Abstracts

Annual Meeting Swiss Society of Gastroenterology (SGG)
Swiss Society of Visceral Surgery (SGVC)
Swiss Association for the Study of the Liver (SASL)
Interlaken (Switzerland), September 22/23, 2016
TABLE OF CONTENTS

Orals

2 S O1–O20

Posters Gastroenterology

7 S PG1–PG31

Posters Hepatology

15 S PH1–PH21

Posters Surgery

20 S PS1–PS15

Index of first authors

24 S

Impressum

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CH-4132 Muttenz, Switzerland
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Cover photo:
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The Guidelines for authors are published on our website www.smw.ch
Submission to this journal proceeds totally on-line: www.smw.ch
ISSN printed version: 1424-7960
ISSN online version: 1424-3997

Printed in Switzerland
Full thickness resection device (FTRD): A novel tool for colonic polyp resection. First clinical experience from two tertiary referral centers in Switzerland.

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Background and study aim: Recently a novel endoscopic tool, the so-called "Full Thickness Resection Device" (FTRD, Ovesco, Germany), has been introduced. FTRD allows colonic full thickness resection (FTR) of certain polyps that are not manageable by established techniques, especially non-lifting lesions measuring up to 30 mm in diameter. In addition, FTR is supposed to have a higher diagnostic accuracy in assessing depth of invasion in early cancer as compared to conventional endoscopic polypectomy techniques. We report our first clinical experience with FTRD procedures, assessing technical success, completeness of resection (R0 status), rate of histologically proven FTR and safety.

Patients and Methods: Retrospective analysis of 19 consecutive patients with colonic polyps treated with FTRD during the period of May 2015 through May 2016.

Results: 13 FTRD procedures were performed in the colon, 6 in the rectum. Indications were adenoma recurrence or residual adenoma with non-lifting sign after previous polypectomy (n=7), staging resection following presumed incomplete polypectomy of early carcinoma (n=4), treatment-naïve adenoma with non-lifting sign (n=5) and one adenoma located at the appendiceal orifice (n=1). In one case (polyp at appendiceal orifice) the lesion could not be reached once the FTRD system was mounted, due to diverticular narrowing of the sigmoid. In the 18 remaining cases amenable to FTR, resection was en bloc and histologically complete (R0) in 94.4% (17/18) of patients. Complete FTR was achieved in 83.3% (15/18), i.e. 91.7% (11/12) in the colon and 66.7% (4/6) in the rectum. The mean diameter of resection specimens was 2.6 cm (range 1.8-3.2 cm). Two technical failures occurred in the initial phase of the study (one problem of handling, one malfunction of the device). Two post-procedure minor bleedings were seen (one requiring endoscopic coagulation and adrenalin injection). Otherwise there were no complications during a one-month-follow-up.

Conclusions: According to these preliminary data, the novel technique of colonic full thickness resection by FTRD appears to be feasible, efficacious and sufficiently safe in the treatment of non-lifting polyps of ≤30 mm in diameter. FTR is an adjunct to the armamentarium of established colonic polypectomy techniques, as it offers minimally invasive treatment to a group of patients that would otherwise undergo open surgery. Limitations include a lower rate of complete FTR in the rectum as compared to the colon. This has to be taken into account when dealing with dysplastic polyps or early carcinoma, where the purpose of FTR includes assessment of depth of invasion. Further prospective studies will have to corroborate this concept.

Electrical Stimulation (ES) of the Lower Esophageal Sphincter (LES) to address Gastroesophageal Reflux Disease (GERD) in Patients after Sleeve Gastroctomy (SG)

Yves Borbély1,2, Dino Kröll3, Johannes Lenglinger1, Radu Tutuian1,2, Beat Mugelli1, Philipp Nett1
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Background: SG is the most commonly performed bariatric procedure. It results in new-onset GERD and may worsen pre-existing GERD. Patients 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 and might provide an alternative to RYGB.

Methods: 9 Patients with LSG and symptomatic GERD despite maximum antireflux-therapy underwent laparoscopic placement for electrodes of ES with hiatal closure if needed and were prospectively recorded. Electrical stimulation was delivered at 5mA, 220Usec pulses in 12 30-minute sessions daily. GERD outcomes pre and post-stimulation were evaluated.

Results: 5 patients were female (56%), median BMI was 41kg/m2 (min 31- max 53). Median time after SG was 3.2 years. There were no perioperative complications; one patient was readmitted for pain. At follow-up after 6 months (n=6), esophageal acid exposure normalized in 5 patients (83%), 2 patients were on PPI for reasons other than GERD.

Conclusions: Preliminary results of patients with refractory GERD after LSG treated with ES of LES revealed this therapy to be safe and efficient. It results in a significant improvement in GERD symptoms and esophageal acid exposure.

Portomesenteric Reconstruction during Whipple Procedures: Feasibility and Rational for on demand Intraoperative Xeno-Pericardial Self-Made Tube Graft

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Objective Achieving R0 Resection by reconstruction of SMV or SMV-PV in pancreatic tumor has been shown to be asociated with low rates of perioperative morbidity and similar survival compared to standard pancreatectoduodenectomy. We evaluated the feasibility and safety of self made tube grafts for venous reconstruction.

Methods
Tension-free end-to-end-anastomosis was not feasible because of advanced portomesenteric infiltration. Selfmade tube grafts were performed on demand. Graft patency was intra- and postoperatively tested by doppler assessment.

Results
Two cases of extensive portomesenteric infiltration in pancreatectoduodenectomy. SMV reconstruction was performed by on demand manufactured interposition xenograft. Venous occlusion was below 30 minutes. No postoperative bleeding or abnormal laboratory tests occurred. Intraoperative and postoperative graft patency were without pathological findings.

Conclusion
On demand manufactured bovine tube xenografts showed to be safe. Selfmade tube grafts offer immediate intraoperative availability without preoperative planning and without additional morbidity and mortality. Beside the procedure is effective in costs it offers equivalent behaviour to autologous grafts in septic complications.

To-hydroxy-4-cholesten-3-one for Diagnosis and Management of Bile Acid Malabsorption: first year clinical experience.

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1 Gastroenterology, UVCN: Visceral Surgery, UVCN and University Institute of Clinical Chemistry 1, University Hospital Bern

Introduction
The hydroxy-4-cholesten-3-one (THCO) is a reliable method to diagnose bile acid malabsorption (BAM). Since THCO is an intermediate metabolite in the bile acid synthesis, increased levels reflect bile acid production, which is the case in BAM. The procedure is effective in aortic coarctation and stenosis in patients with aortic valve malfunction or aortic regurgitation. In patients with aortic valve malfunction or aortic regurgitation, the procedure is effective in assessing depth of invasion.

Methods
We evaluated retrospectively, prospectively collected clinical data during the first year after implementation of a new test using ultra-high performance liquid chromatography coupled to mass spectrometry to measure THCO. In adult patients with clinical suspicion of BAM, unexplained diarrhea and a subgroup with obesity THCO was measured. Levels < 30 ng/ml are considered as normal values. The decision to treat with cholestyramine was at the discretion of the treating physicians.

Results
We performed 126 THCO analysis in 112 patients (62% female, mean age 51 ± 16 years) with a mean level of 84 ± 91 ng/ml. Cholestyramine treatment was more likely initiated in patients with Cronh’s disease (RR 1.8; 95%CI 0.8-3.7) or after ileocolonic resection (RR 3.1; 95%CI 1.7-5.7). Diazepam improved in 60% of patients with a THCO level above 40 ng/ml. Thresholds of 60 or 100 ng/ml do not improve prediction of response to cholestyramine treatment.

Table: THCO measurement in subgroups

| Subgroups | Number | Mean (ng/ml) | SD | Range
<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>Cholestyramine induced diarrhea</td>
<td>14</td>
<td>92</td>
<td>66</td>
<td>45-300</td>
</tr>
<tr>
<td>No diarrhea</td>
<td>33</td>
<td>59</td>
<td>71</td>
<td>&lt;5-300</td>
</tr>
<tr>
<td>Cholestyramine treated</td>
<td>29</td>
<td>87</td>
<td>105</td>
<td>61-300</td>
</tr>
<tr>
<td>Cholestyramine untreated</td>
<td>15</td>
<td>84</td>
<td>105</td>
<td>47-298</td>
</tr>
<tr>
<td>Cronh’s disease (CD)</td>
<td>16</td>
<td>182</td>
<td>105</td>
<td>13-300</td>
</tr>
<tr>
<td>Ileocolonic resection (IR)</td>
<td>26</td>
<td>157</td>
<td>105</td>
<td>28-300</td>
</tr>
<tr>
<td>CD + IR</td>
<td>13</td>
<td>214</td>
<td>95</td>
<td>41-300</td>
</tr>
</tbody>
</table>

p<0.05; *p<0.001; *Validation. Range 5-300 ng/ml

Conclusion
A THCO measurement above 40 ng/ml seems to be associated with a good response to cholestyramine treatment, which suggests clinical bile acid malabsorption. However, most patients have higher levels, particularly in Cronh’s disease after ileocolonic resection. These preliminary results warranted confirmation on a larger scale.
Misdiagnosis of a metastatic metastatic neuroendocrine tumor of the cecum

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Background

Neuroendocrine tumors of the mid gut can vary in their presentation depending on localization and stage. We present a case report where surgery was performed for a supposed metastatic neuroendocrine tumor of the cecum.

Methods

A 73-years-old male patient was sent to additional diagnostics because of slight abdominal pain and rising CRP, no pulmonary or other focuses. An abdominal CT-scan revealed a tumor in the ileocecal area which was PET positive with multiple PET positive lymph nodes and multiple liver metastases, a coloscopy showed a polypoid lesion in the cecum. Due to PET/CT and an elevated chromogranin A we had a strong suspicion of a metastasized carcinoid with local infiltration and locoregional lymphadenopathy. After presentation to our interdisciplinary tumor board we decided to do a hemicolectomy and an intraoperative excision of one of the liver tumors.

Results

Intraoperatively the situs presented an infiltrated and metastasized tumor similar to a cecum carcinoma. Surprisingly the histology showed an inflammation with central caseating necrosis with parts of rod-shaped bacteria. After positive result of mycobacterium in the bronchoalveolar lavage we started the specific drug therapy. The postoperative recovery was uneventful.

Conclusions

Tuberculosis of the cecum is rare and can be misdiagnosed as a malignant tumor. Even if this disease is rarely seen in clinical practice and even if there are no specific (e.g. pulmonary) symptoms, it should be considered in the differential diagnosis of abdominal pain and intestinal tumor.

Population-Based Screening for HBV and HCV Infections: Interim Analysis

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Background and aim: Further improvements in the management of HBV and HCV infections will depend on treatment impact at a population level for which screening is an essential step. Here, we report interim data of an ongoing large-scale screening study for HBV and HCV.

Methods: Individuals between 18 and 80 years attending the pre-operative consultation prior to minor surgery in a general surgical outpatient clinic are being tested. HBsAg, anti-HBc and anti-HCV since November 2014. The presence of anti-HCV was confirmed by an Immunodot test. HBV DNA and HCV RNA are determined in HBsAg- and anti-HCV-positive individuals.

Results: Among 1345 individuals tested so far, two were positive for HBsAg (0.2%) and one of these had detectable HBV DNA. Five individuals were positive for anti-HCV (0.4%) and two of these had detectable HCV RNA. When compared to those without, people with anti-HCV antibodies had already been screened more frequently for HCV (100% vs. 12%, p<0.001) as well as for HBV (80% vs. 20%, p<0.001), had more frequently anti-HBc antibodies (40% vs. 4.5%, p<0.001), and had used intravenous drugs (80% vs. 0.2%, p<0.001), nasal drugs (80% vs. 6.4%, p<0.001), or cannabis (80% vs. 7.3%, p<0.001) more frequently. None of them were immigrant from an endemic area. The median age of individuals with anti-HCV antibodies was not different from those without (49 years [range: 39-62] vs. 44 years [95% CI: 43-45], p=0.6).

