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Article

2013

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## Right colon cancer : left behind ?

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### How to cite

GERVAZ, Pascal, BOUCHARDY MAGNIN, Christine, USEL, Massimo. Right colon cancer : left behind ?  
In: British journal of surgery, 2013, vol. 100, n° s5, p. 8. doi: 10.1002/bjs.9154

This publication URL: <https://archive-ouverte.unige.ch/unige:90372>

Publication DOI: [10.1002/bjs.9154](https://doi.org/10.1002/bjs.9154)

## Swiss Society of Surgery



The following abstracts will be presented at the 100th Annual Congress of the Swiss Society of Surgery, held in Berne 12–14 June 2013.

### Visceral

#### Effect of intra-operative infiltration with local anesthesia on the development of chronic pain after inguinal hernia repair. A randomized controlled triple-blinded trial

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**Objective:** Chronic pain is a common complication after inguinal hernia repair irrespective of the surgical technique. The objective of this randomized controlled triple-blinded trial is to assess the effect of intra-operative infiltration with local anesthesia versus placebo on the development of chronic pain after inguinal hernia repair.

**Methods:** Patients eligible for inguinal hernia repair were randomized into two groups between June 2006 and February 2011. One group (experimental group) received an injection of 20ml Carbostesin® (Bupivacain) 0.25% and the other group (placebo group) received an injection of 20 ml 0.9% Saline at the end

of the operation according to a standardised protocol. The patient, the surgeon and the outcome assessors were blinded. Clinical follow-up investigations were performed after one day, 2 weeks, 1, 3, and 12 months postoperatively. Three interim analyses with data monitoring committee meetings were performed to check whether stopping criteria were met or the sample size had to be adapted. The study was stopped after the third interim analysis for futility reasons because it was unlikely that significance could be reached within an adequate sample size and time. Chronic postoperative pain was estimated by means of a Visual Analogue Scale (VAS) and defined as any pain (VAS > 0) 3 months postoperatively.

**Results:** A total of 402 hernias in 356 patients were randomized. Baseline characteristics such as age, gender, and BMI were comparable between both groups. The incidence of chronic pain at rest three months postoperatively was 41% (n = 71) in the placebo and 47% (n = 82) in the intervention group (p = 0.216). One year postoperatively chronic pain was present in 50% in both the placebo and intervention group. VAS at rest at three and 12 months postoperatively in both groups was nearly identical with median 0 (interquartile range (IQR) 0–2 with the exception of the intervention group at one year with an IQR 0–3). Duration of surgery, length of hospital stay, postoperative complications, return-to work, and recurrence rate one year postoperatively were comparable between the two groups in a preliminary analysis.

**Conclusion:** There is no evidence that intraoperative infiltration of local anesthesia had an influence on the development of chronic postoperative pain at rest.

### Complications after Roux-en-Y gastric bypass: a 13-year experience with 1468 patients with analysis of risk factors

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**Objective:** Roux-en-Y gastric bypass (RYGBP) is one of the commonest performed bariatric procedures. Despite technological advances, improvements in surgical technique and anesthesia, it remains a technically challenging operation in high risk patients. This study reviews all early postoperative complications over a 13-year period in our series of RYGBP.

**Methods:** Our prospectively established database has been assessed to review early postoperative complications developing within 30 days of surgery or during the same hospital stay. For its grading, a validated score system (Clavien-Dindo) was used. Minor (Clavien-Dindo I-IIIa) and major (Clavien-Dindo IIIb-V) complications were separately recorded. Patient-related (e.g. age, gender, BMI, smoking, arterial hypertension) and procedure-related (e.g. surgical approach, surgical experience) factors were analyzed by performing a univariate analysis to identify potential risk factors.

**Results:** Between 1999 and 2011, 1468 patients underwent RYGBP, 343 males and 1125 females with a mean age of 40.7 years (18–67) and a mean BMI of 44.9 (17.7–76.2). 184 procedures were reoperations. Overall, 164 (11.2%) of the patients developed at least one complication. Major complications occurred in 43 patients (2.9%), leading to death in one case (0.06%). Risk factors for early complications were operative experience ( $p < 0.001$ ), reoperation ( $p = 0.002$ ), open ( $p < 0.001$ ) and prolonged ( $p = 0.002$ ) surgery. There was a trend for more overall complications in males ( $p = 0.08$ ). Major complications were associated with early experience ( $p = 0.002$ ) and smoking ( $p = 0.011$ ). There was a trend for patients aged  $> 50$  years ( $p = 0.09$ ) and for those with hypertension ( $p = 0.07$ ) to have more major complications. Other factors like BMI, diabetes, sleep apnea, teaching status, were not significantly associated with results.

**Conclusion:** The most significant individual risk factor for early complications after RYGBP is limited surgical experience and open surgery. RYGBP should be performed by experienced teams with a large case-load, and the laparoscopic approach should be preferred. Smoking should be discontinued several weeks before surgery. Care should be taken in older patients and in the presence of arterial hypertension.

### Anesthetic conditioning in liver transplantation. Results of a multicenter randomized controlled trial

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**Objective:** To evaluate the impact of pharmacological conditioning with the volatile anesthetic sevoflurane in liver transplantation.

**Background data:** In the age of organ scarcity and the increased use of older and steatotic organ grafts, protective strategies during transplantation are gaining importance. Volatile anesthetics such as sevoflurane attenuate ischemia-reperfusion injury in liver resection and lead to improved outcome. The aim of the present randomized controlled trial was to evaluate whether volatile anesthetics change clinical outcome also in liver transplantation.

**Methods:** Cadaveric liver recipients were randomized from 03/2009 to 08/2012 at three University Centers (Zurich, Sao Paulo, Ghent). Standard liver transplant patients were randomly assigned to propofol anesthesia (control group) or conditioning with sevoflurane (sevoflurane group), the anesthetic was accordingly applied for the entire liver implantation surgery. Postoperative peak of the aspartate transaminase (AST) was defined as primary endpoint. Secondary endpoints were in-hospital complications, hospital- and ICU stay.

**Results:** Ninety-eight patients, who underwent liver transplantation, were randomized to propofol ( $n = 48$ ) or sevoflurane ( $n = 50$ ). Peak AST after transplantation was 925 U/l (512–3274) in the propofol group ( $p = 0.73$ ) and

1097 U/l (interquartile range 540–2633) in the sevoflurane one. While the overall complication rate was not different, there was a trend towards less severe complications in the sevoflurane group: median complication score was grade IIIa (IQR II-IVb) for the propofol and grade II (IQR 0-IIIb) for the sevoflurane group (Odds ratio 0.51, 0.24 to 1.09,  $p = 0.08$ ). In the propofol arm 11 patients (23%) experienced delayed graft function, 7 (14%) in the sevoflurane one (Odds ratio 0.64 (0.20 to 2.02,  $p = 0.45$ ).

**Conclusion:** This first multicenter trial with different anesthesia regimens in liver transplantation showed comparable surrogate markers postoperatively, but a trend towards less severe complications in the sevoflurane group. Future trials should be adequately powered to assess complications and identify subgroups, which might benefit from anesthetic conditioning.

### Equal effectiveness of laparoscopic Sleeve Gastrectomy and Roux-Y-Gastric Bypass: one year results of the prospective randomized Swiss multicentre bypass or sleeve study (SM-BOSS)

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**Objective:** Laparoscopic Sleeve Gastrectomy (LSG) has been proposed as an effective alternative to the current standard procedure, the laparoscopic Roux-Y-Gastric Bypass (LRYGB). Prospective data comparing both procedures are rare. Therefore, we performed a randomized clinical trial assessing the effectiveness of the two operative techniques.

**Methods:** Two hundred and seventeen patients were randomized at four bariatric centres in Switzerland. Hundred and seven patients underwent a LSG and 110 patients underwent a LRYGB. The mean BMI of all patients was  $44 \pm 11.1$  kg/m<sup>2</sup>, the mean age was  $43 \pm 5.3$  years, and 72% were female. We looked at weight loss, reduction in co-morbidities, increase of quality of life according to GIQLI, and complications one year postop.

**Results:** Follow-up rate was 100%. Excessive BMI loss one year after the operation was similar between the two groups (LSG:  $72.3 \pm 22\%$  and LRYGB:  $76.6 \pm 21\%$ ,  $p = 0.2$ ). Except for GERD, which showed a higher resolution rate after LRYGB, the comorbidities were significantly improved after both procedures. Quality of life increased significantly in both groups (LSG: 99 to 127, LRYGB 99 to 127.5 points). Complications during the first postoperative year were equal in terms of the incidence of micronutrient deficiencies, and no reoperations. Two patients of the LSG group suffered from extreme GERD, in the LRYGB group there was one anastomotic ulcer and one stricture at the gastroenterostomy.

**Conclusion:** The two procedures are almost equally efficient regarding weight loss, improvement of comorbidities and quality of life one year after surgery.

