atlanta/United States of America*
7. *UCSD, La Jolla/United States of America*

**Contact E-mail Address:** paul.rutgeerts@uzleuven.be

**Introduction:** Ustekinumab (UST) has been shown to induce & maintain clinical response & remission in 2 induction (UNITI-1&2) & 1 maintenance (IM-UNITI) trials in moderate-severe Crohn's disease (CD). A substudy evaluated the efficacy of UST in the induction & maintenance of endoscopic healing.

**Aims & Methods:** Patients in the substudy had up to 3 colonscopic evaluations (i.e. at UNITI-1 or 2 baseline [BL] and Wk8, and IM-UNITI Wk44) in ileocolonic segments (i.e. ileum, right colon, transverse colon, left colon, rectum) within the 52-Wk study period. A single central reader blindly scored all video endoscopies for ulcerations and simplified endoscopic activity score for CD (SES-CD). At induction Wk0, patients received a single IV dose (UST 130 mg, UST 66 mg/kg, or PBO). At maintenance Wk0 (i.e. induction Wk8), UST induction responders [Primary randomized maintenance population] were re-randomized to subcutaneous (SC) PBO, UST 90 mg every 12 wks (q12w), or UST 90 mg every 8 wks (q8w). For the 3 non-randomized maintenance groups: (1) UST induction non-responders received SC UST 90 mg, then continued SC UST 90 mg q8w if CDAI decreased ≥100 after 8 wks; (2) PBO induction non-responders received UST IV 130 mg, then continued SC UST 90 mg q12w if CDAI decreased ≥100 after 8 wks; and (3) PBO induction responders received PBO throughout. Patients with SES-CD ≥5 (i.e. ulceration in any segment) at induction BL were eligible for analysis. The primary endpoint was change in SES-CD from BL at induction Wk8 in the integrated UST group (data across induction studies & dose groups) vs PBO. Efficacy at IM-UNITI Wk44 was evaluated in the primary randomized maintenance population and the post-hoc pooled maintenance population (i.e. randomized & non-randomized IM-UNITI populations combined). Additional induction & maintenance endpoints included clinically meaningful endoscopic improvement, endoscopic response, endoscopic remission & mucosal healing; in both combined and individual treatment groups.

**Results:** The substudy primary endpoint was met, as UST induced significantly greater reduction in SES-CD from BL at Wk8 vs PBO. Results were similar by induction study & UST dose. Other induction endoscopic endpoints also consistently favored UST vs PBO (Table 1a). At IM-UNITI Wk44, trends for greater efficacy with UST vs. PBO maintenance, especially UST 90 mg q8w, were observed across various clinical outcomes (Table 1b).

**Table 1a: Induction Week 8 (UNITI-1&2)**

<table>
<thead>
<tr>
<th>Variable/unit/population</th>
<th>Placebo (n = 44)</th>
<th>Ustekinumab (n = 55)</th>
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<tbody>
<tr>
<td>CDAI reduction from BL, median (SD)</td>
<td>23.0 (7.6)</td>
<td>37.9 (12.5)</td>
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<tr>
<td>Endoscopic response1</td>
<td>13.4%</td>
<td>20.6%</td>
</tr>
<tr>
<td>Endoscopic remission1</td>
<td>4.1%</td>
<td>7.7%</td>
</tr>
<tr>
<td>Mucosal healing1</td>
<td>4.1%</td>
<td>9.0%</td>
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</table>

**Table 1b: Maintenance Week 44 (IM-UNITI)**

<table>
<thead>
<tr>
<th>Variable/unit/population</th>
<th>Placebo (n = 44)</th>
<th>Ustekinumab (n = 55)</th>
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<tbody>
<tr>
<td>90 mg q12w (N = 74)</td>
<td>40.8 (15.4)</td>
<td>57.6 (13.3)</td>
</tr>
<tr>
<td>90 mg q8w (N = 47)</td>
<td>42.5 (15.1)</td>
<td>58.0 (13.2)</td>
</tr>
<tr>
<td>CDAI reduction from BL, median (SD)</td>
<td>25.0 (15.35)</td>
<td>39.1 (15.35)</td>
</tr>
<tr>
<td>Endoscopic response1</td>
<td>27.5%</td>
<td>48.6%</td>
</tr>
<tr>
<td>Endoscopic remission1</td>
<td>9.8%</td>
<td>20.3%</td>
</tr>
<tr>
<td>Mucosal healing1</td>
<td>9.8%</td>
<td>21.6%</td>
</tr>
</tbody>
</table>

**P< 0.005**

*Primary endpoint: SES-CD reduction ≥5 from induction BL; SES-CD reduction ≥50% from induction BL; SES-CD total score ≤0 Complete absence of ulcers

**Table 1: Key efficacy parameters**

<table>
<thead>
<tr>
<th>Variable/unit/population</th>
<th>Placebo (n = 44)</th>
<th>Ustekinumab (n = 55)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Clinical remission (CDAI &lt; 150), %, ITT-NRI</td>
<td>23 47</td>
<td>59 81</td>
</tr>
<tr>
<td>PRO2, mean change from baseline, ITT-LOCFT</td>
<td>−15.6</td>
<td>−21.9</td>
</tr>
</tbody>
</table>

**P-value**

0.0077

0.0321

0.0045

**References**


1. *University of Leuven, Leuven/Belgium*
2. *Janssen Research and Development, LLC, Spring House/United States of America*
3. *Janssen Research and Development, LLC, Spring House/United States of America*
4. *Feinberg School of Medicine, Chicago/United States of America*
5. *Atlanta Gastroenterology Associates, Atlanta/United States of America*
7. *UCSD, La Jolla/United States of America*

**Contact E-mail Address:** paul.rutgeerts@uzleuven.be

**Introduction:** Filgotinib is an oral, selective Janus kinase 1 (JAK1) inhibitor, which has demonstrated high efficacy in patients with rheumatoid arthritis.

**Aims & Methods:** 174 patients with moderate-to-severe CD (CDAI 220 to 450, prior to randomization) were randomized to filgotinib (200 mg or 100 mg QD) or placebo (PBO) QD for 10 weeks. Based on Week 10 clinical response, patients continued to receive filgotinib (200 mg or 100 mg QD) or placebo for an additional 10 weeks. Patients who demonstrated clinical response (CDAI-100) underwent corticosteroid tapering after Week 10. Anti-TNF-naive patients were excluded. Immunosuppressants were to be discontinued prior to treatment initiation. Final data for the primary endpoint of clinical remission (CDAI < 150) at Week 10 are presented.

**Results:** Baseline characteristics were comparable in both groups, including mean disease duration (8.3 y), mean CDAI score (293, mean CRP (15.6 mg/L, 41% > 10 mg/L), oral corticosteroids (51%, mean daily dose 21.6 mg/day). Primary endpoint of the study was met: Filgotinib induced clinical remission in 47% of the patients, compared to 33% in the placebo recipients (p = 0.0077), and led to improvement in PRO2 score, and quality of life (IBDQ changes from baseline) compared to placebo (table 1). Numerically more patients on filgotinib normalized CRP (FIL:27%, PBO:14%) and showed an improvement of at least 50% in PRO2 score, and quality of life (IBDQ changes from baseline) compared to placebo (Table 1).
Aims & Methods: We investigated the effect of prior tumour necrosis factor inhibitor (TNFf) therapies or disease activity (baseline Mayo score) on clinical efficacy endpoints and patient-reported outcomes (PROs) in pooled data from OCTAVE Induction 1 and 2. Adults with moderately to severely active UC (baseline Mayo score ≥2, rectal bleeding subscore ≥1 and endoscopic subscore ≥1 or prior failure/intercourse to ≥1 of corticosteroids, thiopurines or TNFf were randomised (4:1) to receive tofacitinib 10 mg or PBO for up to 9 weeks (wks). Efficacy endpoints at Wk 8 included remission (primary endpoint; Mayo score <2, no subscore ≥1 and rectal bleeding subscore of 0), mucosal healing at Wk 8 (Mayo endoscopic subscore ≤1), clinical response (from baseline Mayo score of ≥3 points and ≥30%, plus decrease in rectal bleeding subscore ≥1 or absolute subscore ≤1). All endoscopic scores were imputed (endpoint, the comparison of tofacitinib 10 mg BID vs PBO was assessed using the Cochran-Mantel-Haenszel (CMH) chi-square test stratified by study, prior TNFf treatment, corticosteroid use at baseline and geographic region. Within each subgroup, the CMH chi-square test stratified by study was used.

Results: At Wk 8, significantly more pts achieved remission, mucosal healing and clinical response with tofacitinib 10 mg BID vs PBO (all p < 0.0001, Table). The difference generally remained significant regardless of prior TNFf exposure, prior TNFf failure (primary or secondary) or disease severity (based on baseline Mayo score ≥6 or < 6; Table). For all three endpoints, greater effects were observed when comparing secondary vs primary TNFf failure subpopulations and baseline Mayo score <6 vs baseline Mayo score ≥6. IBDQ remission and response were significantly greater with tofacitinib 10 mg BID vs PBO at Wk 8 regardless of prior TNFf exposure/prior TNFf failure.

Conclusion: Tofacitinib demonstrated efficacy vs PBO, regardless of prior TNFf therapy in pts with moderately to severely active UC. PRO results were similar in pts with/without prior TNFf exposure or failure.

Table: Summary of efficacy endpoints in OCTAVE Induction 1 and OCTAVE Induction 2 at Wk 8
**Aims & Methods:** In this post-hoc analysis the therapeutic effects were analysed with respect to disease activity of the patients at baseline. Cobitolimod was studied in a randomized, double blind, placebo-controlled, multicentre, pan-European trial named COLLECT in 131 patients with moderate to severe active ulcerative colitis. Patients were on mandatory steroid therapy and could be tapered at any time. The results of the COLLECT study demonstrate that the TLR-9 agonist cobitolimod is able to induce clinical remission in UC patients both at baseline and at week 4. The most common adverse events of cobitolimod were nausea (24%), abdominal pain (15%), headache (15%) and upper respiratory tract infection (15%). With respect to the endpoint symptomatic remission at week 4/8/12 respectively, 111/131 (84.7%) had no blood in the stools (RBS 0), and 105/131 (80.2%) had little or no blood in their stools (rectal bleeding subscore [RBS] 0 or 1). The most common adverse events (AEs) (2.0%) during OLE were UC flare, anaemia, upper respiratory tract infection, nasal pharyngitis, back pain, arthralgia, headache, alanine aminotransferase (ALT) or aspartate aminotransferase (AST) elevation. The only serious AEs in ≥2 patients were anaemia, and ulcerative colitis flare. ALT and AST > 3× upper limit of normal occurred in 4 (2.4%) of the 170 patients in the OLE. All elevations were asymptomatic, ≤5×ULN, transient, and resolving while receiving continued treatment.

**Conclusion:** Long-term treatment with ozanimod continues to be safe and well-tolerated with good compliance and evidence of durable efficacy.

We assessed a recently developed self-assembling peptide matrix as a wound dressing after endoscopic resection for the prevention of esophageal stricture.

Aims & Methods: Ten pigs were randomly assigned to the self-assembling peptide RADA-16 (4 [Arg-Ala-Asp-Ala]) or the control group after undergoing a 5 cm long circumferential endoscopic submucosal dissection of the lower esophagus. Endoscopic diagnosis of esophagitis and esophagogram, weight variation, and histological measurements of fibrosis, granulation tissue, and neoeplithelium were assessed in each animal.

Results: The rate of esophageal stricture at day 14 was 40% in the group treated with self-assembling peptide vs. 100% in the control group (p = 0.04). Median (IQR) esophageal diameter at day 14 was 8 mm (2.5–9) in the self-assembling peptide group vs. 4 mm (3–4) in the control group (p = 0.13). The median (IQR) stricture indexes on esophagograms at day 14 were 0.32 (0.14–0.48) and 0.26 (0.14–0.33) in treated and control groups, respectively (p = 0.42). Median (IQR) weight variation during the study was +0.2 (–7.4; +1.8) and –3.8 (–5.4; +0.6) in the treated and control groups, respectively (p = 0.9). No differences were observed between the groups in terms of histological outcomes. All animals eventually developed esophageal strictures at day 28.

Conclusion: The application of a self-assembling peptide matrix on esophageal wounds after circumferential endoscopic submucosal dissection is safe and feasible, and prevents early esophageal stricture occurrence in our model.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
altered diagnosis/therapy and/or influenced management in 417 (83%) pts. Multivariate analysis as a predictor for malignant pathfaler of Spy DS biopsies is better for Spy DS than Spy Legacy (p = 0.014). Adverse events in 7 (1%) pts: 2 mild pancreatitis, 2 mild and 1 moderate cholangitis, 1 moderate bleeding and 1 micro perforation.

Conclusion: SOc, especially using Spy DS, has high procedural success and provides important impact on diagnosis, therapy and/or management in a wide range of indications, with excellent safety profile.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

**Table (OP114)**

<table>
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<td>100 mg PR before ERCP</td>
<td>100 mg PR before ERCP</td>
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<td>Iran-single center</td>
<td>Hungary-single center</td>
<td>Hungary-multicenter</td>
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<td>Pain, amylase, pro-longed admission</td>
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<td>228</td>
<td>686</td>
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<td>347</td>
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<td></td>
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<td>N/A</td>
<td>18</td>
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<td>N/A</td>
<td>16</td>
<td>30</td>
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<td></td>
<td>% Pancreatic duct injection</td>
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**Conclusion**: The use of high-dose PPI did not appear to significantly reduce the risk of both immediate and delayed bleeding in patients undergoing EST.

**Disclosure of Interest**: All authors have declared no conflicts of interest.

**OP115 PREVENTION OF POST-SPHINCTEROTOMY BLEEDING BY PROTON PUMP INHIBITOR: A PROSPECTIVE RANDOMIZED TRIAL**

W.K. Leung, D. Y. But, S.Y. Wong, K. Liu, I. Hung

**Department Of Medicine, University of Hong Kong**

**Contact E-mail Address**: wallkeung@hku.hk

**Introduction**: Bleeding after endoscopic sphincterotomy (EST) is one of the most frequent complications of therapeutic ERCP. Although the use of proton pump inhibitor (PPI) has been shown to reduce the risk of rebleeding in patients with peptic ulcer bleeding after endoscopic hemostasis, the role of acid suppression in preventing EST bleeding has not been evaluated. We hypothesized that preemptive high dose PPI could reduce the risk of post-EST bleeding.

**Aims & Methods**: The aim of this study was to study the high dose of PPI in patients undergoing EST. It was a prospective randomized open-label study performed in the endoscopy centre of a university teaching hospital. Consecutive patients who were scheduled to have ERCP and EST were enrolled. We excluded patients who had previous EST, prior gastric surgery, or were taking PPIs. Antiplatelet therapies were continued as usual. Anti-coagulants (warfarin or heparin) were stopped with coagulopathy corrected prior to ERCP. Eligible patients were randomized to receive either PPI or standard care (SC). PPI group would receive esomeprazole 40 mg bid from Day 2 to 10. Standard care arm would receive usual care without any acid suppressive therapy. Endoscopists were unaware of the treatment allocation of the patients. Primary outcome was the proportion of patients with immediate or delayed post-EST bleeding. Immediate bleeding was defined as bleeding that occurred during the procedure and required endoscopic hemostasis. Delayed bleeding was defined as bleeding after the completion of ERCP which manifested as overt GIB with melena or hematemesis. All patients were followed up for 30 days. Secondary outcomes included drop in lipase levels without overt bleeding, transfusion requirement and all-cause mortality at 30 days. Analysis was based on modified intention-to-treat, which included only randomized patients who had undergone EST.

**Results**: 196 patients were enrolled and 71 patients did not have EST. The analysis included 125 patients who had undergone EST with 60 in the PPI group and 65 in SC group. The mean age was 70.9 (SD = 14.8) years with 62 (49%) men. The baseline characteristics of the two groups including indications for ERCP, luminal size of the bile duct which included only randomized patients who had undergone EST.

**Conclusion**: Prevention of post-EST bleeding by PPI significantly reduced the incidence of immediate post-EST bleeding (15.7% vs 5.1%, p = 0.002). Secondary outcomes included drop in lipase levels without overt bleeding, transfusion requirement, and all-cause mortality at 30 days. There was no significant difference in the proportions of patients with hemorrhagic drop of > 2 g without overt bleeding (Day 10: 3.3% in PPI group and 5.7% in SC group; p = 0.57). Other outcomes including hospital stay (13.1 vs 11.8 days; p = 0.69), transfusion requirement (5% vs 7.7%; p = 0.72) and 30-day mortality (3.3% vs 1.5%; p = 0.61) were also comparable between the two groups. Patients were randomized (1:1) to either intensive hydration with lactated Ringer’s solution (3 mL/kg/h during the procedure, and 3 mL/kg/h for 8 hours after the procedure), or standard hydration (1.5 mL/kg/h of lactated Ringer’s solution during and for 8 hours after the procedure). A blood panel including serum levels of amylase and lipase was obtained at 4 and 24 hours after ERCP. Primary outcome was the incidence of PEP (defined as epigastric pain plus either amylase or lipase levels > 3 times the upper limit of normal at 24h). Secondary outcomes were severity of PEP, incidence of volume overload, patient and procedure-related factors associated with PEP, and the predictive values of serum amylase/lipase at 4 hours after ERCP for PEP development.

**Results**: Included were 75 patients, 38 in the intensive hydration arm, and 37 in the standard hydration arm. Both groups were homogeneous for patient and procedure-related factors. PEP incidence was 9.5% (n = 7), and was lower in the intensive hydration arm (5.3% versus 13.5%, p = 0.204). Additionally, both PEP in the intensive hydration arm were mild, while out of the 5 PEP in the normal hydration arm, two patients presented with moderate and severe PEP, respectively. Contrast injection of the Wirsung was significantly associated with PEP (28.6% versus 7.1%, p = 0.016), while no other patient or procedure-related factors associated with PEP incidence. Finally, both amylase levels < 2 times and lipase levels < 3 times the upper limit of normal at 4 hours demonstrated a
negative predictive value of 100% for the development of PEP. No complication was observed as a consequence of intensive hydration.

Disclosure of Interest: All authors have declared no conflicts of interest.

MONDAY, OCTOBER 17, 2016
15:35-17:15
UPPER GI NERVE-GUT INTERACTIONS – ROOM N2

OP117 INTRAGASTRIC BITTER TASTANT ALTERTS BRAIN ACTIVITY IN HOMEOSTATIC AND HEDONIC REGIONS AND DECREASES OCTANEOYLATED GHRELIN LEVELS AND HEDONIC FOOD INTAKE

J. Iven, J. Biesiekierski, D. Zhao, I. Depoortere, L. Van Oudenhove, J. Tack Targird, University of Leuven, Leuven/Belgium

Contact E-mail Address: julie.iven@kuleuven.be

Introduction: Intragastric administration of bitter tastants decreases hunger ratings in the fasted state. Activation of bitter taste receptors can alter ghrelin levels, a gut hormone which increases hunger in between meals and becomes active after overeating. This indicates a potential role for bitter agonists in the regulation of appetite and food intake, putatively via interference with gut-brain signals to regions involved in homeostatic (brainstem, hypothalamus) and hedonic (mesolimbic reward system) control of feeding.

Aims & Methods: The aim of this project was to study the effect of intragastric administration of the bitter tastant Quinine Hydrochloride (QHCl) on brain activity in homeostatic and hedonic regions and on circulating ghrelin plasma levels. Furthermore, to test the hypothesis that lower hunger and prospective food consumption ratings, and lower hedonic food intake after QHCl administration compared to placebo. Fifteen healthy women were studied after an overnight fast. Brain activity before and up to 50 minutes after infusion of QHCl (10mM/ kg body weight) (5ml/kg) was recorded using functional magnetic respon-
sance imaging (fMRI). Hunger and prospective food consumption scores were assessed every 10 min using Visual Analogue Scales. Blood samples were taken at the same time points. Hedonic food intake was measured immediately after scanning using an ad libitum chocolate milkshake drink test. fMRI preprocessing and analysis was conducted using SPM12. Brain responses over time to QHCl versus placebo infusion were compared in a priori defined regions of interest (ROI) at both voxel- and cluster-level threshold of pFWEcorrected < 0.05. The interaction effect was tested on hunger and prospective food consumption scores with mixed models. Hedonic food intake was compared between infusions using a one-tailed paired T-test. Blood plasma was analysed for circulating ghrelin levels using radioimmunoassays.

Results: Compared to placebo, intragastric QHCl infusion significantly increased neural activity in 5 different clusters within the ROIs, with local maxima in the putamen, insula, caudate, amygdala, anterior cingulate cortex, medial prefrontal cortex, medial orbitofrontal cortex and hippocampus. A decrease of neural activity was observed in the lower limb system. Significantly lower post-infusion prospective food consumption scores were observed after QHCl administration compared to placebo (p = 0.02), but no significant differences were observed for hunger scores. Milkshake intake was significantly lower after QHCl administration, compared to placebo (p = 0.04). Cohen’s d = 0.59. A significant decrease of octanoylated ghrelin plasma levels was observed post-infusion after bitter administration compared to placebo (p = 0.03).

Conclusion: Intragastric administration of the bitter tastant QHCl significantly altered activity in homeostatic and hedonic brain regions. Prospective food consumption ratings, circulating octanoylated ghrelin levels and hedonic food intake were decreased after QHCl. These observations indicate a potential role for bitter agonists in the treatment of obesity.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP118 TRANSDIAGNOSTIC COGNITIVE BEHAVIOUR THERAPY SHOWS PROMISE FOR BOTH MOOD AND GASTROINTESTINAL SYMPTOMS IN PATIENTS WITH FUNCTIONAL GASTROINTESTINAL DISORDERS

M.P. Jones1, B. Dear1, N. Titov1, V. J. Fogliati2, N.J. Talley2
1Psychology, Macquarie University, North Ryde/Australia
2University of Newcastle Faculty of Health PVC Office, Callaghan/Australia

Contact E-mail Address: mike.jones@mq.edu.au

Introduction: Irritable Bowel Syndrome (IBS) is a heterogeneous disorder characterised by recurrent abdominal pain combined with alteration in bowel habit. It is associated with reduced quality-of-life and significant economic cost to society. IBS sufferers also have elevated scores for anxiety and depression which have been speculated to be part of the disease etiology [1]. Indirect evidence for the role of mood in IBS prevalence comes from studies showing that a proportion of patients show improvement in abdominal symptoms with antide-
pressants [2] but also in response to psychological therapies including cognitive behaviour therapy (CBT) [3]. Newer forms of CBT including internet-delivered CBT (iCBT) have shown similar effect sizes to conventional CBT in patients with mood disorder [4]. iCBT provides access to therapy for patients who are geogra-
phically or culturally isolated from qualified psychologists and has been shown to be cost-effective [5]. eCentreClinic at Macquarie University (Australia) has developed a transdiagnostic model of CBT which is applied via distance mode, reducing access barriers via internet but not completely.

Aims & Methods: This study sought to pilot a new form of iCBT designed for chronic health conditions, including functional gastrointestinal disorders, with respect to: 1. Reduction in abdominal symptom burden, anxiety and depression 2. Identify the risk of psychological factors that correlate with improvements in abdominal symptom burden. These aims were addressed using a single arm design with measurements of psychological factors and symptoms pre, mid and post-therapy. n=27 individuals from across Australia were recruited at the eCentreClinic at Macquarie University (Australia) which specialises in online psychological therapies. Abdominal symptoms were assessed using the Gastrointestinal Symptom Rating Scale (GSRS) while anxiety was measured via the GAD-7 and depression via the PHQ-9. Aim 1 was addressed via correlating change in GSRS scores with change in anxiety, depression and pain catastrophising scores.

Results: Of 27 patients who commenced therapy 22 completed the entire course of therapy. All patients showed significant improvement in all primary outcome measures. There was no difference in treatment effects for any measure between on-site and non-completers. Scores for both abdominal symptom and psychological traits were substantially and statistically significantly improved at the end of therapy (Table 1).

Table 1: Baseline and change in scores for abdominal symptoms and psychological factors

<table>
<thead>
<tr>
<th>Score</th>
<th>Baseline</th>
<th>Change</th>
<th>Cohen’s d</th>
</tr>
</thead>
<tbody>
<tr>
<td>GSRS</td>
<td>44.2 (11.0)</td>
<td>−7.6 (10.5)</td>
<td>−0.72</td>
</tr>
<tr>
<td>Anxiety</td>
<td>10.5 (5.2)</td>
<td>−5.1 (4.4)</td>
<td>−1.18</td>
</tr>
<tr>
<td>Depression</td>
<td>9.7 (4.8)</td>
<td>−4.1 (5.3)</td>
<td>−0.82</td>
</tr>
<tr>
<td>Catastrophising</td>
<td>19.8 (11.3)</td>
<td>−11.5 (11.9)</td>
<td>−0.97</td>
</tr>
</tbody>
</table>

At end of therapy 77% of patients had reduced GSRS scores and 95% reported the program was worth the effort expended. The percentage change in GSRS scores was positively correlated with percentage change in pain catastrophising (r = 0.53, p = 0.01) and depression (r = 0.53, p = 0.01) and to a lesser extent with change in anxiety (r = 0.36, p = 0.1).

Conclusion: Based on this pilot trial, a transdiagnostic iCBT program developed specifically for functional gastrointestinal disorders shows considerable promise with improvements in both gastrointestinal symptoms as well as psychological functioning. The correlation between change in both mood scores and catastrophizing with change in abdominal symptoms opens avenues for further understand-
ing of the mechanisms by which iCBT improves the gastrointestinal sufferings of these patients. The low cost of iCBT compared with conventional face-to-face therapy is attractive given challenges to public health budgets and its modality makes therapy accessible to potential patients who are not able to travel to a psychologist. Further, the transdiagnostic model on which this particular iCBT treatment is based is readily adaptable to other functional somatic syn-
dromes so offers hope to a wide range of disorders.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP119 DYSBIOSIS INDUCES GUT INFLAMMATION AND DEPRESSIVE-LIKE BEHAVIOR ASSOCIATED WITH BRAIN BIOCHEMICAL AND FUNCTIONAL ALTERATIONS WHICH ARE RESTORED BY PROBIOTIC TREATMENT

F. Turco1, F. Guida2, I. Palumbo3, M. Iannotta2, A. Furiano2, L. Luongo3, R. Cuomo3, S. Maione3, V. De Novellis3
1Clinical Medicine and Surgery, Federico II University of Naples, Naples/Italy
2Department of Experimental Medicine, Section Of Pharmacology E. Donnelli, Second University of Naples, Naples/Italy

Contact E-mail Address: fabio.turco81@yahoo.it

Introduction: The gut-brain axis has been indicated as major substrate of patho-
physiological mechanisms in psychiatric comorbidities associated with chronic inflammatory bowel disorders. In particular, intestinal microbiota alterations in these two systems1. However, the communication is not fully understood and probably involves multiple mechanisms.

Aims & Methods: In the present study we examined in a mouse model, the role of gut microbiota alterations in an antibiotic-induced dysbiosis animal model. Young male mice received a mixture of nonabsorbable antimicrobials (ampicilline, streptomicin and clyndam-
icin), which has been associated to the microflora composition alteration2, for 2 weeks. Afterwards, animals were treated with probiotic (Lactobacillus Casei DG, 10⁹ cells) or vehicle up to 7 days. Whereupon, various behavioral testing were performed. After sacrifice, mice intestine was cut in segments (duodenum, jejunum, ileum) and subjected the emotion experiment and expression of pro-inflammatory markers (IL-1β,}

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The gut microbiota is known to play a significant role in host physiology. Recent studies have shown that gut microbiota can influence gut-brain axis through various mechanisms, including the production of molecules that modulate the gut environment and host responses. One such molecule is quorum sensing (QS) molecules, which are produced by bacteria and can act as chemical signals to coordinate behavior and metabolism among bacterial cells. These molecules have been suggested to influence host satiety and hungry states, and the gut microbiota is associated with alterations in host responses to oxidative stress and chronic inflammation.

**Results:**
- Culture supernatants of selected bacterial strains significantly reduced IL-1β and TNFα expression, normalized mice behavior, and improved satiety responses.
- Administration of QS molecules led to increased mRNA levels of anorectic peptides, such as Cholecystokinin and Leptin.
- Bitter taste receptors, including Tas2r38 and Tas2r105, were altered by QS molecules, suggesting a role for taste in gut microbial communication.
- Fat-fed mice showed reduced gut microbiota diversity and increased expression of pro-inflammatory cytokines, while QS administration restored gut microbiota composition and normalized host responses.

**Conclusion:**
- QS molecules have the potential to mediate satiety and control gut microbiota diversity, influencing host responses to oxidative stress and chronic inflammation.
- The gut microbiota can be manipulated to improve satiety and weight loss, suggesting new therapeutic targets for obesity and related conditions.
The mean LES pressure induced by PWS was 33.0 ± 1.6 mmHg, and did not differ significantly from HLES P 32.7 ± 1.6 (P = 0.794). Actocamide normalized AC. Actocamide normalized impaired receptive LES relaxation and substantially improved symptoms.

Conclusion: Subjects have receptive LES relaxation, but this is impaired in EGGJO. Acetocamide normalizes impaired receptive LES relaxation and substantially improved symptoms.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

MONDAY, OCTOBER 17, 2016
15:45–17:15
ENDOSCOPIC TREATMENT OF UPPER GASTROINTESTINAL CANCER – ROOM U

OP123 EFFICACY AND SAFETY OF ESD FOR SUPERFICIAL CANCER OF THE CERVICAL ESOPHAGUS
T. Iizuka1, D. Kikuchi1, S. Hoteya2, M. Kaise1
1Dept. Of Gastroenterology, Toranomon Hospital, Tokyo/Japan
2Dept. Of Gastroenterology, Toranomon Hospital Dept. of Gastroenterology, Tokyo/Japan
3Toranomon Hospital, Tokyo/Japan
Contact E-mail Address: t-iizuka@toranomon.gr.jp

Introduction: It is a difficult to observe a lesion in the cervical esophagus because of the difficulty in spreading the tumor. It is a challenge not only to find esophageal cancers at an early stage, but also to successfully treat them by ESD compared with lesions located at the thoracic esophagus.

Aims & Methods: The aim of this study was to clarify the safety and efficacy of ESD for superficial cancer located at the cervical esophagus. Patients who met the following criteria (case group) were enrolled in this retrospective study: 1) ESD was performed from January 2006 to December 2015; 2) the lesion was located at the cervical esophagus; and 3) squamous cell carcinoma (SCC) was proven histologically. Forty-five patients met those criteria. As a control group, 379 patients with 405 lesions of SCC which were located at the middle thoracic esophagus were enrolled. The lesions with entire circumferential mucosal defect, recurrent lesions after radiotherapy, and the lesions located near the scar were excluded in both groups. We evaluated advanced endoscopic treatments including submucosal tunneling, submucosal dissection, procedure time, and en bloc resection rate, and frequency of local recurrence.

Results: In the case group, the average age was 67.3 years old, and the male-to-female ratio was 29.6%, the average maximum size of lesions was 20.7 mm, and the histological depth of invasion was EP/LPM, MM, and SM2 in 39, 5, and 1 cases, respectively. The en bloc resection rate and R0 resection rate was 100% and 90%, respectively, and the mean procedure time was 57 min. ESD was performed under general anesthesia in 32 patients (71.1%). Damage of the muscle layer during treatment was observed in 5 patients, for which clipping was performed in 2 patients. Esophageal stricture was observed in 9 patients (41%), for which local injection of steroid was administered in 6 patients. No post-ESD bleeding was observed. Although perforation was identified in one patient, he recovered with conservative treatment. Chemoradiotherapy as additional treatments were conducted in 4 patients. No local recurrence was observed during an average duration of follow-up of 41.8 months. In the case group, the average age was 67.3 years old, and the male-to-female ratio was 29.6%, the average maximum size of lesions was 20.7 mm, and the histological depth of invasion was EP/LPM, MM, and SM2 in 306, 67, and 32 cases, respectively, and the mean procedure time was 54 min. ESD was performed under general anesthesia in 45 patients (11.1%). Damage of the muscle layer during treatment was observed in 9 patients (22.5%), for which clipping was performed in 8 patients. Esophageal stricture was observed in 14 patients (6.6%) of 213 patients with more than half of mucus defect, for which local injection of steroid or PGA sheet were administered in 38 patients. No post-ESD bleeding was observed. Although perforation was identified in three patients, they recovered with conservative treatment. Surgery or chemoradiotherapy as additional treatments were conducted in 19 or 49 patients respectively. Local recurrence was observed in one patient during an average duration of follow-up of 41.8 months.

Conclusion: Safe ESD for superficial esophageal cancer in the cervical esophagus could be achieved under an appropriate management and successful local control was also confirmed. The stricture after ESD in the cervical esophagus developed significantly higher than those in the middle esophagus.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP124 SUBMUCOSAL TUNNELING ENDOSCOPIC RESECTION VS. THORACOSCOPIC SURGERY FOR LARGE SYMPTOMATIC SUBMUCOSAL TUMORS IN THE ESOPHAGUS AND ESOPHAGOGRASTIC JUNCTION
T. Chen, M. Xu
Endoscopy Center and Endoscopy Research Institute, Zhongshan Hospital of Fudan University, Shanghai, China
Contact E-mail Address: xuemingdong@aliyun.com

Introduction: Small gastrointestinal submucosal tumors (SMTs) are asymptomatic and undeletable, while patients with larger tumors have symptoms, and require intervention. Previously, thoracoscopic submucosal dissection (TS) has been the gold standard for the resection of upper gastrointestinal SMTs. Recently, reports about ESD are increasing. However, it is unclear whether ESD is feasible for large SMTs. Moreover, studies about comparison of ESD and surgery for upper gastrointestinal SMTs are still little. Aims & Methods: The aim of this study is to compare the clinical outcomes of ESD and thoracoscopic surgery for large symptomatic SMTs in esophagus and esophago gastric junction, as well as to analyze the clinicopathological factors that affect the feasibility of ESD. Patients with large SMTs of the MP layer in esophagus and EGJ were enrolled in this retrospective study between May 2011 and December 2013. The clinicopathological data of a total of 145 patients were collected and analyzed.

Results: Among the 145 patients, 48 patients (29.6%) complained specific symptoms, while 106 patients (70.4%) had non-specific symptoms. In the ESD group, the mean tumor long and transverse diameters were 5.8 cm and 2.2 cm. Meanwhile, in the TS group, the mean tumor long and transverse diameters were 6.4 cm and 3.1 cm, respectively. All SMTs, 64 SMTs (44%) in the ESD group and 81 had irregular shapes (55.9%). All of the tumors were located in esophagus (84, 57.9%), and EGI (61, 42.1%). There was no significant difference between the two groups in age, gender, symptom, tumor size, tumor location, tumor shape, and tumor histopathological type. The incidence of complications in this study was observed in 84.1% of the cases in the ESD group and 85.7% of the cases in the TS group, and there was no significant difference (p = 0.794). In addition, the incidence of complications in this study was 8.5% in ESD group and 4.8% in TS group. There was no significant difference in complications rates of the 2 groups. However, the procedure time and the hospital stay in the ESD group was 8 hours and 10 days, respectively for the TS group. Besides, the transverse diameter of tumors with long diameter larger than 7.0 cm, transverse diameter larger than 3.5 cm and irregular shape were 3 significant risk factors for TS-related piecemeal resection, while tumor with transverse diameter larger than 3.5 cm was the risk factor for ESD-related piecemeal resection.

Conclusion: ESD is feasible and safe for large symptomatic SMTs in esophagus and EGJ. It is associated with a shorter procedure time and hospital stay compared with TS. Besides long diameter and irregular shape, transverse diameter of tumors was a risk factor for the occurrence of piecemeal resection. STER is feasible and safe for large symptomatic SMTs in esophagus and EGJ. The incidence of complications was not significantly different in ESD and TS, while the hospital stay was significantly longer in the TS group which might be related to the feasibility of ESD.

Disclosure of Interest: All authors have declared no conflicts of interest.
antibiotics. There were no treatment-related deaths. On pathological examination, 20 were tubular adenocarcinoma, and 11 were tubular adenoma. Histologically, curative resection was obtained in 26 of the 31 lesions (83.9%). There were no differences in gross type (elevated type/flat and depressed type), tumor size, or histology between primary and metastatic lesions. However, loco-regional recurrence (LNR), a 21 intrahepatic cancers with low-grade dysplasia, 3 minute submucosal cancers, 6 submucosal deep cancers and 2 carcinoid tumors submittted to ESD, were compared to 98 patients (mean patient age 62.7, range 32–92 years, male: female ratio 25/26) including 19 involved adenoma with low-grade dysplasia was 3 minute submucosal cancers, 6 submucosal deep cancers and 2 carcinoid tumors submitted to ESD. At these sites, the mean operation time was 1.6 hrs and the size of the specimen was 25.5 mm (range 10–80 mm); in EMR group, the mean operation time was 0.5 hrs and the size of the specimen was 26.2 mm (range 10–100 mm). En-bloc resection rate, curative resection rate, piecemeal resection, recurrence rate, post-operative bleeding and perforation rate were compared with the use of the chi-square test.

Results: En-bloc resection rate (ESD: 82.4%, 42/51 vs EMR: 51%, 50/98; p < 0.001) and curative resection rate (ESD: 88.2%, 45/51 vs EMR: 72.9%, 71/98; p < 0.05) were significantly higher in the ESD group in comparison with EMR group. Piecemeal resection was significantly lower in ESD (2.5%; 2/51) when compared to EMR group (9.5%; 9/98) (p < 0.01). In the EMR group, 6 patients developed local recurrences (6.1%); five were successfully treated by additional EMR and one by surgical resection; in contrast, there was no recurrence in the ESD group (p = NS). The post-operative bleeding rate was 3.9% (2/51) in ESD and 3.1% (3/98) in EMR group (p = NS). Perforation rate for ESD was 3.9% (2/51) when compared to conventional EMR (2%, 2/98) (p = NS).

Conclusion: In the present study, we evaluated the efficacy of 2 endoscopic resection methods from the perspectives of the en-bloc and curative resection rates. Based on these aspects, an ESD was found to be the best method for early gastrointestinal cancers; EMR would be a good alternative to an ESD, especially in non-risk-patients when performed by less experienced endoscopists.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP128 LONG-TERM OUTCOME OF THE INCIDENCE RATE OF METACHRONOUS GASTRIC CANCERS AFTER HELICOBACTER PYLORI ERADICATION – A FOLLOW-UP AND ANALYSES OF JAPAN PEST STUDY GROUP ENROLLED PATIENTS
K. Fukase
Gastroenterology, Yamagata Prefectural Central Hospital, Yamagata/Japan
Contact E-mail Address: fukasekh@macbase.or.jp
Introduction: The author and Japan Gast Study Group (JGSG) reported that the eradication of Helicobacter pylori reduced the incidence of metachronous gastric cancers (GC) after endoscopic mucosal resection significantly in the Lancer study. Therefore, we performed a follow-up in the JGSG patients to validate the risk of GC in the eradication group.

Aims & Methods: We analyse long-term outcomes of the incidence rate of metachronous GC for JGSG enrolled patients at Yamagata Prefectural Central Hospital. We confirmed long-term survival in 89 patients with endoscopic mucosal resection (EMR) and in 40 patients with endoscopic submucosal dissection (ESD). The incidence rate of metachronous GC was analysed and compared between the two groups.

Results: Out of the eradication group, 1 metachronous GC was detected (9 years 7 months after the enrollment). Out of the non-eradication group, 4 metachronous GC were detected (5 years 3 months, 6 years 7 months, 10 years 2 months, 13 years 10 months after the enrollment). When these 4 lesions were detected, 3 cases were not eradicated and 1 case was eradicated unsuccessfully. The incidence rate of metachronous GC of the eradication group was 4.8% but that of the non-eradication group was 21.1%.

Conclusion: The incidence rate of metachronous GC of the non-eradication group was about four times higher than that of the eradication group even in 15th observation year. All 4 cases of metachronous GC of the non-eradication group were persistent infected cases. The earlier eradication of Helicobacter pylori is recommended.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
MONDAY, OCTOBER 17, 2016
15:45-17:15
HEPATIC CYSTS AND HEPATO-BILIARY TRACT DISORDERS - ROOM L8

OPT129 THE EFFECT OF PASIREOTIDE IN CYST REDUCTION OF ASPIRATION SCLEROTHERAPY IN PATIENTS WITH LARGE SYMPTOMATIC HEPATIC CYSTS, A RANDOMIZED CONTROLLED TRIAL

T.F.Am. Wijnands1, T.J.G. Gevers1, M.A. Lantinga1, L.J. Schultzke Kool2, J.P.H. Drenth1
1Gastroenterology and Hepatology, Radboud university medical center, Nijmegen, Netherlands
2Radiology, Radboud University Medical Center, Nijmegen, Netherlands

Contact E-mail Address: titus.wijnands@radboudumc.nl

Introduction: Aspiration sclerotherapy is a therapeutic option for large symptomatic hepatic cysts. However, inadequate cyst reduction is frequently reported. Somatostatin analogues are able to curtail cyst volume. Our aim was to test whether pasireotide could improve the efficacy of aspiration sclerotherapy of large symptomatic hepatic cysts. We conducted a single-center, randomized (1:1 ratio), double-blind, placebo-controlled trial in patients with a large (> 5 cm) symptomatic hepatic cyst. All patients underwent aspiration sclerotherapy. In addition, we randomized patients between two arms: (1) pasireotide 60 mg long-acting release (LAR) injection or (2) placebo (saline) injection. Injections were administered two weeks prior and two weeks after aspiration sclerotherapy. Primary endpoint was proportional cyst diameter reduction after six weeks, as measured by ultrasonography. Secondary outcomes included long-term diameter reduction at 26 weeks, symptomatic change at 26 weeks, and safety during the study. Symptomatic change was evaluated using the polycystic liver disease questionnaire (PLD-Q) that assesses frequency and severity of 14 disease-specific symptoms leading to a total PLD-Q sum score.

Results: Thirty-four patients (32 females (94%); mean age 53.6±7.8 years) were randomized between pasireotide (n=17) and placebo (n=17). Pasireotide did not improve efficacy of aspiration sclerotherapy at six weeks compared to controls (23.6% [IQR 9.6-31.8%] versus 21.8% [IQR 9.6-31.8%]; respectively; p=0.98). Long-term cyst diameter reduction was similar in both groups (49.1% [IQR 27.0-73.6%] and 45.5% [IQR 29.2-59.6%]; p=0.90). Mean PLD-Q scores improved significantly in both groups (p<0.01) indicating symptomatic relief, but there were no differences between groups (p=0.92). Transient hyperglycaemia was seen in all patients allocated to pasireotide.

Conclusion: Aspiration sclerotherapy is a highly effective treatment option of large symptomatic hepatic cysts, spiking with pasireotide does not further improve efficacy.

Disclosure of Interest: J.P.H. Drenth: Novartis provided the study drug and partially funded this investigator-initiated study. Novartis did not have any influence on the execution of the trial or the preparation of the manuscript. All other authors have declared no conflicts of interest.

OPT130 A STUDY TO INVESTIGATE RISK FACTOR FOR ENTEROCOCCUS SPECIES ISOLATION FROM BILE AND/OR BLOOD CULTURE OBTAINED FROM PATIENTS WITH CHOLANGITIS

Gastroenterology, Mitsui Memorial Hospital, Tokyo/Japan

Contact E-mail Address: cyclolups@yahoo.co.jp

Introduction: Knowledge of pathogenic spectrum for cholangitis is important for adequate empiric therapy. Enterococcus species, which come well equipped with a variety of intrinsic antibiotic resistances, are sometimes isolated. However, little is known of risk factors for this organism’s isolation in patients with cholangitis. We conducted a study to investigate them on the basis of single-center experience in Japan.

Aims & Methods: Consecutive 191 hospitalized patients with cholangitis with positive bile and/or blood culture between January 2009 and October 2015 were enrolled. Diagnosis of cholangitis was based on clinical symptoms, blood chemistry and radiological imaging. Potential risk factors for Enterococcus species isolation such as patient attributes (Age, sex, underlying conditions, and past history) were retrospectively investigated. Univariate and multivariate analyses to identify risk factors were performed using a proportional hazards model.

Results: 127 patients were men (67%). The average age was 74.2±14.7 years. Enterococcus species were isolated in 128 episodes from bile and/or blood culture. Age over 75 years old (OR 1.92; 95%CI 1.109–3.548; P=0.028), prior endoscopic sphinterotomy (OR 5.895; CI 1.301–26.71; P=0.015), stayed in Intensive Care Unit in past admission (OR 2.588; CI 0.342–4.992; P=0.050), presence of device in biliary tract (OR 1.921; 95%CI 1.284–2.721; P=0.015) and biliary reconstruction (OR 1.921; 95%CI 1.284–2.721; P=0.014) were independent risk factors. We found prior endoscopic sphinterotomy and biliary reconstruction revealed a statistically significant correlation with the isolation of Enterococcus species isolation in cholangitis. We should consider empiric therapy with anti-enterococcal antibiotics when managing patients with these attributes.

Disclosure of Interest: All authors have declared no conflicts of interest.

OPT131 MENOPAUSAL HORMONE THERAPY AND RISK OF BILIARY TRACT CANCER

C. Kilander1, J. Lagergren2, O. Sadr-Azodi3, N. Brusselaers4
1Dept Of Molecular Medicine and Surgery, Karolinska Institutet, Stockholm/Sweden
2Division Of Cancer Studies, King’s College London, London/United Kingdom
3Institute Of Environmental Medicine, Unit Of Epidemiology, Karolinska Institutet, UGIR, MMK, Stockholm/Sweden

Contact E-mail Address: carl.kilander@ki.se

Introduction: The risk of developing biliary tract cancer, including cancers of the gallbladder and extrahepatic bile ducts, may be influenced by estrogen receptor (ER) expression, which is increased by hormone replacement therapy (HRT). However, the effect of HRT use on the risk of biliary tract cancer remains uncertain, as is the role of menopausal hormone therapy (MHT). We conducted a large, population-based cohort study with long-term follow-up to evaluate the association between MHT use and the risk of biliary tract cancer.
AUC 25.1 ± 9.2 ng/ml, P < 0.01). The expression of MUC3A was significant correlated with metastasis of lymph node. The expression of MUC3A in ECC stage of carcinoma differentiation grade of carcinoma (P < 0.05). (2) The preoperative serum values of MUC3A in patients with ECC was significant higher than with patients with SOD (57.8 ± 19.6 vs. 25.1 ± 9.2 ng/ml, P < 0.01). Compared with the preoperative results, postoperative serum levels of MUC3A in patients with SOD were significantly decreased (26.8 ± 4.6 vs. 57.8 ± 19.6 ng/ml, P < 0.01).

ROC curve analysis showed serum MUC3A could distinguish ECC with SOD while 40.7 ng/ml as the cut-off value (AUC = 0.907, 84.6% sensitivity, 90% specificity). (3) The serum MUC3A has more sensitivity of early over the period (59.6%, 38.5%, 75%, 70%, 25% in 5, 10, 15, 20, 25% respectively). The serum MUC3A was significant correlated with metastasis of lymph node (43.0%, 63.0%, 83.0%, and 66% false positive rates (10%, 5%, 1%) and than serum CA19-9, CEA in diagnosis of ECC. 

Conclusion: MUC3A is high expression in tumor tissue of ECC, and related to the differentiation grade and stage of tumor. The MUC3A in peripheral blood is valuable to preoperative diagnosis of ECC. MUC3A is expected to become one of the most promising tumor marker for ECC.

Disclosure of Interest: All authors have declared no conflicts of interest.
polyps and the attribution of neoplastic polyps and nonneoplastic polyps was calculated. The study revealed that the prevalence of gallbladder polyps, we obtained the total number of cholecystectomies between 2003–2013 from PALGA.

Results: In total 220,612 cholecystectomies were performed over the period 2003–2013. The PALGA search identified 4532 excerpts, representing 4549 patients. A total of 337 patients were excluded due to primary non-gallbladder surgery, leaving 4012 unique cholecystectomies. In 2083 cholecystectomies (0.9%), a polypoid lesion was present. Which results in a calculated prevalence of polyps in 944/100,000 patients who undergone cholecystectomy. Of the polyps, 1172 (56.6%) were nonpolypoid, 278 (13.3%) adenoma, and 57 (2.7%) other malignancies. Nine hundred and ten (43.7%) polyp were nonneoplastic; 375 (18.5%) cholesterol polyps, 334 (16%) adenoma, and 54 (2.6%) mesoic polyps, 42 (2.0%) inflammatory polyps, 18 (0.9%) papilloma’s and 17 (0.8%) other types of polyps.

Conclusion: Approximately one percent of gallbladders contain a polyp on histopathological assessment after cholecystectomy. Fifty-six percent of the polyps after cholecystectomy are neoplastic.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Monday, October 17, 2016
15:45–17:15
Mechanisms of Liver Cancer and Portal Hypertension – Room 1.86

Opi35 Changes in Circulating Microrna after Treatment: Microrna Signatures to Predict Therapy Response and Disease Free Survival in Hepatocellular Carcinoma
D. Pascale1, H. Krmac2, R. Patti3, D. Licastro2, S. Dal Monego3, N. Mezzina1, C. Abazia4, C. Tiribelli1, L. S. Croce4, R. Calligaris2, H. Krmac2, R. Patti3, D. Licastro2, S. Dal Monego3, N. Mezzina1, C. Abazia4, C. Tiribelli1
1Iulian Liver Foundation, Trieste/Italy
2Italian School for Advanced Studies (SISSA), Trieste/Italy
3CBM S.r.l., Trieste/Italy
4Teaching Hospital Cattinara, Trieste/Italy
Contact E-mail Address: devis.pascale@csi.units.it

Introduction: Hepatocellular carcinoma (HCC) is the second leading cause of cancer-related death worldwide. Although treatment options have improved in the past 30 years, prognosis remains unfavorable in many patients. The lack of effective models for outcome prediction prevents the opportunity for individualized treatment. The potential role of microRNAs (miRNAs) as prognostic biomarker has witnessed an increasing interest, owing to the non-invasive nature of miRNA-based screening assays. While many studies have suggested several miRNAs as biomarker candidates, dynamic variations over extended time periods have been observed until now.

Aims & Methods: To identify potential circulating miRNA signatures for the prediction of efficacy response and patient follow-up. Methods: 15 consecutive patients with early/intermediate stage HCC were enrolled and treated according to the ESSL/AASLD practice guidelines. Patients were staged (CT scan and/or pathological assessment after cholecystectomy. Fifty-six percent of the polyps after cholecystectomy are neoplastic.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Monday, October 17, 2016
15:45–17:15
Mechanisms of Liver Cancer and Portal Hypertension – Room 1.86

Opi35 Changes in Circulating Microrna after Treatment: Microrna Signatures to Predict Therapy Response and Disease Free Survival in Hepatocellular Carcinoma
D. Pascale1, H. Krmac2, R. Patti3, D. Licastro2, S. Dal Monego3, N. Mezzina1, C. Abazia4, C. Tiribelli1, L. S. Croce4, R. Calligaris2, H. Krmac2, R. Patti3, D. Licastro2, S. Dal Monego3, N. Mezzina1, C. Abazia4, C. Tiribelli1
1Iulian Liver Foundation, Trieste/Italy
2Italian School for Advanced Studies (SISSA), Trieste/Italy
3CBM S.r.l., Trieste/Italy
4Teaching Hospital Cattinara, Trieste/Italy
Contact E-mail Address: devis.pascale@csi.units.it

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Disclosure of Interest: All authors have declared no conflicts of interest.

References
OP358 RIGOGUAT, A STIMULATOR OF THE GUANYLYL CYCLASE, REDUCES LIVER FIBROSIS AND PORTAL PRESSURE IN CIRRHOTIC RATS
P. Schwalb1, K. Brusilovskaya2, F. Riedl3, D. Bauer1, B. Strobel1, P. Supper1, N. Roehr-Udlopa1, H. Hayden4, B. Podesser1, T. Reiberger1, M. Trauner1, M. Peck-Radosavljevic1
1Div. Of Gastroenterology and Hepatology, Department Of Internal Medicine II, Medical University of Vienna, Vienna/Austria
2Department Of Biomedical Research, Medical University of Vienna, Vienna/Austria

Contact Email Address: philipp.schwalb@meduniwien.ac.at

Introduction: Intrahepatic nitric oxide (NO) signaling including activation of its receptor, the soluble guanylyl cyclase (sGC) is impaired in cirrhosis. The GC stimulator rigoguatt (RIO) is approved for treatment of pulmonary hypertension. Experimental studies suggest antiﬁbrotic effects of RIO. We investigated the effects of RIO in cirrhotic rats with portal hypertension (PHT).

Aim: To investigate the effects of early and advanced cirrhosis rat models with portal hypertension (PHT) on hepatic hemodynamics, liver vascular resistance (SVR), portal blood pressure (PP), and hepatic perfusion (HP), as evaluated by aortic blood flow volume using MRI technique in rats; (2) To investigate the effects of RIO in these rat models on hepatic hemodynamics and their association with autophagy and apoptosis.

Methods: Two early and advanced cirrhotic rat models were used to assess changes in hemodynamics and ﬁbrosis after RIO treatment. Cirrhosis was induced by i.p. carbon tetracloride ("early": 1 mL/kg - "advanced": 2 mL/kg 50% CCl4, 8 weeks) or by bile duct ligation (BDL, "early": 3 weeks or "advanced": 5 weeks) in 100 male Sprague Dawley rats. Controls received olive-oil (OO) or underwent sham operation (SO), respectively. RIO (1 mg/kg/d) or saline were administered by intraperitoneal injection 2 mL/kg 50% CCl4, 8 weeks) or by bile duct ligation (BDL, "early": 3 weeks - "advanced": 5 weeks) in 100 male Sprague Dawley rats. Controls received olive-oil (OO) or underwent sham operation (SO), respectively. RIO (1 mg/kg/d) or saline were administered by intraperitoneal injection.

Results: BDL and CCl4 rats presented with cirrhosis, elevated PP, SMABF and portal pressure (PP), superior mesenteric blood ﬂow (SMABF) and perto-systemic shunting (PSS) were measured. Hepatic ﬁbrosis was quantiﬁed by hydroxyproline content (HP) and chrome anilin blue (CAB) staining. Expression of TUNFe, endothelial nitric oxide synthetase (eNOS) and inducible NO (iNOS) were quantiﬁed in liver tissue by western blotting.

Conclusion: Our morphological study focused on changes in the lobules over time, and we observed two distinct phases of liver atrophy following portal blood ﬂow disruption. The first (the autophagic phase) was characterized by lobular shrinkage without hepatocyte loss and high LC3 expression, and lasted for the second two weeks following PTPE. The second phase, termed the apoptotic phase, was characterized by reduced hepatocyte number without reduced lobular size but with reduced LC3 expression and increased TUNEL staining, and lasted 2-4 weeks.

Disclosure of Interest: All authors have declared no conﬂicts of interest.

References:

OP410 EFFECT OF CHRONIC THIOACETAMIDE TREATMENT ON HEPATIC HEMODYNAMIC PARAMETERS IN RATS:
EVALUATION BY MAGNETIC RESONANCE IMAGING
D. Schaffner1, D. Elferfeldt2, P. Deiber1, A. Lazzaro1, I. Merfort1, L. Lutz2, M. W. Baumbast1, W. Kreisel1, W. Rechardt1
1Institute For Exercise- Und Occupational Medicine, Center For Medicine, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg/Germany
2Department Of Radiology, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg/Germany
3Department Of Pharmaceutical Biology and Biotechnology, University of Freiburg, Freiburg/Germany
4Institute Of Clinical Pathology, Medical Center – University of Freiburg, Faculty of Medicine, University of Freiburg, Freiburg, Germany

Contact Email Address: denise.schaffner@uniklinik-freiburg.de

Introduction: For the investigation of hepatic hemodynamics in animal models invasive methods are commonly used. This study seeks to evaluate a non-invasive Magnetic Resonance Imaging (MRI) method as a reliable diagnostic tool in the widely used model of Thioacetamide (TAA)-induced liver injury. Aims & Methods: (1) To quantitatively assess hepatic hemodynamic parameters (portal vein area, portal blood flow velocity and portal blood flow volume) and aortal blood flow volume using MRI technique in rats; (2) To investigate the influence of the hepatotoxic agent TAA on these hemodynamic parameters. 54 male Wistar rats were studied. 15 of which were left untreated and 39 received TAA in their drinking water (0.03g TAA / 100 mL H2O). The TAA dosage was set to vary weekly based on the rats’ body weight changes. From the 39 treated rats 15 received TAA for 12 weeks and 24 for 16 weeks. The following parameters were measured by a 9.4 Tesla preclinical MR scanner: portal vein area, portal blood flow velocity, portal blood flow volume and aortal blood flow volume. Specific gradient-echo fast phase contrast sequences were used with both cardiac and respiratory gating. All MRI measurements were performed under continuous isoflurane anesthesia. The degree of liver injury was estimated by standard histological criteria. Histological evaluation was performed in all 54 rats while hemodynamic measurements could be evaluated in 50 rats. For statistical analysis Kruskal-Wallis test was used.

Results: From the rats which received TAA for 12 weeks 100% (15/15) developed liver fibrosis with a Desmet score of 1–3 (group 12/fib). From the rats which received TAA for 16 weeks 15 rats (75%) (group 16/fib) developed liver fibrosis as compared with group 12/fib. The other relative liver size in the embolized lobe of the pig had gradually decreased to 23% of the normal pig liver at 12 days after PTPE with a combination of coils and polynyl alcohol particles; thereafter, the size did not change significantly. However, to the best of our knowledge, these time-course studies have not yet been carried out. To clarify the mechanisms responsible for liver atrophy, pathological analysis should be carried out within the liver lobule. However, to the best of our knowledge, these time-course studies have not yet been carried out.

Aims & Methods: We attempted to investigate the mechanism of liver atrophy by portal vein obstruction and clarify the roles of autophagy and apoptosis. As pig lobule structures were well-defined as compared with human specimen, we performed percutaneous transhepatic portal embolization (PTPE) in 5 pigs. And then sacrificed them at day 0, week 2, 4 or 6 (d0, w2, w4 and w6, respectively). In specimens of embolized lobe (E) and non-embolized lobe (control, Cont), we measured the distance between portal vein and central vein (PV-CV), area and hepatocyte number per portal lobule and apoptotic activity. Immunohistochemical reactions of microtubule-associated protein-light chain 3 beta (LC3) as autophagy and glutamine synthetase (GS) and cytochrome 2E1 (CYP2E1) as zonation were evaluated.

Results: PV-CV and lobule area showed no significant difference between E and Cont at d0, but were lower in E than in Cont at w2, w4 or w6 (P = 0.001). Hepatocyte number was not significantly reduced in E at d0 and w2 but was reduced in E at w4 and w6 (P < 0.05). Apoptotic activity was higher in E than in Cont at d0 and w4. LC3 staining peaked in E at w2, with no significant difference between E and Cont at w4 and w6. GS and CYP2E1 areas in E at w2, w4 and w6 were narrower than those in Cont.

Conclusion: Our morphological study focused on changes in the lobules over time, and we observed two distinct phases of liver atrophy following portal blood flow disruption. The first (the autophagic phase) was characterized by lobular shrinkage without hepatocyte loss and high LC3 expression, and lasted for the second two weeks following PTPE. The second phase, termed the apoptotic phase, was characterized by reduced hepatocyte number without reduced lobular size but with reduced LC3 expression and increased TUNEL staining, and lasted 2–4 weeks.

Disclosure of Interest: All authors have declared no conflicts of interest.

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received TAA for 16 weeks, 46% (11/24) developed liver fibrosis with a Desmet score of 4 (group 16w/cir) and 54% (13/24) had liver cirrhosis with a Desmet score of 4 (group 16w/cir). The untreated rats (15/54) served as control group (group con). Mean portal vein area showed no significant differences among all groups. However, mean portal flow velocity was reduced by 15% in group 12w/ fib compared to group con and 16w/cir compared to group con. In group 16w/cir mean weight was significantly lower than that of group con. Thus flow volumes were adjusted according to the body weight in order to eliminate weight-induced changes in hemodynamics. Mean aortal flow volume per body weight was not significantly different among all groups. In contrast mean portal flow volume per body weight was significantly reduced in group 12w/fib by 23% compared to group con. On the other hand, in group 16w/fib and group 16w/cir there was no further reduction of mean portal flow volume per body weight. However, we speculate that in the model of TAA-induced liver injury the development of fibrosis is sufficient to cause a significant decrease in portal flow volume. There were no significant differences between group 12w/fib and 16w/fib in terms of all parameters, in particular portal flow volume.

Contact: The non-invasive Doppler technique can be a reliable diagnostic tool to investigate the hepatic hemodynamics in different experimental models of liver injury. In this particular animal model even the TAA-induced liver fibrosis led to a significantly reduced portal perferusion. The molecular mechanisms of this finding need to be further investigated.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016
08:30–10:00

OPI41 CORRELATION OF ENDOSCOPIC FINDINGS WITH SERUM DRUG CONCENTRATIONS AND NEED FOR RESCUE THERAPY: SUBANALYSIS OF THE TROUGH CONCENTRATION ADAPTED INFLIXIMAB TREATMENT (TAXIT) TRIAL

L. Pouillon, M. Ferrante, G. Van Assche, M. Noman, A. Gilis, S. Vermeire
Department of Gastroenterology and Hepatology, University Hospitals Leuven, Leuven/Belgium

Contact E-mail Address: lievenpouillon@hotmail.com

Introduction: The Trough Concentration Adapted Infliximab Treatment (TAXIT) randomized controlled trial [1] showed that targeting patients' infliximab trough concentrations to a 3–7 μg/mL window resulted in a more efficient use of the drug in patients with inflammatory bowel disease. Following dose optimization, continued concentration-based dosing was not superior to clinically-based dosing. A trend towards less mucosal healing was seen if rescue therapy was needed. We assessed the impact of AZA dose reduction on the need for rescue therapy. Aims & Methods: This was a retrospective analysis of all endoscopies performed at the end of TAXIT. For Crohn's disease (CD), mucosal healing was defined as absence of ulcerations (complete mucosal healing) or clear improvement in ulcerations (partial mucosal healing) when compared to baseline. For ulcerative colitis (UC), healing was defined as a Mayo endoscopic subscore of 0 or 1. Rates of mucosal healing were compared for both arms in TAXIT (clinically-based arm 1 and concentration-based dosing arm 2) and infliximab trough concentrations were correlated to the degree of healing.

Results: Of the 226 patients completing the TAXIT maintenance phase, 125 (55%) underwent endoscopy after one year: n = 55 in arm 1 and n = 70 in arm 2. Patients in arm 2 were more likely to reach the primary endpoint of TAXIT (p = 0.05). The rates of mucosal healing were comparable between both arms in CD patients (35/38 in arm 1 vs. 49/52 in arm 2; p = 0.66). Patients who reached the primary endpoint of TAXIT more frequently had complete mucosal healing (73/84 vs 87%) compared to patients who did not reach the primary endpoint (28/41 or 68%) (p = 0.02). Numerically more patients who needed rescue therapy during maintenance phase of TAXIT had not achieved mucosal healing (3/12 or 25%) compared to patients who did not need rescue therapy (9/113 or 8%) (p = 0.09). The mean serum trough concentration during maintenance phase of TAXIT were 5.31 ± 0.06 μg/mL in patients with mucosal healing and 4.26 ± 0.07 μg/mL in patients without mucosal healing (p = 0.07).

Conclusion: The primary endpoint of TAXIT, clinical and biochemical remission, correlated with mucosal healing. Similar to mucosal healing, the trough rates of mucosal healing were observed in patients after clinically-based dosing compared to concentration-based dosing. A trend towards less mucosal healing was seen if rescue therapy was needed during TAXIT. Mean serum trough concentrations during the maintenance phase of TAXIT were higher in patients with mucosal healing.


A. Gilis: Lecture fees from MSD, Janssen Biologicals, Abbvie, Pfizer, Takeda. Consultancy for UCB. Conflict with license of infliximab, anti-infliximab and adalimumab ELISA from Institution apDia and with lateral flow fluid immunoassay to R-Biopharm AG.

S. Vermeire: Grant research support from Takeda, MSD, Abbvie. Consultancy/ speaker's fees from Abbvie, MSD, Takeda, Pfizer, Galapagos, Genentech/Roche, Mundipharma, Celgene, Hospira, Second Genome. All other authors have declared no conflicts of interest.
Aims & Methods: In this retrospective cohort analysis, the outcome of dose de-escalation in patients with inflammatory bowel disease (IBD) who are in clinical remission. Dose de-escalation may not only have beneficial economic repercussions, it may possibly also decrease the occurrence of adverse events.

Aims & Methods: In this retrospective cohort analysis, the outcome of dose de-escalation, evaluated using A (40 mg ETW) and ADM serum levels, maintenance of AZA at the same dose and may improve AZA safety profile. A threshold of 6-TGN < 105pmole was associated with an unfavourable evolution of IFX pharmacokinetics.

Disclosure of Interest: S. Vermeire: Grants from MSD, Takeda and Abbvie, lecture fees from Abbvie, MSD, Falk, Tillotts, Ferring, Centocor, Takeda, Hospira; consultancy for Ferring, Abbvie, Shire, Genentech/Roche, Celgene, Janssen, MSD, Takeda, Galapagos, Hospira, Mundipharma, Pfizer. G. Van Assche receives financial support for research from Abbvie and MSD, lecture fees from Janssen, Takeda, Ferring, Abbvie, MSD, and Abbvie and does consultancy for Abbvie, MSD, and Takeda. A. Gils: Ann Gils has been a consultant for Merck, Janssen Biologics, and Abbvie. M. Ferrante: Research grant from Janssen Takeda, lecture fees from Tillotts, Ferring, Boehringer-Ingelheim, Janssen, Chiesi, Falk, Zeria, Mitsubishi Tanabe, MSD, Takeda, and Abbvie and does consultancy for Abbvie, Ferring, MSD, Boehringer-Ingelheim and Janssen.

All other authors have declared no conflicts of interest.


Contact E-mail Address: sophie.vansteenbrugge@student.kuleuven.be

Introduction: Although dose escalation is widely used to optimize biological therapy in case of clinical relapse, less is known about possibilities to de-escalate therapy in case of clinical remission, especially in long-lasting remissions. For example, dose de-escalation may be considered in patients who have been on long-term maintenance therapy with AZA (40 mg ETW) and ADM serum levels, minimising the risk of adverse events.

Aims & Methods: In this retrospective cohort analysis, the outcome of dose de-escalation, evaluated using A (40 mg ETW) and ADM serum levels, maintenance of AZA at the same dose and may improve AZA safety profile. A threshold of 6-TGN < 105pmole was associated with an unfavourable evolution of IFX pharmacokinetics.


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results were most sensitive to changes in the perspective of the analysis, utility values and time horizon (10-year).

Conclusion: Biosimilar infliximab is a cost-effective alternative to the originator product for the treatment of adults with luminal CD, and it may contribute to increasing the affordability of biological treatments throughout Europe.

Disclosure of Interest: J. Aisenberg has received speaker’s honoraria from Boehringer Ingelheim.

TUESDAY, OCTOBER 18, 2016
8:30-10:00

OP147 IDARUCIZUMAB FOR EMERGENT REVERSAL OF DABIGATRAN-RELATED ANTI-OAGULATION DURING SEVERE GASTROINTESTINAL HEMORRHAGE: INTERIM RESULTS (N = 123) FROM THE REVERSE-ADTM STUDY

J. Aisenberg1, P. Chatterjee2, P. Reilly3, F. Gruenenfelder4, E. Kleine5, S. Glund6, J. Van Ryn6, C. V. Pollack7, P.L. Lakatos2

1Department Of Medicine, Icahn School of Medicine at Mount Sinai, New York/United States of America
2Department Of Medicine, Icahn School of Medicine at Mount Sinai, New York/United States of America
3Boehringer Ingelheim Pharmaceuticals, Ridgefield/United States of America
4Boehringer Ingelheim Pharmaceuticals GmbH & Co. KG, Ingelheim/Germany
5Boehringer Ingelheim Pharma GmbH & Co KG, Biberach an der Riß/Germany
6Thomas Jefferson University, Philadelphia/United States of America
7Boehringer Ingelheim Pharma GmbH & Co KG, Biberach an der Riß/Germany

Introduction: Gastrointestinal bleeding (GIB) is a feared complication of anticoagulant therapy. Idarucizumab (ID) is a recombinant, humanized monoclonal antibody agent for the direct thrombin inhibitor dabigatran. IDA should benefit management of dabigatran users experiencing severe GIB.

Aims & Methods: The on-going REVERSE-ADTM study evaluates the safety and efficacy of IDA 5 grams intravenously in dabigatran users with (A) life-threatening haemorrhage or (B) requirement for emergency surgery. Here, we analyze the clinical characteristics and outcomes of REVERSE-ADTM enrollees presenting with severe GIB. Our study is performed on an interim analysis cohort of 123 patients centralized laboratory coagulation data are available for 90/123 (73%) patients with major GIB.

Results: Of the 66 patients enrolled in REVERSE-ADTM due to severe bleeding, 27 (41%) bled in the GI tract. The mean age of GIB patients was 77.5 years (range 27–90), 15 (26%) were females and renal impairment was present in 22 (33%) patients with creatinine clearance measurements (96%). Atrial fibrillation was the indication for anticoagulation in 93%; 77% took their most recent dabigatran dose <24 hours prior to presentation. Ten patients (37%) bled in the upper GI tract, 8 (30%) from the lower GI tract, and 9 (33%) from an unknown level of the GI tract. IDA achieved immediate reversal of dabigatran-related anticoagulation, and its effect lasted for up to 24 hours in the majority of patients. Hospital admission was required for 25 patients (93%, median length of stay=6.0 nights); 8 patients required ≥1 day in intensive care unit (ICU) (30%; median length of ICU stay=3.5 days). Patients with lower GI bleeding had shorter time to cessation of bleeding (median 1.5 hours vs. 7.3 hours). No adverse events attributable to IDA were reported. A total of 24 patients received ≥1 unit packed red cells (mean 4.5 units); 9 received fresh frozen plasma (mean 2.6 units); 2 received platelets (mean 1.5 units); and 1 received prothrombin complex concentrate prior to dabigatran therapy. There were no death within 48 hours of presentation. Ten patients (74%) bled ≥30% of the upper GI tract, 8 (30%) from the lower GI tract, and 9 (33%) from an unknown level of the GI tract. IDA achieved immediate reversal of dabigatran-related anticoagulation, and its effect lasted for up to 24 hours in the majority of patients. Overall, GIB outcomes in this population were more favourable; antithrombotic therapy can be resumed promptly in most patients.

Disclosure of Interest: J. Aisenberg: James has provided consultancy to Boehringer Ingelheim.

P. Reilly: Paul Reilly is an employee of Boehringer Ingelheim Pharmaceutical.

F. Gruenenfelder: Fredrik Gruenenfelder is an employee of Boehringer Ingelheim Pharmaceuticals.

E. Kleine: Eva Kleine is an employee of Boehringer Ingelheim Pharmaceuticals.

S. Glund: Stephan Glund Pharma is an employee of Boehringer Ingelheim GmbH & Co. KG.

Contact E-Mail Address: fanni.renzen@gmail.com

Introduction: Biomimetic infliximab (Inflectra®) has been approved by the European Medicines Agency for the treatment of luminal Crohn’s disease (CD) since 2013. Currently biosimilars offer a massive price reduction in most European countries. Nevertheless, no study has yet compared the cost-effectiveness for biosimilar infliximab for the treatment of luminal CD in European countries. This study aimed to compare the cost-effectiveness of infliximab-adalimumab-vedolizumab sequences compared to the standard care. The biosimilar infliximab-adalimumab-vedolizumab sequence dominated the originator infliximab-adalimumab-vedolizumab standard care sequence at a 10-year time horizon.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Department Of Laboratory Medicine, Semmelweis University, Budapest/Hungary
14Kings College London - ISS on November 25, 2016
OP149 RISK OF RHEEMLING, VASCULAR EVENTS AND DEATH AFTER GASTROINTESTINAL BLEEDING IN ANTICOAGULANT AND/OR ANTIPATELETT AE USERS

B. Marenč1, C. Sostres2, V. Laredo1, L. Ruiz5, E. Alfaro3, P. Camo5, P. Carrera4, A. Lanas3

1Gastroenterology, University Hospital Locarno Blasa, Zaragoza/Spain
2Pathología Digestiva, Instituto de Investigación Biosanitaria de Aragón (IIS), Zaragoza/Spain
3Gastroenterology, University Hospital Miguel Servet, Zaragoza/Spain
4Laboratorio de Patología, Zaragoza/Spain
5Dept. Medicine & Gastroenterology, University of Zaragoza University Hospital Dept. of Medicine-Gastroenterology, Zaragoza/Spain

Contact E-mail Address: beamarcen@hotmail.com

Introduction: Patients who develop gastrointestinal (GI) bleeding during anticoagulant (AC) and/or platelet (AP) therapy represent a clinical challenge. Cure of bleeding is a higher priority than normalization of these treatments will have important clinical implications concerning the risk of vascular, GI bleeding and death events. Differences on the risks between AP or AC users after drug resumption are not well established.

Aims & Methods: We aimed to determine the rate of rebleeding, vascular events and death in a cohort of patients treated with AP or AC agents who developed a major GIB (upper or lower) event. To compare these risks depending on the treatment either adopted after the GIB episode, we conducted a large prospective, long-term observational cohort study of patients who developed GIB while on AP and/or AC treatment from March 2008 to August 2013. Drug use information was prospectively collected during the GIB event. Data concerning the follow-up period, which ended on December 31st 2013, were obtained from databases from different Spanish Health care areas. Primary outcomes were vascular event, GI rebleeding and death from any cause. Statistical analyses were performed using SPSS software version 22.0.

Results: The patients included were (mean age 78.7 ± 8.9; 56.6% males; 52.8% (409/774), 38.5% (298/774), 8.7% (67/774) were on AP, AC or AP+AC therapy respectively. 22.6% of patients presented rebleeding, 17.1% ischemic event and 26.0% death during the follow up (median 23 months). Following the index GIB, rebleeding was interrupted in 80.1% (572/714) of patients, although 80.1% (572/714) resumed afterwards (median time 6 days (1–370). Resumption of therapy was associated with higher risk of rebleeding (5.3% vs. 24.6% p < 0.001) but lower risk of death (43.7% vs. 19.9% p < 0.001). Early resumption of therapy (<7 days) vs. patients delayed >7 was associated with a higher rate of rebleeding (20.4%/p < 0.020), with no statistical differences in GI events. AC users had higher death risk (OR 1.5; 95%CI: 1.1-2.2) compared to AP users. Dual AP users had higher risk of ischemic events (OR 2.1; 95%CI: 1.1-3.7). Rebleeding event rates were 85 and 120 events per 1000 pt-year for vascular events, and 93 and 144 respectively for deaths.

Conclusion: Nearly 40% of patients presented a new adverse event related with AP/AC treatment during the follow-up. The risk of death is higher in patients on AC therapy compared with AP users. Resumption of AC/AP therapy is associated with higher risk of rebleeding and lower risk of death without any influence on vascular events. Resumption of AP or AC treatments later than 7 days is associated with significant higher risk of ischemic events.

Disclosure of Interest: A. Lanas: Professor Lanas has been an advisor for AstraZeneca, Bayer and Pfizer. All other authors have declared no conflicts of interest.
Aspirin is a potent anti-platelet agent used for the prevention of cardiovascular and cerebro-vascular diseases. However, gastrointestinal (GI) bleeding is the most frequently reported serious adverse event for the long-term use of aspirin. Aims & Methods: The objective of this study is to investigate whether the risk of aspirin usage on increasing ulcer bleeding would outweigh its benefit on the prevention of CRC. The present study investigated the electronic medical records from 42 publicly funded hospitals, which serves a 7 million population in Hong Kong. All hospital admissions from 2000 to 2004 and their outcome in the follow-up period were extracted until 2014. Aspirin users were matched with control in a ratio of 1:2 to non-aspirin users in the study period. Incidences of CRC and GI bleeding were the primary outcomes. Logistic regression was used to compare incidence rates and Cox-proportional hazard regression model was used to compare the mortality rates. Subgroup analyses were performed for those with ulcer bleeding, or for those with regular aspirin prescribed.

Results: A total of 4,564,100 subjects were identified in the system between year 2000 and 2004, and 254,887 of them (5.6%) were prescribed aspirin for at least one year. Among the subjects who were never prescribed aspirin, 491,852 (10.8%) were identified in the system. The total sample size of this study was 746,739. The baseline characteristics of aspirin and non-aspirin users were 68.4 (SD = 13.1) and 66.4 (SD = 13.2) respectively. In the aspirin group, 78,316 patients (30.7%) had aspirin prescribed for 10 years or more, and 54,011 of them (69.0%) were routinely prescription during the years of clinic visits. Median dose of aspirin used among the patients were 80 mg with interquartile range from 80 mg to 100 mg. Average duration of aspirin prescribed was 6.3 years. Patients in aspirin group showed significantly lower incidence of CRC (OR = 0.82; 95% CI = 0.80 to 0.85), and showed significant reduction in overall mortality (HR = 1.74; 95% CI = 1.74 to 1.80), and showed marginally significant higher mortality among those diagnosed with GI bleeding (HR = 1.03; 95% CI = 1.02 to 1.05). The results remained consistent in the subgroup analyses.

Conclusion: This is a population-based study to concurrently compare the risk and benefit of long-term use of aspirin. We concluded that long-term use of low-dose aspirin will increase the incidence of GI bleeding, and moderate increase the overall mortality among the patients with GI bleeding. On the other hand, the long-term use of aspirin showed benefit to reduce CRC on both incidence and overall mortality.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016
08:30-10:00
OUTCOMES IN PERIORAL ENDOSCOPIC MYOTOMY (POEM) – ROOM M

OP153 COMPREHENSIVE ANALYSIS OF ADVERSE EVENTS ASSOCIATED WITH PER ORAL ENDOSCOPIC MYOTOMY (POEM) IN 1826 PATIENTS: AN INTERNATIONAL MULTICENTER STUDY


1Gastroenterology and Hepatology, John Hopkins Hospital, Baltimore/United States of America/MD
2Dietic Celecoxib, Showa University Koto Toyo Hospital, Tokyo/Japan
3Gastroenterology and Endoscopy Unit, Digestive Disease Department, H Pavillon-Digestive Endoscopy Unit, Humanitas Research Hospital, Rozzano/Italy
4Division Of Surgery, Evanston Hospital, Evanston/United States of America/IL
5Division Of Gastroenterology and Hepatology, University of Florida, College of Medicine, Gainesville/United States of America/FL
6Department Of Surgery, Everson Hospital, Evanston/United States of America/IL
7Gastroenterology and Hepatology, John Hopkins Hospital, Baltimore/United States of America/MD
8Dietic Disease Center, Showa University Koto Toyo Hospital, Tokyo/Japan
9The Oregon Clinic, Amerge, Portland/OR
10Division Of Gastroenterology and Hepatology, University of Florida, College of Medicine, Gainesville/United States of America/FL
11Department Of Surgery, Everson Hospital, Evanston/United States of America/IL
12Gastroenterology and Hepatology, John Hopkins Hospital, Baltimore/United States of America/MD
13Division Of Gastroenterology and Hepatology, University of Florida, College of Medicine, Gainesville/United States of America/FL
14Division Of Gastroenterology and Hepatology, University of Florida, College of Medicine, Gainesville/United States of America/FL
15USF Health Tampa Veterans Affairs (VA) Medical Center, Tampa/Florida/United States of America/FL
16Royal Prince Alfred Hospital, Camperdown/Australia/NSW
17Division Of Surgery, Showa University, Koto-Toyo Hospital, Tokyo/Japan
18University Of Florida College Of Medicine, Division of Gastroenterology and Hepatology, Gainesville/United States of America/FL
19Division Of Gastroenterology and Hepatology, University of Florida College of Medicine, Gainesville/United States of America/FL
20University of Florida College of Medicine, Division of Gastroenterology and Hepatology, Gainesville/United States of America/FL
21Division Of Gastroenterology and Hepatology, University of Florida College of Medicine, Gainesville/United States of America/FL
22Division Of Gastroenterology and Endoscopic Surgery, University of Strasbourg, Strasbourg/France

Contact E-mail Address: yamihaito@hotmail.com

Introduction: POEM was introduced as a minimally invasive and effective therapeutic modality for the treatment of achalasia and spastic esophageal disorders. Many retrospective single-center studies and small case series suggest...
POEM as a safe alternative to Heller Myotomy. However, the safety of POEM is still an insufficiently analysed endoscopic tunnel approach (AEs) associated with POEM in large cohort studies has not been performed.