Conclusions: This interim analysis of an ongoing population-based screening study shows a lower than expected prevalence of HCV infection. Persons with HCV infection would have been identified by a risk-based screening approach.

A Specific Mutation (PDGFRA) Helped Classify an Atypical Inflammatory Fibroid Polyph

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Introduction: Inflammatory fibroid polyps (IFP) are rare, benign mesenchymal lesions of the gastrointestinal tract. Recent molecular studies have identified platelet-derived growth factor receptor-α (PDGFRA) mutations, suggesting possible neoplastic qualities to IFPs. IFPs usually demonstrate typical histomorphological features including CD34-positive spindle cells arranged concentrically around submucosal vessels, extension into the mucosa and abundant eosinophils. However, signs of regression can make the diagnosis difficult based on morphology alone.

Case description: We report the case of a 51-year-old female with ulcerative colitis (diagnosed 2007), who underwent colonoscopy for surveillance as well as to assess mucosal healing under anti-TNF therapy. An ileal polyp was found and endoscopically resected.

Results: Conventional histology as well as immunohistochemistry was not conclusive to categorize this spindle cell tumor (negative for ckit, DOG1, SMA, S-100, ALK and Staff, normal expression of β-Catenin, positivity for CD34 (initially considered non-specific in context of morphology)). Molecular analysis found a mutation in Exon 18 (c.2525A>T) in PDGFRA. Molecular analysis revealing a PDGFRA-mutation led to the diagnosis of an IFP after other possible lesions (GIST, neural lesion or inflammatory pseudotumor) were excluded.

Conclusions: Molecular analysis revealing a PDGFRA-mutation led to the diagnosis of an IFP after other possible lesions (GIST, neural lesion or leiomyma) were excluded by immunohistochemistry. The absence of the typical appearance could be a result of regressive changes within the polyp. Based on this finding, a CT-scan was performed, which showed no further lesions. We also plan a gastroscopy, as gastric GISTs frequently occur in the recently described PDGFRA mutant syndrome. This entity and possibly genetic counseling should be considered when the diagnosis of IFP is made, something we plan to discuss with the patient.
Prophylactic mesh implantation for prevention of incisional hernia: A randomized controlled trial  
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Background  
Occurrence of incisional hernia is a frequent complication after open abdominal surgery, which often needs surgical repair. We hypothesized that patients at high risk for development of incisional hernia can benefit from prophylactic mesh implantation during primary surgery. 

Methods  
a randomized controlled trial was performed in patients undergoing elective open abdominal surgery at our institution. Patients with two or more risk factors (male gender, diagnosis of a malignant tumor, body mass index above 25 kg/m2 and history of previous laparotomy) were included. In the intervention group a double-layered polypropylene mesh was placed intraperitoneally in addition to standard abdominal closure. The primary endpoint was the incidence of incisional hernia. 

Results  
169 patients were included in the study, baseline characteristics were similar between the two groups. The cumulative incidence of incisional hernia one year postoperatively was 22% in the control group versus 4% in the intervention group (p=0.01). Perioperative complications were similar between the two groups. Abdominal pain 6 weeks postoperative was reported by 65% of patients in the intervention group versus 44% in the control group (p=0.02). One year postoperatively there was no significant difference in patients reporting abdominal pain. 

Conclusions  
Prophylactic mesh implantation in patients at risk for incisional hernia is safe and effective to prevent hernia occurrence. Patients with implanted mesh experience more abdominal pain early after operation, however long term pain perception is similar to patients without mesh. 

Into the mediastinum and out of the Papilla - minimal invasive extraintestinal endoscopic therapy in two body cavities  
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GZO-Spital Wetzikon, 1Department Innere Medizin, Abteilung Gastroenterologie, 2 Department Radiologie 

Background: A 48 years old patient with chronic ethylic pancreatitis presented with fever and dysphagia. CT scan revealed a cystic parasphageal structure and two small retroperitoneal cysts. 

Methods: On transesophageal EUS-FNA pus and elevated amylase confirmed the diagnosis of an infected pancreatic pseudocyst (pp). Subsequently drainage catheters were inserted transesophageally and stentcoccus anginosus was treated with iv-penicillin. Using the 10Fr Spyscope-DS, we entered the pp, located and passed the transhiatal fistula and reached the caudally located smaller pp. A guide wire (0.035 inch) was passed under visual guidance through the pp into the pancreatic duct (pd), advanced into the duodenum and extracted orally. By holding it tightly on both ends we were able to place a 5Fr 13cm plastic stent via the pp into the pd and the duodenum. The proximal end was placed visually in the small pp and the distal end in the duodenum. The esophago-cystic access was closed with hemoclipps. 

Results: Subsequently both the thoracic and the abdominal pp collapsed totally and the patient recovered completely. She is without symptoms after removing the stent completely five months later. 

Conclusions: This is the first reported endoscopic procedure passing a single endoscope extra-intestinally into both the thoracic and abdominal cavity. Thus we were able to treat an infected transhiatal pp by precisely placing a stent under visual guidance. The Spyscope-DS technology enables procedures outside the range of normal endoscopes even outside intestinal structures on both sides of the diaphragm. 

Adherence to Recommendations and Quality of Endoscopic Colorectal Cancer Surveillance in Long-standing Ulcerative Colitis  
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1Service of Gastroenterology, CHUV, Lausanne; 2Crohn and Colitis Center, Lausanne; 3Division of Gastroenterology, Basel University Hospital; 4Institute of Social & Preventive Medicine (IUMSP), CHUV, Lausanne 

Background: Current guidelines recommend endoscopic CRC screening in UC patients after 8 years of disease duration, with a procedure repeated then every 1-2 years. The aim of this study is to assess the adherence to guidelines and the quality of endoscopy in swiss long-standing UC. 

Methods: Retrospective cohort study with patients included in the Swiss IBD cohort. 

Results: we analyzed 391 colonoscopies in 94 patients (Men:51.1%, mean age at diagnosis: 30.5 years). 35.6% of the colonoscopies were performed with explicit indication for cancer screening. Out of those colonoscopies, 59.4% occurred after 8 years. Mean (SD) time until the next screening colonoscopy was 2.4 (1.5) years. Quality of colonoscopy was as followed: Caecal intubation 85.2%, good bowel preparation 48.6%, mean withdrawal time 15.8 minutes, chromoendoscopy: 2.6%, mean number of colonic biopsies: 14. Dysplasia/DALM was found in 14 cases (3.6%). Adenoma were found in 13 (3.3%) 

Conclusion: Despite current international recommendations, a significant number of patients were not included in a surveillance program. Patients undergoing surveillance colonoscopy were often inadequately prepared and chromoendoscopy was used in a minimal number of patients. Our data suggest that adherence to screening guidelines and endoscopic quality should be promoted and standardized. 

Survival of apoptosis-primed activated hepatic fibroblasts is Bcl-xL-dependent  
Anja Monsek1 (1), Achim Weber (2), Beat Müllhäuser (1), Christian Fingas (3), Joachim C. Mertens (1) 
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Background: Activated stromal fibroblasts (ASF) are the main stromal cell population in liver fibrosis and desmoplastic liver cancers and have been implicated in the development of these liver diseases. ASF display an activated phenotype and an increased sensitivity to apoptosis. This 'apoptotic priming' has been linked to changes in the cellular profile of apoptosis regulating Bcl-2 proteins. Targeting of Bcl-2 proteins in ASF could be explored for novel anti-fibrotic and anti-tumor therapies in the liver. Thus, our aim was to investigate the mechanisms of stromal cell activation with focus Bcl-2. 

Methods: For in vitro studies, fibroblasts were either treated with platelet derived growth factor (PDGF) alone or in combination with inhibitors of the anti-apoptotic Bcl-2 proteins (BH3 mimitics) and examined for activation and apoptosis induction. To investigate an anti-fibrotic potential of these compounds in vivo, the MDR2 mouse model of liver fibrosis was employed. 

Results: In vitro treatment of fibroblasts with PDGF results in downregulation of Bcl-2 and upregulation of Bax and Bcl-xL. Addition of BH3 mimetics with selective specificity reveals that survival of activated fibroblasts is Bcl-xL-dependent. In vivo studies demonstrate that pro-apoptotic BH3 mimetics reduce liver fibrosis in MDR2 mice. 

Conclusions: Treatment of ASF with Bcl-xL inhibitors could represent a potential target for the therapy of liver fibrosis and desmoplastic liver cancers.
HEV ORF3 Protein Forms Membrane-Associated Oligomers

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Background and aim: Hepatitis E virus (HEV) infection is believed to be the most common cause of acute hepatitis and jaundice in the world. HEV is a positive-strand RNA virus encoding 3 open reading frames (ORFs), namely ORF1, ORF2 and ORF3. The aim of this study is to investigate the structure and function of HEV ORF3 protein. HEV ORF3 protein interactions were investigated by co-immunoprecipitation and fluorescence resonance energy transfer (FRET). Wheat germ-based cell-free and mammalian cell expression systems displayed different apparent fluorescent protein (GFP) were examined by confocal laser scanning microscopy (CLSM) as well as membrane floatation assays. Glycosylation acceptor site tagging was used to define the capsid protein. Co-immunoprecipitation and FRET revealed oligomers to be secreted into the extracellular milieu together with the ORF2 protein. Results: Sequence analyses revealed the presence of a potential signal peptide and of a transmembrane (TM) segment within the N-terminal half of HEV ORF3 protein. CLSM combined with membrane floatation analyses and glycosylation acceptor site tagging demonstrated the existence of two TM segments of which the first serves as a signal peptide. ORF3 traffics to the plasma membrane to be secreted into the extracellular milieu together with the ORF2 capsid protein. Co-immunoprecipitation and FRET revealed oligomerization of the ORF3 protein through the N-terminal TM segment. Finally, HEV ORF3 proteins produced in cell-free and mammalian cell expression systems displayed different apparent molecular weights. Proteolytic processing or posttranslational modifications possibly explaining this difference are currently being investigated by mass spectrometry.

Conclusions: This study provides a basis for our ongoing efforts aimed at elucidating the three-dimensional structure of the HEV ORF3 protein and its function in the HEV life cycle.

HEV as a Cause of Acute Hepatitis Acquired in Switzerland

Montserrat Fraga, Christoph Doerig, David Semela, Florian Bihl, Beat Mühlpert, Benedetta Terzini Beretta-Piccoli, Felix Brunner, Amalio Telení, Gilbert Greub, Roland Sahli and Darius Moradpour

1Centre Hospitalier Universitaire Vaudois, University of Lausanne, 2Cantonal Hospital St. Gallen, 3Ospedali Regionali di Bellinzona e Mendrisio, 4University Hospital Zürich, 5Epatocentro Ticino, Lugano, and 6University Hospital Berne, Switzerland

Background: Autotochthonous hepatitis E is increasingly recognized as a zoonotic infection in western Europe. Serologic assays have a wide variety in sensitivity and specificity. Therefore, we implemented nucleic acid testing to diagnose and characterize hepatitis E virus (HEV) infection acquired in Switzerland.

Methods: Quantitative HEV RNA determination and genotyping were performed as described previously (Doerig C et al. EASL ILHC 2014 | J Hepatol 2014;60 Suppl 1:S302) in patients presenting with symptomatic acute hepatitis. Patients with a travel history to an endemic region as well as immunocompromised individuals with chronic hepatitis E were excluded from the present analysis.

Results: Sixty-nine cases of acute hepatitis E were recorded between November 2011 and May 2016; additional cases are still being fully characterized. Median HEV RNA was 6.0 × 10^6 copies/ml (range, 7.4-6.0 × 10^10 copies/ml). Complete serology was available in 59 patients; of these, 4 (7%) were negative for anti-HEV IgM and one was negative for both IgM and IgG. Genotyping was thus far successful in 56 cases, revealing infection with genotype 3 in 52 and with genotype 4 in 4 cases. Median ages were 59 years (range, 20-80 years); 53 were men (77%) and 35 of these (66%) were ≥ 50 years old. The clinical course was particularly severe in patients with underlying chronic liver disease, with fatal outcome in two patients with preexisting cirrhosis. At least three cases of brachial neuritis and one case of severe rhabdomyolysis were observed. One patient with brachial neuritis was treated with ribavirin in the acute phase, with a favorable outcome.

