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A randomized trial comparing cost & effectiveness of bipolar vessel sealers Versus clips and vascular staplers in laparoscopic colectomy

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Background: A variety of vascular control devices are used in spite of limited comparative data. This study assesses cost & effectiveness of 2 standard techniques for vascular control in laparoscopic colectomy.

Methods: Patients were randomized to bipolar vessel sealer (BVS: Ligasure Atlas, Covidien) or clips and vascular staplers (CVS: EndoClip & EndoGIA, Covidien). Time and ability to control vessels, as well as instruments costs were evaluated. Diagnosis, duration of procedure, body mass index (BMI), presence of adhesions, abscess or phlegmon, as well as estimated blood loss (EBL) were used to adjust multivariate models.

Results: Of 114 patients randomized, 5 and 9 were excluded and 100 patients were analyzed, of which 55 were operated with BVS and 45 with CVS. Fourty-one right colectomies, 50 left colectomies and 9 total colectomies were performed for neoplasia (60), diverticulitis (26), and colitis (14). Diagnosis, procedure, occurrence and severity of adhesions and abscess, median BMI (27.7kg/m2), operative time (157min), EBL (50ml), and length of stay (3 days) were similar between groups. An average of 1.6 vascular staplers and 1.2 clip appliers were used per procedure. Ten instruments failed, 5 in the CVS arm and 5 in the BVS arm. Overall, there was a borderline significant cost saving of $120.9 in favor of the ligasure (p=0.05). In multivariate analysis, the type of procedure influenced operative time (p=0.0001), while randomization group (p=0.03), procedure (p=0.01), and surgical time (p=0.001) influenced the cost of surgery. For total colectomies, BVS reduced operative time by 96 min. (182 min. Vs 278 min., p=0.04) and instrument costs by $507 (p=0.03), while reducing cost by $159 (p=0.04) in left colectomies. There were no differences for right colectomies.

Conclusions: BVS reduce instrument costs for laparoscopic colectomies. This gain in cost-effectiveness is prominent in total and left colectomies.

Therapy response in chronic hepatitis C patients is affected by common *Vitamin D Receptor (NR 1I1)* polymorphisms

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Background: Chronic hepatitis C virus (HCV) infection represents a leading cause of end stage liver disease. Non-parenchymal hepatic mediators of inflammation and fibrogenesis such as sinusoidal endothelial cells, Kupffer cells and hepatic stellate cells express VDR mRNA and functionally active VDR protein. Given the established role of vitamin D as an immunomodulator, we investigated a potential effect of common polymorphisms (SNP) in the *VDR (NR1I1)* gene on hepatic inflammation & therapy response in a large Swiss cohort of HCV-patients.

Methods: 166 patients with available blood samples and liver biopsies were included for *VDR* genotyping (*Cdx2* rs11568820, bat genptype: *Bsm* rs1544410, *Apa* rs 7975232 and *Taq* rs 731236). Exclusion criteria were HBV or HIV coinfection, alcohol >40 g/day and morbid obesity. Statistical associations with Metavir inflammation score (A) and sustained virological response (SVR) to PEG-interferon/ribavirin standard therapy were calculated.

Results: The *ApaI* (CC) and *TaqI* (TT) genotypes showed a significant correlation with HCV-therapy failure (non-SVR vs. SVR; *ApaI* P=0.037; CC vs. CA/AA P=0.012; OR 2.66; *TaqI* P=0.018; CC vs. CA/AA P=0.002; OR 6.05). Likewise, the most frequent bAt-haplotype (*Bsm* CC_*Apa* CC_*Taq* TT) was associated with non-SVR vs. SVR (P=0.005 vs. any other haplotype; P=0.009 vs. all other haplotypes combined; OR 2.66). 62.2% of bAt-haplotype patients are non-SVR. In addition, Cdx2 TT is also associated with non-SVR (P=0.016 for TT vs. CT/CC) but the small number of TT non-SVR (n=5) limits definite conclusions. Logistic regression analysis between the observed haplotypes confirmed *ApaI* CC and *TaqI* TT as two significant (for *ApaI* CC P=0.043; for *TaqI* TT 0.019) and frequently coexisting SNPs with respect to all occurring haplotype combinations. No significant association was observed for any VDR genotype or haplotype to Metavir inflammatory activity.

Conclusions: VDR SNPs are significantly associated with the therapeutic response to interferon/ribavirin in chronic HCV-patients. Whether substitution of vitamin D during antiviral therapy may be an attractive appr oach remains subject of future clinical studies.

Impact of 18F-FDG-PET on Re-Staging and Prediction of Tumor Response of Patients with Locally Advanced Rectal Cancer

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Objective: Neoadjuvant chemoradiotherapy (CRT) has become a standard practice for locally advanced rectal cancer. Complete pathologic response can be achieved in up to 20% and discussions about a "watch-and-wait" strategy in these patients are going on. Reliable methods to detect patients with a complete pathological response after CRT are not known. One possible method may be the 18F-FDG-PET. The aim of this study was to evaluate the change in tumor maximum standardized uptake value (SUVmax) before and after CRT and to correlate the change with the pathologic response.

Methods: Between 7/2005 and 2/2010 110 patients (39 females, 71 males) with locally advanced rectal cancer were treated by preoperative CRT in a prospective study. A18F-FDG-PET scan was performed in 98 patients before and 4 weeks after CRT. For each scan SUVmax was measured in the tumor. Surgical approach was a sphincter saving total mesorectal excision or an abdominoperineal amputation 6 weeks after CRT. SUVmax at re-staging was correlated with pathologic response and tumor regression grade.

Results: Mean tumor uptake was 12.2 ± 0.7 before and 3.8 ± 0.4 after CRT ($p<0.001$). 31 % of patients showed a complete metabolic response in the 18F-FDG-PET with a SUVmax of 0. 19 % of patients had a complete pathologic response with a tumorstage ypT0 ypN0. 69% of patients without metabolic uptake still had viable tumor cells in the specimen. Accuracy for 18F-FDG-PET for prediction of a complete pathologic response was 48%. Sensitivity for 18F-FDG-PET in re-staging was 33%.

Conclusion: 18F-FDG-PET does not seem to be a good method for prediction of complete tumor response after CRT for locally advanced rectal cancer. A "watch-and-wait" strategy should absolutely not be performed in patients with a negative PET.

Dysregulation of the Myeloid Cell Response Exacerbates Acute Colitis by Impairing Mucosal Healing

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Background: Granulocyte-macrophage colony-stimulating factor (GM-CSF) therapy elicits myeloid cells that promote mucosal healing during acute colitis in the mouse. We hypothesized that a dysregulation of the myeloid cell response results in defective repair functions and increases susceptibility to acute colitis. **Methods**: Dextran sulfate sodium (DSS) colitis was induced in either untreated or clodronate liposome-treated wild-type mice, or in chimeric mice harboring myeloid cells devoid of GM-CSF receptor (GM-CSFR). Clinical parameters of colitis were scored. Mucosal damage and epithelial repair were analyzed on histological sections after BrdU incorporation. Spleen and colon CD11b cells were tested for their propensity to promote in vitro wound closure in epithelial cell monolayers. **Results**: Mice with dysregulated myeloid cell responses, due either to phagocyte depletion or absence of GM-CSFR-driven activation, displayed a higher susceptibility to DSS colitis, with a marked increase in fecal blood score and extent of mucosal ulceration, compared to untreated wild-type mice. Dysregulation of the myeloid cell response was associated with a strong reduction in numbers of proliferative epithelial cells in ulcer-adjacent crypts, suggesting defective repair functions. Accordingly, spleen and colon CD11b cells isolated from mice with defective myeloid cells were clearly inferior in promoting in vitro wound closure, compared to wild-type counterparts. **Conclusions**: A tightly regulated myeloid cell mobilization in the colonic mucosa is mandatory for an efficient response to acute colitis including mucosal healing. Defective acute inflammation may predispose Crohn's disease patients to defective mucosal repair and to subsequent chronic activation of immune responses.

Novel and Simple Preoperative Score Predicting Complications Following Liver Resection

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Background: While liver surgery has enjoyed major development, the incidence of non-lethal, complications remain high. No scoring system is available to identify those patients at higher risk for a complicated course. **Methods**: Complications were prospectively assessed in 615 consecutive non-cirrhotic patients undergoing liver resection at one institution. In randomly selected 60% of the population, multivariate-logistic-regression analysis was used to develop a score to predict severe complications defined as complications grade III, IV and mortality (grade V) (Dindo classification). The score was validated within the remaining 40% of the patients. **Results:** Grade III-V complications occurred in 26 % of the patients (159/615) after liver resection, 15% (90) were grade III, 8% (48) grade IV, and 3% (21) grade V. Four preoperative parameters were identified as independent predictors including ASA category, transaminases levels (AST), extend of liver resection (>3 *vs.* < 3 segments) and the need for an additional hepatico-jejunostomy or colon resection. A prediction score was calculated ranging from 0 to 10 points. The risk to develop serious postoperative complications was 16% in "low risk" patients (0-2 pts), 37% in "intermediate risk" patients (3-5 pts) and 60% in "high risk" patients (6-10 pts). The validation of the score showed a high similarity of the calculated and the observed risks throughout the different risk categories (Hosme Lemeshow = 0.8). The score was significantly associated with hospital stay as well as costs. **Conclusions:** This novel and simple score accurately predicts postoperative complications after liver resection. Early identification of patients at risk may impact not only on decision-making for surgical intervention, but also on quality assessment and reimbursement.

Macrophages from Crohn's disease patients exhibit deficient pro-repair functions

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Background: We previously reported that myeloid cells can induce mucosal healing in a mouse model of acute colitis. Promotion of mucosal repair is becoming a major goal in the treatment of Crohn's disease. Our aim in this study is to investigate the pro-repair function of myeloid cells in healthy donor (HD) and Crohn's disease patients (CD).

Methods: Peripheral blood mononuclear cells (PBMC) from HD and CD patients were isolated from blood samples by Ficoll density gradient. Monocytic $CD14^+$ cells were positively selected by Macs procedure and then differentiated ex-vivo into macrophages (Mφ). The repair function of PBMC, $CD14^+$ monocytic cells and macrophages were evaluated in an in vitro wound healing assay.

Results: PBMC and $CD14^+$ myeloid cells from HD and CD were not able to repair at any tested cell concentration. Remarkably, HD Mφ were able to induce wound healing only at high concentration (10^5 added Mφ), but, if activated with heat killed bacteria, they were able to repair even at very low concentration. On the contrary, not activated CD Mφ were not able to promote healing at any rate, but this function was restored upon activation.

Conclusion: We showed that CD Mφ in their steady state, unlike HD Mφ, are defective in promoting wound healing. Our results are in keeping with the current theory of CD as an innate immunodeficiency. Defective Mφ may be responsible to the mucosal repair defects in CD patients and to the subsequent chronic activation of the adaptive immune response.

IFN Stimulated Gene Expression in the Liver is a Better Predictor of Treatment Response in Chronic Hepatitis C than the *IL28B (IFNλ3)* Genotype

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Background: Therapy of chronic hepatitis C (CHC) with pegIFNα/ribavirin achieves a sustained virologic response (SVR) in ~55%. Pre-activation of the endogenous interferon system in the liver is associated with non-response (NR). Recently, genome-wide association studies described associations of allelic variants near the *IL28B (IFNλ3)* gene with treatment response and with spontaneous clearance of the virus. We investigated if the *IL28B* genotype determines the constitutive expression of IFN stimulated genes (ISGs) in the liver of patients with CHC.
Methods: We genotyped 93 patients with CHC for 3 *IL28B* single nucleotide polymorphisms (SNPs, rs12979860, rs8099917, rs12980275), extracted RNA from their liver biopsies and quantified the expression of *IL28B* and of 8 previously identified classifier genes which discriminate between SVR and NR (*IFI44L, RSAD2, ISG15, IFI22, LAMP3, OAS3, LGALS3BP* and *HTATIP2*). Decision tree ensembles in the form of a random forest classifier were used to calculate the relative predictive power of these different variables in a multivariate analysis.
Results: The minor *IL28B* allele (bad risk for treatment response) was significantly associated with increased expression of ISGs, and, unexpectedly, with decreased expression of *IL28B*. Stratification of the patients into SVR and NR revealed that ISG expression was conditionally independent from the *IL28B* genotype, i.e. there was an increased expression of ISGs in NR compared to SVR irrespective of the *IL28B* genotype. The random forest feature score (RFFS) identified *IFI27* (RFFS = 2.93), *RSAD2* (1.88) and *HTATIP2* (1.50) expression and the HCV genotype (1.62) as the strongest predictors of treatment response. ROC curves of the *IL28B* SNPs showed an AUC of 0.66 with an error rate (ERR) of 0.38. A classifier with the 3 best classifying genes showed an excellent test performance with an AUC of 0.94 and ERR of 0.15. The addition of *IL28B* genotype information did not improve the predictive power of the 3-gene classifier.
Conclusions: *IL28B* genotype and hepatic ISG expression are conditionally independent predictors of treatment response in CHC. There is no direct link between altered IFNλ3 expression and pre-activation of the endogenous system in the liver. Hepatic ISG expression is by far the better predictor for treatment response than *IL28B* genotype.

Sequence-Based Hepatitis B Virus Antiviral Resistance Testing in Switzerland

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Background: A growing number of patients with chronic hepatitis B is being treated for extended periods with nucleoside and/or nucleotide analogs. In this context, antiviral resistance represents an increasingly common and complex issue.

Methods: Mutations in the hepatitis B virus (HBV) reverse transcriptase (rt) gene and viral genotypes were determined by direct sequencing of PCR products and alignment with reference sequences deposited in GenBank.

Results: Plasma samples from 60 patients with chronic hepatitis B were analyzed since March 2009. The predominant mutation pattern identified in patients with virological break-through was rtM204V/I ± different compensatory mutations, conferring resistance to L-nucleosides (lamivudine, telbivudine, emtricitabine) and predisposing to entecavir resistance (n = 18). Complex mutation patterns with a potential for multidrug resistance were identified in 2 patients. Selection of a fully entecavir resistant strain was observed in a patient exposed to lamivudine alone. Novel mutations were identified in 1 patient. Wild-type HBV was identified in 9 patients with suspected virological breakthrough, raising concerns about treatment adherence. No preexisting resistance mutations were identified in treatment-naïve patients (n = 13). Viral genome amplification and sequencing failed in 16 patients, of which only 2 had a documented HBV DNA > 1000 IU/ml. HBV genotypes were D in 28, A in 6, B in 4, C in 3 and E in 3 patients. Results will be updated in August 2010 and therapeutic implications discussed.

Conclusions: With expanding treatment options and a growing number of patients exposed to nucleoside and/or nucleotide analogs, sequence-based HBV antiviral resistance testing is expected to become a cornerstone in the management of chronic hepatitis B.

Short-term individual nutritional care as part of routine clinical setting improves outcome and quality of life in malnourished medical patients

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Background: Strategies to treat malnutrition lack practicability in the hospital setting. The present study aimed at developing and evaluating a routinely manageable concept for an improved nutritional care of malnourished in-hospital patients.

Methods: A randomized controlled intervention study was conducted. 132 risk patients defined by Nutritional Risk Screening 2002 were randomised to individualised nutrition support (intervention group, n=66) or standard hospital care (control group, n=66). Body weight, plasma vitamin levels, quality of life (SF-36), complications, antibiotic therapies, readmissions and mortality were assessed.

Results: Nutrition interventions led to higher intakes (mean [standard deviation]) in energy (1553 [341] kcal vs. 1115 [381] kcal, p<0.001) and protein (65.4 [16.4] g vs. 43.9 [17.2] g, p<0.001). Intervention patients kept their bodyweight in comparison to control patients (0.0 [2.9] kg vs. -1.4 [3.2] kg, p=0.008). Positive effects on plasma ascorbic acid level (46.7 [26.7] µmol/l vs. 34.1 [24.2] µmol/l, p=0.010), SF-36 function summary scale (37 [11] % vs. 32 [9] %, p=0.030), number of complications (4/66 vs. 13/66, p=0.035), antibiotic therapies (1/66 vs. 8/66, p=0.033) and readmissions (17/64 vs. 28/61, p=0.027) were recorded.

Conclusions: Malnourished patients profit from nutrition support regarding nutrition status and quality of life. They have fewer complications, need fewer antibiotics and are less often re-hospitalised.

Unsedated transnasal esophago-gastroduodenoscopy at 4559m – Endoscopic findings in healthy mountaineers after rapid ascent to high altitude

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Background: The causes of gastrointestinal (GI) symptoms of acute mountain sickness (AMS) are uncertain. We aimed to assess the incidence of mucosal lesions of the upper GI tract in healthy mountaineers following rapid ascent to high altitude and their association with GI symptoms.
Methods: 26 healthy mountaineers (16m, 22-60y, 8 with a history of high altitude pulmonary edema (HAPE)) underwent unsedated transnasal fiberoptic esophago-gastroduodenoscopy (UTF-EGD, Pentax FG-16V, 5.3mm) under lidocaine nasal analgesia and 2l oxygen supplement in Zurich (490m) and on two test days (d2+d4) at Capanna Regina Margherita high altitude laboratory in the Alps (4559m), where they spent four days after rapid ascent from 1130m. On each test day arterial oxygen saturation (sO2) was measured and preprandial AMS scores were assessed by self assessment questionnaires (Lake Louise Score (LLSAS), AMS-C). Gastroparesis cardinal symptom index (GCSI), dyspeptic symptoms and hunger scores (10cm visual analogue scale) were recorded. Mucosal lesions were treated with high doses of a proton pump inhibitor (PPI). Dexamethasone 8mg bid was administered if LLSAS in the evening of d2 was >4 or >2 in HAPE susceptible individuals.
Results: 23/26 mountaineers who underwent UTF-EGD at ground level had at least one endoscopy at 4559m (d4). 18/23 also had UTF-EGD on d2. The procedure was generally well tolerated and safe. Arterial sO2 was lower on d2 and d4 than in Zurich (75±1 and 80±1 vs. 96±1; p<0.001). One mild reflux esophagitis was observed at ground level. Of those that underwent UTF-EGD on d2, 5/18 (28%) had peptic mucosal lesions: duodenal erosions/ulcers (4), hemorrhagic gastritis after 500mg aspirin intake (1). On d4 lesions were found in 14/23 (61%); duodenal erosions/ulcers (5), gastric erosions/ulcers (5), hemorrhagic gastritis/duodenitis (5), reflux esophagitis (1). Peptic lesions diagnosed on d2 resolved on d4 under PPI in 1 subject. AMS-C scores on d2/d4 were higher than in Zurich (0.99±0.14/0.39±0.14 vs. 0.05±0.14; p<0.03). Subjects with peptic lesions on d4 had lower hunger scores than those with normal UTF-EGD (37±7 vs. 67±9mm; p<0.02). Lesions were not associated with nausea, fullness, AMS and GCSI scores, the arterial sO2 or with the use of dexamethasone.
Conclusions: GI mucosal lesions are common findings in healthy mountaineers after rapid ascent to high altitude independent of dexamethasone use. The presence of mucosal disease was associated with the loss of appetite, a key symptom of AMS. Patho-physiological mechanisms might include hypoxia and disturbed GI microcirculation in a hostile environment.

C.Gingert, K. Wolff, C. Grübel-Krieger, J. Borovicka, U. Beutner, FH.Hetzer

Percutaneous Tibial Nerve Stimulation - A new treatment for faecal incontinence

Objective:
Percutaneous Tibial Nerve Stimualtion (PTNS) is a new treatment option for patients with faecal incontinence, especially for patients complaining of urge-incontinence. Up to now few studies addressed this technique. We present our first experience with this promising approach.

Methods:
We performed the pTNS by insertion of a small needle (34 gauge) adjacent to the tibial nerve in the ankle and stimulation over 30 min. The initial sessions were done weekly for 12 weeks. We then continued the therapy when patients improved their incontinence and started a maintenance therapy. Faecal incontinence was monitored at baseline, 6 weeks and 12 weeks by using the Wexner and Vaizey Score. Well-being was assessed by the Visual Analogue Scale (VAS). Patient satisfaction was assessed at 12 weeks.

Results:
From August to December 2009 13 patients (12 female) median age 65.7(range 38.4-85.8) were included into the study. Ten patients complained of faecal urgency and 2 of passive faecal incontinence. Median Wexner Score before pTNS was 11(7-13) and median Vaizey Score was 14(10-17). After 6 weeks of pTNS treatment, the Wexner Score significantly decreased to 8(4-10) (*P*=0.0078), while the Vaizey Score declined to 10(4-13),(*P*=0.0039). VAS was 5(2.5-6) before treatment, and it improved at 6 weeks 6.2(4.5-8,1)(*P*=0.0029). No complications or side effects occurred. Five patients completed the initial therapy sessions with a subjective success rate of 100% and started a maintenance therapy. No recurrence of the urge symptoms was reported.

Conclusion:
PTNS may be a safe and effective treatment for patients with faecal urgency and involuntary stool lost. It is a simple to perform and minimal invasive approach tackling a frustrating disorder.

Genetic and Functional Analysis of Intestinal Organic Cation / L-Carnitine Transporter (OCTN) in Crohn's Disease.

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Background: The IBD5 locus has been repeatedly implicated as a genetic risk factor for Crohn's Disease (CD). This locus codes for the organic cation/carnitine transporters (OCTN1 & 2) that transport carnitine. Two variants of OCTN have been associated with susceptibility to CD and a modified function of OCTN-1 was shown *in vitro*. Aims: To investigate the function of intestinal OCTNs in inflammatory bowel disease (IBD) in relation to genetic polymorphisms. Methods: Intestinal tissue was obtained from endoscopic biopsies (n=55) and surgical resections (n=28) in consenting IBD and control patients. OCTN protein levels were measured by Western Blot. Carnitine transport was mesured on brush border membrane vesicles from intestinal resections using H^3 radiolabeled substrate. Common OCTN1 & 2 polymorphisms were carried out using leukocytes. Results: OCTN1 & 2 were shown at 65 KDa in IBD and controls. OCTN1 protein levels were significantly higher in ileum compared to colon (2.3% ± 0.4 vs 0.7% ± 0.2, p<0.0002). OCTN1 expression was higher in CD patients with homo or heterozygous mutations (0.6% ± 0.1 vs 3% ± 0.8, p<0.02). No difference in carnitine transport was found comparing CD and control groups (0.45 ± 0.12 vs 0.51 ± 0.12 nM carnitine/mg prot/min). Carnitine transport tended to be higher, but non significantly, in tissue from patients with homo or heterozygous OCTN1 mutations (0.19 ± 0.03 vs 0.59 ± 0.12). Conclusions: The present data reveal the presence of higher OCTN protein levels in intestinal tissue from IBD patients. Our results suggest that ileal carnitine transport is similar in CD and control groups. However, there was a trend towards higher carnitine transport in patients with OCTN1 mutations.