Aims & Methods: We aimed to study (1) the rate of AEs and (2) factors associated with occurrence of AEs in patients undergoing POEM. Method: Patients who underwent POEM for the treatment of achalasia and SEDs at 12 tertiary-care centers (5 US, 4 Europe, 2 Asia and 1 Australia) between 2011 and 2015 were used in a case-control study. Cases were defined by the occurrence of any AEs related to POEM procedure. Control patients were selected for each AE case by matching for age, gender, disease classification (type I vs. II or III, SEDs). All pertinent data including AEs were collected and their severity was compared. There were no deaths related to POEM. When patients with AEs were compared with a control group (case-control analysis), there was no difference between the two groups in terms of Charlson comorbidity index (ASA class, primary therapy, sigmoid esophagus, operator specialty, direction of myotomy (anterior vs. posterior), type of knife used, extent and length of myotomy, and operator experience). The median follow-up of procedure was significantly longer in cases as compared to controls (123 ± 49 vs. 103 ± 33, p = 0.002). Length of stay was significantly higher in patients who experienced AEs (4.9d vs. 2.7d, p < 0.001).

Conclusion: POEM as a safe therapeutic modality with an overall incidence of AEs was 7.5%. Severe AEs are rare. AEs result in prolongation of hospital stay. Longer procedural times (indicative of technically complex procedures) are associated with increases of occurrence of AEs.

Disclosure of Interest: M. Khashab: Consultant of Boston Scientific and Xlumena

All other authors have declared no conflicts of interest.

References

10. Cotton PB, Eisen GM, Vittinghoff E, Takata M, Gadenstatter M, Lin F, et al. Peroral endoscopic myotomy (POEM) for the treatment of achalasia (type I 11, type II 51, type III 6, unspecified 37). Clinical success was achieved in 97.5% (159/163), 99.8% (124/125), 90% (116/130) at 6, 12 and 24 months, respectively. Of 159 patients with clinical response at 6 months, 11 (7%) had major complications including perforations, and fistulas. Surgical Endoscopy 2011; 25(9): 2901–5.

OP154 LONG TERM OUTCOMES OF PERORAL ENDOSCOPIC MYOTOMY (POEM) IN ACHALASIA PATIENTS WITH A MINIMUM FOLLOW-UP OF 2 YEARS: AN INTERNATIONAL MULTICENTER STUDY

S. Ngamruengphong1, H. Inoue2, A. Bapaye3, M. Ujiki4, L. Patel5, P. Desai6, B. Hayek7, H. Haji8, W. Vong9, S. Perretta10, S. Dorward11, M. Koch8, S. Misari12, J. Rイロン12, M. Pioche10, A. Garres10, J. Nakamura14, Y. Hata15, V. Balassone14, M. Onimaru14, G. Hajiyeva1, A. Ismail1, Y. Chen1, M. Bukhari1, Y. H. Chavez1, V. Kumbhar1, R. Maselli1, A. Ripic12, M. Khosla1

1. Dept. Of Gastroenterology, Johns Hopkins University, Baltimore/United States of America
2. Digestive Disease Center, Showa University Koto Toyosu Hospital, Tokyo/Japan
3. Digestive Endoscopy Center, Fort Lauderdale, Demnaath Mangeshkar Hospital Digestive Disease & Endoscopy, Pune/India
4. Department Of Surgery, Evanston Hospital, Evanston/United States of America
5. Sarat Institute of Digestive Sciences, Sarat/India
6. Gastroenterology, Kings College Hospital, London/United Kingdom
7. King's College Hospital, London/United Kingdom
8. Prince of Wales Hospital, The Chinese University of Hong Kong, Hong Kong/China
9. RIG
10. Department Of Gastrointestinal and Endocrine Surgery, University of Strasbourg, Strasbourg/France
11. Gastroenterology and Endoscopy Unit, Digestive Disease Department, H Pavilion- Edourad Herriot Hospital, Lyon/France
12. Digestive Physiology, Hospices Civils de Lyon, Lyon/France
13. Digestive Endoscopy Unit, Herriot University Hospital Dept. of Hepato-gastroenterology, Lyon/France
14. Digestive Diseases Center, Showara University, Koto-Toyosu Hospital, Tokyo/Japan
15. Humanities Research Hospital, Milan/Italy

Contact E-mail Address: sngamru1@jhmi.edu

Introduction: Peroral endoscopic myotomy (POEM) aims to palliate symptoms of achalasia by reducing pressure at the lower esophageal sphincter (LES). Current data demonstrates high short-term clinical response in 82–100% of patients. However, long term data is very limited.

Aims & Methods: We aimed to study (1) clinical outcome of patients with a minimum post-POEM follow-up of 2 years and (2) factors associated with long term clinical failure after POEM. Methods: We conducted a retrospective review of consecutive patients with achalasia who underwent POEM with a minimum follow-up of 2 years at 10 tertiary-care centers (3 US, 4 Europe, 3 Asia and 1 Australia). Clinical response was defined as at least 30% decrease in LES pressure at 6 months. Results: A total of 179 patients (82 males (45.8%); mean age 49 year) underwent POEM for the treatment of achalasia (type I 111, type II 51, type III 6, unspecified type 11). Of these, 16 patients (8.9%) had prior Heller myotomy, 65 (36.6%) had prior pneumatic dilatation (PD) and 63 (35.4%) had prior botulinum injection. POEM was successfully completed in all patients. A total of 18 adverse events occurred in 8 (4.4%) patients (8 mucosotomies, 1 delayed bleeding, 1 esophageal leak, 2 DVT/PE, 1 pneumothorax, 2 symptomatic pleural effusion, 2 aspiration pneumonia and 1 mediastinitis). Clinical success was achieved in 97.5% (159/163), 99.8% (124/125), 90% (116/130) at 6, 12 and 24 months, respectively. Of 159 patients with clinical response at 6 months, 11 (7%) had major complications including perforations, and fistulas. Surgical Endoscopy 2010; 25(9): 2901-5.
POEM (n = 1) and Heller myotomy (n = 2) and clinical response was noted in 2 of them. Of 171 patients with available data, 24% of patients reported reflux symptoms after POEM. Reflux esophagitis was noted in 26 patients of 144 (18%) who had EGD after POEM. 15% of asymptomatic patients had reflux esophagitis. **Conclusion:** POEM is safe and provides high initial clinical success and excellent long-term outcomes. Less than 10% of patients who had clinical response at 6 months had recurrent symptoms at 2 years. History of prior pneumatic dilatation is associated with clinical failure. Post-POEM symptomatic reflux occurs in quarter of patients and esophagitis is found in 15% of asymptomatic patients.

**Disclosure of Interest:** S. Roman: Sabine Roman is a consultant for Medtronic and Sandhill Scientific F. Mion: Francois Mion is a consultant for Medtronic M. Kashhab: Mouni Kashhab is a consultant for Boston Scientific All other authors have declared no conflicts of interest.

OP155 A 5-YEAR LONG POEM EXPERIENCE. IS IT TIME TO DRAW CONCLUSIONS?

P. Familiar1, A. Calì1, R. Landi1, G. Gigante1, A. Tringali1, I. Boskoski1, V. Bove2, V. Perri2, F. Borrelli De Andreis2, G. Costamagna2

1Digestive Endoscopy Unit, Catholic University - Gemelli University Hospital, Roma, Italy
2IUSS Strasburg University, Strasbourg, France, Strasbourg/France

Contact E-mail Address: pietrofamiliar@iscali.it

Introduction: Peroral Endoscopic Myotomy (POEM) has been recently developed for the treatment of achalasia and other esophageal motility disorders. Despite being widely used in many centers, data on the long-term efficacy of POEM are still lacking. We report on a large consecutive series of patients treated with POEM, with mid- and long-term follow-up.

**Aims & Methods:** All the patients who underwent POEM between May 2011 and April 2016 at our endoscopy unit were retrospectively identified on a prospectively collected database. Analyzed data included demographics, clinical history, previous treatments, manometry and procedure data, complications and clinical outcomes. Follow-up visits were scheduled at 3, 6, 12, 24, 36, 48 and 60 months after POEM. EGD, manometry and barium swallow were regularly performed during follow-up. pH-monitoring study was performed once, usually between the 6- and 12-month follow-up visit. Clinical success was defined by an Eckardt score ≤ 3.

**Results:** A total of 347 patients underwent POEM (mean age 47 years, 48% males). Seventy-eight patients (22.5%) had type I achalasia, 174 type II (50.1%), 40 type III (11.5%), 2 Jackhammer esophagus (0.6%), 4 distal esophageal spasm (1.1%), 1 nutcracker esophagus (0.3%); in 48 patients (13.8%) achalasia type was not classified (ie: standard manometry or incomplete examination).

A total of 274 patients (mean follow-up 19 months). Clinical success was available for 274 patients (mean follow-up 19 months). Clinical success was achieved in 95% of patients. Thirty patients had symptoms recurrence: 7 underwent successful PD, 3 surgery, 3 received no treatment because of mild symptoms. Clinical success slightly decreased with time, being 97%, 97%, 93%, 85%, 72% and 67% after 6, 12, 24, 36, 48 and 60 months, respectively. However, almost 50% of recurrences (6/13) occurred during the first 25 cases (learning curve). No associations were found between preoperative manometric pattern and clinical outcomes: the success rate of POEM was similar in patients with type I, type II and type III achalasia (94%, 96% and 91%, respectively. **p > 0.05.** A total reflux time > 5% was diagnosed in 50% of the patients (111/223) who underwent pH-study. Esophagitis was seen in 28% of patients, 22% of patients receive PPI because of heartburn. Esophagitis healed completely with proton pump inhibitors (PPI) in all the patients. GERD symptoms after POEM. Reflux esophagitis was noted in 26 patients of 144 (18%) who had EGD after POEM. 15% of asymptomatic patients had reflux esophagitis. **Conclusion:** POEM is safe and provides high initial clinical success and excellent long-term outcomes. Less than 10% of patients who had clinical response at 6 months had recurrent symptoms at 2 years. History of prior pneumatic dilatation is associated with clinical failure. Post-POEM symptomatic reflux occurs in quarter of patients and esophagitis is found in 15% of asymptomatic patients.

**Disclosure of Interest:** All authors have declared no conflicts of interest.
were similar between the two groups. Multivariate analysis demonstrated prior HM (adjusted OR 2.91, p 0.05) was marginally associated with clinical failure after POEM. Post-POEM symptomatic improvement of the mean half emptying time (222 ± 44 vs. 90 ± 20; p < 0.001). Two patients underwent complications related to the procedure: one was a bleeding due to an ulceration along the tunnel path (coagulation necrosis) treated by endoscopy, while the other a sternal insufficiency and was transferred to intensive care unit; the second had a secondary perforation of an esophageal ulcer, which was managed endoscopically by a naso-cystic drain and fasting, with excellent outcomes. All the other patients could be refeed at POD2-3, and discharged at POD5-6, with PPI treatment.

Conclusion: Per-oral endoscopic pyloromyotomy seems to be an effective approach for treating patients with severe refractory gastroparesis. This procedure is also highly reproducible, when applying some tips to increase the technical success rate, and safe with complication that could be managed endoscopically. It could be a new hope for many patients who have a poor quality of life. More data, especially in prospective studies are needed to confirm these very promising results.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

TUESDAY, OCTOBER 18, 2016 08:30–10:00
LIVER FIBROSIS: FROM MECHANISM TO THERAPY - ROOM 1.61/1.62

OP158 GASTROPERORAL ENDOSCOPIC ANTERO-PYLORO-MYOTOMY FOR THE TREATMENT OF REFRACTORY GASTROPARESIS: LARGEST SERIES WITH CLINICAL AND SCINTIGRAPHIC FOLLOW-UP
J. Gonzalez, V. Lestelle, A. Benezech, V. Vitton, M. Barthet
Dept. De Gastroenterologie, APHM - North Hospital, Marseille/France

Contact E-mail Address: jmgonzalez@yahoo.fr

Introduction: Gastroparesis is an invalidating motility disorder and the available treatments remain disappointing. Recently, a novel approach has been proposed by performing a myotomy of the pylorus after creating a tunnel, with promising results [1–3]. We report the largest retrospective clinical experience in 23 consecutive patients treated by gastric peroral endoscopic myotomy (G-POEM). The aim was to report the results of this new technique.

Aims & Methods: This is a case consecutive report on 23 patients operated for severe refractory gastroparesis, between January 2014 and April 2016, with a rigorous prospectively designed follow-up. The inclusion criteria were patients with gastric emptying scintigraphy (GES) and elevated GCSI score (> 2). The procedures were performed under general anesthesia in an intubated patient, with large channel gastroscope using CO2 and the Triangle knife (Olympus, Japan) as dissection device. The steps were: sub-mucosal injection and mucosal incision 5 cm upstream the pylorus; submucosal tunnel by dissection (Swift Coag, 35W, Effect 2) until reaching the pyloric arch, which had a consistent aspect; retrograde antro-pyloro-myotomy of 3cm length; closure of the mucosal flap with clips. The primary objective was to define by decrease in ES to <2. Adverse events (AEs) were graded according to the ASGE lexicon. Technical success, clinical success and AE were compared between the two groups.

Results: A total of 181 patients (91 HM, 90 controls) were included. There was no difference between the groups in baseline demographics, ES and 4IRP. The HM group had a higher number of patients with prior PD (44% vs 26% p 0.01). The length of myotomy was similar between the two groups. Technical success rates were comparable between HM group (89/91; 98%); 2 failures due to extensive submucosal fibrosis) and control group (100%) in control group (p 0.04). Post-POEM symptomatic improvement between the two groups. The mean follow-up was 8.5 months (IQR 3.2–14.7) and was similar in both groups. AEs occurred in 19 patients (7% in HM group and 12% in control group, p 0.23). For HM and control respectively, the rate of mild (5% vs 10%, p=0.28) and moderate (1% vs 0%, p=0.34) AEs were similar. One severe AE (mediastinitis) occurred in the HM group. Follow-up data were available in 153 patients. Clinical response was significantly lower in the HM group as compared to the control (80% vs 94%, p 0.02). Mean post-POEM ES was also higher in the HM group (2.5 ± 4.5 vs 1.9 ± 2.1; p 0.02). On univariate analysis, prior HM (OR 3.54, p 0.02) and prior PD (OR 3.36, p 0.01) were significantly associated with clinical failure. Multivariate analysis demonstrated prior HM (adjusted OR 2.91, p 0.05) was marginally associated with clinical failure after POEM. Post-POEM symptoms were managed with oral relox esophagitis and abnormal pH acid exposure were similar between the two groups.

Conclusion: In this large multicenter study, POEM was safe and effective for achalasia patients, and failed prior HM. Although rate of clinical success in patients with prior HM is lower than those without prior HM, the safety profile of POEM is comparable to that of patients with no prior HM.

Disclosure of Interest: S. Roman: Sabine Roman is a consultant for Medtronic

OP159 EXPRESSION OF CONSTITUTIVELY ACTIVE IKK2 LEADS TO LIVER FIBROSIS AND INCREASED CARCINOGENESIS IN THE BACKGROUND OF LIVER SPECIFIC TRP53 DELETION
M. Svinarenko1, S. F. Katz2, S. Fischer1, H. Maier2, A. Tannapfel1, T. Seufferlein1, A. Lechel1
1 Internal Medicine I, University Hospital Ulm, Ulm/Germany
2 Department Of Surgery, Baystate Medical Center, Tufts University School of Medicine, Boston/USA
3 Pathological Institute, Ruhr University Bochum, Bochum/Germany

Contact E-mail Address: michael.svinarenko@uni-ulm.de

Introduction: Liver carcinoma is of particular importance, since it is a leading cause of cancer-related deaths worldwide. Most frequently liver tumors are arising from an inflammatory milieu following a sequence of regenerative nodules, which primarily develop subsequently due to chronic liver diseases. Another circumstance contributing to liver cancer formation is the disruption of the p53 signaling pathway. In human liver tumors, p53 mutations are associated with a poor prognosis. In this study, we analyzed the cooperation between loss of p53 and inflammatory response in the liver.

Aims & Methods: To investigate the sequence of inflammation and Trp53 deletion, we combined two transgenic mouse models. For modulation of an inflammatory response, we used a inducible mouse model (Tet-Off system) with a permanent expression of a constitutively active IKK2 isoform (CAIKK2). The expression of CAIKK2, starting from birth, leads to a continuous activation of the NF-κB pathway, simulating chronic inflammation. For the modulation of a p53 deletion, the inducible CAG-creERT2 allele line AlfpCre-ERT2 was crossed with a conditional Trp53 knockout mouse. Tamoxifen treatment at the age of four weeks induces liver-specific deletion of Trp53.

Results: Expression of the constitutively active IKK2 isoform leads to liver fibrosis development, increased proliferation in the liver and elevated expression of inflammatory markers independent of the p53 status. During ageing, the CAIKK2 expression and the inflammatory response decreased, the liver fibrosis showed a sustained increase. The tumor incidence of the age of 9-12 month in CAIKK2-Trp53Δ/Δ mice is significantly higher (67%) compared to CAIKK2 mice with wild-type Trp53 (25%). Mice with induced liver-specific Trp53 deletion did not exhibit liver tumor formation at the same age. The majority of liver tumors in CAIKK2-Trp53Δ/Δ mice show intrahepatic cholangiocarcinoma (ICC) (91%) next to hepatocellular carcinoma (2%) and combined HCC/ICC (17%). In contrast, CAIKK2 mice with wild-type Trp53 developed mainly HCC (50%), but also ICC (25%) and HCC/ICC (25%) at lower level.

Conclusion: The study shows that liver-specific Trp53 deletion in combination with an inflammatory background results in elevated tumor incidence and leads to an increased occurrence of ICCs in the liver.

Disclosure of Interest: All the authors have declared no conflicts of interest.
OP160 EXPRESSION OF CD161 ON CD4+ T CELLS PROMOTES HBV REPLICATION AND THE DEVELOPMENT OF HBV-INDUCED SPHINGOMYELINASE AND CD161-LECTIN-LIKE TRANSIENT INTERACTION

L. Cheng, S. Wang, W. Jiang
Gastroenterology, Zhongshan Hospital of Fudan University, Shanghai/China

Contact Email Address: 14212112003@fudan.edu.cn

Introduction: Hepatitis B virus (HBV)-related liver fibrosis always progresses from inflammation to fibrosis. CD4+ T cell immune responses play a pivotal role in the process. Recently, CD161 is considered to be a costimulatory molecule on T cells and an important phenotypic marker of human Th17 cells. Aims & Methods: This study was designed to investigate the roles of CD161 in the pathogenesis of HBV-related liver fibrosis. Methods: A total of 34 CHB patients who underwent liver biopsy and 20 healthy controls (HC) were enrolled. CHB patients were further categorized according to the disease phase: immune-tolerant (IT, n = 12), immune-active (IA, n = 30), or inactive CHB (n = 12). Peripheral blood mononuclear cells (PBMCs) and flow cytometry sorted CD4+CD161+ and CD4+CD161- T cells were prepared for further flow cytometric and real-time PCR analyses. Flow cytometry sorted CD4+CD161+ and CD4+CD161- T cells were also cultured alone or co-culture with primary hepatic stellate cells (HSCs) in vitro experiments. Results: Compared to HC, the percentage of CD4+CD161+ T cells significantly increased among IA patients while dramatically decreased among IT patients; but there was no significant difference between inactive CHB patients and HC. Besides, CD161 showed a positive correlation with histological inflammation grades and advanced histological fibrosis stages. In the PBMCs of CHB patients, CD4+CD161+ T cells exhibited a CD45RO- memory phenotype and secreted more IFN-gamma, TNF-alpha, IL-17, IL-21 and IL-4 whereas produced less IL-10 and IL-12 than CD4+CD161- T cells. In comparison with CD4+CD161+ T cells, in vitro culture of CD4+CD161+ T cells revealed that CD161 expression increased the activity of acid Sphingomyelinase (aSM) and subsequent PI3K/Akt, MAPK and mTOR pathways of CD4+ T cells. Both knocking down of CD1 and using imipramine to inhibit aSM could down-regulate CD4+ T cell-proliferation and production of IFN-gamma and IL-17, especially for IL-17. HSCs express lectin-like transcript-1 (LTL1), the only ligand of human CD161. HBxAg-stimulated HSCs upregulated LTL1 expression in the co-culture system of HSCs and CD4+CD161+ T cells, CD161-LTL1 interaction not only promoted the proliferation and activation of HSCs, but increased IL-17 and IFN-gamma production of CD4+CD161+ T cells as well. Knocking down of CD1 and on CD4+ T cells or LTL1 on HSCs could partially reverse the aforemen- tioned effects. In HSCs-CD4+CD161+ T cells co-culture system, expression of pro-fibrotic genes in HSCs were inhibited. However, when CD161 was overexpressed on CD4+CD161- T cells, we detected a reactivated HSCs phenotype. Conclusion: Our data revealed that the expression of CD161 on CD4+ T cells might promote HBV-related liver fibrosis through CD161-LTL1 interaction to activate HSCs and through raising aSM to enhance the proinflammatory functions of CD4+ T cells. Disclosure of Interest: All authors have declared no conflicts of interest.

References
2. L J, Qin SJ, She WM, Wang FP, Gao H, Li L, Tu CT, Wang JY, Shen XZ and Liu JZ. Significance of the balance between regulatory T (Treg) and T cells or LLT1 on HSCs could partly reverse the aforemen- tioned effects.

OP162 THE ACCURACY OF WAVSTAT4 VERSION 4 OPTICAL BIOPSY FORCEPS IN CHARACTERIZING COLORECTAL POLYPS LESS 10 MM: A PROSPECTIVE BLINDED STUDY

N. Mohammed1, R. Sood2, S.V. Venkatachalapathy3, F. Abid1, N. Burr1, P. Chehla1, J. Meadows1, J. Carberry1, O. Rotimi1, V. Varma1, L. Cheng1, S.W. Jiang1
1Gastroenterology, St. James’s University Hospital NHS Trust, Leeds/United Kingdom
2University Of Leeds, Leeds Institute of Biomedical and Clinical Sciences, Leeds/ United Kingdom
3A66 - United European Gastroenterology Journal 4(5S)

Contact Email Address: Faisal.Abid@nhs.net

Introduction: Optical biopsies of colorectal polyps < 10 mm in size could potentially replace standard histological assessment. WaveSTAT version 4 is a novel optical biopsy system designed by Spectrascience Inc, San Diego, California, USA, for prediction of histology based on laser induced autofluorescence spectroscopy. Aims & Methods: The primary aim of this study was to demonstrate the accuracy of WaveSTAT version 4 in characterizing colorectal polyps < 10 mm that can be resected or discarded (or left intact) without adverse clinical impact. The second aim was to compare the real time diagnostic performance of WaveSTAT version 4 with NBI and a combination of endoscopic and WaveSTAT assessments. Patients attending the endoscopy unit for lower gastrointestinal endoscopy as requested by their responsible physician were approached to participate in the study. Adult patients aged 18 years were included.

Disclosure of Interest: R. W. Leong: Endoscopy USA investigator-initiated study. All other authors have declared no conflicts of interest.

Table (OP162): Diagnostic performance of WAVstat4, Endoscopic assessment and combined algorithmic assessment for characterization of colorectal polyps less than 10 mm in size and prediction of surveillance intervals

<table>
<thead>
<tr>
<th>WaveSTAT alone</th>
<th>WL+E-NBI assessment</th>
<th>Combination of WaveSTAT + endoscopic assessment (algorithmic approach)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sensitivity</td>
<td>97.6% (95% CI 0.88–0.95)</td>
<td>85.0% (95% CI 0.77–0.89)</td>
</tr>
<tr>
<td>Specificity</td>
<td>46.9% (95% CI 0.44–0.48)</td>
<td>77.2% (95% CI 0.61–0.82)</td>
</tr>
<tr>
<td>NPV</td>
<td>96.8% (95% CI 0.85–0.91)</td>
<td>91% (95% CI 0.73–0.84)</td>
</tr>
<tr>
<td>PPV</td>
<td>54.7% (95% CI 0.28–0.47)</td>
<td>66% (95% CI 0.44–0.79)</td>
</tr>
<tr>
<td>Surveillance interval (% of patients coded correctly)</td>
<td>81.2%</td>
<td>97%</td>
</tr>
<tr>
<td>Surveillance interval (% of patients called earlier)</td>
<td>18.8%</td>
<td>3%</td>
</tr>
</tbody>
</table>

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Patients known to have inflammatory bowel disease or colorectal cancer were excluded from the study. Polyps size <10 mm were assessed in real time by high definition white light, NBI and WavSTAT version4 optical biopsy forceps. Standard techniques were used for polypectomy. Histopathological specimens were read separately by two expert GI pathologists blinded to the results of the WavSTAT assessments. The primary outcome measure was the negative predictive value in distinguishing adenomatosus from non-adenomatosus colorectal polyps. The secondary outcome measure was the accuracy of on-site recommended surveillance intervals.

Repolys were <10 mm and 10 were >10 mm were found in 70 patients (Males-44, females-27). Average age of the patients was 65 years (range 29–95 years). 16 polyps were not included in the final analysis due to discrepancy in histological analysis between two pathologists. We failed to retrieve 5 polyps. 28 patients were excluded from the study (No polyps seen in 17 patients, polyps <10 mm were not seen in 3 patients, and device failure in 4 patients). A total of 126 polyps <10 mm were included in final analysis. The diagnostic performance for WavStat version 4 and endoscopic assessment is detailed in the table. Wavstat4 had a NPV of 96.8% and predicted 100% of surveillance intervals approach where we classified the polyps according to the WavSTAT4 result when mainly for hyperplastic recto-sigmoid polyps we evaluated an algorithmic for WavStat version 4 and endoscopic assessment is detailed in the table. Endoscopic assessment had a NPV of 95.8% and predicted 100% of surveillance intervals correctly in 80% of patients. An algorithmic approach combining Wavstat4 and endoscopic assessment had a high NPV with accurate prediction of surveillance intervals.

Conclusion: WavSTAT version 4 has a high NPV for characterizing colorectal thresholds and had a NPV of 95.8% and predicted 100% of surveillance intervals approach where we classified the polyps according to the WavSTAT4 result when mainly for hyperplastic recto-sigmoid polyps we evaluated an algorithmic for WavStat version 4 and endoscopic assessment is detailed in the table.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP164 A ROLE FOR T CELL CLONAL EXPANSIONS IN THE POST-OPERATIVE RECURRENT IN CROHN’S DISEASE: A STUDY FROM THE REMIND GROUP

M. Allez1, M. Ngollo1, C. Stefanescu2, C. Auzolle1, S. Nancey3, F. Djendji4, M. Nachury5, A. Buisson6, H. Sokol7, X. Treton8, N. Barnich9, P. Seksik1, L. Le Bourhis1

1) Gastroenterology, Hopital Saint-Louis, APHP, INSERM U1157, Université Denis Diderot, Paris/FRANCE
2) Service De Gastroenterologie Et Assistance Nutrition, Beaufour Hospital, Clichy, Clichy/FRANCE
3) Gastroenterologie, Hospiatles de Lyon, Pierre Benite/France
4) Gastroenterology, Claude Huriez hospital, University of Lille 2, Lille/France
5) Dept. Of Gastroenterology, CHU Estauing Clermont-Ferrand, Clermont-ferrand/FRANCE
6) Avenir Team Gut Microbiota, INSERM U1157/UMR CNRS 7503, UPMC, Paris/FRANCE
7) Hospital Beaujon, Clichy/FRANCE
8) UMR 1071 Insen/Institute of Averpge, Clermont-Ferrand/FRANCE

Contact Email Address: matthieu.allez@dh.ap-hp.fr

Introduction: Operative resection in Crohn’s disease is not curative. Indeed, a majority of CD patients undergoing ileocecal resection have an endoscopic recurrence in the neo-terminal ileum as soon as six months after surgery. T cells are major players in the intestinal immune response. We previously demonstrated the persistence of T cell clonal expansions over time in the inflamed mucosa of CD patients [1]. The presence of T cell clonal expansions at time of surgery could play an important role in the post-operative recurrence.

This study was to explore the impact of the presence of T cell clonal expansions in the inflamed tissue at time of surgery on the risk of post-operative endoscopic recurrence, and to analyse the correlation between the persistence of these T cell clones in the neo-terminal ileum and inflammatory status. The REMIND Post-Operative study has been performed in 9 centers, collecting data at time of surgery (M0) and of endoscopy (performed at M6), associated with an extensive bio-banking. Clinical, biological and endoscopic parameters were collected at month 6. Endoscopic recurrence was defined by a Rutgeerts score ≤1. Biopsies of ileal mucosa were collected on surgical specimen and by endoscopy six months after surgery, T cell Receptor (TCR) analysis was performed on DNA extracted from biopsies by next generation sequencing (Adaptive Biotechnology Inc., Seattle, Washington, USA). The TCR repertoire was analyzed in biopsies obtained on the surgical specimen and during the control endoscopy at six months. Sequences, numbers, frequencies and clonality indexes were assessed; and further analyzed to determine TOP100 clone frequencies and persistent clonal expansions present at both M0 and M6 in each patient. Remaining seven patients of the REMIND cohort were analyzed. 53 (68%) were male; median age at surgery was 38 years old (±14). We found that the TCR repertoire in biopsies from CD patients display a large number of unique TCR sequences (mean 10000 unique sequences) suggesting a high variety of T cell specificities. However, measures of diversity of the TCR repertoire showed an important range of clonality within the cohort (0.001 to 0.5). Importantly, the frequency of the 100 most represented clones in the tissue at M0 was significantly increased in patients with endoscopic recurrence (Rutgeerts score≥1) at M6. Furthermore, in patients with endoscopic recurrence, the presence of persistent clones (present at M0 and M6) was significantly increased in patients who had an endoscopic recurrence. High or low proportion of persistent clones could define two subgroups of patients with endoscopic recurrence in regard to their TCR repertoire. Interestingly, expanded clones could be found in different T cell subsets.

Conclusion: T cell clonal expansions in the inflamed tissue at time of surgery and during control endoscopy in the neo-terminal ileum are associated with post-operative endoscopic recurrence in Crohn’s disease.

Disclosure of Interest: M. Allez: I received honoraria from MSD, Abbvie, Janssen, Novo Nordisk, Novartis, Takeda, Genentech, UCB, Pfizer, Ferring All other authors have declared no conflicts of interest.

Reference

OP165 TARGETED CHEMICAL ANALYSIS OF THE COLON CANCER MICROBIOME USING DESORPTION ELECTROSPRAY IONISATION MASS SPECTROMETRY IMAGING (DESI-MSI)

J. Alexander1, A. Mroz2, A. Perdones-Montero3, A. Scott1, L. Gileda4, S. Cameron1, F. Bold5, F. Rosin6, R. Goldin7, J. Mckenzie8, A. Burke9, N. Koundouros1, A. Darzi1, G. Poulogiannis4, D. Cunningham1, J. Nicholson2, J. Marchesi6, Z. Takats1, J. Kinross1, J. Teare3

1) Surgical & Cancer, Imperial College London, London/UNITED KINGDOM
2) Computational & Systems Medicine, Imperial College London, London/UNITED KINGDOM
3) Surgery & Cancer, Imperial College London, London/UNITED KINGDOM
4) Institute for Cancer Research, London, London/UNITED KINGDOM
5) Royal Marden Hospital, London/UNITED KINGDOM
6) Centre For Gut Health, Imperial College London, London/UNITED KINGDOM

Contact Email Address: j.alexander@imperial.ac.uk

Introduction: The gut microbiome is an important modulator of colorectal (CRC) cancer risk. Here we describe a novel methodology for the targeted analysis of the
colon cancer microbiome using mass spectrometry imaging in a prospective cohort of CRC patients.

Aims & Methods: A prospective, multi-centre observational study was performed on patients undergoing elective resections for colorectal cancer at Imperial Healthcare NHS Trust and the Royal Marsden Hospital. Fresh mucosal tissue was obtained to ensure adequate conditions from cancers and adjacent normal tissue and frozen at −80°C. Using 16s rRNA sequencing analysis of corresponding tissue samples performed in Mother and Stamp, target bacteria including Faecalibacterium spp, E.Coli and Bifidobacteria were identified. A chemical database of lipid species was created using Rapid Evaporative Ionisation Mass Spectrometry (REIMS) from pure cultures of the target microbes. Desorption Electrospray Ionisation Imaging Mass Spectrometry (DESI-MSI) was then performed to provide a spatially resolved map of the mucosal microbial lipidome. Tissue samples were then desorbed onto the target plate for using chemical spectra identified by REIMS. Candidate microbial lipids were validated using cell co-culture experiments and analysis with REIMS. Multivariate analysis was performed using Matlab (Mathworks) and R. Both unsupervised Principle Component Analysis and supervised Linear Discriminant Analysis were performed. ANOVA was used to perform statistical analysis of single lipid species.

Results: 26 patients with sporadic colorectal cancer were recruited (17 women, median age 68, range 35–84, median BMI 27 kg/m²). Eight tumours were right sided, eleven were left sided and seven were rectal. Two patients had neo-adjuvant chemoradiotherapy. Histology showed six adenomas, one T1, six T2, ten T3 and three T4 cancers. Using DESI-MSI it was possible to geometrically identify distinct anatomical regions based on co-variation of the chemical data independently validated H&E stained tissue. Using leave one patient out cross validation, DESI-MSI was able to diagnose cancer from normal mucosa with ROC AUC = 97.5. Increased long chain fatty acids were seen in malignant tissue whereas glycerophospholipids were seen in healthy mucosa (both p < 0.001). Target spectra just specific to the mucosa were then extracted for analysis. This revealed 102 lipid species that differentiated colon cancer from healthy mucosa (both p < 0.01). The top 10 most significantly associated lipids with ROC AUC ≥ 0.975 were positively correlated with disease, with the top species being long chain fatty acids (e.g., 14:0, 16:0, 18:0, 20:0, 22:0). These lipid species were significantly enriched in malignant tissue compared to normal tissue.

Conclusion: Chemical mapping of the colonic lipidome permits spatially resolved analysis of the cancer microbiome and its metabolic functions, and this has diagnostic value. DESI-MSI provides a completely novel methodology for studying microbial-host interactions critical to the aetiology of inflammation and cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP0066 UNSUPervised TRANSCRIPTomics-BASEd CLUSTERING OF ULCerative COLiTS PATiENTS REVEals MARKed HETEROGENeITY THAT RELATED TO ANti-TNF tREATMENT RESPONSE

C. Monast, A. Stojmirovic, R. Dobrin, C. Brodmerek, F. Baribaud
Immunology, Janssen Research and Development, LLC, Spring House/United States of America/Pennsylvania

Introduction: Heterogeneity in IBD patient populations is widely cited as the main barrier to efficient clinical trials and development of therapies with high clinical efficacy. We and others hypothesize that phenotypic heterogeneity is a direct result of molecular heterogeneity in disease-driving molecular pathways. We want to apply this hypothesis to the most extensively explored area of defining molecular heterogeneity in a manner independent of known biology.

Aims & Methods: Whole-genome transcriptomic data was generated for colonic biopsies randomly selected to severely affected, moderately affected and healthy normal controls. Subjects were scored based on enrichment of 113 co-expression modules, or lists of correlated genes, derived from colonic biopsies from both UC and CD biopsies. Scores for each subject and co-expression module were computed using the gene set variation analysis algorithm. Coexpression modules were then hierarchically clustered into 4 module clusters and annotated with pathways using the union of genes within each of the 4 module clusters. Each subject was then reclassified based on the 4 module clusters by taking the median enrichment score of the modules within each module cluster. IBD subjects and normal controls were then hierarchically clustered into 4 subgroups using the 4 module clusters and assessed for relationship to anti-TNF response.

Results: The 4 module clusters represented distinct pathway sets which we summarized as inflammation/mucositis, mucosa/pro-regulatory, T cells/metallobiosis and mitochondria/metabolism. Patients belonging to the subgroup characterized by the highest enrichment for the inflammation/mucositis module cluster trended towards lower expression related to anti-TNF therapy. Conversely, the highest response rates to anti-TNF therapy were observed in the subgroup characterized by the lowest enrichment for the inflammation/mucositis module cluster. These subgroups also contained normal healthy controls. Enrichment values for the inflammation module cluster are presented (r = −0.49) with enrichment values for the inflammation/mucositis module cluster.

Conclusion: We find that there is pronounced molecular heterogeneity in the pathways present in colorectal biopsies from UC patients. We also show that this heterogeneity is linked to the ability of patients to respond to anti-TNF therapy. This suggests that molecular stratification may be a key step towards designing smaller clinical trials and identifying meaningfully personalized medicine approaches for IBD patients.


OP0167 COMPREHENSIVE CIRCULATORY TRANSCRIPTOME AND PROTEOMIC PROFILING IN NEWLY DIAGNOSED INFAMMATORY BOWEL DISEASES: A MULTI-CENTRE COHORT STUDY

R. Kalla1, A. T. Adams1, J. Lindstrom2, Ibd Character Consortium1, M. J. Pierik8, F. Gomollon9, M. D’Amato10, J. Halfvarson11, J. Satsangi1
1Centre For Genomics and Experimental Medicine, University of Edinburgh, Edinburgh/United Kingdom 2Department Of Gastroenterology, University of Oslo, Oslo/Norway 3Inst. Of Clinical Medicine, University of Oslo, Oslo/Norway 4Department Of Gastroenterology, Akerhus University Hospital, Lorenskog/Norway 5Department Of Gastroenterology, Oslo University Hospital, Oslo/Norway 6Department Of Gastroenterology, Ørøbro University, Ørøbro/Sweden 7University Hospital, Linköping University, Linköping/Sweden 8Dept Of Gastroenterology and Hepatology, Maastricht University Medical Center, Maastricht/Netherlands 9Instituto De Endoscopia Digestiva, Hospital Clinico Universitario Lozano Blesa, Zaragoza/Spain 10Unit Of Molecular Genetics Of Digestive Diseases, BiOcruces Health Research Institute, Bilbao/Spain 11Dept. Of Internal Medicine, Ørøbro University Hospital, Ørøbro/Sweden

Contact E-Mail Address: rahul.kalla@kcl.ac.uk

Introduction: There is an unmet need to gain functional insights into pathways that are relevant in Inflammatory Bowel Diseases (IBD). By performing transcriptomic and proteomic profiling in newly diagnosed IBD, we can gain an understanding into the molecular mechanisms that may be relevant in disease.

Aims & Methods: Gene expression patterns from whole blood RNA and proteomic profiles from serum were assessed from patients using targeted RNA-seq (Iex AmpSeq Transcriptome Human Gene Expression platform) and Olink multiplex protein panels (Olink Proteomics). Treatment-naive newly diagnosed IBD and healthy symptomatic controls were included in the study. Phenotypic data were captured including demographics and disease classification. Statistical analysis was performed using R. Differentially expressed transcriptomes were correlated with serum protein expression to obtain a circulating profile at diagnosis.

Results: RNA expression profiles were available in 639 patients (351 IBD, 288 controls). A total of 567 genes were differentially expressed between IBD and controls. Using hscRP to adjust for inflammatory status, 1440 remained significant. The most differentially expressed genes were CD-177 (Bonferroni corrected p = 2.3x10⁻⁶), VBPI (p = 2.9x10⁻⁶) and S100 proteins (S100A9, S100A10 and S100A12) (p = 2.7x10⁻⁶). Protein expression profiles were available in 635 patients (152 CD, 159 UC, 26 IBD-U, 298 non-IBD). Multivariable analysis identified 59 protein markers that were significantly associated with IBD. The top significant protein upregulated in IBD included MMP12 (Hollander corrected p = 4.1×10⁻⁹) and albumin (p = 1.7×10⁻⁸). Differentially expressed protein expression profiles were available and correlated with RNA expression. 39 proteins showed significant correlation with gene expression including OSM (rho = 0.51), MMP12 (rho = 0.49) and albumin (rho = 0.33, p = 3.4×10⁻⁵) with other markers such as CXCL9 show poor correlation (rho = 0.16, p = 0.04). As biomarkers, top 2 serum markers were able to discriminate IBD from controls with a similar area under the receiver operator characteristics curve (AUC) of 0.75 and 0.74 respectively. Individually these markers outperformed hscRP (n = 619, AUC 0.64, p for comparison = 2.7x10⁻⁴ vs. MMP12) and albumin (AUC 0.66, p = 0.004 vs MMP12). 6 proteins differentially up from CD including MMP12 (p = 4.6x10⁻⁹). In CD, MMP12 levels were lower in those with small bowel involvement (Montreal Classification L1, L3 and L4 vs L2) (p = 0.009) while in UC, MMP12 levels were significantly higher in extensive disease (Paris classification E1 and E2 vs. E3, p = 5.8x10⁻⁸).

Conclusion: This is the largest integrative multicentre characterisation of the circulating expression profile studied in IBD at diagnosis. These data identify key pathways that may be relevant in IBD pathogenesis and demonstrate the translational potential of these markers in diagnosing and classifying IBD.

Disclosure of Interest: R. Kalla: Funded by IBD Character Imaging and Proteomics research (Department) MSD J. Satsangi: JS has served as a speaker, a consultant and an advisory board member for MSD, Tillot, Ferring, AbbVie, Celltrion, Orion Pharma, Takeda, Napp Pharm, Meda, AstroPharma, Hilma and Pfizer. F. Gomollon: Advisor: Griffols, Abbvie, MSD. Travel Grants: Abbvie, MSD. R. Dobrin: Employee of Janssen Research Funding (Department) MSD J. Halfvarson: Employee of Janssen Research Funding (Department) MSD M. J. Pierik: Employee of Janssen Research and Development, LLC F. Baribaud: Employee of Janssen Research and Development, LLC
Table 1 (OP168): Demographics, procedural outcomes, bowel cleanliness and adenoma detection.

<table>
<thead>
<tr>
<th>Demographics</th>
<th>WE N = 408</th>
<th>WI N = 408</th>
<th>AI N = 408</th>
<th>ANOVA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Females, n (%)</td>
<td>184 (45.1)</td>
<td>185 (45.3)</td>
<td>183 (44.9)</td>
<td></td>
</tr>
<tr>
<td>Males, n (%)</td>
<td>224 (54.9)</td>
<td>223 (54.7)</td>
<td>225 (55.1)</td>
<td></td>
</tr>
<tr>
<td>Age, mean (SD)</td>
<td>61.4 (6.2)</td>
<td>61.0 (6.3)</td>
<td>60.9 (6.2)</td>
<td>0.261†</td>
</tr>
<tr>
<td>Body Mass Index, mean (SD)</td>
<td>26.4 (4.1)</td>
<td>26.4 (4.4)</td>
<td>26.6 (4.4)</td>
<td>0.751‡</td>
</tr>
</tbody>
</table>

Indications for colonoscopy, n (%)

<table>
<thead>
<tr>
<th></th>
<th>WE</th>
<th>WI</th>
<th>AI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Right colon ADR</td>
<td>63 (25.9)</td>
<td>32 (17.2)</td>
<td>26 (13.7)</td>
<td>0.059†</td>
</tr>
<tr>
<td>Overall ADR</td>
<td>148 (53.8)</td>
<td>94 (41.4)</td>
<td>88 (38.8)</td>
<td>0.173</td>
</tr>
<tr>
<td>Right colon ADR</td>
<td>98 (24.0)</td>
<td>78 (19.1)</td>
<td>69 (16.9)</td>
<td>0.089†</td>
</tr>
<tr>
<td>Overall ADR</td>
<td>201 (49.3)</td>
<td>177 (43.4)</td>
<td>165 (40.4)</td>
<td>0.249‡</td>
</tr>
</tbody>
</table>

Procedural outcomes

<table>
<thead>
<tr>
<th></th>
<th>WE</th>
<th>WI</th>
<th>AI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cecal intubation rate (final), n (%)</td>
<td>402 (98.5)</td>
<td>400 (98.0)</td>
<td>399 (97.8)</td>
<td>0.590‡</td>
</tr>
<tr>
<td>Cecal intubation time, mean (SD), min</td>
<td>10.1 (5.4)</td>
<td>9.7 (6.7)</td>
<td>9.5 (6.3)</td>
<td>0.870‡</td>
</tr>
<tr>
<td>Withdrawal time without polypectomy, mean (SD), min</td>
<td>24.8 (11.7)</td>
<td>23.3 (11.0)</td>
<td>22.9 (9.3)</td>
<td>0.920‡</td>
</tr>
<tr>
<td>Withdrawal endoscopists' correct guesses of insertion method</td>
<td>392 (96.7)</td>
<td>391 (96.3)</td>
<td>387 (95.2)</td>
<td>0.217</td>
</tr>
<tr>
<td>Overall Boston Bowel Preparation Scale (BBPS) score, mean (SD)</td>
<td>7.9 (1.5)</td>
<td>7.5 (1.7)</td>
<td>7.4 (1.6)</td>
<td>0.005†</td>
</tr>
<tr>
<td>Right colon BBPS score (SD)</td>
<td>7.0 (1.2)</td>
<td>6.9 (1.9)</td>
<td>6.7 (1.3)</td>
<td>0.004†</td>
</tr>
<tr>
<td>Infused water during insertion, median (range), mL</td>
<td>550 (50–6500)</td>
<td>400 (50–2000)</td>
<td>408 (50–2000)</td>
<td></td>
</tr>
<tr>
<td>Aspirated water during insertion, median (range), mL</td>
<td>500 (0–600)</td>
<td>50 (0–1000)</td>
<td>408 (0–1000)</td>
<td></td>
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</tbody>
</table>

Adenoma detection

<table>
<thead>
<tr>
<th></th>
<th>WE</th>
<th>WI</th>
<th>AI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall ADR, n (%)</td>
<td>201 (49.3)</td>
<td>197 (48.7)</td>
<td>193 (47.1)</td>
<td>0.473</td>
</tr>
<tr>
<td>Right colon ADR, n (%)</td>
<td>98 (24.0)</td>
<td>78 (19.1)</td>
<td>69 (16.9)</td>
<td>0.005†</td>
</tr>
<tr>
<td>Male, n (%)</td>
<td>94 (24.0)</td>
<td>78 (19.1)</td>
<td>69 (16.9)</td>
<td>0.005†</td>
</tr>
</tbody>
</table>

Medicine at UCLA, Los Angeles/United States of America/CA

F.W. Leung9

Department Of Surgical Sciences, University of Cagliari, Cagliari/Italy

Gastroenterology Unit, Valduce Hospital, Como/Italy

Dept. Of Gastroenterology, Ospedale Valduce Gastroenterology Unit, Como/Italy

Digestive Endoscopy Unit, St. Barbara Hospital, Iglesias/Italy

1Digestive Endoscopy Unit, St. Barbara Hospital, Iglesias/Italy

2Digestive Diseases Center, Vitkovice Hospital, Ostrava/Czech Republic

3Dept. Of Gastroenterology, Ospedale Valduce Gastroenterology Unit, Como/Italy

4Vitkovice Hospital, Digestive Diseases Centre, Ostrava/Czech Republic

5St. Barbara Hospital, Digestive Endoscopy Unit, Iglesias/Italy

6Dept. Of Gastroenterology, Gastroenterology Unit, Ospedale Valduce, Como, Italy, Como/Italy

7Gastroenterology Unit, Valduce Hospital, Como/Italy

8Department Of Surgical Sciences, University of Cagliari, Cagliari/Italy

9Sephreda Ambulatory Care Center, VAGLAHS and David Geffen School of Medicine at UCLA, Los Angeles/United States of America/CA

Contact E-mail Address: cadonisiorgio@gmail.com

Introduction: Adenoma detection rate (ADR, proportion of patients with at least one adenoma) is the primary quality indicator of colonoscopy, due to its correlation with the risk of post-colonoscopy interval cancer and mortality [1,2]. Data from U.S. male veterans [3], patients in Taiwan [5] and Europe [6], suggest that water exchange (WE, infusion of clean water in an airless lumen and removal of dirty water during insertion), but not water immersion (WI, infusion of water as adjunct to insufflation and removal of residual water during withdrawal) significantly increases ADR in the proximal (cecum-splenic flexure) and right (cecum-ascending) colon, when compared with standard air insufflation (AI). Limitations of these studies were their retrospective analysis and/or investigators unblinded to the insertion method.

Aims & Methods: In a prospective, multi-site randomized controlled trial we tested the hypothesis that WE, but not WI, significantly increases ADR (primary outcome measure) compared with AI. The study population was represented by 50–70 years-old asymptomatic subjects, undergoing colonoscopy as primary screening test or after positive fecal occult blood test. A total of 1224 (672 males) patients were enrolled at three centers and randomly allocated 1:1:1 to WE, WI and AI. Split-dose bowel preparation was adopted to ensure optimal pre-procedure cleansing. To overcome the limitation of previous reports of unblinded colonoscopist performing withdrawal inspection, after reaching the cecum another investigator blinded to the insertion method performed the withdrawal. To assess adequacy of blinding the withdrawal, the second endoscopist was asked to guess the insertion technique.

Results: All results are reported in Table 1. Demographics, clinical features, indications, cecal intubation rates and procedure times were comparable. Compared with AI (40.4%), WE (49.3%) but not WI (43.4%) achieved significantly higher overall ADR (p=0.011 and 0.092, respectively). Compared with AI (14.2%), WE (19.4%) but not WI (17.2%) achieved significantly higher advanced adenoma detection (ADR) (p=0.049 and 0.249, respectively). In the right colon, WE (24%) but not WI (19.1%) achieved significantly higher ADR than AI (16.9%) (p=0.012 and 0.413, respectively). Even after split-dose preparation, WE was associated with higher overall and right colon BBPS scores. The impact was most notable in patients with excellent BBPS, adjusted entire and right colon ADR of WE were significantly higher than those of WI and AI. Multivariate logistic regression showed that WE, compared with AI, was an independent predictor of adenoma detection in the entire colon [OR (95% CI), 1.18 (1.03–1.36)] and in the right colon [OR (95% CI), 1.29 (1.04–1.60)]. The results indicate the one-and-done approach. Volumes of water infused negatively impacted by the one-and-done approach. Volumes of water infused and suctioned suggested that WE, WI and AI methods were correctly used.

Conclusion: The current study shows that in European screening patients, WE significantly increased adenoma detection by 18% in the entire colon and by 24% in the right colon. Moreover, compared with the two other methods, WE improves the quality of colon cleaning. A type II error could account for the absence of statistical significance between unadjusted ADR in the WE and WI groups, further direct comparisons between WE and WI are required.

Disclosure of Interest: S. Cadoni: Recipient of the 2013 ESGE Research Grant

All other authors have declared no conflicts of interest.

References


**Conclusion:** Endocuff-assisted colonoscopy enabled a significantly higher polyp detection rate in patients increased by 12% (62% vs. 50%, \(P = 0.001\)) during withdrawal in the Endocuff group but no major complication occurred. The polyp detection rate in patients increased by 12% (62% vs. 50%, \(P = 0.001\)) with the use of Endocuff. The advanced adenoma detection rate was higher in the Endocuff group but no statistically significant difference was found (6.1% vs. 3.2%, \(P = 0.17\)).

**Results:** There were no differences between the groups in cecal intubation rate, withdrawal time, polyp score. Cecal intubation was achieved in 235 patients (98.8%) in the Endocuff group. In four patients, the Endocuff-assisted examination had to be stopped in the sigmoid colon due to severe stenosis caused by diverticula or cancers. These examinations were completed with a standard colonoscope. Superficial mucosal erosions occurred in 54 patients (23.0%) during withdrawal in the Endocuff group but no major complication occurred. The polyp detection rate in patients increased by 12% (62% vs. 50%, \(P = 0.001\)) and the adenoma detection rate increased by 15% (55% vs. 40%, \(P = 0.001\)) with the use of Endocuff. The advanced adenoma detection rate was higher in the Endocuff group but no statistically significant difference was found (6.1% vs. 3.2%, \(P = 0.17\)).

**Conclusion:** Endocuff-assisted colonoscopy enabled a significantly higher polyp and adenoma detection rate than standard colonoscopy. This attachment improved important quality measures used for screening colonoscopy.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**OP170 DEVELOPMENT AND VALIDATION OF A SIMPLE CLASSIFICATION SYSTEM FOR IN VIVO DIAGNOSIS OF COLORECTAL POLYPS USING THE NEWLY INTRODUCED OPTICAL ENHANCEMENT (OE) TECHNOLOGY**

**Aims & Methods:** Primary objective was to develop and validate a simple classification system allowing differentiation of hyperplastic and adenomatous colorectal polyps using optical enhancement technology (OE). This study assessed for the first time the utility of OE to predict colorectal histology. Thirdly, the validity of the classification was evaluated among inexperienced raters, including medical students, nurses and GI fellows. At least, a pilot clinical evaluation was performed during real-time colonoscopy.

**Results:** A simple classification system for differentiating hyperplastic and adenomatous colorectal lesions by using OE was developed and validated. Diagnosis was made in 85% to 90% of polyps with high-confidence. Sensitivity ranged from 92% to 96% and specificity varied from 86% to 93%, respectively. During real-time colonoscopy, diagnosis was made with high-confidence in 90% of polyps with sensitivity of 96%, specificity of 92%, and accuracy of 95%. Positive and negative predictive values were 96% and 93%, respectively.

**Conclusion:** We have developed and validated for the first time a simple and effective classification system for differentiating hyperplastic and adenomatous colorectal lesions by using the newly introduced OE-technology during real-time colonoscopy. These findings need to be evaluated in future prospective, controlled, and blinded clinical trials.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

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**OP171 FREQUENCY AND PREDICTORS OF ADVANCED HISTOLOGY IN LARGE NON-PEDUNCULATED COLORECTAL POLYPS: EXPERIENCE-BASED DATA AT A UNIVERSITY HOSPITAL**

**Introduction:** Endoscopic resection of large non-pedunculated colorectal polyps (LNPcPs) is challenging, with a significant proportion of them containing malignant or premalignant lesions. The potential to improve diagnostic and therapeutic outcomes of CRC, aims of this study were to examine the frequency of LNPcPs in clinical practice, endoscopic and histopathologic features and predictors for advanced histology.

**Aims & Methods:** We previously trained all endoscopists (9 faculty and 14 trainees) at Maastricht UMC+ on detection, diagnosis and endoscopic resection of colorectal neoplasms using a stepwise training program: Phase 1: Training on detection and diagnosis of colorectal neoplasms, with special attention for non-polyoid (flat and depressed) colorectal neoplasms using lectures, videos and individual feedback. Phase 2: Training in endoscopic resection techniques using video-tuition and hands-on training with experienced colonoscopists. Then, we embarked in a prospective study of all consecutive colonoscopies performed at our institution from February 2008 to February 2012. Quality indicators (cecal intubation rate, adenoma and polyp detection and resection rate) were monitored. We recorded patient characteristics (age, gender) and lesion characteristics, i.e. location, size, shape using Paris classification (including polyp size measurement) and histology. We defined LNPcPs as large (≥ 20 mm) non-pedunculated (i.e. sessile, flat, depressed, combinations) colorectal neoplasms (Rutter et al, Gut 2015). We paid special attention to laterally spreading tumors (LSTs), defined as superficially growing lesions along the mucosa instead of growing up- or downwards. We conducted a logistic regression analysis to identify predictors for advanced histopathology, defined as high-grade dysplasia or early colorectal cancer (pT1).

**Results:** A total of 7166 neoplasms were identified in 9533 patients (mean age 58.9 years, 46.0% male), of which 1097 (1.9%) in 176 (1.9%) patients (mean age 68.3 years, 56.3% male) were LNPcPs. The majority (65.9%) of LNPcPs were located in the proximal colon. Mean size was 30 mm (20-100 mm). Ninety-six LNPcPs (46.8%) were sessile and 109 (55.2%) LSTs. LNPcPs contained low-grade dysplasia adenoma (26.8%), high-grade dysplasia adenoma (17.1%), early colorectal cancer (17.1%), sessile serrated adenoma/polyp (6.6%), hyperplasia (8.8%), and traditional serrated adenoma (0.5%). Sessile-LNPcPs more often contained advanced histopathology than LST-LNPcPs (61.5% vs. 34.9%, \(p < 0.001\)). After adjusting for age and gender, distal location (OR 3.1, 95% CI 1.6–6.0, \(p < 0.001\)), size of lesion (OR 2.7 for LNPcP ≥40 mm compared to 20–29 mm, 95% CI 1.1–6.2, \(p = 0.023\)) and sessile shape (OR 2.3, 95% CI 1.2–4.4, \(p < 0.001\)) were all independent predictors for advanced histopathology. The overall bleeding rate to surgery was decreased from 17.0% in the first half of the study period to 16.7%. Delayed bleeding occurred in 6 (5.6%) cases after endoscopic resection, none requiring surgical intervention. No perforations were reported.

**Conclusion:** In this real-life prospective cohort, 1.9% of all patients undergoing a colonoscopy had a LNPcP. Lesion size, sessile shape and distal location were independent predictors of advanced histology. Careful case selection which considers both patient-related factors and endoscopic prediction may improve advanced histology is critical to optimize the outcomes of endotherapy for LNPcP. 

**Disclosure of Interest:** S. Sanduleanu: Consultancy: Pentax Europe All other authors have declared no conflicts of interest.

**Reference**


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**OP172 HEALTH EFFECTS AND COSTS DUE TO POST-COLONOSCOPY COLORECTAL CANCER**

**Aims & Methods:** The aim of this study was to estimate the loss of health and workdays due to CRC-diagnosis due to PCCRC in Sweden. A...
recent register study of colonoscopies in Sweden during 2001–2010 revealed that 18,244 individuals were diagnosed with CRC within 6–36 months after a colonoscopy. A CRC was defined as a PCCRC if it was detected within 6–36 months after a colonoscopy in which no cancer was detected. A total of 1,473 (8.1%) PCCRCs were found in the register study and included in this study. A lifelong mathematical Markov model was employed to calculate the lifelong health effects and resource usage for PCCRC. The effects were calculated by simulating the hypothetical lives of the individuals diagnosed with PCCRC if their condition had instead been diagnosed at the time of colonoscopy. These lives were then compared with simulated lives of individuals diagnosed with PCCRC, in terms of life expectancy, quality of life and costs. The simulation model was constructed by using Swedish registry data, supplemented with data from the published scientific literature and databases.

Results: Our simulation indicated that if the CRC of the individuals diagnosed with PCCRC had been diagnosed at the time of colonoscopy, there would have been a down-staging of the cancer. The proportion of patients at each cancer stage shifted from 53% in stage I-II, 35% in stage III and 9% in stage IV at the time of the index colonoscopy, to 47% in stage I-II, 31% in stage III and 22% in stage IV, respectively, when diagnosed as a PCCRC. Additionally, on our simulations 3% of the PCCRC was expected to be at an adenoma stage at the time of the colonoscopy and were, thus, theoretically able to prevent. The 1,473 PCCRCs were associated with a loss of 1351 life-years, or, expressed differently, 1275 quality-adjusted life-years, compared to being ones detected at colonoscopy. Additionally, the delay in detection was also associated with higher lifetime costs due to an increased need of health care services related to CRC. The cumulative cost was estimated to be €192, 000 less if the patients had been diagnosed at the time of the prior colonoscopy. The extra cost per case is €1305.

Conclusion: Our simulation results imply that false negative colonoscopies cause significant loss of life-years and quality of life in the affected individuals. This, together with higher costs, motivates further efforts to improve the quality of colonoscopies.

Disclosure of Interest: All authors have declared no conflicts of interest.

OPT13 COMPARISON OF COLONOSCOPY, SIGMOIDOSCOPY AND MULTIPLE ROUNDS OF FIT-BASED COLORECTAL CANCER SCREENING: LONG-TERM FOLLOW-UP
E.J. Grobbe1, M. Van Der Vlugt2, A.J. Van Vuuren3, A.K. Stroobants4, R.C. Mallant-Hen1, I. Landsorp-Vogelaar3, P.M. Bossuyt1, E.J. Kuipers5, E. Dekker1, M.C.w. Spaander1

1Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam/Netherlands
2Gastroenterology and Hepatology, Academic Medisch Centrum, Amsterdam/Netherlands
3Gastroenterology and Hepatology and Urology, VU University Medical Center, Amsterdam/Netherlands
4Department Of Public Health, Erasmus University Medical Center, Rotterdam, Netherlands
5Department Of Gastroenterology and Hepatology, Erasmus MC University Medical Center, Rotterdam, Netherlands

Introduction: Comparison of colonoscopy (C) and fecal immunochemical testing (FIT) for screening colorectal cancer (CRC) was the focus of recent screening studies. A method was mainly focused on one-time endoscopic screening to one-time FIT screening. A fair comparison of diagnostic yield (DY) of FIT would comprise cumulative DY after multiple rounds of FIT screening. The aim of our study is to compare the DY of multiple rounds of FIT-screening to one-time screening by sigmoidoscopy and colonoscopy.

Aims & Methods: Demographic data of 30,007 randomly chosen individuals aged 50–74 were obtained from municipal population registers in the city of Rotterdam (n = 50,769). From 2005 to 2010; of these 15,046 were invited for four rounds of FIT, 8,407 for one-time sigmoidoscopy, and 6,600 for one-time colonoscopy screening. We compared 2 rounds of FIT to one-time sigmoidoscopy and 4 rounds of FIT to one-time colonoscopy. Cumulative (cum.) participation rate, positivity rate, number of colonoscopies, and diagnostic yield were calculated for each method. The DY was calculated relative to eligible invitees and participants. Between-group differences for participation, number of colonoscopies and DY were evaluated using multivariable logistic regression analysis adjusted for age and gender.

Results: In total, 28,515 eligible persons (median age 60 years, IQR 55–66; 50% males) were invited. Cum. participation was significantly higher for FIT (77%) than for sigmoidoscopy (31%; p < 0.001) and colonoscopy (24%; p < 0.001). Number of colonoscopies performed relative to eligible invitees was highest for colonoscopy (24%) compared to FIT (13%; p < 0.001) and sigmoidoscopy (3%; p < 0.001). For invitees, DY for advanced neoplasia (AN) was significantly higher after two rounds of FIT compared to one-time sigmoidoscopy (3.1% vs 2.3%; p < 0.001) and after four rounds of FIT compared to one-time colonoscopy (4.5% vs 2.2%; p < 0.001). For participants, DY for AN was significantly higher for endoscopic screening; 4.7% for 2 rounds of FIT compared to 7.3% for sigmoidoscopy (p < 0.001), and 6.1% for 4 rounds of FIT compared to 9.1% colonoscopy (p < 0.001).

Conclusion: In this population-based CRC screening cohort, we demonstrated that multiple rounds of FIT screening detects significantly more advanced neoplasia per invitee compared to one-time sigmoidoscopy and colonoscopy screening, and with significantly fewer colonoscopies needed. Colonoscopy detected more advanced neoplasia per participant. However, due to low participation in colonoscopy screening, FIT seems most effective in population-based CRC screening.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016
08:30-10:00
SURGERY IN IBD – ROOM L7

OPT14 OUTCOMES OF EMERGENCY ADMISSIONS WITH CROHN’S DISEASE IN ADULTS IN ENGLAND BETWEEN 2004 AND 2014
J. Rees1, J. Mytton2, F. Evison3, P. Patel4, R. Cooney5, N. Trudgill1
1Dept. Gastroenterology, Sandwell General Hospital, West Bromwich/United Kingdom
2Informatics, University Hospitals Birmingham NHS Foundation Trust, Birmingham/United Kingdom
3Urology, University Hospitals Birmingham NHS Foundation Trust, Birmingham/United Kingdom
4Gastroenterology, University Hospitals Birmingham NHS Foundation Trust, Birmingham/United Kingdom

Contact E-mail Address: jamesrees@doctors.org.uk

Introduction: Between 2006 and 2010, the UK national audit of adult inflammatory bowel disease admissions revealed a small but non-significant fall in mortality for John’s disease (6% from 1.3% to 0.8%, p = 0.64), an increase for the rate of prescription of anti-TNF therapy on admission from 3.9 to 8.6% and a fall in surgery from 23% to 18%.

Aims & Methods: Hospital Episode Statistics (HES) is an administrative database of data on all elective and emergency care episodes in hospitals in England. Using HES, patients aged between 18 and 60 years coded with a first emergency admission with CD were identified. The influence of demographic factors, comorbidity and infused anti-TNF therapy on mortality, surgery and emergency readmissions was examined using multivariable logistic regression.

Results: Between 2004 and 2014, 24,830 patients (55% female, mean age of 35 (IQR 25–44)) were identified. Mortality was 0.22% at 30 days, 0.29% in hospital and 0.81% within 1 year. During admission, 19.2% of patients underwent surgery (median time to surgery 2 days (IQR 1–6)) and 1.9% received infused anti-TNF therapy. Surgery during admission rose from 16.1 to 22.9% (OR 1.52 (95% CI 1.02–2.27), p = 0.03). Infusion of anti-TNF therapy on admission rose from 0.77% to 0.81% within 1 year. During admission, 19.2% of patients underwent surgery (median time to surgery 2 days (IQR 1–6)) and 1.9% received infused anti-TNF therapy. Surgery during admission rose from 16.1 to 22.9% (OR 1.52 (95% CI 1.02–2.27), p = 0.03). Infusion of anti-TNF therapy on admission rose from 0.77% to 0.81% within 1 year. During admission, 19.2% of patients underwent surgery (median time to surgery 2 days (IQR 1–6)) and 1.9% received infused anti-TNF therapy. Surgery during admission rose from 16.1 to 22.9% (OR 1.52 (95% CI 1.02–2.27), p = 0.03). Infusion of anti-TNF therapy on admission rose from 0.77% to 0.81% within 1 year. During admission, 19.2% of patients underwent surgery (median time to surgery 2 days (IQR 1–6)) and 1.9% received infused anti-TNF therapy.
of relapse than those of the TNF/C11
tine after surgery had higher risk of relapse despite retreatment with anti-TNF
/ C11 tion of TNF
factors predicting relapse in patients with anti-TNF
received anti-TNF
p ment of anti-TNF
TNF-alpha agents (anti-TNF
is effective for patients who underwent ‘Reset’ surgery. The aim of
Introduction: Anti TNF-alpha agents (anti-TNF
clinicians medictions before and after surgery, labora-
data before surgery, and the residual of the affected intestine after surgery, etc.
clear patients undergoing proctocolectomy or preoperative anti-TNF
therapy. In addition, clinical factors predicting relapse in patients with anti-TNF
therapies were evaluated. The evaluated factors were clinical backgrounds, dura-
tion of TNF therapy, concomitant medications before and after surgery, labora-
datory data before surgery, and the residual of the affected intestine after surgery, etc.
other surgery. The rate of overall CD recurrence was inversely correlated with disease activity at the moment of the interview.
Aims & Methods: From July 2005 to November 2015, 65 CD patients underwent intestinal resection at Okayama University Hospital. Of these, 34 patients received anti-TNF therapy after surgery. We compared proctocolectomy or completion proctectomy in inflammatory bowel disease (IBD) patients. Endpoints were postoperative perineal complications, and healing at 6 months after total mesorectal excision (TME) surgery. Patients were assessed. Adult patients undergoing proctocolectomy or completion proctectomy, compared to CD with higher healing rates.
Conclusion: The ‘Reset’ surgery was not so effective for CD patients refractory to anti-TNF therapy. In particular, patients with the residual of the affected intestine after surgery had higher risk of relapse despite retreatment with anti-TNF therapy. Those patients may need additional treatment besides anti-TNF therapy or increase in the dosage amount of the anti-TNF agent.
Disclosure of Interest: All authors have declared no conflicts of interest.
OP176 IMPACT OF MINIMALLY INVASIVE SURGERY ON QUALITY OF LIFE AFTER SURGERY FOR CROHN’S DISEASE TERMINAL ILEITIS
I. Angriman1, O. Zini1, R. D’Inca2, G.C. Storniolo1, R. Bardini4, M. Scarpa4
1Dept. Of General Surgery, University of Padova, Padova/Italy
2Division of Gastroenterology, Padova/Italy
3Gastroenterology, Padua University Hospital, Padua/Italy
4Department Of Surgery, Oncology and Gastroenterology, University Of Padua, School Of Medicine, Chirurgia Generale, Padova/Italy
5Esophageal and Digestive Tract Surgical Unit, Regional Centre For Esophageal Diseases, Veneto Institute of Oncology - 0943, Padova, Italy
Contact E-mail Address: imero.angriman@unipd.it
Introduction: Crohn’s disease (CD) is a chronic inflammatory disease that interferes with the daily life of those affected. Surgical treatment is required in about 70% of CD patients during the course of disease and risk of surgery is among the highest rated concerns among them. Quality of life is often worsened by intestinal surgery.
Aims & Methods: The aim of the study is to assess the impact of minimally invasive surgery on quality of life after surgery for Crohn’s disease terminal ileitis. From June 2010 to December 2015, one author (O.Z.) interviewed by telephone and responded to the generic European Quality of Life (CQOL) questionnaire and the Body Image Questionnaire (BIQ). Their disease activity was defined as Harvey-Bradshaw Index (HBI). Comparisons and correlations were carried out with non-parametric tests. Survival analysis was performed with log rank test.
Results: In our study group 46 patients had minimally invasive surgery for terminal ileum CD while 66 had open surgery for the same indication. Twenty seven patients had a recurrent CD. The total CQOL score and its single items (quality of life, disease activity, quality of life and emotional health) were significantly higher (and thus, better) in the laparoscopy group patients. Similarly, all the BIQ items were significantly better in patients who had a minimally invasive surgery compared to those who had open surgery. At univariate analysis, total CQOL score was directly correlated with minimally invasive surgery (rho = -0.44, p = 0.001) and inversely correlated with disease activity at the moment of the interview (rho = -0.40, p = 0.001), the use of steroids (rho = -0.20, p = 0.02) and recurrent CD as indication for surgery (rho = 0.19, p = 0.05). At multivariate analysis, only disease activity at the moment of surgery and steroid use were revealed to be independent predictors of quality of life. Finally, minimally invasive surgery tended to be associated to a less frequently CD recurrence (p = 0.08)
Conclusion: Minimally invasive surgery was associated to a better quality of life and body image perception. This results is probably due to the beneficial effect of minimally invasive surgery on body image but also by the less severe disease of these patients (less recurrent CD as indication for surgery or simpler surgery). Quality of life is essentially predicted by current disease activity and minimally invasive surgery. Finally, minimally invasive surgery tended to be associated to a less frequent CD recurrence.
Disclosure of Interest: All authors have declared no conflicts of interest.
OP177 CLOSE RECTAL DISSECTION VERSUS TOTAL MESORECTAL EXCISION IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE UNDERGOING PROCTECTOMY
1Surgery and Gastroenterology & Hepatology, AMC, Amsterdam/Netherlands
2State University Maastricht, Maastricht University Medical Centre, Maastricht, Netherlands
3Tyring Institute For Liver and Intestinal Research & Gastroenterology & Hepatology, Academic Medical Center, Amsterdam/Netherlands
4Dept. Of Surgery, Academic Medical Center Dept. of Surgery, Amsterdam/Netherlands
5Dept. Of Gastroenterology, Academisch Medisch Centrum, Amsterdam/Netherlands
6Deptartment Of Surgery, Academisch Medisch centrum, Dept. Of Surgery, Amsterdam/Netherlands
7Colorectal Surgery, Academic Medical Center, Amsterdam/Netherlands
Contact E-mail Address: e.j.degroof@amc.uva.nl
Introduction: Proctectomy or completion proctectomy in inflammatory bowel disease patients is frequently complicated by disturbed perineal wound healing and presacral abscess formation. Close rectal dissection (CRD) has been proposed as an alternative technique for colorectal surgery that could reduce this complication by leaving the rectal mesentery in situ to minimize dead space cavity compared to total mesorectal excision (TME).
Aims & Methods: The aim of this study was to compare perineal wound healing between colorectal resection for right-sided (UC) and left-sided colorectal tumor (TME) or CRD. Since it has been suggested that Crohn’s mesenteric adipose tissue is involved in CD pathology with reduced regulatory potential of wound healing microenvironment. A total of 80 patients undergoing proctectomy or ileoanal pouch formation were assessed. Adult patients undergoing proctectomy or completion proctectomy without resection for UC or CRD (2005–2015) were included. Endpoint were postoperative perineal complications, and healing at 6 and 12 months. Rectal mesentery was cultured and walk-out cells were analysed by flow cytometry. CD45+ immune cells were identified, with phenotyping of wound healing macrophages by regulatory markers CD206 and CD14.
Results: Fifty-nine patients (17 UC/42 CD) were included (46.4% male, mean age 45.5 (±14.5)). CRD was performed in 8 UC (47.1%) and 32 CD patients (76.2%). In UC, significantly less perineal complications (17.6% versus 47.6%, p = 0.033) and a higher healing rate at 6 months (87.5% versus 64.3%, p = 0.066) were seen. No significant differences in outcome between the techniques in UC. Perineal complications occurred frequently in CD patients who underwent TME compared to CRD, (20.0% versus 56.3%, p = 0.045), with higher healing rates at 6 months after TME (90.0% versus 53.3%, p = 0.052). Perineal healing rate at 12 months was 87.5% in the TME group versus 65.5% in the CRD group (p = 0.443). Analysis of rectal mesentery showed an enhanced infiltration of CD45+ immune cells in CD patients with the balance between CD3+ T cells and CD14+ myeloid cells skewed significantly towards the myeloid population (UC vs CD median 24% versus 53%, p < 0.01. In addition, macrophages in CD patients showed significantly less expression of the wound healing marker CD206, in line with a more pro-inflammatory and less wound healing profile of CD rectal mesentery. Strikingly, these alterations were maintained in patients with a defunctioning stoma.
Conclusion: In UC, significantly less perineal complications were seen after proctectomy or completion proctectomy, compared to CD with higher healing rates. >50% of CD patients had perineal complications and impaired healing, which was seen more frequently after CRD. These findings can probably be explained by the increased pro-inflammatory myeloid cell population with decreased wound healing macrophages, irrespective of the presence of a
Type: This was a prospective, observational, non-randomised, uncontrolled, single-centre study conducted in one teaching hospital in Manchester, UK. Patients were assessed at the time of diagnosis and then at 3 months of follow-up. The primary endpoint was the proportion of patients who achieved clinical remission (Haller’s index ≤ 2) by 3 months. Secondary endpoints included the proportion of patients with a marked clinical response (Haller’s index ≤ 2 at the first visit) and the proportion of patients who achieved clinical remission at 6 months.

Results: A total of 100 patients were enrolled, with a median age of 29 years and a median disease duration of 8 months. The majority of patients (87%) had a history of previous surgery. At the time of diagnosis, 76% of patients were in clinical remission and 52% were in clinical remission at 3 months. The proportion of patients in remission increased to 66% by 6 months.

Conclusion: This study demonstrates the potential role of octreotide in the management of IBD, particularly in patients with refractory disease. Further research is needed to confirm these findings and to evaluate the long-term efficacy and safety of octreotide in this patient population.
microbiota-based drug candidate targeted at recurrent CDI, is sourced from human-derived microbes from extensively screened donors and manufactured using standardised, quality-controlled processes. Aims & Methods: To compare the bacterial abundance in the source material for RBX2660 (DS) with the bacterial abundance in the finished drug product (DP) used in the Phase 2B PUNCH CD 2 study. A total of 70 DS samples sourced from 17 unrelated donors (mean age 27; range 18 to 57 years; 94% male) from August 2014 to February 2016 were compared with 70 matched DP samples using the GA-map Dysbiosis Test (GA-test), Genetic Analysis AS, Oslo, Norway. The GA-test used 54 probes targeting V3 to V7 of the bacterial 16S rRNA gene to characterise and identify bacteria present. Approximately 300–400 bacteria at different taxonomic levels are covered, providing for an assessment of the microbial community using multiple variable regions. The GA-test enables serial assessment of the faecal bacterial abundance profile as well as potentially clinically relevant alterations in the microbiome over time. These capabilities of the GA-test were used to assess the production processes for RBX2660. The differences in bacterial abundance between the DP and DS were calculated from log10 fold changes (DP/DS); averaging the differences.

Results: The GA-test found that the bacterial abundance in the RBX2660 DP was lower than in the DS in 38 of the 54 probes; equal in number in 6 of the probes; and higher in 10. More specifically, Firmicutes and Actinobacteria showed reduced signal strength in the DP compared with the DS. Bacteroides increased signal strength in the DP compared with the DS, while Proteobacteria demonstrated equal signal strength in both samples. The comparative abundance in the DP vs. the DS is shown in Table 1. Accuracy was as high as 83.4% at cross-validation. Principal component analysis found that the bacterial profiles in the RBX2660 DP, though lower than in the donor source material, were largely kept intact during the production process for all 17 donors.

Table 1: Comparative Signal Strength of Bacteria

<table>
<thead>
<tr>
<th>Bacteria</th>
<th>Signal Strength in DP vs. DS</th>
<th>Mean Difference (95% CIM)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bacteroides</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bacteroides fragilis</td>
<td>Increased</td>
<td>0.07 (0.03, 0.11)</td>
</tr>
<tr>
<td>Parabacteroides</td>
<td>Increased</td>
<td>0.12 (0.07, 0.17)</td>
</tr>
<tr>
<td>Allistipes</td>
<td>Increased</td>
<td>0.17 (0.11, 0.23)</td>
</tr>
<tr>
<td>Firmicutes</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lachnospirae</td>
<td>Decreased</td>
<td>−0.13 (−0.15, −0.11)</td>
</tr>
<tr>
<td>Streptococcus</td>
<td>Decreased</td>
<td>−0.16 (−0.20, −0.13)</td>
</tr>
<tr>
<td>Negativicutes</td>
<td>Increased</td>
<td>0.03 (0.01, 0.06)</td>
</tr>
<tr>
<td>Clostridia</td>
<td>Decreased</td>
<td>−0.18 (−0.20, −0.16)</td>
</tr>
<tr>
<td>Actinobacteria</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bifidobacterium</td>
<td>Decreased</td>
<td>−0.33 (−0.38, −0.28)</td>
</tr>
<tr>
<td>DP = drug product</td>
<td>DS = drug source</td>
<td>CIM = confidence interval of mean</td>
</tr>
</tbody>
</table>

Conclusion: GA-test analysis confirmed that RBX2660 can be manufactured in a consistent and reliable manner with the preservation of key bacterial diversity believed critical for protection from recurrent CDI. Disclosure of Interest: C. Jones: Employee of Rebiotix Inc., Roseville, MN USA

References

OPI82 A METHYL DONOR MOLECULES-SUPPLEMENTED DIET ERADICATES E. COLI POPULATION AND METHYLATED CEACAM6 PROMOTER DECREASING ITS EXPRESSION IN COLONIC EPITHELIAL CELLS IN MICE

E. Gimier1, A. Agas2, N. Barnich1, J. Denizot3
1M2iSH Uda/Inserm U1070, Clermont-Ferrand/France
2M2iSH Uda/Université d’Auvergne Inra Usc 2018, University of Clermont Auvergne, Clermont-Ferrand/France
3Clermont Université, M2iSH, UMR 1071 INSERM/Université d’Auvergne, Clermont-Ferrand, France Unite Sous Contrat 2018 Institut National de la Recherche Agronomique, Clermont-Ferrand/France
Contact E-mail Address: elodiegimier@hotmail.fr
Introduction: Adherent-invasive E. coli are clearly involved in triggering and maintaining ileal CD. AIEC bacteria adhere to the enterocytes through high affinity interaction between their variant type one pili and abnormally expressed CEACAM6 protein on host cells. We previously reported an original mechanism of CEACAM6 regulation depending on DNA methylation and transcription factor HIF1-binding site (HIF, Hypoxia responsive element) in the promoter of the gene. We observed that an unmethylated HRE site allows HIF-1 to bind the promoter and to induce CEACAM6 expression in intestinal epithelial cells (IEC). Decreasing CEACAM6 expression in CD intestinal cells is one strategy that could prevent AIEC bacteria colonization of the intestinal mucosa and subsequent inflammation. This work aims at studying the effect of a methyl-donor enriched diet (HMD: High Methyl Diet) on microbiota composition, on DNA methylation and on genes expression in CD intestinal cells.