Conclusions: Middle-aged and elderly men constitute the majority of patients presenting with symptomatic acute hepatitis E acquired in Switzerland. Asymptomatic hepatitis E genotypes are currently being further investigated. Brachial neuritis represents a typical extrahepatic manifestation of HEV genotype 3 infection.

Targeting the Unfolded Protein Response Program Exhibits Potent Cytotoxic Effects in Liver Angiosarcoma Cells

Christian Perez-Sibilia, Marianne Kraus, Christoph Drissen, David Semela


Background: Hepatic angiosarcoma is an aggressive tumour with very dismal prognosis. In the last years, anti-angiogenic drugs targeting signalling pathways in endothelial cells have emerged as promising therapy for angiosarcoma. However, clinical trials with anti-angiogenics showed only minor efficacy. Therefore, new therapeutic approaches targeting other signalling pathways in liver angiosarcoma are needed. Our aim is to characterize our recently described liver angiosarcoma cell line at molecular level in order to target new pathways.

Methods: Molecular characterization was assessed by gene expression analysis using whole transcriptome Affymetrix microarrays. In vitro screening for effective compounds was evaluated measuring cell metabolic activity after treatment. Identified compounds were further assessed using in vitro tube formation on Matrigel by dye cytometric analysis activity was assessed by using proteasome-specific activity based probes.

Results: Molecular analysis of our angiosarcoma cell line revealed dysregulated genes associated with the unfolded protein response (UPR) and endoplasmic reticulum (ER) stress program i.e. Tcp1, Hsp, Ddit3, Eif2ak1. We exploited these pathways by using the proteasome inhibitors Carfilzomib and LU102 and the protease inhibitor Lopinavir. These inhibitors showed cytostatic effects in liver angiosarcoma cells. We have identified clinically available compounds with potent effects against difficult to treat angiosarcoma. Combinatory treatments showed synergistic effects and are therefore promising candidates for liver angiosarcoma treatment currently being tested in vivo.
Stump Appendicitis: a Challenging Diagnosis
Sebastian D. Sgardello, Carolina Bianco, Ahmed Abdelghany, Roberta Codecà, Carlo Coduri, Nicola E. Ghisletta

Background: Stump appendicitis (SA) is the interval repeated inflammation of any residual appendicular tissue following primary appendectomy. Incomplete removal of appendix leaves a stump that can cause recurrent appendicitis. We report a case of SA treated with laparoscopic completion appendectomy.

Methods: A 39-year-old female was referred to our emergency department with a 4-day history of upper and right lower quadrant abdominal pain (RLQ), raised inflammatory markers, leucocytosis, signs of local peritonism in the RLQ. A CT scan (CTS) showed thickening of the caecum wall and a suspect perforated appendicular stump with abscess formation. The patient was admitted to hospital with a 4-day history of upper and right lower quadrant abdominal pain (RLQ), raised inflammatory markers, leucocytosis, signs of local peritonism in the RLQ. A CT scan (CTS) showed thickening of the caecum wall and a suspect perforated appendicular stump with abscess formation. The patient was discharged on postoperative day 6 with no complications.

Results: Heightened awareness in recognizing SA is fundamental to avoid serious complications. Factors leading to SA are a retrocecal, subserous or duplicated appendix. SA occurs in open and laparoscopic appendectomy irrespective of how the appendiceal stump is closed. Neither inversion of the stump or simple ligature can prevent SA. Treatment is either open or laparoscopic completion appendectomy. An ileocolic resection may be necessary in case of significant inflammation around the ileocecal valve. Conclusion: SA is rare (1 in 50,000 cases). Diagnosis can be challenging and should be considered in cases of RLQ pain post-appendectomy. Treatment of choice is open or laparoscopic completion appendectomy. To minimize the risk of SA, in primary appendectomy, correct identification of the base of the appendix is mandatory and appendicular stump length should be <= 3mm.

Assessment of nutritional status through bioelectrical impedance is a key determinant of outcome in alcoholic hepatitis: a prospective study

Alcoholic hepatitis (AH) is a severe complication of alcoholic liver disease with an elevated mortality rate on the short term in spite of corticosteroids. A concomitant poor nutritional status is highly prevalent and has through bioelectrical impedance is a key determinant of outcome in alcoholic hepatitis: a prospective study. We explored the specific role of malnutrition in a prospective cohort of patients with regards to clinical outcome at 6 months. The results obtained so far show that there is a significant reduction of species richness (alpha-diversity) in CD samples in patients with AH. The incidence of inflammatory bowel diseases (IBD), including Crohn’s disease (CD) and ulcerative colitis (UC), is increasing throughout the world, particularly in developed countries. Although the etiology of IBD remains still largely unknown, recent studies indicate an altered gut microbiota in combination with an aberrant immune response against it are involved in genetically susceptible hosts. Here, we molecularly profiled the intestinal microbiota of phenotypically and genotypically well-characterized Swiss IBD cohort (SIBDC) patients.

A total of 540 biopsy samples from a combined 125 CD and 98 UC patients were processed. The microbiota composition at the site of biopsy was determined by 16S Amplicon sequencing on theIonTorrent platform. Data were analyzed using the QiIME pipeline.

The results obtained so far show that there is a significant reduction of species richness (alpha-diversity) in CD samples compared to UC samples. Additionally, UniFrac distance between IBD patients (β-diversity) implies the compositional difference between communities. More in-depth analysis demonstrated a higher abundance of Bacteroidetes and Proteobacteria in CD patients versus a higher abundance of Firmicutes and Actinobacteria in UC patients. The data presented here show that IBD patients are associated with a dysbiosis of the mucosa-associated microflora detected on biopsies. Combining the microbial profile data with phenotypic and genotypic information from these patients, we next aim to identify possible biomarkers that may help to predict disease predisposition, activity, and responsiveness to therapy.
The maternal microbiota drives early postnatal innate immune development

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Aims: Postnatal colonization of body surfaces and the intestine with microbes has been assumed to drive postnatal immune development. There is evidence that signals originating from commensals during early life or from maternal microbiota before birth are required to shape the neonatal immune system.

Material and methods: Reversible colonization of germ-free mice with an engineered E. coli strain allowed transient colonization of germ-free mice exclusively during pregnancy (gestational colonization). The dams then delivered and nursed their pups germ-free and offspring were never exposed to live bacteria.

Results: Gestational colonization increased intestinal NKp46+ class 3 innate lymphoid cells (ILC3) and F4/80+CD11c+ mononuclear cells in the pups. Intestinal epithelial transcriptional profiles of the offspring were extensively reprogrammed, including increased expression of genes for antibacterial peptides and metabolism of microbial molecules. These effects were independent of Toll-like receptors, but in some cases were dependent on maternal antibodies that retain microbial molecules and transmit to them the offspring during pregnancy and via milk. Using 13C-isotopically fully-labeled E. coli HA107 for gestational colonization and mass spectrometry, we followed specific bacteria-derived metabolites from the mother to the maternal milk and offspring tissues. Gestational bacterial metabolite exchange included natural microbial ligands for the any hydrocarbon receptor (AHR). Feeding pregnant mice with the AHR ligand indoles-3-carbinol was sufficient to increase intestinal NKp46+ ILC3s in the offspring, revealing the AHR pathway as one important factor in maternal microbiota-dependent shaping of the neonatal immune system. The offspring born to gestationally colonized mothers were primed to avoid inflammatory responses to microbial molecules and limit penetration of intestinal microbes during postnatal colonization.

Conclusion: Our data demonstrate that the maternal microbiota determine the composition and function of neonatal innate immunity.

Impact of bowel cleansing on the mucosa-associated microbiota in healthy volunteers: a pilot trial

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Changes in the microbiota composition induced by bowel preparation have been reported in stool samples. However, it is not yet established whether this is also the case for mucosa-associated microbiome, which is clinically more relevant. Therefore, we investigated mucosal biopsies and luminal content/stool samples harvested before (sightscopy) and after purging (PicoPrep: Natrium-Picosulfat) using ileocolonoscopy and sigmoidoscopy within 6, 12 and 24 hours from 3 healthy volunteers in 16S rDNA amplicon sequencing techniques. A marked reduction in abundance of main phyla being present before purging was detected in each volunteer at ileocolonoscopy and/or at 8 hours later. This was accompanied by an increase of Proteobacteria phyla. Within 24 hours an almost complete restoration of original microbiota in terms of main consortia could be observed.

Conclusion: Purging significantly induces marked changes in the mucosa-associated microbiome. The personal microbiota is being restored to initial microbiota within a day. This underscores the high dynamic nature of human microbiome and its capacity to replenish rapidly.

Circular long-distance endoscopic submucosa dissection in the esophagus for complex multilevel high-grade dysplastic long-segment Barrett esophagus: not a guarantee for curature

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Case: 69 y old female patient was referred with long-standing long-segment Barrett’s esophagus C11M11 (Prague classification) and development of high-grade dysplasia (HGD) being detected in a targeted biopsy as well as multi-level low grade dysplasia. After first endoscopic mucosa resection (EMR) of the target lesion other visible lesions were likewise removed by EMR. However, surveillance showed development of more visible lesions and hence, circular long-distance endoscopic submucosa dissection (ESD) was performed showing multiple HGD. However, 9 months later another visible lesion with histologically proven adenocarcinoma was detected and hence, en-bloc esophagectomy was performed revealing a pT1a pN0 (0/39), L1, V0, G1, R0 adenocarcinoma.

Conclusion: Despite an aggressive endoscopic resection approach utilizing a long-distance circular ESD in complex long-segment Barrett’s esophagus with multiple visible lesions this does not indicate cure. Close endoscopic surveillance is mandatory to detect the development of early cancer and provide the appropriate treatment.

Seated Evaluation of anorectal function by High Resolution Manometry: A randomized comparison of measurements in the seated and left lateral positions

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Introduction: High Resolution Anorectal Manometry (HR-ARM) is an emerging test for diagnosis of defecatory disorders. Important concerns remain about the validity of all manometry measurements because a proportion of healthy individuals appear to have dyskinesia during simulated defecation. This maybe because current investigations are usually performed not in the normal upright, seated position (SP), but in the left lateral position (LLP). The effects of position on anorectal function and patient behavior have not been well defined.

Aim: To test the hypothesis that position impacts on HR-ARM and balloon expulsion time (BET) measurements and to assess patient preference for SP vs. LLP.

Methods: Healthy volunteers (HV) and patients with obstructive defecation (OD) and fecal incontinence (FI) were recruited. HR-ARM and BET were performed in randomized order in SP and LLP using a solid-state catheter with 12 circumferential sensors and a rectal balloon secured by a probe holder (Given Imaging, Yooprof, Israel). Resting tone, "squeeze" pressure on voluntary contraction, recto-anal pressure gradient (RAGP) and BET during simulated defecation were assessed in both positions. Agreement between HR-ARM and BET with MR Defecography is shown in table.

Results: 20 HV (32 ± 15yrs; 11 female), 20 OD patients (OD; 51 ± 15yrs; 11 female; WS 2.3; CCS 13.3) and 20 fecal incontinence (FI; 52 ± 13 yrs; 10 female; Weaver Score (WS) 8.3; Cleveland Constipation Score (CCS) 3.3) were studied. A large majority (53/60) preferred investigation in SP. Resting and squeeze pressure were not affected by position (data not shown). During simulated defecation, abdominal pressure was lower in LLP than in OD and FI (Δ-23±7 mmHg, p=0.002; Δ-18±6mmHg, p=0.003) respectively; however, RAGP was reduced in LLP only in OD (Δ-58±7, p=0.001). Overall, 7/20 HV showed normal simulated defecation in SP but dyskinesia in LLP (p=0.016). Similarly, more individuals had pathological BET (>1 min) in LLP than in OD (19 vs. 6 HV; 19 vs. 6 OD; p=0.001).

Agreement between HR-ARM and BET with MR Defecography is shown in table.