### Primary wound closure with a limberg flap vs. secondary wound healing after excision of a pilonidal sinus: long term results of a Swiss multicenter randomized controlled study

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**Objective:** To compare primary wound closure with a limberg flap to secondary wound healing after excision of a pilonidal sinus. The short-term results were presented at the congress of the Swiss Surgical Society 2012. There was no significant difference in perioperative pain score, intake of pain killers when leaving hospital, and overall satisfaction three weeks after surgery.

**Methods:** From January 2006 to July 2012  $n = 103$  patients with excision of a pilonidal sinus were randomized to group A (primary wound closure with a Limberg flap,  $n = 51$ ) or to group B (secondary wound healing,  $n = 52$ ). Apparent abscesses were treated with incision and antibiotic therapy for at least 10 days prior to the randomization and definitive surgical treatment. Follow up was done after 3 weeks by examination and after 1 year by phone call.

**Results:** Baseline data: presence of recurrent disease 9% in group A vs. 18% in group B ( $p = 0.234$ ), presence of pori not located in the midline 35% in group A vs. 24% in group B ( $p = 0.269$ ), mean distance of the pori from the anus 5.8cm in group A vs. 5.9 in group B ( $p = 0.751$ ), presence of pus 10% in group A vs. 12% in group B ( $p = 1.000$ ), mean wound volume 35ml in group A vs. 39ml in group B ( $p = 0.828$ ), mean number of pori 1.7 in group A vs. 2.1 in group B ( $p = 0.029$ ). The median (range) of operation time was 60 (30–80) min. in group A vs. 30 (10–75) min. in group B ( $p < 0.001$ ). At long term follow-up median (range) of duration of incapacity for work was 4(0–16) weeks in group A vs. 4(0.5–14) weeks in group B ( $p = 0.515$ ) and overall satisfaction was 5.5(0–6) in group A vs. 5(3–6) group B ( $p = 0.973$ ). The procedure-specific overall complication rate was 49% in group A vs. 17% group B ( $p < 0.001$ ). Relapse occurred in 13% in group A vs. 6% in group B ( $p = 0.317$ ). Other complications were: seroma (6%), wound dehiscence (45%), necrosis (10%), hematoma (6%), infection (4%) in group A and wound inertia (6.5%) in group B.

**Conclusion:** At 1 year follow-up, excision of a pilonidal sinus and primary wound closure with a limberg flap has no advantage over excision alone and secondary wound healing.

#### Randomized clinical trial on the effect of coffee on postoperative ileus following elective colectomy

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**Objective:** Postoperative ileus is a common problem after abdominal surgery. Coffee is a popular beverage, and its effects on general well-being, the central nervous system and the cardiovascular system are well known. Although coffee may stimulate bowel function in certain healthy volunteers, there has been no prospective evaluation of its impact on intestinal function after elective colectomy. The aim of this randomized clinical trial was to assess whether coffee consumption accelerates the recovery of bowel function after elective colectomy.

**Methods:** This was a multicentre parallel open-label randomized trial. Patients with malignant or benign disease undergoing elective open or laparoscopic colectomy were assigned randomly before surgery to receive either coffee or water after the procedure (100 ml three times daily). The primary endpoint was time to first bowel movement; secondary endpoints were time to first flatus, time to tolerance of solid food, length of hospital stay and perioperative morbidity. To detect a clinically relevant absolute difference of 24 h in time to the first bowel movement with a two-sided significance level of 0.05 and a power of 80 per cent, it was calculated that 36 patients per study arm would be required. With an estimated dropout rate of 10 per cent, a total of 80 patients were needed.

**Results:** A total of 80 patients were randomized, 40 to each group. One patient in the water arm was excluded owing to a change in surgical procedure. Patient characteristics were similar in both groups. In intention-to-treat analysis, the time to the first bowel movement was significantly shorter in the coffee arm than in the water arm (mean (s.d.) 60.4 (21.3) versus 74.0 (21.6) h;  $P = 0.006$ ). The time to tolerance of solid food (49.2 (21.3) versus 55.8 (30.0)h;  $P = 0.276$ ) and time to first flatus (40.6 (16.1) versus 46.4 (20.1)h;  $P = 0.214$ ) showed a similar trend, but the differences were not significant. Length of hospital stay (10.8 (4.4) versus 11.3 (4.5) days;  $P = 0.497$ ) and morbidity (8 of 40 versus 10 of 39 patients;  $P = 0.550$ ) were comparable in the two groups. No patient died within 30 days of operation and the overall morbidity rate was 22 per cent, with no significant difference between the two groups.

**Conclusion:** Coffee consumption after colectomy was safe and was associated with a reduced time to first bowel action.

#### Roux-en-Y gastric bypass (RYGB) surgery leads to reduced bone mineral density (BMD) and metabolic acidosis in rats

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**Objective:** A decrease in BMD has been reported after RYGB surgery, potentially associated with vitamin D (VD) and calcium (Ca) malabsorption and consequential secondary hyperparathyroidism. However, because these conditions are frequently present in the obese population, it is unclear if they are the primary cause for bone changes after RYGB. We investigated changes in bone metabolism and Ca balance in rats after RYGB compared to a body-weight matched (BWM) control group.

**Methods:** Adult male Wistar rats were randomized for RYGB ( $n = 15$ ) or sham ( $n = 17$ ) surgery. Part of the sham rats were food restricted and BWM ( $n = 8$ ) to the RYGB animals. Pre-op and at 2, 7 and 14 weeks post-op, BMD was measured by m computed tomography (CT). 24 h Ca intake and fecal and urinary Ca loss were measured and blood sampling was performed for blood gas analysis and to determine Ca, VD, parathormone (PTH) and osteocalcin (OC) levels.

**Results:** BMD progressively decreased in RYGB rats in the first two post-op CT scans but then remained stable until week 14. Fecal Ca loss was only increased in RYGB rats 2 weeks after surgery, while urinary Ca loss remained elevated. RYGB rats had a lower blood pH, lower bicarbonate levels and higher lactate levels. Ca, PTH, and OC levels were unchanged, but active VD was significantly increased.

**Conclusion:** We conclude that RYGB rats are in metabolic acidosis, which may contribute to increased bone resorption. Potentially due to higher VD activation, Ca malabsorption was only present early after surgery and seems not to be the only cause of the bone loss.

#### Purse-string closure of the stoma site leads to fewer wound infections: results from a multicenter randomized control trial

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**Objective:** Surgical Site Infection (SSI) after stoma reversal is common. We hypothesized that a near-complete purse-string (PS) closure compared to conventional primary (CP) closure leads to fewer SSIs of the stoma site.

**Methods:** We performed a randomized controlled trial comparing PS and CP closure of ileostomy and colostomy sites from December 2008 through August 2012 at two university medical centers. The primary endpoint was SSI isolated to the stoma site within 30 days of surgery. Secondary endpoints were overall SSI and delayed healing (defined as a wound requiring a dressing beyond 30 days postoperatively). In a subset of patients, we determined time to complete epithelialization of the wound ( $n = 51$ ) and patient satisfaction with wound appearance ( $n = 55$ ) on postoperative days 7 and 30 using a 5-point Likert scale. We compared continuous variables using Student *t* tests and categorical data using chi-square and Fisher exact tests. Cox proportional regression and multiple logistic regression models were used to calculate hazard ratios for SSI and delayed healing adjusting for potential confounders.

**Results:** We enrolled 125 patients during the study period. Twelve patients were excluded because of protocol violations or insufficient follow-up. Baseline demographics, patient comorbidities, and perioperative variables were comparable between groups. Stoma site SSI was significantly lower in the PS group than in the CP closure group (2% vs. 15%,  $p = 0.0015$ ), but time to complete epithelialization was significantly longer (34.6  $\pm$  20d vs. 24.1  $\pm$  17d,  $p = 0.016$ ). Incidence of delayed healing was not significantly different (21% vs 15%,  $p = 0.392$ ). There was no difference in patient satisfaction between groups. Conventional primary closure was found to be a significant and independent predictor of stoma site SSI (HR 46.3, 95% CI 1.9–1117.7). Stoma site SSI was a significant independent predictor of delayed healing (OR 14.6, 95% CI 1.3–160.7).

**Conclusion:** PS closure of the stoma site after ileostomy or colostomy takedown has a significantly lower risk of stoma-site SSI than CP closure though wounds take longer to heal using this approach.

#### Portal vein resection during duodenopancreatectomy: a case-match analysis about safety and survival

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**Objective:** Portal vein (PV) and superior mesenteric vein (SMV) resections are nowadays considered as meaningful surgical approaches in case of pre- or intraoperatively suspected venous tumor invasion of a pancreatic head cancer. The oncological benefit in patients with histologically proven venous tumor infiltration remains unclear. The aim of our study was to analyze the results of pancreatic head resection with PV-SMV resection in patients with histologically proven venous tumor infiltration.