Aims & Methods: CEABAC10 female mice were fed a HMD (supplemented in folate, biotin, B12 vitamin, zinc, methionine) for 2 weeks before pregnancy. After weaning, the colonic epithelial cells from offspring were purified using EDTA. qPCR analysis with different primer sets for CEACAM6 mRNA revealed that the E. coli population was quantified using a qPCR approach. DNA methylation was measured at a global level and on the CEACAM6 promoter using bisulfitesequencing. qPCR was used to quantify CEACAM6 mRNA. RNA-seq data was also used to highlight transcriptomic changes in colonic cells in the both conditions tested.

Results: We observed that mice fed a HMD show a significant decrease in basal lipocalin-2 level in stools compared to mice receiving a conventional diet suggesting a beneficial effect on gut microbiota and inflammation. No significant differences were observed on histological sections following HMD. Microbiota analysis revealed a 1000-fold decrease in E. coli population in fed HMD compared to mice receiving a conventional diet. As expected, global DNA methylation in colonic epithelial cells revealed a global increase in DNA methylation in mice fed a HMD compared to mice fed a conventional diet. Bisulfitesequencing revealed a hypermethylation of the CEACAM6 promoter, especially on the HRE sites. This hypermethylation of the promoter was associated with a significant decrease in CEACAM6 expression as measured by qPCR and Western-blot. RNA-seq data confirmed the decrease in CEACAM6 expression and highlighted many misregulated genes following HMD, among them, many genes involved in adaptive immunity.

Conclusion: This work shows that the addition of a few vitamins and oligo-elements to the diet could interfere with the DNA-methylation metabolism leading to changes in genes expression such as a decrease in CEACAM6 and modify microbiota composition leading to eradication of the E. coli population in the intestine. A diet-based strategy could help decreasing AIEC colonization in CD patients by modulating CEACAM6 expression.

Disclosure of Interest: All authors have declared no conflicts of interest.

OPI83 COMPARATIVE GENOMICS AND SINGLE NUCLEOTIDE POLYMORPHISM DISTRIBUTION BETWEEN ADHERENT-INVASIVE ESCHERICHIA COLI (AIEC) AND NON-AIEC STRAINS FROM THE HUMAN INTESTINE

Biology, University of Girona, Girona/Spain
Contact E-mail Address: c.camprubi@gmail.com
Introduction: The molecular basis of Adherent-invasive Escherichia coli (AIEC) pathogenicity, a pathotype associated with Crohn’s disease, still needs to be well resolved. Nowadays the identification of the pathotype is performed with time-consuming techniques based in phenotypic screening of cultured bacteria; obtaining new molecular tools would therefore be of great significance.

Aims & Methods: Our aim was to identify putative genetic elements involved in AIEC phenotype to gain insight into the mechanisms of its pathogenicity and to find molecular targets for its identification. To achieve this objective we performed comparative genomics of three E. coli strain pairs consisting in one AIEC and one non-AIEC of identical pulsed field gel electrophoresis fingerprint. Each pair belonged to a distinct phylogroup. This approach was designed in order to increase the chance of finding sequences AIEC-specific and not strain-specific. The six strains’ genomes were sequenced de novo by combining paired-end libraries of HiSeq Illumina and PacBio. Two different approaches for comparative genomics were used: i) assembly with Velvet and genome comparison with arranging and comparing AIEC genome to AIEC genome and ii) SPAdes- Kraken software and comparative genomics between pairs in relation to a genome of reference (AIEC UM146) with Mauve. Only non-synonymous Single Nucleotide Polymorphisms (SNPs) in coding regions were selected. Sanger sequencing was performed to confirm the presence of SNPs and to evaluate the distribution of the SNPs in a collection of 22 AIEC and 29 non-AIEC isolates. Nucleotides for each SNP were analysed taking into account AIEC phenotype, adhesion and invasion indexes of isolated by χ² test or ANOVA as required.

Results: Genome sizes of Velvet assemblies for AIEC strains ONT-HNT-D, O6:H1-B2 and O22:H7-B1 were 4.86, 5.16 and 4.79Mb respectively. When SPAdes was used, they presented +95,362bp, +47,933bp and +30,178bp respectively. Comparative genomics of the first approach reported 114, 80 and 31 SNPs, whereas the second resulted in 19, 27 and 31 SNPs respectively. Six SNPs were found with both strategies. From all, 23 SNPs were confirmed by Sanger and analysed among the study collection. These SNPs were comprised in 14 genes from which 3 were involved in metabolic processes, 2 in stress tolerance and 5 in adhesion and invasion pathways. Most of the SNPs were strain-specific, except from one found in a gene putatively implicated in adhesion/invusion, that was differentially distributed among AIEC and non-AIEC strains (p = 0.029).

Interestingly, this SNP plus 3 other SNPs positions located in the same gene were associated with invasion (p = 0.024) and one of them also with adhesion (p = 0.04).

Conclusion: To conclude, we have detected SNP variations in a single gene that could be associated with AIEC phenotype. However, further studies with site-specific mutations are needed to confirm the implication of this gene in the AIEC pathogenicity and the SNP effects. Our study indicates that there is not an AIEC-specific genetic marker and widely distributed in all AIEC.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP1B4 ENTEROHEMORRHAGIC ESCHERICHIA COLI TROPISM TO Peyer’s PATCHES OF LONG POLAR Fimbria AND INHIBITION BY A PROBIOTIC YEAST
C. Cordonnier1, J. Ramboz2, J. Thévenot1, L. Etienne-Mesmin1, A. Rougeron1, S. Renier1, S. Barnich1, S. Blanquet-Diot1, V. Lirello1

1Université d’Auvergne, M2SH, Microbes, Infection, Inflammation et Spécificités des Pathogènes, Clermont-Ferrand, France
2EA CIDAM, Clermont-Ferrand/France

Contact E-mail Address: charlotte.cordonnier@uamail.fr

Introduction: Enterohemorrhagic Escherichia coli (EHEC) are food-borne pathogens associated with diarrhea, hemorrhagic colitis and life-threatening complications such as hemolytic-uremic syndrome. EHEC interact with the Folicule-Associated Epithelium (FAE) of Peyer’s patches of the distal ileum in humans and translocate across the intestinal epithelium via M cells. Molecular mechanisms are still unknown but Long Polar Fimbriae (Lpf) which contribute to interactions with host cells should be involved. Currently, no specific therapeutic strategy is available in EHEC infections and use of antibiotics remains controversial. Probiotic could be an alternative strategy.

Aims & Methods: The objectives of the study were to investigate the role of Lpf in EHEC tropism to Peyer’s patches, and to explore the influence of probiotic yeasts on EHEC interactions with intestinal mucosa. The expression of Lpf genes (encoded by two lpf operons) of EHEC O157:H7 strain EDL933 was analyzed using in vitro models of the human ileocecal or gastrointestinal tract and large intestine. To investigate the involvement of Lpf in the ability of EDL933 to target Peyer’s patches, we generated the DlpfA1, DlpfA2, DlpfA1-DlpfA2 isogenic mutants and pre-treated them with Lpf genes. Lpf interaction with M cells was assessed using an in vitro model of specialized intestinal epithelial cells. In vivo interactions of EHEC with murine Peyer’s patches were analyzed in ileal loop assays. Mice were infected with a mixture of two bacterial strains, and the numbers of Peyer’s patches-interacting bacteria were determined using a competitive index analysis. To investigate the effect of probiotic yeasts, mice were given the probiotic for 7 days before ileal loops assays were conducted with O157:H7 wild type.

Results: Lpf isogenic mutants (i) were not able to interact with ileal biopsies containing Peyer’s patches compared to the wild type strain in competitive colonization assays and (ii) translocated across M cells at levels significantly lower than those observed for the wild type strain. Trans-complementation of the mutants with the cloned lpf genes restored their ability to interact with Peyer’s patches, indicating that expression of lpfA1 or lpfA2 genes is required for interactions with Peyer’s patches. Bloodshot Peyer’s patches were macroscopically observed following EHEC infection of murine ileal loops. We showed that pre-treatment with yeasts significantly inhibited O157:H7 interaction with Peyer’s patches and reduced the number of hemorrhagic Peyer’s patches in murine ileal loops. Since yeast cell surface is rich in mannose, the role of carbohydrates in EHEC interactions with Peyer’s patches was investigated. Among the carbohydrates tested, only mannose specifically limited the interaction of EHEC with Peyer’s Patches.

Conclusion: We conclude that Lpf is involved in the interactions of EHEC with murine Peyer’s patches and are needed for an active translocation across M cell monolayer. Tropism of EHEC to Peyer’s patches can be limited by probiotic yeasts and by specific carbohydrates.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP1B5 CURRENT OR PAST CLOSTRIDIUM DIFFICILE INFECTION IS ASSOCIATED WITH INCREASED MORTALITY, MORBIDITY AND RISK FOR HOSPITALIZATION AMONG PATIENTS HOSPITALIZED FOR CROHNS’ DISEASE: RESULTS OF A NATIONWIDE ANALYSIS
P. Kroner1, M. S. Abougergi2

1Medicine, Mt. Sinai St. Luke’s / West Hospitals, New York/United States of America/NY
2Catalyst Medical Consulting, Baltimore/United States of America/MD

Contact E-mail Address: thomaskroner@gmail.com

Introduction: Multiple factors have been associated with an acute flare of Crohn’s disease, including cigarette smoking and non-steroidal anti-inflammatory drug use. Recently, Clostridium difficile infection (CDI) has been added to this list. CDI can become chronic or recurrent in 20% of patients. To date, the impact of CDI on patients’ mortality and other outcomes among patients with Crohn’s disease has not been investigated.

Aims & Methods: The aim of this study is to explore the impact of past or current CDI on mortality, morbidity and resource utilization among patients hospitalized for Crohn’s disease. This was a retrospective cohort study using the 2012 National inpatient sample, the largest publically available inpatient database in the United States. The inclusion criteria were: 1- a principal diagnosis of Crohn’s disease 2- A principal diagnosis of intestinal hemorrhage, obstruction, fistula, or abdominal abscess with a secondary diagnosis of Crohn’s disease. There were no exclusion criteria. The primary outcome was in-hospital mortality. The secondary outcomes were morbidity as measured by shock, intensive care unit (ICU) admission, colectomy or intestinal resection rate and resource utilization as measured for Crohn’s disease. This analysis included patients who had either past or current diagnosis of CDI. Patients with CDI had similar a colectomy rate (OR: 1.16, CI: 0.75–1.77, p = 0.5), ICU admission rate (OR: 2.77, CI: 0.93–8.29, p = 0.07) and shock rate (OR: 3.06, CI: 0.94–9.97, p = 0.06) but a lower intestinal resection rate (OR: 0.26, CI: 0.08–0.82, p = 0.02) compared with patients without CDI. When resource utilization was examined, patients with CDI had higher LOS (adjusted mean (mean): 2.54 days, CI: 1.78–3.30 days, p < 0.01), higher TPN use (OR: 2.71, CI: 1.92–3.82, p = 0.02), higher total hospital charges (mean: $14,259 CI: $8,473-$20,026, p < 0.01) and similar abdominal CT scan use (OR: 1.41, CI: 0.78–2.59, p = 0.25) compared with patients without CDI.

Conclusion: Current or past CDI is associated with increased mortality among hospitalized patients with Crohn’s disease. However, patients with CDI have similar colectomy rates, shock or ICU admission rate compared with patients without CDI. Finally, CDI has a profound effect on resource utilization with longer length of stay, increased TPN use and substantially higher total hospitalization charges.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 08:30–10:00

OP1B6 SELF-EXPANDABLE METALLIC STENT AS BRIDGE TO SURGERY IS MORE SUPERIOR THAN TRANSMUCAL DRAINAGE TUBE AT QUALITY OF LIFE FOR THE PATIENTS WITH PRIMARY MALIGNANT COLORECTAL OBSTRUCTION
K. Kojima1, N. Toda1, S. Kuroasaki1, K. Funato2, S. Kawamura1, Y. Karasawa2, S. Maeshima1, T. Oki1, M. Seki1, K. Tagawa1

1Gastroenterology, Mitsui Memorial Hospital, Tokyo/Japan
2Mitsui Memorial Hospital, Tokyo/Japan

Contact E-mail Address: kenken.kojiken.529@gmail.com

Introduction: Self-expandable metallic stents (SEMS) or transmucosal drainage tube (TDT) is endoscopic decompression for malignant colorectal obstruction. SEMS is said to be superior to TDT at quality of life (QOL) for the patients, but the comparison between SEMS and TDT for malignant colorectal obstruction was few reported include the clinical efficiency, safety and prognosis.

Aims & Methods: The aim of this study is to evaluate QOLs, clinical efficiency and safety between SEMS and TDT for the patients with malignant colorectal obstruction. We retrospectively analyzed 69 patients who underwent SEMS or TDT insertion for malignant colorectal obstruction from April 2009 to March 2016 on the basis of single-center experience in Japan. SEMS was inserted for bridge to surgery (BTS) or palliation, and TDT was inserted for BTS or bridge to SEMS insertion.

Results: There were 27 patients in SEMS group (male 37.0%, median age 73±(17.0years) and 42 patients in TDT group (male 54.8%, median age 65±(15.2 years). Technical success rate was 100% of SEMS group and 95.2% of TDT group (p=0.15). The endoscopic decompression as BTS for primary colorectal cancer was performed in 57.1% of SEMS group and 85.7% of TDT group (p=0.02). Among these patients, the duration for surgery after decompression was longer in SEMS group (14.9±7.9 days vs 10.5±6.6 days, p=0.044), because the rate of temporary discharge was significantly higher in SEMS group (41.7% vs. 0.0%, p<0.001). No significant difference was shown about the hospitalization in both group (36.1±23.5 days vs 46.4±36.0 days, p=0.36). Oral intake (at least soft solids) was significantly higher in SEMS group (88.9% vs 25.0%, p<0.001). The Colonic Stent Safe Procedure Research Group Colorectal Obstructive Scoring System (CROSS) score before decompression was not a significant difference in both groups (1.1±0.9 vs 1.2±0.7, p=0.49), but CROSS score after decompression was significantly improved in SEMS group (3.7±0.8 vs 2.3±0.5, p<0.001). The complications after procedure, such as perforation, migration, re-obstruction, had no significant difference in both group.

Table: Patients characteristics and results

<table>
<thead>
<tr>
<th>Sex</th>
<th>Value</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Male</td>
<td>73 (53.4%)</td>
<td>25 (40.3%)</td>
</tr>
<tr>
<td>Age (years)</td>
<td>65 ± 15.2 years</td>
<td>65 ± 15.2 years</td>
</tr>
<tr>
<td>Age &gt; 85 years</td>
<td>9 (33.3%)</td>
<td>7 (17.1%)</td>
</tr>
<tr>
<td>Obstructed location (left side)</td>
<td>23 (85.2%)</td>
<td>38 (90.5%)</td>
</tr>
<tr>
<td>Primary colorectal cancer</td>
<td>21 (77.8%)</td>
<td>28 (70.0%)</td>
</tr>
<tr>
<td>Palliation</td>
<td>12 (44.4%)</td>
<td>24 (66.7%)</td>
</tr>
</tbody>
</table>

- Bridge to SEMS insertion | 2 | 7 | N.S. |
- Emergent surgery | 2 | 1 | N.S. |
- Metastatic colorectal cancer | 6 (22.2%) | 12 (30.0%) | N.S. |
- BTS | 0 | 5 | N.S. |
| Palliation to SEMS insertion | 2 | 5 | N.S. |
- Palliation | 0 | 1 | N.S. |
| Technical Success | 27 (100%) | 40 (95.2%) | N.S. |
| Complications | 27 (100%) | 40 (95.2%) | N.S. |
Aims & Methods: This study aimed to clarify the clinical factors associated with the technical difficulty of SEMS placement for malignant colorectal obstruction. This study represents the largest material from a single centre ever published.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP191 IMPACT OF MORTALITY FROM SURGICAL ADENOMA REMOVAL ON THE EFFECTIVENESS OF COLORECTAL CANCER SCREENING

M. Buskermolen1, M.P. Van Der Meulen1, E. Toes-Zoutendijk2, M. Van Loerden3, M.C.W. Spaander4, H. De Koning5, I. Lansdorp-Vogelaar5
1Public Health, Erasmus MC, Rotterdam/Netherlands
2Dept. Of Gastroenterology, Netherlands Cancer Institute, Amsterdam/Netherlands
3Department Of Public Health, Erasmus Medical Center, Rotterdam, Rotterdam/Netherlands
4Erasmus MC, Rotterdam/Netherlands
5*Department Of Public Health, Erasmus University Medical Center, Rotterdam, Rotterdam/Netherlands

Contact E-mail Address: m.buskermolen@erasmusmc.nl

Introduction: Implementation of colorectal cancer (CRC) screening programs results in an increase in the number of adenoma diagnoses. Some of the advanced adenomas (AADs) cannot be endoscopically removed and patients may then be referred for surgery. However these surgical resections have an associated mortality. We aimed to discuss the negative impact of surgery on the effectiveness of CRC screening.

Results: Overall survival in this observational cohort did not differ significantly from that of colorectal cancer patients in the same period (p = 0.14). One-, five- and ten-year survival was not statistically different in both groups (95.9% vs 79.0%; 54.7% vs 51.2%; 41.0% vs 35.6% respectively). Additionally, for tumour stage II, III and IV no statistical differences between both cohorts were found (p = 0.21, p = 0.58, p = 0.10 respectively). Technical success rate was 94.8%. Seventy patients did not experience any complication. Stent migration occurred in 9 patients, whereas stent-related micro- and macro perforations were observed in 14 patients, without influencing survival. Incidence rates of periprooperative mortality did not differ significantly between patients with and without any type of perforation (22.2% vs 15.2% respectively, p = 0.47). On average, surgery took place 16.6 days after colonic stenting, ranging from an operation on the same day as the endoscopic procedure, to an interval of maximal 124 days. In 82.5% of the cases a laparoscopic resection of the tumor was performed. Five point two per cent of the patients got primarily open surgery. In 5.2% of the patients a laparoscopic procedure was converted to laparotomy, because of adhesions or peritonitis. Stoma rates were low (5.2%).

Conclusion: These data indicate that stenting before surgery is effective and safe in the treatment with curative intent of patients with obstructive colon cancer and reinforce the debate on stenting as a BTS.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP192 THE OCCURRENCE OF ANAEMIA AND ANAEMIA SUBTYPES DURING THE FIRST YEAR OF DISEASE IN AN EAST-WEST EUROPEAN INCEPTION COHORT – AN ECCO-EPICOM COHORT STUDY


1Department Of Gastroenterology, North Zealand University Hospital, Frederiksberg/Denmark
2Center For Quality, Region of Southern Denmark, Odense/Denmark
3Division Of Gastroenterology and Hepatology, Karolinska Institutet, Stockholm/Sweden
4Division Of Gastroenterology and Hepatology, University Hospital Center Zagreb, University of Zagreb, Zagreb/Croatia
5Division Of Gastroenterology and Alimentary Tract Surgery, St. Olavs Hospital, Trondheim/Norway
6Clin Endosc
7Div. Of Endocrinology and Gastroenterology, Tartu University Hospital, Tartu/Estonia
8Medical Department, National Hospital of the Faroe Islands, Torshavn/Faroe Islands
9Department Of Gastroenterology and Hepatology, Ben-Gurion University of the Negev BeerSheva, Beer Sheva/Israel
10Division Of Gastroenterology and Hepatology, Gent Hospital, Ghent/Belgium
11Division Of Gastroenterology and Hepatology, Medical School of Ioannina, Ioannina/Greece
12Department Of Gastroenterology and Hepatology, University of Copenhagen, Copenhagen/Denmark
13Division Of Gastroenterology and Hepatology, Tampere University Hospital, Tampere/Finland
14Division Of Internal Medicine, Medical School of Ioannina, Ioannina/Greece
15Department Of Gastroenterology and Hepatology, Ben-Gurion University of the Negev BeerSheva, Beer Sheva/Israel

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 10:30–12:00 COMPLICATIONS IN IBD – ROOM F2

TUESDAY, OCTOBER 18, 2016 10:30–12:00 COMPLICATIONS IN IBD – ROOM F2

Conclusion: Screening colonoscopies in population over 70 years of age in our study were safe, with higher detection of neoplasias, but with lower completion rate. There was higher number of colonoscopies after positive FOBT than primary colonoscopies in seniors considering local od significance of 35.

Results: 1677 screening colonoscopies were performed in total, 333 in group 70 years and more, 1344 in group under 70 years. Polyp detection rate (PDR) and quality of bowel preparation in both groups were comparable. There were significantly more neoplasias (ADR), advanced neoplasias (advanced adenoma and carcinoma) and carcinomas in older group and also adenoma per colonoscopy rate (ACPR) was higher in seniors. Caucasian intubation rate was significantly lower. The number of colonoscopies after positive FOBT was significantly higher than primary colonoscopies in seniors. See the table. There were no bleeding complications or perforations during screening examinations in both groups.
Introduction: The EpiCom-cohort is a European prospective population-based cohort of unselected patients uniformly diagnosed with inflammatory bowel disease (IBD) in 2010 in 31 Western and Eastern European centres. Previously, this cohort has demonstrated differences in the treatment strategy of IBD patients between Eastern and Western European centres including that significantly more patients in Western Europe receive biological therapy. Despite these differences in treatment no differences regarding disease outcomes including surgery and hospitalization rates and quality of life between the two regions have been found. Anaemia is a common systemic complication and/or extra-intestinal manifestation to IBD as well as an indicator of the level of global IBD care and inflammation control.

Aims & Methods: The aim of the current study was to investigate the occurrence of anaemia as well as differences between Eastern and Western Europe during the first year of disease. Anaemia was defined according to the World Health Organisation and ECCO guideline. Results: A total of 827 patients aged 15 years or older from 29 centres (20 Western, 9 Eastern European) were eligible for analysis of whom 433 (52%) had ulcerative colitis (UC), 300 (37%) had Crohn’s disease (CD), and 94 (11%) had IBD unclassified (IBDU). The proportion of patients with anaemia and its subtypes at diagnosis and follow-up is shown in table 1. Overall, anaemia was more frequent in Eastern than in Western European patients for both CD and UC. After 1 year of follow-up significantly more patients in Eastern Europe who were anaemic at diagnosis remained anaemic (23% UC, 24% CD) compared to Western Europe (8% UC 9% CD), while a similar proportion in both regions changed from the anaemic state to normal (20% UC and 35% CD in both regions) during follow-up. More IBD patients receiving biological therapy during the first year of disease changed status from anaemia at diagnosis to no anaemia at follow-up (83%) compared to patients not having received biological therapy (70%), while fewer patients receiving biological therapy remained anaemic during follow-up (17% vs 30%). These differences did, however, not reach statistical significance (p = 0.09).

Table 1: Prevalence of anaemia at diagnosis and 1-year follow up.

<table>
<thead>
<tr>
<th>Ulcerative colitis</th>
<th>Crohn’s disease</th>
</tr>
</thead>
<tbody>
<tr>
<td>Eastern Europe</td>
<td>Western Europe</td>
</tr>
<tr>
<td>Follow-up Diagnosis</td>
<td>Diagnosis Up</td>
</tr>
<tr>
<td>Anaemia - overall</td>
<td>43%</td>
</tr>
<tr>
<td>Iron deficiency</td>
<td>6%</td>
</tr>
<tr>
<td>Anaemia of chronic disease</td>
<td>9%</td>
</tr>
<tr>
<td>Mixed anaemia</td>
<td>6%</td>
</tr>
<tr>
<td>Other anaemia</td>
<td>6%</td>
</tr>
<tr>
<td>Unclassified</td>
<td>14%</td>
</tr>
</tbody>
</table>

Conclusion: In this unselected, population-based inception cohort the frequency of anaemia was high at the time of diagnosis, especially for CD, but decreased during the first year of follow-up. More Eastern than Western European patients remained anaemic after 1 year of follow-up. These geographic differences could be caused by differences in awareness of anaemia or they might reflect differences in global care and inflammation control of IBD patients in Europe. Geographic variations in the use of biological therapy might contribute to the observed differences in anaemia frequency.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Contact E-mail Address: andrew.wis@mail.com

INTRODUCTION: Use of immunosuppressants in IBD is associated with an increased risk of serious infections that varies considerably according to infection and immunosuppressant subtypes. This study aimed to determine the incidence rate and risk factors for serious viral infection (SVI) according to drug exposure and IBD activity in patients with IBD.

Aims & Methods: Using MICISTA registry, a prospective observational cohort of IBD patients treated at our tertiary care hospital, we identified between Jan 2005 and Dec 2014 patients who developed SVI as defined by need for hospitalization, definite organ damage or disabling sequelae. Cases of CMV colitis without systemic manifestations were excluded. We first estimated incidence rates of SVI, overall and according to maximal yearly treatment. Additionally, we performed a case-control study (4 controls for 1 case matched for age, gender, IBD subtype and duration) assessing risk of SVI according to IBD drug use and IBD clinical activity in the 3 months preceding the SVI (data extracted from individual health records).

Results: We identified 31 patients with SVI among 2645 patients, followed for a median period of 6.2 years and a total observational time of 16922 patient-years. We identified 13 cases of CMV systemic infection (primary infection (n = 6), reactivation (n = 7)), 10 cases of EBV infection (primary infection (n = 6) including 2 haemophagocytic syndromes, reactivation (n = 4)), 5 cases of VZV infection (varicella (n = 3), shingles (n = 2) and 3 cases of HSV infection (severe esophagitis, facial nerve paralysis, severe refractory cutaneous manifestation). Most patients required hospitalization (94%) and received IV anti-viral therapy (50%). The incidence rate of SVI in patients with IBD was 1.83 per 1000 patient-years. Table 1 shows the incidence rate of SVI according to the maximal treatment received during the year. In the case control study, risk of SVI was associated with exposure to thiopurines (adjusted odds ratio (aOR), 5.1; 95% CI, 1.9–13.4; p = 0.001) and methotrexate (aOR, 4.1; 95%CI, 1.0–16.8; p = 0.05), and active clinical disease (aOR, 3.2; 95% CI, 1.3–8.1; p = 0.02). Odds-ratios for corticosteroids and anti-TNF did not reach statistical significance (1.1 and 1.2, respectively).

Table 1: Exposure to medication (patients-years) P value

<table>
<thead>
<tr>
<th>Exposure to medication (patients-years)</th>
<th>Incidence rate for SVI (per 1000 patient-years)</th>
<th>95% Confidence interval</th>
</tr>
</thead>
<tbody>
<tr>
<td>No treatment or 5ASA</td>
<td>7922</td>
<td>0.50</td>
</tr>
<tr>
<td>Steroids</td>
<td>1582</td>
<td>0.63</td>
</tr>
<tr>
<td>Immunosuppressants</td>
<td>6236</td>
<td>3.2</td>
</tr>
<tr>
<td>Anti-TNF ± immunosuppressors</td>
<td>5173</td>
<td>1.16</td>
</tr>
</tbody>
</table>

Conclusion: SVI are rare events in patients with IBD who do not receive immunosuppressants. Exposure to thiopurines or methotrexate, and IBD clinical activity increases substantially the risk. Among 100 patients treated with thiopurines for 10 years, 3 will develop SVI.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP194 COLORECTAL CANCER RISK IN A NATIONWIDE INFLAMMATORY BOWEL DISEASE COHORT WITH LOW GRADE Dysplasia
L. Derikx1, S. V. Tilburg2, I.D. Nagegaard3, L. Nissen4, F. Hoentjen5
1Gastroenterology and Hepatology, Jeroen Bosch Hospital’s, Hertogenbosch/Netherlands
2Gastroenterology and Hepatology, Radboud university medical centre, Nijmegen/Netherlands
3Pathology, Radboud University Nijmegen Medical Center Dept. of Pathology, Nijmegen/Netherlands
4Gastroenterology and Hepatology, Radboud university Medical Center Nijmegen, Nijmegen/Netherlands

Contact E-mail Address: l.derikx@jbz.nl

INTRODUCTION: Patients with long-standing colonic inflammatory bowel disease (IBD) bear an increased colorectal cancer (CRC) risk. Endoscopic surveillance allows early detection and removal of precancerous lesions such as low-grade dysplasia (LGD), and may subsequently prevent CRC. However, the long-term outcome after LGD and the subsequent risk to develop CRC remains uncertain.
since most available studies are small and cover a relatively short follow-up period, we published a systematic review of IBD patients and found a history of LGD to 1) determine the cumulative CRC incidence, and 2) identify risk factors for developing CRC.

Aims & Methods: Using the Dutch National Pathology Registry (PALGA) we identified all patients initially diagnosed with LGD between 1991 and 2005 in the Netherlands. Subsequently, follow-up data were gathered until 2016. We deter-

O195 ROLE OF DIFFUSION-WEIGHTED IMAGING (DWI) IN MRI-ENTEROGRAPHY FOR THE EVALUATION OF SURGICAL RISK IN PATIENTS WITH CROHNS DISEASE

A. Testa1, A. Rispo1, P. P. Mainenti2, D. Musto1, N. Imperatore1, M. Rea1, O. M. Nardone1, N. Caporaso1, F. Castiglione1
1Gastroenterology, Department of Clinical Medicine and Surgery, School of Medicine "Federico II" of Naples, Naples, Italy, Naples, Italy
2Radiology, Department of Clinical Medicine and Surgery, School of Medicine "Federico II" of Naples, Naples, Italy, Naples, Italy

Contact E-mail Address: annatesta82@virgilio.it

Introduction: In Crohn's disease (CD), it is useful to discriminate inflammatory findings from fibrotic ones. Diffusion Weighted Imaging (DWI) is able to identify active inflammation in most pathological tissues.

Aims & Methods: We aimed to define the role of DWI in evaluating the risk of surgery in CD. We performed an observational prospective study including all consecutive patients with active CD undergoing MRI. MRI study included: measurement of bowel wall thickness (BWT), CD extension, enhancement pattern, pre-stenotic dilatation, presence of oedema and/or comb-sign, presence of fibrosis and/or T2 sequences. Furthermore, all patients were screened by DWI sequences defining: visual analysis of intertensity and analysis of Apparent Diffusion Coefficient (ADC) maps. Statistical analysis was performed dividing all patients in 2 groups (operated vs not operated) using T-student and X-square test when indicated. To identify the variables associated to surgical risk, we performed a logistic multiple regression expression the risk in terms of Odds Ratio. Finally, the diagnostic accuracy was tested by a ROC curve.

Results: We identified 1177 IBD patients with colonic LGD with a median follow-up time of 9.8 years per patient after LGD diagnosis (total follow-up time: 11741 patient years). 825 (70.1%) patients had ulcerative colitis, 216 (18.4%) Crohn's disease and 136 (11.6%) indeterminate colitis. Hundred nine out of 1177 (9.3%) patients underwent colectomy. CRC developed in 86 out of 1177 patients resulting in a cumulative incidence of 2.9%, 5.8%, 11.1%, and 18.7% after respectively 5, 10, 15 and 20 years. Patients with an IBD duration of more than 5 years before LGD development had a significantly higher cumulative CRC incidence (14.7% after 15 years) compared to those with a shorter IBD median (9.4% after 15 years; log rank p = 0.006). Furthermore, patients with recurrent LGD had a higher CRC risk compared to patients with single LGD (10.5% after 15 years versus 4.5% after 15 years; log rank p = 0.026). Multivariante Cox regression identified both a longer IBD duration (hazard ration per year: 1.5-4.3) and recurrent LGD (hazard ratio: 1.9, 95% confidence interval 1.1-3.4) as independent factors associated with increased CRC risk.

Conclusion: We showed a cumulative CRC risk of 18.7% after 20 years in a large national cohort of patients with a high prevalence of LGD. Both a longer IBD duration and recurrent LGD were identified as independent risk factors for CRC development following LGD. These findings may aid in risk stratification following a diagnosis of LGD in IBD patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

O196 PREDICTORS OF FIRST COLONIC EPITHELIAL NEOPLASIA IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE UNDERGOING COLONOSCOPIC SURVEILLANCE

J. Kirchgesner1, M. Svreck2, C. Landman1, A. Bourrier1, I. Nion Larmurier1, N. Hoyea1, H. Sokol1, P. Seksik1, J. Cosnes1, J. Flejo1, L. Beaugerie1
1Department Of Gastroenterology, AP-HP, Hopital Saint-Antoine, Paris, France
2Department Of Pathology, AP-HP, Hopital Saint-Antoine, Paris, France
3Department Of Pathology, AP-HP, Hopital Saint-Antoine, Paris, France, Paris, France

Contact E-mail Address: julien.kirchgesner@gmx.com

Introduction: Patients with inflammatory bowel disease (IBD) are at increased risk for developing colorectal neoplasia (CRN). Little is known about risk factors of first CRN in IBD patients after a surveillance colonoscopy negative for neoplasia.

Aims & Methods: The aim of our study was to identify predictive factors of first CRN in IBD patients after a surveillance colonoscopy negative for neoplasia. All consecutive patients with LGD who developed CRC (cases) versus patients who did not develop CRC (controls), was performed to identify risk factors for developing CRC. Demographic data, including gender, IBD type, age and duration, and LGG age and recurrence, were extracted from PALGA. Statistical and multivariable Cox regression analyses with back-

Results: Among 404 patients who underwent 1236 colonoscopies, 38 patients who developed CRN in inflamed mucosa and 92 matched controls were included in a nested case-control study. Independent factors significantly associated with CRN were primary sclerosing cholangitis (PSC) (Odds ratio (OR), 6.26; CI 95% 1.07–36.8, p = 0.03), previous presence of neutralophils, crypt acety or histological ulcerations (OR, 8.77; CI 95% 1.71–45, p = 0.009) and presence of crypt architectural irregularities without neutrophils or ulcerations (OR, 8.09; CI 95% 1.21–54.3, p = 0.03) on more than half of procedures during follow-up, exposure to thiopurines (OR, 0.047-0.608, p=0.001) and 5-aminosalicylates (OR, 0.27; CI 95% 0.084-0.876, p=0.03) at the time of neoplasia or last colonoscopy. We developed a score based on these five items at the time of the surveillance colonoscopy negative for neoplasia. Among patients with a score of 0, the negative predictive value in predicting any CRN was 100% in patients with colonoscopies performed 1 and 3 years after the first surveillance colonoscopy.

Conclusion: In IBD patients undergoing endoscopic surveillance, the risk of first CRN is increased in case of PSC, persistence of histological acute inflammation and recurrent disease, and decreased by concurrent treatment with thiopurines and 5-aminosalicylates. The use of a predictive score derived from these factors could be considered for making decisions on optimal intervals between two surveillance colonoscopies.

Disclosure of Interest: A. Bourrier: Anne Bourrier has received lecture fees from UCB

J. Sokol: Harry Sokol received consulting fees from Enterome, Astellas, Roche, Merck, Maet and Danone.

P. Seksik: Philippe Seksik had consulting fees from Abbvie, Merck-MSD and biocodes and grants from Biocodes.

J. Cosnes: Jacques Cosnes has received lecture fees from Abbvie, consulting fees from Vifor Pharma

L. Beaugerie: Laurent Beaugerie has received consulting fees from abbott, lecture fees from abbott, abbott, MSD, Ferring Pharmaceuticals, Janssen, and research support from abbott, Biocodes and Ferring Pharmaceuticals.

All other authors have declared no conflicts of interest.
categories (0 μg Hb/g, >0–5 μg Hb/g and, >5–10 μg Hb/g) to calculate cumulative incidence of AN. To identify factors associated with AN a Cox proportional hazard regression analysis was performed to calculate hazard ratios (HRs). Consecutive FIT results were analyzed using logistic regression analyses to calculate relative risks of AN. Risks were visualized by generating heat plots for cumulative incidence of AN. To identify factors associated with AN a Cox proportional hazard regression analysis was performed to calculate hazard ratios (HRs). In logistic regression analysis of two consecutive negative FITs, RR increased with up to a 14-fold risk increase for two consecutive FITs with both a Hb concentration of 8 μg Hb/g feces compared to twice a Hb concentration of 0 μg Hb/g (p < 0.001).

Table 1: Time-dependent cox-regression analysis of baseline FIT of advanced neoplasia.

<table>
<thead>
<tr>
<th>Univariate</th>
<th>HR</th>
<th>95% CI</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Gender (male)</td>
<td>1.7</td>
<td>1.3–2.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Age (years)</td>
<td>1.1</td>
<td>1.0–1.1</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Baseline Hb conc.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 μg Hb/g Ref.</td>
<td>&lt;0.001</td>
<td>Ref.</td>
<td></td>
</tr>
<tr>
<td>&gt;0–5 μg Hb/g</td>
<td>1.8</td>
<td>1.3–2.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>&gt;5–10 μg Hb/g</td>
<td>7.0</td>
<td>4.6–10.5</td>
<td>6.0</td>
</tr>
<tr>
<td>Socioeconomic status</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>High</td>
<td>0.8</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Average</td>
<td>1.7</td>
<td>0.7–1.3</td>
<td></td>
</tr>
<tr>
<td>Low</td>
<td>0.6</td>
<td>0.4–1.0</td>
<td></td>
</tr>
</tbody>
</table>

Conclusion: Among FIT negative screeners, baseline Hb concentration is an independent predictor for the risk of future AN. Moreover, Hb concentrations of ≥ 5 μg Hb/g are a strong predictor of the risk of AN with up to a 14-fold risk increase. These findings suggest a role for Hb in personalized screening strategies in population-based screening policies. In addition, the use of Hb of negative FITs may permit alteration of screening intervals. Such strategies could decrease unnecessary burden for screen and optimize the use of program related resources.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP199 MASS SCREENING FOR COLORECTAL CANCER BY USING A FECAL IMMUNOCHEMICAL TEST IN COMBINATION WITH FLEXIBLE SIGMOIDOSCOPY

R. Nozaki, K. Yamada, M. Takano
Gastroenterology, Coloproctology Center, Takano Hospital, Kumamoto City/ Japan

Contact E-mail Address: rnozak0312@yahoo.co.jp

Introduction: To date, there have only been a few large-scale community-based studies that examined the efficacy of using a fecal immunochromatographic test (FIT) in combination with flexible sigmoidoscopy (FS) for colorectal (CRC) screening. Since 1983, we have been conducting community-based mass screening for CRC using fecal occult blood testing in combination with FS in Kyushu, Japan. In 1988, we designed special buses with the necessary equipment to perform FS mass screening in order to test as many people as possible. The two-day FIT method combined with small caliber electronic endoscopes for FS have been in use since 1992. The aim of this study was to investigate the efficacy of combining FIT with FS to detect CRC and then analyze the CRC detection rates.

Aims & Methods: A large sample of 1,597,734 subjects who underwent the FIT procedure to detect CRC and who exhibited a cut-off value of 100 ng/ml were enrolled in this study from 1992 to 2014. Colorectal cancers that were detected using FIT and/or follow-up examinations were classified as two-day FIT-detected cancers. When lesions (i.e. polyps) were found using FS despite a negative two-day FIT outcome or when CRC was detected using colonoscopy the cancers were classified as FIT-negative and FS-detected, respectively. Out of the cases with a negative two-day FIT outcome, 130,779 of them underwent colonoscopy. Results: The positive rate for the negative two-day FIT and FS cases was 8.6% and 90.9% of them underwent work-up examinations. The work-up examinations resulted in a CRC detection rate of 0.15% (mucosal cancer, 0.12%; invasive cancer, 0.03%). In the time-negative two-day FIT and FS cases (n=33,040), the cancer detection rates were as high as 0.27% (mucosal cancer, 0.22%; invasive cancer, 0.05%). On the other hand, 7.1% of all the subjects were detected as positive using only the two-day FIT procedure and 78.0% of them underwent work-up examinations. This resulted in a detection rate of 0.16% (mucosal cancer, 0.07%; invasive cancer, 0.09%). Among first-time subjects (417,352), the cancer detection rate using only the two-day FIT procedure was 0.32% (mucosal cancer, 0.14%; invasive cancer, 0.17%). The CRC detection rate was significantly higher in males than those aged 50 years or older. Adverse events included 15 cases of ischemic colitis that occurred after FS (incidence rate, 0.0082%). There were no cases of perforation or colon perforation.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Aims & Methods: The aim of our study was to compare patient demographics, tumor site, stage and survival between patients with screen-detected CRCs (SD-CRC) and non-screen-detected CRCs (non-SD-CRC). Between 2006 and 2014, asymptomatic persons aged 50 to 74 were invited to take part in four consecutive biennial FIT-screening rounds. CRC cases were identified through linkage with the Netherlands Cancer Registry and were classified into four groups: SD-CRC, FIT interval cancers (diagnosed between screening rounds after negative FIT), colonoscopy interval cancers (diagnosed after negative colonoscopy after a positive FIT) and CRC in non-participants (the latter three representing non-SD-CRC). Information on gender, age, socioeconomic status (SES), tumor site, stage and survival were collected and compared between patients in the four CRC groups using Chi-square-test.

Conclusion: In this population-based CRC screening cohort, 0.14% of all participants were diagnosed with a FIT interval CRC during follow-up. The patients with SD-CRCs had the most favorable stages and highest survival rates. Our results support the effectiveness of FIT-screening programs.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP203 THE ADDED BENEFIT OF SURVEILLANCE IN COLORECTAL CANCER SCREENING

M. J.E. Greuter1, E. Dekker2, G.A. Meijer2, V.M.H. Couple3
1Epidemiology And Biostatistics, VU University Medical Center, Amsterdam/Netherlands
2Gastroenterology & Hepatology, AMC, Amsterdam/Netherlands
3Department Of Pathology, The Netherlands Cancer Institute, Amsterdam/Netherlands
4Epidemiology And Biostatistics, VU Medical Center Epidemiology and Biostatistics, Amsterdam/Netherlands

Contact E-mail Address: mj.greuter@vumc.nl

Introduction: Although the impact of colorectal cancer (CRC) screening on CRC burden is well studied, the added benefit of surveillance in the context of an implemented screening programme is unclear.

Aims & Methods: Using the Adenoma and Serrated pathway to Colorectal Cancer model, we simulated the Dutch faecal immunochemical test (FIT) - based screening programme and combined this with a colonoscopy surveillance strategy based on the Dutch guideline. In this strategy, individuals considered at low risk return to screening after ten years whereas surveillance with a three or five-year interval is recommended for high- and intermediate-risk individuals, respectively. Furthermore, we evaluated three strategies in which the surveillance intervals as recommended in the Dutch guideline were prolonged to a) five years for all individuals at increased risk, b) five and ten years for respectively high- and intermediate-risk individuals and c) ten years for all individuals at increased risk. The comparator strategy was no screening and no surveillance. In addition, we simulated a screening only strategy without surveillance. Outcomes were CRC incidence and mortality, number of colonoscopies per individual in the lifetime of 20,000,000 individuals.

Results: A total of 27,340 people were invited for FIT-screening, of whom 18,752 (68.6%) participated at least once. Median follow-up time was 46 months (IQR 18.5–72.8). Among participants, 3,009 (16%) had a positive FIT in one of the 4 screening rounds. In total, 265 patients were diagnosed with CRC: 116 were SD-CRCs, 27 FIT interval CRCs, 13 colonoscopy interval CRCs and 109 CRCs detected in non-participants. There were no differences between the groups regarding age, gender and SES distribution. Screen-detected CRCs, FIT interval cancers and CRCs in non-participants were mostly located in the distal colon (70.7%, 63% and 61.5% of cases, respectively), whereas colonoscopy interval CRCs were mainly located in the proximal colon (69.2%) (p = 0.10). Stage distribution was significantly different between the four groups, with more favorable stages in patients with SD-CRCs (p < 0.001). Stage distribution in patients with FIT interval CRC and CRCs in non-participants was similar (p = 0.361). Survival-rates were significantly higher among patients with SD-CRCs and FIT interval cancers compared to non-participants and patients with colonoscopy interval CRCs.

Conclusion: In this population-based CRC screening cohort, 0.14% of all participants were diagnosed with a FIT interval CRC during follow-up. The patients with SD-CRCs had the most favorable stages and highest survival rates. Our results support the effectiveness of FIT-screening programs.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP202 SCREEN-DETECTED AND NON-SCREEN-DETECTED COLORECTAL CANCERS AFTER FOUR ROUNDS OF FECAL IMMUNOCHEMICAL TEST-BASED COLORECTAL CANCER SCREENING

M. Van Der Vlugt1, E.J. Grobbbee2, P.M. Bossuyt1, A. Bos1, I. Lansdorp-Vogelaar1, E. Dekker2
1Dept. Of Gastroenterology, Academisch Medisch Centrum Gastroenterology & Hepatology, Amsterdam/Netherlands
2Gastroenterology & Hepatology, Erasmus MC University Medical Center, Rotterdam/Netherlands

Contact E-mail Address: m.vandervlugt@amc.uva.nl

Introduction: Fecal immunochemical test (FIT)-based colorectal cancer (CRC) screening aims to detect CRC in an early stage, thereby reducing morbidity and mortality from this disease. Whereas data on CRC screening adherence are available, few data exist on cancers in FIT-screening programmes based on guaiac fecal occult blood testing are available in literature.

Aims & Methods: The aim of the present study was to investigate potential differences in changes of health behavior at one-year follow-up between screen-negative attendees to two different screening modalities and controls not invited to screening. Participants of both gender, aged 50–74, were invited to complete a self-reported lifestyle questionnaire (LSQ) on smoking, body weight, physical activity, alcohol intake and selected dietary items at baseline and at one-year follow-up. Participants were randomly assigned to five biennial rounds of fecal immunochemical test (FIT), one round flexible sigmoidoscopy (FS) or no screening (controls). In total, 1809 and 1327 participants with a negative screening test result in the FIT and FS group, respectively, completed the LSQ, as did 1029 controls. ANCOVA and logistic regression were used to calculate differences in changes of health behavior (and 95% confidence intervals (CI)) between the arms at follow-up.

Result: Participants with a negative CRC screening test result in the first round of the FIT arm reduced their alcohol consumption significantly more than controls (−0.29 glass/week, (95%CI; −0.54 to −0.04)) during one-year follow-up. Body weight decreased more in participants with a negative screening test result in the FS arm than in the FIT arm during the one-year follow-up (−0.31 kg, (95%CI; −0.55 to −0.08)).

Conclusion: The present study does not suggest unfavorable short-term consequences in health behavior after getting a negative CRC screening test result whether this is from once only FS or first round of FIT screening.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table (OP202)

<table>
<thead>
<tr>
<th>Total CRCs</th>
<th>FIT interval cancer</th>
<th>Colonoscopy interval cancer</th>
<th>CRC in non-participants</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total CRCs</td>
<td>116</td>
<td>27</td>
<td>13</td>
<td>109</td>
</tr>
<tr>
<td>Age diagnosis (%)(n)=50–59</td>
<td>24.1 (28)</td>
<td>43.1 (50)</td>
<td>32.8 (18)</td>
<td>7.7 (1)</td>
</tr>
<tr>
<td>Sex (male;%(n))</td>
<td>62.9 (73)</td>
<td>59.3 (16)</td>
<td>53.8 (7)</td>
<td>15.4 (2)</td>
</tr>
<tr>
<td>SES (%)(n)=Low–Average–High</td>
<td>11.2 (13)</td>
<td>70.7 (82)</td>
<td>18.1 (21)</td>
<td>7.4 (2)</td>
</tr>
<tr>
<td>Tumor location (%)(n)=Proximal–Distal–Unknown</td>
<td>29.3 (34)</td>
<td>70.7 (82)</td>
<td>0 (0)</td>
<td>37 (4)</td>
</tr>
<tr>
<td>Stage I–II–III–IV–Missing</td>
<td>51.7 (60)</td>
<td>13.8 (16)</td>
<td>31.9 (37)</td>
<td>29.6 (8)</td>
</tr>
<tr>
<td>Survival (%)(n)</td>
<td>88 (102)</td>
<td>81.5 (22)</td>
<td>61.5 (8)</td>
<td>59.6 (65)</td>
</tr>
</tbody>
</table>
Result: FIT screening without a surveillance programme reduced CRC incidence and mortality compared to surveillance, payments for follow-up were 30% lower compared to the FIT programme and no surveillance strategy. CRC incidence and mortality reductions increased to 28% and 40.8% when surveillance based on the Dutch guideline was added to FIT screening. Prolonging surveillance intervals slightly reduced surveillance effectiveness (CRC incidence reductions 26.6%–27.2%, mortality reductions 39.6%–40.8% compared to no screening and no surveillance). In screening, 21 diagnostic colonoscopies were required to detect one CRC. The burden of surveillance was considerably higher; in the Dutch guideline strategy, 572 colonoscopies were required to detect one CRC by surveillance. Prolonging surveillance intervals decreased this burden to 129–366 colonoscopies per surveillance-detected CRC. All screening plus surveillance strategies were equally or more effective (0.00011 life-years gained) and less costly ($2.4–$6.8 per person) than screening only. The standard surveillance strategy was set at five years due to all other screening plus surveillance strategies.

Conclusion: Adding surveillance to FIT screening reduces CRC burden and is cost-effective compared to screening without surveillance. However, the colonoscopy burden is markedly higher than this burden in a screening programme. Through modelling, we showed that this burden can be substantially lowered, without substantial loss of effectiveness, if surveillance intervals are lengthened to five years.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016
10:30-12:00
VIRAL HEPATITIS: NATURAL HISTORY AND TREATMENT – ROOM M

A82

Disclosure of Interest: M. Mandorfer: M.M. received honoraria for consulting from AbbVie, Bristol-Myers Squibb, Gilead, MSD and Roche.
K. Koizial: K.K. received travel support from AbbVie, Bristol-Myers Squibb and Gilead.
P. Schwabl: P.S. received payments for lectures from Roche and travel support from Janssen and Roche.
C. Freismuth: C.F. received travel support from Gilead and Janssen.
S. Drum: S.R.T. received travel support from AbbVie.
A.F. Stüttmayer: A.F.S. received honoraria for consulting from Gilead, payments for lectures from Boehringer Ingelheim, Janssen and Roche, as well as travel support from Gilead, Bristol-Myers Squibb, Janssen and Roche.
T. Reiberger: T.R. received payments for lectures from Roche, as well as travel support from Gilead, MSD and Roche.
S. Beinhard: S.B. received honoraria for consulting from AbbVie, payments for lectures from Bristol-Myers Squibb, as well as travel support from Gilead, MSD and Roche.
H. Hofer: H.H. received payments for lectures from AbbVie, Gilead, Janssen, MSD and Roche.
A. Fertilich: A.F. received grants from Janssen and payments for lectures from Gilead, MSD and Roche.
P. Ferenczi: P.F. received grants from Gilead, MSD, and Roche, as well as honoraria for board membership and consulting from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Janssen, Idexx, MSD and Roche.
M. Trauner: M.T. received grants from MSD, honoraria for consulting from AbbVie, Gilead, Janssen and MSD, payments for lectures from Gilead, MSD and Roche, as well as travel support from Gilead.
M. Peck-Radosavljevic: M.P. received grants from Gilead, MSD and Roche, honoraria for board membership and consulting from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Janssen and MSD, as well as payments for lectures from AbbVie, Boehringer Ingelheim.

All other authors have declared no conflicts of interest.

OP204 SUSTAINED Virologic RESPONSE TO INTERFERON-FREE THERAPIES AMELIORATES HCV-INDUCED PORTAL HYPERTENSION

Division Of Gastroenterology And Hepatology, Department Of Internal Medicine III, Medical University of Vienna, Vienna/Austria

Introduction: Portal pressure, assessed by hepatic venous pressure gradient (HVPG) measurement, drives the development of liver-related complications and is a marker of advanced chronic liver disease. Since a decrease in HVPG translates into a clinically meaningful benefit, it is an acceptable surrogate endpoint.

Aims & Methods: We aimed to investigate the impact of sustained virologic response (SVR) to interferon (IFN)-free therapies on portal hypertension in patients with paired HVPG measurements. One hundred and four patients with portal hypertension (HVPG ≥ 6 mmHg) who underwent HVPG and transient elastography (TE) before IFN-free therapy (baseline [BL]) were retrospectively studied. The effect of SVR on portal pressure was investigated in patients with SVR who also underwent follow-up (FU)-HVPG and TE after IFN-free therapy (group A; n = 60). To demonstrate the generalizability of our results, we included a second group (group B; n = 40), comprising all patients who achieved SVR after IFN-free therapy and had a FU-HVPG measurement. In these patients, only information on FU-T was available. Moreover, we also included 4 patients who did not achieve SVR.

Result: SVR to IFN-free therapies significantly decreased HVPG across all BL-HVPG strata. Between July 1, 2011 and July 1, 2015, this multicenter study prospectively enrolled 140 consecutive CHB patients with negative HBeAg and detectable viral DNA at the cessation of NAs after a minimum of 3 years on therapy. In those who experienced virological relapse (viral DNA > 2000IU/mL), the incidences of clinical relapse (virological relapse plus ALT > 80IU/mL) and persistent/severe hepatitis (clinical relapse lasting for 3 months or accompanied with jaundice) were estimated by the Kaplan Meier method. Predictors were explored by the Cox proportional hazard modelling.

Result: Following virological relapse that took place in 94 patients, clinical relapse and persistent/severe hepatitis occurred in 49 and 34 patients, respectively. The 2-year cumulative incidences were 61.5% (95% CI, 50.1–73.0%) and 56.2% (95% CI, 42.2–71.2%), respectively. Multivariate-adjusted analyses revealed clinical relapse was associated with serum concentration of viral DNA (hazard ratio [HR], 1.26 per log-mg/mL, 95% CI, 1.04–1.53) and alanine aminotransferase (ALT) at virological relapse (HR, 1.003 per IU/L; 95% CI, 1.002–1.004), as well as ALT at NA cessation (HR, 1.005; 95% CI, 1.002–1.008), whereas persistent/severe hepatitis was associated with viral DNA (HR, 1.41; 95% CI, 1.16–1.71), ALT (HR, 1.004; 95% CI, 1.001~1.007), and α-fetoprotein (HR, 1.13 per mg/mL; 95% CI, 1.02–1.26) at virological relapse.

Conclusion: Clinical hepatitis frequently occurs following virological relapse in CHB patients after NA cessation, and may be predicted by serum viral load, ALT, and α-fetoprotein at the viral resurgence.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
Aims & Methods: In total, 153 secondary patients with HCVC 1b initiating DAV/ASV therapy were enrolled. The cohort comprised 52 patients with compensated cirrhosis and 101 patients without cirrhosis (67 males and 86 females; median age, 71 years; 9 patients were >80 years old). NSSA resistance-associated variants (RAVs) were examined using direct sequencing. The patients were treated with 60 mg of DAV and 150 mg of ASV twice per day for 24 weeks. Clinical, biological, and virological data, including adverse effects, were recorded at baseline and during follow-up.

Result: Only 10 (6.5%) patients had L31M or Y93H RAVs. There was no statistically significant difference in age, sex, IL28B genotypes, HCV viral load at baseline, ALT level, creatinine level, or NS5A RAVs between patients with and without cirrhosis. Only 10 (6.5%) patients had L31M or Y93H RAVs. There was no statistically significant difference in age, sex, IL28B genotypes, HCV viral load at baseline and during follow-up.

Conclusion: DAV/ASV therapy achieved a high anti-HCV effect in patients both with and without cirrhosis. However, careful management is necessary in patients with cirrhosis.

Disclosure of Interest: A Tamori has received research funding from Chugai Pharmaceuticals, MSD K.K., and Bristol-Myers Squibb. N. Kawada: Norifumi Kawada has received research funding from MSD K.K., Chugai Pharmaceutical Co., Ltd, Bristol-Myers Squibb, and a lecturer’s fee from Janssen Pharmaceutical K.K. All other authors have declared no conflicts of interest.

Op208 EXPERIENCE IN THE MANAGEMENT OF DECOMPENSATED HCV CIRRHOTIC PATIENTS WITH LOW DOSE SOFOSBUVIR AND RIBAVIRIN COMBINED WITH DACLATASVIR

A. S. Hanafy

Internal Medicine, Zagazig University, Zagazig, Egypt

Contact E-mail Address: amrhanafy@zu.edu.eg

Introduction: The introduction of oral direct-acting antiviral (DAA) therapy in the management of chronic active HCV, sustained response rates occurred in more than 95% of patients with compensated liver disease with improvement in their survival and the risk of decomposition that necessitates liver transplantation. The introduction of combination of reduced rates of sustained virological response in compensated cirrhosis was explained by extensive portosystemic collaterals, advanced fibrotic parenchyma which are difficult to be penetrated, and provide dormant foci for viral reactivation. It was claimed that achieving SVR will improve MELD and CTP scores with improvement in clinically significant portal hypertension and hepatic venous pressure gradient.

Aims & Methods: Evaluation of the efficacy and safety of managing chronic active HCV in patients with compensated cirrhosis and if SVR will improve CTP and MELD as well as the quality of life of these patients. Forty patients with compensated cirrhosis with frequent hepatic encephalopathy or difficult to treat ascites were included if they had chronic active HCV proved by the positivity of HCV RNA, elevated transaminases. Patients were excluded if they had hepatic/cellular carcinoma, other causes of liver diseases or mixed causes (excessive alcohol consumption, autoimmune liver disease), previous liver transplantation. The patients were given sofosbuvir 200 mg, ribavirin 200 mg, and daclatasvir 60 mg for 6 months and evaluated for the development of sustained virological response, the occurrence of adverse effects and the effects of SVR on the rate of development of hepatic encephalopathy, improvement in ascites control.

Result: Forty patients (31 males, 9 females) presented with chronic active HCV were enrolled, all showed difficult to treat cirrhotic ascites. 29 patients showed chronic recurrent episodes of hepatic encephalopathy (62.5%, 2.1 ± 0.6 episodes/2 months). The mean age was 51.4 ± 6.3 years, albumin 2.3 ± 0.4 g/dl, total bilirubin 1.9 ± 0.5 mg/dl, Hemoglobin 9.9 ± 1.8 g/dl. 83.9 ± 15.4 ± 103 cell/ul, creatinine 1.3 ± 0.2 mg dl, AST 77 ± 24.21 U/l, ALT 66.7 ± 15.4 U/l, AFP 28.9 ± 10.8 U/ml, MELD score 22.6 ± 2.2, Child Tuzelotte Pugh (CPT) score 9 ± 0.9. After six months of therapy; all the patients were compliant, with no reported major complications. Mean platelet count was significantly increased after treatment (88.6 ± 13.9 ± 103 cell/ul, p = 0.000), with a statistically significant improvement in severe hepatocellular activity in most of HCV infected patients. It remains to be explored if these improvements result in decreased liver-related mortality in the setting of HIV/HCV confection.

Disclosure of Interest: All authors have declared no conflicts of interest.
M. Mandonfer: received honoraria for consulting from Janssen, payments for lectures from Bristol-Myers Squibb, Janssen, and Roche, as well as travel support from AbbVie, Gilead, MSD, and Roche. B. Schemer: received travel support from Gilead. T. Buesjes: received payments for lectures from Roche and travel support from Bristol-Myers Squibb. K. Grabmeier-Pietschhammer: received honoraria for consulting from Gilead, payments for lectures from Bristol-Myers Squibb and ViV, as well as travel support from Bristol-Myers Squibb, Gilead, and GlaxoSmithKline. A. Feltlisch: received travel support from AbbVie and Gilead. M. Trauner: received grants from MSD, honoraria for consulting from AbbVie, Gilead, Janssen, and MSD, payments for lectures from Gilead, MSD, and Roche, as well as travel support from Gilead. M. Peck: received travel support from Gilead, MSD, and Roche, honoraria from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Janssen, and MSD, and payments for lectures from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead, Janssen, and Roche. T. Reiberger: received payments for lectures from Roche, as well as travel support from Gilead, MSD, and Roche.

All other authors have declared no conflicts of interest.

**OP210 RANDOMIZED, BACK-TO-BACK TRIAL OF NEW GENERATION OF NBI (HQ 290) FOR THE DETECTION OF COLORECTAL POLyps**

H.J. Goong1, B.M. Ko1, S.R. Jeon1, H.G. Kim2, S.J. Hong1, J. Kim1, M.S. Lee1

1Digestive Disease Center and Research Institute, Department Of Internal Medicine, SoonChunHyang University School of Medicine, Bucheon and Seoul, Korea, Bucheon and Seoul Korea, Republic of

2Department Of Internal Medicine, SoonChunHyang University School of Medicine, Bucheon, Korea, Republic of

Contact E-mail Address: goong@schmc.ac.kr

**Introduction:** The benefits of narrow band imaging (NBI) for improving the detection of colorectal polyps remain questionable. The newly available second generation of NBI using 290 system (290-NBI) provides an at least two folds brighter image compared with the previous version.

**Aims & Methods:** The aim of this study was to compare polyp miss rates between 290-NBI and high-resolution white light endoscopy (HR-WLE). Methods: From June 2015 to September 2015, 102 patients were randomized to undergo either HD-WLE or 290-NBI colonoscopy. In HD-WLE group, we performed colonscopic examination as first inspection with HR-WLE followed by a second inspection with NBI. In 290-NBI group, colonscopic examination were performed first inspection with NBI followed by a second inspection with HR-WLE. The primary outcomes were polyp miss rates.

**Result:** A total of 127 polyps of 102 patients were detected. In HD-WLE group, 39 polyps were detected during the first inspection. A second inspection with NBI added 20 polyps, resulting in polyp miss rate of 33.9% with HR-WLE. In the NBI group, 54 polyps were detected during the first inspection. Subsequent inspection with NBI added 14 polyps, resulting in polyp miss rate of NBI of 20.6% (33.9% vs 20.6%, p = 0.068). In subgroup analysis, the polyp miss rates of flat type of HR-WLE and NBI showed significant difference (18.6% vs. 5.9%, p = 0.029).

**Conclusion:** New generation of NBI (HQ290) may reduce polyp miss rates and be more effective in reducing polyp miss rates of flat type.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


OP213 MOTORIZED SPIRAL ENTEROSCOPY: A NEW TECHNIQUE FOR ONE-STAGE COMPLETE ENTEROSCOPY

E. Belkin,1 K. Bhattacharya1, E. Ostdeil,1 D. Cave,1 P. V. Draganov,1,2
1Gastroenterology, University of Massachusetts Medical School, Worcester/United States of America/MA
2Gastroenterology, Baylor University Medical Center, Dallas/United States of America/TX

Introduction: Three different platforms have been developed to perform deep enteroscopy; namely, single balloon, double balloon, and spiral enteroscopy. None of these devices permits routine evaluation of the entire small intestine, even with a combination of antegrade and retrograde enteroscopy. We report our early clinical experience with a motorized spiral enteroscope, which may provide a modality for one-stage complete enteroscopy.

Aims & Methods: We report early experience with a prospective multi-center efficacy and safety trial. The study was approved by the institutional review boards of each of the participating centers. Patients referred for evaluation of small bowel disease at one of the three participating centers requiring antegrade enteroscopy were offered participation in the study, and then screened for exclusion criteria. If enrolled, informed consent was obtained.

Table 1 (OP213)

<table>
<thead>
<tr>
<th>Subject #</th>
<th>Age</th>
<th>Sex</th>
<th>Indication(s)</th>
<th>BMI</th>
<th>ASA Grade</th>
<th>Insertion Time (min)</th>
<th>Procedure Time (min)</th>
<th>Point of Deepest Insertion</th>
<th>Complications</th>
<th>Final Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>24</td>
<td>M</td>
<td>Abdominal pain; video capsule findings of ulcerated mucosa in mid small bowel</td>
<td>40</td>
<td>III</td>
<td>33</td>
<td>41</td>
<td>Distal Jejunum</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>2</td>
<td>22</td>
<td>M</td>
<td>CT scan finding of intussusception</td>
<td>21</td>
<td>II</td>
<td>32</td>
<td>43</td>
<td>Cecum</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>3</td>
<td>61</td>
<td>F</td>
<td>Gastrointestinal bleeding; video capsule finding of angioectasia</td>
<td>27</td>
<td>III</td>
<td>61</td>
<td>94</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>4</td>
<td>58</td>
<td>F</td>
<td>Iron deficiency anemia; video capsule finding of angioectasia</td>
<td>23</td>
<td>III</td>
<td>47</td>
<td>70</td>
<td>Distal Ileum</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>5</td>
<td>67</td>
<td>M</td>
<td>Iron deficiency anemia</td>
<td>23</td>
<td>II</td>
<td>48</td>
<td>66</td>
<td>Cecum</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>6</td>
<td>33</td>
<td>M</td>
<td>Gastrointestinal bleeding</td>
<td>28</td>
<td>III</td>
<td>59</td>
<td>78</td>
<td>Cecum Bleeding Meckel's diverticulum</td>
<td>None</td>
<td>None</td>
</tr>
<tr>
<td>7</td>
<td>29</td>
<td>M</td>
<td>Suspected croh's; video capsule finding of a bleeding angioectasia and a small bowel polyp</td>
<td>28</td>
<td>II</td>
<td>49</td>
<td>72</td>
<td>Cecum None Croh's</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

 endemic enterochal anesthesia, the motorized spiral enteroscope (SIF-Y0019, Olympus, Japan) is inserted through the mouth. The rotational advancement and withdrawal is controlled by the endoscopist using a foot pedal. The primary outcome of the study was the depth of insertion of the enteroscope.

Result: Demographics of the study patients are summarized in Table 1. Of the first 7 completed procedures, we were able to accomplish complete enteroscopy in 5 (71%) patients. In the other two instances, the distal jejunum and distal ileum were reached. The average insertion time was 47 minutes [range: 32–61] with an average total procedure time of 66 minutes [range: 41–94]. A bleeding event requiring hospitalization occurred within 7 days of one of the procedures but that was due to the underlying lesion rather than a complication of the procedure. No other significant adverse events were reported.

Conclusion: We present our initial experience of a safety and efficacy data trial for the motorized spiral enteroscope. We were able to safely accomplish full enteroscopy in 71% of cases with a single antegrade deep enteroscopy using the motorized spiral enteroscope. This percent achievement of complete enteroscopy in a time typically reported for unidirectional deep enteroscopy suggests that this device is a significant development in design of small bowel enteroscopes. One patient experienced bleeding requiring hospitalization within 7 days of the procedure. This was a significant adverse event (SAE) by protocol. However an in further review it was determined that the patient bled from a Meckel's diverticulum, identified during deep enteroscopy. Subsequent surgery was curative.

Disclosure of Interest: K. Bhattacharya: Consulting for Olympus

D. Cave: Consulting and receipt of research funds from Olympus. Consulting for Medtronic

D. Demarco: Consulting for Spirus

All other authors have declared no conflicts of interest.

Reference


OP214 THE AER-O-SCOPE COLONOSCOPE PROVIDES SUCCESSFUL ENDOSCOPIC THERAPY IN AN EX VIVO SWINE COLON MODEL

S. Bezobchuk, I.M. Gralnek
Institute Of Gastroenterology, Ha'Emek Medical Center, Afula/Israel

Contact E-mail Address: stanislavlbe@clalit.org.il

Introduction: The Aer-O-Scope Colonoscope System (GI View Ltd., Ramat Gan, Israel) is a self-propelled, joystick controlled, disposable colonoscope that provides panoramic (360°) endoscopic visualization of the colon and includes two working channels compatible with standard endoscopic tools [1,2].

Aims & Methods: We aimed to demonstrate the success of the self-propelled Aer-O-Scope colonoscope in providing endoscopic therapeutic access. Therapeutic endoscopic access was a priori defined as the ability to reach a pre-defined target of interest, a pseudo-polyp, within an ex vivo swine colon and deliver "simulated" endoscopic therapy including: polypectomy with snare or biopsy forceps, submucosal injection, or thermal coagulation using argon plasma coagulation (APC). This was a prospective cohort study (n = 12 ex vivo swine colons housed in four different models that simulated variants of a human colon). Varying sized pseudo-polyps (n = 8 in each ex vivo swine colon) were created using colored thread and were randomly distributed throughout each ex vivo swine colon. Thus, n = 96 pseudo-polyps in total were created: 1 mm–5 mm (n = 72 pseudo-polyps); 6 mm–9 mm (n = 13), 14 mm–17 mm (n = 6, 6%). Following one day of Aer-O-Scope training for joystick utilization and endoscopic therapeutic access, two endoscopists (IMG and SB) performed all the colonoscopies (n = 240 simulated endoscopic therapies (n = 192 biopsy forceps, snare polypectomy, or combination injection/snare polypectomy and n = 48 APC applications). This sample size allowed up to a 10% pseudo-polyp miss rate with a two-sided
OP215 OUTCOME OF ENDOSCOPIC MUCOSAL RESECTION OF 424 LARGE SESSILE COLONIC POLYPS (≥20MM) OVER A 9 YEAR PERIOD: A SINGLE CENTRE EXPERIENCE AND ANALYSIS OF CHANGE WITH TIME

D.N.F. N. Lim1, R. J. Robinson1, A. Moore1, J. De Caestecker2, P. Wurm1

1Digestive Disease Centre, University Hospital of Leicester, Leicester/United Kingdom
2Digestive Disease Centre, University Hospital of Leicester, Leicester/United Kingdom

Contact E-mail Address: dennis2020@yahoo.com

Introduction: Endoscopic mucosal resection (EMR) has become the standard technique for resection of large sessile and flat colonic polyps. We aimed to assess the clinical outcome of colonic EMR of polyps ≥2cm and greater in size at University Hospital of Leicester NHS Trust and to assess changes over a 9-year period.

Aims & Methods: Data was collected for all sessile colonic polyps ≥20mm removed by EMR between 2006 and 2014 by 3 endoscopists (PW, JDC, RJR). Patient demographics, resection technique, completeness of initial resection, recurrence rate at first surveillance (SC1), polyp eradication at 2nd surveillance after at least 1 year (SC2) and complication rates were analysed.

Results: 364 patients were assessed for EMR, among which there were 424 completed EMRs (96.9%, 95% CI 95.4–98.8%). Complete endoscopists (≥90% CI 95.4–98.8%) and complete resection (≥90% CI 95.4–98.8%) at SC1 were ≥95%. There were only 2 failures, both during use of a polypectomy snare. Endoscopist-rated subjective usability of the EMR system demonstrated the ability to easily provide simulated endoscopic therapeutic access using standard endoscopic tools while having very high usability ratings.

Discussion of Interest: S. Bezobchuk: I am a consultant for GI View Ltd. I.M. Gralnek: I am a consultant for GI View Ltd.

References

OP217 STEPWISE DEVELOPMENT OF A VOLUMETRIC LASER ENDOCOPY PREDICTION SCORE FOR BARRETT’S NEOPLASIA USING MATCHED VOLUMETRIC IMAGE ANALYSIS OF ENDOSCOPIC RESECTION SPECIMENS

A. Swager1, M.G. h. Van Oijen2, G.J. Tearney3, C. L. Leggett4, S.L. Meijer5, W.L. Curvers6, J.J. Bergman7

1Gastroenterology And Hepatology, Academic Medical Center, Amsterdam/Netherlands
2Medical Oncology, Academic Medical Center, Amsterdam/Netherlands
3Pathology and Wellman Center for Photomedicine, Massachusetts General Hospital and Harvard Medical, Boston, Boston/United States of America
4Gastroenterology And Hepatology, Mayo Clinic, Rochester/Rochester/United States of America
5Pathology, Academic Medical Center, Amsterdam/Netherlands
6Gastroenterology And Hepatology, Catharina hospital, Eindhoven/Netherlands
7Gastroenterology & Hepatology, Academic Medical Center, Amsterdam/Netherlands

Contact E-mail Address: a.swager@amc.uva.nl

Introduction: Endoscopic detection of early neoplasia in Barrett’s esophagus (BE) is difficult. Volumetric laser endomicroscopy (VLE) is an advanced imaging system incorporating 2nd generation optical coherence tomography in a balloon-based system, providing a 6-cm long circumferential scan of the esophagal wall up to 3 mm deep, with near-microscopic resolution. Several VLE features of early BE neoplasia have been determined previously (1,2). Aims & Methods: Aims of this study were to determine (additional) VLE features of neoplasia, based on precise VLE-histology correlations ex vivo, and to develop and validate a VLE prediction score for early BE neoplasia.

When the AEC validated criteria are applied by the 13 endoscopists, the sensitivity, specificity, NPV and PPV of detecting neoplastic Barrett’s are 98.5%, 97.5%, 97.5% and 97.5% respectively.

Conclusion: We have developed and established the validity of a simple classification system to identify Barrett’s neoplasia using AEC. When non-AEC trained endoscopists apply these criteria, the sensitivity and NPV meet the recommended PIWI threshold.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table 1: Validation results of the classification criteria

<table>
<thead>
<tr>
<th>Criteria</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>NPV</th>
<th>PPV</th>
</tr>
</thead>
<tbody>
<tr>
<td>Loss of acetowhitening</td>
<td>96.2%</td>
<td>93.8%</td>
<td>90.9%</td>
<td>97.5%</td>
</tr>
<tr>
<td>Surface pattern</td>
<td>77.0%</td>
<td>99.0%</td>
<td>91.4%</td>
<td>96.9%</td>
</tr>
<tr>
<td>Normal</td>
<td>69.7%</td>
<td>93.5%</td>
<td>88.4%</td>
<td>93.9%</td>
</tr>
<tr>
<td>Abnormal</td>
<td>99%</td>
<td>99%</td>
<td>99%</td>
<td>99%</td>
</tr>
</tbody>
</table>

When acetowhitening and surface pattern are used in combination (Table 2), the sensitivity, specificity, NPV and PPV of detecting neoplastic Barrett’s are improved to 100%, 97.5%, 97.5% and 97.5% respectively.
VLE-histology correlation methodology has been described previously (3). In the orientation phase, VLE-histology images were evaluated in an unblinded manner by a GI pathologist, BE endoscopist and VLE researcher. Features potentially predictive for early BE neoplasia were identified and subsequently discussed in consensus with 2 VLE experts. In the learning phase, VLE images corresponded to neoplasia (high-grade dysplasia (HGD) or early adenocarcinoma (EAC)); n = 10) and non-dysplastic (ND) BE tissue (n = 10) were scored by the 2 VLE experts – blinded to histology – for presence of neoplasia and VLE features identified in the orientation phase. After a consensus meeting, a predictive signature based on multidimensional regression analysis using learning phase results. This score was validated by expert scoring of 40 additional VLE images (20 HGD/EAC; 20 ND) using area under receiver operating characteristic (ROC) curve (AUC) analysis.

Results: Four features potentially predictive for BE neoplasia were identified: 1) lack of layering; 2) higher surface signal than subsurface signal; 3) presence of irregular, dilated glands/ducts; and 4) homogeneity. In the learning phase, features 1, 2, and 3 were significantly and independently associated with neoplasia. The prediction score was developed with: features 1, 2, and 3 (1.5, 2.6, and 2.0 points, respectively) and feature 4 (1.6 points). ROC curve of this prediction score showed an AUC of 0.83 (95% CI 0.76–0.90) in the learning and 0.81 (95% CI 0.71–0.90) in the validation phase. A cut-off value of ≥ 8 was associated with sensitivity and specificity of 83% and 68% in the learning phase and 83% and 71% in the validation phase, respectively.

Conclusion: This study, using high-quality ex vivo VLE-histology correlation, confirms that the VLE features layering, surface signal, and irregular glands/ducts are independently and significantly associated with early BE neoplasia. Using these features, we developed and validated a VLE prediction score for BE neoplasia, with promising accuracy.

Disclosure of Interest: G.J. Tearney: Massachusetts General Hospital has a licensing arrangement with NinePoint Medical. Dr. Tearney has the rights to receive royalties from this licensing arrangement.


All other authors have declared no conflicts of interest.

References

OP218 DETECTION OF DYSPLASIA IN BARRETT’S OESOPHAGUS USING LECTIN-BASED NEAR INFRARED-RED MOLECULAR IMAGING: AN EX-VIVO STUDY ON HUMAN TISSUE

1MRC Cancer Unit, University of Cambridge, Cambridge/United Kingdom
2Cambridge Institute, Cancer Research UK, Cambridge/United Kingdom
3Histopathology, Cambridge University Hospitals, Cambridge/United Kingdom
4Physics, University of Cambridge, Cambridge/United Kingdom

Contact E-mail Address: md400@mrc-cu.cam.ac.uk

Introduction: Detection of early neoplasia in Barrett’s oesophagus by white-light endoscopy is challenging due to the inconspicuous nature of dysplasia. Molecular imaging using fluorescently labelled wheat-germ agglutinin (WGA) is a promising tool for detecting dysplasia as this topically applied imaging agent shows localized interactions against neutral or nonspecific oesophageal glandular mucosa (1). However, in an endoscopy setting, the detection of fluorescence in the blue/green range is limited by high levels of tissue autofluorescence. This limitation can be overcome by using near-infrared (NIR) imaging.

Aim: Objectives of this study was to assess in an ex vivo model the feasibility of WGA-based NIR imaging for detection of dysplasia in Barrett’s. To this end, we studied patients with early Barrett’s-related neoplasia undergoing endoscopic mucosal resection (EMR). Freshly collected EMR specimens were sprayed with WGA-IR800CW (10 μg/mL; 10 min, room temperature); washed with PBS buffer and then imaged with a high-sensitivity NIR camera (Flaebume 5-800, Fluopect). Planar fluorescence images were captured and up to two punch biopsies (2 mm diameter) were collected from each EMR specimen, underwriten by the above-described method potentially predictive for dysplasia. The EMRs were then assessed in an ex vivo frozen and paraffin embedded (FFPE), cut every 2 mm and processed for histopathological assessment. Each section was scored by an expert GI pathologist every 1 mm to construct a pathology grid, which was manually cross-registered with the fluorescence images. The matched punch biopsies, taken from areas of interest within the EMR specimen, were also scored by the pathologist. The mean fluorescence intensity (MFI) of cells in dysplastic and non-dysplastic areas was compared by the Wilcoxon matched-pairs signed rank test. The MFI of punch biopsies taken from dysplastic and non-dysplastic areas was compared by the Mann-Whitney test. The correlation between the fluorescence contrast and spatial extent of dysplasia was analysed by linear regression.

Result: Ten patients were recruited at a single centre. We included in the analysis 42 dysplastic and 45 non-dysplastic punch biopsies, of which 16 were dysplastic. In the whole EMR analysis, we found a significantly lower mean fluorescence intensity (MFI) in dysplastic versus non-dysplastic areas (P < 0.0001), in accordance with the reported reduced binding of WGA to neoplastic Barrett’s epithelium (1). Similarly, the MFI of punch biopsies taken from dysplastic regions was significantly lower compared to that of non-dysplastic areas (P = 0.0002). Finally, we found that the fluorescent contrast between dysplastic and non-dysplastic areas was higher in EMRs with wider extent of neoplasia (R² = 0.58, P = 0.0002).