Gastric emptying, dyspeptic symptoms and eating behavior in healthy mountaineers after rapid ascent to 4559 m

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Background: Loss of appetite and nausea are frequent symptoms of acute mountain sickness (AMS). It is hypothesized, that direct effects of hypoxia on gastrointestinal (GI) motor and sensory function may be the origin of these symptoms. Therefore our aims were to assess gastric emptying (GE), dyspeptic symptoms and appetite in healthy mountaineers after rapid ascent to 4559 m.
Methods: 25 participants [(15m, 22-60 y, 8 with a history of high altitude pulmonary edema (HAPE)] were studied at ground level (GL) in Zurich (490 m) and on two occasions (d2+d4) at Capanna Regina Margherita in the Alps (4559 m), where they spent four days after a rapid ascent from 1130 m. On each occasion we recorded AMS symptoms by self assessment questionnaires [Lake Louise Score (LLSAS)], gastroparesis cardinal symptom index (GCSI) and pharmacotherapy with dexamethasone before the participants ingested a solid lunch meal (400 kcal) labelled with 100 mg ^{13}C-octanoate for a GE breath test. Samples were obtained at regular time intervals over 4 h. $^{13}C/^{12}C$-isotopic ratio was determined by a spectroscopic method (IRIS, Wagner, Germany) and gastric emptying coefficient (GEC) and half emptying time (T_{50}) were calculated. Postprandial dyspeptic symptoms (fullness, nausea, bloating, pain) and appetite scores were assessed by a 10cm visual analogue scale and analysed as $AUC_{0\text{-}4h}$ and $AUC_{2\text{-}4h}$. Dexamethasone 8 mg bid was administered if LLSAS in the evening of d2 was >4 or >2 in HAPE susceptibles. **Results:** LLSAS was highest at d2 and d4 (5.6±0.6 and 3.8±0.6 vs. GL: 1.12±0.5, p<0.001). Compared to ground level GE increased at high altitude at d4 (GEC: 3.5±0.1 vs. 4.0±0.1; T_{50}: 146±7min vs. 111±8min; p<0.001). GE increased further from d2 to d4 (GEC: 3.9±0.2 vs. 4.0±0.1, p=0.06; T_{50}: 135±9min vs. 111±8min, p<0.01). Mean GCSI increased on d2 compared to GL (0.6±0.2 vs. 0.2±0.1, p<0.05) and returned to baseline (GL) on d4 (0.4±0.1). GCSI was not associated with GE parameters. Dyspetic symptoms increased at high altitude at d2 (for all $AUC_{0\text{-}4h}$ p<0.05) and returned to baseline at d4. Two hours after meal ingestion appetite scores increased but were lower on d2 compared to GL (for all $AUC_{2\text{-}4h}$ p<0.05) and returned to baseline at d4. Dexamethasone treatment in 14 participiants did not influence GE, GCSI, dyspeptic symptoms and appetite (p>0.2).
Conclusions: This study is the first description of GE and GI sensory responses to feeding during the acclimatization phase at high altitude. Higher initial dyspeptic symptoms and lower appetite scores return rapidly to baseline independent of dexamethasone use. In addition accelerated solid GE counterbalances the well known increase in energy expenditure at high altitude.

Mapping the Membrane Topology of Hepatitis C Virus Nonstructural Protein 4B

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Background: Nonstructural protein 4B (NS4B) plays an essential role in the formation of the hepatitis C virus (HCV) replication complex. It is an integral membrane protein that has only poorly been characterized to date. In particular, a precise membrane topology is thus far elusive. Here, we explored a novel strategy to map the membrane topology of HCV NS4B.

Methods: Selective permeabilization of the plasma membrane, maleimide-polyethyleneglycol (mPEG) labeling of natural or engineered cysteine residues and immunoblot analyses were combined to map the membrane topology of NS4B. Cysteine substitutions were introduced at carefully selected positions within NS4B and their impact on HCV RNA replication and infectious virus production analyzed in cell culture.

Results: We established a panel of viable HCV mutants with cysteine substitutions at strategic positions within NS4B. These mutants are infectious and replicate to high levels in cell culture. In parallel, we adapted and optimized the selective permeabilization and mPEG labeling techniques to Huh-7 human hepatocellular carcinoma cells which can support HCV infection and replication.

Conclusions: The newly established experimental tools and techniques should allow us to refine the membrane topology of HCV NS4B in a physiological context. The expected results should enhance our understanding of the functional architecture of the HCV replication complex and may provide new opportunities for antiviral intervention in the future.

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The effects of alcohol on gastric emptying and symptoms during and after ingestion of a high calorie, high fat Swiss fondue meal: a randomized cross over trial

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Background: Many competing claims are made concerning the effects of alcoholic vs. non-alcoholic beverages on postprandial gastric function and symptoms; however the interpretation of existing studies is hampered by sub-optimal measurement techniques and/or study design. Gastric emptying (GE) of high fat, high caloric meals and the effect of peri- and postprandial beverage intake have so far only been insufficiently characterised.

Aims: To assess the effects on gastric emptying and symptoms of white wine vs. black tea during, and the effect of schnapps after ingestion of a high calorie, high fat meal.

Methods: A Swiss cheese fondue meal (780 kcal ,32% fat) was labelled with 150mg 13 C Octanoate for breath test measurement (binding stable in presence of alcohol) and consumed with either 300ml white wine (12% alcohol) or tea on 2 study days in a randomised, cross over study. 90 minutes after the meal either 20cl digestive (cherry schnapps (kirsch), 40% alcohol) or water were administered according to a second randomization. At baseline and fixed intervals over 4 hours breath samples for 13CO2 excretion and alcohol and also symptom scores by visual analogue scale (VAS) were collected. Gastric emptying (GE) was evaluated by area under curve of the percentage dose of 13C recovered (AUC PDR) in the breath. Dyspeptic symptoms and a normalized appetite score derived from hunger, satiety, desire to eat and quantity to eat were assessed.

Results: 20 healthy volunteers (14 male; mean age 37.5, mean BMI 23.6) completed the study. GE was faster for the combination of tea/water than for wine/kirsch (AUC18.1 (95% CI 15.2-20.9) vs. 7.4 (95% CI 4.6-10.3),p<0.001). Detailed results showing comparisons between individual study interventions from mixed model analysis are shown in the table.

Study Intervention (Comparison)	Difference	Lower CI	Upper CI	p
(Tea-Wine).Water	8.1	4.1	12.2	0.0006
(Tea-Wine).Kirsch	7.0	2.9	11.0	0.0021
Tea.(Water-Kirsch)	3.6	−0.4	7.7	0.0750
Wine.(Water-Kirsch)	2.5	−1.6	6.5	0.2200

Higher breath alcohol levels correlated with slower postprandial gastric emptying (e.g. wine/kirsch r= 0.82). Scores for dyspeptic symptoms were minimal in all groups and there was no consistent effect of alcohol on appetite; however, after a meal with wine, the digestive reduced the appetite score. (0.33 (95%CI 0.01-0.79); p<0.046).

Conclusion: On consuming a high fat, high calorie meal, such as Swiss fondue, alcohol significantly slowed gastric emptying whether taken during or after the meal. Moreover, at the highest dose applied (wine followed by schnapps), alcohol appeared to reduce appetite for dessert.

Expression of Thymidin Phosphorylase (TP), Dihydropyrimidin Dehydrogenase (DPD) und Thymidylat Synthase (TS) in Pretherapeutic Rectal Cancer and Correlation with Tumor Stage and Regression Grade.

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Background: Neoadjuvant chemoradiotherapy (CRT) has become a standard practice for locally advanced rectal cancer. Complete pathologic response can be achieved in 20-25%. Molecular markers could be helpful to detect responders from non-responders prior to CRT. The aim of the study was to examine the correlation between TP, DPD and TS expression and histopathologic tumor regression grade.
Methods: Rectal biopsy tissue from forty-seven patients receiving neoadjuvant CRT with 50.4 Gy and capecitabine was investigated. Total RNA from paraffin-embedded tissue was isolated. Quantification of TP, DPD and TS was performed by RT-PCR. Results were correlated with the tumor regression grade according to Dworak. Patients with complete histopathologic response (ypT0 ypN0 and Dworak 4) were considered "responders", patients with Dworak 0-3 "non-responders".
Results: Histopathologic examination revealed 9 responders (19%) and 38 non-responders (81%). Median expression of TP, DPD and TS in responders was 69.48, 3.48 and 1.13 respectively; in non-responders 62.59, 4.9 and 1.45 (p=n.s.)
Conclusion: Levels of TP, DPD and TS in pretherapeutic rectal cancer tissue do not show any significant difference in correlation to the final tumor stage after CRT. These markers can not be used as a predictor for complete histopathologic response.

Zinc salts provide a novel, prolonged and rapid inhibition of gastric acid secretion

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Backround: The overproduction of acid and the associated illnesses linked to hypersecretion effects approximately 25 million patients per year. Although a variety of pharmaceutical agents have been employed to reduce the production of acid, alarming new evidence questions the long term efficacy and safety of the agents. These issued coupled with the delayed onset of action and the return of symptoms to over 60% of the patients is less than satisfactory.
Aim: The purpose of the present study was to determine if administration of a zinc salt could lead to a rapid and sustained increase in gastric pH in both animals and in humans and provide a new rapid acid suppression therapy.
Methods: Intracellular pH was measured with BCECF in both human and rat gastric glands following an acid load +/- a secretagogue. In a separate series of studies whole stomach acid secretion was monitored in rats. A final study used healthy human volunteers while monitoring with a gastric pH measurement received either: placebo, zinc salt, or a zinc salt and PPI.
Results: We demonstrate that exposure to $ZnCl_2$ immediately abolished secretagogue induced acid secretion in isolated human and rat gastric glands, and in intact rat stomachs. Chronic low dose zinc exposure effectively inhibited acid secretion in whole stomachs and isolated glands. In a randomized cross-over study in 12 volunteers exposure to a single dose of $ZnCl_2$ raised intragastric pH for over 3 hours including a fast onset of effect.
Conclusion: Our findings demonstrate that zinc offers a novel rapid and prolonged therapy to inhibit gastric acid secretion in human and rat models.

Effect of gastric secretion on measurement of liquid gastric emptying by ^{13}C-Acetate breath test in humans – a combined magnetic resonance imaging (MRI) and ^{13}C breath test study

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Background: Previous intraduodenal validation studies of ^{13}C Acetate (Ac) labeled meals (Neurogastroenterol Motil 2009) have shown that, theoretically, the flow rate of gastric emptying (GE) can be derived from $^{13}CO_2$ excretion curves. However, in higher caloric meals gastric secretion may dilute the ^{13}C GE marker, which could result in lower $^{13}CO_2$ exhalation irrespective of the actual rate of GE. To asses the effect of gastric secretion on $^{13}CO_2$ exhalation, we applied in parallel a newly developed MRI technique allowing the assessment of the intragastric dilution of a test meal (MRM 2007). **Methods:** After ingestion of a glucose drink (500ml, 200kcal) homogeneously labelled with 1200µmol/l Gd-DOTA and 100mg Ac, 12 healthy volunteers were treated with pentagastrin (0.6µg/kg/h i.v.) and placebo (0.9% NaCl i.v.) over a period of 60min on two different days in double-blind randomised order. MRI (1.5T Achieva, Philips Healthcare) assessed gastric content volume [GCV = meal (MV) + secretion volume (SV)] and Gd-DOTA concentration within the meal every 5min over a period of 90min. Antral Ac concentrations (cAc) were identified in individual anatomical maps of Gd-DOTA concentrations. MV and SV were calculated from total gastric Gd-DOTA concentration and GCV. $^{13}CO_2$ in breath was measured by a spectroscopic method and expressed as maximal and cumulative percentage dose rate (PDR_{max}, cPDR). Gastric secretion and emptying were expressed as maximal SV (SV_{max}), minimal cAc (cAc_{min}) as well as area under the curve (AUC) of cAc and MV. A multiple linear regression model was applied to assess the effect (weighted by partial correlations of predictors) of gastric secretion and antral meal dilution on $^{13}CO_2$ excretion during treatment. Effects of treatment were compared by Wilcoxon test. **Results:** Pentagastrin increased SV_{max} and AUC-MV and reduced antral cAc and AUC-cAc, respectively (all p<0.05). cPDR and PDR_{max} were smaller under pentagastrin (all p<0.01). Regression analysis showed that cPDR and PDR_{max} were influenced by intragastric AC dilution and delayed meal emptying whereas Ac dilution had only a minor association with $^{13}CO_2$ excretion. (**PDR_{max}:** R^2=0.72, p<0.001, partial correlations: AUC-MV: r=-0.86, p<0.001, cAc_{min}: r=-0.58, p=0.012, AUC-cAc: r=0.58, p=0.013; **cPDR:** R^2=0.56, p=0.001; AUC-MV: r=-0.78, p<0.001; cAc_{min}: r=-0.68, p=0.002; AUC-cAc: r=0.67, p=0.003).
Summary: Gastric secretion delays meal emptying and dilutes ^{13}C-Acetate in the gastric antrum. This is reflected by lower $^{13}CO_2$ exhalation. Results indicate that delayed meal emptying rather than marker dilution is the main effector of this phenomenon. **Conclusion:** Gastric emptying rates as assessed by stable isotope breath tests are likely to be underestimated by marker dilution, especially for high caloric meals. Underlying mechanisms need to be assessed for an experimental onset in which gastric secretion is induced by physiological meals.

Vitamin D deficiency and a CYP27B1-1260 promoter polymorphism are associated with chronic hepatitis C and poor response to interferon-alfa based therapy

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Background: Vitamin D is an important immune modulator and preliminary data indicated an association between vitamin D deficiency and sustained virologic response (SVR) rates in patients with chronic hepatitis C. We therefore performed a comprehensive analysis on the impact of vitamin D serum levels and of genetic polymorphisms within the vitamin D cascade on chronic hepatitis C and its treatment. ***Methods:*** Vitamin D serum levels, genetic polymorphisms within the vitamin D receptor and the 1α-hydroxylase were determined in a cohort of 468 HCV genotype 1, 2 and 3 infected patients who were treated with interferon-alfa based regimens. ***Results:*** Chronic hepatitis C was associated with a high incidence of severe vitamin D deficiency compared to controls ($25(OH)D_3$<10 ng/mL in 25% versus 12%, p<0.00001), which was in part reversible after HCV eradication. $25(OH)D_3$ deficiency correlated with SVR in HCV genotype 2 and 3 patients (63% and 83% SVR for patients with and without severe vitamin D deficiency, respectively, p<0.001). In addition, the CYPB27-1260 promoter polymorphism rs10877012 had substantial impact on 1-25-dihydroxyvitamin D serum levels and SVR rates in HCV genotype 1, 2 and 3 infected patients. ***Conclusions:*** Chronic hepatitis C virus infection is associated with vitamin D deficiency. Reduced 25-hydroxyvitamin D levels and CYPB27-1260 promoter polymorphism are associated with failure to achieve SVR in HCV genotype 1, 2, 3 infected patients.

Toll-Interacting Protein Deficiency Leads to Increased Susceptibility to Acute and Chronic Colitis.

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Background: Sensing of bacterial products via Toll-like receptors is critical to maintain gut immune homeostasis. The Toll-Interacting Protein (Tollip) inhibits downstream signaling through the IL-1 receptor, TLR-2 and TLR-4. Here,we aimed to address the role of Tollip in acute and chronic inflammatory responses in the gut.
Material and methods: WT or Tollip-deficient mice were exposed to dextran sulfate sodium (DSS) 1.5% in the drinking water during 7 days. To generate bone-marrow chimeras, WT or Tollip deficient mice were 900-rads irradiated, transplanted with WT or Tollip deficient bone-marrow cells and challenged with DSS 2-3 months after transplantation. IL-10 deficient mice were bred with Tollip deficient mice and colitis was compared at various time points.
Results: Upon DSS exposure, Tollip-deficient mice had increased body weight loss and increased pro-inflammatory cytokine expression compared to WT controls. Challenge of bone-marrow chimeras showed that colitis susceptibility was also increased when Tollip deficiency was restricted to non-hematopoietic cells. DSS-exposure lead to a disorganized distribution of zona-occludens-1, a tight junction marker and increased number of apoptotic, cleaved caspase 3 positive, epithelial cells in Tollip-deficient compared to WT mice. Chronic colitis was also affected by Tollip deficiency as Tollip/IL-10 deficient mice had more severe histological stigmata of colitis and higher IL-17 expression than IL-10 deficient controls.
Conclusion: Tollip in non-hematopoietic cells is critical for adequate response to a chemical-induced stress in the gut and to hamper chronic bacteria-driven colitis. Modulation of epithelial cell integrity via Tollip likely contributes to the observed defects.

Common *Vitamin D Receptor (NR 1I1)* gene polymorphisms promote fibrosis progression in chronic hepatitis C patients

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Background: Alterations in the vitamin D receptor (VDR) pathway have been described as an important event in hepatic disorders. VDR signalling has antiinflammatory and antifibrotic effects on stellate cells, and 25-OH-vitamin D levels are reduced in increasing stage of fibrosis and severity of inflammation in chronic HCV pts. We hypothesized that *VDR* gene polymorphisms (SNP) may lead to increased hepatic inflammation and fibrogenesis in HCV pts irrespective of vitamin D levels.
Methods: 223 HCV pts were included for *VDR* genotyping (*Cdx2* rs11568820, *bat* haplotype: *Bsm* rs1544410, *Apa* rs 7975232, *Taq* rs 731236). Exclusion criteria: HBV/HIV coinfection, alcohol >40g/d, morbid obesity. Hepatic mRNA expression of MMP-9 and TIMP-1 was quantified in 22 pts with early fibrosis (F0-F2). Statistical associations of *VDR* genotypes with liver function tests, Metavir F-stage, fibrosis progression rate and hepatic gene expression were calculated. **Results:** Overrepresentation of Apa CC, Bsm CC, Taq AA genotypes and the bAt (CCA) haplotype was observed in HCV pts compared to caucasian HapMap controls. For serum markers of cell injury/inflamma-tion, a significant correlation of GGT to Apa CC (p=0.005) and the bAt haplotype (p=0.005) was observed, with a strong analogous trend for ALT levels. 28.3% of Apa CC pts were cirrhotic and a significant correlation between CC vs. CA vs. AA (p=0.02) and between CC vs. CA/AA (p= 0.009, OR 2.67) could be identified. For the Taq, Bsm and Cdx2 SNPs no significant correlation was detected. The CCA (bAt) haplotype was significantly correlated with presence of cirrhosis (OR 2.49; p=0.02). 21.1% of the HCV pts with the bAt haplotype were cirrhotic. Similar findings for Apa CC (OR 2.323; p=0.04) and the CCA (bAt) haplotype (OR 2.027; p=0.007) were observed for the fibrosis progression rate (<1.01 vs >1.01 U/year). Hepatic MMP-9 mRNA expression was significantly elevated for Apa CC (p=0.03) and close to statistical significance for the CCA (bAt) haplotype (p=0.09). **Conclusions:** Key finding is a strong correlation of a specific *VDR* gene SNP and the common bAt haplotype with the presence of cirrhosis and fibrosis progression rate in chronic HCV pts. Increased liver cell injury/inflammation is accordingly reflected by elevated serum liver function tests and hepatic and MMP-9 mRNA expression in respective *VDR* geno- and haplotypes. This study elucidates for the first time a pathomechanistic relationship between VDR signalling and fibrogenesis in chronic HCV pts.

Demographics and outcomes of severe Herpes simplex virus hepatitis: a registry-based study

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Abstract

Herpes simplex virus (HSV) hepatitis is a rare, but severe disease, thus far only documented by case reports and short series. The present study was based on the SRTR registry, and included all listed patients for liver transplantation from 1985 to 2009 with a diagnosis of HSV hepatitis. We assessed demographics and outcome of all listed patients, and further conducted a case-control study, matching each transplanted patient with 10 controls. Matching criteria included: transplant status, Model for End-Stage Liver Disease score ± 5, transplant date ± 6 months and age at transplant ± 5 years. During the study period, 30 patients were listed for HSV hepatitis. Patients were distributed into two groups, young children (with most ≤5 months) and adults. Twelve listed patients were not transplanted, including seven spontaneous recoveries and five deaths. The chance of recovery was significantly higher in children than in adults (7/9 vs. 0/11, p=0.02). Ten children and eight adults were transplanted. In children, survival was similar between HSV patients and the matched controls (5-year survival: 69 vs. 64%, log-rank p=0.89). Conversely, survival was poor in adult HSV recipients (5-year survival: 38 vs. 65%, log-rank p=0.006), with 62% of them dying within the first 12 months. In addition, all three reported post-transplant deaths in children were independent from HSV, while 4/7 adults deaths were infection-related. *Conclusion*: Children listed for HSV hepatitis have a significantly better survival than adults both prior and after liver transplantation. While HSV fulminant hepatitis is an appropriate indication for liver transplantation in children, it should only be performed in selected adult patients in otherwise good condition.

Effects of Radiofrequency Ablation (RFA) in combination with Sorafenib in a 2-Tumor Rat Model of Hepatocellular Carcinoma.

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Background: Radiofrequency ablation (RFA) is a widely employed local ablative therapy for hepatocellular carcinoma (HCC). The multitkinase inhibitor sorafenib prolongs survival of advanced-stage HCC patients and is currently under investigation for adjuvant treatment in clinical trials. We examined the effects of RFA in combination with sorafenib in a two-tumor rat model of HCC.

Methods: Morris Hepatoma cells (MH) were injected subcutaneously into donor ACI rats. After 14day the resulting tumors were removed and dissected into 1mm^3 cubes. Tumor cubes were subsequently implanted into the right and left liver lobe of syngeneic ACI rats. Animals were randomized into four treatment groups and administered sorafenib (7.5mg/kg/d) or its vehicle (placebo) p.o., starting day 12 after tumor implantation. RFA of the left lobe tumor or sham operation was performed on day 15 after tumor implant. Group 1 was subjected to vehicle treatment and a sham operation. Group 2 had vehicle treatment and RFA therapy. Group 3 had sorafenib treatment and a sham operation. Group 4 had sorafenib treatment and RFA therapy. MRI scans were performed at day 14 and day 20 post-implant for volumetric assessment of tumor size. Animals were sacrificed at two timepoints: day 18 and 30 post-implant (n=10 per group). Tumor samples, surrounding liver tissue and blood samples were collected at harvest.

Results: Most animals developed two distinct tumors. When comparing the size of the unablated right lobe tumors at day 30, the largest tumor volumes were observed in the control group (831 ± 264 mm^3). In the RFA-only group, right lobe tumors were significantly smaller (580 ± 129 mm^3, p<0.05). Sorafenib treatment alone further reduced tumor growth when compared to controls (367 ± 177 mm^3, p<0.001) and to the RFA-only group (p<0.05). Finally, combined sorafenib treatment and RFA therapy resulted in maximal tumor growth inhibition (282 ± 118 mm^3 vs control group, p<0.0001; vs RFA-only group, p<0.001).
There were no significant differences in tumor volume between the 4 groups for the animals harvested 3 days after RFA (day 18 post-implant).

Conclusions: Radiofrequency ablation therapy and sorafenib treatment alone both result in a significant reduction of the unablated right tumor volume, with a more prominent effect for the sorafenib treatment. The smallest right lobe tumors developed under combination of sorafenib treatment and RFA therapy, suggesting a beneficial effect of combining the 2 modalities in HCC patients scheduled for local ablative therapy.

Graft survival and long term complications 12 years after laparoscopic gastric banding for morbid obesity.

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Background: Laparoscopic adjustable gastric banding (LAGB) has been considered by many as the treatment of choice for morbid obesity, because of its simplicity and encouraging early results. The aim of this prospective study was to critically assess the effects, complications and outcome after LAGB in the long term, based on a 12-year experience. *Methods:* Between June 1998 and June 2009 all patients with implantation of a LAGB have been enrolled in a prospective clinical trial. Results were recorded and classified, with special regard to long term complications, re-operation rate and graft survival. *Results:* LAGB was performed in 167 patients (120 female, 47 male) with a mean age of 40.1±5.2 years. Operative mortality was 0%, overall 1.2% (not band-related). Overall patient follow-up was 94.0%. Mean excess weight loss (EWL) after 1, 2, 5, 8 and 10 years was 31.1±7.5% (p<0.005), 44.2±6.5% (p<0.001), 50.3±6.9% (p<0.001), 51.7±6.3% (p<0.001) and 48.8±6.0% (p<0.001). The non-responder rate (EWL<30%) after 2, 5, 8 and 10 years was 24.5%, 18.3%, 12.5% and 16.6%. The early complication rate (<30 days) was 7.8% (13/167), with 10 minor and 3 major complications. Late complications (>30 days) occurred in 40.1% (67/167), of whom 7 were minor and 60 were major complications (3 band infections, 2 band migrations, 11 band leakages, 2 slippings/pouch dilatations, 2 band intolerances and 40 esophageal dilatations). The overall re-operation rate was 20.4% (34/167). The graft survival of the implanted band after 2, 5, 8, 10 and 12 years was 98.8%, 94.0%, 86.8%, 85.0% and 85.0%. The failure rate of the procedure after 2, 5, 8 and 10 years was 25.7%, 24.3%, 25.7% and 31.6%. *Conclusions:* In the present long term high participation follow-up study LAGB is a safe and effective surgical treatment for morbid obesity. However, the high complication, re-operation and long term failure rates lead to the conclusion, that LAGB should be performed in selected cases only, until reliable criteria for patients at low risk for long term complications are developed.