**Methods:** Out of 370 pancreatic resections performed at our institution from 2000 to 2012, 44 patients needed PV and/or SMV resection. We selected a subgroup of patients operated before 2012 in order to measure survival. We identified 21 patients with pancreaticoduodenectomy and PV-SMV resection for histologically proven venous tumor infiltration. These patients were matched with similar patients without PV-SMV resection one to one for age, gender, R status, N status and tumor size representing the most important predictors of survival.

**Results:** The PV-SMV resection group included 12 male and 9 female patients with a mean age of 68 years compared to 11 male and 10 female patients with a mean age of 66 years in the group without venous resection. In each group, 12 patients (57%) had R0 resection, 20 patients (95%) had N1 status, and mean tumor size was 37mm. Mean operative time was 430 min in case of PV-SMV resection compared to 354 min in the control group ( $p=0.006$ ); and mean blood loss were 768 ml and 620 ml, respectively ( $p=0.47$ ). Reconstruction could be performed with direct anastomosis in 15 patients, while 6 patients needed a vascular prosthesis. Mortality was identical in both groups (2 patients) and postoperative morbidity was 86% and 57%, respectively ( $p=0.088$ ). Of note, bleeding complications were not significantly different. Median survival, 1-year survival and 3 year-survival was 13 months, 53% and 28% in case of PV-SMV invasion compared to 11 months, 48% and 28% without venous resection ( $p=0.59$ ), respectively.

**Conclusion:** PV-SMV resection during pancreaticoduodenectomy in histologically proven venous invasion in patients with pancreatic adenocarcinoma is not associated with an impaired long-term survival. Despite prolonged operative times; postoperative morbidity and mortality are not increased. Thus PV-SMV resection should be recommended as standard in oncologic pancreatic resection if necessary.

#### Complications after cytoreductive surgery and Hyperthermic intraperitoneal chemotherapy (HIPEC)

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**Objective:** Cytoreductive surgery (CRS) and hyperthermic intraperitoneal chemotherapy (HIPEC) are criticized for high mortality and morbidity rates in the literature. A potential bias is an ongoing controversy on the use of a diagnosis-based grading system, as suggested by the consensus conference Milan 2006. Otherwise, a therapy-based classification system gained wide acceptance in the surgical literature. Here, we analyzed types, incidence and severity of complications after CRS and HIPEC. In addition, the two classification systems were compared and critically evaluated.

**Methods:** Postoperative complications were prospectively recorded in 114 consecutive patients. Grading of complications was defined by consensus in a weekly morbidity conference. All complications were graded by senior surgeons with both classification systems, both using five categories. In a second step, residents ( $n=40$ ) without experience with any of the two systems were randomized to evaluate a list of selected complications, either with the therapy- or the diagnosis-oriented classification system.

**Results:** The majority (68%) of patients had no postoperative complication. Pulmonary events were most frequent (11%), followed by prolonged ileus (11%), and anastomotic leaks/fistulas or pancreatic fistula (6%). Reoperation or readmission to intensive care was necessary in 10 (8.8%) patients, and most often due to anastomotic leaks/fistula, abscess formation or ileus. In-hospital mortality was 1.8% (2/114). Expert grading revealed a lower incidence of major (grades 3–5) complications in the therapy-based system compared to the diagnosis-based classification (16.7% vs. 29.9%,  $p=0.05$ ). The diagnosis-based system was not conclusive in 24% of cases for experts. Residents needed three times more time ( $P=0.001$ ), felt less safe ( $P=0.006$ ), and made twice more mistakes ( $P=0.001$ ) using the diagnosis-based system.

**Conclusion:** This is the first large series of CRS and HIPEC published in Switzerland, demonstrating that CRS and HIPEC can be performed safely with acceptable morbidity and low mortality. The diagnosis-based classification system should no longer be regarded as the standard for classification of complications after CRS and HIPEC. Instead, the therapy-based system is more simple and rapid, allows comparison with other major procedures, and should therefore be uniformly used to compare outcomes.

#### Molecular upstaging of lymph node negative colon cancers by one-step nucleic acid amplification (OSNA): results of the prospective, European, multicenter study

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**Objective:** Approximately 20% of colon cancer patients classified as lymph node (LN) negative by standard histology will suffer from recurrence. A new diagnostic semi-automated system, One Step Nucleic Acid Amplification (OSNA), detects cytokeratin (CK) 19 mRNA in LN metastases of colon carcinomas. The objective of this prospective, European, multicenter study was to assess whether histopathology pN0 patients can be upstaged to stage UICC III by OSNA.

**Methods:** From 103 colon cancer patients who were classified as LN negative after standard histology (single haematoxylin & eosin (H&E) slice), the LN were subjected to OSNA analysis. An OSNA result revealing a CK19 mRNA copy number exceeding 250 was regarded as tumor positive based on previous investigations.

**Results:** In total, 1594 pN0 LN from 103 colon cancers (median LN/patient: 14, range: 1–46) were analyzed with OSNA. From 103 pN0 patients 26 had OSNA positive LN, resulting in an upstaging rate of 25.2%. Hereunder were 6/37 (16.2%) stage UICC I and 20/66 (30.3%) stage UICC II cases. Overall, 38 LN were OSNA positive: nineteen patients had 1, three had 2, three had 3, and one patient had 4 OSNA positive LN.

**Conclusion:** OSNA resulted in an upstaging of over 25% of initially LN negative patients after conventional H&E analysis. OSNA is a standardized, observer-independent technique allowing the analysis of the whole LN. Therefore, the use of OSNA avoids sampling bias due to not investigated lymph node tissue and results in a more accurate staging in colon cancer patients.

#### A randomized controlled trial comparing emergency cholecystectomy first versus sequential common bile duct endoscopic assessment/cholecystectomy for suspected gallstone migration

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**Objective:** The management of patients with a clinical diagnosis of gallstone migration into the common bile duct (CBD) is a matter of debate. Endoscopic

CBD exploration is often performed prior to cholecystectomy, but most stones migrate spontaneously to the duodenum and many of these explorations are unnecessary. The present study explores the opportunity to perform an emergency cholecystectomy first, with the aim to decrease the length of stay, the number of required invasive endoscopic procedures and morbidity.

**Methods:** This randomized controlled trial included patients with a suspected diagnosis of acute gallstone migration (right upper quadrant pain, documented gallstone and increased liver function tests). Exclusion criteria were radiologically-proven CBD stone and/or acute pancreatitis, acute cholangitis and medical conditions preventing surgery or informed consent. Patients were 1:1 randomly assigned to a “control group” with the standard management of sequential CBD endoscopic exploration and cholecystectomy, vs. a “cholecystectomy first” group undergoing emergency cholecystectomy/per-operative cholangiogram first, and subsequent endoscopic stone extraction when required (power 90%, alpha 5%). Length of stay was the primary end-point.

**Results:** Forty-five patients were included in each arm. Both groups were similar regarding age, gender, BMI and the presence of an associated cholecystitis (21 versus 24,  $p=0.74$ ). Patients in the “cholecystectomy first” group had a shorter hospital stay ( $6.95 \pm 5.83$  vs.  $9.45 \pm 5.25$  days,  $p=0.040$ ), and underwent fewer invasive endoscopic procedures (16 versus 59,  $p < 0.0001$ ). Conversion to laparotomy was necessary in two “cholecystectomy first” and in one control patients ( $p=0.561$ ). Eleven patients in each group required the extraction of a remaining CBD gallstone, representing 22% of all patients. Severe complications (Dindo/Clavien grade III or IV) were seen in one “cholecystectomy first” (severe pancreatitis) and four control patients (abdominal abscess, severe pancreatitis, intestinal perforation and cystic duct bile leakage,  $p=0.17$ ); all four control patients required re-surgery/drainage (4 vs. 0,  $p=0.041$ ).

**Conclusion:** This study shows that patients with a suspected diagnosis of gallstone migration should undergo a cholecystectomy first, allowing for a shorter hospital stay, fewer invasive endoscopic procedures and a lower risk of severe complications.

#### Total tumor volume/alpha fetoprotein score for the selection of liver transplant candidate with hepatocellular carcinoma: a prospective validation

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**Objective:** The selection of liver transplant candidates with hepatocellular carcinoma (HCC) is currently validated based on Milan criteria (one HCC up to 5 cm or up to 3 HCCs each up to 3 cm), but the use of extended criteria is a matter of debate. The objectives of the present prospective multicentric study are to validate the previously proposed Total Tumor Volume (TTV  $\leq 115$  cm<sup>3</sup>) / alpha fetoprotein (AFP  $\leq 400$  ng/ml) selection score.

**Methods:** Patients were recruited in view of liver transplantation according to the TTV/AFP score and were prospectively followed-up. Data were collected and managed through an online database.