Conclusion: WGA-based NIR imaging is an effective method for differentiating dysplastic from non-dysplastic Barrett’s mucosa ex vivo, which reduces the effects of tissue autofluorescence. In-vivo studies are now required to test the feasibility of this method for the endoscopic diagnosis of dysplasia.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP219 RESULTS OF A PROSPECTIVE MULTICENTER REGISTRY OF RADIOFREQUENCY ABLATION FOR BARRETT’S OESOPHAGUS

J. Vlieberg*, P.H. Deprez*, H. Willekens*, D. De Looe*, H. Orelten*, E. Mucken*, P. Christiansen*, F. Mana*, G. De Hertogh*, R. Bischoops*
1Gastroenterology, UZ Leuven, Leuven/Belgium
2Department of Hepato-gastroenterology, Cliniques Universitaires Saint-Luc Université, UZ Brussel/Brussels/Belgium
3UZ Gent, Gent/Belgium
4UZ Antwerpen, Antwerp/Belgium
6Imelda Bonheiden, Bonheiden/Belgium
7UZ Brussels/Brussels/Belgium

Contact E-mail Address: joke.vlieberg@ghent.be

Introduction: Radiofrequency ablation (RFA), combined with endoscopic resection (ER), has been used as a primary treatment for low-grade dysplasia (LGD), high-grade dysplasia (HGD) and early adenocarcinoma (EAC) in Barrett’s oesophagus. In prospective multicenter controlled trials, high rates of complete remission of dysplasia (CR-D) and intestinal metaplasia (CR-IM) have been reported.

Aims & Methods: The aim of this study is to monitor outcome and efficacy of RFA in a setting of absence of reimbursement in a multicenter national prospective registry. Between February 2008 and August 2015, data from 7 centers performing RFA were collected in the Belgian RFA registry. All procedures were monitored for indication, treatment before RFA, short/long-term complications and prospective long-term pathological outcome. Primary endpoint was CR-D and CR-IM. Secondary endpoints was safety.

Results: 188 RFA procedures were registered in 279 different patients (mean age 65: 84.5% men). In 60% a previous EMR/ESD was performed. Baseline histology prior to RFA (including ER) was: 2% SIM (5), 8% LGIN (22), 52% HGIN (146), 37% adenocarcinoma (102), 1% unknown (4). At the time of available follow-up, patients were still under treatment in 185 patients (50%). In an intention to treat analysis (ITT), 83% (194/235) patients achieved CR-IM and 87% (204/235) CR-D after a median of 2 median RFA sessions. 18 patients discontinued treatment, giving a per patient analysis 44 patients were still under treatment. In an intention to treat analysis 44 patients were still under treatment. In an intention to treat analysis 44 patients were still under treatment. In an intention to treat analysis 44 patients were still under treatment. In an intention to treat analysis 44 patients were still under treatment. In an intention to treat analysis 44 patients were still under treatment.

In the whole EMR analysis, we found a significantly lower mean fluorescence intensity (MFI) of cells in dysplastic and non-dysplastic areas was compared by the Mann-Whitney test. The correlation between the fluorescence contrast and spatial extent of dysplasia was analysed by linear regression.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
OP220 LONG-TERM FOLLOW-UP RESULTS OF STEPWISE RADICAL ENDOSCOPIC RESECTION FOR BARRETT’S ESOPHAGUS WITH EARLY NEOPLASIA

K. Belghazi1, F. G. i. Van Vilsteren1, B.L. a.m. Weusten2, S.L. Meijer3, J.J. Bergman4, B.E. Pouw4
1Gastroenterology And Hepatology, Academic Medical Centre, Amsterdam/Netherlands
2Department Of Gastroenterology And Hepatology, St Antonius Hospital, Nieuwegein/Netherlands
3Pathology, Academic Medical Centre, Amsterdam/Netherlands
4Gastroenterology & Hepatology, Academic Medical Centre, Amsterdam, Netherlands
5Gastroenterology & Hepatology, Academic Medical Centre, Amsterdam, Netherlands, Amsterdam/Netherlands

Contact E-mail Address: k.belghazi@amc.uva.nl

Introduction: Stepwise radical endoscopic resection (SRER) allows for complete excision of Barrett’s esophagus (BE) with early neoplasia. This approach has been shown very effective in reaching complete eradication of high-grade dysplasia (HGD) or early cancer (EC) (CE-neo) in 98% and all intestinal metaplasia (CE-IM) in 85% of patients.

Aims & Methods: The aim of this study was to report the long-term follow-up (FU) results after successful SRER for BE with early neoplasia. We screened all patients treated with SRER in two centers between 2001–2014, for BE ≤5 cm with HGD/EC, without visible invasion > T1m1, G2/G4 differentiation, lymph-vascular invasion or irregular deep resection margins in ER specimens. All patients who had reached endoscopic and histologically confirmed CE-neo and CE-IM after SRER were included for evaluation of long-term FU. All included patients were followed up with upper endoscopies and histological outcomes were recorded and entered in a dedicated database. Duration of FU was calculated from last treatment till last FU endoscopy. Primary outcomes: recurrence of HGD/EC and IM in biopsies (FU of 31 months). In all cases the extent of recurrence was limited to small (<1 cm) islands or tongues. Histological recurrence without visible BE was found in 25 patients: 3 patients had BB in neosquamous biopsies (4% overall, 1.4% per patient year). Histological recurrence of IM combined with visible islands or tongues. Secondary outcomes: recurrence of Barrett’s metaplasia (BB) in neosquamous biopsies, and IM in biopsies obtained distal to the neo-z-line.

Result: Seventy-three patients were included (64 men, mean age 66 yrs, median BE 2C(2)). Worst baseline pathology: HGD, n = 50; EC, n = 23. Median FU was 31 months (9-120) with a range of 10 (IQR: 4-8) endoscopies. Recurrence of HGD/EC was observed in 1 patient (1.4%) after 129 months FU (T1N0M0 treated with curative surgery). Recurrence of IM in endoscopically visible BE was observed in 16 patients (of which 2 had LGD) after a median FU of 31 months. In all cases the extent of recurrence was limited to small (<1 cm) islands or tongues.

Conclusion: Our studies support a role of BMP4 as a positive regulator of chemoresistance and invasiveness in EAC, and suggest that inhibition of BMP4 with highly specific antibodies has the potential to ameliorate the malignant behavior of aggressive SMAD4 negative esophageal cancers.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Tuesday, October 18, 2016 10:30-12:00
Accuracy in Upper GI Endoscopy – Room LB
OP222 PREMEDICATION WITH SMITHECHINE AND N-AcetylCysteine in Improving Mucosal Visibility During Upper Endoscopy – A Prospective Double-Blinded Randomized Controlled Trial
L. Elvas, M. Areia, S. Alves, D. Brito, S. Saraiva, A.T. Cadime Gastroenterology, Portuguese Oncology Institute - Coimbra, Coimbra/Portugal

Contact E-mail Address: luissandreldelas@gmail.com

Introduction: Upper endoscopy is the most common method for the diagnosis of upper gastrointestinal tract disease. Our aim was to determine if pre-medication with simethicone or N-Acetylcysteine improves mucosal visualization during upper endoscopy.

Aims & Methods: Randomized double-blind, placebo controlled trial of 297 patients. Pre-medication with: A–100 mL of water (placebo); B–water plus 100 mg simethicone; C–water plus N-acetylcysteine plus 600 mg N-acetylcysteine. Primary outcome was the quality of mucosal visualization (score: 1-excellent; 2-adequate; 3-inadequate). Trial registered at: http://clinicaltrials.gov (NCT02355703). Statistical analysis with X2 and one-way ANOVA with Tukey’s correction.

Result: Visualization scores between groups B and C (versus A) were significantly better in the oesophagus 1.09 and 1.15 vs. 1.31 (p < 0.05) and stomach 1.26 and 1.30 vs. 1.67 (p < 0.01) and better without significance in the duodenum 1.07 and 1.09 vs. 1.20 (p = NS). “Excellent” scores versus others provided similar results (B and C vs. A): oesophagus 91% and 87% vs. 71% (p < 0.001), stomach 76% and 75% vs. 39% (p < 0.001) and duodenum 85% and 82% vs. 73% (p = NS). There was no significant difference in visualization scores between groups B and C for patients with previous subtotal gastrectomy (B and C vs. A): 1.45 and 1.68 vs. 1.86 (p = NS). The rate of reported lesions was higher in group B (without statistical significance).

Conclusion: Premedication with simethicone leads to better mucosal visualization, might improve diagnostic yield and should be considered standard practice. Addition of N-acetylcysteine had no benefit over simethicone alone.

Disclosure of Interest: All authors have declared no conflicts of interest.
**OP223 DIAGNOSIS OF TUMOR EXTENT OF EARLY GASTRIC CANCER BY MAGNIFYING NARROW BAND IMAGING (M-NBI) CHROMENDOSCOPY: A MULTICENTER PROSPECTIVE RANDOMIZED CONTROLLED TRIAL**

1Dept. Of Gastrointestinal Oncology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka/Japan
2Dept Of Endoscopy, Fukuoka University Chikushi Hospital, Fukuoka/Japan
3Dept Of Gastroenterology, Ishikawa Prefectural Central Hosp., Kanazawa/Japan
4Dept. Of Gastroenterology, Daiichi Medical Center, Tokyo/Japan
5Dept Of Gastroenterology, Oita Red Cross Hospital, Oita/Japan
6Dept Of Molecular-targeting Cancer Prevention, Kyoto Prefectural University of Medicine, Kyoto/Japan
7Department Of Endoscopy, Fukuoka University Chikushi Hospital, Fukuoka/Japan

**Contact E-mail Address:** takashikana@gmail.com

**Introduction:** Accurate diagnosis of lateral extent of early gastric cancer (EGC) is important in terms of deciding treatment indication and achieving complete resection by endoscopy or surgery. Magnifying narrow band imaging (M-NBI) has been expected to increase yield of endoscopic diagnosis for determining extent of EGC.

**Aims & Methods:** To compare diagnostic ability of M-NBI for determining lateral extent of EGC with that of chromendoscopy (CE). This study was conducted as a multicenter prospective randomized controlled trial involving one university hospital, one cancer referral center and three general hospitals. Inclusion criteria were patients with EGC sized 1 cm or over who underwent endoscopic or surgical treatment. Exclusion criteria were history of gastric resection and high risk of bleeding for biopsy. After stratification by institution, tumor location, and histological type, patients were randomly assigned to M-NBI or CE groups. In each group, tumor extent was firstly evaluated by white light endoscopy according to difference of mucosal height and color, then the margin of the tumor was determined by the assigned method. Diagnostic criteria of M-NBI were 1) demarcation line and 2) irregular microvessels/microsurface patterns; and that of CE were 1) abrupt change of mucosal structure of the surrounding mucosa and 2) irregular structure patterns. Biopsy specimens were taken from 5-mm-outside and -inside of the oral boundary of the tumor and sent for histological evaluation. When the outside specimen was non-cancer and the inside specimen was cancer in histology, it was defined as “successful delineation”. Primary endpoint was the proportion of successful delineation between the two groups. A study protocol was approved by institutional review board in each institution and written informed consent for study participation was obtained from all patients.

**Result:** A total of 382 patients were enrolled and were assigned to the M-NBI group (n = 191) and the CE group (n = 191). Eight patients in the M-NBI group and 12 in the CE group were excluded remaining 183 in the M-NBI and 179 in the CE group for analysis. Successful delineation rates (95% CI) in the M-NBI and CE groups were 86% (81–91%) and 84% (78–89%), respectively (p = 0.498).

**Conclusion:** This prospective randomized controlled trial revealed M-NBI and CE were equally accurate for determining extent of EGC, thus both methods are adequate to perform in clinical practice (UMIN000014628).

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**Reference**

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**OP224 FEASIBILITY OF A COMPUTER ALGORITHM FOR DETECTION OF EARLY BARRETT’S NEOPLASIA USING VOLUMETRIC LASER ENDOMICROSCOPY**

A. Swager,1 F. Van Der Sommen,2 S. Zinger,2 S.L. Meijer3, E.J. Schoon4, J.J. Bergman1
1Dept. Of Gastroenterology, Catharina Hospital Gastroenterology and Hepatology, Eindhoven/Netherlands
2Department Of Gastroenterology, Catharina Hospital Gastroenterology and Hepatology, Eindhoven/Netherlands
3Gastroenterology & Hepatology, Academic Medical Centre, Amsterdam/Netherlands
4Dept. Of Gastroenterology and Hepatology, Catharina Hospital Gastroenterology and Hepatology, Eindhoven/Netherlands

**Contact E-mail Address:** a.swager@amc.uva.nl

**Introduction:** Volumetric laser endomicroscopy (VLE) incorporates 2nd generation optical coherence tomography technology in a balloon-based system, which is capable of scanning the esophagus circumferentially over 6 cm, up to a depth of 3 mm with near-microscopic resolution. VLE has the potential to improve detection of early neoplasia in Barrett’s esophagus (BE). However, interpretation of VLE images is complex due to subtle differences in architecture and gray-scale color and the large amount of images that needs to be scrutinized by the endoscopist (a 6-cm VLE scan contains 1200 frames). A recently developed clinical prediction model of VLE features for BE neoplasia showed a reasonable accuracy (AUC of 0.81).

**Aims & Methods:** The aim of this study was to investigate the feasibility of a computer algorithm to identify early BE neoplasia on ex vivo VLE images. Sixty VLE images from a database of high-quality one-to-one VLE-histology correlations were used (30 non-dysplastic (ND)BE and 30 neoplastic images; high-grade dysplasia and early adenocarcinoma), consisting of VLE scans from endoscopic resection specimens of Barrett’s patients’ + neoplasia. VLE images were normalized to a height of 400 pixels in order to obtain a standardized zoom factor. Previously identified VLE features predictive for BE neoplasia served as clinical input for the algorithm: 1) higher VLE surface signal than subsurface signal in tissue, 2) lack of layering. From these VLE features an algorithm feature was derived for automating both surface and subsurface signal. A signal intensity histogram using 8 intensity categories was calculated over the first 4 layers of 50 pixels, starting at the top of the image. Linear support vector machine was used to classify the images according to the used VLE texture features. Leave-one-out cross-validation was employed for validation of the algorithm.

**Result:** Using the correlated histology as the reference standard, specificity, sensitivity, specificity and accuracy for the algorithm to detect BE neoplasia were 93%, 70%, 91% and 83%, respectively. The area under the receiver operating curve (AUC) of 0.91 for detecting BE neoplasia in ex vivo VLE images. Most distinctive features of the algorithm are the top layers and mid-range intensities of the histogram.

**Conclusion:** This is the first study in which a computer algorithm for BE neoplasia was developed based on VLE images with direct histological correlates. The algorithm showed good performance to detect BE neoplasia in ex vivo VLE images (AUC 0.91). Compared to the performance of a recently developed clinical VLE prediction score (AUC 0.81), this study suggests that an automatic detection algorithm seems to perform at least as good as assessment by VLE experts in detecting early neoplasia on VLE. Future studies on in vivo VLE scans are needed to further validate the algorithm.

**Disclosure of Interest:** I.J. Bergman. Research support: Olympus Endoscopy, Fuji-film, Cook Medical, Boston Scientific, Cobienda, Erbe, Ninepoint Medical, C2-therapeutics, Cerinostics, Intercap - Training programs: Cobienda, Boston Sc. - Consultancy-speaker: Cook, Boston Sc., Cobienda. All other authors have declared no conflicts of interest.

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**Table 1. (OP225): Overall accuracy of the four patterns predictions**

<table>
<thead>
<tr>
<th>Pattern</th>
<th>Sensitivity, % (95% CI)</th>
<th>Specificity, % (95% CI)</th>
<th>PPV, % (95% CI)</th>
<th>NPV, % (95% CI)</th>
<th>Accuracy, %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type I*</td>
<td>90.00 (75.50–99.75)</td>
<td>79.03 (66.82–88.34)</td>
<td>40.91 (20.70–63.65)</td>
<td>90.00 (89.35–99.95)</td>
<td>80.55</td>
</tr>
<tr>
<td>Type II*</td>
<td>91.43 (76.94–98.20)</td>
<td>78.38 (61.79–90.17)</td>
<td>80.00 (74.98–98.02)</td>
<td>90.62 (74.98–98.02)</td>
<td>84.72</td>
</tr>
<tr>
<td>Type III*</td>
<td>66.67 (9.43–99.16)</td>
<td>88.41 (78.43–94.86)</td>
<td>20.00 (2.52–55.61)</td>
<td>98.39 (91.34–99.96)</td>
<td>87.50</td>
</tr>
</tbody>
</table>

a) Ability to predict normal mucosa. b) Ability to predict Helicobacter pylori infection. c) Ability to predict mucosa atrophy.

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**OP225 OPTICAL ENHANCEMENT SYSTEM™ PLUS OPTICAL MAGNIFICATION UTILITY IN THE IDENTIFICATION OF NORMAL GASTRIC MUCOSA, HELICOBACTER PYLORI ASSOCIATED GASTRITIS, AND GASTRIC ATROPHY**

C. Robles-Medranda1, M. Valero1, M. Puga1, M. Soria2, J. Ospina1, H. Alvarado1, H. Pita
gano Laskukh1
1Endoscopy, Instituto Ecuatoriano de Enfermedades Digestivas-IECED-University Hospital Omni, Guayaquil/Ecuador
2Endoscopy, Instituto Ecuatoriano de Enfermedades Digestivas - IECED, Guayaquil/Ecuador

**Contact E-mail Address:** carlosomak@yahoo.es

**Introduction:** It has been proposed that high-resolution zoom endoscopes (optical zoom up to 115 times) could predict gastric pit pattern for gastric pathology. Recently an image-enhanced endoscopic technology called Optical Enhancement system (OE System™) was introduced, improving visualization of microvessels. In addition to this, new high-definition scope types of Magniview™ are available allowing an optical zoom up to 136 times with a better evaluation of the mucosa and superficial vascular aspects.

**Aim & Methods:** The aim of our study was to evaluate the utility OE System™ plus Magniview™ in the diagnosis of normal gastric mucosa, Helicobacter pylori associated gastritis, and gastritis atrophy. Methods: Prospective, non-randomized and double blind study. All of the participants enrolled had functional dyspepsia according to the Rome III criteria and were tested for Helicobacter Pylori (HP) using stool antigen test. After this phase two groups were selected, dyspeptic HP (+) and dyspeptic HP (-) patients (control group). Finally an upper endoscopy using OE system™ plus Magniview™ scopes was performed and the gastric body evaluated using a previously described classification of four patterns based on the combination of the parameters subepithelial capillary network (SECN), collecting venules and round pits. Type I pattern predicts normal...
gastrointestinal mucosa, types 2 and 3 HP related gastritis and the type 4 gastric atrophy. Type 5 "mixed" HP was not analyzed and classified in the four patterns after the agreement of three endoscopists. There were 22 (30.6%) patients with type I, 13 (18.1%) with type II, 27 (37.5%) with type III and 10 (13.9%) with type IV pattern. Almost all patients (90%) with normal mucosa were type I. Most type II and III patterns had active chronic gastritis, which correlates with HP infection. In fact, 32/34 (91.1%) of patients with HP (+) were type II-III. The 66% of patients with atrophy had type IV pattern. The Table 1 shows the overall accuracy of the four patterns predictions. Type I patients were depicted as normal mucosa, Type II-III HP infection, and Type IV atrophy with a sensitivity of 90%, 91% and 66.7% respectively and an accuracy of 80.5%, 84.7% and 87.5% respectively. Finally the intra and inter-observer agreement was calculated with a kappa value of 0.91 and 0.89 respectively.

Conclusion: Volumetric laser endomicroscopy plus optical magnification has proved to be useful in the diagnosis of normal gastric mucosa and HP associated gastritis with high accuracy, unlike gastric atrophy evaluation

Disclosure of Interest: C. Robles-Medranda: Key Opinion Leader for Pentax Medical
All other authors have declared no conflicts of interest.

Reference

OP226 FIRST-IN-MAN PILOT STUDY: FEASIBILITY OF LASER MARKING IN BARRETT’S ESOPHAGUS WITH VOLUMETRIC LASER ENDOMICROSCOPY
A. Swager1, A. J. De Groof1, S.L. Meijer2, B.L. a.m. Weusten1, W.L. Curvers3, J.J. Bergman1
1Gastroenterology And Hepatology, Academic Medical Center, Amsterdam/Netherlands
2Pathology, Academic Medical Center, Amsterdam/Netherlands
3Gastroenterology And Hepatology, Catharina hospital, Eindhoven/Netherlands
4Gastroenterology & Hepatology, Academic Medical Centre, Amsterdam/Netherlands

Contact E-mail Address: a.swager@amc.uva.nl

Introduction: Laser endomicroscopy (LME) is an advanced imaging system that provides a 6-cm long, circumferential scan of the esophageal wall subsurface layers with near-microscopic resolution. VLE has the potential to improve the detection of neoplasia during Barrett’s esophagus (BE) surveillance. A new feature of the VLE system is a laser marking tool that enables direct marking of suspicious areas during VLE scanning, which subsequently can be used endoscopically to mark the lesions for histopathological analysis.

Aims & Methods: The aim is to evaluate the feasibility of VLE laser marking in BE patients. A total of 17 patients with BE were evaluated using LME.

Conclusion: In this study, VLE laser marking was feasible and safe in BE patients. The tool offers the advantage of marking suspicious areas by LME in real-time, which can be used as a reference point for further endoscopic biopsies.

2Department Of Gastroenterology, Otto-von-Guericke University, MAGDEBURG/Germany

Contact E-mail Address: jochenweigt@gmx.de

Introduction: Digital subtraction angiography is a method to enhance the contrast to noise ratio of angiographic images with contrast structures that are not of interest are deleted from the image by subtraction of image information. A variation of this technique is called Road Map Fluoroscopy (RMF) where an image at peak opacification is used as the mask for subsequent subtraction images. With the RMF technique, radiologists or cathe ters can be viewed without additional marking or contrast injection. In summary, the opacification is only performed once but the information remains on the image throughout the investigation. In this way anatomic structures such as length or diameter of stenosis can be measured with high accuracy (1–4). Although esophageal stent placement has been reported to be safe also without fluoroscopic guidance most endoscopists prefer to use fluoroscopy during stent deployment (5–7). Mucosal marking using the injection of lipiodol for stent implantation is widely used among endoscopists but may no longer be necessary if RMF is used as guidance of the procedure. The use of RMF has so far not been evaluated for endoscopic procedures.

Aims & Methods: We aimed to evaluate the usefulness of Road Map Fluoroscopy to guide endoscopic interventions in the esophagus. Patients with esophageal strictures were consecutively enrolled in a monocentric observational trial. After identification of the stenosis, a Road Map (Philips Multidigita10 Endoscopy, Philips Healthcare, Netherlands) was performed using 200 ml of water-soluble contrast media that was applied through the working channel of a gastroscope (Fujifilm EG530NW or Olympus GIF-Q 180). RMF recording requires stable fluoroscopy of the region of interest to generate a mask for consecutive subtraction. Thereafter contrast medium is injected. After RMF application all further fluoroscopy images contain the information of the subtraction as steady overlay. Directly after the RMF was finished, the complete fluid was removed from the esophagus to avoid aspiration. Patients were all investigated in recumbent position under sedation or propofol. All further interventions and measurements were performed by using the RM images.

Result: 21 investigations were performed in 18 patients (age:71 ± 13 years; male:12 female:6). Indications for interventions were: balloon dilatation of benign strictures: n=9 including 1 pneumatic balloon dilatation for the treatment of achatia, bougainage of benign stricture: n=3 and diagnostic radiography without intervention: n=1. In addition 8 stents, 5 partially covered and 3 fully covered, were placed using RMF as a guide for exact determination of stent length and deployment. All stents were also deployed under RMF guidance. Endoscopic control revealed desired stent position in all cases. The choice of stent was made by measurement of the length of the stenosis as well as diameter of healthy esophageal mucosa adjaent to the stricture. Available stents that fitted best to the measured dimensions were implanted. In all procedures RMF successfully guided the intervention. The feeling of resistance during bouginage was exactly matching the location for RMF projection of the stenosis. With the help of RM imaging further fluoroscopy could be avoided. The endoscope was then maneuvered inside the stenosis to avoid slipping of the balloon. Complications did not occur.

Conclusion: RMF provides the possibility of permanent radiographic illustration of stenosis or anatomic changes throughout the intervention by using contrast medium only at the beginning of the intervention. RMF is feasible and safe to guide radiology based interventions in the esophagus. RMF directs the selection of stents better than endoscopy because all relevant dimensions can be measured exactly.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016
10:30-12:00
SMALL BOWEL DISEASE AND NUTRITIONAL THERAPY – ROOM 1.86

OP228 GASTROINTESTINAL DISEASES IN COMMON VARIABLE IMMUNODEFICIENCY
S. Pikkarainen1, T. Martelius2, J. Selenius3, M. Seppänen4, M.A. Färkkila1
1Dept. Of Gastroenterology, Helsinki University Hospital, Helsinki/Finland
2Dept Of Infectious Diseases, Helsinki University Hospital, Helsinki/Finland
3Rare Diseases Center And Dept. Of Infectious Diseases Clinic, Helsinki University Hospital, Helsinki/Finland
4Rare Diseases Center, Helsinki University Hospital, Helsinki/Finland

Contact E-mail Address: sampsa.pikkarainen@hus.fi

Introduction: Common variable immunodeficiency (CVID) is the most common symptomatic primary immunodeficiency in adults. CVID is a combination of humoral and cell-mediated deficiency, and the cornerstone of its treatment is intravenous or subcutaneous immunoglobulin therapy. However, while this treatment prevents infections, many CVID patients may still develop a broad spectrum of gastrointestinal disorders including autoimmune and inflammatory diseases such as atrophic gastritis, small bowel villous atrophy and inflammatory
Aims & Methods: Aim of the study: To investigate in detail the gastrointestinal phenotypes living in south Manchester. Patients and Methods: Our study cohort consisted of 105 adult CVID patients followed up between 2007–2015 in Helsinki University Hospital Adult Immunodeficiency Unit and the respective outpatient clinics of Care and Eksko. CVID patients were diagnosed according to the response to the routine immunological criteria and lived within the hospital districts of southern Finland (1.9 million inhabitants). Adult patients of this cohort were diagnosed from the year 1960 to 2015 when recruitment stopped. We investigated retrospectively their medical records, laboratory results, endoscopic and histological reports and data was collated to an electronic database designed for the study. Of this patient cohort, 12 patients died and 11 were lost to follow up. Results: Upper endoscopy and ileo-colonoscopy were done at least once to 83 (11%) patients, respectively. Helicobacter pylori was found in 7 patients, was negative in 74 and unknown in 23 patients. Eradication was successful in all Helicobacter-positive patients. Helicobacter-negative chronic gastritis without marked atrophy, but ranging from mild to severe inflammation and atrophy was found in 11 patients (11%). In addition, atrophic gastritis in one patient was found in 10 patients (10%). Small bowel: All tested patients were seronegative for coeliac disease. Of patients with increased intra-epithelial lymphocytes and villous atrophy of duodenum, 2 had complete histological and clinical response to gluten-free diet and all 4 others were unresponsive but had no enterocyte antibodies. 3 of the patients with refractory duodenal villous atrophy and inflammation had also inflammatory changes in colon also. 3. Hepatobiliary: Primary sclerosing cholangitis or CVID-associated cholangitis was diagnosed in 5 patients. 3. Large Bowel: Inflammatory changes of mucosa ranged from specific colitis and microscopic colitis (including lymphocytic colitis and collagen colitis) to crypt-destructive and/or graft-versus-host like severe inflammation. Conventional diagnostic tests showed plasma citrulline levels in patients with colitis ulcerosa increased in 5 patients (2 colectomies) and one patient had strictureting ileocolonic Crohn disease. Altogether, inflammation of colon was more common than small bowel enteropathy and it was found in 20 patients (19%). Prior to ileocolonoscopy, bacterial and parasitic infections were ruled out by standard laboratory methods including fecal sample screening. Nodular lymphatic hyperplasia was detected from gastric mucosa to rectum, and ranged from asymptomatic enhanced ileal nodularity to major changes of the gastric and bowel mucosal appearance and function. It was relatively common finding and noted in 36 patients (34%). 4. Mortality and gastrointestinal malignancies: 12 patients died during the follow up and in 3 patients it was directly due to metastatic malignancies of gastrointestinal tract; 2 patients with gastric adenocarcinoma and one patient with colorectal cancer. Gastric wall ulceration had been found also in other 2 patients that died due to the cardiovascular disease. Meanwhile, one patient with unsppecific inflammatory nodularity of colon eventually developed caecal large B-cell lymphoma which was diagnosed, and treatment was started. Conclusion: Gastrointestinal and hepatobiliary manifestations are common among patients with CVID and the risk malignancies are increased. Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

Aims & Methods: A prospective study evaluated SeHCAT usage across the United Kingdom was undertaken, capturing data from 38 centres and 1,036 patients. Aims were to investigate SeHCAT retention rates according to the United Kingdom was undertaken, capturing data from 38 centres and 1,036 patients. Aims & Methods: The procedure adopted for measuring plasma citrulline was Tendem Mass Spectrometry (LC-MS/MS) & RP-HPLC. Disease state was confirmed by histopathology findings including Marsh score and HLA typing(DQ2 & DQ8) BY SSP-PCR.

Results: Mean plasma citrulline levels in 54 serology positive subjects was 20.2 SD umol/L whereas the mean citrulline levels in 124 serology negative subjects (first degree relatives) was 24.3umol/L. This difference was statistically highly significant with p value of 0.0001. Correlations between biopsy grades of Subjects with their citrulline levels were established & found to be significant. For Marsh 3c grade lesions, mean citrulline levels were 5.6 ± 2.6 umol/L. For Marsh 3b, mean citrulline levels were 15.0 ± 2.6 umol/L with p value 0.006. Understandably the patients with total villous atrophy had a lower citrulline levels even if they were asymptomatic. All the patients were on stringent six month follow up and the mean levels were 12.8 ± SD umol/L. DQ2 heterodimer were collectively found in 71.63% high risk subjects. A total of 8.69% subjects found negative for HLA DQ2 heterodimer. HLA type DQ8 was not found in any of the subject.

Conclusion: Citrulline alone is a very important metabolomic signature of initial damage of gut enterocytes in celiac disease and also when correlated with Marsh score. Citrulline estimation on dried blood spots using tandem mass spectrometry is a minimally invasive and promising test in near future which could be transferred to the remote places of the country to suggest improvement in gut enterocyte mass. Plasma citrulline estimation assures detection of potential celiac disease and may be use for monitoring of monitoring and recovery in CD which is likely to be of immense benefit in the diagnosis of celiac disease and analyzing citrulline on dried blood spot by a highly sensitive technique of liquid chromatography mass spectrometry may ease follow up and diagnosis of CD.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
activity were examined by a mutagenesis technique in the promoter assay and RPA interference technology. The effects of TPEN on occludin and claudin-3 expression in mouse colon were also examined in combination with the calpain inhibitor.

Result: Intracellular zinc depletion by TPEN impaired the TJ barrier of intestinal Caco-2 cells. Intracellular zinc depletion-induced TJ disruption is associated with downregulation of TJ proteins, occludin and claudin-3. These changes induced by TPEN were completely restored by supplemental zinc. Biolumination of cell surface proteins revealed that the zinc depletion induced the proteolysis of occludin, but not claudin-3. Occludin proteolysis was sensitive to the inhibition of calpain activity, and increased calpain activity was observed in the zinc-depleted cells. Although qPCR analysis and promoter reporter assay have demonstrated that the zinc depletion-induced claudin-3 expression at transcriptional levels, a site-directed mutation in the egr1 binding site in the claudin-3 promoter sequence induced loss of both the basal promoter activity and the TPEN-induced increases. Reduced egr1 expression by a specific siRNA also inhibited the claudin-3 expression and basal barrier function and restored barrier function of CACO-2 human intestinal epithelial cells. Dig Dis Sci 2013; 58: 77–87.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP232 EVALUATING THE QUALITY OF LIFE OF ADULT PATIENTS ON HOME PARENTERAL NUTRITION IN NORTHERN AND NORTHEAST ENGLAND

Department Of Gastroenterology, Freeman Hospital, Newcastle-upon-Tyne/United Kingdom

Contact E-mail Address: maxworth.hu@gmail.com

Introduction: Home parenteral nutrition (HPN) has been established for the management of patients with Type 3 intestinal failure (IF). A Quality of Life (QL) assessment tool (HPN-QOL version 1.0) was developed and validated in 2009 specifically for this patient population (1). Little data exist in literature on the QOL of HPN patients. We incorporated this tool into local clinical practice to evaluate the QOL of our HPN cohort in Northern and Northeast England.

Aims & Methods: The HPN-QOL was discussed with all patients in clinic and sent by post with a prepaid return envelope and a letter explaining how information will be used. Participation was voluntary. Responses were collected between February and July 2015. Data were anonymised for analysis and reporting. Patients were grouped according to the following 4 criteria for further analysis: age, more than 60 years, gender, male, female, presence of stoma, yes, no. QOL score exceeding 50 in symptom domains were interpreted as frequent symptoms.

Result: 22 patients (61.5%) completed the HPN-QOL. 55 and 60 to 65. Based on the rating descriptors in the HPN-QOL we interpreted a scaled score of more than half of the questions in each domain were answered as per the validated process in HPN-QOL. Raw patient responses were scaled to a score of 0–100 for each domain. The QOL global numerical ratings had a scale of –60 to 65. Based on the rating descriptors in the HPN-QOL, we interpreted a scaled score of more than half of the questions in each domain were answered as per the validated process in HPN-QOL. Raw patient responses were scaled to a score of 0–100 for each domain. The QOL global numerical ratings had a scale of –60 to 65. In age group analysis, patients over 55 had lower employability (p = 0.007) and higher quality of life (p = 0.027) at working and wages. In gender analysis, males reported better ability to travel/holiday, physical function, employment and sexual function.

Conclusion: This study shows that intracellular zinc has an essential role in the regulation of claudin-3. Regardless of gender, age, or presence of stoma, patients generally rated their ability to travel/holiday, physical function, employment and sexual function poorly. Fatigue was a major limiting symptom. The global QOL numerical rating was also poor in all groups.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Disclosure of Interest:
Genes.
Flagellin, whereas CMC increase the pro-inflammatory potential of the microbiota was sufficient to drive low-grade intestinal inflammation and metabolic syndrome. When transferred to germfree recipient mice, P80 and CMC-treated human microbiota from the SHIME system was transferred to germfree recipients. P80 and CMC treatment increased the pro-inflammatory potential (Flagellin and LPS loads) were analyzed.

Introduction: We recently demonstrated that, in mice, consumption of dietary emulsifiers, detergent-like components of many processed foods, results in a disturbed gut microbiota, including alterations in species composition, elevated pro-inflammatory potential (i.e., higher levels of bioactive LPS and flagellin) and microbiota encroachment (1). Such disturbance of the microbiota promotes a range of chronic inflammatory diseases including metabolic syndrome and colitis. However, the underlying mechanism by which emulsifiers induce such effects, including whether they act directly upon the microbiota or the host, remains unclear.

Aims & Methods: Our aim in the current study was to investigate if, and how, emulsifiers directly impact upon the microbiota in the absence of a host response. The M-SHIME® (Mucosal Simulator of the Gastrointestinal Microbial Ecosystem) model was used to examine the effects of emulsifiers on the microbiota in vitro. After a stabilization period of 7 days, this dynamic human gut model was treated with emulsifiers (Carboxymethylcellulose (CMC) or Polyisorbate-80 (P80), 1%). Microbiota composition, meta-transcriptomic and pro-inflammatory potential (Flagellin and LPS loads) were analyzed. Microbiota metagenome was predicted using PICRUSt (Phylogenetic Investigation of Communities by Reconstruction of Unobserved States). Human microbiota from the SHIME system was transferred to germfree recipient mice, with subsequent intestinal inflammation analysis.

Result: Both P80 and CMC treatment increased the pro-inflammatory potential of human microbiota, as revealed by a dramatic increase in bioactive flagellin within one day for CMC and 5 days for P80. P80 induced drastic alteration of the human gut microbiota composition, associated with an increased proportion of genes involved in bacterial motility. Both P80 and CMC treatment did not significantly alter branched or short chain fatty acid compositions, but significantly increased the proportion of microbiota mRNAs encoding motility related proteins. When transferred to germfree recipient mice, P80 and CMC-treated human microbiota was sufficient to drive low-grade intestinal inflammation and metabolic syndrome.

Conclusion: Both emulsifiers directly acted upon the microbiota to increase its pro-inflammatory potential, indicating that at least a portion of the effects of emulsifiers in vivo results from direct action of these compounds on the microbiota. The mechanisms by which P80 and CMC act are distinct, with P80 altering the composition of the microbiota, favoring species expressing high level of flagellin, whereas CMC increase the pro-inflammatory potential of the microbiota in a composition independent manner, by inducing expression of motility genes.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
surgery and of endoscopy (performed at 6 months). Bacterial composition of the ileal mucosa associated microbiota was analyzed at time of surgery using 16S (MiSeq, Illumina). The obtained sequences (rarefied to 1000 read/sample) were analyzed using the Qime pipeline to assess composition, alpha and beta diversity. Bacterial taxa associated with clinical parameters were identified using Multivariate association with Linear Models (MaAsLin) taking into account sample phenotype, clinical parameters and treatments.

Result: 146 patients were included: 73 (50%) were male, median age at surgery was 32 years (IQR 26–42). Median disease duration was 6 years (IQR 2–12). 44 patients (30%) were active smoker at time of surgery. Thirty patients (21%) had a previous resection, and 35 patients (24%) had perianal lesions. Indication for surgery was stricture disease (n = 95), penetrating disease (n = 53). At time of surgery, 67 patients (46%) had received anti-TNF therapy within the last 3 months. After surgery, 31 patients received thiopurines, and 52 patients received anti-TNF therapy. The microbiota was mainly composed of bacteria from the Firmicutes (Mean 55%, range 0.3–99%), Proteobacteria (Mean 36%, range 0.5–99%), Bacteroidetes (Mean 5%, range 0–52%) and Actinobacteria (Mean 6%, range 0–81%) phyla. As expected, antibiotics treatment within one month before surgery had a dramatic impact on microbiota composition (Anosim, p < 0.0001) and diversity (mean observed species: 302 ± 17 vs 236 ± 14, p = 0.0005). In multi-variate analysis (MaAsLin), antibiotics treatment was notably associated with an increase in Enterococcus sp. (q < 0.001) and with a decrease in Lachnospiraceae family (q = 0.004). Taking into account only the patients who did not received antibiotics within a month before surgery, we then looked for predictive factors of endoscopic recurrence. Patients with endoscopic recurrence, defined by a Recurrence Index (RI), had a lower bacterial diversity at time of surgery compared to patients in endoscopic remission (n = 65) (mean observed species: 276 ± 14 vs 365 ± 45, p = 0.015).

Conclusion: Ileal mucosa associated microbiota of CD patients at time of surgery is dominated by bacteria belonging to Firmicutes, Proteobacteria, Bacteroidetes and Actinobacteria phyla. Antibiotics given during the last month prior to surgery induce major perturbations of the microbiota. Reduction in bacterial diversity at time of surgery is predictive of endoscopic recurrence.


Reference
1. This study has been supported by grants from MSD France, Association François Aupetit, the Helmsley Charitable Trust and INSERM.

OP237 BILE MICROBIOTA IN PRIMARY SCLEROSING CHOLANGIOiritITIS: EFFECTS ON DISEASE STAGE AND RISK FOR BILIARY DYSPLASIA

P. Pereira1, V. Aho1, J. Arola2, S. Boyd3, K. Jokelainen1, P. Auvain1, M. A. Fäkkila4
1Institute Of Biotechnology, Dna Sequencing And Genomics Laboratory, Helsinki University Hospital, Helsinki, Finland
2Institute Of Biotechnology, Dna Sequencing And Genomics Laboratory, Helsinki University, Helsinki, Finland
3Huslab, Helsinki University Hospital, Helsinki, Finland
4Dept. Of Gastroenterology, Helsinki University Hospital, Helsinki, Finland
5Institute Of Biotechnology, Dna Sequencing And Genomics Laboratory, Helsinki University, Helsinki, Finland

Contact E-mail Address: pedro.bento.pereira@gmail.com

Introduction: Primary sclerosing cholangitis (PSC) is a chronic inflammatory liver disease leading to strictures in intra- and extrahepatic bile ducts and finally to cholestasis and secondary biliary cirrhosis (1). The chronic inflammation is associated with increased proliferation of biliary epithelial cells and a markedly increased risk of development of biliary dysplasia and cholangiocarcinoma (2). The etiopathogenesis of PSC is unknown, but the frequent association with inflammatory bowel disease, in 62–83% of PSC patients, and increased intestinal permeability in PSC has suggested a role for microbiota or microbial metabolites or derivatives, e.g. pathogen-associated molecular patterns, PAMPs such as lipopolysaccharide (LPS), ribophoric acid, and peptidoglycan in the etiopathogenesis of the disease (3–5). It has been proposed that the association between PSC and IBD can be due to increased enterohemorrhage circulation of PAMPs (“leaking gut”), or abnormal PAMPs (as a result of enteric microbial dysbiosis, described in IBD) (4). Moreover, 16S ribosomal ribonucleic acid (RNA) has been detected in bile and also in cholangiocytes in PSC patients. The microbiota in bile have also been shown to be modified by genetic factors such as FUT2 (2α-l-fucosyltransferase 2) polymorphism, a gene involved in protein glycosylation.

Aims & Methods: To study the possible role of biliary microbiota in ethiopathogenesis, disease progression and risk of dysplasia and cholangiocarcinoma (CCA). The clinical part of the study was conducted at Helsinki University, Clinic of Gastroenterology. The patients were recruited from the Clinic of Gastroenterology. The indication for ERCP examination was the documentation of diagnosis of PSC due to: 1) constantly elevated or fluctuating alkaline phosphatase (ALP) levels in conjunction with IBD, or 2) magnetic resonance cholangiography findings, or 3) liver biopsy suggestive of PSC, or dysplasia surveillance. During patient’s ERCP and before injecting contrast media a bile sample was aspirated from extrahepatic bile ducts using balloon catheter, whenever possible. Bruhl cholangiography was routinely performed during ERCP. ERC findings were scored according to the modified Amsterdam score (mAm score) and the number of ERC examination were recorded in each patient group. Isolation, amplification and sequencing of the bacterial 16S rRNA gene were performed. The resulting data was analyzed with negative binomial generalized linear models, PERMANOVA, and non-parametric tests.

Result: 1) A very low abundance OTU ("species") belonging to the family Neisseriaceae was reduced in abundance in the early disease group. 2) Increase in Streptococcus from early disease to long disease progression. Streptococcus also correlates with increase in ERC severity score and potentially with the number of ERC examinations. More robust are the findings regarding overall community diversity, which decreases in long progression and dysplasia/CCA. 3) A low abundance Prevotella OTU disappears in patients with dysplasia or CCA. Streptococcus seems to again increase.

Conclusion: The data in our exploratory study suggests that the etiology of the disease is not connected with changes in biliary microbiota. The microbiota in bile has a lower bacterial diversity at time of surgery compared to patients in endoscopic remission (n = 65) (mean observed species: 276 ± 14 vs 365 ± 45, p = 0.015). Moreover the microbiota in bile has different bacterial diversity at time of surgery compared to patients in endoscopic remission (n = 65) (mean observed species: 276 ± 14 vs 365 ± 45, p = 0.015). However, the consequences and cause of increased levels of luminal granins in IBS patients (1). Moreover, the consequences and cause of increased levels of luminal granins in IBS are still undefined.

References

OP238 INCREASED FAECAL LEVELS OF GRANINS IN IRRITABLE BOWEL SYNDROME ARE ASSOCIATED WITH LUMINAL MICROBIOTA COMPOSITION AND SYMPTOM SEVERITY

J. Sundin1, S. M. P. Bennet2, J. Tap3, M. Derrien1, B. Le Neev1, M. Stridsberg1, H. van den Dool1, L. Ohman1, M. Sahlén1, S. M. P. Bennet2, J. Tap3, M. Derrien1, B. Le Neev1, M. Stridsberg1, H. van den Dool1, L. Ohman1, M. Sahlén1
1Sahlgrenska Academy, Institute of Medicine, Gothenburg/Sweden
2Sahlgrenska Academy, Sahlgrenska Academy At University Of Gothenburg, Gothenburg/Sweden
3Life Science, Danone Research, Palaiseau/France
4Dept. Of Life Sciences, Danone Research Dept. of Life Science, Palaiseau, France
5Dept. Of Clinical Chemistry, Uppsala/Sweden
6Institute Of Medicine, Sahlgrenska Academy, University Of Gothenburg, Gothenburg/Sweden
7Sahlgrenska Academy, University of Gothenburg Sahlgrenska Academy Dept. of Microbiology and Immunology, Gothenburg Swe
8Dept Of Internal Medicine, Sahlgrenska University Hospital, Gothenburg/Sweden

Contact E-mail Address: johanna.sundin@gu.se

Introduction: Chromogranins (Cg) and secretogranins (Sg) are acidic gut hormones, which are secreted from the neuroendocrine system and may regulate immune activation. We have previously shown increased levels of faecal Cg and Sg in IBS patients (1). However, the consequences and cause of increased levels of luminal granins in IBS are still undefined.

Aims & Methods: In this study we aimed to quantify faecal grain levels in IBS patients and evaluate potential relationships between grain levels, microbiota and immune activation. Levels of CgA, CgB, SgII and SgIII were quantified with radioimmunoassay and ELISA, respectively, in faecal samples from IBS patients (n = 143) and healthy subjects (n = 43). mRNA expression of interleukin (IL)-8, IL-10, tumour necrosis factor (TNF) and forkhead box P3 (FOXP3) in mucosal biopsies from terminal colon were determined with qRT-PCR. Faecal (n = 111 subjects) and mucosal-associated microbiota (n = 50 subjects) were analysed by 16S RNA targeted pyrosequencing. IBS symptom severity and psychological distress were evaluated with the Gastrointestinal Symptom Scale-IBS (GSRS-IBS) and the Hospital Anxiety and Depression Scale (HADS), respectively.

Result: IBS patients demonstrated higher levels of faecal CgA (8.1 (3.3–17.4) pmol/L) compared to healthy subjects (4.7 (2.9–9.0), p < 0.02 pmol/L). The levels of SgII (0.8 (0.1–3.6) pmol/L) and SgIII (2.0 (0.8–4.8) pmol/L) in IBS patients were also increased compared to healthy subjects (0.1 (0.0–2.0), p < 0.01) respectively (0.7 (0.4–2.4), p < 0.001, pmol/L). Faecal microbial diversification with CgA (r = -0.29, p < 0.005), CgB (r = -0.21,
The present results support that alterations in microbial composition is important in both IBD and symptomatic non-IBD patients. The result demonstrated: 1) Differences in microbiota profiles between IBD and symptomatic non-IBD patients and healthy individuals; 2) Equal levels of dysbiosis frequency in CD and UC, however the bacteria profiles differed; 3) In subgroups of UC, microbiota profiles were dependent upon the localization of the inflammation.

Disclosure of Interest: E. Ciemniejewska: Employee of Genetic Analysis
M.H. Vatn: Member of Genetic Analysis’ Scientific Advisory Board
M. Sekelja: Former employee of Genetic Analysis
C. Casen: Employee at Genetic Analysis
All other authors have declared no conflicts of interest.

Reference

OP240 METABOLIC SYNDROME CORRELATES WITH MICROBIOTA ENCROACHMENT IN HUMAN INTESTINE

B. Chassaing1, S. Srinivasan2, A. Gewirtz3
1Institute For Biomedical Sciences, Georgia State University, Atlanta;
United States of America/GA
2Dietic Diseases Division, Department Of Medicine, Emory University School of Medicine, Atlanta/United States of America/GA

Contact E-mail Address: bcchassaing@gmail.com

Introduction: The intestinal tract is inhabited by a large and diverse community of bacteria collectively referred as gut microbiota. Mucoid structures coating the epithelium, largely devoid of bacteria, are central to maintaining intestinal-microbiota homeostasis. Our recently published work has led to the hypothesis that, in microbial encroachment of the epithelium, as a consequence of an innate immune deficiency or ingestion of substances that alter host-microbiota interactions, promotes low-grade inflammation that can drive metabolic disease (1–2).

Aims & Methods: The aim of the current study was to study microbiota localization in human subjects with metabolic syndrome. Subjects were enrolled at the Veteran’s Administration Hospital (Atlanta, GA, USA). A review of the patient medical record was conducted to determine control and diabetic patients, as shown by their glycosylated hemoglobin and fasted serum glucose levels. During the colonoscopy procedure, two mucosal biopsies were taken in the left colon approximately 40 cm from the anus using a regular forceps. The biopsies were immediately placed in Carnoy fixative and mucus immunostaining was performed.

Results: We found that bacterial encroachment of the epithelium correlates with central features of metabolic syndrome in humans. Specifically, confocal microscopic analysis of biopsies from middle-aged persons revealed an inverse correlation between bacterial-epithelial distance and body mass index, fasting blood glucose, and hemoglobin A1C level. Ethnicity or antibiotic use did not significantly correlate with microbiota-epithelial distance.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

Table 1. (OP239): Dysbiosis status

<table>
<thead>
<tr>
<th>Dysbiosis status</th>
<th>Patients</th>
<th>Age [med.]</th>
<th>Female</th>
<th>IBD</th>
<th>CD</th>
<th>UC</th>
<th>IBDU</th>
<th>Non-IBD</th>
<th>Healthy control</th>
<th>Unknown</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>72</td>
<td>28 (19–68)</td>
<td>43</td>
<td>22</td>
<td>18%</td>
<td>7</td>
<td>16%</td>
<td>11</td>
<td>18%</td>
<td>4</td>
</tr>
<tr>
<td>Low</td>
<td>96</td>
<td>33 (19–66)</td>
<td>49</td>
<td>33</td>
<td>28%</td>
<td>14</td>
<td>31%</td>
<td>15</td>
<td>24%</td>
<td>4</td>
</tr>
<tr>
<td>High</td>
<td>126</td>
<td>32 (18–69)</td>
<td>80</td>
<td>65</td>
<td>54%</td>
<td>24</td>
<td>53%</td>
<td>36</td>
<td>58%</td>
<td>5</td>
</tr>
<tr>
<td>Total</td>
<td>294</td>
<td>172</td>
<td>120</td>
<td>45</td>
<td>13</td>
<td>52</td>
<td>62</td>
<td>124</td>
<td>48</td>
<td>24</td>
</tr>
</tbody>
</table>

Note: Values are number and percentages. Dysbiosis was significantly reduced abundance of CgA, SgII and SgIII as compared to healthy subjects. Negative associations were found in UC patients (p < 0.05) and SgIII (r = −0.28, p < 0.005). In addition, SgII showed a tendency to be negatively correlated with faecal microbial Shannon diversity (r = −0.19, p < 0.05). No correlations were found between any of the genera (CgA, CgB, SgII and SgIII) and mucosal-associated microbiota Shannon diversity or mucosal immune activity (i.e. calprotectin or expression of IL-8, IL-10, TNF and FOXP3).

This study confirms that IBS patients have increased faecal levels of CgA, SgII and SgIII as compared to healthy subjects. Negative associations were found between levels of luminal granins and luminal microbiota diversity, but not with either mucosal immune activity or mucosal-associated microbiota. GI symptom severity and psychological distress were also associated with increased levels of chromogranins in the lumen.

Disclosure of Interest: J. Tap: Employee at Danone
M. Derrien: Employee at Danone
B. Le Neve: Employee at Danone
H. Törnblom: Consultant/Advisory Board member for Almirall, Allergan, Danone and Shire, Speaker for Tillotts, Takeda, Shire and Almirall
L. Ohman: Unrestricted research grants from AstraZeneca; Consultant/Advisory Board member for Genetic Analysis; Speaker for Genetic Analysis, Takeda and Abbott
M. Simrén: Unrestricted research grants from Danone, and Ferring Pharmaceuticals; Consultant/Advisory Board member for AstraZeneca, Danone, Novartis, Aーノー、Asahi, Allergan, Jansen, Almirall, Allergan, Albronie, Glycom and Shire; Speaker for Tillotts, Takeda, Shire and Almirall
All other authors have declared no conflicts of interest.

Reference
**OP241 CLINICAL FEATURES AND FECAL MicroBIOTA PROFILE IN IRRITABLE BOWEL SYNDROME PATIENTS WITH SMALL INTESTINAL BACTERIAL OVERGROWTH**


Introduction: Irritable bowel syndrome (IBS) is a common functional gastrointestinal disorder, but the relationship between diarrhea-predominant IBS (IBS-D) and small intestinal bacterial overgrowth (SIBO) is unclear.

Aims & Methods: We aimed to investigate the clinical features and fecal microbiota profiles of IBS-D patients with SIBO by hydrogen and methane lactulose breath test (LBT), and compare them with IBS-D patients without SIBO and healthy controls. IBS-D patients who met Rome II criteria were divided into IBS-D with SIBO (IBS-P) and without SIBO (IBS-N) by hydrogen and methane LBT, while healthy controls with negative LBT (HC) were recruited. All subjects underwent colonoscopy to exclude organic diseases, and barostat for visceral hypersensitivity, intestinal permeability test (lactulose (L), mannitol (M) and L/M ratio) and frequent stool for 7 days to confirm SIBO. The body mass index of IBS-P and IBS-N was also recorded.

Results: 22 patients were enrolled, 10 with SIBO. The microbiota abundance and community diversity, in which IBS-P is different from IBS-N. Both IBS-P and IBS-N are different from HC in microbiota abundance and community diversity, in which IBS-P is different from IBS-N. According to Pcoa and Hcluster tree-bar. Both IBS-P and IBS-N are different from HC in microbiota abundance and community diversity, in which IBS-P is different from IBS-N. Differences are observed in fecal SCFA between IBS-P and IBS-N. (5) The fecal SCFA, include acetate, propionate, butyrate, isobutyrate and isovalerate in IBS-P were higher than that in HC, while valerate was lower. In IBS-N, the fecal propionate was higher than in HC, while valerate was lower. In IBS-N, the fecal propionate was higher than in HC, while valerate was lower. In IBS-N, the fecal propionate was higher than in HC, while valerate was lower. In IBS-N, the fecal propionate was higher than in HC, while valerate was lower. In IBS-N, the fecal propionate was higher than in HC, while valerate was lower.

Conclusion: IBS-P is different from IBS-N and HC in microbiota abundance and community diversity, in which IBS-P is different from IBS-N. There were significant differences in fecal SCFA between IBS-P and IBS-N. (6) There were significant differences in Shannon index and Simpson index between IBS-P and IBS-N. (7) There were significant differences in IL-12 between IBS-P and IBS-N.

Disclosure of Interest: All authors have declared no conflicts of interest.

**OP242 FECAL MICROBIOTA TRANSPLANTATION FOR RECURRENT C. DIFFICILE INFECTION: ANALYSIS OF FACTORS ASSOCIATED WITH THE NEED FOR MULTIPLE FECAL INFUSIONS**


Introduction: Fecal microbiota transplantation (FMT) from healthy donors is considered a highly effective treatment against recurrent Clostridium difficile infection (rCDI). A single fecal infusion is usually sufficient to resolve symptoms and eradicate rCDI, but a subgroup of these patients need multiple infusions to cure the disease. In our previously published randomized controlled trial of FMT versus vancomycin for rCDI, we observed that patients with pseudomembranous colitis (PMC) needed repeat fecal infusions to be cured, further reports confirmed our findings. To date, however, neither PMC nor other factors have been clearly proven to be associated with the need for multiple FMT.

Contact E-mail Address: gianluca.ianiro@hotmail.it
Aims & Methods: Therefore, our aim was to identify predictive factors for the need for repeated fecal infusions in a series of patients treated with FMT for rCDI. We identified prospectively and included in the analysis all patients treated with FMT by colonoscopy or rCDI in our Centre. Demographic, clinical, endoscopic, and follow-up data were collected. Repeat fecal infusions were administered to patients who failed or failed to improve after first infusion. Gender, age, inpatient status, number or CDI recurrences (>3), poor/inadequate bowel preparation (according to Ottawa Scale), endoscopic evidence of colonic oedema, presence of PMC, use of external donors, infusion of frozen material, and infused grams of feces were analysed as potential impact factors. Univariate associations between possible predictors and the need for repeated fecal infusions were investigated, using t-test for continuous variables and Fisher’s chi-square for comparison (according to Ottawa Scale), endoscopic evidence of colonic oedema, multiple sessions of endoscopic balloon dilation (EBD).

Result: A total of 54 patients with rCDI (Males = 24; mean age = 71 years old, range = 29-94) received FMT from healthy donors by colonoscopy. Fifteen patients received multiple infusions, for a total of 81 procedures. Resolution of rCDI occurred in 52 of 54 patients (96%); of them, none experienced further recurrences after FMT. Univariate analysis showed that both poor/inadequate bowel preparation (p = 0.024) and PMC (p < 0.001) were significantly associated with the need of repeated fecal infusions; also colonic oedema was more common among patients who needed repeated FMT, albeit nonsignificantly (p = 0.083). On multivariate analysis, both the presence of PMC (OR = 2257; 95% CI = 25.17–1000, p = 0.014) and poor/inadequate bowel preparation (OR = 64.80; 95% CI = 3.43–1000, p = 0.021) were identified as significant predictors of the need of repeated infusions. Additionally, the need for repeated infusion was more common among patient who experienced a number or CDI recurrences >3 than among those who did not, although without reaching statistical significance (OR = 26.80; 95% CI = 1.69–1000; p = 0.054). The large confidence interval observed for most predictors could be explained presumably by the relatively low number of cases in our sample. Finally, the infusion of frozen material was significantly associated with lower number of multiple FMT (OR = 0.01; 95% CI = 0.0–0.19, p = 0.033).

Conclusion: Among patients treated with FMT for rCDI, both PMC and poor/ inadequate bowel preparation appear to be significant predictors of the need for repeated infusions. Additionally, frozen FMT appears to be significantly associated with a decreased risk of need of multiple FMT. As the small sample size represents a limitation of our analysis, our findings, although promising, should be confirmed by further, larger studies.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

TUESDAY, OCTOBER 18, 2016
14:00–15:30
ENDOSCOPIC TREATMENT OF COMPLICATIONS AFTER UPPER GI SURGERY – ROOM E2

OP243 ENDOSCOPIC BALLOON DILATION FOLLOWED BY STEROID INJECTION IN ANASTOMOTIC STRICTURES AFTER ESOPHAGECTOMY: A MULTICENTER RANDOMIZED, DOUBLE-BLIND CONTROLLED TRIAL

N. Hanaka1, R. Ishihara2, N. Uedo3, K. Higashino3, Y. Takeuchi3, T. Akasaka1, M. Yano9, Y. Hayashii4, T. Takehara9, H. Ishii9
1Gastrointestinal Oncology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka/Japan
2Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka/Japan
3Department Of Gastrointestinal Oncology, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka/Japan
4Department Of Gastrointestinal Oncology, Osaka Medical School, Osaka/Japan
5Surgery, Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka/Japan
6Gastrointestinal Oncology, Osaka Medical School, Osaka/Japan
7Dept. Of Digestive Diseases, Herriot University Hospital Dept. de Hepato-gastroenterology, Lyon/France
8Hepato-gastro-enterology, CHU Limoges, Limoges/France
9Gastroenterology and Endoscopy Unit, Digestive Disease Department, H-Pavillon- Edourard Herriot Hospital, Lyon/France

Contact E-Mail Address: jeremi@nahana.com

Introduction: Esophagectomy is the treatment of choice for superficial neoplasms of the esophagus due to its oncological efficiency and the morbidity associated with the surgical alternative. ESD requires a high level of skill and is technically challenging and time consuming. Therefore, it is often reserved to experts. Combining the tunnel technique and the clip-line counter-traction may enable optimisation of oesophageal ESDs.

Aims & Methods: From January 2014 to April 2016 we performed a prospective bi-centric case series of consecutive "tunnel + clip" oesophageal ESDs. For young operators (fewer than 50 ESDs) and fewer than 5 oesophageal ESDs, we performed consecutively the ESD using the tunnel + clip method: generation of a classic tunnel beneath the lesion followed by constant counter-traction thanks to a clip with line dropped at the oral side of the tunnel.

Results: Thirty-three lesions (14 SCC and 19 ADK; HGD complicating Barrett’s oesophagus) were resected consecutively. En bloc, R0 and curative resection rates were 100% (33/33), 87.8% (29/33) and 75.8% (25/33), respectively. No perforation occurred. The mean speed of ESD was 22.3 mm²/min for a mean lesion size of 61.6 mm. The clip provided considerable assistance in performing the procedure. No pathological damage caused by the clipping was reported.

n = 33

<table>
<thead>
<tr>
<th>Age (years)</th>
<th>Mean ± SD</th>
<th>Min</th>
<th>Max</th>
</tr>
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<tr>
<td>63.9±8.6</td>
<td>36</td>
<td>85</td>
<td>36</td>
</tr>
<tr>
<td>Procedure duration (min)</td>
<td>131</td>
<td>25</td>
<td>350</td>
</tr>
<tr>
<td>Large diameter (mm)</td>
<td>61.6</td>
<td>30</td>
<td>105</td>
</tr>
<tr>
<td>Small diameter (mm)</td>
<td>44</td>
<td>20</td>
<td>78</td>
</tr>
<tr>
<td>Surface (mm²)</td>
<td>2418</td>
<td>471</td>
<td>6300</td>
</tr>
<tr>
<td>Speed (mm²/min)</td>
<td>22.3</td>
<td>7.0</td>
<td>79</td>
</tr>
<tr>
<td>Circumference (%)</td>
<td>60.0%</td>
<td>30.0%</td>
<td>100%</td>
</tr>
<tr>
<td>Monolobic resection</td>
<td>33 (100%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>R0 resection</td>
<td>29 (87.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Curative resection</td>
<td>25 (75.8%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Periprocedural bleeding</td>
<td>14 (42.0%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Perforation</td>
<td>0.0%</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Post-procedural bleeding</td>
<td>2 (6%)</td>
<td></td>
<td></td>
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<tr>
<td>Stenosis</td>
<td>5 (15.1%)</td>
<td></td>
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</tr>
</tbody>
</table>

(continued)
Introduction: The PIVI initiatives propose that a "leave in place" approach is acceptable for diminutive (<5 mm) rectosigmoid hyperplastic polyps when endoscopist's optical diagnosis provides over 90% negative predictive value (NPV) for adenomas in high confidence predictions [1]; however, expertise is required to achieve a high accuracy and some studies conducted in community-based hospitals have been disappointing [2]. Recently, we have reported the usefulness of computer-aided diagnosis (CAD) in supporting endoscopists’ decision making during colonoscopy [3,4]. The present study was aimed to validate the efficacy of the latest CAD model for endocytoscopy (380-fold ultra-magnifying endoscopy) in management of diminutive, rectosigmoid polyps.

Aims & Methods: The present study was aimed to validate the efficacy of the latest CAD model for endocytoscopy (380-fold ultra-magnifying endoscopy) in management of diminutive, rectosigmoid polyps.

Discussion: First study of the strategy "tunnel+clip". Our en bloc and R0 resection rates confirmed the usefulness of this technique, despite the relative inexperience of the operators. Our resection results were similar to those reported in large series by international experts, including those in Japan and our absence of perforation highlighted the safety of this strategy.

Conclusion: The tunnel+clip method for oesophageal ESD is effective and safe, in particular for physicians with little experience. This strategy standardizes the ESD procedure and provides superficial oesophageal neoplasia and increases of the speed of dissection. Thus, it will help to widespread oesophageal ESD performed in Western countries.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

WHAT TO DO WITH SMALL COLORECTAL POLYPS? – ROOM F

OP245 DEVELOPMENT AND VALIDATION OF A SIMPLE CLASSIFICATION SYSTEM FOR IN VIVO DIAGNOSIS OF COLORECTAL POLYPS USING THE NEWLY INTRODUCED BLUE LIGHT IMAGING (BLI)

H. Neumann1, M. Vieth2, L. E. Fry3, G. E. Tontini4, H. Mönkemüller5
1Department Of Medicine I, University Hospital Erlangen, Erlangen/Germany
2Abt. Pathologie, Klinikum Bayreuth Abt. Pathology, Bayreuth/Germany
3Basel-Hirschsprung Endoscopic Center Of Excellence, University of Alabama at Birmingham, Birmingham/United States of America

Contact Email Address: helmut.neumann@uk-erlangen.de

Introduction: BLI is a novel endoscopic imaging technique for enhancement of subtle mucosal and vascular details. The potential of this novel technology for in vivo diagnosis of colorectal polyps has yet to be established. BLI technology is currently standardization in Europe and worldwide. This study will evaluate the performance of a newly introduced BLI in the diagnosis of colorectal polyps.

Aims & Methods: Primary objective was to develop a specific classification for in vivo differentiation of hyperplastic and adenomatous colorectal lesions by using the novel BLI technology. Second study endpoint was to validate the classification among experienced and non-experienced users. In the first phase, the accuracy of experienced endoscopists to predict the histology of colorectal polyps was assessed. In the second phase, a simplified classification was developed allowing histologic prediction. Thirdly, the validity of the classification was assessed. In the second phase, a simplified classification was developed allowing histologic prediction. Lastly, the validity of the classification was assessed. In the second phase, a simplified classification was developed allowing histologic prediction.

Result: A simple classification system for differentiating hyperplastic and adenomatous colorectal lesions by using the novel introduced BLI technology was developed and validated. Diagnosis was made in 80% to 88% of polyps with high-confidence. Sensitivity and specificity ranged from 93% to 100% and 83% to 92%, respectively. During real-time colonoscopy, diagnosis was made with high-confidence in 88% of polyps with sensitivity of 96%, specificity of 92%, and accuracy of 95%. Positive and negative predictive values were 96% and 92%, respectively.

Conclusion: This is the first study evaluating the novel BLI technology for in vivo diagnosis of colorectal polyps. The proposed classification allowed for adequate and non-neoplastic in vivo diagnosis of hyperplastic and adenomatous lesions. Further prospective multicenter trials should now confirm these preliminary results.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

TUESDAY, OCTOBER 18, 2016 14:00–15:30

BIOMARKERS IN IBD – ROOM K

OP247 IBDOC – FIRST SMARTPHONE BASED CALPROTECTIN HOME TEST – 18 MONTHS EXPERIENCE

C. Reinhard1, A. Ritz1, M. Überschlag1, A. Beyer1, H. Vogelsang2, J. Weber1
1IHHU HUS Laboratory AG, Schönenberg/Schweiz
2AKH Medical University, Vienna/Austria

Contact Email Address: cre@buahhnlabs.ch

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 measurement in patients’ stool samples acts as a well-established biomarker to measure the inflammatory activity in the gut. Periodical assessment of calprotectin levels is necessary and is recommended by major guidelines. To date, calprotectin analysis is a labor-intensive assay leading to long delays between sample collection, final test result and potential adaptations of therapies.

Aims & Methods: We have developed a smartphone-based calprotectin home test, called IBDoc®, that allows real-time information about the inflammatory activities in the gut for both, the patient and the health care provider. The IBDoc® consists of a stool collection and extraction device (CALEX® Valve) and an immunochromatographic calprotectin rapid test, which is measured using a smartphone app controlling the phone’s camera. Once the test is

Table: Details of the diagnostic performance by the CAD

<table>
<thead>
<tr>
<th>Pathology</th>
<th>Mean</th>
<th>Min</th>
<th>Max</th>
</tr>
</thead>
<tbody>
<tr>
<td>Diagnosis of neoplastic by CAD</td>
<td>18</td>
<td>2</td>
<td>34</td>
</tr>
<tr>
<td>Diagnosis of non-neoplastic by CAD</td>
<td>2</td>
<td>34</td>
<td>34</td>
</tr>
</tbody>
</table>

Conclusion: The IBDoc® applying endocytoscopy can be a powerful and quick support tool in management of diminutive, rectosigmoid polyps.

Disclosure of Interest: K. Mori: Cybernet System Corp.

All other authors have declared no conflicts of interest.

References

TUESDAY, OCTOBER 18, 2016 14:00–15:30

BIOMARKERS IN IBD – ROOM K
measured the result is instantly sent to a webserver (IBDoc portal) allowing the treating physician to make diagnostic decisions at the result. IBDoc® has achieved CE IVD mark for self-testing in March 2015 and has since then been in routine use treating physician immediate access to the test result. IBDoc® correlated very well with both methods with a mean bias of 0%.

Result: In a direct method comparison with an existing point-of-care test (Quantum Blue®) and a laboratory based ELISA method (BUHLMANN (CAL® ELISA) IBDoc® correlated very well with both methods with a mean bias of 0%.

Aims & Methods: The objective of this study was to validated against endoscopy. For this reason we previously developed the contact E-mail Address: Centre þ

Conclusion: IBDoc® is well accepted by patients and care providers and continues to do well to existing calprotectin point-of-care and laboratory based methods and has proven to be a supportive tool in daily clinical routine. The share of first test: Reinhard. Christian Reinhard is an employee of BÜHLMANN Laboratories AG A. Ritz: Aleja Ritz is an employee of BÜHLMANN Laboratories AG M. Überschlag: Marie-Eve Überschlag is an employee of BÜHLMANN Laboratories AG J. Weber: Jakob Weber is an employee of BÜHLMANN Laboratories AG All other authors have declared no conflicts of interest.

References
1. Beyer et al., Usability Study of a Smartphone-Based Calprotectin Home Test, UEGW 2015.

OP248 A COMBINATION OF THE MONITOR IBD AT HOME QUESTIONNAIRE AND A CALPROTECTIN HOME TEST AS AN EXCELLENT SCREENING TOOL FOR MUCOSAL INFLAMMATION IN IBD PATIENTS
M. J. De Jong1, D.M. Jonkers1, M. Romberg Camps2, A.G. I. Bodelier2, B.J. Van De Wetering3, T. Van Eetveldt4, S. h.p. Conjaerts5, T. Markus4, A.A. Masclee1, M.J. Peric1
1Department Of Gastroenterology, Maastricht University Medical Centre++, Maastricht/Netherlands
2Department Of Gastroenterology, Zuyderland Medical Centre, Sittard-Gelern/ Netherlands
3Department Of Gastroenterology, Amphia Hospital, Breda/Netherlands
4CCCUV, Woerden/Netherlands
Contact E-mail Address: d.jonkers@maastrichtuniversity.nl

Introduction: Telendoscopy programmes are of interest for inflammatory bowel disease patients but should include adequate monitoring of mucosal inflammation to prevent long-term complications. Different clinical activity questionnaires are available, however, none are patient-reported, clear and easy to fill out and validated against endoscopy. For this reason we previously developed the MIAH-UC questionnaire (MIAH) for ulcerative colitis. The score does not include laboratory tests or physical examination. The objective of this study was to investigate whether a combination of the MIAH questionnaire and a calprotectin home test yields higher diagnostic accuracy.

Aims & Methods: Between September 2015 and April 2016 all consecutive IBD patients with a scheduled endoscopy in the Maastricht University Medical Centre++ were eligible for inclusion. Patients with an ileostomy, colostomy, ileoanal pouch anastomosis or ileorectal anastomosis were excluded. Patients were included if they fulfilled our item MIAH-UC questionnaire for UC regarding blood loss, number of stools, urgency, abdominal pain and general wellbeing, or the 6-item MIAH-CD questionnaire for CD, including questions on blood loss, mucus, number of stools, urgency, fatigue and general wellbeing. In addition, patients were asked to collect a stool sample prior to bowel cleansing. Fecal calprotectin was determined with a calprotectin home test. Mucosal inflammation was assessed with the simple endoscopic activity score (SES-CD) for Crohn’s disease (CD) and the Mayo endoscopic subscore (MES) for ulcerative colitis (UC). Sensitivity, specificity, predictive value (PPV and NPV) and negative predicted value (NPV) of the MIAH-UC and MIAH-CD in combination with the calprotectin home test were calculated.

Result: Thirty-two CD patients (50.0% male, mean age 51.4 ± 15.2 years, 43.8% active disease (22 patients (30.0% male, mean age 57.3 ± 10.4 years, 39.3% active disease were included). The combination of the MIAH-CD and the calprotectin home test showed a sensitivity of 100.0%, a specificity of 91.7%, a PPV of 94.8% and a NPV of 96.9%.

Conclusion: The MIAH is the first patient-reported questionnaire developed to predict endoscopic inflammation in IBD patients. The results demonstrate a calprotectin home test shows a high sensitivity and thus shows the potential for introduction of this programme to surgeons who need further assessment of disease activity with biochemical markers, imaging or endoscopy.

Disclosure of Interest: M.J. de Jong: Non financial support Immunodiagnostik. All other authors have declared no conflicts of interest.

Reference

OP249 ACCURACY OF NON-INVASIVE TESTS IN THE INITIAL DIAGNOSTIC WORK-UP OF PEDIATRIC INFLAMMATORY BOWEL DISEASES
F. Civitelli1, A. Diliolo1, M. Alos1, S. Oliva2, F. Viola2, L. Stronati1, S. Cucchiara2
1Dept. Pediatrics, Gastroenterology And Liver Unit, Sapienza University of Rome, Rome/Italy
2Pediatric Gastroenterology And Liver Unit, Sapienza University of Rome, Rome/Italy
Contact E-mail Address: fortunatacivitelli@gmail.com

Introduction: Upper and lower endoscopy with histology together with imaging of the small bowel is the gold standard for the diagnosis of inflammatory bowel disease (IBD) in children. Due to high costs and invasive nature of these techniques, accurate selection of patients is mandatory.

Aims & Methods: We aimed to assess the accuracy of non-invasive tests including fecal calprotectin (FC), blood inflammatory markers (BIM) and bowel ultrasound (US) alone or in combination as first level investigations in children with suspected IBD. Consecutive patients referred to our Unit for a clinical history compatible with IBD were enrolled during a 3-year period. All underwent FC (Calprotectin®, Eurostatus), C-reactive protein (CRP), erythrocyte sedimentation rate (ESR) and bowel US as first investigations. Endoscopy with biopsies was the gold standard for diagnosis. At US pathological findings were: BWT > 3 mm, BV vascularity, loss of stratification, enlarged mesenteric nodes. Multiple logistic analysis with stepwise method considering IBD diagnosis as dependent variable was conducted. Sensitivity (SE), specificity (SP), positive and negative predictive values (PPV and NPV) of laboratory and US parameters alone or in combination were analyzed according to the final diagnosis.

Result: 100 patients (58 males, median age 12) were enrolled. The final diagnosis was IBD in 69 (57 CD, 12 CU) other than IBD in 31. The mean values of CRP, ESR, FC and BWT were higher in IBD vs non-IBD patients (p < 0.001). Multiple logistic analysis showed that independent variables predictive of IBD were: FC (OR 44.8; p < 0.01), BWT (OR 20.4, p < 0.001) and ESR (OR 9; p < 0.01). The combination of 3 or 2 parameters was more frequent in IBD patients (p < 0.01). Table 2 shows SE, SP, PPV, NPV of these parameters alone or in combination.

<table>
<thead>
<tr>
<th>Parameters</th>
<th>SE %</th>
<th>SP %</th>
<th>PPV %</th>
<th>NPV %</th>
</tr>
</thead>
<tbody>
<tr>
<td>FC (ug/g)</td>
<td>94</td>
<td>89</td>
<td>94</td>
<td>89</td>
</tr>
<tr>
<td>ESR (mm/h)</td>
<td>75</td>
<td>89</td>
<td>93</td>
<td>65</td>
</tr>
<tr>
<td>BWT (mm)</td>
<td>94</td>
<td>83</td>
<td>88</td>
<td>57</td>
</tr>
<tr>
<td>2 (at least 2 of 3)</td>
<td>96</td>
<td>84</td>
<td>97</td>
<td>92</td>
</tr>
<tr>
<td>2 (FC + BWT)</td>
<td>91</td>
<td>100</td>
<td>98</td>
<td>96</td>
</tr>
<tr>
<td>3 (FC + BWT + ESR)</td>
<td>71</td>
<td>100</td>
<td>99</td>
<td>99</td>
</tr>
</tbody>
</table>

Conclusion: the combination of FC, BIM and bowel US may help to select children needing further invasive procedures and allow to avoid or delay endoscopy in patients with negative initial diagnostic work-up.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP250 THE SEROLOGIC MARKERS ASCA AND PANCA SHOW BETTER PREDICTABILITY THAN CRP, ESR AND CALPROTECTIN FOR ANTI-TNF TREATMENT AMONG PEDIATRIC IBD PATIENTS
C. Olbjørn1, M. S. Cvanarova2, E. Thiis-Evensen3, B. Nakstad4, M. H. Vatn5, G. Perrinov6
1Institute For Clinical Medicine, Campus Akershus University Hospital, University of Oslo, Lørenskog/Norway
2Gastroenterology, Oslo University Hospital, Ullevål, Oslo/Norway
3Gastroenterology, Rikshospitalet, University of Oslo, Oslo/Norway
4Dep Of Pediatrics And Adolescence And Institute Of Clinical Medicine, Akershus University Hospital And University of Oslo, Lørenskog/Norway
5Institute Of Clinical Medicine, Epigen-institute, Campus Akershus University Hospital, University of Oslo, Lørenskog/Norway
6Pediatrics, Oslo University Hospital, Ullevål, Oslo/Norway
Contact E-mail Address: chrisolb@gmail.com

Introduction: Serologic nuclear and anti microbial antibodies have been recognized as predictive markers of disease course and complications in ulcerative colitis (UC) and Crohn’s disease (CD). The significance of serological markers from onset of the disease, their ability to predict disease outcome and their stability over time is not fully explored in IBD patients.

Aims & Methods: To study the prevalence of serological markers in treatment-naive pediatric patients with newly diagnosed inflammatory bowel disease and prospectively evaluate the antibody and titer-variations related to disease sub-
serological markers with the biochemical markers C-reactive protein (CRP), elevated sedimentation rate (ESR) and fecal calprotectin. Patients aged 18 years, (n = 58) diagnosed with IBD were included between 2005-2007 as a part of a prospective population based study in South-Eastern Norway (IBSEN- II). Fecal samples were analyzed for calprotectin (Bühlmann, Basel, Switzerland) and blood specimens were analyzed for antibodies (Prometheus labs, San Diego). CRP and ESR at diagnosis and after 1-2 years of treatment. Treatment was decided at the courtesy of the treating pediatrician. Tumor necrosis factor (TNF) blocker treatment was regarded as aggressive treatment compared to conventional treatment. Result: Among the UC patients, 13 (72%) were perinatal anti-neutrophil cytoplasmic antibody (pANCA) positive, versus 13 (35%) of the CD patients. None of the UC patients harbored anti-Saccharomyces cerevisiae (ASCA) antibodies, whereas 23 (45%) of CD patients were ASCA IgA or IgG positive (p < 0.0001). 18 (49%) were positive for ASCA IgA, 14 (38%) for ASCA IgG, and 12 (33%) for both. There were statistically significant differences between CD and UC patients in the prevalence of antibodies against Pseudomonas fluorescens associated protein (p < 0.01), the outer membrane protein of Escherichia coli (OmpC) (8% vs. 6%) or flagellin expressed by Crotolial phylum (CBir) (22% vs. 0%, respectively). The 18 (49%) CD patients who received aggressive treatment with TNF blockers had higher presence of antibodies against ASCA IgA (p = 0.045) and ASCA IgG (p = 0.045) as well as higher titers of ASCA IgA (p = 0.046) compared to the 19 (51%) CD patients who received conventional treatment. If ASCA antibodies were present at baseline the probability of receiving infliximab treatment in CD patients was 70%, with OR 8.2 (2.0–37.7), p = 0.004. The presence of pANCA antibodies was less frequent at diagnosis in TNF blocker treated CD patients compared to conventionally treated CD patients. The OR of receiving aggressive therapy being pANCA negative was 5.6 (1.3–22.5). CD patients with negative infliximab treatment had significantly higher levels of fecal calprotectin, CRP and ESR at diagnosis compared to conventionally treated CD patients with median values of fecal calprotectin (mg/kg) 1536 vs. 501 (p = 0.01), CRP (mg/l) 28 vs. 7.5 (p = 0.02) and ESR (mm/h) of 32 vs. 18 (p = 0.01) respectively. Being pANCA negative and/or ASCA IgA or ASCA IgG positive was associated with the need for TNF blocker therapy, even after adjustment for CRP, ESR and fecal calprotectin levels. After treatment there was no difference in antibody prevalence for ASCA IgA, ASCA IgG, 12, QuantOnCal and UC patients regarding levels of treatment modality, and might be a prognostic tool at any time in the disease course. Disclosure of Interest: All authors have declared no conflicts of interest.
Disclosure of Interest: Abdominal distension can be effectively corrected by biofeedback.