COLOX: a new blood-based test for colorectal cancer (CRC)screening

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Background: The objective is to develop a cost-effective, reliable and non invasive screening test able to detect early CRCs and adenomas. This is done on a nucleic acids multi-gene assay performed on peripheral blood mononuclear cells (PBMCs). **Methods:** A colonoscopy-controlled study was conducted on 179 subjects. 92 subjects (21 CRC, 30 adenoma >1 cm and 41 controls) were used as training set to generate a signature. Other 48 subjects kept blinded (controls, CRC and polyps) were used as a test set. To determine organ and disease specificity 38 subjects were used: 24 with inflammatory bowel disease (IBD),14 with other cancers (OC). Blood samples were taken and PBMCs were purified. After the RNA extraction, multiplex RT-qPCR was applied on 92 different candidate biomarkers. After different univariate and multivariate analysis 60 biomarkers with significant p-values (<0.01) were selected. 2 distinct biomarker signatures are used to separate patients without lesion from those with CRC or with adenoma, named COLOX CRC and COLOX POL. COLOX performances were validated using random resampling method, bootstrap. **Results:** COLOX CRC and POL tests successfully separate patients without lesions from those with CRC (Se 67%, Sp 93%, AUC 0.87), and from those with adenoma > 1cm (Se 63%, Sp 83%, AUC 0.77). 6/24 patients in the IBD group and 1/14 patients in the OC group have a positive COLOX CRC. **Conclusion:** The two COLOX tests demonstrated a high Se and Sp to detect the presence of CRCs and adenomas > 1 cm. A prospective, multicenter, pivotal study is underway in order to confirm these promising results in a larger cohort.

Improved glucose metabolism 1 year after bariatric surgery: Comparison of laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic sleeve gastrectomy (LSG) - a prospective randomized trial

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Background. Bypass of the foregut is thought to play a major role in the rapid improvement in the metabolic control of diabetes after gastric bypass.
Objective. In this randomized, prospective, parallel group study, we sought compare the effects of LRYGB with those of LSG on fasting, and meal-stimulated insulin, glucose levels as well as gut homone levels of the foregut (Ghrelin, CCK) and the hindgut (GLP-1, PYY).
Methods. Thirteen morbidly patients were randomized to LRYGB and 14 patients to LSG. The mostly non-diabetic patients were evaluated before, 1 week, 3 months, and 1 year after surgery. A standard test meal was given after an overnight fast, and blood samples were collected before and after food intake in both groups.
Results. Body weight decreased markedly (P<0.002) and comparably after either procedure. Excess BMI loss was similar at 3 months (35±10% for LRYGB and 31±8% for LSG) and at 12 months 79±23% and 64±20% (p=0.08). After surgery, patients had markedly increased postprandial plasma insulin and GLP-1 levels, respectively, (p<0.01), resulting in an improvement of the HOMA-index as early as 1 week post-op. After 3 months and 1 year, no significant difference was observed with respect to insulin and GLP-1 secretion between the two procedures. Ghrelin was decreased and CCK increased significantly more after LSG.
Conclusion. Both procedures markedly improved glucose homeostasis: insulin, GLP-1 and PYY levels increased similarly after either procedure, however ghrelin decreased and CCK increased significantly more after LSG. Bypass of the foregut does not seem to be the only mechanism in glucose homeostasis.

Effects of weight loss after bariatric surgery on adipokines and metabolic parameters: Comparison of laparoscopic Roux-en-Y gastric bypass (LRYGB) with laparoscopic sleeve gastrectomy (LSG) - a prospective randomized trial

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Background: Adipokines are closely linked to obesity and insulin-resistance. Both LRYGB and LSG improve insulin-sensitivity.
Objective: In this randomized, prospective, parallel-group study, we sought to compare the one-year follow-up results of LRYGB with LSG on weight loss, metabolic control and fasting adipokine levels.
Methods: 12 non-diabetic morbidly obese patients were randomized to LRYGB and 11 to LSG. Patients were investigated before, 1 week, 3 months, and 12 months after surgery. Fasting levels of glucose, insulin, triglycerides, cholesterol (total, HDL and LDL) and adipokines (leptin, adiponectin, and fibroblast growth factor 21 (FGF21)) were analyzed. The adipokines were correlated to weight loss and fat mass measured by DEXA.
Results: Body weight and BMI decreased markedly (P < 0.001) after either procedure corresponding to % weight loss of 16.4±1.3% at 3 months, 24.8±1.7% at 6, and 34.5±2.7% at 12 months after LRYGB and 13.1±1.1%, 20.7±1.5%, and 27.9±2.6% respectively after LSG. HOMA index declined from preop 8.0±1.5 to 5.8±0.4 at 1 week and 3.4±0.3 after 3 months and 2.9±0.2 at 12 months in both groups. Lipid profiles were normalized. Concentrations of circulating leptin levels dropped almost 50% as early as one week and continued to decrease until 12 months postop. Leptin per kg fat mass decreased by 30% after 12 months. Adiponectin increased progressively with weight loss after surgery and adiponectin/kg fat mass increased three fold after weight loss. FSG-21 levels did not change over time. There was no difference found between LRYGB and LSG.
Conclusion: Both procedures were followed by a marked reduction in body weight associated with resolution of the metabolic syndrome. Serum leptin levels decreased and adiponectin levels increased with weight loss, paralleled by improved insulin sensitivity. No change was found for FGF21.

Notch1 Signaling Through Ephrin B2/EphB4 Pathway Maintains Ultrastructure, Differentiation and Function of Liver Sinusoidal Endothelial Cells

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Background: Notch signaling plays a pivotal role in embryonic vascular development as well as in normal vascular remodeling. We have reported that Notch1 KO in mice leads to nodular regenerative hyperplasia (NRH). The pathogenesis of NRH is still unclear; several clinical reports have linked NRH to vascular injury of the sinusoids. The aim of our study is to elucidate the role of Notch1 signaling in NRH focusing on liver sinusoidal endothelial cells (LSECs).

Methods: We used MxCre Notch1 lox/lox mice as a tissue-unspecific conditional KO mouse model. A hepatocyte-specific KO was created by crossing Notch1 lox/lox with AlbCre+/- mice. Morphological assessment of the liver was performed (proliferation by BrdU IHC, hepatic stellate cell (HSC) activation by alpha-SMA IHC). Morphology of hepatic vasculature was assessed by scanning electron microscopy (SEM). Portal vein pressure was measured in anesthetized KO mice. *In vitro* angiogenesis was studied using LSECs on matrigel with primary hepatocyte conditioned medium (CM) from either Notch1 KO mice or control mice.

Results: MxCre induced KO mice developed NRH within 14 days after deletion of Notch1 in the absence of fibrosis or HSC activation. BrdU staining showed a persistently increased LSEC proliferation rate in MxCre Notch1 KO mice (p=0.0058, day 6 up to week 14). SEM of vascular casts showed that loss of Notch1 leads to dedifferentiation and dramatic vascular remodeling of the hepatic sinusoidal microvasculature with increased branching and diameter (p<0.001) as well as active intussusceptive angiogenesis. Fenestrae and sieve plates of LSEC were strongly reduced (p<0.005). Expression analysis of Notch1 key targets in liver homogenates (RT-PCR, WB) showed upregulation of EphB4 and downregulation of EphrinB2. Further, MxCre Notch1 KO mice developed portal hypertension (p=0.0041) and upregulated endothelial CD34 as marker of capillarisation. In contrast, hepatocyte-specific Notch1 KO mice were phenotypically normal. Accordingly, no difference was found in LSEC proliferation and tube formation with Notch1 CM compared to control CM.

Conclusions: Notch1 signaling through EphrinB2/EphB4 is required for vascular homeostasis of hepatic sinusoids by inducing quiescence and differentiation of LSEC in adult mice. Disruption of Notch1 pathway leads to LSEC proliferation, loss of fenestrae, vascular remodeling and portal hypertension without fibrosis or HSC activation. The lack of phenotypic changes in hepatocyte-specific Notch1 KO mice suggests that the development of NRH in our model is secondary to vascular remodeling induced by loss of Notch1 signaling in LSEC.

Ficolin-2 as a possible new serum marker for disease activity in CD patients

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Background and Aims: The ficolins represent microbial pattern recognition receptors that can activate the lectin pathway of complement. We found that in the serum of IBD patients, especially in Crohn's disease (CD), ficolin-2 (L-ficolin) had an acute-phase like expression pattern. With the present study we further investigated the acute-phase like expression of ficolin-2 in CD patients including a possible correlation with disease activity.

Methods: Ficolin-2 concentrations were measured in the sera of IBD patients by ELISA. For the same patients also C-reactive protein (CRP) and fecal calprotectin concentrations were determined. Harvey-Bradshaw index, Mayo score and medication were assessed at the time point of sample collection. Sera and stool samples were collected in a prospective manner from 48 patients of our local IBD cohort.

Results: In our IBD cohort serum concentrations of ficolin-2 were significantly increased in CD patients compared to healthy controls. It was also increased in UC patients compared to HC but this was not statistically significant. The increase of ficolin-2 was higher than 40% compared to healthy controls and a moderate but significant correlation with CRP concentration was measured. Furthermore, CD patients with a Harvey-Bradshaw index (HBI) >3 had significantly higher ficolin-2 concentrations than patients with a HBI ≤3.

Conclusion: Ficolin-2 in CD showed an expression pattern like an acute-phase protein. Ficolin-2 was the only marker in this study that was significantly correlated with disease activity represented by the HBI. Therefore, ficolin-2 may represent a new, easy measurable serum marker, to objectively assess disease activity of CD patients.

Yeast mannan differentially influences maturation of dendritic cells from Crohn's patients compared to healthy controls

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Background and Aims: Yeast mannan more efficiently inhibits T cell proliferation in mixed leukocytes reactions (MLR) from healthy controls (HC) compared to patients with Crohn's disease (CD). This inhibition is mediated via antigen-presenting cells (APC). We aimed to assess yeast mannan-induced regulation of gene expression in monocytes-derived dendritic cells (moDC) from CD patients compared to HC during allogeneic MLR or upon maturation with LPS.

Methods: moDC were generated from monocytes of patients and controls with GM-CSF and IL-4. moDC were matured in co-culture with allogeneic lymphocytes or with LPS, 1 mg/ml yeast mannan, or both. Gene expression was assessed using Affymetrix global gene expression chips. Expression of selected genes was assessed by custom-made TaqMan qPCR array (Applied Biosystems).

Results: After 8 h of allogeneic MLR in the presence or absence of mannan, a number of genes were differentially regulated in sorted moDC. Twenty-two differentially regulated genes related to DC function were compared in LPS- and/or mannan-matured moDC from patients and controls. Strong mannan-induced upregulation was found for the metallothionein (MT) isoform MT1G, with the highest expression in moDC from CD patients. The MT isoform MT2A was also induced by mannan but also by LPS, with a higher expression in both CD and UC compared to HC. Furthermore, LPS significantly upregulated IL-2Rα (CD25) and CCR7 (CD197) mRNA expression in moDC from CD compared to HC and UC. Increased CD25 and CD197 expression was confirmed by FACS.

Conclusions: MT1G is exclusively upregulated by mannan. MTs influence immune responses by regulating zinc homeostasis. Increased IL-2Rα upregulation may lower the threshold for functional maturation of DC from CD. Increased CCR7 upregulation may indicate superior priming for Th1 T cell responses. *In vivo*, increased CCR7 expression may enhance migration of DC to draining lymph nodes for T cell priming.

Deficiency of complement factor c5 prevents the progression of biliary fibrosis in bile duct-ligated mice

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Background: Fibrogenesis represents the universal response of the liver to chronic liver injury. Complement c5 has been linked to fibrogenesis in murine toxic liver injury as well as human chronic hepatitis C. c5 may also play a central role in fibrogenesis of cholestatic disorders, since FXR has been characterized as an activator of the rodent c3 gene. Additionally, increased levels of complement activation products have been detected in human cholestatic disorders. Aim of this study was therefore to further elucidate complement activation in the pathogenesis of biliary fibrosis in the BDL model.

Methods: One week BDL and sham-laparatomy was performed in c5 deficient mice (Hc-/-) and WT controls (n=5-6). Histological examination included H&E and Sirius red and IF. mRNA expression of several genes involved in bile acid homeostasis, inflammation and fibrogenesis was quantified by real-time PCR. Respective protein expression levels were determined by Western blot. Bile acid levels are monitored by RIA.

Results: One week BDL leads to the development of fibrosis in WT animals whereas fibrosis is almost absent in Hc-/- mice. Serum bile acids are more pronounced in Hc-/- compared to WT mice. The expression of retrograde "overflow" transporters is more prominent in Hc-/- mice compared to WT controls. Inversely, expression of inflammatory cytokines is decreased in Hc-/- mice. In parallel TGFβ and αvβ6integrin mRNA expression is less pronounced in Hc-/- mice whereas expression of the MMP9 is significantly increased in WT animals.

Conclusions: The deficiency of complement c5 during biliary obstruction leads to a significant reduction of fibrosis. Besides the absent complement activation increased expression of bile acid overflow transporters in Hc-/- mice may further contribute to a reduction of inflammatory and profibrotic mediators. Our study highlights the particular pathogenetic role of complement activation in chronic cholestatic liver disease.

Efficacy of Tacrolimus Rescue Therapy in Severe Treatment-Resistant Ulcerative Colitis

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Background: Ulcerative colitis (UC) patients refractory to steroids and immunomodulators (Azathioprine, 6-mercaptopurine) are under increased risk for undergoing colectomy. Several rescue therapies such as cyclosporine, tacrolimus and anti-TNF-α agents are available for these cases. We aimed to investigate the efficacy of tacrolimus in treatment-resistant UC patients during a severe flare-up.

Methods: UC patients treated with tacrolimus between January 2008 and April 2010 were retrospectively analysed. Clinical response was defined as a >3 point decrease in the Mayo score.

Results: Thirteen patients (10 male/ 3female) were included. Co-medication: all patients were under either azathioprine or 6-MP and additionally steroids. Infliximab was given in 7/13 (54%). Overall, 8/13 (62%) showed a clinical response under tacrolimus. Five out of 6 patients (83%) that were naive to infliximab (IFX) responded to tacrolimus, whereas the response rate in the IFX pre-treated group was 3/7 (43%, P = 0.135). One IFX-naïve patient unresponsive to tacrolimus later responded to IFX. Tacrolimus had to be applied as maintenance therapy in three of the responders (37%) because of worsening of disease activity upon termination of tacrolimus rescue therapy. Four patients that did not respond to tacrolimus treatment required colectomy at a later time. No side effects of tacrolimus were observed.

Discussion: Tacrolimus is an effective treatment in a subgroup of steroid/immunomodulator- or anti-TNF treatment-resistant UC patients. A subgroup of patients that failed anti-TNF therapy still responded to tacrolimus rescue therapy.

Effects of Pentoxifylline on Liver Regeneration: A Double-Blinded Randomized Controlled Trial in 101 Patients Undergoing Major Liver Resection

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Background: Recent experimental data suggest that Pentoxifylline (PTX), a TNFα inhibitor, enhances liver regeneration and reduces ischemic injury through activation of the IL-6 signaling pathway. However, the clinical impact of PTX in patient undergoing major liver surgery is unknown. **Methods:** 101 consecutive non-cirrhotic patients undergoing major liver surgery with inflow occlusion were included in a double-blinded RCT at a single tertiary care center (2006–2009). 51 patients received intravenous PTX starting 12 hours before and ending 72 hours after surgery, while 50 control patients received a placebo infusion. Primary endpoint was liver regeneration as assessed by 3D-volumetry based on MR tomography at POD 8 compared with preoperative images. Secondary endpoints were transaminases, cytokines and postoperative complications. **Results:** Treatment with PTX resulted in significantly better volume regeneration for small remnant livers (RLBW ratio ≤1.2%) whereas no beneficial effect was observed for RLBW ratio >1.2%. There was a 3.6-fold stronger induction of *IL-6* mRNA for the PTX group ($p<0.001$). Postoperative AST levels were signifycantly decreased for the PTX group on the second postoperative day (442 *vs.* 585 U/L, $p= 0.025$). No significant benefit could be identified regarding the number and severity of postoperative complications as well as median ICU and hospital stay. However, the PTX group had significantly more drug-related adverse events (23 *vs.* 8, $p=0.007$). **Conclusions:** This is the first RCT evaluating the effects of PTX on liver regeneration after major liver resection. The study demonstrates beneficial effects of PTX on regeneration of small remnant livers (RLBW ratio ≤1.2%) which appears to be mediated by IL-6.

Alex Straumann, Sébastien Conus, Lukas Degen, Christian Bussmann, Alain Schoepfer, Hans-Uwe Simon

Maintenance-Treatment of Eosinophilic Esophagitis with Budesonide (BEE-M Trial)

Background Eosinophilic esophagitis (EoE) is a chronic-inflammatory disease of the esophagus, characterized by esophageal symptoms and a dense tissue eosinophilia, both refractory to proton pump inhibitors. Topical corticosteroids have proven effective in inducing clinical and histologic remission. However, the long-term management of this chronic disease is not yet defined.

Methods In a randomized, double-blind, placebo-controlled, long-term trial, we evaluated the efficacy of twice daily 0.25 mg swallowed budesonide in maintaining a remission in adult EoE who had shown a prior response to induction therapy. Pre- and post-treatment disease activity was assessed clinically, endoscopically, histologically, by immunofluorescence and by high-resolution endosonography (EUS). The primary endpoint was the therapy's ability to maintain EoE in histologic remission. Secondary endpoints were the efficacy in symptom control and in preventing tissue remodeling.

Results Despite treatment of quiescent EoE with low-dose budesonide, the esophageal eosinophilic load increased considerably during a 50-week period, from 0.4 to 31.8 eosinophils/hpf; nevertheless, with placebo, the increase was even significantly larger, from 0.7 to 65.0 eosinophils/hpf (P=0.024). At the end of the study period, 35.7% (5/14) of the budesonide patients were still in complete, and 14.3% (2/14) in partial, histologic remission, whereas under placebo, no patient was in complete, but 28.6% (4/14) were in partial, histologic remission (P=0.0647). Similarly to eosinophils, other biomarkers indicating inflammation were also elevated in esophageal tissues in spite of budesonide therapy, but usually less dramatic when compared with placebo. In parallel, the symptom score increased under budesonide (0.79 to 2.29 points), but again markedly less so than under placebo (0.71 to 4.00) (P=0.0875). When compared to healthy controls, patients with active EoE had a significantly thickened esophageal wall, as measured by EUS (3.05 mm vs. 2.18 mm; P<0.0001). Budesonide therapy was associated with a significantly reduced thickness of the mucosa (0.75 mm to 0.45 mm; P=0.025). Histomorphometric determination of the epithelial thickness did not reveal any signs of atrophy under the influence of budesonide (261.22 μm vs. 277.23 μm, P=0.733).

Conclusions After therapy-induced remission, low-dose budesonide maintained histologic and clinical remission in half of the patients, whereas under placebo, inflammation and symptoms flared up in the majority of patients. Signs of remodeling showed a trend toward normalization. Long-term administration of topical corticosteroids was well-tolerated and did not induce epithelial atrophy. (ClinicalTrials.gov number: NCT00271349)

Quality assurance of endoscopic sphincterotomy: A prospective single-center survey

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Background: To the best of our knowledge there there is a lack of studies regarding quality assurance of endoscopic sphincterotomy (EST) in Switzerland. The aim was to assess quality and outcome of EST for benchmarking and to identify potential risk factors for post interventional complications.
Methods: Over 2 years 471 ESTs were performed in a single tertiary referral center. Patient– and procedure-related variables were prospectively recorded with support of a multicenter international sphincterotomy registry. Multivariate analysis was performed.
Results: The overall post interventional complication rate was 9.3% (Pancreatitis 5.5%, bleeding 2.1%, perforation 1.3%, cholangitis 0.4%). In multivariate analysis following variables remained highly significant and predictive for complications: 'Papilla only in lateral view' (p=0.001); antiplatelet therapy (p=0.024) and opacification up to the pancreatic tail (p=0.001). The rate of post interventional pancreatitis did not differ significantly with/without prophylactic pancreatic stent (p=0.56).
Conclusions: The outcome of EST in our clinic matches with large international trials. Prevention of post-ERCP pancreatitis by stents is controversial, and has no influence on outcome.

Efficacy and Safety of Certolizumab Pegol in an Unselected Crohn's Disease Population: 26 Week Data of the FACTS II Survey.

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Background: Certolizumab pegol (Cimzia®, CZP) was approved for the treatment of Crohn's disease (CD) patients in 2007 in Switzerland as first country worldwide. This prospective phase IV study aimed to evaluate the efficacy and safety of CZP over 26 weeks in a multicenter cohort of practice-based patients. **Methods:** Evaluation questionnaires at baseline, week 6 and 26 were completed by gastroenterologists in hospitals and private practices. **Results:** Sixty patients (38F/22M) were included, 53% had complicated disease (stricturing or penetrating), 45% had undergone prior CD related surgery. All patients had prior exposure to systemic steroids, 96% to immunomodulators, 73% to infliximab, and 43% to adalimumab. A significant decrease of Harvey Bradshaw Index (HBI) was observed under CZP therapy (12.2±4.9 at week 0 vs 6.3±4.7 at week 6 and 6.7±5.3 at week 26, both $P<0.001$). Response and remission rates were 70% and 40% (week 6) and 67% and 36% respectively (week 26). The complete perianal fistula closure rate was 36% at week 6 and 55% at week 26. The frequency of adverse drug reactions attributed to CZP was 5%. CZP was continued in 88% of patients beyond week 6 and in 67% beyond week 26. **Conclusions:** In a population of CD patients with predominantly complicated disease behaviour, CZP proved to be effective in induction and maintenance of response and remission. This series provides the first evidence of CZP's effectiveness in perianal fistulizing CD in clinical practice.

Role of Protease-activated receptor in vaccine-induced protection against Helicobacter infection

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Background & Aims: Despite the proven ability of immunization to reduce *Helicobacter* infection in mouse models, the precise mechanism of protection has remained elusive. Protease-activated receptor (PAR2) has been implicated in inflammatory responses as well as in modulating of various gastric functions. This study explores the role of PAR2 in vaccine-induced protection against *Helicobacter* infection ***Methods:*** Immune responses and vaccine-induced protection to *Helicobacter* were assessed in PAR2 deficient mice ($PAR2^{-/-}$) and wild type (WT) mice that were previously immunized with *H. pylori* urease. Infection persistence, cellular responses and gastric pathology were assessed by the rapid urease test (RUT), qPCR, flow cytometry and histology. ***Results:*** Vaccinated $PAR2^{-/-}$ mice were unable to reduce *Helicobacter* burden following infection. This observation correlated with a reduction in inflammation-induced stomach tissue damage and lower recruitment of $CD4^{+}IL\text{-}17^{+}$ T cells into the gastric mucosa of vaccinated $PAR2^{-/-}$ mice post bacterial challenge. Interestingly, splenic denditic cells (DC) from vaccinated $PAR2^{-/-}$ mice at day 14 post *Helicobacter* infection exhibited a weaker activated phenotype in comparison to their WT counterparts. Finally, adoptive transfer of WT DCs into vaccinated $PAR2^{-/-}$ mice prior to *Helicobacter* challenge was able to enhance vaccine-induced protection. ***Conclusion:*** Signaling pathway initiated following PAR2 activation on DCs appear to be critical in the generation of vaccine-induced protection against *Helicobacter* infection.