**Results:** From January 2007 to March 2012, 162 patients with HCC were listed for liver transplantation (28 females-134 males;  $56.8 \pm 6.2$  years). Of them, 134 patients were within Milan criteria, and 28 beyond Milan. The average follow-up from listing was  $35.4 \pm 21.1$  months. The risk of drop-out was higher for patients beyond Milan but within TTV/AFP (14/28, 50%) than for patients within Milan (19/132, 14.4%,  $p < 0.001$ ). Similarly, intent-to-treat survival from listing was lower in the patients beyond Milan but within TTV/AFP (49.6% vs. 79% at four years,  $p < 0.001$ ). After a mean waiting time of  $11.9 \pm 12.1$  months (median: 8), 88 patients were transplanted. Patients within Milan, and those beyond Milan but within TTV/AFP demonstrated similar post-transplant survivals (86.8 vs. 77.5 at four years,  $p=0.378$ ) and recurrence rates (4.5% vs. 10.5%,  $p=0.319$ ).

**Conclusion:** Increased dropout on the waitlist can be anticipated with the use of extended criteria for the selection of HCC liver transplant candidates. However, the present multi-centric prospective study confirms that the TTV ( $\leq 115$  cm<sup>3</sup>) / AFP ( $\leq 400$  ng/ml) score leads to stable post-transplant outcomes

(similar to Milan and non-HCC recipients), promoting its use in centers with at least 12-month waiting time.

#### What is the prevalence of intracranial bleeding in patients with mild traumatic brain injury and GCS 14–15: a retrospective study in 3088 patients

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**Objective:** Mild traumatic brain injury (MTBI) is a central issue in health care and is related to both the identification of individuals at risk and feasible treatment strategies. Until now there is only limited data on the prevalence of intracranial bleeding (ICB) in a large consecutive group of European patients with MTBI and GCS 14–15 on admission.

**Methods:** A retrospective study was conducted. Using our electronic patients records, we identified all patients presenting with isolated MTBI and GCS 14–15 at our emergency department that underwent cranial CT between 2002 and 2011. Cranial CT was performed according to the ‘Canadian CT Head Rules’. In case of ICB, patients were either submitted for further neurosurgical treatment or kept under surveillance for at least 24 hours. Pearson’s correlation coefficient was used to correlate the incidence ICB with age, intake of coumarins, thrombocyte aggregation inhibitors, heparins, or gender.

**Results:** A total of 3088 patients were identified. Mean age was  $41 \pm 20.5$  (7–99) years. Sixty-one percent were male. 149 patients (4.8%) were found to have ICB on CCT (62% male). No patient with ICB died or deteriorated neurologically. Three patients (<0.01%) required burr whole trepanation. The incidence of ICB after MTBI increased with the age and the intake of anticoagulants. However, there was no clinically relevant correlation of ICB with age ( $R=0.11$ ;  $p < 0.001$ ), intake of anticoagulant drugs ( $R= -0.06$ ;  $p < 0.001$ ) or gender ( $R=0.002$ ;  $p=0.455$ ).

**Conclusion:** Our data show a prevalence of 4.8% for ICB after MTBI. However, neurological deterioration after MTBI seems to be rare and the need for neurosurgical intervention is only required in selected cases. The general need for cranial CT in patients after MTBI is therefore questionable and clinical surveillance may be sufficient when cranial CT is not available.

#### Down-staging of tumor-positive lymph nodes in esophageal cancer by neo-adjuvant treatment: do these patients have the same prognosis as those with an a priori negative nodal status?

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**Objective:** Lymph node status is a well-known factor that impacts on long-term survival in esophageal cancer. Neo-adjuvant treatment is nowadays widely used in the purpose of down-staging advanced primary tumors and positive lymph nodes. Down-staging of positive lymph nodes is of particular interest, since they may be outside the resection field and remain in situ postoperatively. This study aimed to assess whether down-staged positive lymph nodes (cN+ to ypN0) have similar outcome as really negative (a priori) lymph nodes (cN0 and pN0).

**Methods:** Between 2000 and 2011 128 patients underwent esophagectomy for cancer in our institution, and out of them 64 had neoadjuvant treatment. For the present analysis, we included patients who were either preoperatively staged N0 (cN0) and postoperative confirmed N0 (pN0) (group 1), or preoperatively staged N+ (cN+) and histologically confirmed down-staged to N0 (ypN0) (group 2).

Preoperatively, lymph nodes were considered to be tumor positive (N+) either by radiological criteria and/or cytological assessment. Median and overall survival rates were determined by using Kaplan-Meier survival curves. Overall survival was defined as time from the index operation to the date of death. Chi-square test and Hazard ratio were used to determine significance of the different survival rates. Differences were considered significant at  $p < 0.05$ . Median follow-up time was 47 months.

**Results:** Sixty patients were assessed, 34 in group 1 and 26 in group 2. There were 29 male and 5 female patients with a median age of 63.5 years in group 1, compared to 22 male and 4 female patients with a median age of 64 years in group 2. In group 1, 11 patients had T3/4 tumors (32%), 21 out of 34 patients are still alive, median actuarial survival is 77 months. In group 2, 18 patients had T3/4 tumors (69%), 7 out of 26 patients are alive, median actuarial survival is 106 months. Even though survival was better in down-staged patients, the difference did not reach statistical significance (chi-square  $p=0.0524$ , HR, 2.23004, 95% CI 1.0547 to 4.7169).

**Conclusion:** Down-staging of tumor positive lymph nodes by neo-adjuvant treatment has a clear beneficial effect on long-term survival. Despite an increased quota of advanced tumor, patients with down-staged lymph nodes have an at least similar overall survival as patients with a priori tumor negative lymph nodes.

#### Blood substitution has no impact on long time survival after elective colon cancer resection: a propensity score analysis

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**Objective:** Whether peri-operative blood transfusion negatively impact survival is still controversial. The main aim of present study was to assess the putative impact of peri-operative blood transfusions on overall in patients undergoing curative resection of stage III colon cancer applying propensity-scoring methods.

**Methods:** In a single-centre study, 309 patients undergoing curative resection of stage I-III rectal cancer between 1996 and 2008 were assessed. The mean follow-up was 47 ± 38 months. Patients who did and did not receive peri-operative blood transfusions were compared using Cox regression and propensity score analyses.

**Results:** Overall, 148 patients (47.9%) received blood transfusions. Patients' characteristics were highly biased concerning transfusions (propensity score 0.61 ± 0.22 vs. 0.37 ± 0.22,  $p < 0.001$ ). In unadjusted analysis, blood transfusions were associated with a 90% increased risk of overall mortality (hazard ratio 1.90, 95% CI:1.19–3.04,  $p = 0.001$ ). The five-year survival for patients receiving blood substitution was 64.5% (95% CI:56.0%–74.3%) compared to 80.1% (95% CI:72.8–88.2%) for colon cancer patients not receiving blood substitutions. In propensity score-adjusted Cox regression (hazard ratio: 0.87, 95% CI:0.56–1.34,  $p = 0.520$ ) blood transfusions did not increase the risk of overall mortality. After adjustment the five-year survival for patients receiving blood substitution was 66.6% (95% CI:58.0%–76.4%) compared to 68.5% (95% CI:60.0–78.2%) for colon cancer patients not receiving blood substitutions.

**Conclusion:** This is the first propensity-score based analysis providing compelling evidence that worse oncological outcomes after curative colon cancer resection in patients receiving peri-operative blood transfusions are caused by the clinical circumstances requiring transfusions, not due to the blood transfusions themselves. Therefore, concerns about overall and disease-free survival should be no issue in the decision-making regarding peri-operative blood transfusions in patients undergoing curative colon cancer resection.

#### Preoperative assessment of esophageal cancer by using PET/CT: information on tumor behavior related to maximum standardized uptake values of the primary tumor

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**Objective:** Combined positron emission tomography and computed tomography (PET/CT) is increasingly used in diagnostics and monitoring of multimodal treatment of esophageal cancer. Metabolic imaging provides information on tumor localization, lymph node and distant metastases; but it also offers novel insights into tumor biology. This study assessed preoperative maximum standardized uptake values (mSUV) of FDG-PET/CT as a predictive factor for long-term survival, as well as for tumor biology and histology.

**Methods:** From 2005 to 2010, 79 consecutive patients underwent esophagectomy for cancer in our institution. Forty patients had a preoperative FDG-PET/CT; two were excluded from further analysis due to in-hospital death. Median survival and overall survival rates were determined by Kaplan-Meier survival curves. Chi-square test and Hazard ratio were used to determine significance of different survival rates. Differences were considered significant at  $p < 0.05$ . Rank correlation test was used to analyze correlation between mSUV values, tumor grading and histological type. ANOVA tests were used to assess the differences of mSUV for the various types of histology and tumor grading. Median follow-up time was 18 months (range 3–57).