Conclusions: There was a preference for investigation in SP. Measurements of resting and squeeze pressure are similar in both positions; however, assessment of simulated defecation by HR-ARM and BET is affected by position, especially in OD patients. Comparison of HR-ARM with MR suggests more accurate assessment of simulated defecation in the physiologic SP.
Influence of Different Biopsy Forceps Models on Tissue Sampling in Eosinophilic Esophagitis

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Background: Eosinophilic esophagitis (EoE) is a mixed inflammatory and fibrostenotic disease. Unlike superficial inflammatory changes, subepithelial fibrosis is not routinely sampled in esophageal biopsies. This study aims to evaluate the efficacy and safety of deep esophageal sampling with four different biopsy forceps.

Methods: In this cross-sectional study, esophageal biopsies were taken in 30 adult patients by one expert endoscopist in distal esophagus with a static jaw forceps (Olympus, FB-11K-1) and compared to proximal biopsies sampled with a static jaw forceps (Olympus FB-45Q-1), an alligator jaw (Olympus, FB-210K), and a large capacity forceps (Boston-Scientific, Radial Jaw 4). One pathologist evaluated the subepithelial area of epithelial and subepithelial layers in H&E-stained biopsies.

Results: Subepithelial tissue was sampled in 96.7% (static jaw FB-11K-1), 92.5% (static jaw FB-45Q-1), 80% (alligator jaw), and 55% (large capacity). The median [IQR] ratio of the surface area of epithelial to subepithelial tissue was 1.07 [0.65-4.465] (static jaw FB-45Q-1), 1.184 [0.608-2.545] (static jaw FB-11K-1), 2.353 [1.312-4.858] (alligator jaw), and 2.71 [1.611-4.858] (large capacity) (large capacity: a ratio of one signifies that equal amounts of epithelial and subepithelial tissue were sampled). A larger surface area of subepithelial tissue was obtained using the static jaw forceps when compared to that using alligator jaw and the large capacity forceps (p<0.001 and p=0.037) and the large capacity forceps (p<0.001). No esophageal perforations occurred.

Conclusions: The static jaw forceps allowed to sample subepithelial tissue in >90% of biopsies and appear to be superior to alligator or large capacity forceps in sampling larger amount of subepithelial tissue.

Caregiver-Assessed EoE Activity in Children Between 3-9 Years of Age Poorly Correlates With Physican Global Assessment, Endoscopic or Histologic Activity

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Background: We aimed to evaluate the relationship between caregiver-reported symptom severity of pediatric patients with eosinophilic esophagitis (EoE), the disease activity assessed by the physicians, endoscopic and histologic findings.

Methods: Caregivers of children between 3 and 9 years of age provided an overall assessment of symptom severity (CareGA, 7-day recall period). Children underwent EGD with esophageal biopsy sampling. Physicians evaluated patient medical history, symptoms, EoE-associated endoscopic and histologic findings, and provided an overall assessment of EoE activity (PhysGA).

Results: 93 children were included (73% boys, median age 6.0 years). Median CareGA of EoE symptom severity was 2.0 (IQR 0.0-4.0); median PhysGA of EoE activity was 2.0 (IQR 1.0-6.0). CareGA poorly correlated with PhysGA (Spearman’s r=0.01, p = 0.892), peak esophageal eosinophil counts (r=0.18, p=0.17), and increasing severity of endoscopic features (exudates: p=0.43; rings: p=0.19; edema: p=0.53; furrows: p=0.07; strictures: p=0.03). PhysGA of EoE overall activity correlated with peak esophageal eosinophil counts (r=0.81, p<0.001) and increasing severity of endoscopic features (exudates: p=0.01; rings: p=0.015; edema: p=0.001; furrows: p=0.001; strictures: p=0.09).

Conclusions: Caregiver assessment of EoE symptom severity, in contrast to physician global assessment of EoE activity, poorly correlates with physician global assessment of EoE activity, esophageal eosinophilia, and endoscopic activity. These findings must be taken into account when defining outcomes for clinical trials in young children with EoE.
POSTERS GASTROENTEROLOGY

Title: 13C-labeled bacteria metabolomics reveals the identity of bacterial metabolites in the host and the host metabolic responses.

Authors: Yasuhiro Uchimura [1], Tobias Fuhrer [2], Uwe Sauer [2], Kathy D. McCoy [1] and Andrew J. Macpherson [1]

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Background: A combination of physical barriers and innate and adaptive immunity prevents penetration of live bacteria from the intestines to systemic sites within our bodies. Nevertheless, we have found that bacterial products can propagate throughout the host organism.

Methods: In order to identify bacteria-derived metabolites in vivo, we colonized germ-free mice with bacteria that had been fully labeled with carbon-13 and then traced 13C-metabolites in various host sites by mass-spectrometry. In addition, the host metabolic response to bacterial colonization was also analyzed through mass-spectrometry.

Results: We identified bacterial metabolites in more than 25 different host tissues. The pattern of propagation of individual bacterial metabolites depended on their molecular features, such as hydrophobicity. We also found prominal host metabolic responses in the peritoneal cavity and portal organs such as liver and spleen as compared to other sites.

Conclusion: Our study demonstrates that 13C-bacteria metabolomics is a powerful technique to address metabolic relationship between gut microbes and the host.

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Title: Buried Bumper Syndrome: Tissue Dissection by Biopsy Forceps guided Papillotome

Authors: Gian-Marco Semadeni, Jan Borovicka, Romus Frei

Kantonsspital St. Gallen, Klinik für Gastroenterologie und Hepatologie

Background: Percutaneous endoscopic gastrostomy (PEG) is a well established and widely used method of nutrition delivery for patients with persistent inability of oral feeding. Buried bumper syndrome (BBS) is a severe late complication of this method, with an estimated incidence of 1%. The typical symptomatic triad of BBS include inability to insert the tube, leakage and loss of patency. Several techniques to dissect the overgrowing tissue are described, including needle knife dissection, argon plasma coagulation (APC) and papillotome dissection through the shortened cannula.

Methods: We describe two cases of BBS in which the papillotome dissection technique was adapted by endoscopic biopsy forceps guidance of the papillotome as following: Antibiotic prophylaxis with ceftriaxone was given. The PEG tube was cut 2-3cm over skin level and a guidewire was advanced over the cannula. The papillotome (Ultrascope, Boston Scientific) was thereafter advanced over the guidewire and its tip was endoscopically grasped by a forceps (Krokodil, Endo-Flux). While bending and pulling the papillotome, it was positioned as desired by the forceps and the overgrowing tissue was safely dissected in four positions. Subsequently, the liberated internal disc was grasped by the forceps and was pulled into the gastric lumen by additional external force through a savoye bougie. The intervention was completed by placement of a gastrotube over the same tract (see video of the complete intervention).

Results: Two male patients (age 27 with cerebral paresis and age 66 with myotonic dystrophy) with typical symptoms of BBS were endoscopically diagnosed with complete buried disc and persistant fistula orifice. Interventions were performed under general anesthesia due to severe comorbidity. Both cases were successfully treated by this adapted method without complications. Interventions lasted 48min and 27min, respectively.

Conclusions: This adapted method of tissue dissection in BBS by biopsy forceps guided papillotome is easy to perform and seems to be a safe procedure. Guidance of the papillotome allows a precise cutting in the desired directions.

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Title: Indications for PEG tube placement predicts short and long term mortality

Authors: Laurent Bochatay, Emiliano Giorstra, Laurent Spahr, Philippe Bichard, Jean Louis Frossard. Gastroenterology and Hepatology, Geneva University Hospital, Switzerland.

Background: Percutaneous endoscopic gastrostomy (PEG) is a well established and widely used method of nutrition delivery for patients with persistent inability of oral feeding. Buried bumper syndrome (BBS) is a severe late complication of this method, with an estimated incidence of 1%. The typical symptomatic triad of BBS include inability to insert the tube, leakage and loss of patency. Several techniques to dissect the overgrowing tissue are described, including needle knife dissection, argon plasma coagulation (APC) and papillotome dissection through the shortened cannula.

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Conclusions: This adapted method of tissue dissection in BBS by biopsy forceps guided papillotome is easy to perform and seems to be a safe procedure. Guidance of the papillotome allows a precise cutting in the desired directions.

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Title: Role of SpyGlass®-Cholangioscopy: First Clinical Experiences

Authors: Gian-Marco Semadeni, Romus Frei, Christa Meyerbender, Michael C. Sutz, Jan Borovicka

Kantonsspital St. Gallen, Klinik für Gastroenterologie und Hepatologie

Background: Direct cholangioscopy enables not only the direct diagnostic visualisation of the biliary tract, such as the workup of stenosis, but offers also the possibility in treating complicated choledocholithiasis. Hence, the SpyGlass® DS cholangioscope (Boston Scientific) allows a precise examination and treatment of biliary abnormalities. A single operator can advanced into the biliary system as a single operator system. It has got a 10Fr diameter and the application (single operator system) is a further advantage.

Methods: Prospective inclusions of direct cholangioscopies with SpyGlass® DS cholangioscope at a tertiary referral centre in Switzerland.

Results: Since September 2015, 14 cholangioscopies were performed in 11 patients (3 female, 8 male; mean age 62; ASA I-II; general anaesthesia (3), conscious sedation (1)).

Overall, indications were stenosis (6), hepatic-choledocholithiasis (4), stent dislocation (2), recurring haemobilia (1) and bile leakage (1). The following interventions were performed: electrohydraulic lithotripsy (EHL). The SpyGlass® DS cholangioscope (Boston Scientific) is attached to a duodenoscope, inserted into the working channel of the duodenoscope and advanced into the biliary system as a single operator system. It has got a 10Fr diameter and a working channel of 1.2mm. The tip of the SpyGlass® DS catheter is steerable in 4 directions.

Methods: Advantages of SpyGlass®-Cholangioscopy are high visual resolution imaging and its simple directions.

Conclusion: First experiences with SpyGlass®-Cholangioscopy in clinical practice show a therapeutic as well as a diagnostic benefit due to its high resolution imaging. Its simple application (single operator system) is a further advantage.
Comparison of impedance planimetry (EndoFLIP®) and videofluoroscopy for evaluation of esophagogastric junction opening width.

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Background: Impedance planimetry (EndoFLIP®) is a diagnostic procedure to test esophageal distensibility. In this study impedance planimetry and videofluoroscopy were compared for the evaluation of esophagogastric junction (EGJ) opening width in dysphagia patients.

Methods: In 56 patients (40 males, age 50.2 [range 18-83] years) both impedance planimetry and videofluoroscopic swallow studies, followed by a transit test of a 14 mm-tablet, were performed within 90 days. EGJ diameters estimated by impedance planimetry were compared to the corresponding results of videofluoroscopic examinations and passage of a 14 mm test tablet into the stomach.

Results: A significant correlation between EGJ diameter ≤15.0 mm by impedance planimetry and tablet impaction was found (r=0.31, p=0.02). Impaction of the tablet occurred in 31/56 patients. Nine patients showed a moderate delay (>15s), three a short delay (≤15s), and 13 no delay of tablet passage.

Discussion: Impedance planimetry and esophageal videofluoroscopy correlate significantly regarding tablet impaction and esophagogastric junction opening during deglutition. Impedance planimetry and a videofluoroscopic transit test of standardized 14 mm tablet are useful in demonstrating esophageal outflow obstruction in dysphagia patients.

A Rare Case of Collagenous Gastritis

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Background: Collagenous gastritis is defined histologically by a subepithelial collagen band of more than 10 µm thickness and an infiltration of inflammatory cells in the lamina propria. The disease was first discovered in 1989 and is extremely rare: only 60 cases have been described in the English literature so far. There is no standardized therapy due to the lack of randomized controlled studies.