The Fc Fragment of Infliximab Modulates Its Inhibitory Activity in Fibroblasts and Monocytes via Interaction with Fc Receptors

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Background: One of the most important cytokines in the pathogenesis of IBD is tumor necrosis factor (TNF). The aim of this project was to evaluate the efficacy of anti-TNF drugs in blocking TNF- mediated responses in different cell types of the intestinal wall.
Methods: As a model system we used $Caco2_{BBE}$, CCD-18Co, and THP-1 cell lines. Signal transduction and mRNA production were investigated by Western Blot and RT-PCR, respectively. Interaction of anti-TNF drugs with cells was studied by fluorescent microscopy.
Results: TNF activated p38 MAPK, NF-κB and increased mRNA expression levels of IL-8, TNF and ICAM-1 in all cell lines tested. All anti-TNF drugs were efficient in intestinal epithelial cells. Infliximab had limited inhibitory capacity in fibroblasts and monocytes. Fluorescently labeled infliximab, but not adalimumab, accumulated at the surface of fibroblasts. Blocking Fc fragments and isolation of Fab fragments of infliximab partially restored its inhibitory efficacy.
Conclusions: Anti-TNF drugs prevent TNF-mediated responses in intestinal epithelial cells. Infliximab has limited inhibitory capacity in fibroblasts and monocytes, most likely due to the interaction with Fc receptor(s). This mechanism may modulate the bioavailability and effectiveness of anti-TNF drugs when administered in IBD patients.

Alcohol withdrawal promotes regression of pancreatic fibrosis via induction of pancreatic stellate cell (PSC) apoptosis. Alain Vonlaufen[1,2], Phoebe A Phillips[2], Zhihong Xu[2], Xuguo Zhang[2], Lu Yang[2], Romano C Pirola[2], Jeremy S Wilson[2], Minoti V Apte[2]. [1]Service de Gastroentérologie, University Hospital, Geneva, Switzerland and [2]Pancreatic Research Group, The University of New South Wales, Sydney, Australia.
Background: The administration of alcohol and repeated iv endotoxin leads to significant pancreatic fibrosis in rats. Whether fibrosis is reversible upon alcohol withdrawal remains unknown.
Aims: 1) To compare the effects of alcohol withdrawal and alcohol continuation on pancreatic fibrosis and PSC apoptosis. 2) To assess the effects of alcohol ± LPS on PSC apoptosis in vitro.
Methods: 1) SD rats fed isocaloric Lieber-DeCarli diets ± alcohol for 10 weeks were challenged with LPS (3 mg/kg; 1 IV injection / week x 3 weeks). Alcohol-fed rats were switched to a non-alcohol (control) diet or continued on alcohol for 7 days. Pancreatic sections and homogenates were assessed for i) fibrosis / collagen deposition; ii) PSC apoptosis and iii) presence of activated PSCs. 2) Cultured rat PSCs were exposed to ethanol 10mM (E10) ± LPS 1μg/ml (L1) for 48h and effects on induced apoptosis assessed.
Results: 1) Withdrawal of alcohol led to resolution of pancreatic fibrosis via increased PSC apoptosis / loss of activated PSCs. Both alcohol and LPS significantly inhibited PSC apoptosis in vitro: Annexin V staining - % of control (mean±SEM); E10 73.6±8.1; L1 45.4±8.9; E10+L1 36.2±5.5; $p<0.05$ vs Control and E10+L1 vs E10; n=6 separate PSC preparations. Similar results were obtained for caspase-3 and TUNEL.
Conclusions: 1) Withdrawal of alcohol reverses pancreatic fibrosis via increased PSC apoptosis in vivo. 2) Alcohol and LPS inhibit PSC apoptosis in vitro. Induction of PSC apoptosis is a key mechanism mediating the resolution of pathological fibrosis in the pancreas.

Equivalency of conventional and high-resolution manometry analysis parameters to quantifying esophageal motility

G01

Nicola Patuto, Daniel Pohl, Donald O Castell, Radu Tutuian

Background: The evaluation of esophageal motility using high-resolution manometry (HRM) involves a series of novel parameters. While HRM recordings provide more intuitive representations of esophageal peristalsis, there is no information on the advantages of the new analysis parameters over conventional manometry analysis.

Aim: Evaluate the correlation between conventional and high resolution esophageal manometry parameters.

Methods: Consecutive patients referred for esophageal testing underwent HRM included 10 x 5 ml liquid swallows 20-30 seconds apart. For each contraction the software (MMS Solar) calculated distal esophageal amplitude (DEA) as contraction average at 5 and 10 cm above the LES, lower esophageal sphincter residual pressure (LESRP) as the lowest pressure during a relaxation relative to the baseline, distal contractile integral (DCI) as the integral of pressures between the transition zone and proximal LES border and integrated residual pressure (IRP4sec) as the integral of the lowest residual pressure during 4 seconds. Esophageal body parameters (DEA vs. DCI) and lower esophageal sphincter parameters (LESRP and IRP4s) were correlated.

Results: Data from 60 patients (37 F, age 52.4; range 18-72) presenting with dysphagia (N=13), chest pain (N=20) and heartburn/regurgitation (N=27) were reviewed. The correlation was very good (r=0.85) between DEA and DCI and excellent (r=0.93) between LESRP and IRP4sec.

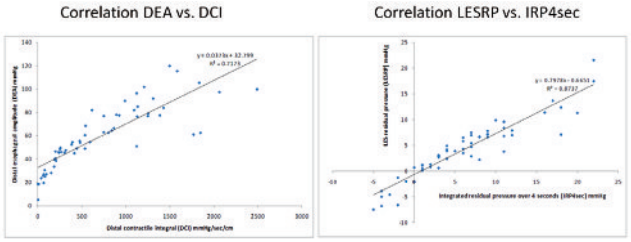

Figure: Correlation between distal esophageal amplitude (DEA) vs. distal contractile integral (DCI) and lower esophageal residual pressure (LESRP) vs. integrated residual pressure over 4 seconds (IRP4sec)

Conclusion: The excellent correlation between conventional and high-resolution manometry parameters indicates their equivalency to quantify esophageal motility.

Multiple rapid swallowing testing in patients with esophageal symptoms: a study using high-resolution manometry

G02

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Background: High resolution manometry offers more detailed analysis of esophageal peristalsis. Multiple rapid swallows (MRS) have been proposed as physiologic challenge for patients with mild or no esophageal motility abnormalities.

Aim(s): Evaluate esophageal peristalsis during standard and multiple rapid swallows in patients with dysphagia, chest pain and GERD symptoms. Assess the reproducibility of measurements during MRS.

Methods: Consecutive patients referred for esophageal testing were asked to rate the intensity and frequency of heartburn, regurgitation, chest pain and dysphagia on a 100mm VAS scale. Primary symptom was defined by highest intensity x severity score. High-resolution manometry included 10 x 5 ml liquid swallows 20-30 seconds apart and 2 sets of 4 rapid swallows 2-3 seconds apart. Standard distal contractile integral (DCI) was calculated by averaging DCI values of individual 10 single swallows. For each MRS sequence the DCI of the final primary contraction at the end of the swallow series was measured.

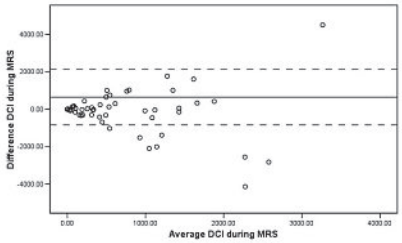
Results: The interim analysis found lower DCI values during standard and multiple rapid swallows (Table) in patients with dysphagia (N=13) compared to those presenting with chest pain (N=20) and/or hearburn/regurgitation (N=27). The reproducibility of DCI during MRS was poor (Cronbach's alpha 0.393) with a trend towards lower DCI values during the second set of MRS (Figure).

Table: Distal contractile integral (mmHg/s/cm) of standard swallows and following multiple rapid swallows; Data are expressed as mean ± SEM

Distal contractile integral (DCI)	Dysphagia (N=13)	Chest pain (N=20)	HB/Regurg (N=27)	p-value
10 swallows	491 ± 122	801 ± 161	736 ± 108	0.33
1st MRS sequence	478 ± 225	915 ± 280	624 ± 154	0.42
2nd MRS sequence	286 ± 120	501 ± 161	809 ± 220	0.22

Conclusion: Evaluating multiple rapid swallows by high-resolution manometry might uncover abnormalities overlook by standard testing. Still, the reproducibility of measurements during MRS warrants caution in interpreting these findings.

Figure: Bland-Altman plot on the reproducibility of distal contractile integral (DCI) measurement during multiple rapid swallows (MRS)



G03

Extraintestinal manifestations in inflammatory bowel disease: frequency and associated risk factors in the nationwide Swiss IBD cohort study (SIBDCS)

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Background: Data on the frequency of extraintestinal manifestations (EIM) in Crohn's disease (CD) and ulcerative colitis (UC) are scarce. Goal: to evaluate prevalences, forms of EIM and risk factors in a large nationwide IBD cohort.

Methods: Data from validated physician enrolment questionnaires of the adult Swiss IBD cohort were analyzed. Logistic regression models were used to identify EIM risk factors. **Results:** 950 patients were included, 580 (61%) with CD (mean age 43yrs) and 370 (39%) with UC (mean age 49yrs), of these, 249 (43%) of CD and 113 (31%) of UC patients had one to 5 EIM. The following EIM were found: arthritis (CD 33%, UC 21%), aphthous stomatitis (CD 10%, UC 4%), uveitis (CD 6%, UC 4%), erythema nodosum (CD 6%, UC 3%), ankylosing spondylitis (CD 6%, UC 2%), psoriasis (CD 2%, UC 1%), pyoderma gangrenosum (CD and UC each 2%), primary sclerosing cholangitis (CD 1%, UC 4%). Logistic regression in CD identified the following items as risk factors for ongoing EIM: active disease (OR 1.95, 95% CI 1.17-3.23, P=0.01), positive IBD family history (OR 1.77, 95% CI 1.07-2.92, P=0.025). No risk factors were identified in UC patients. **Conclusions:** EIM are a frequent problem in CD and UC patients. Active disease and positive IBD family history are associated with ongoing EIM in CD patients. Identification of EIM prevalence and associated risk factors may result in increased awareness for this problem and thereby facilitate their diagnosis and management.

G04

Development of an Activity Index for adult Eosinophilic Esophagitis Patients (ad-EEsAI): International Experts propose Dysphagia, whitish Exudates on endoscopy, and intraepithelial Eosinophil Counts as Items with Closest Association to EoE Activity

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Background and Aims: The international EEsAI study group aims to develop, validate and evaluate the first adult EoE activity index (ad-EEsAI). We report on results of phase 1, which aims to generate candidate items. **Methods:** This study involves 3 phases: (1) item generation, (2) index derivation and testing on a first patient cohort, and (3) validation in a second cohort. In phase 1, item generation, weighting and reduction are achieved through a Delphi process with an international EoE expert group. The experts proposed and ranked candidate items on a 7-point Likert scale (0 = no, 6 = perfect relationship with EoE activity). **Results:** 23 international EoE experts proposed and ranked 37 items (18 clinical, 6 endoscopic, 8 histologic, 5 laboratory items). Rank order for clinical items: dysphagia related to food consistencies (median 6, range 2-6), severity of dysphagia (5, 0-6), duration of dysphagia episodes (5, 0-6), frequency of dysphagia episodes (4, 0-6), swallowing-associated pain (3, 1-5), response to dietary restrictions (3, 0-6); endoscopic items: whitish exudates (6, 3-6), furrowing (4, 2-6), corrugated rings (4, 2-6), linear shearing (4, 2-6), strictures (4, 1-6); histologic items: intraepithelial eosinophil count (5, 4-6), lamina propria fibrosis (3, 2-6), basal layer enlargement (3, 1-5); laboratory items: % blood eosinophils (2, 0-5), total IgE (1, 0-3), Interleukin-5 (0, 0-3). **Conclusions:** These items will now be reduced in further Delphi rounds, tested on a cohort of 100 EoE patients and validated in a second independent cohort resulting in a robust, broadly accepted disease activity index for use in clinical trials and daily care.

G05

Prospective Validation of the Glasgow-Blatchford Bleeding Score to identify Patients with Upper GI Bleedings who need Clinical Intervention. Marc Girardin, Saskia Ditisheim, Alain Vonlaufen, David Bertolini, Isabelle Morard, Thai Nguyen, Emilano Giostra, Antoine Hadengue, Laurent Spahr, Jean-Louis Frossard, Jean-Marc Dumonceau. Gastroenterology and Hepatology Service, Geneva University Hospital.

Background: Upper gastrointestinal (UGI) bleeding is a frequent cause of hospital admission worldwide. The Glasgow-Blatchford bleeding score (GBS) can easily be calculated without endoscopy and has been validated to identify patients who will need clinical intervention, allowing outpatient management and cost reduction for those at low risk (GBS=0). Aim: To prospectively validate the GBS for identifying patients admitted for UGI bleeding in Geneva, who will need clinical intervention. Methods: Consecutive consenting patients with UGI bleeding were included (10/09-03/10). The GBS was calculated, UGI endoscopy was performed and follow-up at 7 and 30 days to evaluate the need for clinical intervention was done in all patients. A clinical intervention was defined as performance of endoscopic haemostasis, blood transfusion or surgery. Results: Eighty-one patients were recruited: 68 included, 13 had missing consent or data. The GBS varied from 0 to 17, with 9 (13%) patients having a GBS = 0. For identifying patients who would need clinical intervention, the GBS had a sensitivity of 100% (40/40), a specificity of 32.1% (9/28), a positive predictive value of 67.8% (40/59), a negative predictive value of 100% (9/9) and an accuracy of 72% (49/68). In the GBS = 0 group, more normal endoscopies were found (44% vs 8%, P<0.02) and no intervention was needed (0% vs 74%, P<0.0001). The length of hospital stay was significantly longer for patient with GBS > 0 (8.3 vs 0.5 d., P<0.0001). Conclusions: The GBS allowed identifying patients admitted with UGI bleeding who needed intervention with a high sensitivity but low specificity (32%). Two thirds of patients who did not require a clinical intervention could not be identified based on the GBS.

G06

20 Years of Eosinophilic Esophagitis in Olten County: Population-based, Prospective Documentation of an Increasing Incidence

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Background and Aims: Eosinophilic Esophagitis (EoE) is reported with increasing frequency over the last two decades. However, it is still unknown whether this reflects a true increase in incidence or just an increased awareness by gastroenterologists. Therefore, we evaluated the incidence and cumulative prevalence of EoE in Olten county over the last 20 years. **Methods:** Olten county is an area of approximately 91,000 inhabitants without pronounced demographic changes in the last two decades. EoE evaluation is based upon two gastroenterology centers and one pathology center. No public programs for increased EoE awareness were implemented in this region. All EoE patients diagnosed from 1989 to 2009 were entered prospectively into the Olten county database.
Results: Fourty-six patients (76% males, mean age 41±16 yrs) were diagnosed with EoE from 1989 to 2009. Ninety-four percent presented with dysphagia. In 70% of the patients concomitant allergies were found. The number of upper endoscopies per year was stable during the entire observation period. An average annual incidence rate of 2/100,000 was found (range 0-8) with a marked increase in the period from 2001 to 2009. A current cumulative EoE prevalence of 43/100,000 inhabitants was calculated. The mean diagnostic delay (time from first symptoms to diagnosis) was 4.3 years from 1989 to 1998 and 4.8 years from 1999 to 2009. **Conclusions:** Over the last 20 years, a significant increase in EoE incidence was found in a stable indicator region of Switzerland. The constant rate of upper endoscopies, the constant diagnostic delay, as well as the lack of EoE awareness programs in Olten county indicate a true increase in EoE incidence.

G07

The Visual Dysphagia Questionnaire: Piloting a New Tool for Assessing Food Consistency-Dependent Dysphagia in Eosinophilic Esophagitis

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Background and Aims: The international EEsAI study group is currently developing the first activity index specific for Eosinophilic Esophagitis (EoE). None of the existing dysphagia questionnaires takes into account the consistency of the ingested food that considerably impacts the symptom presentation. Goal: To develop an EoE-specific questionnaire assessing dysphagia associated with different food consistencies.
Methods: Based on patient chart reviews, an expert panel (EEsAI study group) identified internationally standardized food prototypes typically associated with EoE-related dysphagia. Food consistencies were correlated with EoE-related dysphagia, also considering potential food avoidance. This Visual Dysphagia Questionnaire (VDQ) was then tested, as a pilot, in 10 EoE patients.
Results: The following 9 food consistency prototypes were identified: water, soft foods (pudding, jelly), grits, toast bread, French fries, dry rice, ground meat, raw fibrous foods (eg. apple, carrot), solid meat. Dysphagia was ranked on a 5-point Likert scale (0=no difficulties, 5=very severe difficulties, food will not pass). Severity of dysphagia in the 10 EoE patients was related to the eosinophil load and presence of esophageal strictures.
Conclusions: The VDQ will be the first EoE-specific tool for assessing dysphagia related to internationally defined food consistencies. It performed well in a pilot study and will now be further evaluated in a cohort study including 100 adult and 100 pediatric EoE patients.

G08

Which test should be used to investigate patients after treatment for achalasia?

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Background: Symptomatic relapse after treatment of achalasia occurs in 15-30% of patients within the first year. Symptoms do not correlate with esophageal clearance: there are patients without symptoms but incomplete myotomy or dilation. These patients present often too late for another treatment

Aim: Our aim was to evaluate the predictive value of impedance manometry and timed barium swallow in symptomatic and asymptomatic patients with achalasia after initial successful treatment

Methods: Patients, who underwent treatment (pneumatic dilatation or Heller myotomy) for achalasia earlier, were selected from our database. They were followed up at different time intervals (1 month – 11 years 7 months later) using a structured questionnaire, timed-barium swallow and impedance-manometry. Symptoms were quantified according to the Eckardt score (severity of dysphagia, chest-pain, regurgitation and weight loss), timed barium swallow quantified the height of the barium column at 0.5 - 1 - 3 and 5 minutes after oral contrast and impedance manometry assessed esophageal clearance (total and segmental ant 20, 15, 10 and 5 cm above the LES) during standardized water and viscous swallows and free drinking of 200ml of fluids.

Results: Between Oct 2008 and Jul 2009 23 patients (7 women, age 50.2y; range 26 - 71) underwent investigations. Nine (39%) patients were symptomatic (Eckardt score > 2point). Segmental clearance worsened from the proximal to the distal esophagus and parallel to increased consistency (viscous) and volume (free drinking 200ml). The percentage of patients with measurable barium column decreased from 30 seconds to 5 minutes. There were no differences between symptomatic and asymptomatic patients in the % swallows with complete segmental and total bolus clearance and % of patients with barium retention at 0.5 - 1 - 3 and 5 minutes (table). Neither of the standardized tests as liquid/viscous swallow or barium retention correlated with symptom severity assessed by the Eckardt Score

Conclusion: Currently available methods quantifying esophageal clearance fail short in identifying abnormalities causing symptomatic relapse after treatment for achalasia. Objective parameters to support the clinical assessment in deciding further treatment for symptomatic relapse of achalasia remain to be identified.

Table: Bolus clearance parameters (impedance and timed barium swallow) in symptomatic and asymptomatic patients

Parameter		Asymptomatic (N=14)	Symptomatic (N=9)
% swallows with complete	20cm	96.4 ± 1.6	95.5 ± 3.3
segmental clearance	15cm	81.4 ± 5.9	86.6 ± 5.5
during liquid swallows	10cm	80.7 ± 4.9	81.1 ± 7.1
	5cm	72.8 ± 6.9	64.4 ± 11.9
% swallows with complete	20cm	91.4 ± 2.7	90.0 ± 4.0
segmental clearance	15cm	65.7 ± 7.3	68.8 ± 8.2
during viscous swallows	10cm	59.2 ± 9.2	57.7 ± 11.9
	5cm	52.1 ± 9.0	58.8 ± 11.6
% swallows with complete	20cm	85.7 ± 9.7	88.8 ± 11.1
segmental clearance	15cm	71.4 ± 12.5	77.7 ± 14.6
during free drinking	10cm	50.0 ± 13.8	55.5 ± 17.5
(200 ml)	5cm	42.8 ± 13.7	44.4 ± 17.5
% Swallows with	water	63.5 ± 7.2	57.7 ± 10.6
complete bolus transit	viscous	39.2 ± 8.3	46.6 ± 10.9
% Patients with barium column at	30 seconds	50.0%	33.3%
	1 minute	50.0%	33.3%
	3 minutes	28.6%	22.2%
	5 minutes	14.3%	22.2%

Comparative Socio-economic Evaluation of IBD Patients with and without Infliximab Maintenance Therapy

G09

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Background: The anti-TNFα agent Infliximab (IFX) is used for the treatment of moderate to severe inflammatory bowel disease (IBD) with insufficient response to conventional immunomodulator therapy. IFX maintenance therapy is expensive and it is unknown if indirect costs (eg. by loss of work productivity) can be reduced by this therapy. Goal: to evaluate the direct and indirect costs of an IBD patient cohort under maintenance IFX compared to a cohort under "conventional" immunomodulator therapy. **Methods:** Direct and indirect costs of an IBD cohort under IFX and a reference cohort (similar disease activity and location) under conventional immunomodulator therapy (Azathioprine, or 6-MP, or MTX) were retrospectively evaluated over 12 months (January to December 2008). **Results:** 54 IFX-patients (24f/30m, 37 CD, 10 UC, 7 IC) and 71 non-IFX-patients (38f/33m, 56 CD, 12 UC, 3 IC) were included. IFX patients were younger than non-IFX patients (36 vs. 47 years, P = 0.0003). The mean duration of inpatient stay in hospital (23 in IFX vs. 21 days for non-IFX, P = 0.909) and the hospitalization costs (7,692 in IFX vs. 4,179 SFr for non-IFX, P = 0.4540) did not differ. IFX-patients had significantly more frequently specialist outpatient consultations (8 vs. 4, P < 0.001) and outpatient-related costs (3,633 vs. 2,186 SFr, P <0.001). Total costs for all diagnostic procedures (blood work, endoscopies, radiology) were higher in the IFX-cohort (2,265 vs. 1,164 SFr, P < 0.001). Sixty-five percent of IFX-patients had a 100% job employment compared to 80% in the non-IFX cohort (P = 0.001). **Conclusions:** The direct and indirect costs of maintenance IFX-treated IBD patients are higher compared to IBD patients under conventional immunomodulators. Care should be taken not only to judge the costs as the IFX treated population may represent a cohort with more aggressive disease phenotype, furthermore, quality of life aspects were not assessed.

Loss Of Heat Shock Protein gp96 Does Not Impair Toll-Like Receptor Signalling *In Vitro*

G10

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Background: The heat shock protein gp96 is an endoplasmic reticulum chaperone for multiple protein substrates. We showed that a lack of gp96 in intestinal macrophages of Crohn's Disease (CD) patients is correlated with loss of tolerance against the host gut flora, leading to chronic inflammation. A recent manuscript suggested gp96 to be the major chaperone for TLRs. Therefore, we studied the impact of gp96-knockdown on TLR-function.

Methods: For stable gp96-knockdown a lentiviral system was used. Stimulations were performed with lipopolysaccharide (LPS), a ligand of TLR 4. TLR-folding and -functionality was investigated by Western blotting and flow cytometric analysis.

Results: Flow cytometric analysis of TLR 2 and 4 showed similar patterns on the cell surface of gp96-knockdown cells as well as the mock transduced MM6 cells. Western blot analysis of phospho-IκB/IκB and phospho-NFκB/NFκB ratios did also not reveal a significant difference in TLR mediated NFκB-signalling in these cells.

Conclusions: In contrast to recent reports loss of gp96 does not have pivotal effects on functionality of TLRs in human MM6 cells. These findings indicate that the loss of tolerance against commensal gut flora is caused by different mechanisms yet to be investigated.