**Results:** There was a statistically significant correlation between mSUV and tumor grading (G), in particular comparing G1/2 tumors (mean mSUV 10) vs. G3 tumors (mean mSUV 15),  $p = 0.006$ . However, mSUV values failed to distinguish between adenocarcinoma (mean mSUV 11) and squamous cell carcinoma (mean mSUV 12.7) ( $p = 0.344$ ).

By using mSUV=10 as a bench-mark, median survival was 38.5 months for mSUV < 10 vs. 29 months for mSUV > 10, but the difference was not statistically significant ( $p = 0.3$ ). Overall survival, calculated in patients who already died during the study period, was not correlated to preoperative mSUV values ( $p = 0.55$ ).

**Conclusion:** Preoperative mSUV values do correlate well with tumor grading, in particular to identify undifferentiated tumors (G3). Since survival is related to tumor grading, an increased mSUV > 10 could possibly indicate an impaired long-term survival. Adenocarcinoma and squamous cell carcinoma could not be distinguished because of largely overlapping mSUV values. Although preoperative mSUV value cannot be used as a reliable marker to predict survival, it could be of great value to monitor biological tumor response during preoperative oncological treatment.

#### Primary nonclosure of mesenteric defects during laparoscopic Roux en Y gastric bypass – Reoperations and intraoperative findings in 116 patients

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**Objective:** One of the major life threatening complications after Roux-en-Y gastric bypass (RYGB) are internal hernias, which have been reported with an incidence of 3%–6% in the literature. If not diagnosed early, internal hernias can lead to major morbidity and mortality via bowel incarceration and consecutive necrosis. Therefore strong advice to close mesenteric defects during RYGB has been proposed. The aim of our study is to analyze intraoperative findings in a cohort of 116 patients which had reoperations after primary nonclosure of mesenteric defects during their RYGB.

**Methods:** We searched our prospectively collected database for reoperations in patients with nonclosure of mesenteric defects during the RYGB procedure. Intraoperative findings were collected from the operative notes dictated by the attending surgeon. All operative notes with examined mesenteric defects were included.

**Results:** We identified 116 patients (17 male, 99 female) with a mean age of 44.9 (SD 10.6). 94 patients had reoperations because of pain (34 emergent, 60 elective) and 22 patients had reoperations for other reasons (weight regain, prophylactic inspection of mesenteric defects). Median time from RYGB to the reoperation was 36 months (range 3–144), mean EWL before the reoperation was 61% (SD 20.6). The incidence of internal hernias was 11.2%, with internal hernias at Petersen's space in 5 and internal hernias at mesojejunum space in 8 patients respectively. Petersen's space was found closed spontaneously in 4 and mesojejunum space in 19 cases. Mortality of nonclosure was 1 because of bowel ischemia with consecutive necrosis and death. 111 reoperations were performed laparoscopically and 5 led to conversion to open surgery. Early surgical complications because of the reoperations occurred in 5 patients (1 wound infection, 1 cystic stump leak, 3 bowel obstructions).

**Conclusion:** Nonclosure of mesenteric defects can lead to constant or intermittent pain due to internal hernia with consecutive bowel necrosis and death after RYGB. Spontaneous closure rate of Petersen's or mesojejunum defects is low. Diagnostic laparoscopy is mandatory in patients with primary nonclosure of mesenteric defects and clinical presentation of pain to rule out potential life threatening bowel necrosis. Secondary closure of mesenteric defects can be performed laparoscopically with low morbidity.

### Hypothermic oxygenated machine perfusion (HOPE) prevents biliary injury after transplantation of DCD liver grafts

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**Objective:** The use of livers from donors after cardiac arrest (DCD) is increasing in many countries to overcome organ shortage. Due to an inherent period of warm ischemia before preservation, those grafts are at higher risk of failure and bile duct injury. Several competing rescue strategies by machine perfusion techniques have been developed with however unclear effect on biliary injury after liver transplantation. Here we analyze the impact of an end-ischemic Hypothermic Oxygenated PErfusion (HOPE) approach, applied only through the portal vein for 1hr before graft implantation.

**Methods:** Rat livers were subjected to 30 min in situ warm ischemia, followed by subsequent 4hr cold storage, mimicking DCD-organ procurement and conventional organ transport. Livers in the HOPE group underwent also passive cold storage for 4hr, but were subsequently machine perfused for 1hr before implantation. Outcome was tested in both groups by liver transplantation (LT) at 12 h after implantation (n = 8 each group) and after 4 weeks (n = 8 each group), focusing on early reperfusion injury and later intrahepatic biliary injury.

**Results:** All animals survived after LT. However, reperfusion injury was significantly improved by HOPE treatment after transplantation as tested by hepatocyte injury (AST & HMGB-1 release, TUNEL staining), Kupffer cell activation (CD-68 staining), and endothelial cell activation (sE-selectin staining). In addition, rats receiving non-perfused DCD livers presented four weeks after liver transplantation with less body weight gain, increased bilirubin and severe intrahepatic biliary fibrosis. In contrast, HOPE treated DCD livers were protected from biliary injury 4 weeks after LT, as detected by cholestasis parameter, MRI and by histology (CK-19 and sirius red staining).

**Conclusion:** We demonstrate for the first time in a DCD liver transplant model that end-ischemic hypothermic oxygenated perfusion is a powerful strategy for protection against biliary injury.

### ALPPS is superior to conventional procedures to remove malignant liver tumors not resectable in one procedure

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**Objective:** To compare the clinical efficacy of the new liver resection technique "Associating Liver Partition with Portal Vein Ligation for Staged Hepatectomy" (ALPPS) with conventional techniques of portal vein ligation (PVL) or portal vein embolization (PVE) to achieve a complete tumor resection within 3 months.

**Methods:** Patients undergoing ALPPS in four liver surgery centers 2011–2012 were compared with patients who underwent conventional techniques with PVE and PVL between 2002 to 2012. Primary endpoint was complete (R0) resection at three months without recurrence. Secondary endpoints include 90-day mortality, complications, volume increase of the FLR and tumor recurrence. Multivariate analysis was performed to adjust for potential confounders.

**Results:** patients undergoing ALPPS were compared with 83 patients who underwent conventional PVE/PVL. 77% of ALPPS patients achieved R0 resection at three months compared to 58% in the conventional arm (OR 2.74, p=0.031). 90-day mortality in ALPPS and PVE/PVL was 14.9% and 6.0% respectively (p=0.20). Volume increase per day was 11 times more rapid in ALPPS (35 cc/day; interquartile range (IQR) 26.2–49.5) compared with PVE/PVL (3 cc/day, IQR 1.7–5.8), (p=0.001). Complications  $\geq$  IIB after stage one had a negative impact on volume growth (p=0.004). Systemic and local progression of tumor within 6 months after resection in both groups was comparable.

**Conclusion:** This study provides some evidence that ALPPS is better than PVE and PVL to achieve complete resection of extensive malignant liver tumors. These results support the need for longer follow-up in registries and randomized controlled trials (RCT) to definitively delineate the role of ALPPS in liver surgery.

### Robotic assisted living donor nephrectomy: long-term institutional report and analysis

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**Objective:** The number of living donor kidney transplantations has increased since the advent of minimally invasive surgery; robotic technology has further advanced laparoscopic techniques and facilitates more complex applications. Herein, we report our institutional experience with 750 robotically assisted donor nephrectomies between January 2000 and December 2012.

**Methods:** Donor nephrectomies were performed with the da Vinci Robotic Surgical System. This procedure involves four small trocar incisions and a short infraumbilical midline or Pfannenstiel incision for hand-assistance and extraction of the organ. Donor information and outcomes were retrospectively collected for 750 patients with a date of surgery prior to December 2012. At 1 year after transplant, recipient patient survival and graft survival data was retrospectively collected.

**Results:** Donors included 356 (47%) men and 393 (52%) women with a mean age of 36 years (range, 14–65 years), of which 38% were African American, 32% were Hispanic, 23% were Caucasian. The average body mass index (BMI) was 29 kg/m<sup>2</sup>  $\pm$  6 (range, 17–53), among which 30% of patients had a BMI of 26–29.9 and 39% had a BMI of 30 or more. In 95% of these cases, the left kidney was procured. Vascular anomalies were observed in 196 patients (26%), with a majority of these patients presenting with multiple left renal arteries. The average operative time was 147 min (range, 55–320 min) and 5 patients underwent conversion to open surgery. The median warm ischemia time was 110 s (range, 15–540 s) and the average blood loss was 74 ml (range, 5–1500 ml). Patients remained in the hospital for an average of 3 days (range, 0.8–11 days) and 59 patients (7.9%) were readmitted at a later time point. The average post-donation creatinine level was 1.3 mg/dl at both 6 and 12 months following nephrectomy. For recipients, patient survival and graft survival at 1 year after transplant was 98% and 97%, respectively.

**Conclusion:** In conclusion, robotic-assisted laparoscopic donor nephrectomy is a safe and effective surgical procedure, even in the presence of vascular anomalies and obesity. This represents the largest series of robotically performed living donor nephrectomies to date.