Results: A 24-year-old female patient reported alternating diarrhea and constipation as well as intermittent abdominal cramps for at least one year and a slight body weight loss during the past weeks. Laboratory findings showed an elevated calprotectin (513 mg/kg) without further abnormalities. Colonoscopy revealed normal endoscopic and histological findings. Gastroscopy revealed multiple nodularities in the gastric corpus and a surrounding mucosa that appeared to be atrophic. Histological findings showed a thickened subepithelial collagenous band as well as an increased infiltrate of eosinophils, plasma cells and scattered neutrophils in the lamina propria. Therapy with a proton pump inhibitor as well as oral budesonide was initiated.

Conclusion: Two types of collagenous gastritis are suggested in the literature: a pediatric type with upper gastrointestinal symptoms and an adult type with chronic diarrhea due to an association with coexisting collagenous colitis. While our patient showed no histological involvement of the colon, she did present with diarrhea, making a definitive association with one of the types difficult. Further reports and studies are warranted to better understand the mechanisms of this rare entity.
Coating of commensal microorganisms by SLgA may favor commensal-host mutualism by diminishing the bacterial stress responses

Hai Li, Kathy McCoy, Andrew Macpherson

Background: Secretory IgA (SLgA) is a key component of mucosal immune system. It has been shown involved in gut barrier protection by excluding the direct contact of pathogens and pathobionts to intestinal epithelium. It is well known that a huge amount of IgA is secreted into gut lumen and much of them specific to inhabiting commensal bacteria, and SLgA can be detected on the surface of a large population of gut bacteria, jet it is still elusive what function it has in commensal-host mutualism.

Methods: To investigate the function of SLgA, auxotrophic *E. coli* HA107 were used to induce specific IgA secretion in C57BL/6 and no antibody control. *E*.* coli* MG1655 were then administrated to mice and bacterial RNA were isolated from different gut compartments and sequenced.

Results: By comparing IgA coated and non-coated bacterial transcriptional patterns, we show that the IgA coating reduces the bacterial oxidative stress response, especially in colonic mucus. Further studies determine bile acid is one of the inducer of bacterial stress in the gut.

Conclusions: Our primary data showed the bacteria in the gut is stressed likely by host-derived bile acids and SLgA diminishes bacterial stress. We are trying to figure out the relation between the protection role of IgA and bile acid induced the bacterial stress responses.

Influence of hypoxia on healthy volunteers and patients with inflammatory bowel disease

Stephan R. Varricka, Pedro Ruiz-Castro, Luz Biedermann, Mehdul Medenich, Sylvie Scherf, Michael Scherf, Gerhard Rojas, Jonas Zitz

Background and Aim: Hypoxia can induce inflammation in the gastrointestinal tract and a previous study from our group suggests an impact of hypoxia on the course of inflammatory bowel disease (IBD). We aimed to evaluate prospectively and under standardized conditions what effects hypoxia has on healthy volunteers and IBD patients.

Methods: Ten healthy volunteers, 11 Crohn’s disease (CD) and 5 ulcerative colitis (UC) patients in stable remission underwent 3 hours exposure to hypoxic conditions simulating an altitude of 4300 meters above sea level in a hypobaric pressure chamber situated at the Swiss aeromedical center. Stool samples analyzing cytokines and microbial composition, biopsy samples were collected before and after hypoxia exposure. The results were compared to volunteers and IBD patients.

Results: In the healthy volunteer group (median age 24.8 years), no significant changes on the mRNA levels of IL-1α, IL-1β and IL-6 were revealed in biopsies taken directly after the hypoxic chamber (T2), as well as in biopsies taken after week 1 day before the hypoxic chamber (T1), in biopsies taken directly after the hypoxic chamber (T2), as well as in biopsies taken after 1 week before the chamber (T3). However, the colonic levels of IL-1α, IL-1β and IL-6 increased significantly between T1 and T3 (p<0.05). Furthermore, calprotectin levels increased up to 10 fold of the initial measured value. In UC patients (median age 31.1 years), mRNA levels of IL-1α, IL-1β and IL-6 increased between T1 and T3, and did not reach statistical significance. Calprotectin levels increased up to 10 fold of the initial measured value. One patient in the UC group dropped out of the study because of a flare on T2, another two patients reported increased activity of their disease.

Conclusions: The importance of environmental factors in the pathogenesis including their disease modifying potential are increasingly recognized in IBD. Understanding molecular and microbiologic consequences of intestinal hypoxia may ultimately derive further insights on the pathogenesis of IBD far beyond exposure to low partial oxygen pressure ambient air.

The effects of diet on intestinal microbiota in a gnotobiotic mouse model

Catherine Mouser, Kathy D McCoy, Andrew J Macpherson

Background: The importance of the microbiota in influencing health and disease of the host is well accepted. Indeed, numerous medical conditions related to a Western lifestyle have been associated with a disturbed microbiota. However, the mechanisms driving this relationship remain unexplained. As diet is known to be a major force shaping both the microbiota and the host, we addressed the effects of a fat-enriched and a starch-enriched diet on the microbiota.

Methods: We generated a genetically modified *Escherichia coli* strain expressing a defined helper cell epitope to study antigen-specific systemic antimicrobial CD4+ T cells in gnotobiotic mouse models.

Results: We found that the presence of systemic antigen-specific antimicrobial CD4+ T cells resulted in massively increased bacterial translocation during dextran sodium sulfate (DSS) colitis. Interestingly, this effect was mediated by the presence of a single cognate bacterial neo-antigen peptide as T helper cell epitope.

Conclusions: Systemic antimicrobial CD4+ T cell reactivity may impact adversely on mucosal integrity and homeostasis under conditions of reduced barrier function.
Increased IL-19 Expression in IBD Patients and Colitis Models Indicate Immunosuppressive Function

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Background: Interleukin (IL)-19, a member of the IL-10 cytokine family, has a rather undefined function. We hypothesized an immunosuppressive role of IL-19 and increased concentrations in inflammatory bowel disease (IBD) patients with active disease. Methods: Sera of 30 Cohn’s disease (CD) patients and 41 ulcerative colitis (UC) patients were allocated from the Swiss IBD cohort. We measured IL-19 and the other cytokine family members IL-20 and IL-24 by ELISA. The function of IL-19 was further investigated with a newly generated IL-19 KO mouse strain. Results: Increased IL-19 and IL-20 but not IL-24 concentrations were observed in sera from IBD patients with active disease, correlating with serum CRP levels and inversely associated with patient’s age. Furthermore, Dextran Sodium Sulfate (DSS) colitis leads to an increased IL-19 expression. Bone-marrow derived macrophages but not dendritic cells has been identified as the cellular source for IL-19. Stimulation with Toll-like receptor (TLR) 2, 4, and 9 ligands further up-regulates IL-19 expression by macrophages. Injection of lipopolysaccharide (LPS) leads to increased IL-6 in spleen and liver from IL-19 deficient animals. Conclusion: IL-19 expression is increased in IBD patients with active disease and colitis models. Studies with IL-19-deficient mice indicate that IL-19 suppresses inflammatory cytokine responses.

Low Prevalence of Helicobacter pylori Infection with low Antibiotic Resistance in the Swiss Population

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Background: An infection with Helicobacter pylori is of importance for the development of gastritis, peptic ulcer disease and gastric cancer. In the last decade the prevalence and antibiotic resistance has not been studied in Switzerland. Methods: In a retrospective cross-sectional study the prevalence of H. pylori infection was analyzed in gastroscopy charts and associated histology reports obtained at the Inselspital for the year 2012 (KEK number: BE 135/15). Results: In 184 out of 945 patients an infection with H. pylori was diagnosed based on gastroscopy reports an infection with H. pylori was observed. Fourteen percent of the native Swiss population was infected. Higher prevalence was observed in immigrants with the highest prevalence in immigrants originating from Latin America. The prevalence is low in young people, peaks at an age between 40 and 60 years and declines in old people. In contrast to the Swiss population, immigrants have the highest prevalence at age < 20 years, which declines with age. The infection with H. pylori is associated with a higher prevalence of gastritis, peptic ulcer disease and gastric cancer. After eradication with standard therapy (amoxicillin, clarithromycin, pantoprazole) only 14 patients were followed up, in which a successful eradication was documented with a 13C urea breath test. In only one patient antimicrobial resistance was tested revealing resistance to metronidazole and clarithromycin. Conclusion: We observed a low prevalence of H. pylori in the Swiss population.

Neural control of the esophagogastric junction- Is there a nitrergic innervation of motor endplates in the crural diaphragm of piglets?

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Background: The crural diaphragm (CD) and the lower esophageal sphincter (LES) form the antireflux barrier of the esophagogastric junction (EGJ). Both muscles are simultaneously inhibited during swallowing and transient LES relaxation, the latter is often accompanied by gastroesophageal reflux. The neural control of both muscles is of interest as they show different composition and innervation. The underlying mechanism is still not fully understood but recent findings describe a possible peripheral mechanism based on the action of nitric oxide (NO) and additional vagal fibres that innervate the CD. This study aims to find evidence for a nitricergic co-innervation of motor endplates (MEPs) in the CD in order to gain more insight into the neural control of the EGJ in piglets.

Methods: Tissue blocks from two piglets were processed for cryosectioning and comprised esophageal as well as cranial and costal diaphragm samples. The morphological investigations included NADPH-diaphorase- and AChE staining and fluorescence immunohistochemistry with antibodies against neuronal nitric oxide synthase (nNOS) and vesicular acetylcholine transporter (vAChT).

Results: Nitrergic co-innervation of MEPs in the CD of piglets could not be confirmed so far, whereas the already known co-innervation in the esophagus could be shown in piglets.

Conclusion: The morphological basis for a peripheral mechanism at the EGJ in piglets could not be confirmed in this study, which points to other mechanisms of neural control, possibly via vagal fibres.

Electrical Stimulation (ES) of the Lower Esophageal Sphincter (LES) to address Gastroesophageal Reflux Disease (GERD)

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Background: Fundoplication is an effective treatment for GERD, but is associated with adverse effects, mainly dysphagia, pain and gas-bloat syndrome. ES of LES might provide an alternative as it lacks those complications.

Methods: 7 Patients with GERD at least partially responsive to proton pump inhibitors (PPI) and esophagitis LA Grade A-C received ES of LES after laparoscopic placement of electrodes (20 Hz, 215 µs, 3 – 8 mA in multiple 30-minute sessions). Patients were followed-up with daily symptom and medication diaries, and 24th-impedance-manometry (imp-pH) after 6 months.

Results: Median follow-up was 12 months (min 3 - max 42). There were no major peri- or postoperative complications. Median preoperative esophageal pH<4 was 9.6% (5.0-14), median resting LES pressure (LESp) 7mmHg (0-16). Ineffective esophageal motility was present in 6 patients (86%). Postoperative pH<4 (n=5) was 3.5% (2.1-5.9), LESp 22.8 (9 – 34). After 6 months, 5 patients were completely off PPI. No patient complained of dysphagia or pain.

Conclusions: ES of LES leads to enhanced LES pressures and decreased esophageal acid exposure. It is a safe and effective treatment for GERD and without the typical adverse effects of traditional antireflux surgery.
Background: Endoscopic treatment with endoscopic mucosal resection (EMR) and Radiofrequency ablation (RFA) represents a standard treatment of dysplastic BE. Randomized studies have shown efficacy in selected patient groups. Long-term follow-up results are still awaited. We present outcome data from a Barrett’s cohort at the Kantonsspital St. Gallen.

Methods: Patients were included consecutively for combined endoscopic treatment from 2009 – 2015. After EMR of nodular lesions RFA was performed with the balloon (HALO 360) and sectorial device (HALO 90). Patients were surveyed thereafter at 2 months interval until complete eradication, followed by two 6 months and 12 months interval. Outcome parameters were complete reepithelialisation without dysplasia or resistance or recurrence of dysplasia.

Results: 58 patients were included. Mean age at first intervention was 62 years (range 47-85 years): 14% (8) were female. 40% (23) presented with adenocarcinoma (CA), 53% (31) with high grade dysplasia (HGD) and 7% (4) with low grade dysplasia (LGD). 10% (6) patients underwent surgical resection after EMR, 90% (52) were eligible for endoscopic treatment only. 27% (14) had RFA, 15% (8) EMR and 58% (30) had combined treatment with EMR and RFA. 100% (4) of the LGD-group, 84% (26) of the HGD-group, and 90% (18) of the endoscopic CA-group achieved complete reepithelialisation or no more dysplasia. Resistant or recurrent dysplasia was observed in 8% (4).