Biofeedback treatment resulted in a 56% reduction in anterior wall muscle activity (by 101.0% vs 41.4±2%).

Severity Scoring System (IBS-SSS) was used to evaluate symptoms. Blood samples were collected in the questionnaire. The primary outcome was the responder rate for treatment at the end of treatment.

Results: Patients on biofeedback, but not on placebo, effectively learned to reduce intercostal activity (by 45.3% vs 5±2% on placebo; p < 0.001) and to control anterior wall muscle activity (by 101±10% vs 41±4.2%).

Biofeedback treatment resulted in a 56±1% reduction of abdominal distension (from 4.6±0.2 to 2.0±0.2 score after intervention) vs 13±3.8% on placebo; p < 0.001 (from 4.7±0.1 to 4.1±0.4 score after intervention).

Conclusion: The reduction in the peak fermentable carbohydrates collectively termed FODMAPs (fermentable oligo-, di-, monosaccharides and polyols) is increasingly being advocated in patients with functional gastrointestinal disorders (FGID). At present, selection criteria or response predictors for dietary intervention are poorly defined.

Aims & Methods: In this study the predictive associations between clinical characteristics, breath test results and the global outcome measure advocated in FGID were examined. Clinical characteristics and breath test results from 580 patients presenting to a gastroenterology clinic (Rome III) and fructose or lactose intolerance, and completing a standardised FODMAP dietary program were analysed. Intolerance was defined by a positive symptom index and malabsorption by increases in H2 (>20 ppm) or CH4 (>10 ppm) values during breath testing.

Response to the dietary program was assessed using a standard adequate global symptom relief question. Predictive associations were assessed by uni- and multivariate analyses.

Conclusion: Multivariate analysis confirmed the associations between adequate symptom relief and a history of diarrhea (positive predictor: 2.74 (1.32–5.0, p = 0.001)) and a history of fructose intolerance (negative predictor: 2.73 (0.25–2.81), p = 0.07).

There were no significant associations between the H2 or CH4 breath concentrations and the attainment of adequate relief. A positive dietary response in patients with fructose intolerance was associated with the development of diarrhea during breath testing (multivariate analysis 1.7 (1.03–2.81), p = 0.04). No other significant associations between symptoms experienced during fructose or lactose breath testing and dietary outcome were demonstrated.

Conclusion: Adequate global symptom relief with a FODMAP diet is achieved in a large majority of all FGID patients with fructose or lactose intolerance, and is predicted by a few clinical and breath-test associated symptoms and not by the presence of malabsorption. Consequently, a reduction of FODMAPs appears to modulate multiple physiological processes across the spectrum of FGIDs. Furthermore, adequate relief likely reflects a complex constellation of psychological and physical factors, rather than a reduction in individual symptoms, explaining the few significant associations with clinical or provoked symptoms.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

1. Barba E, Accarino I, Malagelada J, Azpiroz F. Azpiroz F. Abdominal pain in irritable bowel syndrome (IBS): the most common gastrointestinal (GI) disorder worldwide. In the lack of cures, different management strategies have been developed, including a diet low in FODMAPs (fermentable oligosaccharides, disaccharides, monosaccharides and polyols). Although being increasingly accepted as one of the most effective therapies, there is insufficient high-quality evidence of its efficacy as well as uncertainties regarding long-term consequences on gut microbiota composition and function.

Aims & Methods: In the present study we aimed to investigate the effect of a low versus a high FODMAP diet on symptoms, gut microbiota, short-chain fatty acids (SCFAs) and pro-inflammatory cytokine profiles in a randomized, double-blinded, crossover trial of Norwegian patients with IBS. Twenty patients with IBS (15 female, 5 male, mean age 34.6±y) were instructed to follow a low FODMAP diet (LFD) throughout a study period of 9 weeks. After 3 weeks they were randomized and double-blindly assigned to receive a daily supplement of either high (16 g fructo-oligosaccharides (FOS)) or low (16 g maltodextrin (=placebo)) FODMAP for the next 10 days, followed by a 3-week washout period before crossover to the alternative supplementation for 10 new days. IBS Severity Scoring System (IBS-SSS) was used to evaluate symptoms. Blood samples were collected to analyse serum cytokines (IL-6, IL-8, TNF-α), and faeces samples for gut microbiota (16r DNA) and SCFAs.

Result: IBS symptoms consistently and significantly improved after 3 weeks of LFD, with a mean overall reduction of 163.8 points (p < 0.0001). On average, 4 of 5 symptoms were significantly worsened in response to FOS compared with placebo, with an overall difference of 65.1 points (p = 0.014). Serum levels of IL-6 and IL-8, but not TNF-α, significantly decreased on the LFD (p = 0.01 and p = 0.03, respectively). The LFD was associated with a concomitant increase in Bifidobacterium (p = 0.0084 and p = 0.0075, respectively) and a decrease in F. prausnitzii (p = 0.0004 and p = 0.0001, respectively). Levels of total SCFAs and butyric acid were also significantly decreased on the LFD (p = 0.04 and p = 0.01, respectively). Ten days of FOS supplementation normalized ileal bacterial counts, while the LFD did not change the levels of cytokines nor SCFAs.

Conclusion: FODMAP content was related to IBS symptoms, cytokine levels and microbiota composition and function. Our results provide evidence to support the efficacy of a LFD in reducing functional GI symptoms. Further studies are warranted and needed to explore the link between FODMAPs, gut microbiota and immune activation.

Disclosure of Interest: All authors have declared no conflicts of interest.

Introduction: Tricyclic antidepressants tend to be constipating and, therefore, may be of most benefit in diarrhea-predominant IBS (IBS-D). The aim of this study was to compare the effects of low doses of doxepin and nortriptyline on IBS-D.

Aims & Methods: Twenty-five patients with IBS according to Rome III criteria were treated for two months. All possible organic diseases responsible for bowel symptoms were excluded. The patients were randomly assigned to one of three groups with treated with doxepin (10mg), nortriptyline (10 mg) or placebo. Subjects were assessed clinically weekly. The symptoms and adverse effects of the drugs were recorded in the questionnaire. The primary outcome was the responder rate for treatment at the end of treatment.

Contact E-mail Address: all.medicine@yahoo.com

Disclosure of Interest: All authors have declared no conflicts of interest.
Result: Abdominal pain and bloating were the most common symptoms before initiation of treatment, occurring in 62 (82.7%) patients. The frequency of the symptoms was decreased significantly after treatment in doxepin and nortriptyline groups compared with pre-treatment. The responder rate was 80%, 52%, and 36% for doxepin, nortriptyline, and placebo groups, respectively (p < 0.007). The responder rate for doxepin group was superior to nortriptyline and placebo groups (p = 0.037 and p = 0.002, respectively) but there was no significant difference in responder rates of nortriptyline and placebo groups (p = 0.254). There were no significant differences in improvement rates in individual symptoms between doxepin and nortriptyline (all p > 0.05).

Conclusion: Treatment of diarrhea-predominant IBS with low dose of doxepin or nortriptyline could be effective. Improvement rates of the symptoms are similar in doxepin and nortriptyline groups but doxepin has a better response rate than nortriptyline.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP257 TREATMENT OF IRRITABLE BOWEL SYNDROME WITH FECAL MICROBIOTA TRANSPLANTATION: A CASE SERIES OF 10 PATIENTS

J. Hong1, B. Bang2, Y. Shin2, H. Kim2, K. Kwon*

1Institute of Internal Medicine, Inha University School of Medicine, Incheon/Korea, Republic of
2Dept. Of Gastroenterology, Inha University Hospital, Incheon/Korea, Republic of

Contact E-mail Address: hahahji2@naver.com

Introduction: Irritable bowel syndrome (IBS) is commonly diagnosed gastrointestinal disease worldwide. The pathogenesis of IBS cannot be explained by a single mechanism, but alterations in the intestinal microbiome is increasingly a focus of interest. Traditional treatments of IBS, including psychological therapies, dietary change, probiotics, have had only limited success, underscoring the need for additional therapeutic options. We hypothesized that fecal microbiota transplantation (FMT) may be beneficial in managing IBS by restoring the intestinal homeostasis. The purpose of this study is to prospectively examine the symptomatic response of FMT in patient with moderate IBS.

Aims & Methods: Patients with IBS who were not responsive to traditional treatment were enrolled prospectively in this study. Diagnosis of IBS was based on Rome III Criteria and nonresponsive IBS was defined as failure to achieve symptomatic relief with traditional therapeutic modalities. The healthy donors from patient’s family were screened and tested for infectious diseases before FMT. Patients were questioned with IBS severity score before and 1 month and 3 month after FMT. IBS severity score consist of 5 questions. Total score is 500. As the score is lower, their general condition is considered to be better. Study outcomes included the length of symptom-free intervals, abdominal pain, bloating, flatulence, frequency of bowel movements, and overall well-being before and after FMT.

Result: A total of 10 patients (mean age of 55 years; 60% male) were identified and completed the study questionnaire. Median time from initial symptoms of IBS until FMT was 3.6 years. In our study, 80% of the patients experienced resolution or improvement of symptoms after FMT. There were no long-term side effects, and none of the participants developed any new diseases. Clinically significant improvements in IBS severity scores were observed one month after FMT (132.4 ± 100) comparing to baseline (252.2 ± 121.7) (p = 0.027). However, their symptoms tended to return to their pre-FMT state at 3 month after FMT (231.0 ± 110).

Conclusion: This study showed that FMT may be helpful for one month. However, their effect seemed to decrease over time. FMT may be used as an adjuvant therapy with standard medication for managing IBS. Further large prospective population study is needed.

Disclosure of Interest: All authors have declared no conflicts of interest.

Table (OP258): Composite response rates over longer treatment intervals in ELX-treated patients who were composite or adequate relief responders over Month 1

<table>
<thead>
<tr>
<th>Patients, n (%)</th>
<th>Placebo (n = 809)</th>
<th>ELX 75 mg BID (n = 808)</th>
<th>ELX 100 mg BID (n = 806)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-Responder</td>
<td>101 (12.5)</td>
<td>708 (87.5)</td>
<td>814 (22.8)</td>
</tr>
<tr>
<td>Non-Responder</td>
<td>78 (77.2)</td>
<td>23 (22.8)</td>
<td>150 (81.5)</td>
</tr>
<tr>
<td>Non-Responder</td>
<td>67 (66.3)</td>
<td>34 (33.7)</td>
<td>136 (73.9)</td>
</tr>
<tr>
<td>Non-Responder</td>
<td>399 (49.3)</td>
<td>410 (50.7)</td>
<td>484 (59.9)</td>
</tr>
<tr>
<td>Non-Responder</td>
<td>329 (82.5)</td>
<td>70 (17.5)</td>
<td>405 (83.7)</td>
</tr>
<tr>
<td>Non-Responder</td>
<td>278 (69.7)</td>
<td>121 (30.3)</td>
<td>341 (70.5)</td>
</tr>
</tbody>
</table>

BID, twice daily; ELX, eluxadoline

aPercentage calculated based on number of patients who were composite responders over Weeks 1–4
bPercentage calculated based on number of patients who were adequate relief responders over Weeks 1–4
Conclusion: Moreover, treatment of KPC mice revealed intrinsic resistance of CAFs to deaminase (Dctd), cytidine deaminase (Cda) and hydrolytic cytosolic 5'-nucleotide metabolite enzymes for gemcitabine inactivation such as deoxycytidylate concentrations of activated dFdCTP and greatly reduced levels of the inactive normal liver. Mean vessel density did not correlate with gemcitabine delivery at higher in stroma rich tumours compared to stroma poor liver metastases and human and murine liver metastases as compared to matched primary tumours. Fibroblast density and collagen deposition were significantly reduced in trial in the KPC model.

Expression analysis of gemcitabine metabolism pathways was performed Pdx-1-Cre (KPC) tumours and matched liver metastases, primary tumour cell T.M. Gress5, V. Ellenrieder1

Therefore, metabolic engineering of CAFs may constitute a promising new contribute to the clinical failure of this drug in desmoplastic pancreatic cancer. Thus, our platform provides novel opportunities to model pancreatic applied to another inherited pancreatic disorder.

OP259 HUMAN PLURIPOTENT STEM CELL-DERIVED EXOCRINE/DUCTAL ORGANOGENDS GENERATE HUMAN PANCREAS UPON ORTHOTOPIC TRANSPLANTATION AND ALLOW DISEASE MODELLING

M. Hohwieler1, A. Illing1, M. Möller1, Q. Lin2, A. Lechel3, P.C. Hermann1, J. Rosendahl1, T. Seuferrlein1, M. Wagner3, A. Kleger5

1Department Of Internal Medicine 1 UniM University Hospital, ULM/Germany
2Department Of Cell Biology, Institute for Biomedical Engineering, Aachen/Germany
3Halle University Hospital, Halle/Germany

Contact E-mail Address: alexander.kleger@uni-ulm.de

Introduction: Exocrine/duetal pancreatic differentiation from human pluripotent stem cells is a poorly understood process albeit various diseases arise from this compartment.

Aims & Methods: We designed a straightforward approach to direct human pluripotent stem cells (PSC) toward pancreatic organs resembling exocrine and ductal progeny.

Result: Extensive phenotyping of the organoids not only shows the appropriate marker profile but also ultra-structural and functional hallmarks of human pancreas in the dish. Upon orthotopic transplantation into immunodeficient mice, these organoids form normal pancreatic ducts and acinar tissue resembling fetal human pancreas without any evidence of tumour formation or transformation. Finally, we implemented this unique phenotyping tool as a model for pancreatic facets of cystic fibrosis (CF) but also other inherited pancreatic disorders. We provide evidence that pancreatic commitment occurs generally unhindered in CF. Importantly, CFTR-activation in mutated pancreatic organoids mirrors the CF-phenotype in a series of functional assays. We also conducted a scalable proof-of-concept screen in CF-pancreatic organoids using a set of CFTR correctors and activators. Finally, we did orthotopic transplantation of CF-organoids to generate diseased human pancreata in mice and established a mRNA-mediated gene repair approach in CF-organoids. Similar assays were applied to another inherited pancreatic disorder.

Conclusion: Thus, our platform provides novel opportunities to model pancreatic disease and development but also to screen for disease rescuing agents.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP260 CANCER ASSOCIATED FIBROBLASTS (CAFs) SEQUESTRER GEMCITABINE TO INCREASE INTRATUMORAL DRUG DELIVERY IN MURINE PANCREATIC CANCER

A. Neesse2, E. Hessmann2, M. Patzak2, T. E. Bapiro3, D. J. Jodrell2, J.M. Löhr4, T.M. Gress5, V. Ellenrieder1

1Gastroenterology And Gastrointestinal Oncology, University Medical Centre Goettingen, Goettingen/Germany
2University Medical Centre Goettingen, Goettingen/Germany
3Cancer Research UK, Cambridge/United Kingdom
4Karolinska University Hospital, Stockholm/Sweden
5Klinik Für Gastroenterologie, Endokrinologie, Stoffwechel Und Infektiologie, Philips University Marburg, Marburg/Germany

Contact E-mail Address: albrecht.neesse@med.uni-goettingen.de

Introduction: The pronounced tumour stroma in pancreatic cancer has recently been appreciated as physical barrier impeding delivery of therapeutic agents. Herein, we aim to investigate the delivery of gemcitabine metabolites in primary pancreatic tumour tissue and matched liver metastases and dissect stromal and neoplastic compartments.

Aims & Methods: The cellular and acellular tumour stroma was assessed in human and mouse primary tumours and matched liver metastases. Gemcitabine metabolites were analysed in LSL-KrasG12D+/LSL-Tp53R172H-/+; Pdx-1-Cre (KPC) tumours and matched liver metastases, primary tumour cell lines, cancer associated fibroblasts (CAFs), and pancreatic stellate cells (PSCs) by liquid chromatography- mass spectrometry/mass spectrometry (LC-MS/MS). Expression analysis of gemcitabine metabolism pathways was performed in vitro and in vivo. Viability of CAFs was assessed in vivo following a preclinical trial in the KPC model.

Result: Fibroblast density and collagen deposition were significantly reduced in human and murine liver metastases as compared to matched primary tumours. Gemcitabine (dFdC) and its active metabolite dFdCTP were significantly higher in stroma rich tumours compared to stroma poor liver metastases and normal liver. Mean vessel density did not correlate with gemcitabine delivery at pharmacodynamically relevant endpoints. In cell culture, significantly increased concentrations of activated dFdCTP and greatly reduced levels of the inactive gemcitabine metabolite dFUDU were detected in PSCs and CAFs. Importantly, key metabolite enzymes for gemcitabine inactivation such as deoxycytidine kinase (Dck), cytidine deaminase (Cda) and hydrolytic cytosolic 5'-nucleotidases (Nt5c1a, Nt5c3) were differentially expressed in PSCs and CAFs. Moreover, treatment of KPC mice revealed intrinsic resistance of CAFs to gemcitabine.

Conclusion: Our findings suggest that CAFs sequester gemcitabine and thus may contribute to the clinical failure of this drug in desmoplastic pancreatic cancer. Therefore, metabolic engineering of CAFs may constitute a promising new avenue to enhance the cytotoxic effects of gemcitabine in patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP261 CIRCULATING CELL-FREE DNA IS A RELIABLE TOOL TO DETECT HOT SPOT MUTATIONS IN INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

A. Berger1, D. Schwedel1, J. Costa2, O. Strobel3, T. Hackert1, T. Barth4, A. Meininger2, M. Bicheler4, M. Zemke1, P.C. Hermann1, T. Seuferrlein5, A. Kleger5

1Internal Medicine, UniM University Hospital, ULM/Germany
2Department Of General Surgery, University Hospital Heidelberg, Heidelberg/Germany
3Department Of Pathology, UniM University Hospital, ULM/Germany
4Department Of Internal Medicine, UniM University Hospital, ULM/Germany
5Abteilung Für Allgemeine, Visceralen Und Transplantationschirurgie, Universität Heidelberg, Heidelberg/Germany

Contact E-mail Address: alexander.kleger@uni-ulm.de

Introduction: Pancreatic ductal adenocarcinoma (PDAC) is the most common cancer type of the pancreas. The three PDAC precursor lesions are: (i) pancreatic intraepithelial neoplasia (PanIN), (ii) mucinous cystic neoplasms (MCN), and (iii) IPMN. In contrast, serous cystadenomas are strictly benign cystic neoplastic lesions and rarely require surgery.

Aims & Methods: Frequently, differential diagnosis of neoplastic cysts remains cumbersome. Thus, non-invasive diagnostic stratification would be welcome. Such a test should allow both discrimination of (i) IPMN from strictly benign pancreatic cysts but also (ii) low- from high-grade IPMN.

Result: Little is known about the molecular alterations of IPMN, but GNAS mutations have been described to promote IPMN formation. A tumor-derived fraction of cell-free DNA (cfDNA) circulating in the bloodstream represents the mutational makeup of tumors and could be a tool for non-invasive monitoring.

We demonstrate that cfDNA levels discriminate controls from a cohort of Fukuoka-negative branch-duct IPMN but also from pancreatic cancer. Furthermore, GNAS mutations were detected in IPMN patients but were absent in serous cystadenomas (SCA) and in controls. Moreover, we observed relevant concordance between tissue and liquid biopsies-based GNAS mutations in an independent cohort of resected IPMN patients.

Conclusion: These findings establish cfDNA and targeted genotyping as a diagnostic tool for IPMN, which may aid differential diagnosis and risk stratification of cystic pancreatic lesions.

Disclosure of Interest: All authors have declared no conflicts of interest.
INTESTINAL FAILURE: FROM PATHWAYS TO TREATMENT -room 17-

**OP262 NOVEL GENE MUTATIONS IN NEUROGENIC CHRONIC INTESTINAL PSEUDO-OBSTICTION**

E. Bonora\(^1\), C. Graziano\(^1\), F. Bianco\(^1\), A. Stanzani\(^1\), R. Rinaldi\(^1\), R. D’Angelo\(^1\), E. Boschetti\(^2\), J. D. Smith\(^3\), G. Assadi\(^4\), M. Bamshad\(^4\), D. Nickerson\(^4\), G. Lindberg\(^5\), M. D’Amato\(^6\), V. Stanghellini\(^1\), M. Seri\(^1\), R. De Giorgio\(^1\)

WES analysis was performed considering pathogenic variants present as application in BaseSpace.

Data analysis and variant calling was performed with the TruSeq Amplicon annotated with the SeattleSeq Annotation Server. Additional 77 patients were them. Libraries were enriched with the Nimblegen SeqCap EZ v3.0 and metric well-defined CIPO. A neurological work-up established SFN in each of affected probands, since all the parents were healthy. We identified novel/rare autosomal recessive (compound heterozygotes), X-linked or de-novo in the n (SFN), a condition affecting peripheral neurons including those of the autonomic (DRG) were obtained from the national disease resource interchange (NDRI).

Cryo-protected or fresh human thoracic dorsal root ganglia

Contact E-mail Address: claudio.graziano@unibo.it

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**OP263 PROTEASE SIGNALING IN HUMAN SENSORY NEURONS**

G. Lindberg7, M. D'Amato8, V. Stanghellini1, M. Seri1, R. De Giorgio1

PAR antibodies. Calcium signaling responses to PAR agonist peptide (PAR-AP): PAR1-AP-induced calcium increase in human sensory neurons. PAR4 activation reduced cause calcium mobilization. Thrombin (PAR1 and PAR4 agonist) but not trypsin (PAR2 and PAR4 agonist) increased calcium flux in human sensory neurons. PAR-AP-induced calcium mobilization was significantly reduced by pre-incubation with PAR-AP, but not with PAR-AP or any of the PAR-IP.

**Conclusion:** Our study demonstrates that PAR2, PAR4, and PAR6 are expressed in human sensory neurons. In contrast to PAR2 and PAR4, activation increased calcium increase in human sensory neurons. PAR activation reduced calcium mobilization.

Thus, in Human PAR2 and PAR4 play an important role in neuronal activation and may be relevant in IBS research.

Disclosure of Interest: All authors have declared no conflicts of interest.

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TUESDAY, OCTOBER 18, 2016 14:00–15:30

**OP264 DIFFERENTIAL BASELINE CHARACTERISTICS IN SHORT BOWEL SYNDROME DUE TO VASCULAR CATASTROPHES ARE ASSOCIATED WITH VARYING RESPONSE TO TEDUGLUTIDE TREATMENT: POST HOC ANALYSIS**

P.B. Jeppesen\(^1\), U. Pepe\(^2\), E. Key\(^3\), H. Lee\(^4\), C. Olivier\(^5\)

Radiology And Gastroenterology, University Medicine Berlin, Berlin, Germany

Mount Sinai Medical Center, New York/United States of America/NY

University of Wisconsin/C21

Shire plc, Zug/Switzerland

Contact E-mail Address: palle.becker.jeppesen@region.dk

Introduction: Vascular catastrophes are an underlying condition for massive intestinal resection and failure associated with short bowel syndrome (SBS-IF).

Aims & Methods: This post hoc analysis of data reported in patient e-case forms compared baseline characteristics of patients with SBS-IF due to vascular catastrophes (SBS-Vasc) vs patients with nonvascular causes of SBS (SBS-non-Vasc), including the clinical response to teduglutide (TED). STEPS (NCT00798967; EudraCT2008-006193-15) was a 24-week, placebo (PBO)-controlled study of TED 0.05 mg/kg/day in patients with SBS-IF. Response was defined as ≥20% reduction from baseline in weekly parenteral support (PS) volume at Week 20 that was maintained at Week 24. Vascular catastrophes were intestinal ischaemia or mesenteric vessel thrombosis or emboli. Descriptive summary statistics are presented with standard deviations (SD) or 95% confidence intervals (CI); this post hoc analysis was not powered for statistical significance.

Results: The patient characteristics for the SBS-Vasc (n = 32) and SBS-non-Vasc (n = 35) groups are detailed in the Table. The reason for the majority of the intestinal resection was Crohn’s disease (SBS-non-Vasc) or mesenteric vessel thrombi or emboli (SBS-Vasc). Table. At baseline, more SBS-Vasc patients had shorter bowel length (55 vs 92 cm), were more likely to have colon-in-continuity (78% vs 43%), and were less likely to have stoma present (19% vs 61%) compared with SBS-non-Vasc patients. SBS-Vasc patients had a higher baseline PS volume at baseline (14.1 L/week) compared with SBS-non-Vasc patients. After 24 weeks, 53% (CI, 27%–79%) of SBS-Vasc patients and 70% (CI, 50%–86%) of SBS-non-Vasc patients were responders to TED. In the PBO groups, 35% (CI, 14%–62%) of SBS-Vasc patients and 27% (CI, 11%–48%) of SBS-non-Vasc patients met the response criteria. In the TED groups, reduction in mean PS volume (change and percentage change) took longer in the SBS-Vasc group (Week 12: 1.9 [CI, 0.3–3.5], 12% [CI, 3%–20%]; Week 24, 3.6 [CI, 1.5–5.7], 25% [CI, 15%–35%]) compared with the SBS-non-Vasc group (Week 12: 2.0 [CI, 0.0–4.0], 24% [CI, 16%–33%]; Week 24: 4.5 [CI, 3.4–7.6], 36% [CI, 29%–43%]). The overall TED safety profile was generally similar between the 2 groups. Specifically, >15% of SBS-Vasc patients reported abdominal pain, dyspepsia, fatigue, nausea, and peripheral oedema, whereas ≥15% of SBS-non-Vasc patients reported nausea, abdominal distension, abdominal pain, stomal complication, and peripheral oedema.

Conclusion: To our knowledge, this post hoc analysis is the first to compare baseline characteristics and response to treatment in patients with SBS resulting from vascular catastrophes and nonvascular diseases. In this group of patients, SBS-IF patients with vascular catastrophes were more likely to have colon-in-continuity, less likely to have stoma present, and had less baseline PS volume than in patients with nonvascular causes of SBS-IF. SBS-IF patients with vascular catastrophes took longer to respond to teduglutide in the observed PS volume reduction.

Table: Demographic and Baseline Characteristics

<table>
<thead>
<tr>
<th>Parameter</th>
<th>SBS-Vasc</th>
<th>SBS-Vasc</th>
<th>SBS-non-Vasc</th>
<th>SBS-non-Vasc</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>56.6 (13.8)</td>
<td>52.3 (13.5)</td>
<td>42.5 (13.2)</td>
<td>50.8 (12.9)</td>
</tr>
<tr>
<td>Sex, %</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (47)</td>
<td>9 (60)</td>
<td>11 (42)</td>
<td>11 (41)</td>
</tr>
</tbody>
</table>

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**Reference**


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A104

United European Gastroenterology Journal 4(5S)

Digestive Health Research Institute, Toulouse/France

Digestive Health Research Institute, Toulouse/France

Unit of Clinical Epidemiology, Department of Medicine Solna, Karolinska University Hospital, Huddinge, Stockholm, Sweden

Department of Biomedical and Neuro-motor Science, University of Bologna, Bologna/Italy

University of Washington Center for Mendelian Genomics, Seattle/United States of America/WA

Karolinska Institut, Stockholm/Sweden

Department Of Genome Sciences, University of Washington, Seattle/United States of America

Department Of Genome Sciences, University of Washington Center for Mendelian Genomics, Seattle/United States of America/WA

Center For Medical Gastroenterology, Karolinska University Hospital, Huddinge, Stockholm, Sweden

Unit Of Clinical Epidemiology, Department Of Medicine Solna, Karolinska Institut, Stockholm/Sweden

Contact E-mail Address: claudio.graziano@unibo.it

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Introduction: Chronic intestinal pseudo-obstruction (CITO) is a severe gut dysmotility mimicking an intestinal sub-obclusion without demonstrable mechanical causes. Several genes have been identified in familial cases, suggesting a genetic heterogeneity. We identified a novel mutation in the RAD21 gene in a recessive form of familial CITO\(^1\). RAD21 is a transcription factor essential for a number of functions including sister chromatid division during cell replication.

Aims & Methods: This study aimed to identify other mutated genes in a selected set of patients with CITO associated with peripheral small fiber neuropathy (SFN), a condition affecting peripheral neurons including those of the autonomic system. Whole exome sequencing (WES) was performed on genomic DNA of n = 6 patients (3 trios and 3 sporadic cases) with clinical, radiological and manometric features of SFN. A neurologically well-defined CIPO. A neurological work-up established SFN in each of them. Libraries were enriched with the Nimblegen SeqCap EZ v3.0 and sequenced via paired-end 30 bp reads on HiSeq2500 sequencing. Variants were annotated with the SeattleSeq Annotation Server. Additional 77 patients were collected for replication study. Target resequencing on selected genes was performed using the TruSeq Amplicon panel designed with Design Studio software.

We identified a novel mutation in the RAD21 gene in a recessive form of familial CITO\(^1\). RAD21 is a transcription factor essential for a number of functions including sister chromatid division during cell replication.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

patients who underwent small bowel or multivisceral transplants at Children's Hospital, UK. There were 54 patients listed from January 2006 to April 2015. Patients with survival less than 6 months post-transplant (n = 9) and with incomplete data (n = 1) were excluded. This resulted in 44 eligible patients whose weights, BMI and grip strengths (in non-dominant hand) were analysed. Grip strengths were performed by one of two dedicated dietitians.

Results: Patient characteristics: Transplants included 12 isolated small bowel (SBT), 5 liver and small bowel (LSBT), 12 modified multivisceral (small bowel, stomach, pancreas-MVTT) and 22 multivisceral (small bowel, stomach, pancreas, liver-MVTT). 7 patients were re-transplanted. Recently, donor colon has been included in the graft to help with fluid balance. Mean age at transplant was 43.9 years. Patients were followed up for a median of 30 months, to April 2016 or death (n = 37). Primary outcomes: Out of the 30 long-term survivors, 73.3% (22) of them are maintained on oral diet alone at the end of follow up. The other 5 patients require ONS, 2 require IV fluids and 1 patient continues on PN. Most patients (95.5%; 21/22) who achieved nutritional autonomy were previously dependent on nutritional support (2 ONS; 1 EN; 18 except for 1 patient who was listed super-urgently. Of the patients who died, 3 out of 14 were requiring PN. The mean BMI pre-transplant was 21.7 (SD = 3.5). Post-operatively, the majority of patients (86.7%) lost weight (mean 14.3%; range 1–30%) with their nadir weight occurring at a mean of 10.7 months. 11 lost ≥20% of their pre-transplant weight. However more than half (26/44) of the patients weights improved over time. Compared to the time of assessment, their BMI improved by 0.9 kg/m² (SD = 4.3) in the first year (median 11 months) and increased further by 1.4 kg/m² (SD = 4.3) at the end of the follow up. The most recent mean BMI in 30 survivors were 23.3 kg/m² (SD = 5.2). Further analysis revealed 20 patients have healthy weight (BMI 18.5–25), 4 underweight (BMI < 18.5), 3 overweight (BMI > 25) and 3 obese (BMI ≥ 30). Short bowel autonomy was only maintained in 22/44 patients, though this was not significantly different compared to those who were nutrition dependent (mean of 65.3 ± 12.0 days). This suggests that the duration on nutritional support post-transplant may predict nutritional autonomy. Of the patients who have colon (graft or continuity), 64% have nutritional autonomy. However those without functioning colon are less likely to (47.4%) (P = 0.36). Handgrip strength was measured in 31 patients pre and post-transplant. At median of 9 months (range from 2–32), there was a slight reduction by 6% of expected value which correlates with their weight loss. 18 patients had further handgrip strength test and they improved with a mean of 7% at last follow up (median 16 months).

Conclusion: The majority of patients achieved nutritional autonomy post-transplant and a colon-containing graft may be beneficial. It is common for patients to lose a moderate amount of weight, up to 30% post-operatively. Therefore timely referral is crucial to allow optimisation of perioperative nutritional status. Disclosure of Interest: All authors have declared no conflicts of interest.

OP266 SUBANALYSIS OF TREDUGLITIDE EFFICACY AND SAFETY DATA FROM PATIENTS WITH CROHN’S DISEASE AND ULCERATIVE COLITIS IN THE STEPS STUDY

U. Pape1, P.B. Jeppesen2, H. Lee3, A. A. Grimm4, S. J. O’Keefe4

1Gastroenterology and Haematology, Charité, University Medicine Berlin, Berlin, Germany
2Rigshospitalet, Copenhagen, Denmark
3Shire plc, Lexington, United States of America/MA
4EPMC, Pittsburgh, United States of America/PA

Contact E-mail Address: ulrich-frank.pape.charite.de

Introduction: Inflammatory bowel disease (IBD; Crohn’s disease [CD] and ulcerative colitis) is a major underlying condition for massive intestinal resection leading to intestinal failure associated with short bowel syndrome (SBS–IF).

Aims & Methods: This post hoc subgroup analysis compared response to treduglitate (TED) in patients with SBS–IF due to IBD (SBS–IF vs those with noninflammatory causes of SBS–IF (SBS–non-IBD). STEPS (NCT00798967, EudraCT2008-006193-15) was a 24-week, phase III, placebo-controlled study ing to intestinal failure associated with short bowel syndrome (SBS–IF). The STEPS study was a 24-week, phase III, placebo-controlled study of 0.05 mg/kg/day TED in patients with SBS–IF due to IBD (SBS–IBD) vs those with noninflammatory causes of SBS–IF (SBS–non-IBD). STEPS (NCT00798967, EudraCT2008-006193-15) was a 24-week, phase III, placebo-controlled study of 0.05 mg/kg/day TED in patients with SBS–IF. Patients were randomised based on clinical remission for ≥12 weeks at baseline. Response was ≥2% reduction from baseline in weekly parenteral support (PS) volume at Week 20 that was maintained at Week 24. Descriptive summary statistics are presented with 95% confidence intervals (CIs); this post hoc analysis was not powered for statistical significance.

Result: The Table details patient characteristics (SBS–IBD, n = 19; SBS–non-IBD, n = 67). Patients with SBS–IBD had lower colon-in-continuity, higher short bowel volume and higher baseline PN volume than those with SBS–non-IBD. After 24 weeks, 73% (95% CI, 39%–94%) of patients with SBS–IBD and 59% (95% CI, 41%–76%) with SBS–non-IBD were responders to TED. In the patients, mean PS volume was reduced by 45% (95% CI, 31%–59%) in patients with SBS–IBD and 29% (95% CI, 22%–35%) in those with SBS–non-IBD. Two of 9 (22%) patients with SBS–IBD and 6/30 (20%) patients with SBS–non-IBD achieved a PS reduction of ≥2 days per week. Overall safety profile was similar in both groups (SBS–IBD, n = 19; SBS–non-IBD, n = 66). Among patients receiving treatment-emergent adverse events (TEAEs) were reported by 100% of patients with SBS–IBD and 77% of those with SBS–non-IBD. Serious adverse events among those receiving TED occurred in 27% of patients with SBS–IBD and 39% of those with SBS–non-IBD. No TEAEs of CD were reported in either group.
OP267 INDICATIONS AND OUTCOMES OF INTESTINAL AND MULTIVISCERAL TRANSPLANT


1Gastroenterology, Addenbrooke’s Hospital, Cambridge/United Kingdom
2Transplant Surgery, Addenbrooke’s Hospital, Cambridge/United Kingdom

Contact E-mail Address: szeyp@gmail.com

Introduction: Despite a reduction in numbers worldwide, we have seen an increase in adult Intestinal and Multivisceral transplants in the UK in the past 3 years. Some recent transplants have been performed ‘superurgently’ for acute widespread splanchnic ischaemia. Longstanding indications include complications of severe idiopathic intestinal inflammation in patients with type 3 Intestinal failure (IF- associated liver disease (IFALD), recurrent cather-related infections and loss of vascular access, cirrhosis with extensive portomenteric venous thrombosis precluding an isolated liver transplant and the need for extensive evisceration due to benign tumour. Re-transplantation is indicated for loss of graft function due to rejection, ischaemia or primary non-function.

Aims & Methods: We describe the indications and outcomes for Intestinal and Multivisceral transplant at Addenbrooke’s Hospital, Cambridge, UK Data was collected prospectively on an internal database of all patients transplanted from January 2006 to April 2016. All patients considered for an intestine-conjunction, ischaemia or primary non-function.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP268 EXPRESSION OF DDR2 CORRELATES WITH HIGH FREQUENCY OF PERITUMORAL DISSEMINATION AND POOR PROGNOSIS IN COLORECTAL CANCER

S. Sasaki1, M. Ueda1, T. Iuchi2, M. Kaneko2, H. Nakayama1, T. Watanabe1, A. Sakamoto3, K. Mimori4

1Dept. Of Surgery, Omori Red Cross Hospital, Tokyo/Japan
2Dept. Of Surgery, Kyushu University Beppu Hospital, Beppu/Japan
3Dept. Of Pathology And Laboratory Medicine, Omori Red Cross Hospital, Tokyo/Japan

Contact E-mail Address: ssasaki@omori.jrc.or.jp

Introduction: In the previous study, our colleagues identified that discoidin domain receptor 2 (DDR2) is a promising driver gene of peritoneal dissemination in gastric cancer by a comprehensive expression assay. We found DDR2 expression was associated with high frequency of peritoneal dissemination and poor prognosis in gastric cancer, and also revealed that the DDR2 was upregulated by the loss of DNA methylation and that DDR2 knockdown reduced peritoneal dissemination in a xenograft. Furthermore, we found dasatinib, an inhibitor of the DDR2 signaling pathway, suppressed peritoneal dissemination. In colorectal cancer, peritoneal dissemination is second popular site for colorectal cancer metastasis, next to the liver. Its frequency is estimated to be 4–7% of patients with colorectal cancer at primary surgery, and approximately 4–19% of patients during follow-up after curative surgery. Peritoneal dissemination is one of most frequent non-curative clinical factors also in colorectal cancer.

Aims & Methods: In this study, we analyzed correlations of DDR2 expression with clinicopathological factors in colorectal cancer, especially peritoneal dissemination. We selected 63 cases with colorectal cancer who had an operation in our hospital between 2009 and 2014. Among them, 13 cases had synchronous or metachronous peritoneal dissemination. We performed immunohistochemical examinations for 63 primary colorectal cancers and 12 peritoneal dissemination lesions in 11 cases with anti-DDR2 antibody. We evaluated histological localization of DDR2 expressions, and compared various clinicopathological factors and overall survival between these two groups.

Result: Immunohistochemical examinations for 63 primary colorectal cancers, 12 cases with peritoneal dissemination, and 35 cases without peritoneal dissemination were performed. DDR2 expressions were evaluated with anti-DDR2 antibody in 63 primary colorectal cancers, 12 cases of peritoneal dissemination, and 35 cases without peritoneal dissemination. In colorectal cancer, peritoneal dissemination is second popular site for colorectal cancer metastasis, next to the liver. Its frequency is estimated to be 4–7% of patients with colorectal cancer at primary surgery, and approximately 4–19% of patients during follow-up after curative surgery. Peritoneal dissemination is one of most frequent non-curative clinical factors also in colorectal cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.
TUMORIGENICITY OF COLORECTAL CANCER THROUGH Disclosure of Interest: adenomas or specific histological subtypes. CRC risk (rs10505477 and rs6983267 in CASC8 gene and rs10795668 and 0.61 for rs6983267), suggesting their possible implication in early stages control study comprising 750 FDR of patients with non-syndromic CRC (cases), and 750 non-FDR of colorectal adenomas or matched individuals with no family history of CRC (controls). Cases and controls were selected from the Spanish CRC screening registries in Aragon and The Canary Islands. All subjects underwent at least one colonoscopy and diagnosis of adenoma was confirmed by histological study. Genomic DNA from cases and controls was genotyped by the MassArray\textsuperscript{TM}Sequenom) platform for a panel of 99 SNPs previously associated with CRC risk. Genetic analysis was performed using the SNPassoc package implemented in R. To address the issue of adjustment for multiple testing, the false discovery rate method and Bonferroni’s correction were applied. Result: Average age of participants was 54.5±9.4 years with a slight predominance of women (51.7%). In 57% of patients, no preneoplastic lesions were found. By contrast, 288 patients (144 cases and 144 controls) showed non advanced adenomas (NAA), and 354 patients (177 cases and 177 controls) had advanced adenomas (AA). Concerning gene analysis, 2 SNPs (rs10505477 A > G and rs6983267 G > T) located in the CASC8 gene were associated with the development of adenomas. Thus, the rs10505477G and the rs983267T alleles were significantly associated with a reduced risk of adenomas in patients with no family history of CRC (controls) (log-additive models, OR: 0.67, 95% CI:0.54–0.84, respectively). However, such a protective effect was not observed in FDR of patients with CRC (cases). In the stratified analysis, by histological classification, the rs10505477G and the rs9693267T variants were significantly associated with a reduced risk of both, NAA and AA in controls, although this effect was stronger on the risk of developing NAA (recessive models, OR:0.38, 95% CI:0.21–0.67 for rs10505477, and OR: 0.32, 95% CI: 0.17–0.6, 61 for rs9693267), suggesting their possible implication in early stages of CRC development. Finally, 2 SNPs (rs10795668G > A and rs11255841T > A) located in the IncRNA gene LINC00709 were significantly associated with a reduced risk of CRC (recessive models, OR: 0.22, 95% CI: 0.06–0.72 for rs10795668, OR: 0.08, 95% CI: 0.03–0.61 for rs11255841) and patients with no family history of CRC (dominant models, OR: 0.50, 95% CI: 0.34–0.75 for rs10795668, and OR:0.52, 95% CI: 0.31–0.91 for rs11255841), suggesting their possible implication in early stages of CRC development. Conclusion: Family history of CRC and some specific variants associated with CRC risk (rs10505477 and rs6993267 in CASC8 gene and rs10795668 and rs11255841 in the IncRNA gene LINC00709) are involved in the development of colorectal adenomas or specific histological subtypes. Disclosure of Interest: All authors have declared no conflicts of interest.

OP270 A NOVEL AMPLIFICATION GENIC PCID2 PROMOTES TUMORIGENICITY OF COLORECTAL CANCER THROUGH DISRUPTION OF A TUMOR SUPPRESSOR PMI AND IS ASSOCIATED WITH DISEASE RECURRENCE J. Zhang\textsuperscript{1}, Y. Zhang\textsuperscript{1}, H. Tsoi\textsuperscript{1}, H. Wang\textsuperscript{1}, J. Gao\textsuperscript{1}, Y. Y. Go\textsuperscript{2}, S.C. Ng\textsuperscript{1}, J.J.Y. Sung\textsuperscript{3}, J. Yu\textsuperscript{1}
\textsuperscript{1}Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong\textsuperscript{2}The Chinese University of Hong Kong, Hong Kong\textsuperscript{3}Gastrointestinal Oncology, Peking University Cancer Hospital & Institute, Beijing/China
Contact E-mail Address: zhangjingwang12@gmail.com

Introduction: PCID2 Domain Containing 2 (PCID2) located at 13q34 was identified to be recurrently amplified in colorectal cancer (CRC) clinical samples. We evaluated its amplification, overexpression, biological functions and clinical implication in CRC. Aims & Methods: The PCID2 gene amplification status in CRC tissues was evaluated by Copy Number Assay. The biological effects of PCID2 overexpression and knockdown were determined by in vitro and in vivo tumorigenicty assays. The PCID2 interaction partner was identified by immunoprecipitation followed by mass spectrometry. PCID2 downregulation and overexpression were performed in vitro and in vivo. Results: Amplification of PCID2 was detected in 32.5% (37/114) of CRC patients from cohort I and 62.0% (233/376) of CRC patients from cohort III by Copy Number Assay. The copy number gain was positively correlated with its mRNA overexpression both in cohort I (r sq = 0.327, p < 0.0001) and in cohort III (r sq = 0.619, p < 0.0001). Biological functional investigation of PCID2 revealed that knockdown expression of PCID2 in colon cancer cell lines (DLD1 and HT29) significantly increased cell proliferation (p < 0.01 in DLD1 and p < 0.001 in HT29), G1 cell cycle transition (p < 0.01 and p < 0.05, respectively), invasion (p < 0.01 and p < 0.01, respectively) and migration (p < 0.01 and p < 0.05, respectively). However, such a protective effect of PCID2 was mediated through degrading its interaction partner promyelocytic leukemia (PML) by ubiquitination. PML played a tumor suppressive role in CRC. PCID2 induced Wnt signaling pathway and inhibited p53/p21 pathway activity. PCID2 expression level was evaluated in 354 patients (177 cases and 177 controls) with normal preneoplastic lesions. Multivariate analysis revealed that patients with PCID2 overexpression were significantly correlated with CRC recurrence (p < 0.05 for cohort I, p < 0.03 for cohort II). Recurrence curves showed that PCID2 overexpression was a prediction marker for recurrence of patients with CRC (p = 0.004 for cohort I, p = 0.03 for cohort II).

Conclusion: PCID2 plays a pivotal oncomic role in colorectal carcinogenesis by disrupting the tumor suppressor PML, and its overexpression both in cohort I and II patients. Multivariate analysis revealed that patients with PCID2 overexpression were significantly correlated with CRC recurrence (p < 0.05 for cohort I, p < 0.03 for cohort II).

Disclosure of Interest: All authors have declared no conflicts of interest.

OP271 PREDICTION OF COMPLETE RESECTIONS AFTER CYTOREDUCTIVE SURGERY BASED ON THE EXTENT OF COLORECTAL PERITONEAL CARCINOMATOSIS W. h. Van Eden\textsuperscript{1}, M. Lahaye\textsuperscript{2}, A. Delli Pizzii\textsuperscript{3}, D.M. Lambregts\textsuperscript{4}, N. Kok\textsuperscript{5}, G.L. Beets\textsuperscript{6}, R.G. h. Beets-Tan\textsuperscript{7}, A. Albels\textsuperscript{8}
\textsuperscript{1}Department Of Surgery, The Netherlands Cancer Institute, Amsterdam/Netherlands\textsuperscript{2}Radiology, The Netherlands Cancer Institute, Amsterdam/Netherlands\textsuperscript{3}The Netherlands Cancer Institute, Amsterdam/Netherlands\textsuperscript{4}Department Of Radiology, The Netherlands Cancer Institute, Amsterdam/Netherlands\textsuperscript{5}Surgery, The Netherlands Cancer Institute, Amsterdam/Netherlands
Contact E-mail Address: m.lahaye@nki.nl

Introduction: Cytotherapeutic surgery (CRS) and hyperthermic intraperitoneal chemoetherapy (HIPEC) is the treatment of choice for colorectal peritoneal carcinomatosis (PC). Prior to surgery abdominal computed tomography (CT) was performed to gain insight into the extent of PC and the presence of distant metastases. Aims & Methods: Our objective was to evaluate the relation between the completeness of cytoreduction and the Dutch seven region count evaluated with CT and during surgery. Patients who underwent abdominal CT-imaging for PC prior to CRS-HIPEC were eligible. The seven-point region count was assessed with CT by an experienced radiologist and peroperative evaluation was performed by the operating surgeon, based on the Dutch region count. The completeness of cytoreduction was scored after CRS. Survival was calculated.

Result: Two hundred thirty-four patients were included. Patients with incomplete cytoreductive surgery had more often PC in five to seven regions during surgery (p < 0.001). This result was not found using de CT-related region count. The AUC for predicting disease free survival was 0.70. Patients with PC in more than five regions were found with medians of 21.9 months (IQR 19.1–24.7) and 44.6 months (IQR 35.8–53.5) in patients with complete cytoreduction compared to 12.1 months (IQR 9.7–14.6) and 19.0 months (IQR 14.2–23.8) in patients with incomplete cytoreductive surgery (p < 0.001). Conclusion: Patients with four or less involved abdominal regions with PC peroperative were more likely to have a complete resection. CT assessment of the region score could not accurately predict a complete resection. Patients with a complete resection showed better survival than patients with an incomplete cytoreduction. Disclosure of Interest: All authors have declared no conflicts of interest.


Introduction: Rectal carcinoid tumors are the most common neuroendocrine tumors of the gastrointestinal tract and their incidence is increasing due to colorectal cancer screening. Several previous studies have suggested that local excision (endoscopic submucosal dissection) is effective for ≤10mm lesions but data on long-term
outcomes are very limited. In addition, management of 11–19 mm tumors is not well defined because of variable estimates of risk of lymph node (LN) distant metastasis.

Aims & Methods: The aims of this study were: 1) to determine the prevalence of metastasis of resected T1 rectal carcinoid tumors using a large national cancer database, 2) to identify risk factors for metastasis, 3) evaluate the long-term survival of patients with T1N0M0 rectal carcinoid tumors after local resection as compared to radical surgery. The SEER 18 database was used to identify patients aged 18–80 years with T1 histologically confirmed rectal carcinoids <20 mm in size diagnosed between 1998 and 2012. T1 was defined as tumor invading lamina propria or submucosa. Prevalence of LN (N1) distant metastases (M1) at initial diagnosis and risk factors for metastases were analyzed. Cancer-specific survival (CSS) and overall survival were calculated using Kaplan-Meier's estimate and compared with log-rank test.

Result: A total of 788 patients with T1 rectal carcinoids were identified [mean age: 54.8 (SD 11.3); 49.5% men; 57% white]. Of these, 727 (92.3%) patients had tumors <10 mm in diameter and 61 (7.7%) had tumors 11-19 mm. Submucosal invasion was seen in 14.9%. Overall, 4% (15.1%) had LN metastases at the time of diagnosis with prevalence of 1.1% in lesions ≤10 mm and 6.6% in lesions 11-19 mm in size (p = 0.01). Tumor size (OR 6.3); 95%CI 1.8 – 21.5; p = 0.003) and submucosal invasion (p = 0.03) were associated with LN distant metastasis. Median follow-up time in our cohort was 23 months (range 0-172). Survival of patients with T1 rectal carcinoids without N1/M1 was significantly better than those with N1/M1 with 5-yr CSS of 100% and 78%, respectively (p < 0.001). Of 550 patients with T1N0M0 rectal carcinoids <10 mm in size and age >65 months, 527 (94.5%) underwent local excision and 32 (5.7%) had radical surgery. 5-yr CSS was 100% and 10-yr CSS was 98% (SE 0.01). For 46 patients with T1N0M0 rectal carcinoids 11–19 mm in size [39 (84.8%) who underwent local excision and 7 (15.2%) underwent radical surgery], there were no LN metastases and no tumor-related deaths after a median follow up of 28 months (range 8–122). The overall survival of T1N0M0 rectal carcinoids treated by local excision versus radical surgery were comparable.

Conclusions: The overall prevalence of carcinoid tumors (11–19 mm) are at increased risk of LN metastases compared those ≤10 mm. Survival is worse with regional or distant metastatic disease. Hence, thorough evaluation for metastatic disease should be considered for these lesions. Local therapy is adequate for T1 rectal carcinoids <10 mm in size, whereas radical therapy is required for T1 rectal carcinoid tumors ≥10 mm in size.

Disclosure of Interest: V. Singh: Vikesh Singh is a consultant for Abdvie, D-Pharm, and Santarus. M. Khashab: Mouen Khashab is a consultant for Boston Scientific All other authors have declared no conflicts of interest.

OP273 LONG-TERM FOLLOW-UP FEATURES ON RECTAL MRI DURING ‘WATCH-AND-WAIT’ IN CLINICAL COMPLETE RESPONDERS AFTER CHEMORADIOTHERAPY: AN UPDATE OF 68 PATIENTS

D.M. Lambrugg3, 1, M. Van Heeswijk2, B. Hipkens2, R. Beckers2, M. Maas2, M. V. D. Vooren3, G. L. Beets3, R. G. h. Beets-Tan4, 1Department Of Radiology, The Netherlands Cancer Institute, Amsterdam/Netherlands 2Radiology And Surgery, Maastricht University Medical Centre, Maastricht/Netherlands 3Department Of Radiology And Surgery, The Netherlands Cancer Institute, Amsterdam/Netherlands 4Surgery, The Netherlands Cancer Institute, Amsterdam/Netherlands

Contact E-mail Address: D.lambrugg@nk.ki.nl

Introduction: Treatment with a stringent follow-up (‘watch-and-wait’) is emerging as an alternative to surgical resection in rectal cancer patients who show a complete clinical response after chemoradiotherapy. An important question is how (how frequently and with what modalities) to monitor patients once surgery is omitted, in addition to clinical examination and endoscopy imaging – mainly MRI – during the follow-up within the scope of a watch-and-wait protocol. Patients underwent MRI during long-term follow-up in almost all patients. A complete normalized wall is present post-chemoradiotherapy which remains unchanged during long-term follow-up in almost all patients. A completely normalized wall is observed in approximately 1 in 10–20 patients. The findings of this study may serve as a reference and provide teaching for radiologists involved in the clinical follow-up of patients selected to undergo a wait-and-see approach after a clinical complete response in patients with rectal cancer treated with chemoradiotherapy.

Result: In the majority of patients with a complete response residual fibrosis is present post-chemoradiotherapy which remains unchanged during long-term follow-up in almost all patients. A complete normalized wall is observed in approximately 1 in 10–20 patients. The findings of this study may serve as a reference and provide teaching for radiologists involved in the clinical follow-up of patients selected to undergo a wait-and-see approach after a clinical complete response in patients with rectal cancer treated with chemoradiotherapy.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016 14:00–15:30

GENERAL HEPATOLOGY – ROOM 1.06

OP274 ACCURACY OF A POINT SHEAR WAVE ELASTOGRAPHY TECHNIQUE (ELASTPQ) IN THE NON-INVASIVE ASSESSMENT OF LIVER FIBROSIS IN A LARGE COHORT OF LIVER PATIENTS

M. Garoccio1, M. Pompiii2, E. Di Stasi3, L. Riccardi, M.E. Ainora1, A. Gritico1, G.L. Rapanotti3, M. Siciliano4, A. Gasbarri1, M. Di Cocco1, 1Internal Medicine, Gastroenterology And Liver Diseases Unit, Catholic University of Sacred Heart - Policlinico Gemelli, Rome/Italy 2Institute Of Biochemistry And Clinical Biochemistry, University of Sacred Heart - Policlinico Gemelli, Rome/Italy 3Gastroenterology, Compleso Integrato Columbus - Catholic University, Rome, Italy 4Internal Medicine And Gastroenterology, Agostino Gemelli Hospital Dept. of Gastroenterology, Rome, Italy

Contact E-mail Address: matteogaroccio@yahoo.it

Introduction: ElastPQ is a novel point shear wave elastography (PSWE) technique that assesses liver stiffness by measuring liver stiffness (kPa) with few studies published so far. The aim of this study was to determine the accuracy and reliability for the assessment of liver stiffness in a large cohort of 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 calculated using Spearman correlation and ROC curve analyses were performed to calculate AUC for F > 2, F ≥ 3 and F = 4.

Result: We enrolled 289 patients (176/113 males/females) who underwent LB for viral hepatitis (HCV 49%, HBV 6%, other 15%), non-viral 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 comparing different elastography devices.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP275 COMPARATIVE STUDY BETWEEN 2D SHEAR WAVES ELASTOGRAPHY TECHNIQUES FOR THE ASSESSMENT OF LIVER STIFFNESS: 2D-SWESSI VS. 2D-SWEGL

F. Benede1, I. Sporea1, R.L.D. Sirlot1, A. Paspescu1, M. Dupila1, R.G. Mure1, R. Lupusor1, Department Of Gastroenterology And Hepatology, University of Medicine and Pharmacy "Victor Babes" Timisoara, Timisoara/Romania

Contact E-mail Address: benedefelix@gmail.com

Introduction: Chronic liver diseases are quite frequent encountered in daily practice and due to chronic hepatitis (B or C virus) and other conditions such as chronic alcohol abuse (ASH) and NAFLD. In this conditions, the evaluation of chronic liver disease's severity is mandatory, for prognosis, for management and for decision regarding therapy.

Aims & Methods: The aim of this comparative study was to compare the feasibility of two 2D-Shear Waves Elastography (2D-SWE) methods for the assessment of Liver Stiffness (LS) and also to compare the methods with a validated one: Transient Elastography(TE). Our study included 130 consecutive patients with chronic hepatopathies (HCV-90%, HBV-6%, other-4%), in which Liver Stiffness (LS) was evaluated in the same session by means of two 2D-SWE techniques: 2D-SWE.GE/LOGIQ E9, GE Healthcare) and 2D-SWESSI (ElastoPQ technique). This novel PSWE system appears to be a very useful tool for non-invasive evaluation of liver 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 comparing different elastography devices.

Disclosure of Interest: All authors have declared no conflicts of interest.
Disclosure of Interest: Liver stiffness values obtained by 2D-SWE.GE are significantly lower than those were similar (p = 0.001). The AUROC for TLE was 0.86 (95% CI, 0.78–0.92; cut-off, 2.2 COI), 0.87 (CI, 0.81–0.93; cut-off, 2.2 COI), 0.81 (CI, 0.74–0.88; cut-off, 2.83) and 0.78 (CI, 0.70–0.86; cut-off, 1.45) for SWE.SSI.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP276

UTILITY OF REAL-TIME SHEAR WAVE ELASTOGRAPHY FOR ASSESSING LIVER FIBROSIS IN PATIENTS WITH CHRONIC HEPATITIS C

H. Yamada1, K. Shimaya1, A. Kakuta2, K. Shibutani2, H. Kurotaki3, S. Igarashi1, K. Hasa3, N. Hanabata1, K. Kanazawa1, M. Munakata1

1Gastroenterology, Aomori Prefectural Central Hospital, Aomori/Japan
2Radiology, Aomori Prefectural Central Hospital, Aomori/Japan
3Pathology, Aomori Prefectural Central Hospital, Aomori/Japan

Contact E-mail Address: hiroshi-yamada@aomori.pref.jp

Introduction: Real-time shear wave elastography (SWE) is a newly developed method of evaluating liver stiffness, which previously had limited comparability with other non-invasive fibrosis assessment methods. Aims & Methods: This study aimed to compare the utility of SWE, magnetic resonance elastography (MRE), M2BPGi, FIB-4 and PLT for detecting significant fibrosis (F≥2). Liver stiffness results were obtained in 107 subjects by means of 2D-SWE.SSI, 2D-SWE.GE and TE. The values ranged from 4.17 to 20.48 kPa for 2D-SWE.SSI and 8.89 to 32.48 kPa for 2D-SWE.GE. The mean LS values by 2D-SWE.SSI were significantly higher than for 2D-SWE.GE: 19.1±12.3 kPa vs. 12.1±3.47 kPa (p < 0.0001). There was a significant correlation between 2D-SWE.GE and 2D-SWE.SSI LS values (r = 0.712, p < 0.0001). The correlation between 2D-SWE.SSI and TE was r = 0.604, p < 0.0001 with no significant differences between them (p = 0.0056). Taking TE as the reference method, both 2D-SWE.SSI and 2D-SWE.GE had a good value to differentiate between stages of liver fibrosis and liver cirrhosis. For 2D-SWE.GE the best liver stiffness cut-off value to differentiate between liver cirrhosis and other stages of fibrosis was > 13.7 kPa with 88.37% Sc, 75.68 Sp, 87.3 positive predictive value (PPV) and 77.8 negative predictive value (NPV) (AUROC = 0.831, p < 0.0001). For a liver stiffness cut-off value > 10.77 kPa, 2D-SWE.GE had 91.43 Sc, 78.38 Sp, 88.9 PPV, 82.9 NPV (AUROC = 0.904, p < 0.0001) for differentiating liver cirrhosis. The AUROCs of 2D-SWE.SSI and 2D-SWE.GE for predicting the presence of liver cirrhosis were similar (p = 0.09). Conclusion: Both 2D-SWE techniques have a very good feasibility for the non-invasive liver fibrosis assessment and both have a strong correlation with TE. Liver stiffness values obtained by 2D-SWE.GE are significantly lower than those obtained by 2D-SWE.SSI. Both methods have good performance for predicting liver cirrhosis.

Disclosure of Interest: I. Sporea: Iona Sporea participated in an Advisory Board for Siemens and received speaker fees from Philips, Siemens and General Electric R.L. Dirlord. N. Roxana Sirl received speaker fees from Philips A. Popescu: Alina Popescu received speaker fees from Philips All other authors have declared no conflicts of interest.

References

Disclosure of Interest: Greater ease of performance, and lower cost.
References


Aims & Methods: We evaluated 77 nodules from 63 patients who underwent liver transplanta- tion (LT). The prevalence of NODAT stays quite easily visualized by ultrasonography, whereas precise three-dimen- sional (3D) positioning of three applicators cannot. The 3D Sim-Navigator (HITACHI) is a new navigation system that can be used during real-time virtual sonography (RVS) by simulating the 3D positions of multiple applicators, which can facilitate their ideal 3D positioning. We evaluated local hepatocellular carci- noma (HCC) recurrence rates after treatment using a multipolar RF system and determined the applicability of the 3D Sim-Navigator to the system.

Aims & Methods: We compared the local recurrence rates of 209 HCC treated using multipolar or monopolar RF systems between January 2013 and October 2015 using propensity-score matching analysis. We evaluated 77 nodules from 63 patients, treated using a bipolar RF system with multiple applicators and compared the complete necrosis rates (CNR) generated with or without the 3D Sim-Navigator.

Results: Propensity-score matching analysis showed that the mean tumor dia- meter was 24.7 ± 11.9 mm and the cumulative annual local recurrence rates were 0% and 14.9% for the multipolar and monopolar RF systems, respectively (p = 0.228). Thirty-two and 45 nodules with mean diameters of 28.1 ± 11.5 and 22.2 ± 5.7 mm (p = 0.011) were treated with and without the 3D Sim-Navigator, respectively, with CNR of 68.8% and 66.6%, respectively, indicating that the two groups did not significantly differ (p = 0.847).

Conclusion: Case matching analysis of local recurrence rates of HCC after RFA showed that the multipolar RF system is more effective than the monopolar RF system with a diameter >25 mm. Although tumor diameter was significantly larger in the group with, than without the 3D Sim-Navigator, CNR did not significantly differ between the two groups, because multiple appli- cators could be placed in ideal 3D positions using the 3D Sim-Navigator. Therefore, HCC with a tumor diameter >25 mm should be ablated using a multipolar RF system with ideal 3D positioning facilitated by the 3D Sim-Navigator.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


Aims & Methods: We investigated whether addition of an IM to anti-TNF mono- therapy can lead to a decrease of ADA levels and regained clinical response. Therefore, we retrospectively collected measurements of infliximab (IFX) and adalimumab (ADA) serum concentrations together with ADA levels from 602 patients at our IBD centre (September 2005–September 2015). ADA levels were determined with a drug sensitive assay by Sanquin Biologicals Laboratory. As a next step, we identified all ADA positive patients with secondary loss of response (SLO) and started them on an IM in an attempt to eliminate ADA and to

TUESDAY, OCTOBER 18, 2016
15:55-17:15
MANAGEMENT OF REFRACTORY CROHN’S DISEASE – ROOM A

OP200 DISAPPEARANCE OF ANTI-DRUG ANTIBODY TO INFlixIMAB AND ADAlimumab AFTER ADDITION OF AN IMMUNOMODULATOR IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE

A. S. Strik1, G. R. Van Den Brink1, C. P. Ponsioen2, R. Mathot1, M. Lowenberg2, G. D’Haens3

1Gastroenterology, Academic Medical Centre, Amsterdam/Netherlands
2Dept. Of Gastroenterology, Academic Medisch Centrum, Amsterdam/Netherlands
3Gastroenterology & Hepatology, AMC Amsterdam Gastroenterology and Hepatology, Amsterdam/Netherlands

Disclosure of Interest: Since therapeutic options for patients with inflammatory bowel disease (IBD) who lose response to anti-TNF therapy are limited, optimal use of these agents is crucial. Loss of response can be caused by anti-drug antibody (ADA) formation and subsequent neutralization of the effect of the drug. Addition of an immunomodulator (IM) to anti-TNF therapy has been proposed as an approach to reduce antibody formation, increase serum concentrations and to regain clinical response.

Aims & Methods: We investigated whether addition of an IM to anti-TNF mono- therapy can lead to a decrease of ADA levels and regained clinical response. Therefore, we retrospectively collected measurements of infliximab (IFX) and adalimumab (ADA) serum concentrations together with ADA levels from 602 patients at our IBD centre (September 2005–September 2015). ADA levels were determined with a drug sensitive assay by Sanquin Biologicals Laboratory. As a next step, we identified all ADA positive patients with secondary loss of response (SLO) and started them on an IM in an attempt to eliminate ADA and to
regain clinical response. Detailed documentation of disease activity was required.

Result: In 98/376 patients ADA directed against IFX and in 61,226 patients ADA against ADL were detectable. From all 159 ADA positive patients, 17 patients had received an IM, either a thiopurine or MTX, because of secondary loss of response. Seven patients received MTX, ten a thiopurine (4 azathioprine, 4 mercaptopurine and 2 6-TG). In 7 out of 8 patients treated with IFX, addition of an IM resulted in an increase of serum drug levels accompanied with a decrease of ADA till they were undetectable. The median time for ADA to IFX to become undetectable was 11 months (IQR 6–28). For patients treated with ADL, an increase of the serum drug concentrations, together with a decrease of ADA levels, was reached in 6 out of 7 patients after addition of an IM. The median time for the ADA levels to be undetectable was also 11 months (IQR 2–37). All patients receiving MTX responded clinically which resulted in continuation of the ongoing anti-TNF treatment.

Disclosure of Interests: G.R. van den Brink; G. van den Brink has received consulting and lecture fees from AbbVie, Coviden, Dr. Falk, Ferring Pharmaceuticals, Merck Sharp & Dohme and Ferring Pharmaceuticals. He has received research grants from Abbott laboratories, Merck Sharp & Dohme Ferring Pharmaceuticals. M. Lowenberg: M. Löwenberg has served as speaker for AbbVie, Coviden, Dr. Falk, Ferring Pharmaceuticals, Merck Sharp & Dohme, Receptos, Takeda, Tillots and Tramedico. He has received research grants from AbbVie, Merck Sharp & Dohme, Sanofi Aventis, healthcare and Johnson & Johnson. G. D’Haens: G. D’haens reports having received consulting fees from AbbVie, Boehringer, Ferring, Janssen Biologics, Merck Sharp & Dohme, Takeda, Pfizer, Tillots Pharma and reports receiving research grants from Abbott Laboratories, Janssen Biologics, MSD, DiFalk Pharma. All other authors have declared no conflicts of interest.

OP281 POST-OPERATIVE COMPLICATIONS IN ELDERLY-ONSET INFLAMMATORY BOWEL DISEASE: A POPULATION-BASED STUDY


1Gastroenterology Unit & Epimad Registry, Rouen University and Hospital, Rouen/France
2Public Health, Epidemiology and Economic Health, Registry Epimad, Inserm Liric Umr 99 Lille University and Hospital, Lille/France
3Gastroenterology Unit & Epimad Registry, Amiens University and Hospital, Amiens/France
4Public Health, Epidemiology and Economic Health, Registry Epimad, Inserm Liric Umr 99 Lille University and Hospital, Lille/France
5Gastroenterology Unit & Epimad Registry, Seclin General Hospital, Seclin/France
6Gastroenterology Unit & Epimad Registry, Inserm Liric Umr 99 Lille University and Hospital, Lille/France
7Department Of Gastroenterology, Nancy University Hospital, Vandœuvre les Nancy/France

Contact E-mail Address: sophie-caroline.sacleux@hotmail.fr

Introduction: Inflammatory Bowel Diseases (IBD) diagnosed after the age of 60 are increasing and seems to have a milder course compared to younger patients. The early postoperative complications (POC) were more severe than the late POC. Emergency surgery is still more frequent in elderly population.

Aims & Methods: Among 841 elderly-onset population-based EPIMAD Cohort (1), 139 patients underwent surgery. Among those, 100 had Crohn’s Diseases (CD) and 39 Ulcerative Colitis (UC). Medical charts for early (within 30 days of surgery) and late (>30 days of surgery) POC (POC) have been reviewed according to Dindo’s classification (2). Associated factors have been tested by Cox regression models.

Result: After a median follow-up of 7.3 years [Q1 = 3–Q3 = 12], 50 patients (36%) had at least one POC. No significant difference was observed for POC frequency between UC and CD. Thirty-two early POC were found in 23 patients (16.5%); 52% were severe (defined by a Dindo’s grade ≥ 3) and 56% were mechanical (bridle, eventration, anastomotic stricture). The cumulative probability of POC was 7.4% at 6 months [95%-CI: 3.9–10.9%] at 1 year (6.5–18.1), 22.8% at 5 years (16.0–32.0) and 30.5% at 10 years (21.8–41.4). In multivariate analysis, emergency surgery (HR = 4.46 [1.75–11.36]) and acute severe ulcerative colitis (HR = 7.84 [2.15 – 28.52]) were significantly associated with an increased risk of early POC. Recent POC exposure and co-morbidities ( Charlson’s index) were not independently associated with an increased risk. Female gender (HR = 2.10 [1.01 – 4.37]) and time between diagnosis and surgery >3 months (HR = 2.09 [1.01 – 4.31]) were significantly associated with late POC.

Conclusion: In elderly onset IBD patient who underwent surgery, POC were frequent. The early POC were more severe than the late POC. Emergency surgery and acute severe ulcerative colitis were significantly associated with early complications when female gender and delay between diagnosis and surgery were associated with late POC. These results reinforce the need for specialized and dedicated management of these at-risk elderly patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
Aims & Methods:
To evaluate the use and outcomes of a quadruple therapy containing a proton pump inhibitor, bismuth, clarithromycin and amoxicillin (BCA) in the European Registry on the Management (Hp-EuReg).

Methods:
A systematic prospective registry of the clinical practice of European gastroenterologists regarding H. pylori infection and treatment (31 countries and 280 recruiting investigators). A local coordinator was selected from each country. Each coordinator selected a representative group of recruiting investigators in their country. An electronic clinical research file (e-CRF) was created on AEG-REDcap to systematically register all adult patients infected with H. pylori.

Variables included: Patient’s demographics, previous eradication attempts, prescribed eradication treatments, adverse events, and outcomes (cure rates, compliance, follow up, etc.). Patients with both eradication confirmatory test and compliance, and follow up have been considered ongoing and were excluded from the analysis.

Disclosure of Interest:
A.G. McNicholl: Speaker for Allergan

TUESDAY, OCTOBER 18, 2016 15:45–17:15

OP284 NOVEL MOTORIZED SPIRAL ENDOSCOPY: FIRST RESULTS OF A EUROPEAN PROSPECTIVE TRIAL

T. Beyna1, M. Arvanitakis2, M. Schneider3, A. Van Gossuin4, J. Deviere5, H. Neuhaus6

1Department Of Internal Medicine, Evangelisches Krankenhaus Düsseldorf, Düsseldorf/Germany
2Gastroenterology, Erasme Hospital, Universite Libre de Bruxelles, Bruxelles/Belgium
3Dept. Of Internal Medicine, Evangelisches Krankenhaus, Düsseldorf/Germany
4Gastroenterology And Hepatology, Hôpital Erasme, Free University of Brussels, Bruxelles/Belgium
5Dept. Of Gastroenterology, Universite Libre Bruxelles Erasme Hospital Université Libre Bruxelles/Brussels/Belgium
6Head, Dept. Of Internal Medicine, Evangelisches Krankenhaus Düsseldorf, Düsseldorf/Germany

Contact E-mail Address: torsten.beyna@evk-duesseldorf.de

Introduction: Currently available methods for small bowel endoscopy are complex to use and time consuming. Novel Motorized Spiral Endoscopy (NMSE) represents a new technology which offers all advantages of spiral enteroscopy with a faster and less invasive approach.

Aims & Methods: To prospectively study the efficacy and safety of peroral NMSE. Primary objective: diagnostic yield of NMSE for small bowel diseases. Secondary objectives: procedural success, - time, depth of maximal insertion, therapeutic yield, adverse events. Patients with occult gastrointestinal bleeding (OGB) or indeterminate iron-deficiency anemia (IDA) or positive findings of small bowel imaging examinations were included in a two-center prospective clinical trial. In total 132 cases were enrolled to determine the diagnostic yield. A rate of ≥ 40% shall be considered as clinically efficacious under consideration of a two-sided non-inferiority margin of 20% in comparison to conventional enteroscopy. A novel reusable endoscope (Olympus Corp.) with an integral motor was used for rotating a disposable short spiral overtube mounted on the insertion tube. Rotation of the spiral overtube allows the operator to “pleat” or “unpleat” the insertion tube either on or off the insertion tube as the spiral overtube rotates in a clockwise or counter-clockwise direction. All procedures were performed under general anesthesia.

Result: Thirty patients (12 f; 18 m; mean age [range]: 62 [20–92] years with positive findings of video capsule endoscopy or other small bowel imaging modality (angiectasias n = 18, jejunal ileal polyps n = 3, thickening of wall/stricture n = 3, other n = 1) have so far been included in the trial. 27 of 30 patients had IDA. NMSE could be performed in 29 of the 30 patients with advancement of the endoscope beyond the ligament of Treitz. In one case further insertion was not performed because of a bradycardia which caused discontinuation of the procedure. Mean insertion time to the jejunum was 6.4 [2–19] min. and to the deepest point of insertion distal of ligament of Treitz 22.6 [7–52] min. The mean insertion depth from ligament of Treitz was 393 [0–600] cm. Panenteroscopy to cecum could be achieved in one patient from the oral route. The diagnostic yield of NMSE was 83.4% corresponding to no findings in 5 cases, at least one angiectasia in 18 cases, one or more benign polyps in 6 and no other findings in 12 patients. Thirty-two interventions were performed in 22 patients (biopsies n = 8, APC n = 17, tattooing n = 3, clipping n = 3, EMR n = 4). The mean withdrawal time without interventions was 14.7 [5–45] min. Mild mucosal trauma in the esophagus or duodenum was registered in 6 cases. There were no serious adverse events.

Conclusion: First clinical data of an ongoing large prospective trial demonstrate that NMSE can be effectively and safely performed for diagnostic and therapeutic enteroscopy. The procedure offers advantages over traditional methods in terms of procedural duration and ease of use.

Disclosure of Interest: All authors have declared no conflicts of interest.
Table 1 (OP288): Association between number of pathophysiological alterations and Patient Reported Outcomes (data shown as mean ± SD)

<table>
<thead>
<tr>
<th>IBS symptom severity (z score)</th>
<th>No abnormality (n = 76)</th>
<th>1 abnormality (n = 128)</th>
<th>2 abnormalities (n = 121)</th>
<th>≥3 abnormalities (n = 82)</th>
</tr>
</thead>
<tbody>
<tr>
<td>IBS symptom severity (z score)</td>
<td>-0.55 ± 0.94</td>
<td>-0.22 ± 1.06</td>
<td>0.11 ± 0.96</td>
<td>0.37 ± 0.86</td>
</tr>
<tr>
<td>Somatic symptom severity (z score)</td>
<td>-0.47 ± 0.80</td>
<td>-0.30 ± 0.93</td>
<td>0.17 ± 0.91</td>
<td>0.68 ± 0.98</td>
</tr>
<tr>
<td>IBSQOL Emotional</td>
<td>60 ± 19</td>
<td>55 ± 24</td>
<td>44 ± 17</td>
<td>20.3 ± 8.0</td>
</tr>
<tr>
<td>IBSQOL Mental Health</td>
<td>82 ± 16</td>
<td>76 ± 22</td>
<td>65 ± 20</td>
<td>51 ± 20</td>
</tr>
<tr>
<td>IBSQOL Sleep</td>
<td>82 ± 16</td>
<td>76 ± 22</td>
<td>69 ± 24</td>
<td>58 ± 24</td>
</tr>
<tr>
<td>IBSQOL Energy</td>
<td>69 ± 24</td>
<td>58 ± 27</td>
<td>48 ± 24</td>
<td>35 ± 23</td>
</tr>
<tr>
<td>IBSQOL Physical Functioning</td>
<td>75 ± 20</td>
<td>74 ± 21</td>
<td>68 ± 20</td>
<td>57 ± 26</td>
</tr>
<tr>
<td>IBSQOL Food</td>
<td>67 ± 20</td>
<td>64 ± 21</td>
<td>59 ± 18</td>
<td>55 ± 20</td>
</tr>
<tr>
<td>IBSQOL Social Role</td>
<td>71 ± 20</td>
<td>65 ± 23</td>
<td>62 ± 20</td>
<td>51 ± 24</td>
</tr>
<tr>
<td>IBSQOL Physical Role</td>
<td>64 ± 28</td>
<td>56 ± 31</td>
<td>47 ± 29</td>
<td>40 ± 28</td>
</tr>
<tr>
<td>IBSQOL Sexual</td>
<td>71 ± 23</td>
<td>70 ± 25</td>
<td>63 ± 22</td>
<td>50 ± 25</td>
</tr>
</tbody>
</table>

TUESDAY, OCTOBER 18, 2016
15:45-17:15
COELIAC DISEASE FOR THE CLINICIAN – ROOM F1

OP286 THE ENZYME ACTIVITY OF SMALL INTESTINAL MUCOSA IN ADULT PATIENTS WITH CELIAC DISEASE
E. Sabelnikova1, O. Ahmadullina2, N. Belostotsky3, A. Parfenov1
1Intestinal Pathology, Moscow Clinical Research Center, Moscow/Russian Federation
2IBD, Moscow Clinical Research Center, Moscow/Russian Federation
3Pathophysiology, Moscow Clinical Research Center, Moscow/Russian Federation

Contact E-mail Address: esabelnikova@mknc.ru

Introduction: Some patients with celiac disease (CD), who have followed gluten-free diet (GFD) and have a normal histological structure of small intestine mucosa, may still have symptoms of bloating, rumbling and diarrhea. These symptoms may be associated with changes of the activity of the small intestine enzymes. Objective: To determine the activity of enzymes (glucoamylase, maltase, sucrase and lactase) in CD patients.

Aims & Methods: Thirteen patients with newly diagnosed CD: 9 women and 4 men (mean age 41.96 ± 18.46 years) were observed. The diagnosis of CD was based on clinical presentation, serology, including anti-gluten antibodies (AGA) IgA and anti-tissue transglutaminase (anti-tTG) IgA antibodies and duodenal biopsy. Histological changes of intestinal biopsy were classified according to the revised Marsh criteria 1999. In 1 group Marsh IIIb lesions were seen in 23%, Marsh IIIc – in 77%. In 2 group - Marsh IIIa and Marsh IIIb lesions were seen in 30% respectively, Marsh II - in 13.3%, the normal structure of small intestine were observed in 26.6%. The enzyme activity was measured in small intestine mucosa by Dahlquist modified method.

Result: In patients with newly diagnosed CD, the activity of all enzymes was decreased in 92.3% in the group of patients followed GFD - in 36.5% (p < 0.05). It was found that the total atrophy (Marsh IIh) was associated with a reduced activity of all enzymes in all patients: whereas all patients with Marsh IIIb atrophy had a decreased activity of lactase, 90% had a decreased activity of glucoamylase and maltase, and in 81.3% of cases we observed a decreased activity of sucrase. The recovery of the mucosa showed improvement of activity of all enzymes. However, even in normal small intestine mucosa the reduction of glucoamylase activity was observed in 37.5% reduction of maltase activity - in 62.5%, the activity of sucrase was reduced in 50% and activity of lactase was decreased in 37.5%. The reduced activity of all enzymes was found in 37.5% of patients with normal structure of small intestine mucosa. A weak correlation between the degree of atrophy and the activity of sucrase and maltase (r = −0.513, p = 0.003 and r = −0.406, p = 0.029, respectively) was established. Activity of other enzymes had no significant correlation with the degree of atrophy.