Lack of transketolase-like (TKTL) 1 aggravates murine experimental colitis

G11

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Background: TKTL1 is involved in the pentose phosphate pathway which provides the cells with the reducing molecule NADPH. NADPH detoxifies reactive oxygen species (ROS) which contribute to tissue damage during mucosal inflammation. We investigated the role of TKTL1 during experimental dextran sodium sulfate (DSS) induced colitis and its potential function in ROS detoxification.

Methods: Acute DSS colitis was induced in knock out mice ($TKTL1^{-/-}$) mice and wild type mice (WT). mRNA levels of interferon (IFN)-γ, inducible nitric oxide synthase (iNOS), interleukin (IL)-6 and tumor-necrosis-factor (TNF) were determined by quantitative real-time RT-PCR. iNOS protein expression was confirmed by Western blotting. Myeloperoxidase (MPO) was determined in colon tissue for evaluation of anti-ROS neutralizing mechanisms.

Results: DSS colitis was significantly more severe in $TKTL1^{-/-}$ which had a significantly shorter colon and more severe histological score as compared with WT mice. Colitis in $TKTL1^{-/-}$ was associated with increased mRNA levels of IFN-γ, iNOS, IL-6 and TNF as compared with WT DSS. In addition, iNOS protein expression was significantly upregulated in $TKTL1^{-/-}$ mice in comparison with WT mice, both treated with DSS. MPO activity was higher in $TKTL1^{-/-}$ mice as compared with WT during DSS colitis.

Conclusion: DSS induced colitis was more severe in TKTL1 deficient mice as compared to WT mice. We conclude that the loss of function of TKTL1 leads to a higher susceptibility to DSS. Detoxification mechanisms against ROS are enhanced.

Swiss Case Series of Autoimmune Pancreatitis

G12

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Background: Autoimmune pancreatitis (AIP) is a chronic inflammatory disease of the pancreas induced by auto-immunological mechanisms. In most case series an elevation of serum IgG, especially IgG_4 is reported in up to 92%. As in most other autoimmune diseases AIP responds to steroid therapy. Histologically two different entities can be differed, one with a mainly lymphocytic infiltration, particularly occurring in Asian and older individuals and one with mainly granulocytic infiltration, occurring more often in Western and younger individuals. Clinically, patients mainly complain of jaundice, abdominal pain or diabetic symptoms. Most patients are referred to additional diagnostics because of tumor in the pancreas head, less often because of calcification or pseudocyst.
As there has been less information on AIP from European countries the aim of this study was to analyse the demographic data, clinical presentation, histological findings, imaging and laboratory results and response to therapy in Swiss patients with autoimmune Pancreatitis.

Methods: We prospectively collected data of 16 patients with AIP between December 2007 and April 2010 concerning demographic data, clinical presentation, histological findings, imaging and laboratory results and response to therapy.

Results: 75% of patients were men, median age was 45,4years. 88% reported of abdominal pain, 50% were cholestatic, 43,8% had weight loss. Radiologic findings when apparent were a tumor of the head of the pancreas (50%), calcifications (25%) and pseudocyst (25%). IgG_4 was elevated in 81,3%, total IgG in 31,3%, CA 19-9 in 18,8%. 43,8% had a diabetes. 75% responded to steroid therapy, 25%. 25% showed a relapse after initial respond though.

Conclusion: As well as in other countries AIP is a rare disease in Switzerland. The results of our study correlate with results of current literature. In most patients pancreatic cancer, chronic pancreatitis or cystic tumors are suspected. To avoid unnecessary surgery, in all patients IgG_4 should be measured and, if negative, tentative prednisone treatment should be considered.

G13

Should Repeatedly Ingested Sharp Objects In Patients With Borderline Personality Disorder Always Be Removed Endoscopically? An International Survey

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Background: Ingestion of foreign bodies is a frequent clinical problem, but there is no consensus on repeated endoscopies in patients with borderline personality disorders who swallow sharp objects repetitively.

Methods: A survey on endoscopy for sharp foreign body removal in patients with borderline personality disorders was sent to 222 gastroenterologists, surgeons and psychiatrists in Switzerland, Germany and Austria. A case vignette was presented and 9 questions were asked, including personal experience with and judgement on the appropriateness of repeated endoscopies in these patients.

Results: The initial response rate was 58/222 (26%), with 55 replies of sufficient quality. Among responders, 64% had experience with repeated foreign body removal in borderline patients. Almost all responders (95%) agreed that intentionally swallowed sharp objects in a psychiatric patient should be removed promptly. 85% would remove ingested sharp objects repeatedly, with certain variations among specialities. In our case vignette, doctors from another hospital who were initially involved in the presented patients care refused to perform repeated endoscopies. Twenty percent of clinicians asked in our survey said they would accept this decision and not perform an endoscopy (13% of gastroenterologists, 18% of surgeons and 29% of psychiatrists). Twenty percent of clinicians knew of at least one case where endoscopy was refused because sharp foreign bodies were ingested repeatedly. Approval of this approach differed among specialist groups (20% of gastroenterologists, 50% of surgeons, 75% of psychiatrists).

Conclusions: In patients with borderline personality disorders, the main difficulty is not the swallowed foreign body, but the psychiatric disease leading to repeated ingestion of objects. The current results highlight the different opinions on repeated endoscopies. The decision not to remove a swallowed object carries the risk of perforation. Whether this is ethical is debatable. An interdisciplinary and interinstitutional consensus on the management of repeated foreign body ingestion in patients with borderline personality disorders is clearly needed.

G14

The Patient's Perception of Eosinophilic Esophagitis Related Symptoms: a Qualitative Content Analysis

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Background and Aims: The international EEsAI study group is currently developing an activity index for Eosinophilic Esophagitis (EoE). A potential discrepancy between patient and physician reported EoE symptoms has not been assessed yet. Therefore, we aimed to evaluate patient reported items describing their EoE activity and to compare these with the physician's perception.

Methods: A questionnaire was sent to 100 EoE patients in Switzerland. EoE-related symptoms dependent and independent of food intake were reported by patients. Results were analyzed using a qualitative content analysis and compared with symptoms reported by international EoE experts in Delphi rounds.

Results: The questionnaire response rate was 64/100. The following items were developed by combining categories based on patients answers: food-consistency related dysphagia, frequency and severity of dysphagia, food impaction, strategies to avoid food impaction, food allergy, drinking-related retrosternal pain. The following food categories associated with dysphagia were identified: meat, rice, dry bread, French fries, raw, fibrous foods, others. Sports and psychological stress were identified as triggers for non-food intake related EoE symptoms. A good correlation was found between patient and physician's reported EoE related symptoms.

Conclusions: There is a good correlation between patient reported symptoms and the physician's perception of clinical items as reported by international EoE experts. These patient reported outcomes will now be incorporated into the EEsAI questionnaire that measures EoE activity.

G15

Effect of music on patients undergoing endoscopy with propofol-sedation

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Abstract

Background: To assess the effects of music in patients under staff-administered propofol-related analgosedation while undergoing gastroenterologic endoscopic procedures in terms of comfort, dosage and efficiency. Methods: 70 consecutive outpatients were randomized for having music or no music administered by headphones while receiving gastroscopy and/or colonoscopy in staff-administered propofol-related deep analgosedation. The amount of analgetics and propofol and the procedure time were recorded while patient comfort and satisfaction were assessed by interview with standardized items. Results: 70 patients were examined in two groups (gastroscopy/colonoscopy). The amount of required propofol was significantly lower by 39% in gastroscopy with music ($p<0.001$) and 39.5% in colonoscopy with music ($p<0.001$). Procedure comfort and overall satisfaction were significantly higher with music than without music ($p=0.042$ and $p=0.011$). Mean duration of the procedure was shortened with music in gastroscopy and colonoscopy, but the difference did not reach significance. Conclusion: Music decreases the required amount of medication in patients receiving staff-administered propofol-related analgosedation for gastroscopy and colonoscopy.

Gastroscopy group	Gastro total (n=30)	Gastro with music (n=15)	Gastro w/o music (n=15)	p-value
Age in yrs	47.1	47.73	46.47	p = 0.853
Gender (male/female)	10/20	5/10	5/10	
Heigth in cm	168.4	166.8	170	p = 0.184
Weight in kg	68.435	64.6	72.27	p = 0.054
Previous Examination	14 yes 16 no	7 yes 8 no	7 yes 8 no	not done
No of difficult examinations	0	0	0	not done
No of pts with biopsies	29 yes 1 no	15 yes 0 no	14 yes 1 no	not done
Colonoscopy group	**Colo total (n=40)**	**Colo w/o music (n=20)**	**Colo with music (n=20)**	**p-value**
Age in yrs	56.575	59.4	53.75	p = 0.187
Gender (male/female)	20/20	10/10	10/10	
Heigth in cm	171.765	171.1	172.43	p = 0.649
Weight in kg	74.45	73.65	75.25	p = 0.690

Previous Examination	13 yes 27 no	7 yes 13 no	6 yes 14 no	not done
No of difficult examinations	7	4	3	not done
No of pts with biopsies	35 yes 5 no	17 yes 3 no	18 yes 2 no	not done
No of pts with polypectomies	14 yes 26 no	5 yes 15 no	9 yes 11 no	p = 0.185

Table 1: Demographic data of study patients

Gastroscopy group	**Gastro total (n=30)**	**Gastro w/o music (n=15)**	**Gastro with music (n=15)**	**p-value**
Propofol mg	98.335	122	74.67	p < 0.001
Duration min.	9.17	10.67	7.67	p = 0.103
Colonoscopy group	**Colo total (n=40)**	**Colo w/o music (n=20)**	**Colo with music (n=20)**	**p-value**
Propofol in mg	115.25	143.5	87	p < 0.001
Duration min.	20.5	22.45	18.55	p = 0.152

Table 2: Overall results for main criteria

	(n=30)	**(n=15)**	**(n=15)**	
Quality of service	9.865	9.83	9.9	p = 0.695
Information	9.415	9.63	9.2	p = 0.277
Procedure comfort	8.55	8.77	8.33	p = 0.508
Absence of pain	9.75	9.9	9.6	p = 0.398
Attitude for further procedures of the same type	9.265	9.1	9.43	p = 0.552
Overall satisfaction	9.55	9.63	9.47	p = 0.516
Colonoscopy group	**Colo total (n=40)**	**Colo w/o music (n=20)**	**Colo with music (n=20)**	**p-value**
Quality of service	9.675	9.65	9.7	p = 0.832
Information	9.275	9.15	9.4	p = 0.567
Procedure comfort	7.63	6.88	8.38	p = 0.042
Absence of pain	8.59	8.3	8.88	p = 0.402
Attitude for further procedures of the same type	8.755	8.23	9.28	p = 0.108
Overall satisfaction	8.625	7.9	9.35	p = 0.011

Table 3: Quality and comfort questionnaire mean results, answers given by rating from 1 (worst) to 10 (best)

G16

Protein tyrosine phosphatase N2 regulates TNF-induced signalling and cytokine secretion in T_{84} intestinal epithelial cells

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Background: We have previously shown that the Crohn's disease (CD) candidate gene, protein tyrosine phosphatase N2 (PTPN2), regulates IFNγ-induced signalling and effects in intestinal epithelial cells (IEC). Here, we investigated whether PTPN2 is regulated by TNF and controls TNF-induced signalling and effects in IEC.
Methods: T_{84} IEC were used for all studies. Protein analysis was performed by Western blotting, mRNA analysis by RT-PCR. PTPN2 knock-down was induced by siRNA and cytokine levels were measured by ELISA.
Results: TNF treatment elevated PTPN2 mRNA as well as nuclear and cytoplasmic protein levels and caused cytoplasmic accumulation of PTPN2. Pharmacological NF-κB inhibition completely prevented the TNF -induced rise in PTPN2 protein. Knock-down of PTPN2 resulted in elevated TNF -induced ERK1/2 and p38 activity. Loss of PTPN2 potentiated TNF-induced secretion of IL-6 and IL-8. In TNF and IFNγ co-treated cells, loss of PTPN2 enhanced the expression of iNOS and apoptosis as assessed by the amount of cleaved caspases-3 and 7 as well as the number of fragmented nuclei in DAPI-stained cells.
Conclusions: We demonstrate that TNF induces PTPN2 expression in T_{84} IEC and loss of PTPN2 promotes TNF-induced expression of pro-inflammatory mediators. These data indicate that PTPN2 activity may play an important role in the establishment of chronic inflammatory conditions in the intestine, such as CD.

G17

Dying in Yoghurt – The number of living bacteria in probiotic yoghurt decreases under exposure to room temperature

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Background: There are rising numbers of probiotic foods that are commercially available and excessively advertised. They are supposed to beneficially modulate the commensal gut flora and various immune responses. Here, we study whether the number of probiotic bacteria in yoghurts is altered by an interruption of the cold chain.
Methods: Three commercially available probiotic yoghurts from three different companies were either kept on 4°C or put at room temperature (RT) for 6 h or 24 h before analysis. The yoghurts were diluted in PBS and incubated on MRS agar plates at 37 °C for 48 h. Then, colony forming units (CFU) were counted by microscopy.
Results: The first investigated yoghurt contained *Lactobacillae johnsonii* as a probiotic component. The agar plates containing the yoghurt dilutions that had been at RT for 6 h showed a significant decrease in CFU (n=4 for all analyses), which was further pronounced when kept at RT for 24 h. The number of CFU of the second yoghurt, containing *Lactobacillae GG*, was also decreased by 6 h and further diminished by 24 h at RT. The third yoghurt contained *Lactobacillae acidophilus*. In the yoghurt samples that had been at RT for 6 h, 53.8 % CFU remained and in the 24 h RT samples were just about one fourth CFU as compared to control samples.
Conclusions: We demonstrate that the survival of probiotic bacteria in commercially available products is critically dependent on the conditions the products are stored. This represents an important information for the consumers of such probiotic yoghurts.

Titanium dioxide microparticles activate the inflammasome in intestinal epithelial cells

G18

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Background: Microparticles are small, non-biological particles that are used as food additives. The most commonly ingested compound is titanium dioxide (TiO_2). The inflammasome is a multiprotein complex containing NALP3 and caspase-1, which activates pro-inflammatory cytokines IL-1β and IL-18. With regard to recent findings identifying asbestos and monosodium urate as inflammasome activators, we questioned whether TiO_2 might trigger similar effects.
Methods: TiO_2-microparticles were applied to THP-1 cells and to the intestinal epithelial cell (IEC) line Caco-2. Inflammasome assembly was confirmed by Co-IP with caspase-1 antibody and subsequent Western blot for NALP3. IL-1β and IL-18 secretion was determined by ELISA. Electron microscopy and element analysis (EDX) was used to confirm uptake of TiO_2.
Results: Incubation of cells with 5 and 20 µg/ml TiO_2 resulted in assembly of the NALP3-inflammasome, which correlated with increased secretion of IL-1β and IL-18, representing an inflammatory reaction. Electron microscopy with element analysis recognized intracellular particles to contain almost exclusively titanium.
Conclusion: TiO_2 microparticles are taken up by macrophages and IEC, activate the inflammasome and induce IL-1β and IL-18 secretion. In a situation of an impaired mucus barrier as it is the case in IBD patients those food additives could aggravate or perpetuate mucosal inflammation and represent a link between the increasing incidence of IBD and Western diet.

G19

Dietary sphingomyelin-triggered apoptosis in intestinal epithelial cells is mediated by cathepsin D- and Bid-activation

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Background: Sphingomyelin (SM), a lipoid component of the plasma membrane is prevalent in animal products. Recently we could show that dietary SM induces apoptosis of intestinal epithelial cells (IEC) and aggravates inflammation in DSS-colitis. Metabolism of SM in the bowel generates ceramide which acts as bioactive lipid messenger and increases cathepsin D activity. Cathepsin D conducts activation of pro-apoptotic protein Bid. We investigated whether increased SM provides a mechanism to induce the pathway of apoptosis.
Methods: Acute colitis was induced to female C57-BL/6J mice by 2 % dextran sulfate sodium (DSS) in drinking water. Mice received 4 mg SM a day resuspended in drinking water and applied by oral gavage. Mice were sacrificed after 7 days and IEC were isolated *ex vivo*.
Results: After dietary SM intracellular ceramide contents were impressively increased in IEC as shown by immunofluorescence. Activated Bid (tBid) was significantly increased in mice with acute DSS-colitis (4.00 ± 2.45) compared to mice without acute DSS-colitis (1.00 ± 0.69, $p < 0.05$). Execution of the apoptotic cascade via activated caspase-9 and -3 could be confirmed on protein level with immunohistochemistry and Western.
Conclusion: Dietary SM increases intracellular ceramide and initiates tBid mediated apoptosis in IEC during acute DSS-colitis. This shortens the physiological life cycle of IEC and impairs crucial functions of the intestinal mucosa: barrier, defence and nutrient absorption. Our findings provide evidence that ceramide-triggered activation of cathepsin D results in the induction of apoptosis signalling by cleavage of the pro-apoptotic protein Bid.

G20

Regulation of Expression of Heat-Shock Protein Gp96 in Intestinal Macrophages, Monocytes, *in vitro*-differentiated Macrophages and Dendritic Cells

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Background: The ER-residing heat shock protein gp96 is a chaperone with immunological relevance via its peptide-binding capacity. Lack of gp96 protein in intestinal macrophages (IMACs) from Crohn's Disease (CD) patients correlates with loss of tolerance against the host gut flora. Therefore we investigated the expression of this chaperone in the relevant cell types.
Methods: In vitro differentiated dendritic cells (ivDCs) or macrophages (ivMACs) and IMACs isolated from surgical specimens were exposed to cytokines, bacterial cell components and gp96. Expression levels of gp96 were assessed by real-time RT-PCR and Western blots.
Results: Induction of gp96-expression was higher in *in vitro*-differentiated DCs (3- to 7-fold) as compared to *in vitro*-differentiated MACs (1.5 to 2-fold), whereas MOs expressed only basal gp96 levels. The highest expression of gp96 was found in IMACs (to approx. 300-fold as compared with MOs). There was no correlation between expression levels of gp96 and age or gender. Stimulation experiments showed that LPS, MDP, TNF, IL-4, and gp96 induced gp96-expression (3- to 6-fold).
Conclusion: Gp96 expression is induced during the differentiation of monocytic cells to MACs, DCs and especially in the mucosal environment (IMACs). The finding that bacterial envelope components and TNF regulate its expression further supports its role in mucosal tolerance and inflammation.

G21

Long term follow-up after endoscopic ballon dilatation for Crohn's strictures

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Background: Fibrotic strictures are common complications in patients with Crohn's disease resulting in repeated surgery, which may ultimately result in chronic diarrhoea and short bowel syndrome. Endoscopic dilatation of Crohn's disease-related strictures is an alternative to surgical resection in selected patients. The aim of the study was to asses the long-term safety and efficacy of stricture ballon dilatation in a retrospective analysis.

Methods: A total of 48 patients with Crohn's disease were enrolled from the outpatient clinic of the Inselspital Bern. The dilatations were performed with CRE ballons, the final diameter was individually chosen between 8-16mm.

Results: Between 2001 and 2009, 73 dilatations were performed in 48 patients (mean age 43, range 19-90; 50% female) for clinically symptomatic strictures. The strictures (mean length 4cm, range 0.5-5cm, 75% inflamed) were localized in 44% of the patients at the ileocecal valve and in 46% of patients at the ileocecal anastomosis. Immediate success of a first dilatation was 87.5%. The median follow-up was 3.3 years. A second dilatation was required due to recurrent obstructive symptoms in 29% of the patients. Surgery was necessary in another 29% of patients. After a single dilatation 68% of patients came into clinical remission compared to 54% of patients who had two or more dilatations. After the first dilatation 43% had a step-up strategy in their medical treatment with introduction of immunomodulators or anti-TNF antibodies. 57% of the patients whose medical treatment had been changed remained in remission versus 40% of patients without change of medical therapy. The complication rate was low, only one patient with re-stenosis after surgery had a perforation after the second dilatation.

Conclusions: Endoscopic dilatation is generally safe and has a good outcome with the increase of quality of life of the patients. Adaptation of the medical treatment with the goal of mucosal healing is an important factor to maintain the treatment success.

Expression of the G protein-coupled receptor 68 (OGR1) is regulated by the inflammatory cytokine TNF-α G22

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Introduction: Inflammatory bowel disease (IBD) is associated with acidification of intestinal mucosal tissue. The increase in local proton concentration is linked to subsequent inflammatory cytokine release. The G protein-coupled receptor 68 (GPR68; also known as OGR1) functions as a sensor for extracellular protons/pH, thus stimulating inositol phosphate pathways. We studied whether cytokines affect OGR1 expression in the human monocyte cell line Mono Mac 6 (MM6).
Methods: RNA was isolated from cells treated with cytokines IFN-γ, IL-1β, IL-6, TNF-α, or TGF-β, or the differentiating agent PMA. Expression levels were quantified by real-time PCR.
Results: Treatment of MM6 cells (6 and 24 h) with TNF-α, but none of the other cytokines, led to significant upregulation of OGR1 mRNA. Dose-dependence of TNF-α (0-100 ng/ml) induction of OGR1 mRNA was confirmed at the time points 4 and 8 h. Maximal OGR1 induction was reached at a TNF-α concentration 50 ng/ml. Macrophagic differentiation of MM6 cells with PMA led to a highly significant increase in OGR1 expression. We are further studying whether the same signalling pathways are involved in TNF-α and PMA-mediated induction of OGR1 expression and the functional consequences of this regulation.
Conclusion: OGR1 mRNA expression is induced in cells of human macrophage lineage by TNF-α. TNF-α stimulation of OGR1 expression and of its pH-sensing activity may play a role in the molecular pathogenesis of IBD.

Posters Hepatology

H01

Oral glutamine challenge and capillary blood ammonia to detect hepatic encephalopathy : a study in 57 patients with cirrhosis

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Hepatic encephalopathy (HE) is a serious complication of cirrhosis that may be improved by medical therapy. Ammonia (NH3) is central to the pathogenesis of HE, but determination of NH3 in venous blood performs poorly for the diagnosis. Determination of NH3 in capillary (partially arterialized) blood after amino-acid challenge could improve the diagnostic performance of HE. Patients+Methods: 57 patients (age: 56yrs) with cirrhosis (MELD score: 13.5 [7-12]) and portal hypertension (esophageal varices: n=38; HVPG: 16 mmHg), and 13 controls (age: 54yrs) were included. Psychometric tests + capillary blood NH3 (Blood Ammonia Checker Arkray) were performed at T0, T30', T60' after 20 gr oral glutamine load. Diagnosis of minimal HE was based on psychometric tests. Patients were followed-up for 1 year (overt HE, liver-related events). Results: **1**. The test was well tolerated without precipitation of overt HE. **2**. Capillary blood NH3: higher levels in patients than controls (0', 30', 60': 75, 117, 169 vs 52, 59, 78 umol/l, respectively, $p<0.05$). **3**. Diagnosis of HE: baseline neuropsy tests showed 25 patients with criteria for HE. At 60', 38 patients met the criteria (chi2: $p<0.001$). **4**. Diagnostic performance of capillary blood NH3 for HE :

NH3 capillary	Area under curve (AUC)	SE	P value
baseline	0.541	0.08	0.6
60'	0.727	0.07	0.006

5. Patients' follow-up : 34.5% of patients developed either overt HE or a liver-related events. Linear logistic regression analysis identified previous episodes of overt HE (OR 5.761 [1.123-29.542]) and presence of esophageal varices (OR 7.73 [1.239-40.377]), but not NH3, as independent predictors of events.
Conclusion : Determination of capillary blood NH3 following an oral glutamine challenge is feasible, safe, and useful to unmask minimal HE, but a poor predictor of overt HE/liver-related event over time.