Conclusion: Combined endoscopic treatment is a highly effective therapy with 92% success rate, short surveillance interval. Patients were surveyed thereafter at 2 months interval until complete eradication, followed by two 6 months and 12 months interval. Outcome parameters were complete reepithelialisation without dysplasia or resistance or recurrence of dysplasia.
Is smoking cessation linked to new ulcerative colitis cases? A retrospective cohort-based hypothesis.

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Methods: Adult IBD patients included in the Swiss IBD cohort from November 2006 to November 2015 were asked about their smoking status at diagnosis. We compared the proportion of former smokers in 10-year groups of UC and CD patients.

Results: 2361 IBD patients (1386 CD, 995 UC) were included in the analysis. Among them 52% of CD and 24% of UC patients were smokers at diagnosis (proportion of smokers in Switzerland [2014]: 29%). The higher proportion (66%) of former smokers at diagnosis was in the 50 to 60 years old group of UC patients compared to only 26% in CD patients between 40 to 50 years old (p<0.001). On a gender basis, the higher proportion of former smokers is particularly significant high among males 50-60 years old with UC (68%) and persists among them over 60 years old (52%).

Conclusions: The proportion of former smokers at diagnosis increases dramatically and significantly over years in UC patients compared to CD patients. A peak was reached over 50 years old suggesting an indirect impact of smoking cessation on the second peak of diagnosis in ulcerative colitis.

Determinants of Tobacco Consumption in the Swiss IBD Cohort

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Background: Smoking has a differential effect on inflammatory bowel diseases (IBD); deleterious for Crohn’s disease (CD) and protective for ulcerative colitis (UC). Thickness of the mucus layer, immune system (cytokines production), microvasculature and intestinal microbiome are potential mechanistic factors influenced by the nicotine and numerous other substances. It has been hypothesized that smoking cessation is associated with the second peak of diagnosis in UC patients after 50 years old. Our aim was to confirm this hypothesis using data on smoking status at IBD diagnosis.

Methods: Retrospective analysis of prospectively yearly collected data from adult UC and CD patients included in the Swiss IBD cohort study (SIBDCS) from November 2006 to November 2015.

Results: 999 UC and 1388 CD patients were included in the study and separated in three groups (smokers, past-smokers and non-smokers at enrolment). In general, past smokers who succeed in smoking cessation are males, older, with a higher BMI (p<0.001). The disease location was less extensive in UC (modestly left sided colitis and proctitis) (p=0.121) and less ileal in CD (compared to active CD smokers) (p=0.039). Concerning treatment, UC past smokers used significantly more topical treatment and CD past smokers required less anti-TNF and conventional immunosuppressants. The disease severity measured by clinical scores and CRP/albumin showed no significant difference.

Conclusions: UC and CD patients in the Swiss IBD cohort who succeed in smoking cessation seem to be patients with a pattern of disease which is less likely to be influenced by smoking. Further investigations are needed to identify whether this phenotype is due to smoking cessation or likely to ease it.

What kind of IBD patients succeed in smoking cessation? - Insights from the Swiss IBD Cohort Study.

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Methods: Adult UC and CD patients included in the Swiss IBD cohort study (SIBDCS) from Nov. 2006 to Nov. 2015 were asked about their smoking status. Patients were separated in two groups (active smokers vs. non-smokers).

Results: 999 UC and 1388 CD patients were included in the study and separated in three groups (smokers, past-smokers and non-smokers at enrolment). A logistic regression analysis was performed with smoking as main outcome. In the univariate analysis, smoking was positively associated with the female gender in CD patients. Smoking CD patients had more stenosis and used significantly more oral Budesonide, whereas UC patients used more topical treatments. A high anxiety and depression score was significantly associated with smoking among CD patients. The use of invalidity insurance was significantly higher in smoking UC and CD patients in the univariate analysis and was confirmed in the multivariate analysis (OR 1.8 [1.1-3.0], p=0.02 for UC and OR 3.4 [1.3-9.1], p=0.015 for CD).

Conclusions: After adjustment for disease pattern and activity, the only factor significantly associated with tobacco consumption in IBD patients is the need for invalidity insurance. This positive association between active smoking and invalidity insurance is, however, not specific to IBD patients but also known in the Swiss population (Suchtmonitoring Schweiz, www.suchtschweiz.ch; www.addictionsuisse.ch).
PH1

Protective role of specific pathogen free microbiota in bile duct ligated and CCL4 treated mice
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Background: In chronic liver disease the presence of gut-derived bacterial products and the resultant increase in inflammatory cytokines in the splanchic and systemic circulation may contribute to the progression of fibrosis. However, the role of the intestinal microbiota and the host-microbe interaction in the development of liver fibrosis remains largely unknown. We hypothesized that fibrosis would be attenuated in a gnotobiotic model of limited intestinal colonization (altered Schaedler flora, AIF) compared to a more complete colonisation with specific pathogen free flora (SPF). We aimed to investigate the development of fibrosis and portal hypertension in AIF and SPF mice.

Methods: Liver fibrosis was induced by common bile duct ligature (BDL) for 14 days or intraperitoneal (IP) injection of 20% (dilution in saline) cation tetrachloride (CCL4) for 10 weeks in AIF or SPF mice, C57BL/6 mice. Hemodynamic measurements were performed after 14 days in BDL or 10 weeks in CCL4 treated mice. Liver histology and collagen deposition were evaluated using Sirius red staining for determination of fibrosis degree. To assay bacterial translocation, mesenteric lymph nodes, spleen and liver were dissected aseptically and then cultured on Luria-Bertani agar and blood agar plates for aerobic and anaerobic culture respectively.

Results: There were no differences in portal pressure between sham-operated (controls) AIF or SPF mice. After BDL or CCL4 treatment portal pressure (Pp), portal- systemic shunts (PSS) and liver histology and collagen deposition within the liver showed a significant increase in both groups. However, the increase in portal pressure and degree of fibrosis was significantly higher in AIF than SPF mice.

PH2

Alcohol intake increases the risk of hepatocellular carcinoma in hepatitis C virus-related compensated cirrhosis
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Introduction: Whether alcohol intake increases the risk of complications in patients with HCV-related cirrhosis remains unclear. Aim: To determine the impact of alcohol intake and viral eradication on the risk of HCC, decompensation and death.

Patients and methods: We included 764 patients (526 ALD, 157 HCV, 81 NAFLD, 64% of eligible patients) who were seen between January 1999 and December 2012 at a single tertiary care center. Alcohol and viral intake was evaluated using a standardized questionnaire.

Results: 74 patients consumed alcohol (median alcohol intake: 15 g/day); 68 reached viral eradication. During a median follow-up of 58 months, 33 patients developed HCC, 53 experienced a decompensation event, and 39 died. The 5-year cumulative incidence rate of HCC was 10.6% (95% CI: 4.6-16.6) in abstainers (13.8% (95% CI: 13.5-34.1) in consumers (p=0.087), and 2.0% (95% CI: 0.5-8.2) to 3.5% (95% CI: 14.2-29.2) in patients with and without viral eradication (p=0.002), respectively. The lowest risk of HCC was observed for patients without alcohol intake and with viral eradication (0%) followed by patients with alcohol intake and without viral eradication (6.2% (95% CI: 0-18.4)), patients without alcohol intake and with viral eradication (15.9% (95% CI: 7.1-24.7)), and patients with alcohol intake and no viral eradication (29.2% (95% CI: 15.6-54.1)) (p=0.009).

Conclusion: Light-to-moderate alcohol intake increases the risk of HCC in patients with HCV-related cirrhosis. Patient care should include measures to ensure abstinence.
Alcohol abstinence improves the prognosis of alcoholic liver disease related cirrhosis in both compensated and decompensated patients
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Introduction: Alcohol abstinence improves the prognosis of alcoholic liver disease related cirrhosis in both compensated and decompensated patients. Whether abstinence has similar impact on mortality in all stages of the disease remains unclear. Aim: To assess the impact of abstinence on mortality of patients with ALD-related cirrhosis according to the Child–Fugh stage.

Methods: Data related to death were collected during a 21-year period among patients with cirrhosis related to ALD.

Results: 526 patients (68% of male, median age 55 years [95% CI: 54-56]) were included. 48% of the patients belonged to Child–Fugh stages B or C. Median MELD score was 9.3 (95% CI: 8.6-10.0). During a median follow-up of 54 months (95% CI: 47.59), 273 patients died. Causes of death were hepatocellular carcinoma in 12 cases, liver failure in 178 cases and non-liver related in 83 cases.

Sensitivity analyses, abstinence was associated with a reduced mortality rate (HR: 0.40; 95% CI, 0.27-0.59, p<0.001) as well as in stages B and C, and decompensated patients.

Conclusion: Alcohol abstinence improves the prognosis of alcoholic liver disease related cirrhosis in both compensated and decompensated patients.

Portal vein recanalization using a transhepatic approach is feasible and effective in most of non-cirrhotic patients with porto-mesenteric vein occlusion
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Introduction: Portal vein occlusion is a condition that can be associated with gastrointestinal bleeding (GIB), portal biliopathy or intestinal ischemic necrosis. Portal vein recanalization (PVR) without shunting the liver could prevent complications related to portal hypertension and restore a physiological portal perfusion. Aim: To evaluate the feasibility and the efficacy of PVR in patients with chronic portal vein occlusion.

Methods: All non-cirrhotic patients with non tumoral porto-mesenteric vein occlusion in which PVR was attempted using a transhepatic approach were reviewed.

Results: 13 patients were included (10 men, median age: 53 years [95% IC: 39-58]). Indications for portal vein recanalization were GIB in 4 cases, portal biliopathy in 1 case, reduction of portal pressure before surgery in 4 cases and other reasons in 4 cases. Chronic occlusion involved only the main portal vein in 8 cases, together with the mesenteric and/or the splenic veins in 4 cases and only the mesenteric vein in 1 case. Recanalization was successful in 11 cases (85%). One treatment failure was related to unrecognized obliterative portal veinopathy that made recanalization of the portal vein useless. The median follow-up was 38 months (95% CI: 12-60). Anticoagulation was given to 9 patients after recanalization (69%, median duration: 1 month [95% IC: 0-12]). The actuarial probability of stent permeability was 69% (95% CI: 44-94) at 2 years (78% and 55% in patients who received and who did not receive anticoagulation, p=0.4).

Conclusions: PVR using a transhepatic approach is feasible and effective in most of non-cirrhotic patients with chronic porto-mesenteric vein thrombosis.

Durable Response in the Markers of Cholestasis through 18 Months of Open-Label Long-Term Study of OCA in PBC
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Background: Obeticholic Acid (OCA) is a selective FXR agonist developed for treatment of primary biliary cholangitis (PBC). 216 patients were randomized and dosed in a double-blind (DB), placebo-controlled, phase 3 PBC trial (POSE; 97% of patients completing the DB phase enrolled in the open-label extension (OLE). The OLE aim is to assess the durability of OCA on the markers of cholestasis and safety.

Methods: Study inclusion criteria: PBC diagnosis, ALP ≥1.67x ULN and/or total bilirubin (bili) >ULN to <2x ULN, stable UDCA dose or unable to tolerate UDCA. During the DB phase, patients were randomized to: daily Placebo (PBO), 5 to 10 mg OCA titration, or 10 mg OCA. In the OLE, all patients were to be initially treated with 5 mg OCA with the option to increase based on response and tolerability every 3 months.