### Preliminary results of randomized double-blinded controlled trial comparing Sacral Nerve Modulation (SNM) with Pudendal Nerve Stimulation (PNS) for fecal incontinence

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**Objective:** Sacral Nerve Modulation (SNM) is an established treatment of refractory lower urinary tract and bowel dysfunction. For urological patients not yielding satisfactory results with SNM, Pudendal Nerve Stimulation (PNS) has been described and successfully tested. Furthermore some patients with fecal incontinence (FI) not responsive to SNM showed a good response to PNS. We therefore started a study to compare PNS with SNM for the treatment of FI.

**Methods:** Patients with FI were enrolled in a randomized double-blind study. During the screening period SNM and PNS were tested for one week each. We implanted two tined leads, one near a sacral root (S3/4) (SNM) and one near a pudendal nerve (PNS). By modification of the introduction device we developed a quick and easy technique for PNS-testing based on direct physical response. In the following double blind test phase we also randomized the sequence of lead-connection to the external stimulator. Improvement of symptoms of 50% and more was counted as success. If the test was successful in SNM-, PNS- or both test periods, the superior method was selected for permanent stimulation. The

correspondent lead was connected with the permanent neurostimulator (InterStim™ II) in a second procedure. In the case of equivalence PNS was favored.

**Results:** From 2010 to 2012 we included 22 patients, 18 female and 4 male (median age 68yr). In all patients tined leads were placed successfully in the SNM and PNS position (average surgery time 71min ( $\pm 27$ )) without complications. To date 20 patients are available for preliminary analysis because 2 are still blinded. Average pretreatment Wexner score of 15.6 ( $\pm 4.2$ ) improved under SNM and PNS to an average score of 10.9 ( $\pm 5.1$ ,  $p=0.001$ ) and 11.6 ( $\pm 5.4$ ,  $p=0.01$ ), respectively. These results correlated well with a significant improvement in visual analog scale (VAS) both for SNM and PNS ( $p=0.001/p=0.032$ ). Both scores didn't reveal a significant difference in reduction of FI comparing SNM with PNS ( $p=0.883/p=0.717$ ). In 16 (80%, 7 PNS; 9 SNM) of 20 patients either SNM or PNS evaluation or both were successful, leading to permanent implantation.

**Conclusion:** Both SNM and PNS are successful minimal invasive procedures for patients with FI. So far none has shown superiority. If SNM as the gold standard fails in certain patients, PNS should be tested as alternative minimal invasive treatment option.

#### First results on end-ischemic hypothermic oxygenated machine perfusion (HOPE) of human liver grafts donated after cardiac arrest

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**Objective:** To present first results of an end-ischemic hypothermic oxygenated machine perfusion on outcome in human liver transplantation, donated after cardiac death (DCD).

**Background:** Respecting national ethical rules, long donor warm ischemia times may occur in controlled DCD liver transplantation, with potentially high risk of graft failure and bile duct injury. In an attempt to improve these extended criteria DCD liver grafts, we applied hypothermic oxygenated perfusion before implantation.

**Methods:** Five adults received human livers, donated after controlled cardiac death (Maastricht category III), with an extended true warm ischemia time of 30 minutes (MAP < 50 mm Hg to flush). After declaration of death and waiting times, standard cold flush and storage were performed using IGL-1® solution (4 °C). In addition, hypothermic oxygenated perfusion (HOPE) was applied through the portal vein for 1–2 hours during recipient hepatectomy. Perfusate was cooled (10 °C), recirculated and oxygenated (pO<sub>2</sub> 50 kPa) using an ECOPS® device (Organ Assist) and UW machine solution (KPS®). Perfusion pressure was maintained below 3 mm Hg.

**Results:** All machine perfused DCD livers showed an excellent and immediate function after transplantation. Liver enzyme release and kidney function were comparable with matched DBD liver grafts. Median ICU and hospital stay were 2 and 16 days. Within a follow up of at least 6 months, no signs of intrahepatic biliary complications occurred.

**Conclusion:** This is the first worldwide report on cold machine perfusion of human DCD liver grafts and transplantation. End-ischemic hypothermic oxygenated liver perfusion appears safe, and has a great potential for clinical use due to its easy approach. In our early experience we observed no evidence of graft failure or dysfunction despite extended DCD criteria. Further studies are warranted.

#### Outcomes of primary repair of complex ano-rectal fistulas with endo-rectal flap advancement repair

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**Objective:** Although the majority of ano-rectal fistulas may be treated with fistulotomy, patients with higher-lying fistulas or women with anterior fistulas in whom simple fistulotomy may threaten continence present a management dilemma. The endo-rectal advancement flap is a surgical procedure used in the treatment of ano-rectal and rectovaginal fistulas.

**Methods:** A prospective study was performed on 407 consecutive patients receiving endo-rectal advancement flaps during a 10-year period (2000–2010). We excluded from this collective patients with Crohn's disease, post obstetrical injury. Only patients with crypto glandular origin were considered.

**Results:** There were 161 (39.5%) women, and 246 men (60.5%). Primary success was defined as resolution of symptoms for at least a 12-month period without an additional surgical procedure. If resolution of symptoms after flap placement was achieved after an additional minor surgical procedure, it was considered a secondary success. When a new flap procedure or fistulectomy was done it was considered as a recurrence. Primary success was achieved in 272 (66.8%) patients, and a secondary success in 48 (11.8%) recurrences in 87 (21.4%) patients, for a total success of 78.6 per cent. Functional results demonstrate 3 gas incontinence, 1 faecal soiling and 1 sphincter rigidity in a patient operated 11 times before endo-rectal flap.

**Conclusion:** Anal advancement flaps demonstrate a reasonable success rate when utilized in a group of patients with challenging ano-rectal fistulas. The advantage of this technique is the low rate of incontinence.

#### Right colon cancer – left behind?

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**Objective:** Colorectal cancer outcome has dramatically improved in Europe during the past three decades. Colorectal surgeons focused their effort on management of rectal cancer but surgical management of colon cancer has remained virtually unchanged since 1980. We hypothesized that, during the past three decades in Switzerland, improvement in rectal cancer survival was superior to improvement in colon cancer survival.

**Methods:** We performed a survival analysis based on a tumour registry, which includes a comprehensive cancer dataset for a population of about 450,000 since 1980 in a Swiss county. Data analysis was restricted to biopsy-proven adenocarcinomas of the colon and rectum.

**Results:** Data was available for 4,901 patients (right colon = 1,483; left colon = 2,305; rectum = 1,113). 5-year overall survival dramatically increased throughout the study period: it was 42% in 1980–84 and 65% in 2004–09 ( $p < 0.0001$ ). Patients with rectal cancer operated in the 2000s had 50% reduction in their risk of death in comparison with rectal cancer patients operated in the 1980s (Hazard Ratio = 0.48, 95% Confidence Interval .30–.77,  $p = .002$ ). This reduction in the risk of death was also observed for left colon cancer - but not for right colon cancer. After adjusting for age, sex and tumour stage, patients with right colon cancer showed a significantly worse outcome than patients with either left colon or rectal cancers (Hazard Ratio = 0.82; 95% Confidence Interval .75–.91,  $p = 0.0001$ ).

**Conclusion:** Our data indicate that, while the overall prognosis for colorectal cancer has markedly improved in Switzerland since 1980, patients with right colon cancer did not benefit from treatment advances as much as other patients. In 2010, patients with rectal or left-sided colon carcinomas have a better prognosis than patients with right colon tumors. Oncologically adequate right colectomy is oftentimes difficult to perform: this procedure should not be considered as a “big appendectomy” and abandoned to residents with little experience in surgical oncology.

#### Intraoperative signal loss in recurrent laryngeal nerve monitoring in the course of bilateral thyroidectomy – results of a two step strategy

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**Objective:** Intraoperative Neuromonitoring (IONM) has become a standard adjunct for thyroidectomy. In our institution, we have implemented a two step strategy: if signal loss of the recurrent laryngeal nerve (RLN) occurs while operating the first side of a planned bilateral thyroidectomy, surgery is limited to this side to avoid exposure and damage of the contralateral nerve. The second side will only be operated upon after having a laryngoscopically proven, impeccable vocal cord function postoperatively. The use of IONM and a two step strategy has the potential to completely avert the disastrous condition of a bilateral RLN palsy. However, little is known about the outcomes applying this strategy and the potential morbidity of the additional “unnecessary” procedure in case of a false positive signal loss.

**Methods:** This is a retrospective analysis of prospectively collected data on patients scheduled for total thyroidectomy in our institution from January 2008 to December 2012. The data of all patients in which a signal loss occurred on the first side of the procedure were analyzed concerning postoperative RLN-function, morbidity and timing of completion thyroidectomy.