H02

Diagnostic value of faecal calprotectin in patients with liver cirrhosis

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Background. Faecal calprotectin (FC) reliably distinguishes organic disease and functional bowel disorder throughout the intestinal tract. In liver cirrhosis, FC has been reported to correlate with disease severity (1). However, its value to identify organic intestinal disease in patients with liver cirrhosis is unknown.
Methods. In 55 consecutive outpatients with liver cirrhosis (25 alcoholic, 16 viral, 8 NAFLD, 6 others; 43 Child A, 12 Child B) who were referred for upper endoscopy, FC levels were measured in stool samples collected within 24 hours before the investigation using an enzyme-linked immunosorbent assay (Bühlmann AG, Schönenbuch). The final diagnosis was adjudicated in a blinded fashion using all available medical records. Reflux esophagitis Los Angeles grade A and mucosal erythema without erosions were not considered relevant pathological lesions. The presence of a relevant finding in the upper GI tract was the primary endpoint.
Results. Patients with relevant findings (acid-related mucosal damage, including ulcers, n=25) had higher FC levels (median 125µg/g, IQR 83-192) than patients without (n=30, 43µg/g, IQR 14-110, $p=0.02$). The area under the receiver operating characteristics curve to identify a relevant finding was 0.69 (95% CI 0.55-0.80). At the optimal cut-off point (64μg/g), FC provided 80% sensitivity and 67% specificity with a positive and negative likelihood ratio of 2.4 and 0.33, respectively. The overall test accuracy was 73%.
Conclusion. In contrast to patients with normal liver function, the diagnostic value of faecal calprotectin to identify organic upper intestinal disease is limited in patients with liver cirrhosis.

1. Yagmur E, et al. [Elevated concentrations of fecal calprotectin in patients with liver cirrhosis]. Dtsch Med Wochenschr. 2006;131(36):1930-4.

H03

Incidence, management, and outcome of incidental gallbladder carcinoma: analysis of the database of the Swiss association of laparoscopic and thoracoscopic surgery (SALTS)

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Background: Little is known about the long-term survival of patients with incidental gallbladder carcinoma (IGBC). The role of radical resection for this disease is discussed controversially in the literature.
Methods: Eighty-nine patients with histologically confirmed carcinoma of the gallbladder were identified out of 30,960 patients undergoing laparoscopic cholecystectomy. Sixty-nine patients were included in our study. Long-term survival by different T-stage and comparison of patients with extended resection versus simple cholecystectomy were calculated using the log-rank test. The time-to-event data will be demonstrated by Kaplan–Meier curves.
Results: The overall incidence of IGBC in patients who underwent laparoscopic cholecystectomy was 0.28. The comparison of simple cholecystectomy versus extended re-resection of the gallbladder bed and regional lymph node resections showed a significant benefit in overall survival for the pT2 and pT3 group. The pT1b group showed no significant benefit in overall survival ($p = 0.34$).
Conclusion: IGBC has a low incidence (0.28%). We present a large study of patients with IGBC, comparing the overall survival by different histological findings. We observed a significant benefit for the group with pT2 and pT3. Therefore we recommend extended resection of the gallbladder bed and the regional lymph nodes for patient with incidental histologically confirmed pT2 and pT3 carcinoma of the gallbladder after performance of laparoscopic cholecystectomy. For patients with pT1b stage no recommendations can be given based on this study.

H04

Recurrent Hepatitis C After Liver Transplantation - Experience of the First 21 Patients Treated in Lausanne

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Background and aim: Recurrent hepatitis C is a major cause of morbidity and mortality after liver transplantation (LT), and optimal treatment algorithms have yet to be defined. Here, we present our experience of the first 21 patients with recurrent hepatitis C treated in Lausanne.

Patients and methods: Twenty-one patients with histology-proven recurrent hepatitis C after LT were treated since 2003. Treatment was initiated with pegylated interferon-α2a 135 µg per week and ribavirin 400 mg per day in the majority of patients, and subsequent doses were adapted individually based on on-treatment virological responses and clinical and/or biochemical side effects.

Results: On an intention-to-treat basis, sustained virological response (SVR) was achieved in 12/21 (57%) patients (5/11 [45%], 2/3 [67%], 4/5 [80%] and 1/2 [50%] of patients infected with genotypes 1, 2, 3 and 4, respectively). Two patients experienced relapse and 6 did not respond to treatment (NR). Treatment duration ranged from 24 to 90 weeks. It was stopped prematurely due to adverse events in 5/21 (24%) patients (with SVR achieved in 2 patients, NR in 2 patients, and death of one patient awaiting re-transplantation). Of note, SVR was achieved in a patient with combined liver and kidney transplantation. Importantly, SVR was achieved in some patients despite the lack of an early virological response or HCV RNA negativity at week 24. Darbepoetin α and filgrastim were used in 33% and 14%, respectively.

Conclusion: Individually adapted treatment of recurrent hepatitis C can achieve SVR in a substantial proportion of LT patients. Conventional stopping rules do not apply in this setting so that prolonged therapy may be useful in selected patients.

H05

Liver resection for hepatocellular carcinoma in patients with normal, non-normal non-cirrhotic and cirrhotic liver

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Background: The aim of this study was to assess factors predicting post-resection disease-free survival, specifically looking at the presence or absence of underlying liver disease.
Methods: From 1/1983 to 3/2010, 93 patients underwent a liver resection for HCC. Clinical, biological and pathological data were retrospectively assessed, and compared between patients with normal (n=5), non-normal non-cirrhotic (n=34) and cirrhotic (n=54) liver. Disease-free survival (DFS) was the only outcome variable considered.
Results: The three groups were similar regarding age, alcohol consumption, HBV and HCV infection, AFP, number of HCC nodules, micro- and macro-vascular invasions and preoperative HCC treatment. However, patients with cirrhosis demonstrated significantly higher ASA scores, smaller HCCs, but of more advanced grade ($p<0.05$ in all cases).
Patients with normal liver had higher DFS (63 months) compared to patients with non-normal non-cirrhotic (47 m) and with cirrhotic livers (30 m), with a trend towards significance ($p=0.136$, 0.076, log-rank). DFS was similar between patients with cirrhosis and with non-normal non-cirrhotic livers ($p=0.328$). Of all variables, alkaline phosphatase, GGT and AFP, HCV infection, presence of satellite nodule, and extrahepatic disease independently predicted DFS (multivariate Cox analysis).
Conclusions: According to this study, post-HCC resection DFS is both linked to tumor (AFP, satellite nodules, extra-hepatic disease) and patient factors (alkaline phosphatase, GGT, HCV infection). Patients at increased risk should undergo closer post-resection monitoring.

H06

Atypical and anatomical liver resections without Pringle's maneuver are feasible, safe and without major blood loss

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Objective
Pringle's maneuver is performed to reduce blood loss during liver resections. However, this can lead to potentially irreversible cellular ischemia and lethal liver failure.
Methods
From 9/2002 to 4/2010 122 consecutive atypical (specimens > 5 cm) and anatomical liver resections were performed in 94 patients, without Pringle's maneuver. Data, including functional liver tests, were collected prospectively. Water-jet dissection of liver parenchyma was used.
Results
122 liver resections were performed during 113 operations. Preoperative chemotherapy was used in 37.2%. Blood loss was median 500 ml (range 50-6000). The median weight of the resected parenchyma was 553g (range 109-1850). The median time spent in the intensive care unit was 2 days (range 1-44).
No mortality occurred. Morbidity was 8%. Biliary leakage (n=5) was treated conservatively. Liver failure only occurred in one patient suffering from portal vein thrombosis after right hemihepatectomy. However his liver function recovered completely after interventional recanalization.
Conclusions
Atypical and anatomical liver resections without Pringle's maneuver are feasible, safe and accompanied by only moderate blood loss. Performing liver resections without Pringle's maneuver might help to avoid liver failure in the postoperative course.

Acute Liver Failure Requiring Liver Transplantation Due To Accidental Heme Arginate Overdose In A Patient With Acute Intermittent Porphyria

H07

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Background: Acute intermittent porphyria (AIP) is the most common of the acute porphyrias. The mainstay of treatment is glucose and heme arginate (Normosang®) administration which inhibit hepatic ALA synthase and improve clinicial symptoms and biochemical abnormalities.

Methods: Case report of a patient with acute liver failure requiring urgent liver transplantation due to liver failure after erroneous 6-fold overdose of heme arginate.

Results: A 58-year old patient with AIP since 34 years accidentally received a 6-fold overdose of heme arginate (19mg/kg instead of the recommended dose of 3mg/kg) during an acute attack. As recommended in the product information, albumin and charcoal were administered and hemodiafiltration was started. Albumin binds free heme, charcoal reduces enterohepatic recirculation of heme and hemodiafiltration eliminates propylene glycol, the solvent in Normosang®. Transaminases and INR rose within one day. After 2 days, coagulation factor V was <10%. After 2.5 days, transaminases peaked (GOT 4571 U/l) and the patient got anuric. After short-term improvement of liver failure, it deteriorated again on day 5. Factor V fell to 17%, lactate was rising, anuric renal failure persisted, and the patient got hypoglycaemic and had to be intubated due to encephalopathy. The patient was listed for super-urgent liver transplantation and was transplanted six days after the overdose. The explanted liver showed no preexisting liver cirrhosis, but signs of subacute liver injury and starting regeneration. The patient recovered within a short time. She was asymptomatic in relation to liver injury and porphyria, however, still on hemodialysis.

Conclusion**:** To our knowledge, this is the first published case report of acute liver failure requiring urgent liver transplantation after accidental heme arginate overdose. Knowledge of a potentially fatal course is important for the correct management of future cases including early referral to a transplantation center. This case enlarges the limited experience that AIP is cured by liver transplantation, which already has been performed in patients with otherwise untreatable symptoms of AIP.

Endoscopic treament of anastomotic strictures complicating OLT with temporary, maximal, plastic stenting

H08

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Background : Anastomotic biliary strictures complicate 4-13% of orthotopic liver transplantations (OLT); temporary dilation with multiple plastic stents is emerging as the gold standard endoscopic treatment. Methods: Starting in 7/2003, all consecutive patients with anastomotic strictures complicating OLT had temporary stricture dilation with plastic stents. As many stents as possible were inserted by ERCP at each stent replacement scheduled every 3 months, aiming at stent removal after one year. Results: Between 7/2003 and 5/2010, 25 patients of the 211 OLTs performed were included after a median of four (1-114) months following OLT. Seventeen (68%) patients have completed therapy, five (20%) still have stents in place, two (8%) had therapy interrupted because of diffuse ischemic biliary strictures which required evaluation for retransplantation and one (4%) died during treatment due to ischemic colitis with septic shock after conservative management of a duodenal perforation in a patient with terminal cirrhosis on the graft due to HCV recurrence. Patients underwent a median of three (2-6) ERCPs, with a median of 2 (1-3) stents placed during the first ERCP and a median of 3 (1-6) stents placed during the subsequent procedures. Median treatment duration was 10 (1-15) months. During treatment, four (16%) patients experienced cholangitis and three (12%) had asymptomatic elevation of liver tests related to stent obstruction (this was treated by stent replacement earlier than scheduled). All patients who completed treatment achieved stricture resolution with no relapse detected during a median follow-up of 9 (1-73) months. Conclusions: Temporary dilation of anastomotic post-OLT biliary strictures with plastic stents (maximal number with regular replacements by ERCP for one year) is effective and appears to be safe in patients without liver failure and portal hypertension.

H09

TREATMENT OF CHRONIC HEPATITIS C IN 3 PATIENTS WITH HCV-INDUCED SEVERE THROMBOCYTOPENIA

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Background: Thrombocytopenia has been described in HCV infection even in the absence of cirrhosis and splenomegaly. Different mechanisms have been proposed, including immune-mediated platelet (plt) destruction. Here, we report on the treatment of 3 patients with HCV-HIV coinfection and HCV-induced severe thrombocytopenia.

Patients and treatment: All patients had an infection with HCV genotype 3, an intermediate fibrosis stage (Metavir F2 or F3), HIV infection controlled by antiretroviral combination therapy, and severe, steroid-refractory thrombocytopenia. Pegylated interferon-α2a (PEG-IFN-α2a) was started at 45 or 90 µg per week and doses were rapidly increased in the following, while ribavirin (RBV) was prescribed at standard doses. Treatment was pursued for 48 weeks. Two patients received intravenous immunoglobulins (IVIG) during the first weeks of PEG-IFN-α2a and RBV combination therapy.

Results: A significant increase in plt counts (from 17, 39 and 37 G/l, respectively, to > 100 G/l) was observed in the 3 patients while they experienced a virological response. Thrombocytopenia relapsed in one patient together with a relapse of chronic hepatitis C. The other 2 patients achieved a sustained virological response (SVR), with normal plt counts at follow-up in one and persistent mild thrombocytopenia in the other.

Conclusions: Carefully titrated PEG-IFN-α2a and RBV combination therapy may be performed safely in this difficult-to-treat patient population, with close monitoring and eventually concomitant IVIG during the first weeks. SVR can lead to normalization or significant improvement of plt counts, suggesting a causative role of HCV in this condition.

S01

Predictive risk factors for intra- and postoperative complications in 526 laparoscopic sigmoid resections due to recurrent diverticulitis: A multivariate analysis.

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Background: Laparoscopic sigmoid resection is a feasible and frequent operation in patients suffering from recurrent diverticulitis. There is still an ongoing debate about the optimal timing for surgery in patients suffering from recurrent diverticulitis episodes. In elective situations the complication rate for this procedure is moderate, but there are patients at high risk for perioperative complications. The few identified risk factors so far refer to open surgery. Data for the elective laparoscopic approach is still rare. The objective of this study is to identify potential predictive risk factors for intra- and postoperative complications in patients undergoing laparoscopic sigmoid resection due to diverticular disease.
Material and Methods: Uni- and multivariate analyses of a prospectively gathered database (1993-2006) were performed on a consecutive series of 526 patients undergoing laparoscopic sigmoid resection due to recurrent diverticulitis in a single institution. Patients were assessed for demographic data, operative indications, and intra- and postoperative complications. Altogether, we analyzed 17 potential risk factors to identify significant influence on the intra- and postoperative outcome including timing of surgery.
Results: Statistical analysis of specific medical and surgical complications revealed anaemia, prior myocardial infarction, heart failure, experience of the surgeon and male gender, as independent predictive risk factors for postoperative complications.
Patients age >75 years was the only independent risk factor for intraoperative complications in a multiple logistic regression model. Early elective surgery led to increased conversion rate but did not influence the postoperative complication rate.
Conclusion: This large single center study provides first evidence of the significance of predictive risk factors for intra- and postoperative complications in laparoscopic sigmoid resection.

S02

Esophageal dysmotility and dilatation following laparoscopic gastric banding – An underestimated long term complication.

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Background: Esophageal motility disorders and dilatation after laparoscopic adjustable gastric banding (LAGB) have been reported. However, only a few studies present long term follow-up data. The aim of this study was to evaluate the effects of LAGB on esophageal dysfunction over the long term in a prospective study. *Methods:* Between June 1998 and June 2009 all patients with implantation of a LAGB were enrolled in a prospective clinical trial including a yearly barium swallow. Esophageal motility disorders were recorded and classified over the period. An esophageal diameter of 35 mm or greater was considered dilated. *Results:* LAGB was performed in 167 patients (120 female, 47 male) with a mean age of 40.1±5.2 years. Overall patient follow-up was 94%. Esophageal dysmotility disorders were found in 108 patients (68.8% of patients followed). Esophageal dilatation occurred in 40 patients (25.5%) with a mean esophageal diameter of 47.3±6.9 mm (35.0-94.6) after a follow-up of 73.8±6.8 months (36-120), compared to 26.2±2.8 mm (18.3-34.2) in patients without dilatation (diameter of < 35mm) (p<0.01). 34 patients suffered from stage III dilatation (band-deflation necessary) and 6 from stage IV (major achalasia-like dilatation, band removal mandatory). In 29 patients upper endoscopy was carried out because of heartburn/dysphagia. In 18 patients the endoscopy was normal, 9 suffered from GERD, one from a stenosis and one from a hiatus hernia. *Conclusions:* This study demonstrates that esophageal motility disorders after LAGB are frequent, poorly appreciated long term complications. Despite adequate excess weight loss LAGB should probably not be considered the procedure of first choice and should only be performed in selected cases, until reliable criteria for patients with a low risk for the procedures long term complications are developed.

S03

The sphincter's fate in low lying rectum cancer: a decision analysis

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Background: Abdominoperineal resection (APR) is the standard of care for a rectal cancer located within 5 cm from the anal verge. Yet, APR entails a permanent colostomy. Intersphincteric resection (ISR) is an alternative procedure which preserves the anal sphincter. Concerns about a less radical procedure causing worse oncological results or poor fecal continence have precluded the widespread use of ISR. In the absence of data from a randomized controlled trial investigating the relative benefits of ISR and APR, a decision analysis can objectively inform patient and physician decision's making.

Methods: A Markov model was built using data from the nationwide Swedish Rectal Cancer Registry and from a systematic review of the literature (1990-2009). Morbidity, mortality, tumor progression, continence, and quality of life were modelled during 35 years. Quality adjusted life expectancy and crude survival rates of rectal cancer patients undergoing APR or ISR were compared. Extensive sensitivity analysis were performed, including probabilistic sensitivity analysis.

Results: ISR was the preferred strategy with a gain of 1.36 quality-adjusted life years (QALY) over APR (ISR 8.90 QALY Vs APR 7.55 QALY), while both strategies displayed similar 5-year mortality rates (ISR 70.1% Vs APR 69.4%, TNM stage II cancer). APR became the preferred procedure when the mortality, morbidity, or risk of local recurrence following ISR were modelled higher than 11%, 60%, or 94%, respectively. On the other hand, the occurrence of fecal incontinence had marginal influence on the preference of patients for ISR. Overall, the disutility of a colostomy drove the preference for ISR through the model.

Conclusion: From a patient's perspective, ISR is the preferred strategy for resection of a low lying rectal cancer, when technically feasible.

S04

Long-term follow-up of open and laparoscopic repair of large incisional hernia

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Background: Long-term results after laparoscopic repair of large incisional hernia remain to be determined. The aim of this prospective study was to compare early and late complications between laparoscopic repair and open repair in patients with large incisional hernia.

Methods: A total of 428 consecutive patients underwent incisional hernia repair at our institution between February 2003 and June 2009 and were prospectively followed. Only patients with a hernia diameter of ≥ 5cm were included in this study. We compared 56 patients who underwent open incisional hernia repair with 69 patients who underwent laparoscopic repair.

Results: The demographic parameters were not significantly different between the two groups. Conversion to open surgery occurred in seven patients (10%). Median hospital stay (6.0 days, range 1-23 days vs. 7.0 days, range 1-67 days; p= 0.014) and incidence of surgical site infections (SSI) (5.8% vs. 26.8%; p= 0.001) were significantly lower in the laparoscopic group compared with open surgery. Bulging of the implanted mesh was observed in 17.4% in the laparoscopic group and in 7.1% in the open group (p= n.s.). After a median follow-up of 65 months (range 1-80 months) in the open group and 33 months (range 1-62 months) in the laparoscopic group, a recurrence rate of 18% in the open group and 16% in the laparoscopic group was found (p= n.s.). Multivariate analysis revealed width of the hernia ≥ 10cm, SSI, and BMI ≥ 30kg/m^2 as significant risk factors for hernia recurrence.

Conclusions: The incidence of SSI is significantly lower after laparoscopic incisional hernia repair. At long-term follow-up, the recurrence rate is not different between the two techniques. Abdominal bulging is a specific problem associated with laparoscopic repair of large incisional hernia. Size of the hernia, BMI, and SSI are risk factors for hernia recurrence irrespective of the technique.

S05

Operative time and BMI are significant risk factors for surgical site infections in laparoscopic sigmoid resection

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Background: Surgical site infection (SSI) in patients undergoing colorectal surgery is a common complication and associated with increased costs. The aim of this study was to assess risk factors for SSI in laparoscopic sigmoid resection for benign disease.

Methods: 4488 patients undergoing laparoscopic colorectal surgery were collected in a prospective multicenter SALTS-database between 2/1995 and 2/2008. 2571 patients underwent sigmoid resection for benign disease and were included in this study. Uni- and multivariate analysis was used to determine risk factors for SSI.

Results: The incidence of SSI in the observed population was 3.5% (90/2571). Among these patients inicisional superficial infections was found in 71%, incisional deep infections in 22% and organ-space infections in 7%. In univariate analysis, patients age, underlying disease, type of operation (sigmoid and recto-sigmoid resection), and surgeons experience has no impact on SSI (p= n.s.). Univariate and multivariate analysis showed that operation time > 240min. (Odds ratio (OR) 1.7; Confidence interval (CI) 1.0-2.8), BMI $\geq$ 27 kg/m^2 (OR 2.3 (1.3-4.5)), organ lesions (OR 7.9 (2.0-31.8)) and male gender (OR 2.3 (1.2-4.5) are significant risk factors for SSI. Reoperation rate in the SSI-group was significantly higher compared to the No SSI-group (30% vs. 3%; p< 0.001). SSI is associated with a significant longer median hospital stay (15 days, range 2-69 vs. 8 days, range 1-69; p< 0.001) and higher mortality rate (2.2% vs. 0.4%; p= 0.019).

Conclusion: Significant risk factors for SSI are operation time > 240min, BMI $\geq$ 27 kg/m^2, organ lesions, and male gender. SSI is associated with a significant higher reoperation rate, longer hospital stay, and higher mortality rate.

S06

Comparative Study of emergency vs elective Colon Cancer Surgery

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Background
Approximately 20% of colon cancer patients present with conditions requiring emergent operative resection. The aim of this study was to assess differencies in preoperative state (age, BMI, weight loss, nutritional risk score, ASA score), extent of resection, in-hospital morbidity/mortality and tumor stage (pTNM) between emergent and elective operations.
Methods
All patients requiring operative resection for adenocarcinoma of the colon between 01/01/2000 and 12/31/2009 were reviewed.
Results
124 of 529 (23.4%) patients presented with an emergency situation (bowel obstruction 71 (13.4%), perforation 25 (4.7%), obstruction and perforation 18 (3.4%), bleeding 10 (1.9%)). There was no difference in age (median 75.5y emergency vs 74y elective) or BMI (median 24.0 vs 24.8), but a significant difference in preoperative weight loss (mean 3.39kg vs 2.55kg), nutritional risk score (median 3 vs 2) and ASA score (ASA 3-5 50% vs 42%) between emergent and elective operations. Extent of resection was significantly higher in the emergency group (extended/subtotal/total colectomy 21% vs 9.4%). In-hospital morbidity (Dindo II-IV 26.6% vs 17.8%) and mortality (10.5% vs 3.7%) was higher in the emergency group. Emergency operations had more advanced tumor stages (UICC I/II 44.3%, UICC III/IV 55.7%) than elective operations (UICC I/II 55.8%, UICC III/IV 44.2%). The number of positive lymph node (mean 2.18 vs 1.15) and the lymph node ratio (mean 0.11 vs 0.06) was higher in the emergency group.
Conclusion
Emergencies presented with higher ASA and nutritional risk score, had more advanced tumor stages and resulted in higher morbidity and mortality. There is an urgent need for better screening of colon cancer.