Results: Both OCA groups had significant reductions in ALP (UL) after 12 months of DB treatment (PBO: -12 ± 8; OCA Titration: -106 ± 87, p<0.0001; 10 mg OCA: -122 ± 75, p<0.0001). This response was durable through an additional 18 months of the OLE (PBO: -98 ± 70, p<0.0001 OCA Titration: -111 ± 90, p<0.0001; 10 mg OCA: -107 ± 91, p<0.0001). After 12 months of DB treatment, bili (µmol/L) in the PBO group increased (1.5 ± 4.3, p=0.05), but remained stable in OCA Titration and 10 mg groups (-0.6 ± 3.5 and -1.2 ± 4.7). During the OLE, the change from baseline in bili was sustained (PBO: 1.9 ± 14.0, OCA Titration: -0.3 ± 3.9; 10 mg OCA: -1.3 ± 4.5).

Conclusion: OCA treatment improves liver biochemistry, which is sustained throughout 18 months of the OLE.
Hepatic Manifestations of Wilson Disease - The CHUV Experience 2005-2015
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Background and aim: Wilson disease (WD) is an inherited disorder of ATP7B, the gene that encodes a copper transporter necessary for normal copper metabolism. We here describe the adult cases of hepatic WD diagnosed in the Division of Gastroenterology and Hepatology of the CHUV between 2005 and 2015.

Methods: Clinical manifestations, results of diagnostic tests, management and outcome of adult patients with hepatic WD were recorded.

Results: Ten new adult cases of hepatic WD were diagnosed in our center between 2005 and 2015. Five were women and 5 men, with a median age at diagnosis of 26 (range, 18-56) years. Four patients presented with acute liver failure (ALF), 4 with persistently elevated liver function tests, and 2 with compensated cirrhosis. None had neurological manifestations. Only one patient, presenting with ALF, had a Kassey-Flescher corneal ring. Median ceruloplasmin level at diagnosis was 0.19 g/l, median 24 h urinary copper excretion 2.6 (range, 0.3-62.0) µmol/24h, and median hepatic copper concentration 789 (range, 28-1677) µg/g liver dry weight in a patient with WD and a mutation of the ATP7B gene identified in 8 patients; the results of genetic testing are pending in 2 patients. Alethic frequency of the common H1069Q mutation was 19%. Peptide scores were >4 in all patients with a complete diagnostic dataset. Time from presentation to diagnosis varied between 2 hours and 20 years. Three patients presenting with ALF and one with uncompensated cirrhosis underwent successful liver transplantation. One patient with ALF recovered under chelator therapy, as predicted by a Dhawan score <11. D-penicillamine was used as first-line chelator, associated with a subsequent switch to trientine due to adverse effects in 2 out of 6 patients.

Conclusions: The clinical presentation of hepatic WD is highly variable. Three out of 10 patients were diagnosed at an age >35 years. A high index of suspicion in clinically compatible situations is key. The Peptide score is very useful to ascertain a diagnosis of WD.
Verteporfin inhibits hepatocellular carcinoma growth

In vitro and in vivo

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Hepatocellular carcinoma (HCC) is one of the most common malignant tumors worldwide. Angiogenesis and the Hippo signaling pathway (hpo) play an important role in the development and progression of HCC. Here we study the effect of Verteporfin (VP) in vitro and in vivo in HCC without prior light activation, focusing particularly on the mode of action of VP. VP was able to impair HCC cell lines proliferation in a time-dose-dependent manner, as observed by cell viability and clonogenic assays. VP significantly down-regulated the mRNA expression of proliferative genes and differentiation genes interfering with cell-cycle progression and enhancing apoptosis, as assessed by q-PCR and flow cytometry. VP treatment reduced the proliferation and the tube formation capabilities of immortalized microvascular endothelial cell (HMEC-1).

Subcutaneous HCC cell line xenografts in Rag2-/-;γc-/- mice showed significantly reduced tumor growth after two weeks of VP treatment. There was a marked decrease of Ki67 positive cells within the tumor tissue and also a statistically significant down-regulation of proliferative genes expression. VP-treated mice showed a significant decrease of CD31+ cells within the tissue as well as a significant down-regulation of VEGF-A mRNA levels. While previous authors suggest the mechanism of action of VP as the result of a direct binding of VP to the YAP/TEAD complex, our results show, that VP interferes with the autophagic flux, co-localizing in the lysosomes, with VP acting as an early stage autophagy inhibitor. Our results suggest that the antitumour activity of VP in HCC models is due to an inhibition of tumor angiogenesis as well as due to a direct effect on tumor cell proliferation and progression, interfering with the autophagy machinery. Verteporfin may be a promising drug in the treatment of otherwise inoperable, advance HCC.

Deletion of the Hippo core kinases MST1 and MST2 by siRNA rescued liver regeneration in aged mice.

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Background: The Hippo pathway controls organ size by regulating cell proliferation and apoptosis. We investigated how the Hippo pathway is regulated during the physiological process of liver regeneration after PH to define targets to improve the recovery of non-regenerative livers. Moreover by using a non-regenerative aged mouse model we aim to demonstrate that inhibition of the MST1 and MST2 Hippo core kinases has clinical potential to restore liver regeneration following PH.

Methods: Eight week and 12 month old mice were subjected to 67% liver resection. Liver regeneration was assessed by quantification of the Ki67 positive hepatocytes and by the liver to body weight ratio and YAL activation. siRNA was used to knock down MST1 & 2 in the liver.

Results: Following a standard 2/3 PH in young mice we observed an increase in the activation of the core kinases MST1 and LAT1 during the hypertrophic phase of liver regeneration. The return of MST1 and LAT1 to a steady-state levels coincided with the activation of the YAP targets genes (Birc5, Cyclin B and Foxm1) and with the peak of hepatocytes proliferation. Following PH in aged mice we observed an anomalous activation of the MST1 and LAT5 kinases and impairment in the YAP target genes activation in the non-regenerating liver. Silencing the core kinases MST1 and MST2 by siRNA femoral vein injection provoked quiescent hepatocytes to re-enter proliferation and restored liver regeneration in aged mice after PH.

Conclusion: Our data suggest that the Hippo pathway is a component of the liver regenerative process and that targeting the Hippo core kinases MST1 and MST2 could be clinically relevant to restore impaired liver regeneration.

Phenotypic characterisation of human serum albumin (HSA) in cirrhotic patients

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Background. Albumin (HSA) in cirrhotic patients is a potential diagnostic marker for liver disease. Phenotypic alterations of HSA have been described in cirrhosis and early hepatocellular carcinoma, but the extent of these alterations in cirrhosis has not yet been described so far. The aim of our study was to characterise posttranscriptional modifications of the native HSA allowing to discriminate between ASH and NASH and ASH and HCV cirrhosis.

Methods. In 106 consecutive patients undergoing HVPG and TJB in a single tertiary care center in the period December 2014-April 2016, data on fluoroscopy time (FT), absorbed radiation dose, equivalent effective dose (mSv), and volume of iodinated contrast material (ICM) were prospectively collected and reviewed, together with clinical and laboratory data. Incidence and severity of procedure-related complications were assessed. In 29 hospitalised patients creatinine values after 72 hours of the procedure were reviewed to identify contrast-induced nephropathy (CIN).

Results. Median effective radiation dose was 5.4 mSv (IQR 10 mSv). 28.3% of patients exceeded an effective exposure of 10 mSv and 9.4% exceeded 20 mSv. Only age and BMI correlated with radiation dose (R=0.327, p=0.001 and R=0.410, p<0.0001 respectively), and only BMI remained independently associated to an exposure over 20 mSv. Procedure-related complications occurred in 8 patients (7.5%) and were minor in 6 cases. Median ICM volume was 12.5 ml. 6/28 patients met the diagnostic criteria for CIN.

Conclusions. HVPG and TJB show a good safety profile and radiation exposure associated to these procedures is in most of the cases low. In hepatic hemodynamics procedures, efforts should be made to reduce the radiation dose in patients with obesity and to use the minimal possible ICM volume in patients with acute-on-chronic liver failure.
Direct antiviral agent (DAA) treatment of chronic HCV infection results in rapid regression of transient elastography (FibroScan®) and validated fibrosis markers FIB-4 and APRI.

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Background: Acute-on-chronic liver failure (ACLF) may result in death within days to weeks. Therefore, ACLF is associated with high mortality.

Methods: 118 patients with ACLF at admission to hospital. Therefore risk assessment for cirrhotic patients at admission to hospital.

Conclusions: NLR ratio is a simple, rapid and cost-effective marker of systemic inflammation. It was an independent predictor of 28-day mortality for patients with ACLF and admission to hospital.

Isolation, Characterization and Differentiation of Stem Cell Organoids Derived from Gallbladder Tissue

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Background: Recent developments in three-dimensional culture models allowed the expansion of adult stem cells in the form of organoids. We identified the gallbladder as a source of intraepithelial stem cells. Our culture models allow the long term culture and expansion of gallbladder derived organoids. The current focus is to define conditions which drive the differentiation of organoid cells into hepatocytes.

Methods: Organoids are isolated from C57BL/6J entire livers or gallbladders and expanded in Matrigel™. Culture conditions for expansion are based on growth factors including Wnt activation (R-Spondin) and TGF-beta inhibition (Noggin). Differentiation conditions include the removal of R-spondin and Noggin and the addition of dexamethasone.

Results: Isolation of stem cells from non-regenerating mouse livers revealed that gallbladders are a potent source of organoids. Expansion of gallbladder derived organoids is possible for up to one year, independently from the age of the donor mice. Application of differentiation media induces expression of hepatocyte lineage markers, such as HNF4α and albumin.

Conclusions: Organoids can be isolated and expanded long term in vitro and are a potential powerful cell source for the treatment of severely damaged and genetic diseased livers.
The health burden of Primary Biliary Cholangitis in Switzerland

SwissPBC | SASL 36

1Terzioli Beretta-Picozzi B, 1Cerny A, 2Carbone M, 3Giostra E, 4Semela D, 5Mertens J, 6Hessler R, 7Strikker B, 8Yalid-de Bakker C, 9Bihl F, 10Stirnimann G, 11Invernizzi P

Epidemiological data on PBC in Switzerland do not exist. The aim of our study is to assess the disease burden of PBC in Switzerland. This survey should be the basis for a prospective PBC registry in Switzerland.

Methods: This is a nationwide, cross-sectional, multi-centre study involving also family doctors and gastroenterologists outside centres.

Preliminary results: About 500 patients can be recruited from the University Hospitals and hepatology centres. 43/295 gastroenterologists, 406/504 general practitioners answered the survey. 30 out of the 43 replying gastroenterologists have PBC patients, for a total number of 119 patients. 18 gastroenterologists are willing to participate, for a total number of 60 patients. 78 out of the 406 replying GPs have PBC patients, for a total number of 116 patients. 32 GPs are willing to participate, for a total number of 44 alive patients. About 50 PBC patients could be identified but are not available for the study because their physicians are not willing to participate. About 60 patients could be recruited from outside of centres.

Conclusions: Patients recruitment will last until the end of June, data on the precise numbers of the recruited patients and analysis of the collected data will be presented.
Outcomes of 50 consecutive transanal total mesorectal excisions for rectal cancer
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Background
Transanal total mesorectal excision (TaTME) is an alternative to conventional mesorectal excision owing to its ability to achieve clear distal and circumferential resection margin in rectal cancer.

Methods
Consecutive patients treated by TaTME were included in a prospective cohort study. Perioperative and short-term surgical outcomes were measured along regular clinic visits and the results were reported as median and interquartile range (IQR).

Results
50 patients with rectal cancer (7cm to anal verge, IQR 6-8) underwent a TaTME between Feb 2013 and May 2016. Age and body mass index were 66.5 years (IQR 57.25-76.75) and 26.5kg/m² (IQR 22.8-30.1). 33 (66%) patients had neoadjuvant radiochemotherapy. Median surgery time was 355 minutes (IQR 314-419), including an ileostomy. Median length of stay was 13 days (IQR 10-16.25). Dissection of the mesorectum was good (98/50 MercuryI) and all distal and circumferential margins were clear. Median T stage was 3 (IQR 2-3). 13 patients had lymphnode metastases for a median number of retrieved nodes of 24.6 (IQR 18-34). Last, cumulative 30-day morbidity amounted to 26% major complications (Dindo Clavien III-V), including 3 anastomotic leaks (8%) and 32% minor complications (Dindo Clavien I-II).