**Results:** Of the 931 patients undergoing thyroid surgery during the mentioned period, 456 had an intended total thyroidectomy (49%). 9 Patients (2%) showed a signal loss on the first side that led to a limited unilateral resection; 3 of these (33%) had a documented RLN palsy postoperatively. All palsies recovered completely in time. Up to now, 7 patients have undergone completion thyroidectomy after normalization of vocal cord function with a deferment of 2 to 721 days (median 39 days). No RLN palsy occurred in completion thyroidectomies. Apart from 3 (42%) transient and 1 permanent parathyroid insufficiencies, there was no additional morbidity of the completion thyroidectomy. For the one-step bilateral procedure, the rate of transient parathyroid insufficiency was 22.9%. Eight transient (1.7%) and no permanent RLN palsies were observed.

**Conclusion:** The concept of an IONM-guided two step strategy to avert bilateral RLN palsy as the most disabling complication of thyroidectomy is very appealing. Despite a trend towards an increased rate of transient postoperative parathyroid insufficiency, without statistic significance ( $p > 0.05$ ), no additional morbidity compared to a one-step procedure was observed.

#### Prophylactic intraabdominal mesh implantation in high risk patients: preliminary results of a randomized controlled trial

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**Objective:** Incisional hernia is a frequent long-term complication in patients undergoing abdominal surgery and is associated with significant morbidity and cost. Prophylactic mesh implantation possibly reduces the risk of incisional hernia formation. Thus, a prospective randomized study is ongoing in order to evaluate the incidence of incisional hernia after three years in high risk patients undergoing elective abdominal surgery. We present short term results.

**Methods:** Patient were eligible for the study if at least two of the risk factors (male gender, body mass index  $>25\text{kg/m}^2$ , malignant tumor, previous laparotomy) were present and randomized into two groups. Control group: For the closure of the abdominal wall, a standard technique was applied using a running suture of PDS 1 loop. Treatment group: A polypropylene based mesh was placed intra-abdominally and fixed using non-absorbable sutures. Afterwards, the abdominal wall was closed as described in the control group. Up to now 100 patients were randomized into two groups and completed the 3 months follow-up control. Postoperative outcome was compared in 48 patients in the treatment group versus 52 patients in the control group.

**Results:** Demographic parameters such as age, gender, BMI, and number of risk factors were similar in both groups. There was no significant difference between the two groups in terms of duration of operation, hospital stay, and reoperation rate. At 3 months of follow-up the incidence of surgical site infections was comparable between the treatment and the control group (29.7% vs. 32.4%;  $p = 1.00$ ). No mesh infection was found. No intestinal fistula was found in both groups. Incisional hernia was found in one patient in the control group and in no patient in the treatment group (2.7% vs. 0%;  $p = 1.00$ ). In one patient in the control group and in no patient in the treatment group open abdomen was diagnosed (2.7% vs. 0%;  $p = 1.00$ ).

**Conclusion:** The low incidence of intra- and postoperative complications reveals the safety of a prophylactic procedure to prevent a frequent complication such as incisional hernia in high risk patients.

#### Mid-term results after perineal stapled prolapse resection for external rectal prolapse

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**Objective:** The aim of this study was to assess the mid-term recurrence rates, functional results, and patient satisfaction after perineal stapled prolapse resection.

**Methods:** From November 2007 to October 2011, a total of 56 consecutive patients were included in the study.

Recurrence rates, functional results according to the Wexner incontinence scale, and patient satisfaction using a visual analogue scale were determined.

**Results:** The median age was 78.5 years (range, 24–94 years), and 2 patients were men. Mid-term results were available for 46 (82%) of 56 patients after a median follow-up of 25.5 months (range, 2–47 months). In 10 cases (18%) data collection was not possible. The recurrence rate at 3 years was 19.7% (95% CI 4.2–32.7%). The Wexner incontinence score improved from a median of 14.5 pre-surgery to 4.0 points ( $p < 0.0001$ ) after surgery. 25 patients (54%) stated that their bowel movements were regular postoperatively. On a visual analogue scale that measured satisfaction, the median patient score was 9 (range, 0–10), indicating high patient satisfaction.

**Conclusion:** Perineal stapled prolapse resection is an alternative technique for treating rectal prolapse with a recurrence rate similar to the Altemeier-Mikulicz or Delorme's procedures. This technique is a quick and reliable procedure for use in patients with advanced age.

#### Survival assessment of patients with synchronous liver and lung colorectal metastases: a study based on the LiverMetSurvey

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**Objective:** Some studies have suggested that the presence of resectable lung metastasis (LM) should not alter the management of patients with colorectal liver metastasis (CRLM) aiming for a cure. The goal of this study, based on the LiverMetSurvey registry, was to test this assumption and define prognostic factors of survival in patients with synchronous liver and lung metastases.

**Methods:** All patients underwent a CRLM resection, and were allocated to three groups: CRLM only ( $n = 10702$ ), CRLM and resected synchronous LM ( $n = 174$ ), and CRLM and unresected synchronous LM ( $n = 303$ ). Liver and lung metastases were all simultaneous as diagnosed less than three months apart. Liver metastases were considered simultaneous when diagnosed less than one year after the primary colorectal cancer. Univariate survival assessments used Kaplan-Meier curves and log-rang tests, multivariate analyses used Cox regressions (all performed from the time of liver resection).

**Results:** Five-year univariate survivals were similar for patients with CRLM only or with resectable LM (47.1% and 42.1%,  $p = 0.892$ ), but lower in patients with unresectable LM (13.5%,  $p < 0.001$ ). In the multivariate analysis, factors independently associated with worse survivals included synchronous liver metastases (compared to primary), bilateral liver metastases and bilateral lung metastases. Patients with resected LM presented significantly less synchronous and bilateral CRLM, and less bilateral lung metastases (vs. CRLM only,  $p < 0.001$ ). When adjusted for similar risk factors, survival was significantly worse for patients with resected LM compared to patients with CRLM only ( $p < 0.001$ ).

**Conclusion:** Only selected patients with simultaneous colorectal liver and lung metastases can demonstrate similar survivals as those with liver metastases only. However, resection should be offered whenever possible due to the poor survival of patients with unresected lung metastases.

#### Gastrointestinal cancer volumes in Switzerland until 2035 – an estimation based on available national cancer incidences and a scenario for the future development of the Swiss population

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**Objective:** Centralization of major gastrointestinal (GI) surgery is highly debated in Switzerland. Precise estimation of cancer incidence and numbers of patients are pivotal to define health care resources. This study aimed to estimate volumes of esophageal, gastric, colorectal, and pancreatic cancer for the next 25 years.

**Methods:** Swiss Statistics ([www.bfs.admin.ch](http://www.bfs.admin.ch)) provides incidences on various cancer and models of future developments of the Swiss population. Cancer incidences (new cases per 100,000 inhabitants) from 1985 to 2009 were analyzed to estimate trends of future incidences. The most probable scenario of the future development of the population in Switzerland, as proposed by Swiss Statistics, was chosen, considering increased population age and migration phenomena. All data were obtained from the online database (STAT-TAB) of Swiss Statistics. Data of 2010 were used as contemporary baseline for comparisons.

**Results:** Incidences of esophageal, colorectal, and pancreas cancer steadily increased since 1985, and will probably further increase. Gastric cancer incidence reveals an ongoing decrease. In 2010, 505 new esophageal cancer cases were observed. The number of new cases increases to 678 and 817 in 2025 and 2035, respectively. Incidences for men and women for 2025 and 2035 are 11.9 and 4; and 13.9 and 5. Colorectal cancer has the highest incidences and numbers. 4080 new cases were observed in 2010. The number of new cases increases to 4,917 and 5,280 in 2025 and 2035, respectively. Incidences for men and women for 2025 and 2035 are 67.3 and 47.4; and 71.1 and 48.7. In 2010, 1,055 new pancreas cancer cases were observed. The number of new cases steadily increases to 1,359 and 1,451 in 2025 and 2035, respectively. Incidences for men and women for 2025 and 2035 are 14.8 and 16.8; and 15.3 and 17.5. There were only 780 new gastric cancer cases in 2010. A further decrease to 673 and 559 new cases in 2025 and 2035 is estimated. Incidences for men and women for 2025 and 2035 are 9.6 and 6.1; and 8 and 4.7.

**Conclusion:** Oncologic burden of GI cancer will significantly increase during the next two decades. Designated centers will need to massively enlarge health care resources to properly take care of these complex patient groups.

#### Five-year follow-up of patients with type 1 diabetes transplanted with allogeneic islets: the UIC experience

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**Objective:** This report summarizes a 5-year phase 1/2 islet transplantation clinical trial at the University of Illinois at Chicago (UIC). The goal was to test a strategy to achieve insulin independence with a lower islet mass, through the use of a tumor necrosis factor- $\alpha$  receptor antagonist (etanercept) and a glucagon-like peptide-1 analog (exenatide). We have previously reported that this addition to the Edmonton protocol is associated with a significantly lower number of islets required to achieve insulin independence, during a 15-month follow-up. The current study extends our previous report and provides detailed long-term data on the transplant outcomes.