S07

Intrapancreatic accessory spleen misdiagnosed as a non-secreting endocrine tumour: case report and review of the literature

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Introduction: An intrapancreatic accessory spleen may be mis-diagnosed as a non-secreting neuroendocrine tumour of the pancreas. We report a case of an intrapancreatic accessory spleen with review of the literature.
Case report: A 67-year-old woman in good general conditions with a family history positive for pancreatic cancer underwent a routine health check. Her personal history was completely uneventful without any symptoms present. Physical examination was normal and laboratory tests revealed normal AFP, CEA but a slightly elevated CA 19-9. Additional laboratory test as Chromogranine A, NSE, 5-HIA, PP and Substance-P were ordered and beside of a slightly elevated PP normal. The patient underwent CT-Scan investigation which showed a 18 x15x15mm lesion in the tail of the pancreas without any contrast enhancement. An additional Octreotide-Scan was normal. A neuro-endocrine tumour was suspected. The patient underwent a left-sided splenopancreatectomy. Intraoperatively, a dark red but soft tumour was found in the tail of the pancreas. Postoperative histo-pathological examination revealed an intrapancreatic accessory spleen without any signs of a tumour.
Results: In a large series of non-selected autopsy investigations an accessory spleen was found in 10-30%. The second most common site is the pancreatic tail (17%). Pancreatic endocrine tumours are rare tumours (< 10%). However, 50% of these non-secreting endocrine tumours are malignant and require surgical resection. The only possibility to differentiate an accessory spleen from a neuroendocrine tumour are nuclear scintigraphic investigations as 99m Tc-sulphur colloid or Tc-tagged heat-damaged red blood cells scintigraphies. These are investigations which are non-invasive, sensitive and specific tests for detecting splenic tissue.
Conclusion: Nuclear Szintigraphy may provide the definitive diagnosis of an intrapancreatic spleen and therefore prevent patients from unnecessary major surgery.

S08

Esophageal perforation: non-operative treatment is more than an option

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Background: Esophageal perforation (EP) is a live-threatening situation with a high mortality (up to 40%). The role of conservative treatment for EP remains controversial. We want to evaluate the non operative approach with aggressive interventional drainage of collections, insertion of oesophageal, gastric and mediastinal drainage, and the administration of broad-spectrum antibiotics.
Methods: From 2002 to 2009, 28 patients (18 male, 10 females) with EP were treated at our institution and reviewed retrospectively. Diagnosis of EP was confirmed by CT-scan, contrast studies and/or endoscopy.
Results: Mean age was 61 years (range 26-85). The etiology of EP was “spontaneous” in 10, iatrogenic in 10, ingestion of foreign body or acid in 6 and traumatic in 2 patients. Rupture was proximal in 4 (14%), in the mid esophagus in 6 (22%) and distal in 18 patients (64%). Median delay from rupture to treatment was 1.46 days (range 0-8). In 16 (57%) of 28 patients treatment was nonoperative. 12 patients (43%) underwent operative treatment. (6 primary repairs, 4 transhiatal resections, and 2 surgical drainage). Overall mortality was 10.7% (3 patients, 2 of them in the non-operative group, in both cases, however, the patients refused further treatment). In all patients, closure of EP was documented by esophagogram and/or upper endoscopy. Mean hospital stay was 41.9 days (range 5-175) for operated patients and 20.3 days (9-53) for conservatively treated patients.
Conclusion: These results support the concept of a proactive treatment strategy in high-risk patients with EP, yielding a good outcome. While Boerhaave’s perforation may rather be treated surgically, conservative treatment of EP from other etiologies using comprehensive drainage can safely be considered in semi-/stable patients.

Risk Factors for Delayed Gastric Emptying after Pancreaticoduodenectomy

S09

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Background: Delayed gastric emptying (DGE) after partial pancreaticoduodenectomy (PD) is associated with a longer hospitalization and higher costs. The objective of our study was to assess risk factors for DGE after PD.

Methods: Retrospective analysis of a prospective database including 194 consecutive patients who underwent PD between 2002 and 2009. Three grades of DGE were distinguished: Grade A: gastric tube (GT) for 4-7 postoperative days (POD) and delay of solid food diet (DSFD) until 7 POD. Grade B: GT for 8-14 POD and/or DSFD until 14 POD. Grade C: GT longer than 14 POD and DSFD for more than 14 POD.

Results: 53% of all patients suffered from any grade of DGE. The incidence of DGE grade A was 13.9%, grade B 23.7% and grade C 15.5%. Multivariate analysis revealed a decrease of DGE (all grades) with retrocolic reconstruction (odds ratio (OR) 0.33 (confidence interval 0.12-0.9) p=0.03) and in patients without diabetes mellitus (DM) (OR 0.4 (0.2-0.9) p=0.02). Grade C DGE is significantly associated with age above 70 years (OR 2.6 (1.1-5.7) p=0.02), intraoperative blood loss greater than 1000 ml (OR 2.7 (1.5-4.8) p= 0.001) and dissection of more than 20 lymph nodes (OR 2.5 (1.2-5.2) p= 0.02). Mean hospitalization was 18 days in DGE grade A, 22 days in grade B, 35 days in grade C and 16 days for patients without DGE.

Conclusion: Low grade DGE is associated with DM and antecolic reconstruction. Age above 70 years, increased blood loss and dissection of more than 20 lymph nodes are independent risk factors for high grade DGE. These results allow to adjust gastric tube removal in patients undergoing PD. A prospective randomized trial is needed in order to confirm the role of the above mentioned risk factors.

Surgical site infection after ileostomy closure: is it really a problem?

S10

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Background: Surgical site infection (SSI) is the most common complication after closure of an ileostomy and varies between 1.5% and 29%. The aim of this study was to evaluate the SSI rate within 30 days after closure of an ileostomy.

Methods: Our study based on 29 consecutive patients who had undergone closure of an ileostomy at our institution between January 2008 and December 2009. SSI was assessed according to the criteria developed by the Centers for Disease Control and Prevention and all patients underwent clinical examination at least 30 days postoperatively.

Results: Median age of the patients was 67 years (range 32-83), median BMI 25 kg/m^2 (range 19-31) and median ASA-score of 2 (range 1-3). Postoperative complications developed in 6 patients (20.7/%). Whereas SSI was observed only in 1 patient (3.4%) (incisional superficial). Incisional hernia was found in 4 patients (13.8%) and subcutaneous hematoma in 1 patient (3.4%) after a median follow up of 44.5 days (range 30-237). The median operation time was 90 minutes (range 65-235). Primary closure of the skin was performed in all patients whereas subcutaneous drainage was placed only in 4 patients (13.8%). Median hospital stay was 6 days (range 4-16).

Discussion: A low rate of SSI of only 3.4% was observed in our study group. Whereas incisional hernia seems to be a common complication and needs further investigations.

S11

Mesh fixation in totally extraperitoneal laparoscopic repair of inguinal hernias: tack versus fibrin glue

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Background

The laparoscopic repair of inguinal hernias generally involves mesh fixation to avoid displacement and recurrence. We wanted to compare the clinical outcome of totally extraperitoneal endoscopic inguinal hernioplasty (TEEP) using fibrin glue or mechanical stapling for mesh fixation.

Patients and methods

We retrospectively analysed a total of 276 consecutive patients of whom 218 sent us a questionnaire back. The patients were undergoing TEEP operation for unilateral (n=131) or bilateral hernia (n=89) from January 2007 until December 2009. They received mesh fixation by tack (n=109) or by fibrin sealant (n=109). Outcome measures were operative time, length of hospital stay, costs and postoperative outcome (SF-12 questionnaire) and satisfaction.

Results

The two groups of mesh fixation were comparable in age, sex, ASA classification and preoperative rate of recurrent hernia. In the patients with unilateral hernia the operative time did not differ significantly between the two groups (p=0.081). The length of hospital stay was significantly shorter after mesh fixation by glue (2.3 vs. 2.8 days; P = 0.003). Taken both unilateral and bilateral hernia together the difference of hospital stay length is proved (P = 0.013). Furthermore, operative time is then significantly shorter in the fibrin sealant group (57 min vs. 48 min; P = 0.005).Intraoperative complications are rare and did not differ between the two methods. Costs for bilateral and also unilateral hernia are significantly lower for glue (1ml: 197.5 CHF; 2ml: 336.5 CHF) than tacker (514.35CHF). In the tacker group there was one case of nerve entrapment that required a re-operation. In the long-term follow-up patients do not show any clinical differences between tacker and glue concerning life quality and personal satisfaction.

Conclusion

The length of hospital stay as sign of recovery was significantly shorter after mesh fixation by fibrin glue. At same clinical results in the long-term follow-up the material costs for fixation by fibrin glue are significantly lower.

S12

Pelvic floor reconstruction with biomesh after abdominoperineal extendend excision for rectal cancer?

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Background:
In order to achieve a better oncological outcome, the abdominoperineal extended excision (APE) has been recently described by Holmes for patients with advanced low rectal cancer We present our first experiences with a biological mesh (Permacol ™) for closure of this large defect to the pelvic floor.

Methods:
The procedure began in supine position: mobilisation of the rectum, transsection of the sigmoid colon and performing a permanent descendostomy. After closing the laparotomy the patient is moved into jack-knife position. An extrasphincteric excision of the anal canal, including the levator ani is performed. The rectosigmoid is removed through the perineum including the resected coccyx`s tip. Reconstruction of the pelvic floor is performed with a 1.5mm thick sheet of Permacol ™.

Results:
From October 2009 to January 2010, 5 patients (4 male) of median age 52 years (range 37-82), underwent extended APE. All patients had a very low rectal cancer, with a range of 2-4cm from the anal verge or with an infiltration of the pelvic floor, one in the context of ulcerative colitis. Four patients had neoadjuvant radiotherapy. Median operation time was 240min. No intraoperative complications occurred. Postoperatively a vaginal wound dehiscence occurred in one patient which required operative closure. Antibiotics for a perineal wound infection were needed in two patients. At last, all perineal wounds healed without removing the biomesh.

Conclusion:
Reconstruction of the pelvic floor after extended APE with a biomesh is a safe procedure. The perineal wounds healed without removal of the biomesh. Although the five reported cases represent our hospital`s early experience, those results are encouraging and lack of any severe complications.

First Experience with Pudendal Nerve Stimulation for Fecal Incontinence

S13

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Background: Sacral Nerve Stimulation (SNS) is an established treatment of refractory lower urinary tract and bowel dysfunction. For urological patients not yielding satisfactory results with SNS, Pudendal Nerve Stimulation (PNS) has recently been successfully tested. Given the sometimes unsatisfactory results after SNS in fecal incontinence (FI), we tested PNS for this indication.
Methods: We performed PNS following a two stage technique as originally described by Spinelli et al. During the screening period (implanted tinned lead connected to an external neurostimulator), improvement of symptoms of at least 50% was counted as success and lead to implantation of a permanent neurostimulator.
Results: In 2009, we tested PNS in 8 female patients, median age 72 years (range 31-84). FI was due to sphincter defect, pelvic floor surgery or neurogenic factors (some patients with FI of multiple origins). After screening, 7 of 8 (87.5%) patients reported a success (Median reduction of symptoms 70% (range 30-90%)). Six patients had the permanent stimulator implanted; one patient reported paraesthesia and wished explantation of the electrode despite of its very good function.
Conclusion: PNS is a successful minimal invasive procedure for patients who failed SNS in FI. Further studies are ongoing for refined patient evaluation and long-term follow-up.

Results of Distal Gastric Bypass

S14

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Background

Treatment failures of proximal gastric bypass (GBP) procedures in terms of insufficient weight loss (up to 20% for morbid obesity, 40% for superobesity) have inspired us to introduce the distal GBP (dGBP) into our algorithm. The results of our series of primary dGBP will be presented here.

Methods

In a prospective cohort study from 2005-2010 we analyzed all of our primary dGBP regarding weight loss and morbidity. The decision for a primary dGBP was individually made according to certain criteria, e.g. BMI, fat distribution, severity of comorbidities or eating habits. Failure was defined as excess weight loss (EWL) < 50%. The common channel was defined as 10% of total small bowel length. A small pouch of approximately 15-20 ml was created.

Results

From 2005 to 2010 we performed 688 bariatric bypass procedures, of which 319 were primary dGBP. Mean preoperative BMI was 49 kg/m^2. Mean EWL was 75.4% at 2.4y mean follow-up. Follow-up rate was 95.6%. Failure rate was 3.1% compared to 8.8% for the proximal GBP and 19.4% in the first series of proximal GBP before 2005. Long term mortality was 0.31% (n=1, lung cancer), there were 2 leaks at the gastro-jejunostomy (0.63%) and 3 staple line ruptures (0.94%). Albumin levels were unchanged pre- and postoperatively. Complete remission rates for diabetes and hypercholesterolemia were 88% and 94%.

Conclusions

Adding dGBP to the bariatric repertoire significantly reduces the failure rate, while the incidence of hypoproteinemia is not increased.

S15

Effective weight loss in morbidly obese patients: comparison between laparoscopic Roux-en-Y gastric bypass (LRYGB) and laparoscopic sleeve gastrectomy (LSG)

P. C. Nett, Y. Borbely, J. M. Heinicke, D. Candinas, Bern

Laparoscopic sleeve gastrectomy (LSG) is gaining popularity as a procedure for the treatment of morbid obesity. Its indications and long-term results are currently under evaluation. Initially started as a first-stage procedure for superobese patients (BMI>50kg/m2), it is now emerging as a standalone procedure in bariatric surgery. Early results suggest that, at the end of the first year, weight loss and resolution of comorbidities with LSG is comparable to laparoscopic Roux-en-Y gastric bypass (LRYGB). Whether LSG alone can replace LRYGB as a standard bariatric procedure is questionable. The aim of this study is to compare the results, resolution of comorbidities, and complications between LSG and LRYGB.

A retrospective comparative analysis was done of 20 patients in each arm who underwent LSG and LRYGB. Both groups were matched for age, sex, and body mass index. The resolution of comorbidities, percentage of excess weight loss (EWL), and complications were studied at 6 months and 1 year in our study.

The resolution of most comorbidities such as type 2 diabetes, hypertension, dyslipidemia, sleep apnea, joint pains, and percentage of EWL in both groups was comparable at the end of 6 months and 1 year. Though early resolution of type 2 diabetes was seen to be better in the LRYGB group, the results matched up at 1 year. On the other hand, there was an increased incidence of gastroesophageal reflux disease in LSG patients.

Long-term studies are needed to evaluate the efficacy of LSG alone as a procedure for the treatment of morbid obesity and its comorbidities.

S16

Early experience with laparoscopic sleeve gastrectomy as a single-stage bariatric procedure in high risk and/or superobese patients

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Laparoscopic sleeve gastrectomy (LSG) as a single-stage restrictive bariatric procedure is becoming increasingly popular, especially in patients who are high risk and/or superobese (BMI>50kg/m2). The aim of this study was to evaluate the efficacy of LSG as a definitive procedure for morbidly obese patients at our institution.

Prospectively collected data from 29 patients who underwent LSG between July 2007 and December 2009 were reviewed. The average age of the patients was 41±13 years with a preoperative body mass index (BMI) of 55±11 kg/m2. Preoperative indications for LSG included contraindication to laparoscopic Roux-en-Y gastric bypass (n=18), severe coronary artery disease and/or congestive heart failure (n=5), significant liver disease (n=2), and patient preference (n=4). LSG was performed using the Endo-GIA stapler to create a lesser curve gastric tube over a 32-French bougie. Operative time, complication rates, and the percentage of excess weight loss (EWL) were calculated.

The operative time was 146±21 min. There was no conversion to open surgery. Complications within the first 30 days after surgery occurred in 7 of 29 patients (24%): gastric tube stenosis (n=2), port site infection (n=2), nosocomial pneumonia (n=1), subphrenic abscess (n=1), lung embolism (n=1), and one staple line disruption requiring revision surgery. There were no deaths. Preliminary EWL at 3, 6, 9, and 12 months was 34, 49, 59, and 72%, respectively, and many patients had improvement or resolution of obesity-related comorbidities. All patients reported significant loss of appetite.

Early review of our data demonstrates that LSG as a single-stage bariatric procedure can be performed safely and with excellent excessive weight loss in high risk and/or superobese patients (BMI>50kg/m2). Additional follow up will be necessary to better define its long-term safety and efficacy.

S17

Laparoscopic mesh repair in ventral hernia: Sometimes they come to nothing

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Background

The biocompatibility properties of meshes are crucially important for minimizing the development of recurrences after laparoscopic hernia repair. We compared the clinical outcome of two different polypropylene meshes, the large-pored proceed® and the small-pored atrium®.

Methods

We analyzed a total of 120 consecutive patients undergoing laparoscopic hernia repair from 2006 until 2008. Outcome measures were operative time, length of hospital stay, recurrence rate, and re-operation rate.

Results

40 patients received an atrium® mesh, 80 patients received proceed® mesh. 2 patients had a recurrence after implantation of a large-pored mesh; 8 patients suffered from recurrence after small-pored mesh implantation (P = 0.002). The reason for recurrence after large-pored mesh in both cases was the too small mesh size selected in the primary operation. In all recurrences after small-pored mesh shrinkage of the mesh was supposed to be the direct cause (P< 0.001). Bowel adhesions to the mesh were significantly different pronounced (n= 4 in large-pored mesh; n= 9 in small pored mesh; P= 0.004).

Conclusions

We have noted a remarkable shrinkage rate in some of the prosthetic materials. It was astonishing how distinctive the shrinkage in the small-pored meshes was. The recurrence rate associated with laparoscopic hernia repair can be minimized by selecting the correct type of mesh besides its adequate dimension.

Development of a Pediatric Eosinophilic Esophagitis Activity Index (ped-EEsAI): International Experts propose Dysphagia, whitish exudates on endocopy, and intraepithelial Eosinophil Counts as Major Items related to EoE Activity

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Background and Aims: The international EEsAI study group aims to develop, validate and evaluate the first pediatric EoE activity index (ped-EEsAI). We report on results of phase 1, which aims to generate candidate items. **Methods:** This study involves 3 phases: (1) item generation, (2) index derivation and testing on a first patient cohort, and (3) validation in a second cohort. In phase 1, item generation, weighting and reduction are achieved through a Delphi process with an international EoE expert group. The experts proposed and ranked candidate items on a 7-point Likert scale (0 = no, 6 = perfect relationship with EoE activity). **Results:** 23 international EoE experts proposed and ranked 39 items (20 clinical, 6 endoscopic, 8 histologic, 5 laboratory items). Rank order for clinical items: dysphagia related to food consistencies (median 5, range 2-6), severity of dysphagia (5, 3-6), frequency of dysphagia episodes (5, 3-6), regurgitation and vomiting (4, 2-5), response to dietary restrictions (4, 1-6); endoscopic items: whitish exudates (5, 3-6), furrowing (4, 3-6), corrugated rings (4, 2-6), linear shearing (4, 2-6), strictures (3, 2-6); histologic items: intraepithelial eosinophil count (5, 4-6), lamina propria fibrosis (3, 2-6), basal layer enlargement (3, 1-5); laboratory items: % blood eosinophils (3, 0-5). **Conclusions:** These items will now be reduced in further Delphi rounds, tested on a cohort of 100 pediatric EoE patients and validated in a second independent cohort, resulting in a robust, broadly accepted disease activity index for use in clinical trials and daily care.

Traumatic injuries of the pancreas: a rare event and a diagnostic challenge but associated with good long-term prognosis

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Background
Only 1-5% of the patients with blunt abdominal trauma and 8% of the patients with penetrating trauma acquire an injury of the pancreas. Concurrent injuries are present in up to 70% of these patients, explaining the delay in the diagnosis of a pancreatic injuries.
Methods
We performed a retrospective analysis of our prospective trauma database between 2002 - 2009. The primary diagnostic test was a CT scan. Pancreatic injuries were graded according to the Moore classification. Patients were followed by questionnaire, abdominal ultrasound and measurement of blood glucose and stool elastase.
Results
There were 6 patients (4 male, 2 female) with a traumatic injury of the pancreas, out of how 2148 patients with possible abdominal trauma at the emergency station. The median age was 28 years (19-80. We found an even distribution of the injuries: grade I, III, IV and V: 1 patient each, grad II: 2 patients. 5 patients (83%) suffered concurrent intraabdominal injuries, one patient incurred concurrent rib fractures. We found the following accidents: 2 horseback riding with hoof kick, one skiing, one traffic crash and one scooter, 1 penetrating abdominal trauma. Three patients were treated by interventional drain placement, 2 by a left resection of the pancreas and 1 by direct suture of the pancreas. One patient developed a pseudocyst, 2 patients developed a pancreatic fistula Grade A and B; all healed spontaneously. The mean time in hospital was 18 days (10-47). The median follow up was 56 months (1-98). There were no exocrine pancreatic insufficiency, nor diabetes.
Conclusion
Traumatic injuries of the pancreas are rare and should be sought actively in blunt and penetrating abdominal trauma. Although they affect young patients and result in prolonged hospitalization the long-term prognosis is good with a normal exocrine and endocrine function of the pancreas.

Anastomose Colo-anale. Quelle qualité de vie ?

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Buts: Évaluer, à l'aide de formulaires standardisés, les résultats péri-opératoires et la qualité de vie post opératoire des reconstructions colo-anales.
Patients et méthode: De 2003 à 2008, 104 patients ont subis une résection antérieure basse avec anastomose colo-anale et stomie de protection. Cent-une opérations ont été effectuées pour un Carcinome du rectum, deux pour une fistule recto-vaginale après résection sigmoïdienne et une pour sténose rectale après résection sigmoïdienne. La morbidité péri-opératoire a été relevée de façon prospective. Le contrôle à long terme a été effectué à l'aide des formulaires standardisés selon Eypasch(GIQLI) et Wexner.
Résultats: Le collectif comportait 46 femmes et 59 hommes. Chez 35 patients, un réservoir comme remplacement du rectum a été confectionné; chez 69 patients, seule une anastomose latéro-terminale a été effectuée. La durée opératoire était de 250 min pour les 2 types de reconstructions. La morbidité chirurgicale était de 3%: 2 patients ont présenté une fuite anastomotique, l'une d'elle ayant nécessité une amputation et 1 patient a dû être réopéré en raison d'une ischémie colique. La durée d'hospitalisation était de 17 jours. La létalité a été nulle.
Tous les patients encore en vie à l'heure actuelle ont reçu le formulaire de contrôle avec un taux de retour de 85 % (79/92). La durée moyenne entre l'opération et le contrôle était de 2,3 ans. Les scores d'Eypasch et de Wexner étaient comparables pour les deux techniques: 110 (Eypasch) et 7,5 (Wexner).
Conclusion:
L'anastomose colo-anale avec stomie de protection est une technique sûre. La morbidité chirurgicale est faible. Toutefois, la qualité de vie et le score d'incontinence, mesurés à 2 ans, sont clairement plus faibles que dans une population de référence.
Une bonne information des patients est donc indispensable et une stomie définitive devra toujours être discutée.

Successful closure of a gastric leak after open sleeve gastrectomy as a rescue procedure for failed gastric banding by using an endoscopic over-the-scope clip (OTSC)

P. C. Nett, A. M. Ortner, J. M. Heinicke, D. Candinas

Sleeve gastrectomy is increasingly being recognized as a valid rescue procedure after failed gastric banding in morbid obesity. Gastrocutaneous fistulas are uncommon complications accounting for 0.5-3.9% of these operations. When their management is not effective, the mortality rate is high.

A 63-year-old female, 9 and 10 years after laparoscopic gastric banding and open rebanding underwent open sleeve gastrectomy. Three days after surgery a staple line disruption occurred. Although revision surgery was performed, a high-output gastrocutaneous fistula with a diameter of 6mm persisted. Repeated computed tomography scans of the abdomen revealed a large extravasation of contrast material parallel to the gastric sleeve.

Gastrocutaneous fistula was initially treated with conservative measures as antibiotics, jejunal enteric feeding and total parenteral nutrition. The use of a percutaneous radiologically guided drainage permitted to control the leak and to have a controlled fistula. Two months later, fibrin glue as a tissue adhesive was applied endoscopically to the leak without any success. Finally, 4 months after the original surgery, an endoscopic over-the-scope clip (OTSC) was brought to the leak and closed the gastrocutaneous fistula.

Patients with a gastric leak after repeated bariatric surgery should be treated conservatively by antibiotics, percutaneous radiologically guided drainage, jejunal enteric feeding and total parenteral nutrition. When the leak persists, endoscopic sealing by an endoscopic OTSC should be considered before redo surgery, because it is simple, safe, effective and, in some cases, life-saving.