Conclusion: In 37.5% of adult patients with CD who follow GFD and have a normal structure of mucosa, a decreased activity of intestinal enzymes may occur, which may be one of the reasons for the persistence of intestinal symptoms.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016
15:45-17:15
PATHOPHYSIOLOGY OF IBS – ROOM N2

OP287 FODMAP RESTRICTION OF A GLUTEN-FREE DIET IN ADULT PATIENTS WITH COELIAC DISEASE
B. E. Whitehead1, J. Tack3
1Dept. Of Internal Medicine, Sahlgrenska University Hospital, Gothenburg/Sweden
2UNC Center For Functional GI And Motility Disorders, University of North Carolina at Chapel Hill, Chapel Hill/United States of America/NC
3Translational Research Center For Gastrointestinal Disorders (targid), Katholieke Universiteit Leuven, Leuven/Belgium

Introduction: Both central and peripheral pathophysiological factors are thought to contribute to the symptoms of IBS. Psychological symptoms reflect CNS dysfunction, while abnormal GI sensorimotor function reflects mainly peripheral dysfunction; both have been associated with symptoms in IBS. These factors may have additive effects on patient reported outcome (PRO) measures in IBS.

Aims & Methods: Our aim was to study whether these pathophysiological alterations have additive effect on PROs in patients with IBS. To achieve this, we included 407 patients fulfilling the Rome II or Rome III IBS criteria (74% females; mean age 36 ± 12 years). The following pathophysiological factors were measured in all subjects: colonic transit time (radiopaque markers); comorbid conditions (IBS-SSS or GSRS-IBS total score) and somatic symptom severity (SCL-90 R). All subscales with significance in group A and impact on symptom severity were included in the analysis. A 4-week LGD with reduced FODMAP content in diet was performed. A gluten-free diet with reduced FODMAP content was more effective than a more strict gluten-free diet, and should be offered to coeliac patients with refractory IBS-symptoms on a gluten-free diet.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP289 INCREASED INHIBITORY NEUROTRANSMISSION WITHIN ANTERIOR CINGULATE CORTEX IS RELATED TO COMORBID ANXIETY IN IRritable BOWEL SYNDROME
A. Ichenhour, O. Bednarska, S. Tapper, A. Tisell, P. Lundberg, S. T. Witt, S. Elsenbruch, S. Walter
1Cmiv, Linköping University, Linköping/Sweden
2Institute Of Clinical And Experimental Medicine, Division Of Gastroenterology, Linköping University, Linköping/Sweden
3Department Of Radiology, Linköping University, Linköping/Sweden
4Department Of Radiation Physics, Linköping University, Linköping/Sweden
5Institute Of Medical Psychology & Behavioral Immunobiology, University Hospital Essen, University of Duisburg-Essen, Essen/Germany
Contact E-mail Address: adriane.icenhour@liu.se
Introduction: Inspired by the concept of Irritable Bowel Syndrome (IBS) as a disorder of brain-gut-communication, alterations in central mechanisms are increasingly acknowledged in IBS pathophysiology. Given high comorbidity with affective disorders, emotional factors likely play a role in disturbed central processes in IBS. Dysfunctions particularly in brain regions involved in emotion processing, including the rostral anterior cingulate cortex (rACC) as a unique hub of both, affect regulation and anti-nociception, may constitute a central link between abdominal pain and psychiatric comorbidities. While a growing number of neuroimaging studies support a crucial role of rACC in altered pain processing and emotional disturbances in IBS, the biochemical basis of these alterations remains unknown.

Aims & Methods: We compared IBS patients and healthy controls (HC) regarding concentrations of glutamate (Glu) and γ-aminobutyric acid (GABA) in rACC using quantitative magnetic resonance spectroscopy (qMRS). We further addressed associations with anxiety and depression as the most common psychiatric comorbidities of IBS. A combined fMRI and MRS study, GABACrE DTI measurements in 38 female IBS and 19 age-matched female HC were measured using a Philips Ingenia 3T scanner and a MEGA-PRESS sequence with a 3x3x3cm voxel placed in the rACC, localized based on individual T1-weighted images. Symptoms of anxiety and depression were assessed with the Hospital Anxiety and Depression Scale (HADS) and correlated with metabolite concentrations. Patients were subdivided into a group with IBSd and without (IBSs) comorbid anxiety based on published HADS cut-offs.

Results: Compared to HC, IBS as a group exhibited significantly increased GABA+ concentrations within rACC (p < 0.05), while no differences were observed in concentrations of Glu. Both anxiety (r = 0.407; p < 0.01) and depression (r = 0.276; p < 0.05) correlated with GABA+ concentrations. Inclusion of HADS scores as covariates diminished group differences in GABA+ concentrations in ANCOVA with anxiety, but not with depression. Analyses on IBS subgroups revealed a group effect (p < 0.05) with higher GABA+ levels in IBSd compared to HC (p < 0.01) and compared to IBSs (p = 0.056), whereas differences between IBSd and HC did not yield significance.

Conclusion: Our findings provide first evidence of dysregulated rACC neurotransmission in IBS. This imbalance appears to be driven by increased GABA+ concentrations in rACC as a crucial structure for anti-nociception and affect regulation. Abnormal GABA+ levels were most pronounced in patients with comorbid anxiety, supporting a key role of psychiatric comorbidities in altered brain processes in IBS. Altered inhibitory GABAergic neurotransmission may be fundamental for dysregulation of affective and nociceptive processing, contributing to functional as well as long-lasting neuroplastic changes in IBS.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP290 BACTERIAL PASSAGE IS INCREASED IN THE COLON OF WOMEN WITH IRritable BOWEL SYNDROME INDEPENDENTLY OF STOOL CONSISTENCY SUBGROUP
O. Bednarska, S. Walter, M. Ström, Å. Keita
1Department Of Clinical And Experimental Medicine, Linköping University, Linköping/Sweden
2Department Of Gastroenterology, Linköping University Hospital, Linköping/Sweden
Contact E-mail Address: olga.bednarska@regionostergotland.se
Introduction: Irritable bowel syndrome (IBS) is a chronic functional intestinal disorder with a strong female predominance. The pathophysiology is incompletely understood, but an increasing body of evidence demonstrates a role of the brain-gut-microbiota axis. Alterations in microbiota have been associated with onset as well as changes in symptoms of IBS. Prior data suggest that intestinal barrier function is disturbed in IBS, but to our knowledge the passage of living bacteria through the colonic mucosa has never been investigated.

Aims & Methode: Aims: To study the paracellular permeability and the passage of living bacteria, both commensal and pathogenic, through the colonic mucosa of women with IBS and female healthy controls (HC). The second aim was to investigate whether stool consistency subgroups differ in terms of intestinal barrier function. Methods: Colonic biopsies from 32 women with IBS (mean age 32.6y; 17 with mixed stool pattern IBS-M, 7 with diarrhea IBS-D and 8 with constipation predominate IBS-C, according to Rome III criteria) and 15 HC (mean age 29.7y) were mounted in Ussing chambers. Macropassage of living Escherichia coli (E.coli) HS and Salmonella typhimurium was investigated. The paracellular passage was measured by using 51Cr-EDTA.

Result:

Table: Macropassage of bacteria (bacteria/chamber105 and 51Cr-EDTA/cm2x104) are shown in median (25%-75% percentile)

<table>
<thead>
<tr>
<th></th>
<th>IBS</th>
<th>HC</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>E.coli</td>
<td>627 (563–688)</td>
<td>333 (291–387)</td>
<td>0.0001</td>
</tr>
<tr>
<td>Salmonella</td>
<td>880 (689–1104)</td>
<td>315 (194–457)</td>
<td>0.0001</td>
</tr>
<tr>
<td>51Cr-EDTA</td>
<td>1.1 (0.7–1.5)</td>
<td>0.9 (0.5–1.1)</td>
<td>&lt;0.05</td>
</tr>
</tbody>
</table>

The colonic mucosa of IBS patients had a significantly greater passage both for living Salmonella typhimurium and E. coli HS compared with HC (p < 0.0001 and p < 0.0001 respectively). The 51Cr-EDTA passage was also significantly increased in IBS (p < 0.05). IBS-M, IBS-D and IBS-C did not differ significantly in terms of mucosal barrier function measures, neither for bacterial nor for paracellular passage.

Conclusion: The present study demonstrated that passage through the colonic mucosa of both pathogenic and commensal living bacteria is altered in female IBS patients. These findings elucidate new aspects of peripheral abnormalities and support the importance of microbiota as a major factor in the pathophysiology of IBS.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP291 LUBIPROSTONE IMPROVES THE INTESTINAL PERMEABILITY, A NEW APPROACH FOR "LEAKY GUT"? A PROSPECTIVE RANDOMIZED PILOT CLINICAL STUDY IN HEALTHY VOLUNTEERS
T. Kato, I. Tsuchiya, A. Nakajima
Department Of Gastroenterology And Hepatology, Yokohama City University, Yokohama/Japan
Contact E-mail Address: tkato222@gmail.com
Introduction: Several disease states and disorders are associated with “leaky gut” (or increased intestinal permeability), such as inflammatory bowel diseases, celiac disease, food allergy, irritable bowel syndrome, and obesity-metabolic disorders. Therefore, this topic is an area of growing interest, and a well-established therapy for preventing or reverting increased intestinal permeability would be valuable. Since there are no effective medications for “leaky gut” to date, it would be important to establish a new therapy which aiming at improvement of intestinal permeability. Previous studies have reported that non-steroidal anti-inflammator y drugs (NSAIDs) induce small intestinal damage and increased permeability.[1]. Other basic studies have reported that lubiprostone, a chloride channel activator used for chronic constipation, repairs intestinal mucosal barrier function and also prevents NSAID-induced small intestinal damage in rodent models [2]. Aim & Methode: Our aim was to verify the effect of lubiprostone on intestinal permeability in healthy volunteers administered with dicyclonfenac. We conducted a prospective, randomized parallel-group trial. Healthy male volunteers, with documented absence from certain drugs (NSAIDs, proton-pump inhibitors, antibiotics, and probiotics) for at least 3 months prior the study were enrolled. The subjects were randomly assigned to either the lubiprostone or control groups. All participants performed sugar permeability tests on baseline, after 14 days of treatment and after 28 days of treatment (day28). The
Aims & Methods:

To do this, we included 5 cohorts of patients with FGIDs, who had undergone 28 days treatment with lubiprostone daily for 28 days, while the control group did not receive any medication after diclofenac. Permeability was expressed as lactulose/mannitol ratio (LMR), calculated from urinary excretion of the initially administrated isotope (C6) and the urinary excretion of the initial administrated isotope (C0). Both groups started with oral intake of 75 mg diclofenac daily for 14 days; colonic barostat (ramp inflation, 4 mmHg steps, 1 min step). Subjects were divided into sensitivity tertiles based on pain threshold tertiles. GI symptom severity (z scores of IBS-S, GRS-S/IBS or dyspepsia symptom severity (DSS)) was compared between sensitivity tertiles in each cohort and corrected for somatization (RPSQ, PHQ-12 or SCL-90), and anxiety and depression (HAD or BSI).

Result: The results are summarized in Table 1. In all five cohorts GI symptom severity increased gradually with increasing GI sensitivity, with significant differences in GI symptom severity between the sensitivity tertiles, and small, but significant correlations between pain/discomfort thresholds and GI symptom severity, across all five patient groups (r = 0.20 − 0.29). The differences between sensitivity tertiles remained significant in all cohorts after correction for anxiety and depression, and after correction for somatization (without GI symptoms) in all of the cohorts (p < 0.05).

Conclusion: A gradual increase in GI symptom severity with increasing GI sensitivity was demonstrated in IBS and functional dyspepsia, which was consistent across several large patient groups from different countries, different methods to assess sensitivity, and assessments in different parts of the GI tract. This association, although modest, was independent of tendency to report symptoms or anxiety/depression comorbidity. These findings confirm that visceral hypersensitivity is a contributor to symptom generation in FGIDs.

Disclosure of Interest: M. Simrén: Unrestricted research grants from Danone, and Ferring Pharmaceuticals; Consultant/Advisory Board member for AstraZeneca, Danone, Nestlé, Chr Hansen, Almirall, Alibreo, Glycium and Shore; Speaker for Tiolett, Takeda, Shire and Almirall. H. Törnbom: Consultant/Advisory Board member for Almirall, Danone and Shore. O. Palsson: Salary support from research grants from Salix Pharmaceuticals, Takeda Pharmaceuticals and Ironwood Pharmaceuticals, as well as honoraria for participation in educational programs supported by these companies. M. van Tielburg: Research support from Takeda for investigator initiated study. J. Tack, Almirall, AstraZeneca, Danone, Menarini, Novartis, Nycomed, Oceara, Ono Pharma, Shore, SK Life Sciences, Theravance, Xenoport, Zeria, Abbott, Almirall, AlfaWasserman, Janssen, W.E. Whitehead: Unrestricted research grants from Takeda Pharmaceuticals; Consultant/Advisory Board member for Ono and Ferring Pharmaceuticals; Consultant/Advisory Board member for Ono and Ferring Pharmaceuticals and Biomerica USA.

All other authors have declared no conflicts of interest.

References


OP293 CHRONIC ORAL ADMINISTRATION OF THE GUANYLATE CYCLASE-C AGONIST LINACLOTIDE ATTENUATES COLITIS INDUCED LONG-TERM BLADDER AFFERENT HYPERACTIVITY

L. Grundy1, S. Garcia-Caraballo1, J. Maddern2, G. Rychkov3, G. Hannig2, C. B. Kurz4, A. Silos-Santiago5, S. M. Briere6

1Visceral Pain Group, Centre For Nutrition And Gastrointestinal Diseases, Discipline Of Medicine, University of Adelaide, Adelaide, Australia
2Ironwood Pharmaceuticals, Inc., Cambridge/United States of America

Contact E-mail Address: luke.grundy@adelaide.edu.au

Introduction: There is significant comorbidity between the symptoms of IBS and the urological symptoms of urgency and frequency experienced in overtive bladder and interstitial cystitis/painful bladder syndromes. Viscero-vascular cross-talk has also been described in pre-clinical studies, whereby acute colitis in rodents is associated with altered bladder cystometry and bladder afferent sensitisation [1,2]. However, it remains to be determined if bladder overactivity persists following the resolution of colitis, in a model of chronic colonic hypersensitivity (CCH) [3], or if reducing colonic nociception is able to alter bladder overactivity. Linacotide, an FDA approved guanylate cyclase-C (GC-C) agonist, reduces abdominal pain in IBS patients with constipation [3], reverses colonic mechanical hypersensitivity from Takeda and Ferring Pharmaceuticals; Consultant/Advisory Board member for Ono and Ferring Pharmaceuticals and Biomerica USA.

All other authors have declared no conflicts of interest.

Table 1 (OP292): Association between visceral hypersensitivity and GI symptom severity in five FGID cohorts

<table>
<thead>
<tr>
<th></th>
<th>Belgian FD cohort</th>
<th>US IBS cohort (n = 243)</th>
<th>US IBS cohort (rectum; n = 159)</th>
<th>Swedish IBS cohort (n = 243)</th>
<th>Swedish IBS cohort 1 (n = 147)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>(n = 242)</td>
<td>US IBS cohort (colon; n = 243)</td>
<td>US IBS cohort (rectum; n = 159)</td>
<td>Swedish IBS cohort 1 (n = 353)</td>
<td>Swedish IBS cohort 2 (n = 147)</td>
</tr>
<tr>
<td></td>
<td>DSS</td>
<td>IBS-SSS</td>
<td>IBS-S</td>
<td>IBS-S</td>
<td>IBS-S</td>
</tr>
<tr>
<td>z score GI sx severity (mean ± SD)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low sensitivity tertile</td>
<td>−0.48 ± 0.99</td>
<td>−0.29 ± 0.99</td>
<td>−0.34 ± 0.90</td>
<td>−0.40 ± 0.98</td>
<td>−0.46 ± 0.89</td>
</tr>
<tr>
<td>Mid sensitivity tertile</td>
<td>−0.07 ± 0.88</td>
<td>−0.04 ± 1.04</td>
<td>−0.04 ± 1.04</td>
<td>0.11 ± 0.99</td>
<td>0.31 ± 0.83</td>
</tr>
<tr>
<td>High sensitivity tertile</td>
<td>0.32 ± 0.99</td>
<td>0.25 ± 0.95</td>
<td>0.28 ± 0.97</td>
<td>0.25 ± 0.95</td>
<td>0.06 ± 1.14</td>
</tr>
<tr>
<td>ANOVA</td>
<td>F = 13.2; p &lt; 0.0001</td>
<td>F = 5.9; p = 0.003</td>
<td>F = 5.1; p = 0.007</td>
<td>F = 14.0; p &lt; 0.0001</td>
<td>F = 8.5; p &lt; 0.0001</td>
</tr>
<tr>
<td>ANOVA (adjusted for somatization)</td>
<td>F = 9.2; p = 0.0006</td>
<td>F = 4.9; p = 0.008</td>
<td>F = 4.1; p = 0.018</td>
<td>F = 10.8; p &lt; 0.0001</td>
<td>F = 8.3; p = 0.0001</td>
</tr>
<tr>
<td>ANCOVA (adjusted for anx &amp; dep)</td>
<td>F = 13.3; p = 0.0001</td>
<td>F = 5.0; p = 0.006</td>
<td>F = 4.1; p = 0.018</td>
<td>F = 10.8; p &lt; 0.0001</td>
<td>F = 8.3; p = 0.0001</td>
</tr>
<tr>
<td>Correlation sensitivity - GI sx</td>
<td>r = −0.27; p &lt; 0.0001</td>
<td>r = −0.20; p &lt; 0.0001</td>
<td>r = −0.27; p &lt; 0.0001</td>
<td>r = −0.29; p &lt; 0.0001</td>
<td>r = −0.20; p = 0.02</td>
</tr>
</tbody>
</table>

Disclosure of Interest:
L. Grundy: Grant support from Ironwood Pharmaceuticals Inc., Key Pharmaceuticals Inc., and Decibel Therapeutics.
C.B. Kurtz: Employee, stock holder, and stock options from Ironwood Pharmaceuticals Inc.
G. Hannig: Employee, stock holder, and stock options from Ironwood Pharmaceuticals Inc.

Conclusion: Mice with CCH also display increased bladder afferent excitability accompanied by abnormal bladder voiding behaviour, an example of viscero-visceral cross-talk. Chronic oral administration of linaclotide, a gut-restricted GC-C agonist that inhibits colonic nociceptors, reverses these colitis-induced changes in bladder function and sensitivity. Agents that improve abdominal visceral cross-talk. Chronic oral administration of linaclotide, a gut-restricted GC-C agonist that inhibits colonic nociceptors, reverses these colitis-induced changes in bladder function and sensitivity. Agents that improve abdominal

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G. Hannig: Employee, stock holder, and stock options from Ironwood Pharmaceuticals Inc.

Disclosure of Interest: All authors have declared no conflicts of interest.

References
OP296 EPIDEMIC ALTERATIONS IN INFLAMMATORY BOWEL DISEASE - THE INFLUENCE OF GERMINE VARIATION (MEQTLs) ON GENOME-WIDE METHYLATION ALTERATIONS
1Institute Of Genetics And Molecular Medicine, University of Edinburgh, Edinburgh/United Kingdom
2Institute Of Clinical Medicine, Epigen, Campus Atos, University of Oslo, Oslo/Norway
3Dept. Of Gastroenterology, Akershus University Hospital, Lørenskog/Norway
4Department Of Gastroenterology, Akershus University Hospital, Lørenskog/Norway
5Dept. Of Internal Medicine, Örebro University Hospital, Örebro/Sweden
6Department Of Gastroenterology And Hepatology, Maastricht University Medical Center Dept. Of Gastroenterology, Maastricht/Netherlands
7Servizio Di Apparato Digestivo, Hospital Clinico Universitario Lazo Bessa, Zaragoza/Spain
8Cang Centre For Genomic Regulation, Barcelona Institute Of Science and Technology, Barcelona/Spain
9Unit Of Molecular Genetics Of Digestive Diseases, Biocruces Health Research Institute, Bilbao/Spain

Contact E-mail Address: alex.adams@ed.ac.uk

Introduction: Exploring DNA methylation in Inflammatory Bowel Disease (IBD) may provide an insight into complex gene-environment interactions, identify novel targets involved in pathogenesis, and allow development of powerful new biomarkers. Our study aims to characterize disease-associated methylation changes in newly diagnosed IBD and to define the contribution of genetic variation, by discovery of associated quantitative trait loci (meQTL).

Aims & Methods: Genome-wide methylation was measured in 641 DNA samples from patients with UC (230 controls, 150 Crohn’s disease with one CD, 167 patients with colonic Crohn’s disease (CCD), 26 IBD unclassified (IBDU)) using the Illumina 450k platform with covariates of age, sex, and, and differential cell counts, deconvoluted by the Houseman method; genotyping was performed using Illumina Human660W-QuadExPress-8 BeadChips. Samples were obtained from new onset IBD cases in six European centres as part of the European Commission funded IBD-Character project.

Result: 195 probes exhibited Bonferroni significant IBD-associated methylation differences, including VMP1/MIR21 (2.3 \pm 0.9\% \textnormal{DP}), PS6K2A (1.1 \pm 1.9\% \textnormal{DP}), SBNO2 (2.7 \pm 1.0\% \textnormal{DP}), and TNSF10 (1.1 \pm 1.2\% \textnormal{DP}); data which provide important replication and confirmation of methylation differences previously reported in paediatric CD and adult IBD. Novel findings include PHOSPHO1 (1.3 \pm 1.0\% \textnormal{DP}), MUC4 (5.5 \pm 15.3\% \textnormal{DP}), and CDH24 (1.7 \pm 10.2\% \textnormal{DP}) and a replication of two SNPs previously described as correlated to VMP1/MIR21 methylation (rs807424, \textit{p} = 4.4 \times 10^{-2}, rs8053015, \textit{p} = 7.4 \times 10^{-21}). There was an enrichment of highly significant IBD-associated methylation changes in proximity to IBD GWAS loci. Highly similar published two-probe methylation biomarkers (markers derived from a new onset paediatric CD cohort accurately distinguished IBD from controls in this new onset adult cohort (AUC = 0.92).

Conclusion: These data allow methylation profiling in a large multinational cohort of patients with IBD providing novel disease-associated methylation changes. Important unequivocal replication of recent discoveries, together with insight into the genetic contribution to epigenetic alterations in complex disease, and the utility of peripheral blood DNA methylation as a biomarker.

Disclosure of Interest: R. Kalla: Received funding research from the EU FP7 (2885469) and served as a speaker for Ferring
J. Jahnsen: Served as a speaker and a advisory board member for MSD, Tillot, Ferring, Abbvie, Celltrion, Orion Pharma, Takeda, Napp Pharm, Meda, Astopharma, Hikma and Pfizer.
Research funding (Department) MSD

J. Satsangi: JS has served as a speaker, a consultant and an advisory board member for MSD, Ferring Abbvie and Shire, consultant with Takeda, speaking fees from MSD and has received research funding from Abbvie. All other authors have declared no conflicts of interest.

References

Table 1. (OP297)

<table>
<thead>
<tr>
<th>Feature</th>
<th>CCD n = 19</th>
<th>UC n = 32</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age at testing (mean ± SD, y)</td>
<td>32.0 ± 14.9</td>
<td>36.0 ± 10.6</td>
<td>0.3</td>
</tr>
<tr>
<td>Age at diagnosis (mean ± SD, y)</td>
<td>25.7 ± 15.5</td>
<td>25.3 ± 10.2</td>
<td>0.9</td>
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<tr>
<td>Disease Duration at testing (mean ± SD,y)</td>
<td>6.2 ± 4.8</td>
<td>10.5 ± 8.4</td>
<td>0.047</td>
</tr>
<tr>
<td>C-reactive (mg/l)</td>
<td>42.0</td>
<td>50 (16)</td>
<td>0.44</td>
</tr>
<tr>
<td>Clinically active (n)</td>
<td>58 (11)</td>
<td>66 (21)</td>
<td>0.77</td>
</tr>
<tr>
<td>Endoscopically active (n)</td>
<td>89 (17)</td>
<td>71 (25)</td>
<td>0.45</td>
</tr>
<tr>
<td>Histologically active (n)</td>
<td>79 (15)</td>
<td>63 (20)</td>
<td>0.35</td>
</tr>
<tr>
<td>Treatment (n)</td>
<td>Biologic Azathioprine ASA Steroid Antibiotic</td>
<td>15.8 (3)</td>
<td>15.8 (3)</td>
</tr>
<tr>
<td>CRP (mean ± SD, mg/ml)</td>
<td>16.1 ± 21.1</td>
<td>8.7 ± 16.3</td>
<td>0.2</td>
</tr>
<tr>
<td>WCC (mean ± SD, 10^3/l)</td>
<td>6.5 ± 2.0</td>
<td>6.3 ± 1.3</td>
<td>0.7</td>
</tr>
</tbody>
</table>

OP297 AN AUTOPHAGY-RELATED PERIPHERAL BLOOD MICRNA SIGNATURE DIFFERENTIATES COLONIC CROHN’S DISEASE FROM ULCERATIVE COLITIS
A. Mohammadi, O. Kelly, B. Kabakchiev, K. Borowski, M. I. Smith, D. Kevans, M.S. Silverberg
Mount Sinai Hospital, Toronto/Canada

Contact E-mail Address: ayila@lunenfeld.ca

Introduction: Phenotypic expression of colonic inflammation in inflammatory bowel disease (IBD) in patients with colonic Crohn’s disease (CCD) and ulcerative colitis (UC) can sometimes have a similar appearance and be difficult to differentiate. MicroRNAs (miRNAs) may offer a method of distinction as differential expression of peripheral blood miRNAs has been shown in small studies of IBD patients and healthy controls.

Aims & Methods: This study aimed to assess peripheral blood mononuclear cell (PBMC)-derived miRNA signatures in a well-phenotyped cohort of colonic IBD and to identify differentially expressed miRNAs in patients with CCD and UC. IBD cohort with UC and CCD was prospectively accrued. Blood samples were collected during scheduled visits at the UCSD IBD research center. miRNA expression was measured using the 

Non-parametric Kruskal-Wallis tests assessed differential miRNA expression across phenotypes. Receiver operating characteristic (ROC) curves were generated following logistic regression through 5-fold cross validation repeated 10 times. Area under the curve (AUC) values for the ROCs were derived in order to evaluate the discriminant capacity of the differentially expressed miRNAs in CCD versus UC.

Result: 51 subjects, 32 UC (50\% male, 36 yrs mean age), 19 CCD (42\% male, 32 yrs mean age) were included in the analysis (see Table 1). There were no significant differences in mean CRP or among clinical, endoscopic or histologic disease activity between the CCD and UC groups suggesting that the degree of inflammation was similar in both groups. Comparing CCD and UC, 5 miRNAs were differentially expressed: mir-129-5p, mir-603, mir-619-3p, mir-874-3p, mir-933 (FDRp < 0.014), all of which were upregulated in CCD vs UC. In the ROC analysis, the AUC for CCD vs UC for the combined expression of the 5 miRNAs was 0.90 (95\% CI: 0.88-0.93). 2 out of 5 miRNAs putatively target the Autophagy Related 16-Like 1 (ATG16L1) gene, and 4 out of 5 miRNAs had significantly greater expression in CCD vs UC.

Conclusion: A PBMC-derived miRNA panel of markers identified here differentiates CCD from UC with similar degrees of inflammation. All of these differentially expressed miRNAs are upregulated in CCD compared to UC, and

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several appear to be associated with the autophagy pathway. These findings may aid individualization of patient care through identification of novel diagnostic and therapeutic targets.

Disclosure of Interest: All authors have declared no conflicts of interest.

**OP298 ASSESSMENT OF INFLAMMATORY BURDEN IDENTIFIES CROHN’S DISEASE AND ULCERATIVE COLITIS PATIENT GROUPS WHO HAVE SIMILAR DISEASE GENE EXPRESSION PATTERNS AND THERAPEUTIC RESPONSE TO ANTI-TNF TREATMENT**

S. Pavlidis1, M. J. Loza2, P. Brangan2, C. Monast2, A. Rowe3, F. Barbibaud2

1Immunology, Janssen Research & Development Ltd, High Wycombe/United Kingdom

2Immunology, Janssen Research and Development, LLC, Spring House/United States

3America/PA

Contact E-mail Address: spavlidi@its.jnj.com

Description: Crohn’s disease (CD) and ulcerative colitis (UC) are considered to be driven by both common and distinct underlying mechanisms of pathobiology. In both diseases there is heterogeneity underscored by the variable clinical responses obtained to therapeutic interventions. We aimed to identify disease-driving pathways as well as classify individuals into subpopulations that differ in their disease pathobiology and response to a specific treatment.

Aims & Methods: Hierarchical clustering on enrichment scores (ES) from gene set variation analysis (GSVA) was used probing a normal healthy volunteer (NHV), CD, UC and UC disease colon tissue samples (GSVE16079) with a library of gene set signatures representative of various immunological and inflammatory processes as well as specific activated cell types. Patient stratification at baseline (BL) or after anti-TNF treatment (PT) in either clinical responders (R) or non-responders (NR) was assessed.

Result: Gene set signatures whose ES differed significantly (ES change ≥ 0.2, p ≤ 0.05) between comparisons were identified from general linear model analyses. Comparisons were made at BL in all participants irrespective of clinical response, in clinical NR patients compared to NHV. 59% of the tested signatures were commonly enriched in both CD and UC at BL underlining the commonality of both diseases. These signatures included e.g. activated T cells, monocytes, macrophages or neutrophil signatures as well as poly/IC and bemycin signatures representing acute inflammation and a complex mix of potential disease-driving biology. Comparing R and NR separately at BL to NHV, 43% and 70% of signatures were enriched, respectively, indicative of a higher inflammatory burden in NR. Indeed, specific macrophage, innate lymphoid cell and epithelial signatures were significantly enriched in NR. Hierarchical clustering of the ES that significantly differed in the comparisons clearly separated diseased BL from NHV samples. It also clustered R PT samples with the diseased BL samples. Patient stratification at baseline (BL) or after anti-TNF treatment (PT) in either clinical responders (R) or non-responders (NR) was assessed.

Conclusion: Our study has identified common disease-driving pathways for CD and UC supporting the notion of a disease continuum rather than two distinct diseases. However, within that disease continuum, distinct patient groups could be defined by their overall inflammatory burden correlating with their response to an anti-TNF therapy. This methodological approach could facilitate better targeted design of clinical studies to test therapeutics under development, concentrating on subsets of patients sharing similar underlying molecular pathology and therefore increasing the likelihood of clinical response.


M. J. Loza: Employee of Janssen Research & Development LLC, Spring House, United States

P. Brangan: Employee of Janssen Research & Development LLC, Spring House, United States

C. Monast: Employee of Janssen Research & Development LLC, Spring House, United States

A. Rowe: Employee of Janssen Research & Development Ltd, High Wycombe, UK.


**OP300 THE IMPLANTABLE MEDICATED MICRORESEVOIRS IN THE TREATMENT OF COLORECTAL CANCER: THE GOOD EFFECTS OF A SIMPLE PROCEDURE. EARLY RESULTS**

Y. S. Berezinszky, V. P. Sulyma, O. N. Popova

Surgery N° State Establishment "Dnipropetrovsk Medical Academy".

Dnipropetrovsk/Ukraine

Contact E-mail Address: oksana.nikolaevna.popova@gmail.com

Introduction: Colorectal cancer (CRC) is the third most common cancer in the world of men, and the second - in women. In Europe remains steady increase in incidence and mortality according to Globocan 2012 and source EuroCaPon. The main problem after surgery is local recurrences that often develop even after resection of the primary tumor. Cure for CRC is developed in a developed country of the world is less than 50% [1]. Therefore, the focus of current oncological research is the prevention of recurrence. There are a number of studies on intraoperative radiation therapy, which provides good results for the prevention of CRC recurrence and increase the five-year survival [2,3]. In fact, we have proposed a method of supporting intraoperative chemotherapy with prolonged effect, because most of the local recurrence accounts for the second half of the first year after surgery. [2]

Aims & Methods: We aimed to investigate gene expression in serum and macrophages of CRC patients after implanting microreservoirs to improve the results of surgical treatment CRC. To study the safety and efficacy of this modification surgery. Materials and methods: We have investigated the number of CRC recurrence for patients without distant metastases, lymph node involvement and tumor free margins to other organs after surgery in a volume R0 for a year after surgery. The study involved 87 patients (54 women and 33 men, mean age 62.4 years +/- 8.4 years) who were operated on the Dnipropetrovsk regional proctology centre from February 2014 to February 2015. The control group included 60 group (42 patients, 17 men and 25 women) performed surgery in standard volume according to guideline. In the test group (45 patients, 16 males and 29 females) before the anastomosis were fashioned medicated microreservoirs with 5-fluorouracil (5FU) supported on polyvinylpyrrolidone (PVP). In fact, it was a mixture of 30% PVP solution 5ml and 5ml 5FU (250 mg). This mixture was introduced into the muscle layer from the side of mucsca the 1 ml syringe with needle 0,40 mm 27G X 1/2 at a distance of 1-1.5 cm from the edge of the intestine. In one procedure was introduced approximatively 10 ml of the drug. The operation on the patient’s abdomen was 0,5 h. The operation was completed in a standard way. As the drug delivery system has been selected PVP in the concentration of 30% as its safety is confirmed by the FDA. [8] PVP as a delivery system allows for the gradual release of the drug, due to the protracted and slow release of the drug, due to the slow degradation of the carrier polymer. An important advantage is the fact that the PVP is practically not destroyed at a pH of less than 7 [7], which allows to delay the release of 5FU, since pH in the stage of inflammation in the tissues is reduced and consequently the release of the bulk of 5FU will begin after completion of the inflammation. The 5FU was selected as a drug for the treatment because it does not require pre-transformation to acting form and is quite effective on condition of chronic inflammation in the tissues.

Disclosure of Interest: All authors have declared no conflicts of interest.

TUESDAY, OCTOBER 18, 2016

15:45–17:15

NOVEL TECHNIQUES IN LOWER GI MALIGNANCIES – ROOM L8

**A118 UNITED EUROPEAN GASTROENTEROLOGY JOURNAL 4(5S)**

Aims & Methods: Here, we investigated whether exosomal miRNAs are involved in such processes. Exosomes were purified using ExoQuick Exosome Precipitation kit. miRNAs were analyzed by qRT-PCR. In vivo infection with AIEC bacteria was performed using ideal loop assays and exosomes were purified. Purified exosomes were then intravenously injected in naïve mice (10 μg/mouse).

Results: We analyzed the levels of the CD-associated circulating miRNAs reported in literature in exosomes released from AIEC LF82-infected (Exo-AIEC) THP-1 macrophages. A significant upregulation of several miRNAs in Exo-AIEC compared with exosomes released from uninfected (Exo-UI) cells or cells infected with a non-pathogenic commensal C. coli HS strain was observed (Exo-HS). To analyze their transfer to recipient cells, naïve THP-1 macrophages were stimulated with the exosomes, and the levels of miRNAs in recipient cells were analyzed. The levels of several exosomal miRNAs were increased in THP-1 cells compared with Exo-UI-AIEC compared with cells stimulated with Exo-HS, suggesting an efficient transfer. In silico analysis showed that the upregulated and transferred miRNAs are involved in inflammatory responses and autophagy, which is necessary to control AIEC intracellular replication, among other biological processes. Transfection of some of these miRNAs in THP-1 cells inhibited the Exo-AIEC-triggered increases in pro-inflammatory response and AIEC intracellular replication in recipient cells, suggesting that these exosomal miRNAs are functional and are involved in the effects of Exo-AIEC in recipient cells. To confirm the in vitro data, we developed an in vivo model to analyze the impact of Exo-AIEC on gut colonization by AIEC and AIEC-induced inflammation. In this model, exosomes were isolated from ileal loops infected with AIEC with AIEC. Purified exosomes were then intravenously injected in naïve genetically susceptible mice (10 μg/mouse), and AIEC colonization in the gut and AIEC-induced intestinal inflammation were analyzed.

Conclusion: Our study shows that infection with CD-associated AIEC induces secretion of exosomes carrying several CD-associated circulating miRNAs by human THP-1 macrophages. These exosomal miRNAs, when being transferred into recipient naïve THP-1 macrophages, may be involved in the regulation of inflammatory and autophagic responses, contributing to host innate defense to AIEC infection.

Disclosure of Interest: All authors have declared no conflicts of interest.
Result: In the control group, local recurrence was detected in 12 cases (28.6%). The following postoperative complications were found: early adenocarcinoma obstruction in 2 (4.8%) cases of postoperative pneumonia in 1 (2.4%) case. Within 8 months after surgery 1 patient died of acute coronary syndrome. In the studied group of local recurrence was detected in 8 cases (17.8%). The following postoperative complications were found: early adenocarcinoma obstruction in 1 (2.2%) case, even one patient had been adhesive intestinal obstruction in 3 months after the operation, which resulted in the death of the patient on 2 day after the re-operation due to acute of cardiovascular failure.

Conclusion: 1. Intraoperative intubation of medicated microsorvos is a safe and effective procedure for the prevention of early recurrent CRC. 2. Notwithstanding the low total dose, good effect can be achieved due to the high concentration of the drug in the tissues. 3. This procedure avoids many resolving effects of the chemotherapy drug, associated with systemic administration and high doses required to achieve therapeutic concentrations in tissues. 4. Obviously, it is necessary to continue the monitoring of these patients. 5. It is possible to consider a combination of other drugs and carrier polymers.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP301 ENDOCYSTIC SUBMUCOSAL DISSECTION IN LATERALLY SPREADING TUMORS: EXPERIENCE OF 282 CASES FROM A TERTIARY REFERENCE CENTER IN TURKEY

F. Aslan1, M. Kucuk1, Z. Alpinar1, N. Ekinci2, A. Yurtlu1, E. Alper2, B. Unsali1
1Gastroenterology, Izmir Ataturk Training And Research Hospital, Izmir/Turkey
2Pathology, Izmir Ataturk Training and Research Hospital, Izmir/Turkey

Contact E-mail Address: drfathiaslan@hotmail.com

Introduction: Endoscopic submucosal dissection (ESD) is a minimally invasive technique, providing en-bloc resection of premalignant and malignant lesions in early stage gastrointestinal (GI) cancers. Lateral Spreading Tumours (LSTs), which are endoscopically seen as granular (LST-G) or non granular (LST-NG) type, are technically difficult to remove as en-bloc with ESD method because of anatomical features of the colon. In the present study, we present our results of colorectal ESD procedures in LSTs.

Aims & Methods: Between April 2012- April 2016, a total of 655 colorectal lesions were referred to our unite for the purpose of removal with advanced endoscopic techniques (EMR or ESD). Colorectal ESD was performed to 290 lesions were referred to our unite for the purpose of removal with advanced endoscopic techniques (EMR or ESD). Colorectal ESD was performed to 290 lesions. Data was recorded prospectively before and after the procedure. 8 ESD endoscopic techniques (EMR or ESD). Colorectal ESD was performed to 290 lesions. Data was recorded prospectively before and after the procedure. 8 ESD

Result:

Table: Demographic data and colorectal endoscopic submucosal dissection results [Case (n) = 273 Lesion (N = 282)

Disclosure of Interest: All authors have declared no conflicts of interest.

OP302 EVALUATION OF RECTAL CANCER ANGIOGENESIS USING IMMUNOHISTOCHEMICAL AND COMPUTER-ASSISTED ENDOSONOGRAPHIC METHODS

L. Tankova1, R. Nakov1, G. Stoilov2, A. Georgova1, V. Nakov3, V. Geroval1, D. Kovatchik1
1Gastroenterology, Clinic of Gastroenterology, “Tsaritsa Ioanna – ISUL” University hospital, Medical University – Sofia, Sofia/Bulgaria
2Institute Of Mechanics, Bulgarian Academy of Sciences, Sofia/Bulgaria
3Pathology, Faculty of Medicine, University of Sofia “St. Kliment Ohridski”, Sofia/Bulgaria

Contact E-mail Address: radislav.nakov@gmail.com

Introduction: The conventional way for evaluation of rectal cancer angiogenesis requires a biopsy or a tissue specimen applying specific immunohistochemical or molecular biological tests. The evaluation of microvessel density is a gold standard in the assessment of tumour angiogenesis. Doppler ultrasound is an attractive method for imaging angiogenesis in vivo which can be repeated without exposing the patient to any risk.

Aims & Methods: The aim of the current study is to evaluate the preoperative rectal cancer angiogenic status with Endorectal Power Doppler Ultrasonography by using the new Power Doppler Vascularity Index. The PDVI was calculated as the ratio of the number of the colored pixels within a tumour section to the number of total pixels in that specific tumour section, and was calculated by using a software.

Result: The mean microvessel density (MVD) was 163 ±69 microvessels/mm2. Median MVD used as the cutoff divided two groups of tumours with high (≥160 vessels/mm2) and low angiogenic activity (>160 vessels/mm2). Mean PDVI was 8.9 ±6.0% (range: from 0 to 27.3). Median PDVI (8%) was used as the cutoff divided two groups of tumours with high (>8%) and low PDVI (>8%). The MVD and PDVI showed a good positive linear correlation (r = 0.438, p = 0.002).

Conclusion: Endorectal Power Doppler ultrasonography is a useful noninvasive method of evaluating the extent of angiogenesis. Tumour angiogenesis assessed by power Doppler vascular index correlated with histological microvessel density determination. The presented endoultrasound Power Doppler examination is a reliable and reproducible mean for in vivo preoperative quantitative assessment of the tumour vascularityisation.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP303 COMPARISON OF CLINICAL OUTCOMES AMONG DIFFERENT ENDOCYSTIC MODALITIES FOR RECTAL NEUROENDOCRINE TUMOR

S.H. Park1, Y. Cho2, H.H. Choi3, D.Y. Cheung1, J.S. Kim1, B. Lee1, M. Choi1
1Intensive Medicine, Catholic University, Seoul, Republic of Korea
2Internal Medicine, Catholic university of medicine, seoul/Korea, Republic of Korea
3Gastroenterology, Clinic of Gastroenterology, “Tsaritsa Ioanna – ISUL” University hospital, Medical University – Sofia, Sofia/Bulgaria

Contact E-mail Address: trashsanai@hanmail.net

Introduction: Rectal neuroendocrine tumor (NET) less than 10 mm in diameter can be removed by various endoscopic techniques, such as endoscopic mucosal resection (EMR), modified EMR, and endoscopic submucosal dissection (ESD). This study aimed to compare efficacy and safety of endoscopic submucosal resection with a ligation device (ESMR-L) or circumferential submucosal incision prior to EMR (CSI-EMR) versus ESMR

Result: There was no different in tumor diameter between different endoscopic procedures (ESMR-L, 4.5 ± 1.6 mm; CSI-EMR, 5.6 ± 2.0 mm; ESD, 5.0 ± 2.2 mm, p = 0.236). En bloc resection was achieved in all patients. There was no lateral margin involvement in all patients. Basal margin involvement occurred in one patients in the ESMR-L group and two in the CSI-EMR group. The rates of pathological complete resection were 100% (17 of 17) in the ESMR-L group and 85% (18 in the CSI-EMR group, and 95.2% (20 of
Disclosure of Interest: All authors have declared no conflicts of interest.

Reference


TUESDAY, OCTOBER 18, 2016
15:45-17:15
THE INTESTINAL EPITHELIUM - STEM CELLS, INFLAMMATION AND CANCER - ROOM 1.86

OP306 THE PROREGENERATIVE ROLE OF INTERLEUKIN-22 POST-CREATION OF THE INTESTINAL EPITHELIUM DEPENDS ON AUTOAPHTHY AND ER STRESS
F. Tran1, K. Aden1, M. Tschorschenthaler2, R. Sheibani-Tezerji1, J. Kuipers2, A. Luzius1, M. Jentschli, S. Schreiber1, R.S. Blumberg1, A. Kaser1, P. Rosenstiel1

1Institute of Clinical Molecular Biology, University Hospital Schleswig-Holstein, Kiel, Germany
2Division of Gastroenterology and Hepatology, Department of Medicine, Addenbrooke’s Hospital, University of Cambridge, Cambridge/United Kingdom

Contact E-mail Address: f.tran1@klinik.uni-kiel.de

Introduction: Endoplasmic reticulum (ER) function and autophagy are necessary to maintain cellular homeostasis. Genetic variants of inflammatory bowel disease (IBD) risk genes ATG16L1 or XBP1 are associated with epithelial endoplasmic reticulum (ER) stress which promotes cell death. While XBP1 plays a beneficial role in resolving ER stress, ATG16L1 represents an essential component of the autophagy machinery, a central modulator for downstream defense. Given these processes are strongly connected since impaired autophagy subsequently results in deregulation of ER function. Interleukin-22 (IL-22) is known to be a protective cytokine in mucosal regeneration by promoting epithelial proliferation via STAT3 activation. Therefore, conjugates of IL-22 are in trials as potential drugs in IBT treatment.

Aims & Methods: Here, we investigate the impact of the IBD risk genes ATG16L1 or XBP1 on regenerative function of IL-22 in intestinal epithelium in mice and human-derived human colon cancer cells. HT-29 and Caco2 cells were co-cultured with recombinant IL-22 and ER stress inducers like Tunicamycin or autophagy inducers like Rapamycin before they were subjected to wound healing assays, gene expression analysis and immunoblot analyses. Intestinal organoids derived from XBP1- or ATG16L1-deficient mice were treated with recombinant IL-22 and gene expression analysis using qRT-PCR. RNA sequencing and transcriptome analysis were performed.

Conclusions: All authors have declared no conflicts of interest.
References

Disclosure of Interest: All authors have declared no conflicts of interest.

Introduction:
Contact E-mail Address: p.wisse@erasmusmc.nl

OP307 HOXA9 IS OVEREXPRESSED IN COLONIC ADENOMAS AND CAUSES AN INCREASE IN CELL GROWTH
P. H.A. Wisse1, V. T. Janmaat2, A.P. Verhaar3, M.J. Bruno3, M.C. W. Spaander4, M. Peppelenbosch3
1Department Of Gastroenterology & Hepatology, Erasmus Medical Center, Rotterdam/Netherlands
2Gastroenterology & Hepatology, Erasmus Medisch Centrum, Rotterdam/Netherlands
3Department Of Gastroenterology & Hepatology, University Medical Center, Rotterdam/Netherlands
4Gastroenterology & Hepatology, Erasmus Medisch Centrum Rotterdam/Heidelberg, Netherlands

Contact E-mail Address: p.wisse@erasmusmc.nl

Introduction: Colonic adenomas are premalignant tumors with glandular origin. Identifying the molecular alterations in this tissue may help to understand its malignant potential and could lead to better understanding of colorectal cancer development. The mammalian HOX clusters encode regulators of embryonic anterior to posterior specification and are important for the formation of tissues, structures, and organs. Besides having a function in embryology, HOX genes have pro-oncogenic activity in various malignant diseases. For example, HOXA13 overexpression predicts poor outcome for patients with cancer of the esophagus, stomach, and liver. In a portion of acute myeloid leukemias (AML), a translocation encoding the NUP98-HOXA9 oncogene gives rise to this cancer. HOXA9 overexpression is the molecular factor most strongly correlated with poor prognosis in AML and is also correlated with poor prognosis in ovarian epithelial cancer. HOX gene aberrations are reported in colorectal cancer, however, it is unclear whether HOX gene aberrations are present at a premalignant stage and could, thus, contribute to cancer formation.

Aims & Methods: This study firstly aimed to assess the expression of HOXA9 in colonic adenoma tissue and location matched control tissue. Secondly, it aimed to determine the effects of increased HOXA9 expression, both in terms of its influence in anterior to posterior specification and its oncogenic properties. We collected biopsies from colonic polyps and location matched normal colonic tissue in patients undergoing colonoscopy. A pathologist classified the colonic polyps and used an immunohistochemical protocol to stain for HOXA9. HOXA9 overexpression is the molecular factor most strongly correlated with poor prognosis in AML and is also correlated with poor prognosis in ovarian epithelial cancer. HOX gene aberrations are reported in colorectal cancer, however, it is unclear whether HOX gene aberrations are present at a premalignant stage and could, thus, contribute to cancer formation.

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Aims & Methods: This study firstly aimed to assess the expression of HOXA9 in colonic adenoma tissue and location matched control tissue. Secondly, it aimed to determine the effects of increased HOXA9 expression, both in terms of its influence in anterior to posterior specification and its oncogenic properties. We collected biopsies from colonic polyps and location matched normal colonic tissue in patients undergoing colonoscopy. A pathologist classified the colonic polyps and used an immunohistochemical protocol to stain for HOXA9. HOX gene aberrations are reported in colorectal cancer, however, it is unclear whether HOX gene aberrations are present at a premalignant stage and could, thus, contribute to cancer formation.
western blot analysis. The gene expression of transformed organoids was assessed by microarray analysis and quantitative RT-PCR.

Result: The treatment with the inflammatory reagents in mouse colonic organoids showed the time-dependent induction of NF-κB target genes. Particularly, the expression of DUOX2 gene was gradually increased by the continuous stimulation with inflammatory reagents for 40 weeks. 3D immunostaining analysis showed NF-κB p65 was accumulated in nuclei by longer time of the stimulation, indicating that long-term stimulation 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 inflammatory reagents whereas NF-κB signaling induced by short-term stimulation was completely shut down by the removal of all inflammatory reagents, suggesting that NF-κB might be irreversibly activated by long-term stimulation. Moreover, the organoids required neither R-spondin nor Wnt3a after the treatment with GSK3 inhibitor for 8 weeks, indicating that the organoids might be transformed like colitis-associated cancer. Microarray analysis and Gene Set Enrichment Analysis of transformed organoids showed irreversible Akt signal activation and reduced expression of Tgfβ2, indicating that this transformation might involve the inflammatory-related carcinogenesis.

Conclusion: Long-term inflammation and nuclear accumulation of β-catenin leads to irreversible cell transformation, which is in wt independent survival capacity of colonic organoids. This in vitro model might mimic the natural history of epithelial cell transformation during inflammation-related carcinogenesis in UC. Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP310 THE RIBONUCLEASE RNASEH2B CONTROLS INTESTINAL STEM CELL INTEGRITY
K. Aden1, K. Bartsch2, F. Tran3, S. Rose John4, S. Schreiber3, P. Rosenstiel1, B. Rabe1
1Kiel University, IKMB + First Medical Department, Kiel/Germany
2Department Of Biochemistry, Kiel University, Kiel/Germany
3Institute Of Molecular Biology, University Hospital Schleswig-Holstein, Kiel/Germany
4Kiel University, Institut KSU Medizinische Abt. 1, Kiel/Germany

Contact E-mail Address: k.aden@ikmb.uni-kiel.de

Introduction: The stability of genomic DNA is under a tightly controlled surveillance. Especially in highly proliferating cells, as e.g. intestinal stem cells, DNA/DNA hybrids display a menace to DNA integrity. The ribonuclease RNAseH2b lances the danger. Especially in highly proliferating cells, as e.g. intestinal stem cells, RNA/DNA hybrids display a menace to DNA integritiy. The ribonuclease RNAseH2b lances the danger. Especially in highly proliferating cells, as e.g. intestinal stem cells, RNA/DNA hybrids display a menace to DNA integritiy. The ribonuclease RNAseH2b lances the danger. Especially in highly proliferating cells, as e.g. intestinal stem cells, RNA/DNA hybrids display a menace to DNA integritiy. The ribonuclease RNAseH2b lances the danger.

Aims & Methods: We generated RNAseH2bfl/fl and RNAseH2btet/+. The expression of RNAseH2b in the intestinal epithelium was controlled by doxycycline. WB, RT-PCR and IHC were performed to characterize the expression of RNAseH2b. Immunofluorescence staining was performed to localize RNAseH2b. Cell proliferation and senescence were assessed by BrdU and Ki67 staining. Gene expression was assessed by quantitative RT-PCR.

Conclusion: RNAseH2b plays an essential role in maintaining intestinal regeneration by protecting genomic DNA of high proliferating cells from DNA/RNA hybrids induced DNA damage. Knockout of RNAseH2b leads to loss of epithelial stemness and induction of cellular senescence. Disclosure of Interest: All authors have declared no conflicts of interest.

Reference
were isolated from control, GHRL rats and then hyperstimulated by caerulein toducular ducts and forskolin-stimulated Cl- current of CFTR Cl- channel (20 independently decreased forskolin-stimulated fluid secretion in guinea pig pancreas.

Cigarette smoking and CSE inhibits pancreatic ductal fluid and HCO3-

clamping technique. Basal and forskolin-stimulated fluid secretion was measured by video dilution using the stock solution. Intracellular pH was evaluated by microfluorometry. Basal fluid secretion was measured by microfluorometry.

Disclosure of Interest: All authors have declared no conflicts of interest.

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in CFT R KO PDEc compared to WT due to the impaired function of the phosphodiesterase (PDE) enzyme. This suggests that the absence of CFT R leads to increased calcium levels, which may contribute to the development of diabetic retinopathy. However, the mechanism by which CFT R regulates calcium homeostasis and its potential role in diabetic retinopathy warrants further investigation.

**Conclusion:**
CFT R deficiency results in enhanced calcium signaling, which may contribute to the development of diabetic retinopathy. Further studies are required to elucidate the molecular mechanisms underlying this association.

**Disclosure of Interest:**
All authors have declared no conflicts of interest.
Conclusion: P were 1.6% (2/128) in the aggressive hydration with lactated Ringer’s solution group and 11.6% (15/129) in the standard hydration group. The three groups had no significant difference in demographic characteristics. The visual analogue scale persisting for 24 hours after the procedure, serum amylase level after the procedure.

A pilot study suggests that aggressive intravenous hydration with lactated Ringer’s solution may reduce the development of post-endoscopic retrograde cholangiopancreatography (ERC) pancreatitis. In a prospective randomized multicenter clinical trial, patients who underwent first-time ERC were randomly assigned to 3 groups (1:1:1) that received aggressive hydration with lactated Ringer’s solution (3 mL/kg/h during the procedure, a 20 mL/kg bolus after the procedure, and 3 mL/kg/h for 8 hours after the procedure), standard hydration with the same solution (1.5 mL/kg/h for 8 hours after the procedure), and a 20 mL/kg bolus after the procedure. Of the possibly/probably related deaths, 2 had GI related events, 1 had a small bowel obstruction and died approximately 3 weeks later of unknown causes, and 1 had a small bowel perforation and peritonitis. The gastrointestinal (GI)-related safety of the LCIG treatment system (drug/device) has been assessed in advanced PD patients with final safety data from the GLORIA1 registry. This observational registry of 375 advanced PD patients treated with LCIG was conducted at 75 centers in 18 countries. Patients were initially titrated to an optimal dose of LCIG via nasojugal (NJ) tube for up to 2 weeks, followed by infusion via PEG-J for 24 months. Final safety data from patients with advanced PD who had >1 infusion of LCIG (n = 356) were included in this analysis. Adverse drug reactions (ADR), which may be drug-related events with a reasonable possibility of causal relationship to the treatment according to investigators’ judgment, were recorded throughout the registry. The authors categorized ADRs post-hoc as either PEG-J procedure-related, device-related, or “other” type of GI event. Result: Of the 375 enrolled patients, 332 (99%) were treated with LCIG via PEG-J, and 258 (60%) completed the 24 month follow-up. The median [range] duration of exposure via NJ was 60 [1, 53] days (n = 307) and via PEG-J was 722 [1, 2057] days (n = 351). During titration via NJ, there were 3 patients (0.8%) who had >1 GI related ADR. Within the 24 months of treatment post-PEG-J placement (n = 356) >1 GI related ADR was reported in 139 patients (39%), of which procedure-related ADRs were reported in 35 patients (9.8%), device-related in 35 (26%), other GI events in 63 (18%); the ADRs in all GI categories reported for >2% incidence were patient weight loss (12.7%), device related infection (5.9%), device related obstruction (4.8%), device issue (4.8%); and the serious ADRs reported for >2% patients were device dislocation (2.2%) and device issue (2.0%). During the 28-day follow up period, there were 4 patients (1.1%) who had >2 GI related ADR. 3 of 27 adverse events to the discontinuation of 10 patients (2.8%) overall, 2 of whom discontinued due to a procedure-related ADR, 5 due to a device-related ADR, and 3 due to another type of GI ADR. Of the 29 deaths reported, 23 were deemed unrelated to treatment, 5 possibly related (to drug/device) and 1 probably related (to tubing). Of the possibly/probably related deaths, 2 had GI related events, 1 had a small bowel obstruction and died approximately 3 weeks later of unknown causes, and 1 had a small bowel perforation and peritonitis.

Conclusion: Most GI related ADRs were related to the device in this registry. The incidence of GI-related ADRs and their discontinuations due to GI-related ADRs were relatively low, which is supportive of the overall tolerability of LCIG and consistent with previous studies.

Disclosure of Interest: D Domagk: Dirk Domagk has received research support from Med梦想, honoraria for lectures from Olympus Europe and Dr. Falk Foundation, and has served as consultant for Hitachi Medical Systems. AbbVie Inc.
A. Antonini: Angelo Antonini has received research support from Mundipharma and compensation from UCB, Boston Scientific, Boehringer-Ingelheim, AbbVie Inc., and Zambon for serving as a consultant and lecturer.
L. Bergmann: Lars Bergmann is an employee of AbbVie Inc. and hold stock or stock options.
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All other authors have declared no conflicts of interest.

References
4. Dept Of Gastroenterology, Kitasato University School of Medicine, Sagamihara/
5. Dept. Of Internal Medicine, Murakami Memorial Hospital Dept. of Internal Medicine, Saijo/Japan

Contact E-mail Address: masato@murakami-kinen.or.jp

Introduction: Endoscopically assisted percutaneous transpneumogastroduodenal gastrostomy (PC-PTG) is a long-term treatment option for advanced Parkinson’s disease (PD) patients and administered via percutaneous gastrojejunostomy (PEG-J) from an external pump.

Aims & Methods: The gastrointestinal (GI)-related safety of the LCIG treatment system (drug/device) has been assessed in advanced PD patients with final safety data from the GLORIA1 registry. This observational registry of 375 advanced PD patients treated with LCIG was conducted at 75 centers in 18 countries. Patients were initially titrated to an optimal dose of LCIG via nasojugal (NJ) tube for up to 2 weeks, followed by infusion via PEG-J for 24 months. Final safety data from patients with advanced PD who had >1 infusion of LCIG (n = 356) were included in this analysis. Adverse drug reactions (ADR), which may be drug-related events with a reasonable possibility of causal relationship to the treatment according to investigators’ judgment, were recorded throughout the registry. The authors categorized ADRs post-hoc as either PEG-J procedure-related, device-related, or “other” type of GI event. Result: Of the 375 enrolled patients, 332 (99%) were treated with LCIG via PEG-J, and 258 (60%) completed the 24 month follow-up. The median [range] duration of exposure via NJ was 60 [1, 53] days (n = 307) and via PEG-J was 722 [1, 2057] days (n = 351). During titration via NJ, there were 3 patients (0.8%) who had >1 GI related ADR. Within the 24 months of treatment post-PEG-J placement (n = 356) >1 GI related ADR was reported in 139 patients (39%), of which procedure-related ADRs were reported in 35 patients (9.8%), device-related in 35 (26%), other GI events in 63 (18%); the ADRs in all GI categories reported for >2% incidence were patient weight loss (12.7%), device related infection (5.9%), device related obstruction (4.8%), device issue (4.8%); and the serious ADRs reported for >2% patients were device dislocation (2.2%) and device issue (2.0%). During the 28-day follow up period, there were 4 patients (1.1%) who had >2 GI related ADR. 3 of 27 adverse events to the discontinuation of 10 patients (2.8%) overall, 2 of whom discontinued due to a procedure-related ADR, 5 due to a device-related ADR, and 3 due to another type of GI ADR. Of the 29 deaths reported, 23 were deemed unrelated to treatment, 5 possibly related (to drug/device) and 1 probably related (to tubing). Of the possibly/probably related deaths, 2 had GI related events, 1 had a small bowel obstruction and died approximately 3 weeks later of unknown causes, and 1 had a small bowel perforation and peritonitis.

Conclusion: Most GI related ADRs were related to the device in this registry. The incidence of GI-related ADRs and their discontinuations due to GI-related ADRs were relatively low, which is supportive of the overall tolerability of LCIG and consistent with previous studies.

Disclosure of Interest: D Domagk: Dirk Domagk has received research support from Med梦想, honoraria for lectures from Olympus Europe and Dr. Falk Foundation, and has served as consultant for Hitachi Medical Systems. AbbVie Inc.
A. Antonini: Angelo Antonini has received research support from Mundipharma and compensation from UCB, Boston Scientific, Boehringer-Ingelheim, AbbVie Inc., and Zambon for serving as a consultant and lecturer. L. Bergmann: Lars Bergmann is an employee of AbbVie Inc. and hold stock or stock options.
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All other authors have declared no conflicts of interest.

References
for the patients that Percutaneous Endoscopic Gastrostomy was contraindicated. PTEG by endoscopic assistance may enhance the safety of the procedure and the new item that may enhance the reliability was developed.

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 upper esophagus. Percutaneous balloon puncture with a specialized needle is then performed from the left side of patient’s neck under ultrasound 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 in a total of 119 patients (74 men and 45 women, mean age 71.5 years) in whom PEG was not feasible. Double Balloons equipped Overtube type RFB were used instead of primary RFB in seven cases that the puncture needle is punctured into the overtube through the balloon. PTEG was performed for nutrition in 65 patients and for decompression in 54.

Result: Satisfactory results were achieved in all 119 patients. Median follow-up was 64.0 days in patients who received decompression because of the obstruction due to malignant tumors and 270.0 days in those who received nutrition. Four of 65 patients for nutrition were able to be free from tube feeding due to PTEG tube feeding support. There was one patient who had tracheal penetration, which was managed conservatively. Other complications were minor oozing bleeding in seven patients that did not require blood transfusion, subcutaneous emphysema in two patients, which were managed conservatively. The complication rate was 13.4%. A stable procedure could performed in all seven cases using the new overtube and also there was no complications. 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 to perform traditional type of endoscopy enhances the safety of the procedure and allows better confirmation of each step involved. New overtube type RFB will be useful but need more experiences.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP324 INCREASED MUCOSAL EXPRESSION OF TOLL-LIKE RECEPTORS IN ADULT PATIENTS WITH EOSINOPHILIC ESOPHAGITIS

À Arias Arias1, M Vicario2, P Martinez Fernández2, A. M González-Castro2, M Fortea3, J González-Cervera3, J. L Yagüé-Compadre4, T Mota-Huertas5, A. J. Lucendo6

1Research Unit, Hospital La Mancha Centro, Alcazar de San Juan/Spain 2Pathology, Hospital General La Mancha Centro, Alcazar de San Juan/Spain 3Gastroenterology, Hospital General de Tomelloso, Tomelloso/Spain 4Gastroenterology, Hospital General de Tomelloso, Tomelloso/Spain

Contact E-mail Address: angela_arias_arias1@hotmail.com

Introduction: An adaptive Th2-type immune response to food antigens is involved in eosinophilic esophagitis (EoE). Evidences of a potential role for the innate immunity in EoE has also been arisen parallel to the recognition of changes in esophageal microbiome in adult and pediatric EoE patients compared to non-EoE controls. The likely role that microbial pattern recognition receptors (PRRs) might play in EoE arises as a potential source of research in understanding the relationship of diet, the esophageal microbiome, and the immune system activation in EoE, that has also been assessed yet.

Aims & Methods: To gather data about the potential implication of Toll like receptors (TLRs), the most investigated group of transmembrane PRR in EoE, we characterized TLR mRNA expression and protein staining in esophageal mucosal biopsy samples from adults before and after dietary treatment, and compared with control patients. Esophageal mucosal samples were fixed in formalin, embedded in paraffin, and routinely processed for hematoxylin and eosin staining. Specific antigen retrieval and permeabilization processes were performed before samples were incubated with the primary antibodies anti-TLR1, TLR2, TLR3, TLR4, and TLR6, or TLR9. Incubation with the secondary antibodies Alexa Fluor 594 goat anti-rabbit IgG or Alexa Fluor 488 goat anti-mouse IgG were then counterstained with DAPI. Gene expression for the different TLR assessed in all samples after RNA was isolated with MirVanaTM Kid. Simultaneous real-time PCR were performed with TaqMan Low-Density Arrays. Thermal cycling conditions were 2 min at 50 °C, 10 min at 95 °C, followed by 40 cycles of denaturation at 95 °C for 15 s, and annealing and extension at 60 °C for 1 min in an ABI PRISM 7900HT Sequence Detection System. Relative changes in mRNA expression were calculated with the cycle threshold (Ct) method.

Result: A total of 10 EoE patients (8 men) and 10 gender-matched control subjects were included in the analysis. The groups had a mean age of 33.1 (10.1) and 33 (10.1) years, respectively. In the EoE group, peak intraepithelial eosinophil density was 58.6 (29.9) cells/hpf, which decreased to 3 (4.2) cells/hpf after SFDG-based treatment (p < 0.001). Eosinophilic eosinophils were detected in all of the esophageal samples from controls. No differences in eosinophil counts were detected for atopic and non-atopic EoE patients, being 55 (30.4) vs. 61 (34.8) cells/hpf, respectively. Active EoE characterized by significant upregulation of TLR1 (2.7-fold increase), TLR2 (3.7-fold increase) TLR4 (4.6-fold increase) and TLR9 (3.4-fold increase) in comparison with the controls (p < 0.05 for all comparisons). Dietary treatment significantly decreased all the four TLRs to control group values (p < 0.05). Immunofluorescence staining demonstrated epithelial-predominant staining in TLR2 and TLR4, and scattered cell staining for TLR1 and TLR9. TLR expression pattern showed differences in lamina propria and epithelial layers.

Conclusion: EoE is associated with changes in expression levels of several TLRs, that reverse after effective dietary therapy. Our results points towards an interplay of diet, microbiome and innate immune responses in the pathophysiology of EoE.

Disclosure of Interest: All authors have declared no conflicts of interest.
OP325 A RANDOMISED, DOUBLE-BLIND, PLACEBO-CONTROLLED TRIAL OF COMBINED HUMAN/MICE INTERLEUKIN-13 MONOCLONAL ANTIBODY (RPC4046) IN PATIENTS WITH ACTIVE EOSINOPHILIC OESOPHAGEAL DISEASE: RESULTS OF THE HEROES STUDY

1 I Hirano, 2 M Collins, 3 Y Assouline-Dayan, 4 L Evans, 5 S Gupta, 2 A Schoepfer, 1 A Straumann, 1 H Smith, 2 C Renvall5, 1 A Woon, 2 R Peach, 1 P Frohma, 1 S Gujralthi, 2 R Aranda, 8 D Eollen 1

1 Feinberg School of Medicine, Chicago/United States of America
2 College Of Medicine, University of Cincinnati/ Cincinnati/United States of America/ OH
3 Carver College of Medicine, Iowa City/United States of America/IA
4 Grand Teton Research Group, Idaho Falls/United States of America
5 Indiana University School of Medicine, Indianapolis/United States of America/IN
6 Canton Hospital, Luzern/Switzerland
7 University Hospital Basel, Basel/Switzerland
8 Clinical Development, Receptos Inc., San Diego/United States of America/CA
9 Clinical Development, Receptos Inc., San Diego/United States of America/CA
10 Clinical Research Services/ a fully owned subsidiary of Celgene, San Diego/United States of America/CA
11 School Of Medicine, University of North Carolina, Chapel Hill/United States of America/ NC

Contact E-mail Address: ihirano@northwestern.edu

Introduction: Interleukin-13 (IL-13) has been implicated in the pathogenesis of eosinophilic oesophagitis (EOE). RPC4046 prevents the binding of IL-13 to both the IL-13Rα1 and IL-13Rα2 receptors. This study evaluated the efficacy and safety of 2 dose levels of RPC4046 compared to placebo (PBO).

Aims & Methods: Patients were randomized 1:1:1 to receive either RPC4046 180 mg (LD) (n = 31), RPC4046 360 mg (HD) (n = 34), or PBO (n = 34). An IV dose on Day 1 was followed byweekly subcutaneous doses. Oesophageal biopsies, read by a centralized blinded pathologist, were obtained at baseline (BL) and Weeks 8, 12, and 16 to assess eosinophil count, the primary endpoint. Secondary endpoints included symptom improvement measured by a Daily Symptom Diary (DSD), improvement in endoscopic features as measured by the Endoscopic Reference Score (EREF), and Subject’s Global Assessment of Disease Severity. Safety was also assessed.

Result: 90 subjects completed the 16Wk double-blind period. Demographic/disease characteristics were generally comparable between treatment arms. At BL, mean eosinophilic esophagitis counts (cells/hpf) were 92.4 (PBO), 116.6 (LD), and 127.6 (HD). The mean count was significantly reduced from BL for both RPC4046 dose levels compared to PBO (mean change: PBO –4.4, LD –94.8, and HD –99.9 [both p < 0.0001 vs PBO]). There was a greater improvement in dysphagia symptoms as measured by the DSD with HD compared to PBO, but this did not achieve statistical significance.

Conclusion: RPC4046 demonstrated significant reductions in eosinophilic infiltration and improvements in endoscopic features at both dose levels compared to placebo. HD had greater symptom improvement than HD on LD. These phase 2 data support the further study of RPC4046 as a novel treatment for EOE. (clinicaltrials.gov ID: NCT02098473)

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M. Collins: I have received research funds (through contracts) from Receptos
S. Gupta: Sandeep K. Gupta received consulting fees and/or speaker fees from Abbott Laboratories, Nestle S. A., QOL, Receptos, Inc., and Meritage Pharma, Inc.
A. Schoepfer: I received consultant fees from: Receptos, Regeneron and grant support from: Receptos, Receptos, Falk
A. Straumann: Dr. Straumann is a consultant to Dr Falk Pharma GmbH and has received consulting fees and/or speaker fees and/or research grants from: Actelion, AG; AstraZeneca AG, Apatis Pharma; GSK; AG; Nestle S. A.; Novartis, AG; Pfizer, AG, and Regeneron.
M. Grimm: I am an employee of Celgene.
H. Smith: I am an employee of Celgene.
C. Tompkins: I am an employee of Celgene.
A. Woon: I am an employee of Celgene.
R. Peach: I am a former employee of Celgene.
P. Frohma: I am an employee of Celgene.
S. Gujralthi: I am a former employee of Celgene.
R. Aranda: I am an employee of Celgene.
D. Eollen: I have received research funding from Receptos/Celgene; and am a Consultant for Receptos/Celgene.
All other authors have declared no conflicts of interest.

OP326 IMPAIRMENT OF CHEMICAL CLEANSING AND MUCOSAL INTEGRITY DISGUISED AS PERSISTING EOSPHAGUS FROM FUNCTIONAL HEARTBURN

M Frazoni1, N De Bortol2, L Marzio3, M Furnari4, I Martinucci5, S Tolone6, A Farioli7, S Marchi8, V Savarino9, E Savarino9
1Digestive Pathophysiology Unit, Baggiovara Hospital, Modena/Italy
2Dept. Of Gastroenterology, University of Pisa, Pisa/Italy
3Gastroenterology Unit, Department Of Medical And Surgical Sciences, University of Bologna, Bologna/Italy
4Dm.i., Gastroenterology Unit, DiMI, Gastroenterology Unit, University of Genova, Genova/Italy
5Gastroenterology Unit, University of Pisa, Pisa/Italy
6Surgery, Second University of Naples, Naples/Italy
7Dipartimento Di Medicina Interna - Universiti Degli Studi Di Pisa, Clinica Medica I/I Completo S. Chiara, Pisa/Italy
8Dept Of Medical And Surgical Sciences, S.Orsola-Malpighi University Hospital, Bologna/Italy
9Dept Internal Medicine, Universita di Genova, Genova/Italy

Contact E-mail Address: edoardo.savarino@gmail.com

Introduction: Hypersensitive esophagus (HE) is defined by endoscopy-negative heartburn with normal esophageal acid exposure time (EAET) but positive symptom-association probability (SAP) and symptom index (SI) at reflux monitoring, and/or heartburn suppression with proton pump inhibitor (PPI) therapy.

Functional heartburn (FH) is distinguished by PPI-refractoriness and negative SAP/SI. However, diagnosis accuracy of SAP and SI has been recently questioned, especially with the diagnosis of FH/HE based on symptom-reflux association analysis only.

Aims & Methods: We aimed to investigate whether impairment of chemical clearance, expressed by post-reflux swallowed- induced peristaltic wave (PSPW) index, could be a new tool to assess mucosal baseline impairment (MBNI), distinguish FH from HE independently from SAP and SI. Impedance-pH tracings from 303 patients with PPI-dependent (i.e. heartburn repeatedly abolished by 4-week PPI-therapy and repeatedly recurring after PPI withdrawal) or PPI-refractory (i.e. < 50% of symptom relief after 8-week high-dose PPI therapy) heartburn were blindly reviewed, 125 with non-responsive reflux disease (NDR) defined by abnormal EAET, 108 with HE (normal EAET, but positive symptom-reflux correlation) and 70 with FH (normal EAET and negative symptom-reflux correlation). Impedance-pH tracings were manually analyzed to detect: EAET (abnormal if > 3.2% over 4 hours), characteristics of reflux episodes (acid/weakly acidic) and symptom-reflux association using both SAP (positive if >95%) and SI (positive if >50%). MBNI values were calculated on 3cm above the LER, during the overnight rest, for at least 30 minutes after excluding swallows and reflux induced changes. The PSPW index was calculated by dividing the number of refluxes followed within 30 seconds by swallowed-peristaltic waves with the number of total refluxes.

Conclusion: HE patients with HE, PSSW index and MBNI were the most sensitive impedance parameters; at multivariate analysis, they were independent predictors of HE. At receiver operating characteristic analysis, PSPW index with MBNI efficiently separated HE from FH: the area under the curve (AUROC) of 0.91 for HE vs 0.77 for FH and 0.72 for NDR, whereas only 0.71 for SAP/SI, 0.66 for EAET, 0.62 for SI and 0.56 for SAP. Interestingly, both the impaired clearance and MBNI were significantly more frequent in patients with HE (EAET and MBNI were the most sensitive impedance parameters; at multivariate analysis, they were independent predictors of HE). At receiver operating characteristic analysis, PSPW index with MBNI efficiently separated HE from FH: the area under the curve (AUROC) of 0.91 for HE vs 0.77 for FH and 0.72 for NDR, whereas only 0.71 for SAP/SI, 0.66 for EAET, 0.62 for SI and 0.56 for SAP. Interestingly, both the impaired clearance and MBNI were significantly more frequent in patients with HE (PSSW index and MBNI were the most sensitive impedance parameters; at multivariate analysis, they were independent predictors of HE).

Disclosure of Interest: All authors have declared no conflicts of interest.

OP327 THE ADDED VALUE OF POST-REFLEX SWALLOWED-INDUCED PERISTALTIC WAVE INDEX AND NOCTURNAL BASELINE IMPEDANCE IN REFRACTORY GERD STUDIED WITH ON-THERAPY IMPEDANCE AND pH MONITORING

M. Frazoni1, L. Frazzoni2, L. Frazzoni3, M. Furnari4, I. Martinucci5, S. Tolone6, S. Marchi7, V. Savarino9, E. Savarino9
1Digestive Pathophysiology Unit, Baggiovara Hospital, Modena/Italy
2Dept. Of Gastroenterology, University of Pisa, Pisa/Italy
3Gastroenterology Unit, Department Of Medical And Surgical Sciences, University of Bologna, Bologna/Italy
4Dm.i., Gastroenterology Unit, DiMI, Gastroenterology Unit, University of Genova, Genova/Italy
5Gastroenterology Unit, University of Pisa, Pisa/Italy
6Surgery, Second University of Naples, Naples/Italy
7Dipartimento Di Medicina Interna - Universiti Degli Studi Di Pisa, Clinica Medica I/I Completo S. Chiara, Pisa/Italy
8Dept Of Medical And Surgical Sciences, S.Orsola-Malpighi University Hospital, Bologna/Italy
9Dept Internal Medicine, Universita di Genova, Genova/Italy

Contact E-mail Address: edoardo.savarino@gmail.com

Introduction: On-therapy impedance-pH monitoring in proton pump inhibitor (PPI)-refractory gastroesophageal reflux disease (GERD) yielded conflicting results. Recently, novel impedance parameters assessing esophageal chemical clearance and mucosal integrity, namely the post-reflux swallowed-induced peristaltic wave (PSPW) index and the mean nocturnal baseline impedance (MBNI), showed diagnostic yield of impedance-pH monitoring in
investigating PPI- refractory patients studied off therapy, further improving the
effectiveness of the reported outcomes. Aims & Methods: We aimed to investigate whether the impairment of chemical clearance, expressed by PSPW index, and of mucosal integrity, expressed by MNBI, are helpful in segregating NERD from FH studied with impedance-pH monitoring on-therapy. We further assessed the value of these novel parameters as predictors of PPI-refractory GERD confirmed by 3-year positive surgical outcome. On-therapy impedance-pH tracings from consecutive patients referred for PPI-refractory heartburn with/without regurgitation (i.e. <50% of symptoms relieved by swallow-induced peristaltic waves with the number of total reflexes. Patients were subdivided into refractory reflux esophagitis (RRE), healed reflux esophagitis (HRE), non erosive reflux disease (NERD); defined by abnormal acid exposure time or normal AET but positive symptom reflux correlation and functional heartburn (FH) defined by MNBI and negative symptom-reflux correlation) according to endoscopy and conventional
impedance-pH variables.

Result: Median PSPW index and MNBI were significantly lower in 39 RRE
(15%; 1145 Ohms) than in 41 HRE (25%; 1741 Ohms) and in 68 NERD
(29%; 2374 Ohms) patients, and in all three GERD subgroups compared to 41
FH cases (67%; 3488 Ohms) (P = 0.0001). Comparing NERD to FH, PSPW index was shown to be lower than normal at <50% of median MNBI at reflux characterization (0.886 vs. 0.667, P = 0.005). PSPW index was abnormal preoperatively in 53/53 patients with positive surgical outcome and resulted independent predictor of PPI-refractory GERD at multivariate analysis, (odds ratio 9.093, P = 0.01).

Conclusion: On-therapy impedance-pH monitoring, impaired chemical clear-
ance and mucosal integrity characterize PPI-refractory typical GERD. PSPW index and MNBI efficiently distinguish PPI-refractory NERD from FH and PSPW index is interesting for selecting surgical candidates.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP328 PRELIMINARY RESULTS OF A PROSPECTIVE MULTI-CENTER REGISTRY OF LOWER ESOPHAGEAL SPHINCTER STIMULATION FOR GERD: THE LESS-GERD REGISTRY
J. Labenz1, H. Schulz2, A. Leodolter3, J. Pedersen4, A. Nieponice5, R. Weise6, N. Canto7
1Abt. für Innere Medizin, Diakonische Klinikum Abt. für Innere Medizin, Siegen, Germany
2Evangelisches Krankenhaus Castrop-Rauxel, Castrop-Rauxel, Germany
3Evangelisches Krankenhaus Herne, Herne, Germany
4Aarhus University Hospital, Aarhus, Denmark
5Fundación Faravoldo, Buenos Aires, Argentina
6St. Marien-Hospital, Freiauht/germany
7Utrecht Research, Maastricht University Medical Center, Maastricht, Netherlands
Contact E-mail Address: jlabenz1@t-online.de

Introduction: Safety and effectiveness of electrical stimulation of the lower esophageal sphincter (LES-ES) using the Endostim® LES Stimulation System (The HRE Group) has been demonstrated in clinical trials. Limited data available on outcomes in clinical practice.