Conclusion
Transanal total mesorectal excision allows good surgical and oncologic quality to the expenses of a reasonable surgery time and morbidity.

Comparison of robotic-assisted vs laparoscopic resection of rectal cancer after neoadjuvant chemoradiotherapy
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Background
Ongoing studies compare the effectiveness, the technical and oncological outcomes of robotic-assisted vs laparoscopic rectal surgery with total mesorectal excision (TME). For both techniques we analysed our perioperative results in patients with locally advanced rectal cancer and neoadjuvant chemoradiotherapy (CRT).

Methods
Retrospective analysis of prospectively collected data. From January 14 to April 16 a total of 30 patients with rectal cancer underwent a laparoscopic or a robotic-assisted DaVinci Xi TME in our department. In the robotic group (Rob-G) a total of 10 patients (age 64 ± 14, 80% f) were included, in the laparoscopic group (Lap-G) 20 patients (age 61 ± 11, 45% f).

Results
The average operation time was significantly longer in the Rob-G compared to the Lap-G (421 ± 87 min vs 278 ± 54 min; p = 0.05). Severe complications (Clavien-Dindo III or IV) occurred in 15% in Rob-G vs. 10% in Lap-G (p = ns). On the specimen the number of retrieved lymph nodes did not differ significantly (Rob-G 17.5 ± 6.8 vs Lap-G 20.8 ± 7.3, p = ns). The quality of the TME was complete in 100% of the Rob-G and in 90% of the Lap-G (p = ns). The mean hospital stay was 14 ± 5 days in the Rob-G and 14 ± 7 days in the Lap-G (p = ns).

Conclusions:
Although our team is at the beginning of the learning curve with the DaVinci XI TME, we achieve comparable results to the laparoscopic technique in regards to perioperative morbidity, quality of oncological resection and length of hospital stay. The influence on oncological outcomes should be investigated in further studies with a larger patient collective.

Impact of macrophage dependent ATP release via Connexin 43 on abdominal sepsis outcome
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Danger associated molecular patterns, including extracellular nucleotides such as ATP, are released during sepsis. Extracellular nucleotides modulate responses via specific receptors that are present on various immune cells. Here, we explored by which mechanism ATP is released during abdominal sepsis and focused on the importance of hemichannel Cx43 in mediating ATP release from macrophages during sepsis.

Macrophages were isolated from peritoneum and liver from C57Bl/6J mice. The release of extracellular ATP was quantified using luciferin-luciferase assay. In vivo, we used LPS injection and caecal ligation and puncture (CLP) as a model of peritonitis. Macrophages were identified to release ATP in response to toll like receptor (TLR) 2 and 4 agonists. Inhibition of Connexin 43 via specific antagonists reduced extracellular ATP levels. In vivo, Cx43 was not constitutively expressed in liver but was highly induced following LPS injection or CLP. Cells expressing Cx43 in septic livers were identified as infiltrating macrophages and neutrophils. We identified elevated Cx43 expression at the cell surface and in the endoplasmic reticulum of primary M1 macrophages but not M2 macrophages after stimulation with LPS. However, Kupffer cells were Cx43 negative. Blocking of Cx43 during CLP using Gap27 increased serum levels of TNFα and IL1β and prolonged survival significantly compared to PBS treated controls.

In conclusion, LPS induced upregulation of the hemichannel Cx43 on peritoneal macrophages that is associated with elevated ATP release and outcome after peritoneal sepsis in mice.
Robotic Esophagectomy: Concept and First Experience With the New DaVinciXi System
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Background: Esophageal resection is an essential part in the treatment of esophageal cancer but remains a highly delicate procedure. To facilitate the operation and to reduce morbidity, minimal invasive techniques have gained popularity within the last years. Here we present our concept and our first results of robotic assisted operations in esophageal surgery.

Methods: In October 2015 we have started robotic esophageal resection in our institution using the latest DaVinciXi System. Due to our concept we perform the abdominal part in an open procedure using the robotic assistant in the thoracic part of the Ivor Lewis procedure. Gastroesophageal anastomoses were performed completely intrathoracal by using the robotic system without a thoracotomy.

Results: So far 4 patients have been operated on using this new approach. All patients were male, and the average age was 61 years. 3 patients had an adenocarcinoma, one patient had a neuroendocrine tumor. Neoadjuvant radiochemotherapy was applied on 3 patients. In none of the patients conversion to the open procedure was necessary. Anastomoses were performed with a robotic assisted continuous suture. Mean operation time was 476 minutes. RO resection was achieved in all patients, and there was no mortality and no anastomotic leakage. There was one Clavien Dindo I complication, as well as one II and III.

Conclusions: Robotic assisted esophageal resection using the latest DaVinciXi System is feasible and the first results are promising.

Stereotactic Navigation in Minimal Invasive Liver Surgery
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Background: In patients with malignant hepatic disease, local ablation is a tissue-sparing alternative when resection is not feasible. Here, technical accuracy, safety and clinical efficiency in terms of local tumour control using stereotactic minimal invasive navigation for ablation (MINA) of liver lesions is reported.

Methods: Treatment with MINA using microwave ablation (MWA) included malignant liver lesions not amenable to conventional surgery. Indications for using a laparoscopic approach were lesions located peripherally or in proximity to adjacent organs, with planned combined resection and ablation strategies, or with additional diagnostic laparoscopy. A navigation system using a rigid surface registration method was applied for placement of ablation antennas. Technical accuracy (registration and target positioning errors), safety (complications within 90 days), and clinical efficiency (rate of incompletely ablated lesions at 3 month) were analysed.

Results: Laparoscopic MINA: 54 patients with 346 malignant liver lesions at two European Centres treated between 2013 and 2015. Median lesions treated per patient : 3 (1-55). Average registration error: 8.4mm. Complications: grade I-II 13%, grade III 4%. Local recurrence at 90 days: 9% of lesions. Mean LOS: 2 days. Percutaneous MINA: 63 patients with 96 lesions over 28 months. Complications: Grade I-II 5%, grade > II 0%. Median LOS: 2 days. Local recurrence at 90 days 14%, with 23/3 successful early re-ablation with complete tumor control.

Conclusions: Minimal invasive stereotactic navigation allows precise, efficient and safe treatment options and offers new treatment strategies for patients not amenable to conventional surgery or with complicated recurrent disease.

LADD bands causing chronic constipation and small bowel obstruction: Leading symptoms for intestinal malrotation in adults
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Background: During embryonal development a lack of normal peritoneal rotation will be detected more frequent in future.

Methods: We report the case of a 68-year-old male, with a history of diarrhea and flushing, admitted in our Center for small bowel obstruction. The pre-operative CT scan showed a 4 cm ileal solid mass with free peritoneal fluid, without any liver nor thoracic lesions. We performed an urgent explorative laparotomy and about 40 cm from the ileocecal valve, we found a stenotic ileal tumour, with a mesenteric adenopathies and diffuse micro and macronodular peritoneal carcinomatosis. We performed a 30 cm small bowel resection with manual L-L anastomosis. Results: Pathologic evaluation of the resected specimen showed a well differentiated (G1) neuroendocrine tumour 1.4 x 0.5 cm in size, with two metastatic nodes. The tumour presented muscular infiltrations, perineural and lymphatic vessels invasion and multiple mesenteric implants. The immunohistochemistry analysis revealed synaptophysin and chromogranin A positivity and a Ki-67 expression < 2%. Mitotic count was less than 2 x 10 high-power fields (HPF). Our diagnosis was pT2, pN1, M1L1, G1. Conclusions: This case is challenging because the tumour expresses low proliferative index like G1 tumours, but shows an aggressive clinical behaviour such as node metastasis and peritoneal carcinomatosis, which is not considered by the current NETs classifications, and makes it difficult to predict the prognosis.
Evaluation of intraperitoneal mesh implantation managing open abdomen: comparisons of outcome between two tertiary centers
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Background: Patients with open abdomen represent difficult clinical situation that are associated with significant short term and long term morbidity e.g. incisional hernia. Aim of the present study was to compare the outcome between mesh implantation and conventional treatment without mesh implantation.
Methods: In this study the results from two treatment strategies from two tertiary centers (Bern and Vienna) are analyzed. We compared our management technique on the one hand in fascial dehiscence and on the other hand in open abdomen with patients treated in the Surgical Department of Vienna.
Results: In Bern 124 of 200 patients (62%) were treated with mesh implantation, whereas non-resorbable mesh was not implanted in Vienna. Patients in Bern were significantly older compared to the cohort of Vienna (65, range 22-85; versus 56, range 20-88 years). Mean redo surgery after open abdominal treatment was 1 (0-29) in Bern and 4 (0-46) in Vienna. The incidence of fistula was 18% in Bern and 23% in Vienna and the mortality was 17% in Bern and 13% in Vienna.
Conclusion: Mesh implantation is a safe treatment option managing open abdomen without increasing the rate of intestinal fistula.

Pericutaaneous ureteral stent vs. double J stent: Analysis of infectious and urological complications after kidney transplantation
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Background: Ureteral complications remain a long-term complication after kidney transplantation. In this study we compared the outcome between percutaneous ureteral stent vs internal double J stent.
Methods: We retrospectively analyzed all patients undergoing kidney transplantation from 2005-2014 where whether a percutaneous ureteric stent (group A) or an internal double J stent (group B) was used. After excluding patients younger 18 years and multior- gan transplantation, a total of 310 patients were identified.
Results: 217 patients (70%) were treated with percutaneous ureteral stent; 93 (30%) with double J. Type of stent used was related to the period (group A 2005-2010; group B 2011-2014) and the surgeons choice. 99% of ureteric anastomosis were performed using the Lich-Gregor technique. Mean follow up was 64 months in group A and 26 months in group B (p<0.001). There was no difference in terms of urinary tract infections within 6 weeks (p=0.204). In total, 28 (9.0%) developed ureteral complications, 33 (10.6%) vesicoureteral reflux and 54 (17.5%) received urologic redo-intervention during follow-up. In group A, significantly more ureteric complications and vesicoureteral reflux were detected leading to more total redo-urologic interventions (p<0.018, p=0.001 and p=0.003, respectively).
Conclusion: The use of percutaneous ureteric stents is associated with more ureteric complications, vesicoureteral reflux and needed urologic redo Intervention than double J stents after kidney transplantation.
Surgical Site Infection (SSI) Rate in Colorectal Surgery—experience from a Single Centre.
Codecà Roberta, Abdelghany Ahmed, Bianco Carolina, Sgardello Sebastian, Biggiogero Maira, Ghisletta Nicola, Kuhmeier Alfred, Donadini Andrea

Background: Surgical site infections (SSIs) represent a major cause of the postoperative morbidity after colorectal surgery. Treatment consumes important health care resources, and thus, its prevention and optimized treatments are crucial. A Swissnoso report has shown a SSI rate of 12.8%.

Methods: We built a multidisciplinary team to monitor postoperative SSIs (defined as its occurrence within 30 days of surgery). 194 consecutive patients, who underwent colorectal surgery from July 2013 to June 2015, were studied. Patient’s characteristic, operative data and the postoperative course were analyzed.

Results: There were 194 patients (90 male, 104 female, median age 57 years) who underwent colorectal surgery (173 elective, 21 emergency operations). The most common surgical indications were diverticulitis and functional colon disease (103 cases, 53 %) and cancer (91 cases, 47 %); 73% of patients had a laparoscopic approach. The overall SSI rate was 5.15% (10 SSI); whereby 3 SSI were superficial, and 5 were deep, and 2 were organ/space SSI, respectively. Incidences of SSI were different for the type of surgical approach and operative indications. While 5 SSI were treated conservatively, the remaining 5 cases required radiological or surgical interventions. The mean length of hospital stay for patients with SSI was 20 days.

Conclusion: Compared to the national level, we could show a much lower SSI rate at our institutions. Correct timing of antibiotic prophylaxis, a meticulous surgical technique to avoid contaminations and spillage of infectious materials, as well as a laparoscopic approach are key points. Timely recognition and an adequate treatment may limit the consequences of SSIs.