Association between Cogan´s-Syndrome and Inflammatory Bowel Disease: a case series

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Background: Cogan´s syndrome (CS) is a rare autoimmune disease with less than 250 cases reported. It mainly affects the audiovestibular system and the eyes frequently resulting in deafness. Inflammatory bowel disease (IBD) consists of two subtypes, Crohn's disease (CD) and ulcerative colitis (UC), and represents a common form of chronic intestinal inflammation.
Methods: Patient data were collected using a questionnaire that was sent to one of our outpatients and three of the 13 members of the German CS self-help group.
Results: In all Cogan patients with IBD (3 female with UC, 1 male with CD), intestinal disease was diagnosed years before onset of CS. After suffering from a complicated IBD disease course, they suddenly developed CS-related symptoms, such as hearing loss, tinnitus or eye inflammation. Three of them went deaf within few years after diagnosis. Although all of them had been on immunosuppressive IBD therapy, these treatment regimens did not prevent the onset of CS.
Conclusions: Our data suggest a strong association of IBD and CS. Since CS rapidly leads to bilateral deafness, it seems to be a rare, but nevertheless important complication of IBD. Early diagnosis and appropriate treatment could be essential for preventing disease progression.

Laparoscopic conversion of very very long limb Gastric Bypass (VVLL- RYGB) after weight rebound to Biliopancreatic Diversion (BPD)

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Background:
The Roux-en-Y gastric bypass (RYGB) has a long term failure rate of 20- 35%. Biliopancreatic Diversion is one effective procedure after failed weight loss after Roux-en-Y Gastric Bypass. This study reports on our results of a small series of patients who underwent conversion from very very long limb - RYGB to Biliopancreatic Diversion for weight loss failure.

Methods:
The data analyzed included age, BMI, excess body weight loss (EBWL) and peri- and postoperative morbidity rates.

Results:
From 2008 to 2009 7 Patients underwent conversion from RYGB to Biliopancreatic Diversion. Mean BMI before conversion was 43.7 kg/m2. All patients lost excellent weight after conversion to BPD, with a mean BMI and EBWL of 43.7 kg/m2 and 28.7 % before conversion and a mean BMI and EBWL of 34.2 kg/m2 and 58.6 % after conversion at a mean follow up of 5.3 months.

Conclusions:
Laparoscopic conversion of the weight rebounded RYGB into Biliopancreatic Diversion is feasible and highly effective with an acceptable morbidity in short term follow up.

Endoscopic Marsupialisation of a Symptomatic Duodenal Duplication Cyst in an Adolescent

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Background: Duodenal duplication cysts (DDC) are rare congenital malformations. The most common manifestation is acute pancreatitis, due to compression of the papilla of Vater. In rare cases, malignant tumors arising from DDC have been observed. The optimal management of DDC remains a matter of debate. Complete surgical resection has been advocated, but various case reports and a small series[1)] suggest that endoscopic treatment followed by close surveillance is an alternative.

Methods: We describe and illustrate the technique of endoscopic marsupialisation of a juxtapapillary DDC in a 17yr old male patient, after a first episode of acute pancreatitis, whose clinical data we have reported elsewhere[2)].

Results: We punctured the DDC with a needle knife in two locations, inserted a guidewire through these holes and placed the standard papillotome over the guidewire for a semicircular incision across the DDC roof. Thus the DDC roof flipped open and could be resected at its base with a polypectomy snare. Recovery was uneventful. The patient has remained free of recurrence over a follow-up period of five 5 years so far.

Conclusions: As previously shown by others[1)], DDC can be treated safely and effectively by endoscopic means. Various tools are at hand. We describe a technique of marsupialisation using the needle knife, standard papillotome over a guidewire, and polypectomy snare in a sequential manner. In the case presented, successful decompression of the DDC was achieved, without recurrence of pancreatitis or evidence of malignancy over a follow-up period of 5 years.

References:
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VVLL-Magenbypass mit und ohne zusätzliche Magenfundusresektion: vergleichende Studie zum Gewichtsverlauf nach 12 Monaten

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Einleitung
Der VVLL-Magenbypass führt über eine Restriktion der Nahrungsaufnahme, eine moderate Malabsorption und über die Beeinflussung verschiedener hormoneller Achsen zur Gewichtsreduktion. Dem Hormon Ghrelin wird dabei eine entscheidende Bedeutung beigemessen. Dieses Hormon welches vorwiegend im Magenfundus produziert wird dient zur Appetitregulation. Es kann durch Ausschaltung des Magenfundus aus der Nahrungspassage (Bypasschirurgie) oder durch Resektion (Gastric-Sleeve) in seiner Serumkonzentration gesenkt werden.

Methode
Mittels prospektiver Datenerfassung und retrospektiver Datenanalyse verglichen wir zwei Patientengruppen (A: n=36, VVLL Magenbypass mit Fundusresektion, B: n=33, VVLL Magenbypass) bezüglich BMI Verlauf und Excess body weight loss (EBWL) mit einem Follow up von einem Jahr.

Resultate
Die Gewichtsreduktion zeigte einen BMI kg/m2 und EBWL % in der Gruppe A von 29.97 kg/m2 /65.3%, respektive in der Gruppe B von 29.51 kg/m2 /65.59% nach 12 Monaten.

Schlussfolgerungen
Unsere Resultate zeigen im frühzeitigem Follow up von 12 Monaten keinen Vorteil der zusätzlich durchgeführten Fundusresektion bezüglich Gewichtsreduktion. Der mittel- und langfristige postoperative Verlauf ist abzuwarten um zu zeigen ob die Fundusresektion einen zusätzlichen Vorteil bezüglich der Gewichtsreduktion bringt.

Percutaneous, endoscopic assisted removal of gallstones in a critical ill patient: A new and feasible approach

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Backround: Cholecystectomy is associated with a high mortality rate in critically ill patients. As already widely accepted percutaneous cholecystostomy has a high success rate in the acute inflammatory situation in patients with high perioperative risk. There is still an ongoing debate about the necessity of the interval cholecystectomy in critically ill patients with various coexisting diseases who are not qualifying for surgery.
Methods: Here we present a new treatment option for critical ill patients who suffer from cholecystitis and common bile duct stones. An 85 year old woman was admitted to the emergency room and presented with typical symptoms of cholecystitis. After diagnosis of acute colecystitis due to multiple small gallstones in septic condition we indicated an immediate laparoscopic cholecystectomy. Due to cardiopulmonary decompensation and resusication prior to surgery we performed only a cholecystostomy. The patient recoverd well and after 2 weeks we did an endoscopic gallstone removal through a percutaneous applied metallic stent. The common bile duct stones were removed by an endocopic retrograde chiolangiography two days later. The reconvalescence of the patient was uneventfull and she was discharged five days after the ERCP.
Conclusion: This new technique is feasible and safe in critical ill patients who are suffering from severe cholecystitis caused by multiple gall stones and who are not qualifying for cholecystectomy.

Acute Pancreatitis after Roux-en-Y Gastric Bypass Surgery due to Reflux into the Biliopancreatic Limb: a Case Report

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Objective: Whilst bile stones after bariatric procedures are known sequelae in the long term, perioperative acute pancreatis is rather uncommon. Among other known causes, obstruction of the biliopancreatic limb can cause retrograde pressure back into the biliopancreatic ductal system, leading to acute pancreatitis.
Methods and Results: We report the case of a 57-year-old female bariatric patient who developed acute pancreatitis in the early postoperative course following conversion to open proximal Roux-en-Y gastric bypass (RYGBP) and extensive adhesiolysis for therapy-resistent gastroesophageal reflux disease. Due to band intolerance, a gastric band had been removed, and sleeve gastrectomy carried out two years earlier. At the same time, cholecystectomy was performed.
On pod 3, the patient experienced a sudden onset of abdominal pain and fever. Laboratory analysis revealed an acute pancreatitis with mild hyperbilirubinemia. An UGI contrast examination showed reflux of contrast tracer into the biliopancreatic limb, with documented slightly delayed passage into the common limb. Because there was no obvious sign of intestinal obstruction, we decided on conservative treatment. A magnetic resonance cholangiopancreato-graphy (MRCP) to rule out cholangiolithiasis remained inconclusive; in a follow-up no concrements were found. Antibiotic therapy was initiated, and the patient could be discharged from hospital on pod 37.
Conclusion: Acute pancreatitis can arise for a multitude of reasons. With biliary stones as the foremost reason in general, we think the cause in this case was reflux of intestinal content into the biliopancreatic limb, probably complicated by intermittent mechanical obstruction, explaining the mild hyperbilirubinemia.
This potentially fatal complication of RYGBP surgery is very rare and has been described in the literature only once.

Gewichtsverlauf, Resolution der Komorbiditäten (Diabetes Mellitus Typ II, arterielle Hypertonie) und Komplikationen nach laparoskopischem VVLL-Magenbypass

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Einleitung:
Ziel bariatrischer Operationen ist die nachhaltige Gewichtsreduktion und die Behebung von adipositasassoziierter Komorbiditäten wie Diabetes Mellitus Typ II und arterielle Hypertonie. Der Very very long limb Magenbypass ist ein restriktives Verfahren mit einer moderaten Malabsorption. Am eigenen Patientengut haben wir die Nachhaltigkeit dieses Verfahrens untersucht.

Methoden:
Wir führten bei 239 Patienten mit einem laparoskopischen VVLL-Magenbypass und einem Follow up von 0.5-9 Jahren eine prospektive Datenerhebung mit retrospektiver Datenanalyse des Gewichtsverlaufes, Beeinflussung der Komorbiditäten sowie der frühpostoperativen Mortalität/Morbidität durch.

Resultate:
Das mittlere Patientenalter betrug 40 Jahre (21 bis 60), der mittlere präoperative BMI betrug 45.7 kg/m2 (35-73.4), 47.3% (n=113) litten an einer arteriellen Hypertonie und 27.2% (n=65) an einem Diabetes Mellitus Typ II. Der mittlere BMI kg/m2 und der EBWL % betrugen nach 1 Jahr 30.0 kg/m2 /62.7% und nach 5-9 Jahren 31 kg/m2 /61%. Es zeigte sich ein EBWL >50% nach 1 Jahr von 83% und nach 5-9 Jahren von 83% der Patienten. Die arterielle Hypertonie verbesserte sich bei 69% und der Diabetes Mellitus Typ II bei 98% der Fälle. Die Mortalität betrug 1.3%. Eine Proximalisierung des Common Channels aufgrund schwerer Malnutrition war in 1.2% der Fälle notwendig.

Schlussfolgerungen
Die Therapie der Adipositas mittels VVLL-Magenbypass zeigt im kurz- bis mittelfristigem Verlauf eine nachhaltige Gewichtsreduktion und Verbesserung der Komorbiditäten.

Gewichtsrebound bei Magenbandträgerin nach stumpfem Abdominaltrauma mit ungewöhnlicher Ursache

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Einleitung:
Das laparoskopisch platzierte Magenband (LAP Band) stellt ein restriktives Verfahren zur Behandlung der Adipositas dar. Methodische Komplikationen sind die Pouchdilatation, das Slippage, die Bandmigration oder die Ösophagusdekompensation.
Systemassoziierte Probleme sind die Leckagen oder Rupturen die zu Dyskonnektion im Port-Bandsystem führen. Eine traumatische Ruptur des Verbindungsschlauches zum Portsystem wird bisher nicht beschrieben.

Methoden:
Fallbeispiel einer 40 jährigen Patientin mit St.n. LAGB Implantation 2004 mit traumatischer intraperitoneal liegender Ruptur des Verbindungsschlauches.

Resultate:
Die Patientin präsentierte sich 5 Jahre nach Magenbandimplantation in unserer Sprechstunde. Der präoperative BMI betrug 43.5 kg/m2 (105kg,156cm). Bis zwei Monate vor dieser Konsultation stabilisierte sich das Gewicht auf 60kg (BMI 25 kg/m2). Sie berichtete über einen Arbeitsunfall wobei sie einen stumpfen Schlag durch einen Palettenwagen gegen den Oberbauch links erlitt. Danach kam es zunehmend zu vermehrt möglicher Nahrungsaufnahme sowie verspätetem Sättigungsgefühl mit konsekutivem Gewichtsrebound auf 68kg (BMI 28 kg/m2). Eine Gastrografinuntersuchung zeigte eine Ruptur des intraperitoneal liegenden Verbindungsschlauches.

Schlussfolgerung:
Eine traumatisch bedingte Ruptur des Verbindungsschlauches durch ein stumpfes Abdominaltrauma ist möglich. Bisher ist kein solcher Fall in der Literatur beschrieben worden.

Therapie der perforierten Divertikulitis: Back to the roots?

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Einführung:
In den letzten Jahrzehnten wurden die operativen Therapieempfehlungen der perforierten Divertikulitis mehrmals geändert. Anfang des 20. Jahrhunderts wurde ein dreizeitiges Vorgehen empfohlen mit einem doppelläufigen Kolostoma und Lavage des Abdomens, dann die Resektion des befallenen Kolons und in einem dritten Schritt der Verschluss des Kolostomas. In den 80er Jahren ging die Tendenz immer mehr zum zweizeitigen Vorgehen mit einer Operation nach Hartmann und im zweiten Schritt die Wiederherstellung der Darmkontinuität, da man davon ausging, dass das intraabdominale Belassen eines perforierten Kolons ungünstig sei. Seit den 90er Jahren wird vermehrt eine primäre Kolonresektion mit oder ohne protektivem Stoma durchgeführt. Seit einigen Jahren wird die laparoskopische Lavage des Abdomen bei einer perforierten Divertikulitis Hinchey III propagiert und in einem zweiten Schritt Resektion. Back to the roots? Wir berichten über drei Fälle eine perforierten Sigmadivertikulitis mit einer Peritonitis Hinchey III.

Fallvorstellung:
Bei 3 Patienten mit einer perforierten Sigmadivertikulitis wurde eine laparoskopische Lavage des Abdomens durchgeführt. Wichtige Befunde bei Eintritt waren hämodynamische Instabilität, Adipositas permagna, Dyspnoe NYHA IV und Niereninsuffizienz. Etwa 3 Monate postoperativ wurde bei zwei Patienten die laparoskopische Sigmaresektion komplikationslos durchgeführt.

Diskussion:
Die laparoskopische Lavage bei perforierter Divertikulitis mit einer zweizeitigen Resektion ist eine gute Alternative zur primären Resektion bei Patienten mit relevanten Nebendiagnosen. Zeigt sich bei der Laparoskopie eine fäkale Peritonitis empfiehlt sich auf jeden Fall eine Resektion mit protektivem Stoma oder eine Resektion nach Hartmann.

Spontaneous Rupture of a Hepatocellular Carcinoma
A Case Report

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Background
We report a case of haemorrhage due to spontaneous ruptured hepato-cellular carcinoma leading to a state of shock. This is a rare event in Western countries where the incidence of hepato-cellular carcinoma is < 3%.

Methods
A 76 year old male patient, who had been operated for rectal carcinoma 11 months before was referred for syncope. A focal liver lesion was known and had been characterised as focal nodular hyperplasia in contrast enhanced computed tomography and sonography.

Results
After stabilization of vital parameters emergent helical computed tomography showed active bleeding from segment IV of the liver with haemoperitoneum. Emergency laparotomy revealed a necrotic tumor mass of approximately 5cm in diameter with arterial bleeding. Resection of segment IV of the liver was performed after which the bleeding could be stopped. Histopathological work up confirmed the tumor to be a hepato-cellular carcinoma. In the postoperative course no complications ensued.

Conclusion
Haemoperitoneum as a first presentation of HCC is an unusual occurrence. Nevertheless, as this case shows, it has to be included in the differential diagnosis of patients presenting in a state of hypovolemic shock with no adequate trauma. This should raise special concern in patients with known focal liver lesions or underlying liver disease, e.g. cirrhosis.

Laparoscopic repair of a hernia of Morgagni using a mesh technique

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Background: Morgagni's hernia is a rare cause of a diaphragmatic hernia. When symptomatic, a trans-thoracic or trans abdominal repair has been carried out. We report a symptomatic case, presenting in a young patient, repaired successfully using a laparoscopic approach and using a mesh technique.

Case report: An 27-year-old man presented with an 6 month history of intermittent severe upper abdominal pain, associated with episodes of constipation. Clinical examination was unremarkable, abnormal chest radiographic findings and a diagnostic CT scan. The hernia was reduced and the sac fully excised from the mediastinum in a laparoscopic way.

Result: Using the reported technique a safe reduction of the herniated contents and closure of the defect was achieved. The patient made an uncomplicated postoperative recovery, and at 6 months he remains well, with no recurrence of symptoms an no evidence of recurrent herniation.

Conclusion: Laparoscopy provides an excellent route for repair of a Morgagni's hernia. With careful dissection, the hernial sac can be easily removed and, where possible, this should be done. If there is excessive tension on the repair, a mesh repair technique may be a better option.

Duodéno-pancréatectomie céphalique (Whipple) par voie laparosocpique.

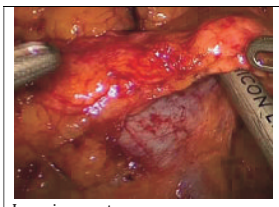
B. Ghavami, Lausanne

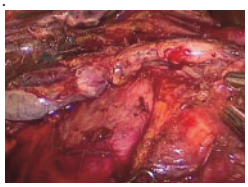
La laparosocpie est de plus en plus la voie préférentielle dans la chirurgie viscérale. De nombreuses interventions complexes sont pratiquées sous coelioscopie. Aujourd'hui de nombreuses enquêtes ont pu démonter la faisabilité de la laparoscopie dans des affections tumorales.

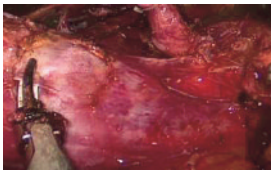
Parmi les opérations avancées on peut citer les colectomies, les gastrectomies, l'hépatectomies, la pancréatectomie caudale, etc. Toutefois cet abord est peu utilisé pour la duodéno-pancréatectomie céphalique, qui constitue une intervention majeure et compliquée. La coelioscopie permet une exploration première pour juger l'opérabilité du patient. L'opération de Whipple sous coelioscopie peut être réalisée dans des tumeurs T1 ou T2.

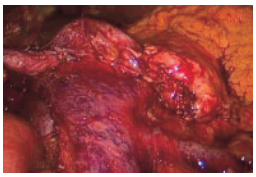
Cette présentation, est sous forme d'une vidéo de 10 minutes, d'une duodéno-pancréatectomie céphalique chez une patiente de 70 ans souffrant d'un AdénoCarcinome de la tête du pancréas, T1 N0 M0 sans ictère.

Elle détaille les différentes étapes de l'opération de Whipple : mobilisation du bloc duodéno-pancréatique, dissection de l'artère mésentérique sup, de la veine porte, lymphadénectomie complète (37 ganglions prélevés), section gastrique et pancréatique.


La veine porte


la dissection de l'artère mésentérique sup


libération de la face supérieure de la V. porte de la tête du pancréas


la veine porte et ses branches et la tranche de section du corps du pancréas

Ein Koagelpropf an der Entero-Enterostomie nach Magenbypassoperation: Eine potentiell lebensgefährliche Frühkomplikation

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Einleitung

In unserer Klinik wurden seit 2000 über 350 Magenbypassoperationen durchgeführt. Eine chirurgisch revisionspflichtige intraluminale Staplernahtreihenblutung im Bereich der Entero-Enterostomie trat nur in einem Fall auf.

Material und Methoden

Fallbeispiel eines 32 jährigen Patienten mit Redo Magenbypass und postoperativem Subileus bei obstruierendem Koagelpropf in der Entero-Enterostomie.

Ergebnisse

Am ersten postoperativen Tag zeigte sich ein Passagestopp des Gastrografins unmittelbar nach der Gastroenterostomie in der postoperativen Durchleuchtung. Die diagnostische Laparoskopie zeigte eine massive Distension des biliopankreatischen Dünndarmschenkels sowie eine massive Dilatation des Restmagens ante perforationem. Nach Eröffnung der Entero-Enterostomie zeigte sich eine Blutung im Bereich der intraluminalen Klammernaht. Der alimentäre und biliopankreatische Schenkel waren mit insgesamt 0.5l gefüllt. Die blutkoagelbedingte Stase im biliopankreatischen Schenkel führte zu einer massiven Distension des Restmagens. Gut 1.5l Verdaungssäfte konnten via Gastrotomie abgesogen werden.

Schlussfolgerung

Eine Tachykardie und eine klinische Verschlechterung des Patienten mit Passagestopp in der postoperativen Gastrografinpassge stellt auch ohne wesentlichen Hb Abfall eine sofortige Indikation zur operativen Revision dar. Eine koagelbedingte Stase im biliopankreatischen Schenkel mit konsekutiver Ruptur im distendierten Restmagen ist eine der schwersten Frühkomplikationen nach Magenbypassoperation.

Spontaneous Rupture of a Hepatocellular Carcinoma
A Case Report

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Background

We report a case of haemorrhage due to spontaneous ruptured hepato-cellular carcinoma leading to a state of shock. This is a rare event in Western countries where the incidence of hepato-cellular carcinoma is < 3%.

Methods

A 76 year old male patient, who had been operated for rectal carcinoma 11 months before was referred for syncope. A focal liver lesion was known and had been characterised as focal nodular hyperplasia in contrast enhanced computed tomography and sonography.

Results

After stabilization of vital parameters emergent helical computed tomography showed active bleeding from segment IV of the liver with haemoperitoneum. Emergency laparotomy revealed a necrotic tumor mass of approximately 5cm in diameter with arterial bleeding. Resection of segment IV of the liver was performed after which the bleeding could be stopped. Histopathological work up confirmed the tumor to be a hepato-cellular carcinoma. In the postoperative course no complications ensued.

Conclusion

Haemoperitoneum as a first presentation of HCC is an unusual occurrence. Nevertheless, as this case shows, it has to be included in the differential diagnosis of patients presenting in a state of hypovolemic shock with no adequate trauma. This should raise special concern in patients with known focal liver lesions or underlying liver disease, e.g. cirrhosis.

Laparoskopische Splenektomie eines Littoral Zell Angioms

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Einleitung:

Das Littoral Cell Angiom (LCA) ist eine seltene vaskuläre Neoplasie der Milz ausgehend von den gleichnamigen Littoral Zellen, erstmals beschrieben von Falk et al 1991.

Material und Methoden:

Bei einem 66 jährigen Patienten wurde computertomographisch bei Pyrexie unklarer Genese eine Splenomegalie mit einer 5,5 cm grossen hypodensen Raumforderung am Unterpol gefunden. Aufgrund der Verdachtsdiagnose Milztumor stellten wir die Indikation zur laparoskopischen Splenektomie.

Ergebnisse:

Der Patient wird in Steinschnittlagerung Antitrendelenburg positioniert. Der Operateur steht zwischen den Beinen und ein Assistent rechts vom Patienten. Es werden 4 Zugänge (1x10mm Optiktrokar, 1x12mm Versaport, 2x 5mm Trokare) gesetzt. Es folgt die Mobilisation des Milzunterpols über Dissektion des Ligamentum splenocolicum und eingehen in die Bursa omentalis unter Durchtrennung des Ligamentum gastrocolicum mittels Ligasure sowie Fortsetzung der medialen Mobilisation mittels Durchtrennung der Arteriae gastricae breves. Nun erfolgt die Absetzung des Milzhilus mittels zweier Staplerapplikationen (Endo GIA, weisses Magazin, Tyco). Die Bergung erfolgt mittels Endo-Catch über eine Erweiterung des Zugangs im linken Oberbauch.

Schlussfolgerungen:

Hinter der Verdachtsdiagnose unklarer Milztumor verbirgt sich selten ein LCA. Seit der Erstbeschreibung 1991 sind weltweit in der englischsprachigen Literatur mehr als 60 Fälle des LCA beschrieben. Aufgrund potientieller maligner Entartung und möglicher Metastasierung empfehlen wir die videotechnische Splenektomie zur Diagnosesicherung und Therapie des LCA.

The numbers refer to the pages of this supplement.