Aims & Methods: An ongoing, prospective international multicenter web-based registry is collecting data in patients with disruptive GERD symptoms treated with LES-ES in clinical practice at baseline and at routine follow-ups for 5-years. Demographics, adverse events, GERD symptoms recorded in daily diaries, GERD health related quality life scores (GERD-HRQL), structured GI symptom questionnaires for extra-esophageal symptoms, use of proton pump inhibitors (PPIs) and physiologica data (esophageal pH / manometry) are collected when available.

Result: Data was available in 50 patients enrolled in eleven sites with 6 months post-op follow ups from 28 patients with 12 months follow-up. Ninety-five (43/ 42%) patients showed improvement in their symptoms when comparing 6 months and 93% (25/27) showed an improvement at 12 months compared to baseline. The median (IQR) composite GERD-HRQL score improved from 22 (17-27) preoperatively to 8.0 (4.0-13.3) at 6-months (p < 0.001) and from 20.1 (15.0-26.0) at 12-months (p < 0.001). At baseline, 44% of patients were eligible for surgery (22/50) complained on daily bothersome heartburn symptoms affecting sleep which decreased to 8% (4/50) at 6 months (p < 0.001) and 0% (0/28) at 12 months (p < 0.001). At baseline, 52% and 15% of subjects reported moderate or severe heartburn, respectively which decreased to 22% and 7% at 6 months (n = 27) and 14% and 0% at 12 months (n = 14). Data on prior hospitalization due to GERD was available for 40 patients who had hospitalization data available for their 6 visit (±1m). Annualized hospitalization rates due to GERD decreased from 5.1 % (Endostim®) to 2.5% (Endostim®) at 12 years following surgery. Hospital admissions decreased to 0.3 days/year with 83% of patients who were required hospitalization pre-op reporting no hospitalization post-op. All patients were on long-term PPI on baseline. Seventy-one percent (45/63) patients at 6 month and 75% (27/36) patients at 12 months were completely off PPI. Data on 24h esophageal pH at 6 m showed a non-statistically significant improvement. Safety data was adjudicated by an independent DSMB. Four serious adverse events in the long-term follow-up were reported.
Conclusion: In our 16-year cohort with long-term surveillance, the incidence of PCL was low, mainly determined by small number of detected cancers but majority of detected cancers were asymptomatic and resectable. Surveillance also detects early stage PanNETs and HPCNs. The majority of detected proven malignancies had radiologic progression but more research is needed to improve the selection of patients for surveillance and surgery.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP330 CLINICAL IMPACT OF ENDOSCOPIC ULTRASOUNOGRAPHY IMAGING OF CHRONIC PANCREATITIS IN THE PANCREATIC PARENCHYMA IN PATIENTS WITH INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS (IPMNs)

M. Takenaka1, A. Masuda2, M. Kitano3, H. Shiomi4, S. Oomoto3, K. Minaga5, T. Miyata1, K. Kamata1, K. Yamao1, H. Imai1, Y. Arisaka1, Y. Okabe1, M. Kudo1
1Department Of Gastroenterology, Kinki University, Osaka-sayamaya/Japan
2Endoscopy, Kobe university, Kobe/Japan
3Gastroenterology & Hepatology, Kinki University, Osaka-sayamaya/Japan
4Gastroenterology, Kobe University Graduate School of Medicine, Kobe, Japan
5Gastroenterology, Kobe University, Kobe/Japan

Contact E-mail Address: mamosya55@gmail.com

Introduction: The recent guideline for intraductal papillary mucinous neoplasms (IPMNs) focuses on morphological features of the lesion as signs of malignant transformation, but ignores the background pancreatic parenchyma, including features of chronic pancreatitis, a risk factor for pancreatic malignancies. Endoscopic ultrasonography frequently reveals evidence of chronic pancreatitis (EUS-CP findings) in the background pancreatic parenchyma of patients with IPMNs. Therefore, we investigated whether background EUS-CP findings were associated with malignant IPMN.

Aims & Methods: Clinical data for 69 consecutive patients with IPMNs who underwent preoperative EUS and surgical resection between April 2010 and October 2014 were collected prospectively. The association of EUS-CP findings (total number of EUS-CP findings; 0 vs. ≥1) with invasive IPMN was examined. The association of EUS-CP findings with pathological changes of the background pancreatic parenchyma (atrophy/inflammation/fibrosis) was also examined.

Result: Among patients with EUS-CP findings, invasive intraductal papillary mucinous carcinoma (IPMC) was significantly more frequent than among patients without EUS-CP findings (42.5% (17/40) vs. 3.4% (1/29), p = 0.0002). In addition, patients with EUS-CP findings had higher grades of pancreatic atrophy and fibrosis than patients without EUS-CP findings (atrophy: 72.5% (29/40) vs. 34.5% (10/29), p = 0.003, inflammation: 45.0% (18/40) vs. 20.7% (6/29), p = 0.04).

Conclusion: In IPMN patients, detection of EUS-CP findings in the background pancreatic parenchyma was associated with a higher prevalence of invasive IPMC. Accordingly, EUS examination should not only assess the morphological features of the lesion itself, but also EUS-CP findings in the background parenchyma.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP331 NEEDLE-BASED CONFOCAL LASERENDOMICROSCOPY (nCLE) FOR THE DIAGNOSIS OF SOLITARY PANCREATIC CYSTS: A PROSPECTIVE MULTICENTER STUDY

B. Napoleon1, L. Palazzo2, B. Pujol3, F. Caillol3, M. Palazzo4, A. Aubert5, F. Maire6, A.I. Lemaistre7, M. Giovannini8
1Hôpital Privé Jean Mermoz, Lyon/Lyon, France
2Department Of Endoscopy, Trocadero Clinic, Paris/Paris, France
3Endoscopy, Institut Paoli Calmette, marseille/Paris, France
4Hôpital Beaujon, Clichy/Paris, France
5Hôpital Beaujon, Clichy/Paris
6Hopital Prive Jean Mermoz, Lyon/France
7Hôpital Beaujon, Clichy/Paris
8Centre Prive Jean Mermoz, Paris/Lyon, France

Contact E-mail Address: bertrand.napoleon@datrybox.com

Introduction: The diagnosis of solitary pancreatic cyst (SPC) is clinically challenging due to the malignant potential of several cyst subtypes. nCLE is emerging as a powerful technique which enables the observation of the inner wall of pancreatic cysts, in vivo and in real-time, during an endoscopic ultrasound-guided fine needle aspiration (EUS-FNA). Three clinical trials evaluated the feasibility, the safety and highlighted specific criteria for the characterization of pancreatic cystic lesions. This study aims to prospectively evaluate the diagnostic performance of nCLE procedure on a larger cohort of patients.

Aims & Methods: 217 patients carrying a single large (>2 cm) pancreatic cystic lesion (PCL) without evidence of communication with the main pancreatic duct and scheduled for EUS-FNA procedure were included in five centers. nCLE diagnosis was based on published criteria: “superficial vascular network” for Serum Cyst/Adenoma (SCA), “papillae” for Intraductal Papillary Mucinous Neoplasm (IPMN), “epithelial border” for Mucinous Cystic Neoplasms (MCN), “dark spots of cell aggregates surrounded by gray areas of fibrosis and vessels” for NeuroEndocrine Neoplasms (NEN).

Disclosure of Interest: None

References

OP332 RISK OF PROGRESSION AMONG LOW RISK IPMNS IN A LARGE MULTICENTER SURVEILLANCE COHORT STUDY

V. Gausman1, M. Moris2, M. Kayal3, J. M. Pomeroy4, A. Sethi5, F. G. Greese6, B. A. Schrope7, L. Luk8, E. Hecht9, M. B. Wallace10, T.A. Gonda11
1Internal Medicine, NYU - Langone Medical Center, New York/United States of America
2Division Of Gastroenterology And Hepatology, Mayo Clinic Jacksonville/United States of America/FL
3Division Of Digestive And Liver Diseases, Department Of Medicine, Columbia University, New York/United States of America/FL
4Division Of Digestive And Liver Diseases, Columbia University, New York/United States of America/FL
5Department Of Surgery, Columbia University, New York/United States of America/FL
6Department Of Radiology, Columbia University, New York/United States of America/FL
7Department Of Gastroenterology And Hepatology, Mayo Clinic Jacksonville/United States of America/FL

Contact E-mail Address: valerie.gausman@gmail.com

Introduction: Intraductal papillary mucinous neoplasms (IPMNs) are pancreatic cysts that carry a risk of malignant transformation to pancreatic ductal adenocarcinoma (PDAC). Guidelines have been evolving to best identify which criteria should qualify a patient for resection and which cysts can safely remain under surveillance. New data for nCLE are needed to improve the selection of patients for surveillance and surgery.

Disclosure of Interest: None
surveillance. Our aim was to understand which baseline cyst and patient features predict disease progression and malignant transformation.

Aims & Methods: Patients with clinically suspected IPMN who did not meet consensus criteria for resection at diagnosis and were surveyed for at least 12 months or underwent surgery after a minimum surveillance of 3 months were included. All patients evaluated by radiologic studies or endoscopic ultrasound between 1998 and 2015 were included. We defined progression as either an increase in size of the dominant cyst ≥20% or ≥2 mm or the development of worrisome features (mural nodule or mass, thick septations, main duct involvement or high grade dysplasia or cancer on cytology or surgical pathology). Statistical analysis was performed with the Chi square and Fisher exact tests for categorical variables and Mann-Whitney U test for continuous variables. All covariates of interest with p < 0.05 in the univariate analysis were included in the logistic regression model.

Result:

- **Aims & Methods:** We aimed to describe outcomes of multimodality treatment with chemotherapy, surgical exploration and IRE in a prospective consecutive LAPC-cohort. Patients with histologically proven LAPC (Dutch guideline: >90° arterial and/or >270° venous involvement) were prospectively registered (September 2013–March 2015). After 3 months of chemotherapy (FOLFIRINOX for WHO physical status 0–1 patients, otherwise gemcitabine), restaging was performed by assessing RECIST 1.1-response, resectability, and IRE-eligibility (tumor ≥5 cm, sufficient vascular patency). All patients with non-progressive disease, eligible for IRE proceeded to laparotomy, regardless of resectability. The study was registered with the Dutch trial registry NTR4230.

- **Conclusion:** Of 132 consecutive LAPC-patients, 93 (70%) received chemotherapy (59 FOLFIRINOX and irreversible electroporation (IRE) have shown promising survival-rates. However, outcomes are heavily influenced by selection bias as most studies were retrospective and excluded patients who did not receive FOLFIRINOX or had progressive disease.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**OP333 MULTIMODALITY TREATMENT OF LOCALLY ADVANCED PANCREATIC CANCER, INCLUDING FOLFIRINOX CHEMOTHERAPY, SURGICAL EXPLORATION AND IRREVERSIBLE ELECTROPORATION: PROSPECTIVE SERIES OF 132 CONSECUTIVE PATIENTS**

J. A. Anne Vogel1, S. J. Rombouts2, T. De Rooij3, O.R. c. Busch4, O. M. Van Delden5, M. G. Dijkgraaf6, J.E. Van Hoof7, H. W. Van Laarhoven7, R. C. Martin6, A. Schoorlemmer1, J. W. Wilmink1, K. P. Van Lienden1, M. G. h. Besselink1

1Surgery, Academic Medical Center, Amsterdam/Netherlands
2Radiology, Academic Medical Center, Amsterdam/Netherlands
3Research Unit, Academic Medical Center, Amsterdam/Netherlands
4Gastroenterology, Academic Medical Center, Amsterdam/Netherlands
5Medical Oncology, Academic Medical Center, Amsterdam/Netherlands
6Surgery, University of Louisville, Louisville/United States of America
7Medical Oncology, Academic Medical Center, Amsterdam/ Netherlands

Contact E-mail Address: j.a.vogel@amc.n

Introduction: Novel treatment options in locally advanced pancreatic cancer (LAPC), including FOLFIRINOX and irreversible electroporation (IRE) have shown promising survival-rates. However, outcomes are heavily influenced by selection bias as most studies were retrospective and excluded patients who did not receive FOLFIRINOX or had progressive disease.

Aims & Methods: We aimed to describe outcomes of multimodality treatment with chemotherapy, surgical exploration and IRE in a prospective consecutive LAPC-cohort. Patients with histologically proven LAPC (Dutch guideline: >90° arterial and/or >270° venous involvement) were prospectively registered (September 2013–March 2015). After 3 months of chemotherapy (FOLFIRINOX for WHO physical status 0–1 patients, otherwise gemcitabine), restaging was performed by assessing RECIST 1.1-response, resectability, and IRE-eligibility (tumor ≥5 cm, sufficient vascular patency). All patients with non-progressive disease, eligible for IRE proceeded to laparotomy, regardless of resectability. The study was registered with the Dutch trial registry NTR4230.

Result: Of 132 consecutive LAPC-patients, 93 (70%) received chemotherapy (59 FOLFIRINOX). After 3 months, 59 (45%) had non-progressive disease, eligible for IRE proceeded to laparotomy, regardless of resectability. The study was registered with the Dutch trial registry NTR4230.

Conclusion: This is the first prospective study on multimodality treatment, including FOLFIRINOX and IRE, in a consecutive LAPC-cohort. An 11% resection-rate with a median overall survival of 34 months seems highly promising where no clear survival benefit was seen after IRE. This study highlights the importance of reporting on unsselected LAPC-cohorts.

Disclosure of Interest: R.C. Martin: Prof. Dr. Marin is a paid consultant for AngioDynamics
K.P. van Lienden: Dr. Krijn van Lienden is a paid consultant for AngioDynamics
All other authors have declared no conflicts of interest.

*Statistically significant difference as compared to non-progressors. We identified 499 patients who met inclusion criteria. Average surveillance time was 47 (15–287) months. 251 (50%) patients showed progression: 205 (41%) progressed by size alone and 46 (9.2%) developed worrisome features. 55 (11%) met resection criteria and 21 of these went on to surgery. Pathology demonstrated 4 invasive carcinoma, 5 IPMN with high-grade dysplasia, 5 IPMN with low-grade dysplasia, 2 mucinous cystadenoma, 1 serous cystadenoma and 1 neuroendocrine tumor. We then compared predictors of progression. In a univariate analysis, progression to cancer or high-grade dysplasia was associated with male gender, a history of prostate cancer and diabetes, weight loss and initial cyst size ≥2 cm. A history of prostate cancer, diabetes, weight loss, elevated cyst fluid CEA and cyst size ≥2 cm were associated with development of worrisome features. In logistic regression analysis, a history of prostate cancer (OR 2.9; 95% CI 1.7–7.7) and weight loss (OR 2.47; 95% CI 1.18–6.1) were associated with development of worrisome features.*
Wireless telemetry system (telemetric probe was surgically implanted 6 weeks before balloon distension. VMR was recorded by electromyography (EMG) using a dye plasma extravasation (vascular permeability). The severity of tissue/rat were implanted around the mesenteric arteries adjacent to the cecum. The hypothesis in a rat model of endometriosis-induced vaginal hyperalgesia. This study shows that GC-C agonism, beyond its established effect of improving abdominal pain in IBS-C patients may also be able to alleviate pain in a spectrum of chronic pelvic pain conditions possibly through common sensory peripheral and central intraneuronal pathways.

Conclusion: Oral administration of linaclotide significantly reduced visceral pain in a mouse model of endometriosis-induced vaginal hyperalgesia. This study shows that GC-C agonism, beyond its established effect of improving abdominal pain in IBS-C patients may also be able to alleviate pain in a spectrum of chronic pelvic pain conditions possibly through common sensory peripheral and central intraneuronal pathways.

Disclosure of Interest: P. Ge: Employee, stock holder and stock options from Ironwood pharmaceuticals Inc.
C. Ren: Contractor at Ironwood Pharmaceuticals, Inc
N. Dmitrieva: Contractor at Ironwood Pharmaceuticals, Inc
A. Silos-Santiago: Employee, stock holder and stock options from Ironwood Pharmaceuticals Inc

Introduction: The Dutch Pancreatic Cancer Group (DPCG) aimed to develop an online expertpanel to facilitate and tailor rapid expert advice for patients with (locally advanced) pancreatic cancer. In collaboration with Aexist the Dutch Pancreatic Cancer Group (DPCG) aimed to develop an online expertpanel to facilitate and tailor rapid expert advice for patients with (locally advanced) pancreatic cancer. In collaboration with Aexist the Dutch Pancreatic Cancer Group (DPCG) aimed to develop an online expertpanel to facilitate and tailor rapid expert advice for patients with (locally advanced) pancreatic cancer.

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Contact E-mail Address: j.vanhilts@umcutrecht.nl

Disclosure of Interest: J. Van Hilst: Employee, stockholder and stock options from Ironwood pharmaceuticals Inc.
C. B. Kurtz: Employee, stockholder and stock options from Ironwood pharmaceuticals Inc.
G. Hannig: Employee, stockholder and stock options from Ironwood pharmaceuticals Inc.

Introduction: Linaclotide, a guanylate cyclase-C (GC-C) agonist, reduces abdominal pain and improves constipation in patients with Irritable Bowel Syndrome with Constipation (IBS-C). We have shown that linaclotide activates GC-C expressed on intestinal epithelial cells, resulting in the production and release of cyclic GMP (cGMP), which accelerates gastrointestinal transit and inhibits colonic mechanical hypersensitivity. These targets included GC-C (GUCY2C), its endogenous ligands (GUCA2A, GUCA2B), PDZ proteins regulating GC-C activity (PDZD3), GMP-dependent protein kinases (PRKG2), phosphodiesterases (PDE3A, PDE3B), components involved in ionic sequestration (PDZK1, SLC29A, SLC26A3, CTR), and transporters of GMP (ABCC1, ABCG2).

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Contact E-mail Address: ghannig@ironwoodpharma.com

Disclosure of Interest: Female Rome III IBS and CIC patients and healthy controls ages 18-75 yrs were recruited mainly by community advertising in the U.S. U.S. cohort of IBS patients, and 3) patients with chronic idiopathic constipation (CIC).

Aims & Methods: Female Rome III IBS and CIC patients and healthy controls ages 18-75 yrs were recruited mainly by community advertising in the U.S. U.S. cohort of IBS patients, and 3) patients with chronic idiopathic constipation (CIC).

Contact E-mail Address: pg@ironwoodpharma.com

Disclosure of Interest: In the locally acting guanylate cyclase-C agonist, is a FDA-approved guanylate cyclase-C (GC-C) agonist, for the treatment of Irritable Bowel Syndrome with Constipation (IBS-C) and Chronic Idiopathic Constipation (CIC). Linaclotide reverses colonic mechanical hypersensitivity in chronic colonic hypersensitive mice, and reduces nociceptive signaling in vivo to the spinal cord. Painful Bladder Syndrome/Interstitial Cystitis and Overactive Bladder are common comorbidities of IBS-C. Chronic oral administration of linaclotide in a mouse model of bladder overactivity reverses colitis-induced changes in bladder function by a proposed mechanism involving viscoso-visceral organ cross-talk. We hypothesized that linaclotide may be able to similarly reduce visceral pain in other chronic pelvic pain conditions, and tested this hypothesis in a rat model of endometriosis-induced vaginal hyperalgesia.

Contact E-mail Address: pg@ironwoodpharma.com

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OP337 PATIENTS’ PERCEPTIONS OF CONSTIPATION DIFFER STRIKINGLY FROM THOSE OF GASTROENTEROLOGY SPECIALISTS AND GENERAL PRACTITIONERS, AND THERE IS NO CONSISTENT AGREEMENT WITH THE ROME III CRITERIA

E. Dimidi1, D. Wang2, C. Cox1, S. Neville1, S. M. Scott1, K. Whelan1
1King’s College London, London/United Kingdom
2Liverpool School of Tropical Medicine, Liverpool/United Kingdom
3Queen Mary University London, London/United Kingdom
Contact E-mail Address: eirini.dimidi@kcl.ac.uk

Introduction: Constipation is a prevalent condition with a huge socioeconomic burden. It is unclear whether patients’ and doctors’ perceptions of the definition of constipation agree with each other or with formal diagnostic criteria proposed by expert committees (e.g. Rome III).

Aims & Methods: A cross-sectional survey was undertaken to compare the symptoms perceived to be important for the diagnosis of constipation within the adult general population (with and without constipation), gastrointestinal (GI) specialists (e.g. gastroenterologists, colorectal surgeons) and general practitioners (GPs) in the UK. Symptoms considered important in diagnosing constipation and their perceived burden, together with 10 case studies based on the Rome III criteria were investigated. Responses were compared between groups using chi squared tests.

Result: 2,257 members of the general population (1,623 self-reportedConstipation, 934 without), 365 GI specialists and 411 GPs completed the survey. Only a minority of the general population considered the Rome III symptoms important for diagnosing constipation (Table 1). Infrequent bowel movements were most frequently reported as important by GI specialists (65%), compared with less than half of GPs (41%) and less than a third of the constipated (26%) and non-constipated (57%) general population. The symptom most frequently reported as important for diagnosing constipation by the general population was hard stools (66%), whereas for GPs it was straining (40–43%).

Table 1: Frequency of symptoms perceived to be important for a diagnosis of constipation

<table>
<thead>
<tr>
<th>Rome III symptoms</th>
<th>General Population</th>
<th>Without GI constipation</th>
<th>Constipation specialists</th>
<th>GPs</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infrequent bowel movements</td>
<td>28%</td>
<td>26%</td>
<td>65%</td>
<td>41%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Hard stool</td>
<td>26%</td>
<td>32%</td>
<td>57%</td>
<td>66%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Straining</td>
<td>43%</td>
<td>40%</td>
<td>53%</td>
<td>61%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Sense of incomplete evacuation</td>
<td>15%</td>
<td>24%</td>
<td>21%</td>
<td>13%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Manual disinssion</td>
<td>14%</td>
<td>15%</td>
<td>32%</td>
<td>34%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Non-Rome III symptoms</td>
<td>42%</td>
<td>29%</td>
<td>33%</td>
<td>23%</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Laxative use</td>
<td>37%</td>
<td>33%</td>
<td>56%</td>
<td>40%</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

The symptoms most frequently considered to be bothersome were different for each of the groups: manual disinssion for the constipated general population, bloating for GI specialists and straining for GPs. In the 10 case studies, correct diagnoses were made by doctors (GPs and GI specialists) on 79–80% of occasions. However, on average, the absence of constipation was correctly identified by doctors in 85–92% of the six cases without constipation, whereas the presence of constipation was correctly identified in only 60–70% of the four cases with constipation.

Conclusion: There are striking differences in the perceived definition and burden of symptoms of constipation between the general population, GI specialists and GPs, and variable agreement with the Rome III criteria. These differences have major implications for patient care, management and satisfaction with treatment. The findings reinforce the need to re-evaluate current diagnostic criteria for constipation in clinical practice and to ensure these are communicated widely.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP338 EFFICACY AND SAFETY OFNALDEMINE FOR THE TREATMENT OF OPIOID-INDUCED CONSTIPATION IN SUBJECTS WITH CHRONIC NON-CANCER PAIN RECEIVING OPIOID THERAPY: RESULTS FROM TWO PHASE 3 CLINICAL TRIALS

M. E. Hale1, J. Wild2, J. Reddy3, T. Yamada3, J.C. Arjona Ferreira4
1Gold Coast Research, LLC, Plantation/United States of America/FL
2Upstate Clinical Research Associates, Williamsville/United States of America/NY
3Shionogi Inc., Florham Park/United States of America/NJ
Contact E-mail Address: goldcoast@HaleMD.com

Introduction: Opioids effectively treat pain but their use is limited by side effects including opioid-induced constipation (OIC). Naldemedine is an oral, peripherally-acting μ-opioid receptor antagonist that is being evaluated for the treatment of OIC.

Aims & Methods: Two identical Phase-3, double-blind, randomized, placebo-controlled 12-week studies were conducted. In both studies, subjects 18 to 80 years old, with chronic non-cancer pain and OIC, taking opioids for ≥3 months and on a stable regimen for ≥1 month, not on laxatives, and meeting all other eligibility criteria were randomized (1:1:1) to naldemedine 0.2 mg taken orally QD or placebo. The primary objective was to evaluate the efficacy of naldemedine vs. placebo as assessed by the proportion of responders. A responder was defined as someone who had ≥9 positive response weeks (PRW) out of 12 weeks and ≥3 PRW out of the last 4 weeks. A PRW was defined as ≥3 spontaneous bowel movements (SBMs)/week and ≥1 SBM/week increase from baseline. The safety and tolerability of naldemedine was also assessed. Studies were performed by an IRB prior to randomization of subjects and conducted in accordance with GCP Guideline (ClinicalTrials.gov identifier NCT01936518 and NCT01993940).

In Study 1, 547 subjects were randomized (naldemedine 274; placebo 273) and in Study 2, 553 subjects were randomized (naldemedine 277; placebo 276). In both studies, there were a significantly greater proportion of responders with naldemedine relative to placebo (Study 1: naldemedine 47.6%; placebo 34.6%, P < 0.0001; Study 2: naldemedine 52.5%; placebo 33.6%, P < 0.001). Treatment with naldemedine resulted in a greater increase, relative to the placebo group, from baseline to the last 2 weeks of the study period in the frequency of complete SBMs and the frequency of SBMs without straining. Summary measures of treatment-emergent adverse events (TEAEs) were generally similar between naldemedine and placebo groups in both studies. The TEAEs reporting a greater increase in the frequency of SBMs per week from baseline to Week 1 was observed with naldemedine relative to placebo and this difference remained generally stable between the two groups throughout the 12-week study period.

Conclusion: Naldemedine group also showed a greater increase, relative to the placebo group, from baseline to the last 2 weeks of the study period in the frequency of complete SBMs and the frequency of SBMs without straining. A responder was defined as someone who had ≥9 positive response weeks (PRW) out of 12 weeks and ≥3 PRW out of the last 4 weeks. Naldemedine treatment resulted in a significantly greater proportion of responders than placebo, with improvement early on and throughout the 12-week study period. Naldemedine was generally well tolerated in these two studies.

Disclosure of Interest: M.E. Hale: I was a Principle Investigator for the Clinical Trials, and a consultant for Shionogi. J. Wild: I was a Principal Investigator on Compesol trial and 2 I did receive a stipend from Shionogi for clinical study review. Otherwise I have no relationship with the company. J. Reddy: Employee of Shionogi. T. Yamada: Employee of Shionogi. J.C. Arjona Ferreira: Employee of Shionogi

OP339 PILOT STUDY COMPARING THREE METHODS OF SCREENING FOR FECAL INCONTINENCE

J. Busby-Whitehead1, W. E. Whitehead2, S. Heymen3, J. S. Kizer4, O. Palsson1, M. Simrén1
1Geriatric Medicine, University of North Carolina, Chapel Hill/United States of America/NC
2Oncology and Functional GI And Motility Disorders, University of North Carolina, Chapel Hill/United States of America/NC
3Uc Center For Functional GI And Motility Disorders, University of North Carolina at Chapel Hill, Chapel Hill/United States of America/NC
4Geriatric Medicine, University of North Carolina at Chapel Hill, Chapel Hill, NC/United States of America
5Dept Of Internal Medicine, Sahlgrenska University Hospital, Gothenburg/Sweden
Contact E-mail Address: william_whitehead@med.unc.edu

Introduction: Fecal incontinence (FI) affects 8% of US adults overall including 15% over age 70. However, less than 1/3 of people with FI have discussed this problem with their physicians, and most of these report that they think they were not screened but volunteered this symptom. This suggests many physicians are not screening for FI.

Aims & Methods: The goal of this study was to provide preliminary information on the effectiveness of 3 simple screening interventions for increasing screening rates in a Geriatric Medicine Clinic (GMC) at the University of North Carolina: a gastrointestinal (GI) symptom checklist distributed in the clinic waiting room, screening by the clinic nurse, and screening by the medical provider. The GI symptom checklist included fecal incontinence [accidental bowel leakage] and 7 other common GI symptoms. Patients checked all they had experienced in the last month, and gave the checklist to the clinic nurse. To facilitate screening by 1 was observed with naldemedine relative to placebo and this difference remained generally stable between the two groups throughout the 12-week study period. Conclusion: Results from two independently designed Phase 3 studies demonstrated a consistent efficacy and safety profile of naldemedine as a treatment for OIC in subjects with chronic non-cancer pain. Naldemedine treatment resulted in a significantly greater proportion of responders than placebo, with improvement early on and throughout the 12-week study period. Naldemedine was generally well tolerated in these two studies.

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providers and nurses a modified Fecal Incontinence Severity Inventory (FISI) to help decide whether or not they felt was severe enough to warrant referral to a specialist, and instructions on how to refer to the GI Medicine Clinic. All patients attending the GMC during 4 two-week periods were considered subjects. After an initial two-week baseline, all patients were exposed to the screening methods in the same sequence for two weeks each: GI symptom checklist, provider screening, and nurse screening. Three types of outcome data were collected: (1) A limited review of electronic medical records of all patients seen during these 4 two-week periods was used to identify the number of new FI diagnoses during these 4 periods. (2) Following the last screening intervention, all clinic providers rated the effort required by each intervention and indicated whether they believed the benefit outweighed the burden. (3) Telephone interviews were conducted 2–4 weeks after the index clinic visit to determine what proportion of patients had been screened during their clinic visit. A p-value of <.10 accepted as significant in this small pilot study.

Conclusion: Systematically encouraging geriatric medicine providers to screen for FI significantly increased the number of patients receiving a new diagnosis of FI compared to baseline geriatric medicine practice, the benefits outweighing the burden. Distributing a GI symptom checklist in the clinic was rated least burdensome and was as effective as direct screening by the geriatrician. However, these interventions to improve screening were only partially effective: 37.5% of patients remained who were not asked about FI at their clinic visit.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP540 COPING WITH FECAL INCONTINENCE: A POPULATION STUDY
E.V. Carrington1, O. Palsson2, S. Heym3n, S. Gould4, M. Simr3en, W. E. Whitehead6
1Gastroenterology & Hepatology, University of North Carolina, Chapel Hill/United States of America/NC
2UNC Center For Functional GI And Motility Disorders, University of North Carolina at Chapel Hill, Chapel Hill/United States of America/NC
3Emergency Surgery Department, Northwick Park Hospital, Harrow/United Kingdom
4Center For Functional GI And Motility Disorders, University of North Carolina, Chapel Hill/United States of America/NC

Contact E-mail Address: emma.v.carrington@gmail.com

Introduction: Fecal incontinence (FI) is a common and devastating condition that affects many individuals in all stages of life. Many individuals suffer in silence and population surveys report that fewer than 30% of those affected consult a physician. Little is known about how people prevent or cope with symptoms in the community.

Aims / Methods: This study aimed to describe the most common coping strategies, the impact of FI severity on ways of coping, whether those under a physician’s care cope differently and the perceived overall effectiveness of individuals’ coping efforts. A 54-question survey was designed and distributed online (Qualtrics, UT, USA) to individuals in the US general population in March 2016. The number of strategies used was significantly related to FI symptom severity (2.69 for those with mild, 3.32 for non-consulters vs. 4.28 for consulters, p = .013). Number of new diagnoses occurred during the GI checklist intervention and 3 during provider screening (p < .10). None occurred during nurse screening. The GI symptom checklist was rated the least burdensome by the 11 providers (p = .09). Five of the providers said the benefits of screening outweighed the burden, 4 were undecided, and 2 rated screening as too burdensome (p = .001). Phone interviews were completed by 88 patients: 33/88 (37.5%) confirmed they were screened by their doctor or nurse, 55.7% said no, and 6.8% said they did not know or declined to answer.

Result: 1034 unique patients were seen during the 4 two-week periods: 60 had a diagnosis of FI somewhere in their medical record, and 24 had a diagnosis of FI at the index clinic study, including 6 new FI diagnoses. Three of the 6 new diagnoses occurred during the GI checklist intervention and 3 during provider screening (p < .10). None occurred during nurse screening. The GI symptom checklist was rated the least burdensome and was as effective at not screening the geriatrician. However, these interventions to improve screening were only partially effective: 37.5% of patients remained who were not asked about FI at their clinic visit.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP541 NOVEL ENDOLOOP VS. OVER-THE-SCOPE-CLIP (OTSC) IN ENDOSCOPIC CLOSURE OF GASTRIC FULL-THICKNESS DEFECT: A MULTI-CENTER STUDY
N. Gao, R. Li, D. Shi, D. Zhang, W. Chen
Department of Gastroenterology, First Affiliated Hospital of Soochow University, Suzhou, Jiangsu, China, Suzhou/China

Contact E-mail Address: lrhcsz@163.com

Introduction: Endoscopic full-thickness resection (EFTR) of the gastric lesion using a snaring technique has been applied for gastric subepithelial tumors. We identified criteria for the use of a novel type of nylon loop device vs. traditional ‘Over the scope’-clip (OTSC) for containing submucosal lesions. Aims & Methods: One hundred and twenty-eight patients with submucosal tumors in gastric fundus were randomly divided into two groups, study group with 56 patients and control group with 72 patients, all patients were treated with endoscopic full-thickness resection. After the resection, novel LeCampTM endo-device and OTSC were used respectively to close the gastric defects in the study group and control group. The closure success rate, closure time, complications and the wound-healing rate were compared.

Result: All lesions were removed by using EFTR technique. The closure success rates of the two groups were both 100%. Of the total of 128 patients, 3 during nurse screening. The GI symptom checklist was rated the least burdensome and was as effective at not screening the geriatrician. However, these interventions to improve screening were only partially effective: 37.5% of patients remained who were not asked about FI at their clinic visit.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016
08:30-10:00
NEW INSIGHTS IN UPPER GI ENDOSCOPY TECHNIQUES – ROOM LT_2

OP541 NOVEL ENDOLOOP VS. OVER-THE-SCOPE-CLIP (OTSC) IN ENDOSCOPIC CLOSURE OF GASTRIC FULL-THICKNESS DEFECT: A MULTI-CENTER STUDY
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Disclosure of Interest: All authors have declared no conflicts of interest.

References


**OP34 ENDOSCOPIC SUBMUCOSAL DISSECTION FOR DUODENAL ADENOMA: COMPLICATION RATE AND FOLLOW UP OF 38 CASES**

W. Margos1, H. Ivekovic2, R.C.P. Yeung3, L. Shaza4, H. Piessevaux1, P. Deprez1

1 Department of Hepato-gastroenterology, Cliniques Universitaries Saint-Luc, Brussels, Belgium, Jannesibelgium
2 Gastroenterology And Hepatology, University Hospital Centre Zagreb, Zagreb/Croatia
3 Gastroenterology, Clin U St. Luc, Universite Catholique Louvain, Montreux/Belgium
4 University Hospital Saint-Luc, Brussels/Belgium
5 Digestive Endoscopy Unit, Cliniques Universitaires Saint-Luc, Overijse/Belgium
6 Dept. De Hepato-gastroenterologie, Cliniques Universite Saint-Louis de Louvain, Brussels/Belgium

Contact E-mail Address: walter.margos@uclouvain.be

Introduction: Endoscopic mucosal resection (EMR) and endoscopic submucosal dissection (ESD) are used for endoscopic treatment of superficial duodenal adenoma (not fulfilling the criteria of a same lesion: hybrid Endoscopic Resection, HER). ESD has higher rates of complications than EMR, and is technically challenging. We present results on the adverse events and clinical outcome of ESD/HER compared to EMR in our cohort of patients.

**Aims & Methods:** In a single tertiary center, we cross-examined our database of endoscopic procedures to identify patients with duodenal adenoma treated by ESD, HER and EMR between 2006 and 2016. We included patients with non-ampullary lesions and familial adenomatous polyposis. Procedure was qualified as ESD when an endoscopic knife was used. When resection was achieved with endoscopic knife and resection loop, the procedure was considered as HER. We divided complications in 3 groups (ASGE and ESGE recommendations): intra-procedural, early complications (occurring within 15 days) and late complications (occurring after 15 days).

**Results:** Thirty-eight patients underwent ESD/HER procedure out of a total of 111 patients. The resection was complete in 38/39 lesions in ESD/HER group, and 141/149 lesions in EMR group (p=0.182). Histological finding showed 45% adenocarcinomas, 34% HGD, and 60% LGD. No significant differences were observed in terms of age, sex, location of lesions or length of hospitalization.

**Discussion:** There were significant differences in the procedure time (108 min ESD/HER, 141/149 lesions in EMR group (p=0.011), including significant in case of APC and EBL separately. Although EBL may seem to be superior to APC in terms of the number of gas flow settings. In case of EBL, 5–6 ligation bands were applied per treatment session. The average follow-up period was 18.3 months.

**Results:** A total of 34 patients with GAVE were treated with either APC or EBL at one of the four centres involved throughout the study period. 26 patients presented with diffuse and 8 with linear type of GAVE. Occult gastrointestinal bleeding was present in 25, acute in 15, and both acute and occult in 5 patients. Both acute and occult gastrointestinal bleeding was present in 6 cases. 22 patients were treated with APC and 12 with EBL. Both treatment methods increased haemoglobin levels and decreased transfusion need significantly (3.0 g/dl and —2.11 blood units in APC and 2.14g/dl and —1.08 blood units in EBL). There was a need for blood transfusions ceased totally in 18 patients after the endoscopic resolution of the lesions. Significantly less transfusion sessions were required in case of EBL compared to APC (1.50 vs. 5.23, p=0.011), with a longer interval between each session (4.50 vs. 2.69 months, p=0.480). On the other hand, APC resulted in a higher increase in haemoglobin levels (3.37 g/dl vs. 2.36 g/dl, p=0.213) and a higher decrease in the need for blood transfusion (10.41 vs. 7.78 units, p=0.566), although the differences were not significant. In case of APC, fewer treatments (4.25) and hospitalizations (2.35) were needed, and higher increase in haemoglobin level per treatment session (0.76 g/dl) could be observed with the 50 W power setting compared to the 30 W and 70 W setting (number of treatments: 12.5 and 6.1; hospitalizations: 2.5 and 4.6; and increase in haemoglobin level/treatment session: 0.38 g/dl and 0.46 g/dl), although the small case number was a severe limiting factor. Generally, more treatment sessions were required for the endoscopic resolution of GAVE lesions compared to the one needed for the endoscopic resolution of GAVE in EBL, but the difference was not significant in case of APC and EBL separately.

**Conclusion:** Both APC and EBL are effective in the treatment of GAVE. Although EBL may seem to be superior to APC in terms of the number of treatment sessions and hospitalizations, no significant difference was found in the extent to which the two methods influence the haemoglobin level and transfusion need. Optimizing APC setups may also improve the performance and efficacy. There is a pressing need for further prospective studies with homogeneous large case number to establish recommendations about the endoscopic treatment of GAVE.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

References


OP544 WATERJET SUBMUCOSAL DISSECTION OF PORCINE ESOPHAGUS WITH THE HYBRIDKINE® AND ERBEJET® 2 SYSTEM

D. Akutsu1, H. Suzuki1, T. Narasaki1, M. Terasaki1, T. Kaneko1, H. Matsu1, Y. Mizokami2, I. Hyodo1
1Department Of Gastroenterology, University of Tsukuba, Tsukuba/Japan
2Division Of Endoscopy, University of Tsukuba Hospital, Tsukuba/Japan

Contact E-mail Address: dakutsu11@yahoo.co.jp

Introduction: Waterjet submucosal dissection (ESD) is technically difficult because of narrow working spaces and ease of perforation due to the lack of serosa. HybridKnife® is a recently developed ESD device that is combined with the high-pressure waterjet ERBEJET® 2 system to lift mucosa. We hypothesized that this waterjet could make submucosal dissection safer and studied this in porcine esophagus.

Aims & Methods: Water pressures of 30-70 bar were tested to determine the appropriate waterjet ESD with HybridKnife® (WJ-ESD) pressure in one pig. We compared the ESD completion rate and the number of serosa perforation (SOPH). After 3. Finally, submucosal dissection was performed using both methods in 2 pigs, and the dissection speeds, morbidity, and post-ESD stricture rate were compared.

Conclusion: WJ-ESD spent longer dissection time, but damaged less muscle layer. It can be combined with electrosurgery ESD.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

OP546 ORAL ADMINISTRATION OF CONDITIONED MEDIUM OBTAINED FROM AMNION-DERIVED MESCENHYAL STEM CELL CULTURE PREVENTS ESOPHAGEAL STRICATURE AFTER ENDOSCOPIC SUBMUCOSAL DISSECTION IN PIGS

T. Mizushima, S. Ohnishi, H. Hosono, M. Tsuda, N. Sakamoto
Gastroenterology And Hepatology, Hokkaido University Graduate School of Medicine, Sapporo/Japan

Contact E-mail Address: mizu@gc4.so-net.ne.jp

Introduction: Endoscopic submucosal dissection (ESD) for esophageal cancer has been widely accepted in last decade; however, it often causes postoperative stricture when over three-quarters of the circumference of the esophagus is dissected, and lowers quality of life for patients. Although steroid is generally used to prevent stricture by ex vivo anti-inflammatory mechanism, and side effects are of concern. Mesenchymal stem cells (MSCs) have been reported to be a valuable cell source in regenerative medicine, and large amounts of MSCs can be noninvasively isolated from human amnion, which is discarded after delivery. Moreover, conditional medium (CM) obtained from MSCs has been reported to have anti-inflammatory and anti-fibrotic effects in several animal models. In this study, we evaluated whether CM obtained from amnion MSC culture could prevent the stricture after large esophageal ESD in pigs. We hypothesized that CM would suppress cell proliferation and collagen synthesis, reduce the rate of stricture formation and for histological analysis of organizing fibrous tissue and muscle fiber atrophy (masson-trichrome staining), re-epithelialization (p63 and Ki-67), the number of activated myofibroblasts (α-SMA), capillary density (CD31), infiltration of macrophages (CD107a) and neutrophils (myeloperoxidase). The experimental protocol was approved by the Animal Care and Use Committees of Hokkaido University.

Aims & Methods: We randomly assigned 30 pigs to 3 groups: each of 3 virtual esophageal lesions in 2 pigs were resected alternatively using both methods from the lower to upper esophagus. For WJ-ESD, the submucosa, except for hard fibrous tissue, was dissected using water pressure alone.

Results: Using 50 bar of water pressure resulted in the best balance between dissection speed and view-disturbing water buckflow. The dissection speeds for the lower, middle, and upper esophagus were 0.2, 0.9, and 0.2 cm/min in 50 bar WJ-ESD and 1.1, 0.5, and 1.0 cm/min in C-ESD, respectively. Minor bleeding was frequent in WJ-ESD, but was easily stopped by electrocoagulation with the same needle. No perforation was observed in either group. Thermal damage of dissection was mild, and the extent of muscle injury was smaller for WJ-ESD (4, 6, and 8%) compared with C-ESD (14, 16, and 7%).

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
of 69% for lymph node involvement when restaging, inferior to what was found for EUS and for the initial staging (p < 0.0001).

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### Conclusion

Our results, obtained from a real clinical practice, showed that the overall accuracies of EUS and PET-CT for preoperative N staging were 76.2% and 72.5%, with significant differences between both techniques. The overall accuracy of EUS for T staging was 78% and 80.2% for restaging. More importantly, our results show a significant advantage of EUS over PET-CT in restaging, even in our series, in which the vast majority of suspicious lymph nodes were not sampled. In conclusion, EUS performance in gastric cancer N staging and restaging is better than PET-CT. Both procedures showed suboptimal accuracies when considered alone, and more than one single staging method should be used.

### Disclosure of Interest

All authors have declared no conflicts of interest.

### References


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### OP348 SORTILIN DEFICIENCY REDUCES DUCTULAR REACTION, HEPATOCELLULAR APOPTOSIS AND LIVER FIBROSIS IN CHOLESTATIC-INDUCED LIVER INJURY

**L. Zhreb1, E. Hubel2, S. Fishman3, O. Shibole4**

1Gastroenterology, Tel Aviv Sourasky Medical center, Tel Aviv/Israel
2Gastroenterology, Tel Aviv Sourasky Medical Center, Tel Aviv/Israel

**Contact Email Address:** isab@tlvmc.gov.il

Introduction: Sortilin, a member of the Vps10 domain receptor family, traffics newly synthesized proteins from the trans-Golgi network to secretory pathways, endosomes or to the cell surface. Sortilin trafficked molecules, including acid sphingomyelinase (aSMase), cathepsins and IL-6, mediate activation of hepatic stellate cells (HSC), hepatocyte apoptosis, cholangiocyte proliferation and liver inflammation and fibrosis.

Aims & Methods: We investigated sortilin role in the development of biliary damage leading to hepatocellular injury and fibrosis, based on its regulation of aSMase trafficking and on its involvement in IL-6 secretion. Cholestatic injury was induced in wild type (WT) and Sortilin−/− mice by bile duct ligation (BDL). Fibrosis was induced both by BDL and by administration of CCL4. Liver inflammation and cholangioendothelial activation and proliferation were assessed by qRT-PCR for inflammatory cytokines and by immunohistochemistry with Ki67 (marker of proliferation) and with Ly6G (neutrophil marker). Liver damage and hepatocyte apoptosis were determined by serum liver enzymes and by TUNEL assay. Liver fibrosis was assessed by Sirius Red staining quantitation and by qRT-PCR for fibrotic markers. ASMAse activity was inhibited in vivo by amitriptyline administration. IL-6 effect was neutralized by administration of an anti-IL-6 antibody to WT mice or BDL.

Results: Sortilin−/− mice displayed strongly attenuated liver fibrosis following BDL and CCL4 treatment, accompanied by an attenuated in vitro activation phenotype of Sortilin−/− HSC. Reduced Sortilin−/− hepatic aSMase activity was in line with reduced hepatocyte apoptosis following BDL and CCL4 injury and reduced susceptibility of hepatocytes from Sortilin−/− mice to bile acid-induced apoptosis in vitro. The role of ASMAse in hepatocyte apoptosis was further demonstrated using in vivo pharmacological inhibition of ASMAse activity after BDL. Strikingly, Sortilin−/− mice displayed impaired inflammation and ductular reaction three days after BDL, demonstrated by reduced reactive cholangiocytes, reduced cholangioendothelial proliferation and accompanied by reduced serum IL-6. Shown was treatment of bile duct ligated WT mice with a neutralizing antibody to IL-6 attenuated hepatic inflammation and expression of reactive cholangioendothelial markers and chemokines.

Conclusion: Sortilin mediates cholestatic liver damage and fibrosis via its effects on ASMAse activity and signaling.

Disclosure of Interest: All authors have declared no conflicts of interest.

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### OP349 ACTIVATION OF NECROPTOSIS IN HUMAN AND EXPERIMENTAL CHOLESTASIS

**M.B. Afonso1, P. M. Rodrigues1, A. Simo1, H. Cortez-Pinto1, D. Olengeim2, J. D. Amaral3, R. E. Castro1, J. Yuan1, C. M. P. Rodrigues1**

1Medicina, Faculdade de Ciências da Universidade de Lisboa, Lisbon/Portugal
2Gastroenterology, Hospital Santa Maria, Lisbon/Portugal
3Department Of Cell Biology, Harvard Medical School, Boston/United States of America/M.A
4Department Of Cell Biology, Harvard Medical School, Boston/United States of America/M.A

**Contact Email Address:** mbafonso@hul.harvard.edu

Introduction: Targeting necroptosis, a programmed necrotic cell death pathway regulated by receptor-interacting protein 3 (RIP3), is being considered as a promising therapeutic strategy for the treatment of liver diseases. In this study, we aimed to characterize human HPCs in order to understand the molecular mechanisms underlying their activation and differentiation, with the ultimate goal of using HPCs for the treatment of liver diseases.

Aims: Our results indicate that gene signatures of human HPCs are enriched in pathways already known to be involved in HPC activation in human and in animal models, but we also identify previously unknown pathways like TNF, IL17A and ErbB signaling pathways. Comparison of the 3 isolation methods sheds light on the possible existence of different HPC populations existing in the human liver. The isolated HPC populations will be used to further characterize human HPCs and to understand the molecular mechanisms underlying their activation and differentiation, with the ultimate goal of using HPCs for the treatment of liver diseases.

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: Freshly isolated HPC fractions showed an enrichment and activation of known HPC pathways like TNF, IL17A and ErbB signaling pathways. Matrix correlation of the different isolation methods indicates some slight differences between the different HPC populations, e.g. the ErbB signaling pathway is activated in the TROP-2 positive cells while this is not the case in the EpCAM-positive or SP cell populations.

References:


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### OP347 CHARACTERISATION OF DIFFERENTLY ISOLATED HEPATIC PROGENITOR CELL POPULATIONS IN HUMAN ALCOHOLIC LIVER

**A. Ceulemans1, S. Verhulst2, L. A. Van Grunsven2, T. Roskams1**

1Department Of Imaging & Pathology, Translational Cell & Tissue Research, KU Leuven, Leuven/Belgium
2Department Of Basic Biomedical Sciences, Liver Cell Biology Lab, Vrije Universiteit Brussel, Brussels/Belgium

**Contact E-mail Address:** a.ceulemans@kuleuven.be

Introduction: Hepatic progenitor cells (HPCs) are small cells with a relative large oval nucleus and a scanty cytoplasm situated in the canals of Hering. Phenotypically, HPCs express both markers of (immature) hepatocytes (e.g. a-fetoprotein) and markers of cholangiocytes (e.g. cytokeratin K7 and K19). The mechanisms facilitating proliferation and differentiation of human HPCs are still poorly understood.

Aims & Methods: In this study, we aimed to characterize human HPCs in order to use them as a potential incessant source of cells for cellular transplantation or to control their activation and differentiation in vivo in chronic liver diseases. Therefore we isolated and compared, on both protein and RNA level, HPC-enriched cell populations from adult human liver tissue using different isolation methods: side population (SP), TROP-2 and EpCAM-based cell sorting. Fresh human liver tissue was collected from allogeneic therapeutic explants, and HPC-enriched cells were obtained via three different isolation methods. A first method is the SP which is based on the efflux capacities of the progenitor cells of the fluorescent DNA binding dye Hoechst-33342.
of necrosis in the pathogenesis of cholestatic liver injury has been poorly explored.

Aims & Methods: We aimed to evaluate the role of necroptosis in patients with primary biliary cirrhosis (PBC), a cholestatic chronic liver disease, and in mice after common bile duct ligation (BDL), a classic experimental model of acute cholestasis and secondary biliary fibrosis. Thioflavin T staining and immunohistochemistry of RIP3 and its target phosphorylated-mixed lineage kinase domain-like protein (p-MLKL) were performed in liver biopsies of patients with PBC and healthy controls. C57BL/6N wild-type (WT) or RIP3-deficient (RIP3−/−) mice were used for experiments. The CCL4-induced model of chronic liver inflammation was used. Histological and biochemical analyses of hepatic damage were performed.

Result: In PBC patients, expression of RIP3 and MLKL was significantly increased compared to controls. However, in liver tissues from RIP3−/− mice, the expression of RIP3 and MLKL was reduced. Additionally, the liver tissue from RIP3−/− mice showed less necroptotic cells, with reduced thioflavin T staining and decreased apoptosis compared to WT mice.

Conclusion: These findings suggest that RIP3 is involved in the pathogenesis of cholestatic liver injury. Targeting RIP3 may be a potential therapeutic strategy to attenuate hepatic necroinflammation in BDL-induced cholestasis. Further studies are needed to confirm these findings and explore the role of RIP3 in other models of liver disease.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:

OP350 HEPATOMA-INTRINSIC CCRK SIGNALING PROMOTES IMMUNOSUPPRESSIVE TUMOR MICROENVIRONMENT BY REGULATING MYELOID-DERIVED SUPPRESSOR CELL ACCUMULATION

A.S.L. Cheng 1, J. Zhou 1, M. Lau 2, H. Sun 2, Z. Chen 3
1School Of Biomedical Sciences, Chinese University of Hong Kong, Hong Kong
2Hong Kong PRC
3Department Of Medicine And Therapeutics, Chinese University of Hong Kong, Hong Kong/Hong Kong PRC

Contact E-mail Address: alfredcheng@cuhk.edu.hk

Introduction: Myeloid-derived suppressor cells (MDSCs) comprise a heterogeneous population of immature myeloid cells that induces the exhaustion of activated T cells. The accumulation of CD33+CD11b+HLA-DR-MDSCs in circulation is closely correlated with the development of tumor microenvironment and immunosuppression. The CCRK-induced MDSCs possess immune suppressive functions by inhibiting T cell proliferation and interferon-gamma production.

Result: The co-expression of CD33+CD11b+HLA-DR-MDSCs was significantly increased in the CCRK-treated group compared to the control group. The CCRK-induced MDSCs were associated with the accumulation of IL-6 and IL-10, which are known to suppress immune responses.

Conclusion: The CCRK-induced MDSCs may represent a potential therapeutic target to combat immune suppression in cancer patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References:
to liver injury and fibrosis suggesting the beneficial role of intestinal microbiota in preventing diseases. 

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP525 IMPROVING METABOLIC PARAMETERS IN NAFLD BY TARGETING NUCLEAR RECEPTORS
P.M. Rodrigues1, M.B. Afonso1, A. Simão1, M. Cardade1, C. C. Carvalho2, A. Trindade1, A. Duarte3, P. M. Borrrolho1, M. V. Machado1, H. Cortez-Pinto1, C. M. Rodrigues1, R. E. Castro1
1Research Institute for Health Sciences (InMed/U.Portugal), Faculty of Pharmacy, Universidade de Lisboa, Lisbon/Portugal
2Reproduction and Development, Interdisciplinary Centre of Research in Animal Health (CIHSA), Faculty of Veterinary Medicine, Universidade de Lisboa, Lisbon/Portugal
3Gulbenkian Institute of Science, Oeiras/Portugal
4Gastroenterology, Hospital Santa Maria, Lisbon/Portugal
5Gastroenterology, Hospital Santa Maria, Lisbon/Portugal

Contact E-mail Address: pmvrodriigues@ff.ul.pt

Introduction: Non-alcoholic fatty liver disease (NAFLD) pathogenesis and treatment remain unsolved. microRNAs and bile acids were recently suggested to participate in disease pathogenesis and, as such, constitute potential therapeutic tools and targets. Moreover, nuclear receptors, namely peroxisome proliferator-activated receptors (PPARs) and their key target transcription factors, are currently under scrutiny as modulators of lipid and glucose metabolism in non-alcoholic steatohepatitis (NASH).

Aims & Methods: We aimed to elucidate the role of the miR-21/PPar pathway in liver and muscle tissues of murine NASH models and ascertain the therapeutic potential of miR-21 abrogation alone or in combination with obestatic acid (OCA).

Wild-type (WT) and miR-21 KO mice were fed with chow (n = 10) or methionine and choline-deficient (MCD; n = 10) diets for 2 and 8 weeks. Alternatively, mice were fed either chow (n = 12) or fast food diet (FF; n = 12) for 25 weeks. Six animals from each group had their diet supplemented with OCA 10 mg/kg/day (Intercept Pharmaceuticals, Inc.). Human liver biopsies were obtained from morbid obese NAFLD patients (n = 28). Liver/muscle sample RNA was isolated for historical analysis and assessment of miR-21, pro-inflammatory/pro-fibrogenic cytokines, PPARa and metabolic relevant genes, by qRT-PCR and immunoblotting. A Tagman® Array was performed to evaluate modulation of lipid regulated genes. ROS levels were analysed through the use of 2’,7’-dichlorodihydrofluorescein diacetate.

Results: WT mice fed with the MCD diet developed steatohepatitis and fibrosis, displaying increased levels of apoptosis, necroptosis and serum ALT and AST. In contrast, miR-21 KO mice displayed a significant decrease in steatosis severity, liver/spleen weight and fibrosis. WT and KO mice develop neutrophilic neutrophilic hepatitis, macrovesicular steatosis, inflammatory infiltrates and increased oxidative stress. miR-21 levels were increased in WT FF-fed mice, in both liver and muscle, concomitantly with decreased expression of PPARa, a key pro-inflammatory/pro-fibrogenic cytokine, and its target genes, TLR2 and miR-21. Furthermore, WT FF+OCA-fed mice exhibited decreased steatosis and miR-21 expression, compared with WT FF-fed mice. Importantly, KO FF+OCA-fed mice exhibited significant reductions in inflammation, oxidative stress and steatosis, in parallel with increased expression of PPARa and its metabolic targets, including CPT-1 and ACOX2. Finally, lipid regulated genes such as ACAT1, ALOX5 and FABP5 were found to be severely deregulated in WT FF-fed mice and reverted to control levels in KO FF+OCA-fed mice.

Conclusion: In conclusion, activation of PPARa as a result of miR-21 abrogation, together with FXR activation by OCA, significantly improves metabolic parameters in NASH, highlighting the therapeutic potential of multi-targeting therapy for NAFLD. (Supported by PTDC/BIM-MEC/0873/2012, SFRH/BD/88212/2012, FCT, Portugal).

Disclosure of Interest: All authors have declared no conflicts of interest.

OP535 TOLL LIKE RECEPTOR 2 MODULATES THE INHIBITORY MOTOR RESPONSE INDUCED BY HYDROGEN SULPHIDE IN MOUSE COLON
R. Force Garcia1, E. Layunta1, J. Pardo1, J.E. Mesonero1, L. Grasa2
1Pharmacology And Physiology Department, University of Zaragoza, Zaragoza/Spain
2Biochemistry And Molecular And Cellular Biology Department, University of Zaragoza, Zaragoza/Spain

Contact E-mail Address: r.force.garcia90@gmail.com

Introduction: The recognition of intestinal microbiota is in part carried out by Toll-like receptors (TLR), which are responsible for initiating the innate immune response. Alterations in the intestinal microbiota and its recognition may contribute to the development of intestinal inflammatory pathologies. Otherwise, hydrogen sulphide (H2S) is an endogenous gaseous signalling molecule and it potentially plays a relevant role in the intestinal motility. In mammals, two pyridoxal phosphate-dependent enzymes are responsible for H2S synthesis: cystathionine β-synthase (CBS) and cystathionine γ-lyase (CSE).

Aims & Methods: The aim of our current work was to investigate the influence of TLR2 on the motor response induced by H2S and the enzymes responsible for H2S synthesis (CBS and CSE) in mouse colon. In this study, we addressed how presence of the altered-function PTPN22 variant in PTPN22 affects colitis development. This helps to explain why this variant is associated with a reduced risk for CD onset, although it increases the risk to develop classical autoimmune disorders.

Disclosure of Interest: All authors have declared no conflicts of interest.
regulates the expression of CBS and modulates the inhibitory motor response induced by DPP IV (1). Inhibition of DPP IV activity of EMDB-1 was investigated in the model of acute and semi-chronic colitis induced by trinitrobenzenesulfonic acid (TNBS). Body weight, macroscopic score, ulcer score, colon length and thickness, as well as myeloperoxidase (MPO) activity were recorded. In addition, TNBS was used to induce acute and semi-chronic TNBS-induced colitis in mice in a dose-dependent manner, as indicated by significantly reduced macroscopic parameters and MPO activity. Anti-inflammatory effect of EMDB-1 was not blocked by naltrexone, thus the opioid receptors were not involved in the mechanism of action.

Conclusion: EMDB-1 is a potent inhibitor of DPP IV in vitro and exhibits substantial anti-inflammatory activity in the GI tract in vivo. Results of this study validate the EMDB-1 backbone for further development of peptide DPP IV inhibitors and suggest its use in the treatment of colitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP355 DIRECT INHIBITION OF HMBGI BY NEUTRALIZING ANTIBODY AMELIORATES EXPERIMENTAL COLITIS IN MICE VIA MODULATION OF MACROPHAGE PLASTICITY

N. Eissa1, F. Rabbi2, M. Metz-Boutigue2, C. Bernstein3, J. Ghia1
1Division of Gastroenterology and Hepatology, University of Zurich, Zurich/Switzerland
2INSERM, Strasbourg/France
3Internal Medicine, Division of Gastroenterology, University of Manitoba, Winnipeg, Canada

Contact E-mail Address: Neur.Eissa@umanitoba.ca

Introduction: Macrophages play a major role in intestinal bowel disease (IBD) pathogenesis through an inappropriate response to migration, and an impaired transition from a pro-inflammatory (classical activated macrophages (CAMs)) to an anti-inflammatory (alternative activated macrophages (AAMs)) phenotype. Therefore, growing awareness of a relationship between Chromogranin (Cg)-A and a susceptibility to inflammatory conditions, the specific interaction between CgA-derived peptides and macrophage plasticity in IBD is unknown. Recently, we have shown a linear correlation between CgA and CAMs with active ulcerative colitis, and colitic CgA-deficient mice demonstrated a significant decrease of colitis associated to a modulation of macrophage plasticity. As CgA is a prohormone, herein, we assessed the functional role of a specific CgA-derived peptides (Chromogranin (CHR); Cg-A;47-66) in the regulation of acute colitis and the functional plasticity of murine macrophages.

Aims and Methods: Colitis was induced in C57BL/6 mice (7-8 weeks old) by administering dextran sodium sulfate (DSS 3%) in drinking water for 5 days. Mice were treated with CHR (2.5 μg/kg) from day 1 to day 7. On day 4, serum level of C-reactive protein (CRP) was quantified using ELISA, and colonic length and thickness were measured by Uchida's T2 test. Results: Treatment with HnAb significantly suppressed colonic inflammation in DSS-C mice by improving colon shortening (6.2 ± 0.4 cm vs. 5.3 ± 0.5 cm, p < 0.05), DAI (2.87 ± 0.5 vs. 3.7 ± 0.3, p < 0.05) and HS (6.0 ± 0.1 vs. 9.6 ± 0.2, p < 0.05). Besides, MPO activity and inflammatory cytokines were evaluated to determine the colonic inflammation severity. Mucosal barrier function was assessed by immunofluorescent staining of mucus layer (muc2) and tight-junction (T-J) protein detection. mRNA was detected by qPCR. T-J protein, HMBGI, TLR4, MyD88 and inflammation scores of DSS-C group (0.69 ± 0.77) were significantly lower than those of HnAb group as compare to DSS-C group (1.61 ± 0.5 vs. 3.04 ± 0.11, p < 0.05), IFN-γ (2.14 ± 06 vs. 7.87 ± 0.21, p < 0.05) and IL-1β (1.53 ± 0.10 vs. 2.48 ± 0.04, p < 0.05) mRNA expression was decreased when treated with HnAb as compared to DSS-C group (p = 0.0001). Relatively intact mucus layer was seen in high colon of HnAb group as compared to DSS-C group. Significantly higher expression of tight-junction protein ZO-1 (0.38 ± 0.01 vs. 0.15 ± 0.05, p < 0.0001), claudin-5 (0.10 ± 0.07 vs. 0.13 ± 0.06, p < 0.0001) and occludin (0.85 ± 0.09 vs. 0.39 ± 0.01, p < 0.0001) was detected in HnAb mice as compared to mice in DSS-C group. Interestingly, colonic HMBGI protein in both nucleus (0.58 ± 0.02 vs. 0.79 ± 0.03, p < 0.0001) and cytoplasm (0.23 ± 0.01 vs. 0.01 ± 0.001, p < 0.0001) were significantly depleted more with HnAb as compared to HMBGI, suggesting that primary inhibition of HMBGI by HnAb blocked sequential HMBGI formation and release. Lastly, TLR4 (0.31 ± 0.03 vs. 0.77 ± 0.08, p < 0.0001) and MyD88 (0.30 ± 0.03 vs. 0.78 ± 0.01, p < 0.0001) protein was significantly reduced in HnAb group than mice in DSS-C group though MyD88 mRNA was relatively higher in HnAb group than DSS-C group (0.69 ± 0.04 vs. 0.38 ± 0.01, p < 0.05).

Conclusion: Administration of HnAb ameliorated DSS-C by suppressing inflammation and strengthening mucosa barrier function possibly through inhibition of HMBGI-TLR4-MyD88 pathway, suggesting a potential interventiontial target of HMBGI in ulcerative colitis treatment. Disclosure of Interest: All authors have declared no conflicts of interest.

OP356 NEW, PEPTIDE INHIBITOR OF DIPEPTIDYL PEPTIDASE IV, EMDB-1 ATTENUATES COLITIS IN MICE VIA TOPICAL ADMINISTRATION

M. Salaga, P. Miosinska, H. Zatorski, M. Zielenka, J. Fichna
Dept. Of Biochemistry, Medical University of Lodz, Lodz; Lodz; Poland

Contact E-mail Address: macieks100@wp.pl

Introduction: PETIR (PEPetide-Targeted ImmuNoregulation) is a novel therapeutic strategy which takes for the purpose restoration of the immune balance by limiting the activity of immune cells and induction of endogenous protective mechanisms, such as TGFβ and glucagon-like peptide-2 (GLP-2) through inhibition of DPP IV-dependent pathways. Experimental data indicate that PETIR results in suppression of cell proliferation and reduced synthesis of pro-inflammatory cytokines without affecting cellular viability. Aims and Methods: The objective of this study was to test the anti-inflammatory activity of a novel DPP IV inhibitor EMDB-1 in the mouse models of colitis. The inhibitory effect of EMDB-1 on DPP IV was checked in vitro in the cell culture medium. HPLC system measuring the degradation rate of endorphin-2 (EM2, natural DPP IV substrate) in the presence of the test compound. The anti-inflammatory activity of EMDB-1 was investigated in the model of acute and semi-chronic colitis induced by trinitrobenzenesulfonic acid (TNBS). Body weight, macroscopic score, ulcer score, colon length and thickness, as well as myeloperoxidase (MPO) activity were recorded. In addition, TNBS was used to induce acute and semi-chronic TNBS-induced colitis in mice in a dose-dependent manner, as indicated by significantly reduced macroscopic parameters and MPO activity. Anti-inflammatory effect of EMDB-1 was not blocked by naltrexone, thus the opioid receptors were not involved in the mechanism of action.

Conclusion: EMDB-1 is a potent inhibitor of DPP IV in vitro and exhibits substantial anti-inflammatory activity in the GI tract in vivo. Results of this study validate the EMDB-1 backbone for further development of peptide DPP IV inhibitors and suggest its use in the treatment of colitis.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP357 CHROMOFUNGIN (CHR) AMELIORATES EXPERIMENTAL COLITIS IN MICE VIA MODULATION OF MACROPHAGE PLASTICITY

E. Nick1, F. Rabbi2, M. Metz-Boutigue2, C. Bernstein3, J. Ghia1
1Gastroenterology and Hepatology, University of Zurich, Zurich/Switzerland
2Institute Of Physiology, University of Zurich, Zurich/Switzerland
3Novartis Institutes for Biomedical Research, Basel/Switzerland

Contact E-mail Address: irina.tcymbarevich@usz.ch

Introduction: Pharmacopeia play a major role in intestinal bowel disease (IBD) pathogenesis through an inappropriate response to migration, and an impaired transition from a pro-inflammatory (classical activated macrophages (CAMs)) to an anti-inflammatory (alternative activated macrophages (AAMs)) phenotype. Therefore, growing awareness of a relationship between Chromogranin (Cg)-A and a susceptibility to inflammatory conditions, the specific interaction between CgA-derived peptides and macrophage plasticity in IBD is unknown. Recently, we have shown a linear correlation between CgA and CAMs with active ulcerative colitis, and colitic CgA-deficient mice demonstrated a significant decrease of colitis associated to a modulation of macrophage plasticity. As CgA is a prohormone, herein, we assessed the functional role of a specific CgA-derived peptides (Chromogranin (CHR); Cg-A;47-66) in the regulation of acute colitis and the functional plasticity of murine macrophages.

Aims and Methods: CHR treatment can attenuate the severity of experimental colitis

Disclosure of Interest: All authors have declared no conflicts of interest.

OP358 DEFICIENCY OF PH-SENSING RECEPTOR TDAG8 AMELIORATES T-CELL TRANSFER COLITIS

I. Tcymbarevich1, C. De Valli`ere1, J. Cosin-Roger1, R. M. Spalinger1, C. A. Wagner1, K. Seuwen1, I. Frey-Wagner1, G. Rogler2
1Gastroenterology And Hepatology, University Hospital Zurich, Zurich/Switzerland
2Klinik Fur Gastroenterologie, UniversitaetsSpital Zurich, Zurich/Switzerland
Introduction: The adaptive immune system plays a crucial role in the pathogenesis of inflammatory bowel disease (IBD). Inflammation in IBD is typically associated with a decrease in local pH. The proton-sensing receptor T-cell death associated gene 8 (TDAG8), also known as G-protein-coupled receptor 65 (GPR65), has been identified as a risk gene for IBD in recent genome wide association studies.

Aims & Methods: We investigated the role of TDAG8 in T cell-mediated pathogenesis in intestinal inflammation using a murine adaptive transfer colitis model. Naive T-cells (CD4+CD25L-), from WT and TDAG8(-/-) donor mice, were intraperitoneally injected. Injection of PBS was used as a control group. The results of colitis were evaluated by weight change, colonoscopy score, spleen weight, H&E staining, IHC and mRNA expression.

Results: Induction of colitis was observed after 3 weeks by weight loss, diarrhea and bloody stool. The WT group showed severe weight loss (p = 0.013), whereas the TDAG8(-/-) group displayed only a minor delay in weight gain. No significant differences were observed in colon length, spleen weight and colonoscopy score between PBS and the TDAG8(-/-) groups. H&E staining of distal and proximal parts of the colon showed severe infiltration and crypt damage in the WT group. The TDAG8(-/-) group displayed significantly less histopathological signs of colitis in comparison to PBS and WT groups. CD3+ and IL-17A immunoreactive cells were rarely detected in colonic tissue of TDAG8(-/-) in comparison to the WT group. Regulation of mRNA expression of pro-inflammatory cytokines (IFNγ, TNF, IL17A) was observed in the TDAG8(-/-) group in comparison with the WT group. No significant differences were observed in mRNA expression levels of Fop1, RORγt and IL18.

Conclusion: Our data demonstrate that TDAG8 deficiency in T-cells ameliorates the development of colitis suggesting an important physiological role of this pH receptor.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016 10:30-12:00
SURGERY MEETS ENDOSCOPY IN THE COLON – ROOM F1

OP359 TRANSCANAL ENDOSCOPIC MICROSURGERY VERSUS ENDOSCOPIC MUCOSAL RESECTION FOR LARGE RECTAL ADENOMAS (N=109) (RCT)

R. M. Barendse1, G. D. Musters1, E.J.R. De Graaf2, F. J. C. Van Den Broek3, E.C. J. Consten4, P.G. Doorneweboch5, J. C. H. Hardwick5, I. C. De Hingh6, P. Fockens7, C. Hoff8, J. M. Jansen8, A.W. Van Milligen De Wit9, G. Van Der Schelling9, E.J. Schoon10, M.P. Schwartz11, B.L.a.m. Weusten12, M. G. Dijkgraaf1, C. Hoff8, J. M. Jansen8, A.W. Van Milligen De Wit9, G. Van Der Schelling9, E.J. Schoon10, M.P. Schwartz11, B.L.a.m. Weusten12, M. G. Dijkgraaf1, E.C. J. Consten4, P.G. Doorneweboch5, J. C. H. Hardwick5, I. C. De Hingh6, P. Fockens7, C. Hoff8, J. M. Jansen8, A.W. Van Milligen De Wit9, G. Van Der Schelling9, E.J. Schoon10, M.P. Schwartz11, B.L.a.m. Weusten12, M. G. Dijkgraaf1, C. Hoff8, J. M. Jansen8, A.W. Van Milligen De Wit9, G. Van Der Schelling9, E.J. Schoon10, M.P. Schwartz11, B.L.a.m. Weusten12, M. G. Dijkgraaf1, C. Hoff8, J. M. Jansen8, A.W. Van Milligen De Wit9, G. Van Der Schelling9, E.J. Schoon10, M.P. Schwartz11, B.L.a.m. Weusten12, M. G. Dijkgraaf1

Aims & Methods: For this randomised controlled non-inferiority trial, patients with rectal adenomas ≥3 cm, without malignant features, from 20 hospitals were included and randomised (1:1) to EMR or TEM, allowing endoscopic removal of residual adenoma at 3 months. Unexpected malignancies were excluded post randomisation. Primary outcomes were recurrence within 24 months and the number of recurrence-free days alive and out of hospital, analysed by intention-to-treat. The trial was designed to demonstrate non-inferiority of EMR with regards to recurrence rate with an upper limit of 10%. Secondary outcomes were quality of life, anal function and costs. This trial is registered in the Dutch Trial Registry (NTR1422).

Results: Between Feb 2009 and Sept 2013, 209 patients were randomised to EMR (n=106) or TEM (n=103). 4 patients withdrew consent. 1 patient had prostate cancer instead of rectal adenoma. The remaining 204 patients (103 EMR, 101 TEM) were treated; 27 (13%) had unexpected cancer and were excluded. One patient had prostate cancer instead of rectal adenoma. The remaining 204 patients (103 EMR, 101 TEM) were treated; 27 (13%) had unexpected cancer and were excluded.

Conclusion: Due to unexpected high recurrence rates after both TEM and EMR, non-inferiority of EMR could not be demonstrated. Taking into account the high rate of unexpected malignancies, a trend towards more severe complications after TEM and the cost-effectiveness of EMR, EMR is the recommended technique in case of similar expertise of TEM and EMR.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016 10:30-12:00
UPPER GI BLEEDING – ROOM M

OP361 MEDIUM- AND LONG-TERM RESULTS OF TREATMENT WITH LANREOTIDE IN CASES OF CHRONIC OR RECURRENT OBSCURE GASTROINTESTINAL BLEEDING OR DUE TO GASTROINTESTINAL ANGIODYSPLASIAS

S. Frago1, L. Ollerol2, M. Lázaro1, E. Peña-Galo3, N. De La Llana1, J. Alcedo1, M. Frago1

Aims & Methods: Our aim is to determine the medium and long-term benefit of lanreotide in cases of chronic or recurrent obscure gastrointestinal bleeding (GIB) or attributable to gastrointestinal angiodyplasias (GIADs). The long-term results with lanreotide are still very scarce.

Contact E-mail Address: sfriego@mac.com

Introduction: Somatostatin analogues have been proposed as a rescue therapy in cases of chronic or recurrent obscure gastrointestinal bleeding (GIB) or attributable to gastrointestinal angiodyplasias (GIADs). The long-term results with lanreotide are still very scarce.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016 10:30-12:00
INTENSIVE SESSIONS - ROOM G

OP362 EFFICACY OF NON-EXPOSED ENDOSCOPIC WALL-INVERSION SURGERY (NEWS) AS AN ADVANCED METHOD OF FULL-THICKNESS RESECTION FOR GASTRIC TUMOR

K. Nimi1, T. Mitsu5, S. Aikou5, S. Koshidama1, N. Yamamichi1, H. Yamashita1, M. Fujishiro1, Y. Seto1, K. Koike1

Aims & Methods: We described previously that endoscopic full-thickness resection (EFTR) for gastric tumors is a novel treatment option especially for node-negative EGC difficult to resect by ESD. The present study compared the efficacy and safety of EFTR with the NEWS technique for the treatment of gastric tumors.

Results: From July 2011 to March 2016, 20 patients (10 females, 10 males) from 2 hospitals were treated with NEWS. The mean age of patients was 68.7 years (range, 35-83 years). The mean size of tumors was 3.4 cm (range, 1.3-6.0 cm). The mean number of sessions was 2.3 (range, 1-4 sessions). The mean number of recurrences was 0.3 (range, 0-1 recurrence). The mean number of days to achieve hemostasis was 0.5 days (range, 0-3 days). The mean hospital stay was 2.7 days (range, 2-4 days). There were no complications.

Conclusion: EFTR is an effective and safe treatment for early gastric cancer. EFTR compared with NEWS is a useful treatment option for early gastric cancer.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016 10:30-12:00
INTENSIVE SESSIONS - ROOM H

OP336 NON-INVASIVE NUCLEAR PHARMACOLOGY AS A TOOL FOR THE STRATEGIC MANAGEMENT OF GASTRIC BLEEDING

K. Kiyoshi, M. Yamashita, K. Niimi

Aims & Methods: We hypothesized that non-invasive nuclear pharmacology would be useful for an effective management of gastric bleeding.

Results: Of the 20 patients, 14 were non-bleeders and 6 were bleeders. The non-invasive nuclear pharmacology was useful for an effective management of gastric bleeding.

Conclusion: Non-invasive nuclear pharmacology is useful for an effective management of gastric bleeding.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP363 MODULATION OF THE ADAMTS13 GENE BY BOX-CORE-BOX ELEMENTS IN THE HUMAN PROMOTER:


Aims & Methods: We investigated the association of ADAMTS13 gene polymorphisms with thrombotic thrombocytopenic purpura (TTP).

Results: Of the 123 patients, 99 were non-bleeders and 24 were bleeders. The non-invasive nuclear pharmacology was useful for an effective management of gastric bleeding.

Conclusion: Non-invasive nuclear pharmacology is useful for an effective management of gastric bleeding.

Disclosure of Interest: All authors have declared no conflicts of interest.

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Comparison in health resources consumption before and after Lanreotide.

<table>
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<th>Variable</th>
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<td>Red cell units - Prior yr-1yr-2yr-3 yr</td>
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<td>4.5</td>
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<tr>
<td>Iron iv doses - Prior yr-1yr-2yr-3 yr</td>
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<td>2.0</td>
<td>2.5</td>
<td>2.6</td>
<td>6.1</td>
<td>6.5</td>
<td>9.5</td>
</tr>
</tbody>
</table>

SD: Standard deviation. Yr: year

Results: Twenty-two patients (median age 76.1 years, range 56–90; 50% male sex) were included. Before starting treatment 19 were ASA III, 22.7% consumed antplatelet and 31.8% anticoagulants. At the end of follow-up only one patient had stopped the anticoagulant. The bleeding was attributed to GIAD in 77.3% and 22.7% was obscure. The bleeding was overt in 68.2% and occult in 31.8%. Before starting lanreotide 4 patients had received endoscopic treatment using argon plasma coagulation (APC), 2 hormonal therapy and 1 thalidomide. Two patients received APC concomitant to lanreotide, and 1 hormonal therapy after stopping this one without reaching bleeding cessation. The average duration of treatment with lanreotide was 28.4 months (range 6–36). Mean follow-up was 32.4 months (range 9–36), with the results shown in the table. Five patients did not complete the follow-up for not related to GIB deaths. No side effects forced to suspend lanreotide.

Conclusion: The use of lanreotide for all 6 months in patients with chronic or recurrent obscure gastrointestinal bleeding or from gastrointestinal angiodysplasia, refractory to or not candidates for other therapies, is safe and is associated with a decrease in consumption of medical resources within the three years following its indication.

Disclosure of Interest: All authors have declared no conflicts of interest.
lower survival. Thus, we hypothesize that CPT class B patients may be a cluster of patients with low hepatic reserve, to whom post-EBL bleeding may impose an additional risk for disease progression, that can significantly impact on survival.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP364 INTERNATIONAL PROSPECTIVE STUDY OF UPPER GI HAEMORRHAGE: DOES WEEKEND ADMISSION AFFECT OUTCOME?
I. A. Murray1, A. Stanley2, H. R. Dalton3, J. H. J. Ng4, S. B. Lausen5
1Gastroenterology, Royal Cornhill Hospital, Truro, Truro/United Kingdom
2Gastroenterology, Glasgow Royal Infirmary, Glasgow/United Kingdom
3Gastroenterology, Royal Cornhill Hospital, Truro, Truro/United Kingdom
4Dept. Of Gastroenterology And Hepatology, Stsinghal, Singapore/Singapore
5Gastroenterology, Odense Universitetshospital, Odense/Denmark

Contact E-mail Address: Adrian.Stanley@rccc.scot.nhs.uk

Introduction: Weekend admissions have been associated with higher mortality. For upper gastrointestinal haemorrhage (UGIH) some studies show significantly increased mortality1 and delayed endoscopy while the UK UGH audit reported no difference2. We studied whether out of hours (OIH) admissions had more morbidity, were stable and/or had higher mortality.

Aims & Methods: Prospective study over 12 months (from March 2014) from 2 UK and 2 international centres. Admission time, demographics, pulse, BP, lab results, endoscopy findings, further procedures and 30d mortality were recorded.

3 pre-endoscopy scores (Glasgow Blatchford (GBS), AIMS65 and admission Aims & Methods: Prospective study over 12 months (from March 2014) from 2 UK and 2 international centres. Admission time, demographics, pulse, BP, lab results, endoscopy findings, further procedures and 30d mortality were recorded.

3 pre-endoscopy scores (Glasgow Blatchford (GBS), AIMS65 and admission were determined. Chi-squared, Fisher’s exact and Kruskal-Wallis tests were used. The estimated mean size of PUD was 13.3 mm (±6.8). The mean number of blood units transfused was 3 (±2.4). Rebleeding occurred in 25% and in-hospital mortality was 2% (p = 0.041), presence of non active non gastrointestinal neoplasia (p = 0.021), high-risk location (p = 0.001), large-ulcers (p = 0.045). Idiopathic-PUD (p = 0.006) were associated with hemoastatic failure. The number of red blood cells (RBC) transfused for bleeding were correlated to hemostatic failure. Forrest classification of the PUD in the second endoscopic therapy, gastric or duodenal location, were not statistically significant different between groups when evaluated the hemostatic success. In the multivariate analysis, large ulcer size (p = 0.014; OR = 7.4, 95% CI 1.5–36.3), previous endoscopic therapy (p = 0.001), presence of hemodynamic instability (p = 0.039; OR = 1.71) were independent risk factors for rebleeding.

Conclusion: In patients with UGI secondary to PUD that require a second endoscopic therapy for rebleeding, the need for higher blood transfusion (>4) and large ulcers (>20 mm) were independent risk factors for hemoastatic failure. Early surgery or angiography should be considered in this group of patients.

Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP366 A HISTORY OF ISCHEMIC HEART DISEASE, HIGH BLOOD UREA NITROGEN AND C-REACTIVE PROTEIN LEVELS, AND LOW HEMOGLOBIN LEVELS: AS PREDICTIVE CLINICAL FEATURES FOR EARLY DEATH AFTER PERCUTANEOUS ENDOSCOPIC GASTROSTOMY
T. Nishimura1, T. Kuwai2, T. Takasago2, Y. Miyasako2, Y. Sumida3, S. Iso2, H. Imagawa1, T. Yamaguchi2, A. Yamaguchi3, H. Kouno4, H. Kohno2
1Gastroenterology, Kure Medical Center and Chugoku Cancer Center, kure/Japan
2Gastroenterology, Kure Medical Center and Chugoku Cancer Center, kure/Japan
3Gastroenterology, Kure Medical Center and Chugoku Cancer Center, kure/Japan

Contact E-mail Address: tomoyukin@kure-nh.go.jp

Introduction: Percutaneous endoscopic gastrostomy (PEG) is accepted as the method that enables enteral feeding in patients with swallowing difficulties. However, complications and early death are considerably prevalent after PEG. To decrease the incidence of early mortality after PEG, it is very important to identify risk factors of this procedure. Aim & Methods: The aim of our study was to determine factors that could predict early death within 30 days following PEG. A retrospective analysis of the records of all patients who underwent PEG at Kure Medical Center and Chugoku Cancer Center from January 2008 to March 2014, and who subsequently underwent examined clinical and preparatory laboratory data and extracted predictive factors of death after PEG by using univariate and multivariate analyses.

Results: A total of 1077 patients (502 female (46.7%) and 575 male (53.3%); mean age 78 y.o.) were assessed. Predictors of poor survival after PEG included history of ischemic heart disease (odds ratio [OR] 2.32, 95% confidence interval [CI] 1.2–4.3, P < 0.01), blood urea nitrogen level ≥30 mg/dl (OR 3.14, 95% CI 1.8–5.5, P < 0.0001), C-reactive protein level ≥2.6 mg/dl (OR 4.04, 95% CI 2.2–7.3, P < 0.0001), albumin level ≤2.7 mg/dl (OR 4.2, 95% CI 1.2–1.2, P < 0.001), and hemoglobin level ≤11.2 g/dl (OR 4.0, 95% CI 2.0–8.0, P < 0.001).

Multivariate analysis on predictive factors of early death revealed a significant correlation between early death and each of the following: history of ischemic heart disease, high blood urea nitrogen and C-reactive protein levels, and low hemoglobin levels. As a predictive clinical feature, history of ischemic heart disease and high blood urea nitrogen levels were associated with early mortality after PEG. Early surgery or angiography should be considered in this group of patients.
Introduction: The Chinese University of Hong Kong, Hong Kong/PRC

Conclusion: A history of ischemic heart disease and laboratory data, such as high blood urea nitrogen and C-reactive protein levels and low hemoglobin levels may be useful predictive clinical factors for early death after PEG. If patients have already had ischemic heart disease, high blood urea nitrogen, high C-reactive protein, or anemia, PEG should be considered carefully.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016 10:30-12:00 IMMUNOTHERAPY IN CANCER – ROOM 1.6/1.62

OP367 GLUTAMINOLYSIS INHIBITION AS A THERAPEUTIC STRATEGY IN GLUTAMINE-ADDICTED KRAS MUTANT COLORECTAL CANCER

C.C. Wong1, J. Xu2, Q. Yun3, X. Li4, W. Kang5, J.J.Y. Sung6, Z. Cai4, J. Yu7, H. Suzuki8, E. Yamamoto1

1Department Of Medicine And Therapeutics, The Chinese University of Hong Kong, Hong Kong/Hong Kong PRC
2Department Of Medicine, The Chinese University of Hong Kong, Hong Kong/Hong Kong PRC
3Gastroenterology, Zhejiang University, Hangzhou/China
4Hong Kong Baptist University, Hong Kong/Hong Kong PRC
5Department Of Pathology And Cellular Pathology, The Chinese University of Hong Kong, Hong Kong/Hong Kong PRC
6Department Of Medicine & Therapeutics, The Chinese University of Hong Kong, Hong Kong/PRC
7Institute Of Digestive Disease And Department Of Medicine And Therapeutics, The Chinese University of Hong Kong, Hong Kong/Hong Kong PRC

Contact E-mail Address: chicichun.wong@cuhk.edu.hk

Introduction: Colorectal cancer (CRC) with KRAS mutations represents an unmet clinical need due to the lack of effective therapies. A defining characteristic of oncogenic KRAS-driven cancers is an altered cellular metabolism, in which glucose and glutamine metabolism are extensively rewired to satisfy their anabolic needs. In this study, we investigated the metabolic dependencies of KRAS-mutant CRC, and established the role of glutaminolysis in KRAS-mutant CRC growth and evaluated the synergism between glutaminolysis inhibition and chemotherapeutic agents.

Aims & Methods: Metabolic dependencies of KRAS mutant CRC cell lines were assessed by colony formation and apoptosis assays. Glutamine metabolism in KRAS mutant CRC cell lines were traced using stable U13C-glutamine labeling and Ultra-high Performance Liquid Chromatography-Mass Spectrometry (UPLC-MS). Role of glutaminase (GLS1) and the mitochondrial glutamate transporter (SLC25A22) in mediating glutaminolysis was evaluated. Finally, functional significance of glutaminolysis inhibition via GLS1 or SLC25A22 blockage was investigated using chemotherapeutic agents and their combinations.

Results: Deprivation of glucose, glutamine or their combination in six KRAS mutant CRC lines (DLD1, HCT116, LOVO, SW480, SW620 and SW1116) and four KRAS WT cell lines (CAO2, SW280, HT29 and SW480) revealed that KRAS mutant CRC cells were profoundly sensitive to glucose depletion as compared with KRAS wild type CRC cells, whilst exhibiting resistance to glucose depletion. This indicates that supply of glutamine is obligatory for KRAS mutant CRC survival. U13C5-glutamine labeling in DLD1 cells and UPLC-MS revealed that a majority of glutamine was metabolized into glutamate, aspartate and the intermediates of the tricarboxylic acid (TCA) cycle, indicating that glutamine-derived carbons were channeled to the mitochondrion for the replenishment of TCA cycle (a process known as glutaminolysis). We further revealed that glutamine was first converted to glutamate by GLS1 at the outer side of inner mitochondrial membrane, which is coupled to SLC25A22 for the import of glutamate into the mitochondrial matrix. Consistent with this model, the silencing of GLS1 or SLC25A22 significantly suppressed cell proliferation in KRAS mutant CRC cells, indicating that their coupled action is indispensable for cell growth. U13C-glutamine tracing in DLD1 cells with SLC25A22 knockdown showed a decreased entry of glutamine-derived carbon into TCA cycle, confirming its involvement in glutaminolysis. Inhibition of SLC25A22-dependent glutaminolysis triggered metabolic stress, suppressed ATP production and promoted oxidative stress. Moreover, a combinatorial approach utilizing SLC25A22 shRNA plus 5-Fluorouracil synergistically suppressed the growth of KRAS mutant CRC in vitro and in subcutaneous xenograft models.

Conclusion: KRAS mutant CRC cells are addicted to glutamine and the blockade of glutaminolysis enzymes GLS1 and SLC25A22 suppressed cell survival. SLC25A22 knockdown relieved therapeutic resistance in CRC and its synergistic effect with chemotherapy warrants further investigation.

Disclosure of Interest: All authors have declared no conflicts of interest.
Disclosure of Interest: All authors have declared no conflicts of interest.

References

OP370 SPONTANEOUS BACTERIAL PERTONITIS – DOES THE INFECTION ACQUISITION SITE MATTER?
A.G. G. Antunes1, C. Teixeira1, P. Costa1, B.M. Santos Peixe2, A. Alves2, S. Oliveira1, C. Sousa1, P. Oliveira3
1Dept. Of Gastroenterology, Centro Hospitalar do Algarve, Faro/Portugal
2Dept. Of Gastroenterology, Centro Hospitalar de Setubal, Setubal/Portugal
3Dept. Of Gastroenterology, Centro Hospitalar de Lisboa Ocidental, Lisboa, Portugal

Contact E-mail Address: sergiojgiao@hotmail.com
Introduction: Spontaneous bacterial peritonitis (SBP) develops in up to 25% of patients with cirrhosis and its associated significant short and long-term morbidity and mortality. With the amelioration of medical care, the use of antibiotics for primary and secondary prophylaxis of SBP, there is some controversy concerning whether the acquisition site of the infection has an effect on the prognosis of SBP and if the international guidelines for antibiotic therapy (mainly based on the acquisition site) are still considered to be the best practice. Aims: To compare clinical, analytical and microbiological features between nosocomial and community-acquired SBP; 2) to assess the influence of the infection acquisition site when evaluated in-hospital mortality and 1 year-mortality. Retrospective cohort study, conducted in 3 tertiary centers that evaluated all cases of SBP between 2010 and 2014. Medical records and laboratory data were reviewed. For defining the acquisition site of the infection, we followed the criteria described by European Center for Disease Prevention and Control (ECDC). Healthcare-associated infections and Nosocomial infections were analyzed as a separate variable. Multiresistant bacteria (MDR) was defined according to the ECDC criteria (resistant to 3 antibiotic families, including beta-lactam antibiotics).

Results: We identified 222 episodes of SBP, from which 110 were considered as community-acquired; in-hospital mortality was 28.8% and 1 year-mortality was 56.9%. In 85 episodes we obtained microbiological isolation (MDR = 28%), with a predominance of gram negative (53.6%). Community-acquired SBPs were more frequently caused by gram negative bacteria and Nosocomial-acquired SBPs were gram positive bacteria - (0,033); SBPs secondary to MDR-bacteria were more frequent in Nosocomial-acquired group (19,64 vs 6,36%; p=0.003). No statistically significant differences were noticed between centers when evaluated microbiological isolation rate, gram staining of MDR isolations. There were no statistically significant differences between Community-acquired SBP and Nosocomial-acquired SBPs for the variables age, gender, Child-Pugh, MELD, Hb, leukocytes, platelets, CRP, Na, INR, bilirubin, albumin, ascites fluid characteristics, gastrointestinal bleeding, acute kidney injury, creatinine, hyperbilirubinemia and in-hospital mortality. No complications were recorded. No Nosocomial-acquired SBPs were associated with long hospitalizations (17,8 vs 11,7 days; p=0.007). No statistically significant difference was detected when analyzed in-hospital mortality (Nosocomial-acquired = 29.5 vs Community-acquired = 28.2%; p=0.88); 1 year mortality (Nosocomial-acquired = 61.6 vs Community-acquired = 55.8%; p=0.22). Nosocomial-acquired SBPs were associated with a worse prognosis (63,0 vs 51,7%; p=0.025).

Conclusion: Nosocomial-acquired SBPs were associated with higher rates of MDR-bacteria, longer hospitalization lengths and higher 1 year-mortality. Clinical and laboratorial features were not significantly different between SBP according to the infection acquisition site; 6,36% of community-acquired SBPs were secondary to MDR-bacteria and so in a relevant percentage of our sample, empiric antibiotic therapy according to the current guidelines would eventually fail.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP372 ENDORING™ INCREASES ADR EVEN IN HIGH-RISK SCREENING COLONOSCOPY: RESULTS OF A SINGLE CENTRE PILOT STUDY
B. Hayee1, G. Chung-Faye1
1Gastroenterology, King’s College Hospital, London/United Kingdom
2Gastroenterology, King’s College Hospital, London/United Kingdom

Contact E-mail Address: b.hayee@nhs.net
Introduction: Colonoscopy remains the gold standard procedure for screening and polyp detection, with adenoma detection rate (ADR) being a widely accepted key performance indicator (KPI). It has been long recognised that even experienced colonoscopists incur an appreciable ‘miss-rate’ and a number of novel devices have been marketed to assist this aspect of practice. The Endorings™ device is a soft simple silicone, single-use device consisting of a series of rings arranged around a central tubular core. As the colonoscope is inserted the rings fold backward to allow intubation and flare on withdrawal to flatten colonic folds and aid inspection.

Aims & Methods: This was a single-centre pilot study to determine the effect of Endorings used in a high-risk cancer screening population (national), when used by experienced accredited ADR. A total of 120 cases (60 ADR) were prospectively assessed. Data was collected during screening colonoscopy (performed by two accredited colonoscopists) and recorded. ADR was calculated as the number of polyps detected at any given procedure. There were no significant differences in completion rates, withdrawal time, use of sedation, and comfort scores. The device was removed in 5/6 procedures due to interference with intubation (in the presence of either an angulated sigmoid or diverticular region).

Results: The ADR without Endorings™ was 49.4% with a per-procedure detection rate (ppr) of 0.97. With the device (n = 66), ADR was 66.7% (p = 0.0006) with ppr of 1.625. This represents a 35% increase in ADR and a 68% increase in the number of polyps detected at any given procedure. There were no significant differences in completion rates, withdrawal time, use of sedation, or comfort scores. The device was removed in 5/6 procedures due to interference with intubation (in the presence of either an angulated sigmoid or diverticular region).

Conclusion: Use of the Endorings™ device was associated with a significant increase in ADR. Qualitatively, the three-ring design was felt to interfere with normal intubation such that insertion technique had to be modified. An updated device with polyp detection device in place. The Endorings™ may offer an advantage in screening colonoscopy and, in this cohort, further prospective investigation is warranted.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP373 THE FIRST RANDOMISED CONTROLLED TRIAL OF ENDOCUFF VISION®-ASSISTED COLONOSCOPY VERSUS STANDARD COLONOSCOPY FOR POLYP DETECTION IN BOWEL CANCER SCREENING PATIENTS (E-CAP STUDY)
R. Bhattacharyya1, F.J.Q. Chegdu2, K. Kandiah2, C. Fogg3, B. Higgins3, B. Hayee4, L. Gadeke1, F.J.Q. Chedgy2, K. Kandiah2, C. Fogg3, B. Higgins3, B. Haysom-Newport4, L. Gadeke1, F. Thursby-Pelham2, R. Ellis1, P. Goggin1, G. Longcroft-Wheaton5, P. Bhandari2, P.J. O’Dwyer1, R. Bhattacharyya1
1Dept. Of Gastroenterology, Queen Alexandra Hospital Dept. of Gastroenterology, Portsmouth/United Kingdom
2Gastroenterology, Queen Alexandra Hospital, Portsmouth/United Kingdom
3Gastroenterology, Portsmouth Hospitals NHS trust, Hampshire/United Kingdom
4Dept. Of Gastroenterology, Portsmouth Hospital Dept. of Gastroenterology, Portsmouth, United Kingdom
5Dept. Of Gastroenterology, Portsmouth Hospital Dept. of Gastroenterology, Portsmouth, United Kingdom

Contact E-mail Address: rupam.bhattacharyya@gmail.com
Introduction: Up to 25% of colonic polyps are missed during colonoscopy. The Endocuff Vision® is a cap with soft flexible arms which are inserted at the end of a colonoscope and improves views during withdrawal. We have performed the first randomised controlled trial to identify the role of Endocuff Vision® in improving polyp detection.

Aims & Methods: Our aim was to investigate the impact of Endocuff Vision®-assisted colonoscopy on polyp detection, as compared to standard colonoscopy, in the UK Bowel Cancer Screening Programme (BCSP). This was a single-centre, single-blinded, randomised controlled trial. Ethics approval was obtained (ref.: 
Table 1: E-CAP results

<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Standard</th>
<th>Endocuff</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>265</td>
<td>266</td>
</tr>
<tr>
<td>Polyps</td>
<td>470</td>
<td>436</td>
</tr>
<tr>
<td>Polyps/patient</td>
<td>1.77</td>
<td>1.67</td>
</tr>
<tr>
<td>ADR</td>
<td></td>
<td>0.441</td>
</tr>
<tr>
<td>Adenomas</td>
<td>359</td>
<td>336</td>
</tr>
<tr>
<td>Adenomas/patient</td>
<td>1.35</td>
<td>1.26</td>
</tr>
<tr>
<td>PDR</td>
<td>185/265 = 69.8%</td>
<td>187/266 = 70.3%</td>
</tr>
<tr>
<td>ADR</td>
<td>167/265 = 63%</td>
<td>162/266 = 60.9%</td>
</tr>
<tr>
<td>Cancer detection rate</td>
<td>15/265 = 5.7%</td>
<td>14/266 = 5.3%</td>
</tr>
</tbody>
</table>

Conclusion: In the UK, the bowel cancer screening is performed by highly experienced endoscopists with special accreditation. Our results suggest that in expert hands, ADR exceeds 60% even without Endocuff. In such settings, Endocuff Vision did not improve polyp detection rates (PDR) or ADR. However, Endocuff did not cause any adverse events, prolong procedure duration or cause additional discomfort. These data demonstrate the safety and feasibility of Endocuff. However, no additional gain was demonstrated in expert hands.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP375 EFFICACY AND SAFETY OF THE NOVEL II. PEG AND ASCORBATE BOWEL PREPARATION NER1006 VERSUS TRISULFATE SOLUTION IN OVERNIGHT SPLIT-DOSING ADMINISTRATION: RESULTS FROM THE PHASE 3 STUDY NOCT1

Contact E-mail Address: LClyaton@norgine.com

Introduction: Successful colon cleansing enables effective colonoscopy. PEG based split dosing preparations are traditionally seen as the gold standard in cleansing, but many still require a high preparation volume intake. NER1006 is a novel 2L PEG3350 aspartate-based bowel preparation, with 3 clinical development. The low volume of NER1006 is achieved through the use of ascorbate in the second dose only.

Aims & Methods: This phase 3, randomised, multicentre, colonoscopist-blinded, non-inferiority study assessed the efficacy, safety and tolerability of a 2-day overnight split-dosing regimen of either NER1006 (NER) or trisulfate solution (TS) in patients undergoing colonoscopy. Two alternative primary endpoints were evaluated: overall bowel cleansing success and ‘Excellent plus Good’ cleansing rating in the colon ascenders using the Harefield Cleansing Scale (HCS). Secondary endpoints included hierarchical evaluation of lesion detection rates (key), and cleansing assessment using the Boston Bowel Preparation Scale (BBPS, supportive). Patient tolerability, acceptability and compliance were assessed using questionnaires. Safety was monitored through adverse events and clinical laboratory evaluation. The threshold for statistical significance in this study was P < 0.025. The confidence interval (CI) for the difference between the groups used a 10% margin to demonstrate non-inferiority vs. TS.

Result: Patients were randomised to receive either N2D (n = 310) or TS (n = 311). For N2D and TS, respectively, the mean age (SD) was 57.7 (10.36) and 57.3 (10.56) years. The distribution of males vs. females was 158 (51.0%) vs. 152 (49.0%). For N2D and 169 (54.3%) vs. 142 (45.7%) for TS. High quality overall bowel cleansing efficacy was achieved in both treatment groups (Table 1). N2D demonstrated non-inferiority (lower CI limit ≥ 10%) to TS for both alternative primary endpoints. Numerically, more patients on N2D achieved an ‘Excellent plus Good’ cleansing rate in the colon ascenders compared with TS. Non-inferiority for N2D in adenoma detection rate in the colon ascenders was not demonstrated; other key secondary endpoints were not formally tested. Tolerability and acceptability as assessed by the Bowel Cleansing Impact Questionnaire (BCIQ) Questionnaire were comparable for N2D and TS (Table 1). Compliance rates were high in both treatment groups. There were no deaths. NER1006 was not associated with any serious treatment-emergent adverse events (TEAEs). The most frequently reported related TEAEs in both treatment groups were nausea and vomiting.

Conclusion: When administered as a 2-day split dosing regimen, and compared to trisulfate solution, NER1006 was non-inferior in overall bowel cleansing success and in achieving an ‘Excellent plus Good’ cleansing rate in the colon ascenders. Both treatments were well tolerated, most TEAEs were mild or moderate in severity and reflected the expected safety profile of respective treatments. The
Table 1 (OP375): Efficacy and safety endpoints

<table>
<thead>
<tr>
<th>Abstract legend</th>
<th>NER1006 2-day split-dosing</th>
<th>Comparator: trisulfate solution</th>
<th>CI for the difference [P value]</th>
</tr>
</thead>
<tbody>
<tr>
<td>Efficacy</td>
<td>Primary analysis set, n = 276</td>
<td>Primary analysis set, n = 280</td>
<td>–8.15%* [0.528]</td>
</tr>
<tr>
<td>Primary endpoint: Patients with successful overall bowel cleansing efficacy (HCS) [n]</td>
<td>235 (85.1%)</td>
<td>238 (85.0%)</td>
<td>n.a.</td>
</tr>
<tr>
<td>Supportive secondary endpoint: Patients with successful overall bowel cleansing efficacy (BBPS) [n]</td>
<td>228 (82.6%)</td>
<td>227 (81.1%)</td>
<td>n.a.</td>
</tr>
<tr>
<td>Primary endpoint: Excellent plus Good cleansing rate in colon ascendens [n]</td>
<td>99 (35.9%)</td>
<td>82 (29.3%)</td>
<td>–1.69%* [0.059]</td>
</tr>
<tr>
<td>Key secondary endpoint: Adenoma detection rate, colon ascendens</td>
<td>14.1%</td>
<td>17.1%</td>
<td>n.a.</td>
</tr>
<tr>
<td>Key secondary endpoint: Adenoma detection rate, overall colon</td>
<td>33.7%</td>
<td>35.0%</td>
<td>n.a.</td>
</tr>
<tr>
<td>Key secondary endpoint: Polyp detection rate, colon ascendens</td>
<td>18.5%</td>
<td>23.9%</td>
<td>n.a.</td>
</tr>
<tr>
<td>Key secondary endpoint: Polyp detection rate, overall colon</td>
<td>45.7%</td>
<td>48.6%</td>
<td>n.a.</td>
</tr>
<tr>
<td>Compliance rate (min 75% of both doses taken) [n]</td>
<td>255 (92.4%)</td>
<td>255 (91.1%)</td>
<td>n.a.</td>
</tr>
<tr>
<td>BOCLIR score [mean (SD)]</td>
<td>39.9 (17.0)</td>
<td>39.6 (17.51)</td>
<td>n.a.</td>
</tr>
<tr>
<td>SAFETY</td>
<td>Safety set, n = 262</td>
<td>Safety set, n = 265</td>
<td>n.a.</td>
</tr>
<tr>
<td>All treatment-emergent adverse events [n]</td>
<td>118</td>
<td>67</td>
<td>n.a.</td>
</tr>
<tr>
<td>Patients with any related treatment-emergent adverse event [n]</td>
<td>39 (14.9%)</td>
<td>25 (9.4%)</td>
<td>n.a.</td>
</tr>
</tbody>
</table>

* = 97.5% 1-sided CI; ** = 95% 2-sided CI; n.a. = not applicable

1I. NER1006 showed high efficacy and safety in overnight split-dosing administration.

Disclosure of Interest: M. DeMicco: Contractor for Norgine through Anaheim Clinical Trials LLC; Principal Investigator for the NOCT study.
L.B. Clayton: Employee of Norgine
R. Ng Kew Shing: Employee of Norgine
M.S. Epstein: Contractor for Norgine through Investigative Clinical Research. Investigator for the NOCT study.

Contact Email Address: alida andrealli@gmail.com

Introduction: Split-dose cleansing regime for colonoscopy is recommended over day-before preparation by practice guidelines and it has been shown to increase the adenoma detection rate. Nevertheless, the compliance with split-dose prescription for early-morning colonoscopy (8–10 am) is poor [1].

Aims & Methods: Present randomized study was aimed at evaluating weather the addition of oral instructions to a self-explanatory booklet for bowel preparation increases compliance with split-dose. We prospectively enrolled consecutive 50–70yr-old outpatients undergoing screening colonoscopy from 8:00 to 10:00 am. Exclusion criteria were inability to provide consent and contraindications to the preparation adopted in the study. All patients received a low-volume preparation. We designed a dedicated booklet underlying the advantages of split-dose regimen including: 1. reduction of the risk of missing neoplastic lesions; 2. improvement of colon cleansing and lower risk of reshadeling the procedure; 3. increase of bowel prep tolerability; 4. reduction in procedure duration. Day-before preparation was left as an alternative and discouraged, secondary option. In order to evaluate whether additional oral explanation, aimed at reinforcing the benefits of split-dose, may further improve compliance, patients were randomized in two groups: group A-only booklet delivered; group B-oral explanation along with booklet. Patients’ data (demography, education, socioeconomic status), along with prep-related and procedural data, were collected by a structured questionnaire on colonoscopy day. Colon cleansing was evaluated by Boston Bowel Preparation Scale (BBPS). Proportions were compared by chi-squared test or chi-squared for trend, as appropriate. A logistic regression analysis was performed to disclose factors associated with compliance to split-dose prescription. A p-value < 0.05 was considered significant for all comparisons.

Results: During the study period (January–April 2016), 286 patients were enrolled (mean age 59.8 ± 7, males 53.7%), 143 in group A and 143 in group B; of them 266 have undergone colonoscopy (group A: 130, group B: 136). The two groups were well balanced as concerns age, gender, education, employment and marriage status. Split-dose was adopted by 106/130 and by 118/136 patients in group A and B, respectively (81.5% vs 86.8%, p = 0.317). Among patients who complied with split-dose the quality of bowel cleansing was good or excellent (BBPS 2 in each segment of the colon) in 215/224 (96.0%). No significant differences between group A and B were observed with regards to adherence to preparation scheme, which were both optimal, (98.1% vs 97.5%, p = 0.693) and to the adequacy of bowel prep (BBPS > 2 in each segment) (97.2% vs 94.9%, p = 0.785). No variable was significantly associated with split-dose uptake at logistic regression analysis.

Conclusion: Present data show an excellent compliance with split-dose prescription for early morning colonoscopy in both written only and oral and written instruction groups, leading to very satisfactory levels of colon cleansing. This finding underlines that the adoption of a self-explanatory booklet clearly describing the benefits of split-dose marginalizes the need of additional oral instructions. This result is relevant in an open-access system, where routine oral education is unfeasible, and does not support ESGE indications, which recommend both oral and written explanation by healthcare professionals. No variable was significantly associated with split-dose uptake at logistic regression analysis.

Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

WEDNESDAY, OCTOBER 19, 2016
10:30-12:00
BURDEN OF LIVER DISEASE - ROOM LT

OP377 THE BURDEN OF OVERT AND OCCULT LIVER CIRRHOSIS IN PATIENTS WITH METABOLIC SYNDROME: ANALYSIS FROM A LARGE GENERAL PRACTITIONERS DATABASE

A. Martin1, E. Cerantola1, A. Gatta2, P. Pontisso3

1Department Of Medicine, University of Padua, Padova/Italy
2Dept Of Medicine, Internal Medicine and Hepatology, University of Padova, Padova, Italy, Padova/Italy
3Dept Of Medicine, Internal Medicine And Hepatology, University of Padova, Padova/Italy

Contact Email Address: andremartin86@gmail.com

Introduction: Liver cirrhosis represents the end stage of chronic liver disease, characterized by high mortality and morbidity (1,2) with relevant health and social costs (3). Metabolic syndrome represents one of the major risk factors of liver disease in western countries (4). The real prevalence of this condition is difficult to assess, since liver disease is silent until clinical decompensation of cirrhosis occurs.

Aims & Methods: The aim of this study was to estimate the prevalence of occult liver disease in the Veneto region and to compare the results with the burden of liver disease in the remaining 65% of liver disease diagnosis in each segment of the colon) in 215/224 (96.0%). No significant differences between group A and B were observed with regards to adherence to preparation scheme, which were both optimal, (98.1% vs 97.5%, p = 0.693) and to the adequacy of bowel prep (BBPS > 2 in each segment) (97.2% vs 94.9%, p = 0.785). No variable was significantly associated with split-dose uptake at logistic regression analysis.

Conclusion: Present data show an excellent compliance with split-dose prescription for early morning colonoscopy in both written only and oral and written instruction groups, leading to very satisfactory levels of colon cleansing. This finding underlines that the adoption of a self-explanatory booklet clearly describing the benefits of split-dose marginalizes the need of additional oral instructions. This result is relevant in an open-access system, where routine oral education is unfeasible, and does not support ESGE indications, which recommend both oral and written explanation by healthcare professionals. Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

WEDNESDAY, OCTOBER 19, 2016
10:30-12:00
BURDEN OF LIVER DISEASE - ROOM LT

OP377 THE BURDEN OF OVERT AND OCCULT LIVER CIRRHOSIS IN PATIENTS WITH METABOLIC SYNDROME: ANALYSIS FROM A LARGE GENERAL PRACTITIONERS DATABASE

A. Martin1, E. Cerantola1, A. Gatta2, P. Pontisso3

1Department Of Medicine, University of Padua, Padova/Italy
2Dept Of Medicine, Internal Medicine and Hepatology, University of Padova, Padova, Italy, Padova/Italy
3Dept Of Medicine, Internal Medicine And Hepatology, University of Padova, Padova/Italy

Contact Email Address: andremartin86@gmail.com

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Reference
was recorded. Sex distribution of these patients was similar to that of the patients without cirrhosis (M:F 90:11, 0.9, respectively), while sex was higher in patients with elevated transaminases [mean age (yrs) = 55.5 vs 48.9, p < 0.0001]. Patients with overt diagnosis of cirrhosis were 0.3% of the overall population, while thrombocytopenia, as indicator of occult cirrhosis, was detected in 1.3% of the remaining patients. The epidemiological profile of these two groups was similar [M:F:1:1.5; mean age (yrs) = 65.6 vs M:F:1:1.67; mean age (yrs) = 65, p = n.s], but significantly different (p < 0.0001) compared to the normal population and to subjects with only liver enzyme alterations. Patients with occult and overt cirrhosis presented a similar prevalence of metabolic syndrome profile (49% and 56% respectively), while these figures were lower in patients without signs of liver disease (33%, p < 0.0001).

Conclusion: In conclusion, a large proportion of patients with biochemical signs of chronic hepatitis and cirrhosis are still undiagnosed. Metabolic syndrome seems to be the major risk factor that characterizes patients with more severe liver disease.

Disclosure of Interest: All authors have declared no conflicts of interest.

References


OP378 THE NATIONAL BURDEN IN FRANCE OF HOSPITAL CARE FOR PATIENTS WITH HEPATIC ENCEPHALOPATHY: DATA FROM THE FRENCH NATIONAL HOSPITAL DATABASE (PMSI)

A. Abergel1, H. Hagege2, R. Benamouzig2, C. Bureau3, C. Blein5, C. Amaz5, A. Radwan5, R. Cipelli4
1CHU de Clermont-Ferrand, Clermont-Ferrand/France
2Cretet Gastroenterologie, CH  Cretet Gastroenterologie, Cretet cedex/Alpes de Haute Provence
3Service Gastroenterologie, Hopital Aricenne, Boigny/77/France
4CHU Purpan, Toulouse/France
3HEYA, Lyon/France
5Alfa-Wasserman Pharma, Levallois-Perret/78/France
6Medical Dept., Norgine Medical Department, Rueil Malmaison/France

Contact Email Address: aabergel@chu-clermontferrand.fr

Introduction: Hepatic encephalopathy (HE) is a complication of cirrhosis characterized by a broad spectrum of neuropsychiatric manifestations. According to the clinical symptoms there are two types of HE: covert and overt HE (OHE). In general, the prevalence of OHE is estimated at 10%-14% in cirrhotic patients in patients with transjugular intrahepatic portosystemic shunt (TIPS). In France, the prevalence of OHE was estimated at 25,000 patients (21,000 to 30,000 patients), yet little is published on the national burden of hospitalisation of patients with hepatic encephalopathy. The first objective of this study was to use the retrospective national PMSI data (Programme Médicalisé des Systèmes d’Information) to assess the public health burden of hospitalisations for OHE, documenting its incidence rate but also to analyse the characteristics of hospitalisations. The second objective was to study the factors independently associated with length of stay in patients with HE.

Disclosure of Interest: All authors have declared no conflicts of interest.

Aims & Methods: A retrospective cohort was performed from the national PMSI database between 2012 and 2013. Given the absence of coding specificity of hepatic encephalopathy via ICD 10 code “K72”, Hepatic failure, not elsewhere classified, an patients hospitalised for HE was implemented according to a medical expertise from the expression of the main symptoms of the disease. A negative binomial regression model was used to estimate the link between lengths of stay and HE presenting characteristics such as age, sex, aminotransferases, malnutrition, renal failure, bacterial infection and respiratory diseases, stays in reanimation, intensive care units and death.

Result: The study collected respectively 13,484 patients on 2012 corresponding to 17,601 hospitalisations and 13,672 patients in 2013 corresponding to 17,491 hospitalisations. The mean age was 63.1±13.8 years in 2013 and 62.7±13.9 years in 2012. Thirty percent of patients were admitted to the intensive care units. In nearly all hospital stays, the illness was medically managed (87% of stays in 2013 and 89% in 2012). Nevertheless, there are 12% of surgical stays (1,664 stays in 2013 and 1,514 stays in 2012). The mean length of HE stay was 15 days (SD 19 days) and the median was 10 days. The length of stay was 48% longer for patients with malnutrition, and 52% longer in case of a bacterial infection. The length of stay was 12% and 14% longer for patients with renal failure and respiratory diseases, respectively. More 40 million euros per year are spent by Social Security in France for HE hospitalisations with a mean cost per overnight stay estimated at €62.411.

Conclusion: The mean length of stay in patients with HE was high (15 ± 19 days). The binomial model confirmed the significant longer length of stay induced by patients with comorbidity such as malnutrition, renal insufficiency, bacterial infection and respiratory disease. The annual economic burden of HE hospitalisations in France amounted to €40 million.

Disclosure of Interest: H. Hagege: Herve Hagege has acted as a medical expert for Norgine and Alfa Wassermann
C. Bureau: Cristophe Bureau has acted as a medical expert for Norgine and Alfa Wassermann
C. Blein: Cécile Blein is an employee of HEVA, who were contracted by Norgine and Alfa Wassermann to participate in this study.
C. Amaz: CAMILLE Amaz is an employee of HEVA, who were contracted by Norgine and Alfa Wassermann to participate in this study.
R. Benamouzig: Robert Benamouzig is an employee of HEVA at the time the study was undertaken.
I. Leurs: Irina Leurs was an employee of Norgine at the time the study was undertaken.

All authors have declared no conflicts of interest.

References


Table 1 (OP379): All-cause resource use pre- and post-RFX initiation

<table>
<thead>
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<th>6 months (n = 114)</th>
<th>12 months (n = 102)</th>
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<tr>
<td></td>
<td>Mean (SD)</td>
<td>n*</td>
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<tr>
<td></td>
<td></td>
<td>Pre-RFX</td>
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<tr>
<td>Hospitalisations with overnight stay per patient</td>
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<td>Total bed days</td>
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<tr>
<td>Total bed days per inpatient</td>
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<td>Critical care bed days per inpatient</td>
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<td>7.9 (10.1)</td>
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<tr>
<td>Emergency room visits per patient</td>
<td>63</td>
<td>1.9 (2.3)</td>
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</table>
OP382 PREGNANCY OUTCOME IN MORE THAN 5000 BIRTHS TO WOMEN WITH VIRAL HEPATITIS IN A POPULATION-BASED COHORT STUDY IN SWEDEN

J. Lubel1

Introduction: Previous studies have shown inconsistent results with respect to hepatitis B (HBV), Hepatitis C (HCV) and pregnancy outcome.

Aims & Methods: The aim of this study was to investigate pregnancy outcome in women with HBV or HCV. In a nationwide cohort of pregnancies between 1997 and 2011 we investigated the risks of adverse pregnancy outcomes in 3,077 births to women with HBV and 2,150 births to women with HCV using data from Swedish healthcare registries. Births to women without HBV (n=1,428) and healthy controls (n=1,429) were served as population controls. Crude and adjusted relative risks (RR) were calculated using Poisson regression analysis.

Results: Women with HCV were more likely to smoke (47.62% vs. 8.65%) and to have alcohol dependence (18.79 vs. 1.07) compared with population controls. Most women were born in non-Nordic countries. HCV was associated with a decreased risk of preeclampsia (aRR: 0.42, 95% CI: 0.25-0.65), an increased risk of late neonatal death (7-27 days; aRR: 4.47, 95% CI: 1.01-12.44) and an increased risk of preterm birth (aRR: 1.31, 95% CI: 1.08-1.59). HCV was associated with an increased risk for preterm birth (aRR: 1.21, 95% CI: 1.01-1.44).

Conclusion: Both HBV and HCV are risk factors for preterm births, while HCV seems to be associated with a protective effect against preeclampsia. Future studies should corroborate these findings.

Disclosure of Interest: All authors have declared no conflicts of interest.

WEDNESDAY, OCTOBER 19, 2016
10:30–12:00
TRANSLATIONAL ASPECTS OF IBD – ROOM L8

OP383 ALTERATION OF THE RENIN-ANGIOTENSIN SYSTEM IN THE CIRCULATION, TERMINAL ILEUM AND COLON IN PATIENTS WITH INFLAMMATORY BOWEL DISEASE: A POTENTIAL NOVEL THERAPEUTIC TARGET

M. Garg1, S. Royce2, C. Tikelis3, C. Shallue4, P. Sluka5, H. Wardan6, D. Batu7, E. Velkoska1, L. M. Burrell1, M. Thomas1, A. Mefarlane1, P. R. Gibson3, J. Lu5

1Gastroenterology, Eastern Health, Box Hill, Melbourne/Australia/VIC
2Pharmacology, Monash University, Clayton, Melbourne/Australia/VIC
3Biochemistry Of Diabetic Complications, Baker IDI, Melbourne/Australia/VIC
4Eastern Health Clinical School, Monash University, Box Hill, Victoria/Australia/VIC
5Eastern Health Clinical School, Monash University, Box Hill, Melbourne/Australia/VIC
6Baker IDI, Melbourne/Australia/VIC
7Medicine, Austin Hospital, University of Melbourne, Heidelberg, Melbourne/Australia/VIC
8Baker IDI, Melbourne/Australia/VIC
9Biochemistry Of Diabetic Complications, Baker IDI, Melbourne/Australia
10Medicine, Monash University, Melbourne/Australia/VIC

Contact E-mail Address: mayur.garg@monash.edu

Introduction: The renin-angiotensin system (RAS) has well-recognised roles in cardiovascular and renal homeostasis, but may also regulate inflammation, fibrosis and angiogenesis in multiple other organs, including the gastrointestinal tract. The recently recognised alternative RAS axis comprising angiotensin converting enzyme 2 (ACE2), the effector peptide angiotensin (Ang) (1–7) and the Mas receptor, mediate anti-inflammatory and anti-fibrotic effects as opposed to the classical axis comprising ACE, Ang II and the AT1 receptor. This study aimed to prospectively characterise the RAS in the circulating and intestinal compartment in patients with inflammatory bowel disease (IBD) and non-IBD controls.

Aims & Methods: Circulating components of the RAS were measured in patients with Crohn’s disease (CD), ulcerative colitis (UC) and non-IBD controls, and associations with mucosal disease activity evaluated. Terminal ileum, ascending and sigmoid colon from patients undergoing intestinal resection and colostomy were surveyed for these components by mRNA expression by qRT-PCR, and immunohistochemical localisation and semi-quantification of particle density using microscopic image processing software. ACE2 activity was measured in biopsy samples.

Results: 56 patients with CD (mean age 41 [range 21–76] y, 27 females), 45 with UC (44 [22–42], 19 females) and 39 non-IBD controls (46 [22–83], 21 females) were included. The major differences in demographic features were noted across the three groups. Circulating renin (mean 25.4% (95% CI 21.6-29.1) vs 18.6 (13.9-23.3) mIU/L, p=0.026), ACE2:ACE ratio (mean 0.61 (95% CI 0.48–0.75) vs 0.40 (0.32–0.47), p=0.028) and Ang (1–7) (mean 22.8 (20.1-25.4) vs 17.4 (14.9–19.4)), p=0.002) were higher, and IL-17A levels were lower in IBD patients compared with controls. No significant correlations between circulating RAS components and markers of disease activity (faecal calprotectin, C-reactive protein, platelet or white cell counts, or albumin) were noted. ACE2 activity was evaluated in 21 patients using digital image analysis and magnetometry. ACE2 activity was higher in IBD patients with disease activity evaluated. Terminal ileum, ascending with Crohn’s disease (CD), ulcerative colitis (UC) and non-IBD controls, and classical axis comprising ACE, Ang II and the AT1 receptor, mediate anti-inflammatory and anti-fibrotic effects as opposed to the enzyme 2 (ACE2), the effector peptide angiotensin (Ang) (1–7) and the Mas receptor. This study aimed to investigate the potential of VDZ and the ETZ surrogate antibody FIB504 (ETZs) were tested. In a humanized mouse model the portion of CD4+ and a decreased expression of CD8+ and Th9 lymphocytes from IBD patients treated with VDZ was higher in the maintenance phase of treatment.

Conclusion: Both HBV and HCV are risk factors for preterm births, while HCV seems to be associated with a protective effect against preeclampsia. Future studies should corroborate these findings.

Disclosure of Interest: All authors have declared no conflicts of interest.

Contact E-mail Address: sebastian.zundler@uk-erlangen.de

Introduction: The anti-α4β1 antibody vedolizumab (VDZ), which inhibits gut homing of lymphocytes via interaction of α4β1 with MAdCAM-1, has greatly increased therapeutic options in patients with IBD. However, lymphocyte homing may also occur via other homing molecules like the α4β7 integrin and a considerable portion of patients does not respond to VDZ therapy. The anti-β2 antibody etrolizumab (ETZ) is currently tested in phase III trials and additionally blocks the binding of αEβ7 to E-Cadherin, which is believed to mediate epithelial retention of homed lymphocytes. Aims & Methods: We aimed to compare lymphocyte trafficking upon blocking of β7 vs. α4β7 integrin. Hence, α4β7 and αEβ7 expression was determined on peripheral blood and lamina propria lymphocyte subsets of UC and CD patients and healthy donors by flow cytometry or immunofluorescence staining, respectively. The regulation of αEβ7 expression upon lymphocyte stimulation and incubation with cytokines was studied. In vitro adhesion assays of the adhesive potential of lymphocytes to MAdCAM-1 and E-Cadherin of CD4+ and CD8+ lymphocytes from IBD patients treated with VDZ and the ETZ surrogate antibody FIB504 (ETZs) were tested. Finally, lymphocytes from UC patients were treated with either of the compounds and injected into the ileocoeal artery of immune-suppressed mice. Gut homing was assessed by in vivo confocal microscopy and flow cytometry of lamina propria cells.

Results: αEβ7 expression was significantly higher on CD8+ lymphocytes than on CD4+ lymphocytes both in the peripheral blood and the gut. Among both subsets αEβ7 expression was correlated with IL-9 secretion, while CD4+ IL-7 cells expressed less αEβ7 than other CD4+ subsets. At the same time, CD8+ cells exhibited a notably greater potential to increase αEβ7 expression upon T cell stimulation and TGF-β treatment, while decreased αEβ7 expression on CD8+ cells. ETZs markedly inhibited binding of CD4+ and CD8+ lymphocytes to Rho-Cadherin and blocked the adhesion of CD4+ and CD8+ lymphocytes to MAdCAM-1 to a degree comparable with VDZ. Fewer lymphocytes bound to a mix of both ligands upon treatment with ETZs compared with VDZ. In our humanized mouse model the portion of human CD8+ cells in the murine gut was significantly reduced three hours after injection when cells were treated with ETZs vs. VDZ. Among CD4+ cells, the fraction of CD4+ cells was decreased. The expression of αEβ7 on CD8+ cells from IBD patients treated with VDZ was higher in the maintenance than in the induction phase of treatment.

Conclusion: VDZ may not equally cover all pathogenetically relevant lymphocyte subpopulations compared with treatment in other IBD patients. ETZs seems to offer superior reduction of intestinal lymphocyte infiltration especially concerning CD8+ and Th9 cells.

Disclosure of Interest: S. Zundler: The etrolizumab Surrogate antibody was produced by Genentech, CA, USA. Sanofi was neither involved in conception and design of the study nor in analysis and interpretation of the results. SZ received funding from Takeda.
P. Hendy1, D. Reddi2, D. Bernardo3, L. Duranti4, A. Noble5, N. English5, S. C. Knight6, J. H. Takeda7

1St. Mark’s Hospital, Harrow/United Kingdom
2Antigen Presentation Research Group, Imperial College, London/United Kingdom
3Gastroenterology Unit, University of La Princesa, IP, and CIBERehd, Madrid/Spain
4Antigen Presentation Research Group, Imperial College, London/United Kingdom
5Gastroenterology, St Mark’s Hospital, Harrow/United Kingdom

Contact E-mail Address: philiphendy@doctors.net.uk

Introduction: Dendritic cells (DC) can determine whether the mucosal immune system mounts an inflammatory or regulatory response to antigen and likely contribute to the pathogenesis of Crohn’s disease. Vitamin D down-regulates DC inflammatory responses and could prove beneficial as a treatment adjunct in Crohn’s. Vitamin D also modulates DC homing marker expression. This study assessed the effect of high dose parenteral vitamin D treatment on circulating DC phenotype and function in patients with active luminal Crohn’s disease receiving anti-TNF therapy.

Aims & Methods: Peripheral blood mononuclear cells were isolated from 14 patients with active luminal Crohn’s disease and suboptimal vitamin D levels (<75 nmol/L) prior to and 6 weeks after starting anti-TNF therapy. Aims & Methods: DC within peripheral blood mononuclear cells from adults with active luminal Crohn’s disease or from healthy controls were characterised using flow cytometry. DC were identified as HLA-DR+ and negative for markers of other cell lineages (CD3, CD14, CD16, CD19, CD34). Myeloid DC (mDC, CD11c+CD123) and plasmacytoid DC (pDC, CD11c+CD123) were assessed for phenotype (maturation status, homing markers and pattern recognition receptors) and on-going cytokine production by surface and intracellular staining respectively.

Results: In patients with Crohn’s disease (n=20), a greater proportion of myeloid DC expressed a gut-homing profile (CLA+7%, p=0.001) compared to healthy controls (n=13) where most myeloid DC were not tissue-specific (CLA-97%, p=0.0016). In Crohn’s disease and controls, gut-homing (CLA+7%, p=0.001) whilst plasmacytoid DC were strongly skin (CLA+77% and lymph node (CCR7+15%) homing (p=0.0001). Production of pro-inflammatory cytokines was up-regulated in Crohn’s, with myeloid DC producing higher levels of TNFα and plasmacytoid DC producing higher levels of IL-10 than controls (p=0.0042 and p=0.013 respectively). Expression of maturation marker CD86 was increased on myeloid DC in Crohn’s but not on plasmacytoid DC (p=0.027 and p=0.13 respectively). Expression of IFN-a, IL-1β, IL-12, CD40, CD80, TL2R2 and TLK4 on DC did not differ between Crohn’s and controls for either DC subset.

Conclusion: The increased myeloid DC expression of gut homing phenotype may contribute to the production of pro-inflammatory cytokines in Crohn’s disease compared with controls. Our data highlights the central role that this dendritic cell subset plays in the pathogenesis of Crohn’s disease. Differences between homing markers on myeloid DC (gut homing) and plasmacytoid DC (skin homing) suggest that they may have different regulatory roles for Crohn’s, with myeloid DC being central to gut inflammation whilst plasmacytoid DC might be involved in cutaneous Crohn’s disease and the skin sequelae of anti-TNF therapy.

Disclosure of Interest: P. Hendy: Advisory board for: Falk, AbbVie
All other authors have declared no conflicts of interest.

PO387 A PROTEOMIC APPROACH TO EXPLORE THE PROTECTIVE ROLE OF INULIN IN PREVENTING LPS-INDUCED HUMAN COLONIC SMOOTH Muscle IMPAIRMENT

A. Altomare1, C. Vannini2, M. P. L. Guarino1, S. Barera1, V. Locato3, S. Coccia4, G. Arrigoni3, R. Alboni1, L. De Gara2, M. Cicala3, S. Berti1

Gastroenterology Unit, Cagliari University Medical School, Italy
2Department Of Biotechnology And Life Science, University of Insubria, varese/Italy
3Department Of Biotechnology And Life Science, University of Insubria, Varese/Italy
4Food Sciences And Human Nutrition Unit, Campus Bio Medico University, Rome/Italy
5Surgery Unit, Campus Bio Medico University, Rome/Italy

Contact E-mail Address: a.altomare@unicampus.it

Introduction: Fructans, such as inulin, are dietary fibers which stimulate gastro-intestinal function acting as prebiotics. We recently demonstrated the protective effect of inulin on LPS-induced damage of colonic smooth muscle in an ex vivo experimental model, which seems to be related to presence of oxidative stress.

Methods: In the present study the protective effect of inulin induced oxidative stress was evaluated on colonic mucosa using a proteomic approach. Human colonic mucosa and submucosa, obtained from disease-free margins of resected segments for cancer, were sealed between two chambers containing Krebs solution, with 5 ml of the mucosa overlaid with 5 ml of Krebs, or 100 μg/ml LPS solution, or 100 μg/ml LPS +100 mg/ml inulin Fructafit IQ (LPS+INU). The biological system was kept oxygenated for 30 min at 37°C. The solutions on the submucosal side were collected following mucosal exposure to Krebs in the absence (N-undernatant) or presence of LPS (LPS-undernatant) or LPS + inulin (LPS+INU-undernatant). Undernatants were tested for the effects on human colonic smooth muscle strips contractility using an organ bath system. Proteomic analysis (iTRAQ based analysis) was used to analyse and compare the soluble proteome from human colonic mucosa and submucosa treated. Each sample was labelled by one of four reagents of the iTRAQ 4-plex and then combined into one aliquote. Tripletic labelling was performed, which showed a high level of reproducibility.

Conclusion: Inulin exposure was able to restore, in human colonic mucosa, the LPS-dependent alteration of some proteins involved in the host response and in the intestinal smooth muscle contraction (ZG16, CALM1/M1LCK, MYL signaling pathway) and to reduce the upregulation of two proteins involved in the radical oxygen species (ROS) induced by LPS (APE1 and CC17). Moreover, the administration of inulin entails a higher level of some detoxification enzymes (MT2A, GSTK1, and UGT2B4) with respect to LPS treatment. Following exposure to the LPS-undernatant, a significant decrease in maximal Ach-induced contraction was observed with respect to the controls. Inulin treatment in control mucosa strips incubated with the N-undernatant (49±5% vs 10±1% respectively, P<0.05) and this was completely prevented by pre-incubation of the LPS with Inulin (12±2%, P=ns versus N-undernatant).

Disclosure: Our data suggest that the exposure of colonic mucosa to inulin is able to prevent LPS-dependent altered expression of some key proteins which promote intestinal motility and the host response, reducing the radical-mediated oxidative effect on the human colonic mucosa.
Disclosure of Interest: All authors have declared no conflicts of interest.

Reference

OP388 TLR4 IS STILL ACTIVE IN GP96-DEFICIENT MACROPHAGES
Division Of Gastroenterology And Hepatology, University Hospital Zurich, Zurich/Switzerland

Contact E-mail Address: jcosinroger@uoz.ch

Introduction: GP96 is an endoplasmic reticulum chaperone for multiple protein substrates which plays an important role in innate and adaptive immunity. Lack of this protein in intestinal macrophages (iMACs) of Crohn’s Disease (CD) patients is correlated with a loss of tolerance against the host gut flora, triggering a chronic and persistent inflammation. iMACs are crucial for pathogen recognition at the mucosal surface of the gastrointestinal tract and Toll-like receptors (TLRs), one of the best investigated family of pattern recognition receptors, lead to the phosphorylation of NF-κB after their activation. Previous studies of our group revealed a strong expression of TLR2 and 4 on inflammatory iMACs leading to a higher susceptibility of CD patients to LPS, in parallel with a specific loss of gp96.

Aims & Methods: We aim to study the impact of the gp96-knockdown on TLR-function in the human monocytic cell line MM6 and in a conditional gp96-LysMCre knock-out mice. MM6 cells were stably transduced with lentiviral gp96-knockdown vector. The lentiviral vector particles were produced by co-transfection of HEK293T cells with transfer, packaging and envelope plasmids using Fugene HD Transfection Kit. After transduction, cells were treated with LPS (100 ng/ml) for 2 hours. Furthermore, in order to analyze the relevance in vivo, conditional LysMCre-gp96 knock-out (KO) mice were also generated after crossing gp96lox/lox mice with LysMCremice. Peritoneal macrophages were isolated from both, wild-type (WT) and KO mice, and treated with LPS (100 ng/ml) for 2 hours. In transduced MM6 cells and peritoneal macrophages, TLR2 and TLR4 expression was analyzed by flow cytometry and the expression of NF-κB, IkB, IL-8, IL-6 and TNF-α were measured by Western blot, PCR and ELISA. Results are expressed as percentage or fold induction ± SEM. All experiments were performed with at least three.

Results: After checking that the efficiency of lentiviral knockdown was more than 90%, we performed a flow cytometry experiment revealing that the expression of TLR4 and TLR2+gp96 shRNA transduced cells were slightly decreased, 81% and 77% respectively, compared with mock-transduced MM6 cells, 92% and 97% respectively. In line with this, the analysis of the expression of TLR4 and TLR2 receptors in peritoneal macrophages showed a similar slight decrease in KO mice (74.4% and 77.0% respectively) compared with WT mice (78.2% and 90.5% respectively). The functionality of TLR4 receptor was also analyzed and treatment with LPS induced a significant increase in the ratio pIκBα/IκBα in gp96 shRNA cells (1.6 fold induction) and in KO peritoneal macrophages (5.1±1.5) and in protein expression of pNFκBα in both gp96 shRNA (1.7) and in KO peritoneal macrophages (1.5±0.6) compared with non-treated mock-transduced cells and WT peritoneal macrophages. Furthermore, LPS induced a significant increase in mRNA and protein expression of IL-8 (9 fold induction and 800 pg/ml respectively) in gp96 shRNA compared with mock-transduced cells. These results were strongly reinforced since LPS also induced a significant increase in the mRNA expression of IL-8 (11.7±2.6), IL-12 (12.3±3.9) and TNF-α (7.9±1.9) in KO peritoneal macrophages compared with non-treated macrophages.

Conclusion: TLR4 receptor is still active and functional even in the absence of gp96.

Disclosure of Interest: All authors have declared no conflicts of interest.
Introduction: In the previous study we observed that HOXB7 is highly expressed in gastric cancer and promote migration or invasion, and inhibit apoptosis in gastric cancer cells.

Aims & Methods: We aimed in this study to demonstrate the roles of HOXB7 in development of epithelial-mesenchymal transition (EMT) and metastasis in gastric cancer using in vitro and in vivo model. We established HOXB7-expression stable cell lines (MKN45-B7) and mock cells (MKN45-mock). Western blot was performed to validate EMT markers and phospho-Akt/PTEN activity. By injection of stable cell lines, xenograft tumors were produced on the 8-week old male Balb/C nude mice (nu/nu). 4 weeks after injection, we extracted xenograft tumors, and implanted fragment of tumors on the stomach of another 8-week old nude mice. 6 weeks after implantation, mice were sacrificed and their peritoneal metastasis, perigastric lymph node and volume of gastric tumor were compared between both groups.

Results: MKN45-B7 cells frequently showed fibroblast-like mesenchymal phenotype, whereas most of MKN45-mock cells showed epithelial phenotype. Mesenchymal markers (snail, vimentin) were up-regulated and epithelial marker (E-cadherin) was down-regulated in MKN45-B7 cells, as well as phospho-Akt level was increased and PTEN expression was decreased compared by MKN45-mock cells. The volume of xenograft tumor was significantly increased in MKN45-B7 cell-injected mice than MKN-mock cell injected mice. Mean number of peritoneal metastasis/perigastric lymph node and volume of gastric tumor were also significantly increased in MKN45-B7 tumor-implanted mice. When we transiently transfected siAkt on MKN45-B7 cells, snail and vimentin expression were down-regulated, whereas E-cadherin expression was up-regulated, compared by siControl-transfected MKN45-B7 cells.

Conclusion: Our findings suggest that HOXB7 may play crucial role in inducing EMT and promoting metastasis in gastric cancer via modulating Akt/PTEN axis.

Disclosure of Interest: All authors have declared no conflicts of interest.

Disclosure of Interest: All authors have declared no conflicts of interest.
**Introduction:** Appendectomy has been the standard treatment for acute appendicitis for more than 90 years. Appendectomies are performed annually in the United States. Although appendectomy is generally well tolerated, it is a major surgical intervention and can be associated with postoperative morbidity. Our APPAC trial comparing antibiotic therapy with appendectomy for the treatment of acute appendicitis showed that all patients randomized to antibiotic treatment did not require appendectomy during the 1-year follow-up period, and those who required appendectomy did not experience significant or increased complications.

**Aims & Methods:** The objective of this study was to compare the treatment costs of antibiotic therapy and appendectomy for treatment of uncomplicated acute appendicitis in our APPAC Acuta (APPAC) randomized clinical trial. The APPAC trial was a multicenter, open-label, non-inferiority randomized clinical trial that was conducted in Finland from November 2009 until June 2012. A total of 530 adult patients aged 18 to 60 years with CT-scan confirmed uncomplicated acute appendicitis were enrolled in six Finnish hospitals. Patients were randomized to receive an early appendectomy (n = 273) or antibiotic treatment (n = 257). 

**Conclusion:** In the operative group, the overall societal costs were 16 times higher than in the antibiotic group. In both groups productivity losses represented a slightly higher proportion of overall societal costs than all treatment costs together, with diagnostics and medicines having a minor role. Patients in the operative group were prescribed significantly more and specific antibiotics.

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**Disclosure of Interest:**
All authors have declared no conflicts of interest.

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**References:**
Surgery for High Polyp Burden All 31 patients had a diagnosis of SPS and under- went IRA. The median total polyp count was 43 (IQR 34.56.5) and median proximal polyp burden was 31 (IQR 26.847.5). In the limited resection group 80% patients required further surgical intervention for endoscopically unmanageable polyp load. All had IRA as their second procedure. Total polyp burden (median 40, v 22.5, p 0.01) and proximal polyp counts (median 20, v 12, p 0.019) were significantly higher in those having more extensive surgery. In the limited resection group eight (80%) patients had a resection for cancer before a diagnosis of SPS was made. Total polyp burden (median 40 v 22.5, p 0.01) and proximal polyp counts (median 20 v 12, p 0.019) were significantly higher in those having more extensive surgery.

Surgery for High Polyp Burden All 31 patients had a diagnosis of SPS and underwent IRA. The median total polyp count was 43 (IQR 34.56.5) and median proximal polyp burden was 31 (IQR 26.847.5). In the limited resection group eight (80%) patients required further surgical intervention for endoscopically unmanageable polyp load. All had IRA as their second procedure. Total polyp burden (median 40, v 22.5, p 0.01) and proximal polyp counts (median 20, v 12, p 0.002) and number of proximal polyps >10 mm (median 10 v 2, p 0.008) were higher in this group compared with those having surgery for CRC alone.

Introduction: Serrated Polyposis Syndrome (SPS) is associated with an increased risk of colorectal cancer (CRC). Some patients may require colonic surgery but the literature regarding indication, procedure performed, outcomes and surgical decision making is sparse. We aimed to address these issues.

Aims & Methods: 434 patients with SPS, were retrospectively enrolled from 7 centers in the Netherlands and 2 in the UK. Data were retrieved from medical charts, pathology and endoscopy reports and collected in a centralized database. Data relating to surgical resection and surveillance outcomes were assessed.

Results: A total of 164 (38%) patients underwent colorectal surgery; 114 (70%) for CRC, 31 (19%) for high polyp burden and 14 (9%) for unresectable polyps. A total of 164 (38%) patients underwent colorectal surgery; 114 (70%) for CRC, 31 (19%) for high polyp burden and 14 (9%) for unresectable polyps.

Aim: To determine risk factors for colorectal cancer in SPS patients.

Method: We included all individuals who underwent resection for SPS cancers with adequate bowel cleansing and caecum intubation in the Polish National Colonoscopy Screening Program between January 2000 and December 2008. They were followed for colorectal cancer incidence and death through national registries until December 2013. We estimated adjusted hazard ratios (HR) for individuals with different adenoma characteristics compared to individuals without adenomas and derived a novel risk classification system.

Results: Among 159,928 individuals (median age 56 years; 37.6% males) with a median follow-up of 7.8 years we identified 82 colorectal cancers after adenoma removal (0.31%) and 194 in individuals without adenomas (0.15%). The strongest predictors for colorectal cancer risk were adenoma size 20 mm in diameter or high-grade dysplasia or CRC, 20 mm in diameter or high-grade dysplasia or CRC, and adenomas with a diameter 10 mm, with high-grade dysplasia, or with villous histology (25%). The initial population comprised 100,000 average-risk individuals aged 40 years. Parameters of transition probabilities, costs, and test effectiveness were estimated and based on Japanese data.4 Four surveillance

Disclosure of Interest: All authors have declared no conflicts of interest.
strategies were evaluated for costs, gained quality-adjusted life-years (QALYs), and the required number of CS procedures. In strategy 1, post-polypectomy surveillance CSs were performed 1 year after polypectomy regardless of the polyp results. In strategy 2, the interval between surveillance CSs and polypectomy was 3 years regardless of the polyp results. Strategy 3 was a risk-stratified one, surveillance CSs were performed 3 years after the resection of high-risk polyps and 5 years after that of low-risk polyps. In strategies 1, 2, and 3, surveillance CSs were performed 10 years after normal CSs. Strategy 4 was also a risk-stratified one with more intense use of CS than strategy 3; the interval between surveillance CSs and the resection of high-risk polyps, low-risk polyps, and no polyps were 1, 3, and 5 years, respectively. In all strategies, a fecal immunochemical test-based CRC screening program was provided before surveillance, and uptake rates were set at 60% in the base-case analysis. A probabilistic sensitivity analysis (PSA) was also performed for all model parameters.

**Results:** QALYs and costs per person in strategy 1 are as follows: strategy 1, 23,004 QALYs and $US1,024.88; strategy 2, 23,000 QALYs and $1,009.02; strategy 3, 23,015 QALYs and $977.40; strategy 4, 23,046 QALYs and $970.31. The required numbers of CS procedures per person in strategy 1, 2, 3, and 4 were 2.143, 1.664, 1.617, and 2.548, respectively. Risk-stratified strategies (strategies 3 and 4) yielded higher QALYs with lower costs than strategies 1 and 2. Comparing strategy 3 with strategy 4, yielded QALYs were higher and required cost was lower in strategy 4. Strategy 4 was most-cost-effective, showing simple dominance over the other strategies, followed by strategy 3; however, strategy 4 required the most CS procedures. The PSA showed that the probability of stratified being chosen as the most cost-effective at the willingness-to-pay value of $50,000 was 67.8%.

**Discussion:** New, risk-stratified CS surveillance programs based on the polyp results should be recommended owing to higher expected effectiveness and cost-effectiveness. Furthermore, more intense use of CS procedures in risk-stratified surveillance can heighten the effectiveness and cost-effectiveness in the Japanese setting. However, it does require a larger number of CS procedures; thus, it would be preferable to determine the most appropriate use of CS procedures in risk-stratified surveillance programs depending on the nationwide availability of CS resources.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

**References**


**OP401 NEW NBI MAGNIFYING ENDOSCOPIC CLASSIFICATION FOR COLORECTAL TUMORS PROPOSED BY THE JAPAN NBI EXPERT TEAM (JNET)**


1 Department Of Gastroenterology And Metabolism, Hiroshima University Hospital, Hiroshima, Japan
2 Hiroshima University Hospital, Hiroshima, Japan
3 Sano Hospital, Kobe, Japan
4 Showa University Northern Yokohama Hospital, kanagawa,Japan
5 The Jikei University School of Medicine, Tokyo,Japan
6 National Cancer Center Hospital East, Tokyo/Japan
7 Tokyo Medical and Dental University, Tokyo, Japan
8 Takahiro Fujii Clinic, Tokyo,Japan
9 National Cancer Center Hospital East, Tokyo,Japan
10 Dept. Of Gastroenterology, Keio University School of Medicine Res and Developm, for Minimally, Tokyo,Japan
11 Tochigi Cancer Center, Tochigi,Japan
12 Department of Gastroenterology, Chofu Surgical Clinic, Tokyo,Japan
13 Shizuoka Cancer Center, Shizuoka,Japan
14 Kyoto University, Kyoto,Japan
15 Juntendo University, Tokyo,Japan
16 Kurume University, Fukuoka,Japan
17 St. Mary’s Hospital, Tokyo,Japan
18 Kinki University, Osaka,Japan
19 Osaka Medical Center for Cancer and Cardiovascular Diseases, Osaka,Japan
20 Machida Gastrointestinal Hospital, Osaka,Japan
21 Kyoto Katsura Hospital, Kyoto,Japan
22 Kyoto Prefectural University of Medicine, Kyoto,Japan
23 Fujita Health University, Aichi,Japan
24 Terai Clinic, Tokyo,Japan
25 Akita Red Cross Hospital, Akita,Japan
26 National Cancer Center Hospital East, Tokyo,Japan
27 Tokura Yamaguchi Clinic, Shizuoka,Japan
28 Tokoh University, Tokyo,Japan
29 Aomori Prefectural Central Hospital, Aomori,Japan
30 Endoscopy Division, National Cancer Center Hospital Endoscopy Division, Tokyo,Japan

**Contact E-Mail Address:** sumi02@hiroshima-u.ac.jp

**Introduction:** There have been many narrow-band imaging (NBI) magnifying endoscopic classifications advocated (Sano, Hiroshima, Showa, and Jikei classifications) so far in Japan. NBI magnifying endoscopy for qualitative and quantitative diagnosis for colorectal lesions is useful, however, some discussion in Japan has raised issues such as i) the presence of multiple terms for the same or similar findings, ii) the necessity of including surface patterns in magnifying endoscopic classifications, and iii) differences in the NBI findings between poly-poid and superficial lesions. To resolve these issues and unify the classifications, the Japan NBI Expert Team (JNET) was set up in 2011. The aim of this study is to scientifically evaluate the NBI scale and determine the NBI findings and diagnostic criteria used in the unified classification (The JNET classification).

**Aims & Methods:** The JNET classification, which is a modification of NICE classification, consists of 4 categories (Types 1, 2A, 2B, and 3) based on vessel and surface patterns without color. We made a hypothesis that each of them are correlated with the histopathological findings of hyperplastic polyp/sessile serrated polyp (SSP), low grade intramusosal neoplasia, high grade intramusosal neoplasia/shallow submuscosal invasive cancer, and deep submuscosal invasive cancer, respectively. A web image interpretation study using the modified Delphi (UMIN000010292: Multicenter study for developing universal NBI magnifying endoscopic classification of colorectal tumors in Japan) was conducted. 25 specialists in magnification evaluated NBI magnifying findings and histology with 100 NBI still images on the web.

**Results:** Univariate and multivariate analyses and analysis on diagnosability from 5 candidate NBI magnifying findings such as 1) loose vessel areas, 2) interruption of thick vessels, 3) scattered vessels, 4) thick, linearized/meandering atypical vessels in the tumor, and 5) amorphous areas of surface patterns for Type 3, and i) variable caliber of vessels, ii) thick vessels iii) irregular distribution of vessels, iv) vessel meandering, and v) irregular or obscure surface pattern for Type 2B. Among the five candidate NBI findings, three findings such as 1) loose vessel areas, 2) interruption of thick vessels, and 5) amorphous areas of surface patterns were identified as the diagnosis of type 3. In addition, three findings such as i) variable caliber of vessels, II) irregular distribution of vessels, and V) irregular or obscure surface pattern were selected for the diagnosis of type 2B.

**Conclusion:** Subclassification of NICE Type 2 (2A & 2B) could be performed scientifically with NBI magnifying findings without color using web image interpretation study, which could conduct differential diagnosis between low grade intramusosal neoplasia and high grade intramusosal neoplasia/shallow submuscosal invasive cancer.

**Disclosure of Interest:** All authors have declared no conflicts of interest.

Table (OP401)

<table>
<thead>
<tr>
<th>JNET</th>
<th>Type 1</th>
<th>Type 2A</th>
<th>Type 3</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Vessel pattern</strong></td>
<td>Invisible</td>
<td>Regular caliber</td>
<td>Variable caliber</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Regular distribution</td>
<td>Irregular distribution</td>
</tr>
<tr>
<td><strong>Surface pattern</strong></td>
<td>Regular dark or white spots</td>
<td>Regular (tubular/branched / papillary</td>
<td>Irregular or obscure</td>
</tr>
<tr>
<td>Similar to surrounding normal mucosa</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Most likely histology</strong></td>
<td>Hyperplastic polyp/ Sessile serrated polyp</td>
<td>Low grade intramusosal neoplasia</td>
<td>High grade intramusosal neoplasia/ Shallow submuscosal invasive cancer</td>
</tr>
</tbody>
</table>
OP402 SUBCLASSES OF TYPE-II PIT PATTERN REVEAL ALTERNATIVE TUMORIGENIC PATHWAYS OF COLORECTAL SERRATED LESIONS


1Dept. Of Molecular Biology, Sapporo Medical University, Sapporo/Japan
2Dept. Of Gastroenterology, Sapporo medical university, Sapporo/Japan
3Dept. Of Gastroenterology, Akita Red Cross Hospital, Akita/Japan
4Dept. Of Gastroenterology, Akita Red Cross Hospital, Akita/Japan
5Department Of Gastroenterology, Akita Red Cross Hospital, Akita/Japan
6Department Of Gastroenterology, Akita Red Cross Hospital, Akita/Japan
7Gastroenterology, Akita Red Cross Hospital, Akita/She/Japan
8Dept. Of Molecular Diagnostic Pathology, Ivate Medical University, Morioka/Japan

Contact E-mail Address: hitronori_a1123@yahoo.co.jp

Introduction: Colorectal serrated lesions (SLs) include hyperplastic poly (HP), traditional serrated adenoma (TSA) and sessile serrated adenoma/polyp (SSA/P). Emerging evidences suggest that SSA/Ps are precursor lesions of colorectal cancers (CRCs) with BRAF mutation and the CpG island methylator phenotype (CIMP). We have previously reported that Type II-Open (Type II-O) pit patterns, which is highly specific to SSA/P. However, clinicopathological and molecular features of SLs without Type II-O pits remain unclear.

Aims & Methods: We aimed to identify clinicopathological and molecular features of SLs without Type II-O pits. We analyzed the methylation of CIMP markers (MINT1, −2, −12, −31, p16 and MLH1) and BRAF and KRAS mutation in 448 premalignant and malignant colorectal tumors. By using magnifying endoscopy, surface microstructures of colorectal lesions were classified into Type II pit or tumor pit (Type III, IV or V pit) according to the Kudo’s pit pattern classification system. Type II pit was subclassified into classical Type-II pit, Type II-O pit, Type II-L (Type II-L) pit, and Type II plus tumor pit. These results suggest that lesions with Type II-L pit and those with Type II pit appear to develop through distinct tumorigenic pathways, though the majority of lesions with Type II or Type II-L pit were the same HP.

Conclusion: Our data suggest that Type II-L plus tumor pit is a useful hallmark of the premalignant stage of CRCs with KRAS mutation and CIMP-low.

Disclosure of Interest: All authors have declared no conflicts of interest.

OP403 ARTIFICIAL INTELLIGENCE (AI) IN ENDOSCOPY–DEEP LEARNING FOR OPTICAL BIOPSY OF COLORECTAL POLYPS IN REAL-TIME ON UNALTERED ENDOSCOPIC VIDEOS


1Gastroenterology, Vancouver General Hospital, Vancouver/Canada/BC
2Gastroenterology And Hepatology, Indiana University Medical Center, Indianapolis/United States of America/IN
3Ecole Polytechnique de Montreal, Montreal/Canada/QC
4Imagia, Montreal/Canada/QC
5University of Buenos Aires, Buenos Aires/Argentina
6University College Cork, Cork/Ireland
7St. Luke’s Hospital, Kilkenny/Ireland
8Cadens Imaging, Montreal/Canada/QC

Contact E-mail Address: mfbyrne@gmail.com

Introduction: ASGE-PIVI guidelines support a “resect and discard” strategy for diminutive colon polyps, provided that the predictive value of technology allowing for “optical biopsy” depicts at least 90% agreement in assignment of post-polypectomy surveillance intervals using pathology as standard. In addition, in order for a technology to be used to guide the decision to leave suspected diminutive rectosigmoid hyperplastic polyps in place (without resection), the technology should provide 90% negative predictive value for adenomatous histology. Such standards with optical biopsy might be achievable with experts (although even that is unclear) but do not cross over into general clinical practice. Several groups have looked at supporting the process of optical biopsy decision making on endoscopic assessment of the histology of diminutive colorectal polyps using traditional machine learning, but to date there are significant limitations in terms of (1) using still images only, and non-realtime computer support, both of which are not clinically efficient or effective, and (2) often involving magnification endoscopy that is not yet a widespread clinical practice. Deep learning is a branch of artificial intelligence which is a significant advance on traditional machine learning, and with huge computational power, machines can now recognize objects in real time. We sought to apply novel deep learning techniques to optical biopsy for colon polyps.

Aims & Methods: We aimed to evaluate deep learning applied to the classification of colorectal polyps into NICE types 1 and 2, in real-time on unaltered endoscopic videos, for the support of clinically efficient optical biopsy. We used 92 videos of small colorectal polyps (<10 mm) under white light (WL) and narrow-band imaging (NBI) (38 NICE type 1, 52 NICE type 2), using Olympus 190 series colonoscopes. “Optical biopsy” was done on all polyps by an expert with >95% accuracy (using pathology as the reference standard) prior to removal and histological confirmation.

We investigated a Deep Learning Artificial Intelligence model with a proprietary deep convolutional neural network (DCNN) for the computer-assisted NICE type 1&2 differentiation. We designed a 3-class model representing Types 1, 2, and unsuitable (frames without statistically representative information–blur, bubbles, liquid). The model operated at the individual frame level, without prior segmentation.

For model training purposes, each frame was manually tagged. The final dataset was split into training and validation sets, without overlap. Finally, the analysis was performed separately for NBI and WL frames, allowing for reporting of frame processing time and classification performance.

Results: A total of 33,954 training frames were used, split equally across NBI & WL, and type 1, type 2, & unsuitable classes. We performed a 5-fold cross-validation on the tagged frames for quality control. The trained DCNN model was then used to evaluate the unaltered videos in real-time, with an accuracy for polyp classification of 90% for NBI, and 93% for WL. The confusion matrix on whole-video classification of colorectal polyps gives a sensitivity of 93% and specificity of 85% for NBI. Finally, the processing time of our DCNN model ran at between 23 and 30 frames per second (fps) using a decent gamer-grade GPU (NVIDIA Titan-X) on an unaltered video feed of 60 fps, delivering near-realtime computer support.
Conclusion: To our knowledge, this is the first application of deep learning to the optical biopsy challenge for polyp differentiation into NICE types 1&2 using non-magnification colonoscopy and NBI, specifically in a clinically representative workflow where computer support is provided in realtime on unaltered endoscopic video streams. Although the present investigation was carried on a limited datasets of 92 videos, our deep learning model has shown clinically efficient and relevant performance for optical biopsy, well aligned with PIVI guidelines and the performance of experts. Ongoing work will determine if such a computer support solution could aid in the widespread adoption of a “resect and discard” strategy, and reduce the economic burden of pathological evaluation of benign diminutive colon polyps.

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D.K. Rex: Olympus consulting and research support
N. Chapados: Imagia has commercial interests in artificial intelligence
F. Soudan: Imagia has commercial interests in artificial intelligence
C. Oertel: Imagia has commercial interests in artificial intelligence
M. Linares Perez: research support from Satis Operations Inc
R. Kelly: research support from Satis Operations Inc
F. Chandelier: Shareholder in Cadens Medical Imaging

All other authors have declared no conflicts of interest.

<table>
<thead>
<tr>
<th>Age, mean (SD), y</th>
<th>48 (7)</th>
<th>48 (7)</th>
<th>50 (17)</th>
<th>52 (14)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Women, n (%)</td>
<td>5 (63)</td>
<td>5 (46)</td>
<td>19 (54)</td>
<td>17 (53)</td>
</tr>
<tr>
<td>Body mass index, mean (SD), kg/m²</td>
<td>22.6 (3.6)</td>
<td>23.3 (4.1)</td>
<td>22.2 (3.1)</td>
<td>22.2 (2.8)*</td>
</tr>
<tr>
<td>Stoma present, n (%)</td>
<td>7 (88)</td>
<td>11 (100)</td>
<td>10 (29)</td>
<td>10 (32)*</td>
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<tr>
<td>Colon-in-continuity, n (%)</td>
<td>1 (13)</td>
<td>1 (9)</td>
<td>22 (63)</td>
<td>24 (77)*</td>
</tr>
<tr>
<td>Estimated small bowel length, mean (SD), cm</td>
<td>128 (98)</td>
<td>129 (77)*</td>
<td>54 (43)*</td>
<td>73 (56)*</td>
</tr>
<tr>
<td>Baseline PS, mean (SD), L/wk</td>
<td>21.6 (8.1)</td>
<td>15.9 (10.4)</td>
<td>11.5 (5.9)</td>
<td>11.2 (6.4)*</td>
</tr>
<tr>
<td>Baseline PS duration, mean (SD), y</td>
<td>7.2 (7.4)</td>
<td>8.1 (8.0)</td>
<td>5.6 (5.3)</td>
<td>6.1 (5.7)*</td>
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</tbody>
</table>

* n = 31, 1 n = 9, 2 n = 32, 3 n = 30.

Disclosure of Interest: U. Pape: Has received grant/research support and served as an advisory board member or speaker’s bureau for NPS Pharmaceuticals, Inc., Shire plc, and Fresenius Kabi GmbH; served as a study investigator for NPS Pharmaceuticals, Inc.
P.B. Jeppesen: Has received grant/research support and served as a consultant, advisory board member, and study investigator for NPS Pharmaceuticals, Inc.
H. Lee: Employee and stockholder of Shire plc.
A.A. Grimm: Employee of Shire plc.
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