**Methods:** In this single center trial, 10 patients received 1–3 transplants. The first 4 subjects received the Edmonton immunosuppressive regimen and the remaining 6 subjects received the UIC immunosuppressive protocol (Edmonton plus etanercept and exenatide). Long-term follow-up included measurement of HbA1c, C-peptide, and glucose every 3 months; renal function tests every 6 months; and advanced metabolic tests, including mixed meal, oral glucose tolerance, intravenous glucose tolerance, and glucagon stimulation, yearly.

**Results:** All 10 patients achieved insulin independence after 1–3 transplants. At five years of follow-up, six of the seven patients remaining in the study were free of exogenous insulin. All patients attained positive C-peptide levels, a HYPO score of 0, and a significantly improved  $\beta$ -score. Most patients maintained HbA1c levels under 6.5%. Five patients changed immunosuppressive medication from sirolimus to mycophenolate mofetil (MMF) due to side effects, and kidney function remained stable or improved. A total of 3 patients were withdrawn before the study end.

**Conclusion:** The steady decline of islet function over time is an unfortunate clinical reality. In order to identify and implement strategies that minimize this temporal decline, reports of long-term follow-up in current clinical trials are of importance. This clinical trial at UIC enabled 60% of initially transplanted patients to achieve insulin-independence five years after their first transplant. Comparison between the 2 groups at the study end was limited by the patient size, given that 3 withdrew. The difference in outcomes between the 2 protocols, supporting potential improvement in graft function with the UIC protocol, needs validation in a larger sample.

#### Mini-laparotomy versus laparoscopically assisted ventriculo-peritoneal shunt placement: a prospective randomized controlled trial

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**Objective:** In ventriculo-peritoneal shunt (VPS) surgery, laparoscopic assistance can be used for placement of the peritoneal catheter. In this single centre randomized controlled trial we compared the rate of shunt complications and failures for laparoscopic assistance versus traditional mini-laparotomy.

**Methods:** 120 patients scheduled for VPS surgery were randomized to laparoscopic or mini-laparotomy (i.e. open insertion) of the peritoneal catheter. Primary endpoint was the rate of overall shunt complication/failure within 12 months from surgery. Secondary endpoints were distal shunt failure rate at 6 weeks, 6 months and 12 months, overall complication/failure at 6 weeks and 6 months, duration of surgery and hospitalisation, and morbidity.

**Results:** Overall shunt complication/failure rate was 15% (9 patients) in the laparoscopic group and 18.3% (11 patients) in the mini-laparotomy group ( $p = 0.404$ ). Patients in the laparoscopic group had no (0%) distal shunt failures compared to the mini-laparotomy group (8%,  $n = 5$ ;  $p = 0.029$ ). Intra-operative complications occurred in two patients (laparoscopic group), and abdominal pain led to catheter removal in one patient per group. Infections occurred in one patient (1.7%) in the laparoscopic group and three in the mini-laparotomy group (5%). Mean duration of surgery and hospitalisation was similar in the two groups.

**Conclusion:** This randomized controlled trial provides compelling evidence that use of laparoscopic shunt placement significantly reduces the rate of distal shunt failure compared to open approach surgery, resulting in a trend towards fewer overall shunt failures.

#### Acute modulation of glucagon-like peptide-1 (GLP-1) signaling is not involved in the control of energy expenditure after Roux-en-Y gastric bypass (RYGB) surgery in rats

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**Objective:** Compared to traditional weight loss strategies, the compensatory decrease in energy expenditure (EE) in response to body weight loss is attenuated after RYGB surgery. Because basal and postprandial GLP-1 levels are increased after RYGB surgery, and because GLP-1 has also been shown to increase EE, we investigated if increased GLP-1 levels are involved in the alterations in EE after RYGB.

**Methods:** Adult male Wistar rats were randomized for RYGB ( $n = 8$ ) or sham surgery ( $n = 17$ ). Part of the sham operated rats were food restricted and body weight-matched (BWm,  $n = 8$ ) to the RYGB animals. The effects of acute subcutaneous administration of the GLP-1 antagonist exendin-9 (30  $\mu\text{g}/\text{kg}$ ) and the GLP-1 agonist exendin-4 (5  $\mu\text{g}/\text{kg}$ ) on EE were tested using indirect calorimetry. Rats were fasted during the light cycle before injections with exendin-9 (ex-9) and exendin-4 (ex-4), respectively. EE was measured in the fasted state for one hour and during ad libitum access to food, and food intake (FI) was recorded.

**Results:** Ex-9 increased FI only in RYGB rats. EE was lower in RYGB and BWm compared to sham operated, ad libitum fed rats, but significantly higher in RYGB compared to BWm. There was no effect of ex-9 treatment on EE in either group of animals. Similarly, ex-4 decreased FI more in RYGB than in sham rats but did not modulate EE.

**Conclusion:** We conclude that acute modulation of GLP-1 signaling is not directly involved in the altered EE after RYGB surgery in rats.

### The remains of the day: bile duct injuries related to single-port laparoscopic cholecystectomy - a meta-analysis of randomized controlled trials.

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**Objective:** Single-port laparoscopic cholecystectomy (SPLC) has recently emerged as a new surgical technique. The initial experience was characterized by a lack of standardized operative techniques and preliminary technical equipment. Its evaluation was done by retrospective analysis of small case series. Thereby, an increased rate of bile duct injuries (BDI) compared to standard laparoscopic cholecystectomy (LC) was detected. Despite the incidence remained low, devastating consequences implied that this rise should be considered as not acceptable. This current study assessed the rate of BDI during SPLC compared to standard LC by performing a meta-analysis of randomized trials that have been published during last years.

**Methods:** A systematic review of the literature was performed from Medline, Embase and Web of Science databases, according to the PRISMA guidelines. Articles published from January 1990 to November 2012 were identified; and from these, only randomized controlled trials (RCT) comparing SPLC versus LC reporting BDI rate were included. Jadad score was used to assess the quality of the studies. The meta-analysis was performed using Review Manager 5.1 software.

**Results:** The review of the literature yielded 499 publications. Of these, 11 RCT including 858 patients were finally integrated into the meta-analysis. While nine RCT had Jadad scores <4, the two remaining studies were considered as high quality (Jadad score 4–5). The rate of BDI was 0.89% for SPLC and 0.24% for LC; the difference was not statistically different (overall effect:  $Z = 0.89$ ,  $p = 0.38$ ). The heterogeneity was zero ( $\text{Chi}^2 = 0.76$ ,  $df = 3$  ( $p = 0.86$ );  $I^2 = 0\%$ ). Forest-plots were only possible of four studies, whereby three of these four studies were in favor of LC.

**Conclusion:** With increasing experience, improved technical equipment and better standardization of the surgical technique, BDI rates of SPLC seems to be comparable to standard LC. However, results must be analyzed with caution as the overall quality of RCT remains low; and they are clearly underpowered. Based on the current evidence, SPLC cannot be recommended as standard technique for laparoscopic cholecystectomy.

### Predictors of failure to reach a sufficient liver volume prior to hepatectomy after portal vein embolization

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**Objective:** Portal vein embolization (PVE) is well established to induce liver hypertrophy in patients with liver tumors and small future liver remnant (FLR) precluding safe hepatectomy. In some cases PVE fails to induce liver hypertrophy which may result in excessive waiting times to hepatectomy leading to increased tumor progression rates. Aim was to describe factors associated with failure of hypertrophy after PVE in patients.

**Methods:** Patients undergoing PVE for malignant disease were extracted from an international multicenter database containing 160 patients treated with multiple methods to induce liver hypertrophy between 2002 and 2012. Demographics, comorbidities, disease-related parameters, pre and post PVE FLR volumes were analyzed. Standardized FLR(%) was determined using a formula based on body surface area. Logistic regression analysis was performed identifying risk factors for failure to reach the recommended cut-off of 30% sFLR prior to hepatectomy.

**Results:** Forty-eight patients (M:F = 28:20 and median age (range) = 60(40–76) years) underwent PVE for malignant disease. Indications were colorectal liver metastases (n = 21), hepatocellular carcinoma (n = 7),

intrahepatic or hilar cholangiocarcinoma (n = 12) and other (n = 8). Complete FLR volume data were available in 46 patients. Median (IQR) pre-embolization sFLR(%) was 24(20–29)%. After a median (range) waiting time of 42 (21–168) days, median (IQR) FLR (%) increased to 32(27–40)%. Nineteen (41%) patients did not reach the cut-off of 30% sFLR prior to hepatectomy. High body mass index ( $\text{kg}/\text{m}^2$ ) ( $p = 0.02$ ), chemotherapy prior to PVE or in waiting interval ( $p = 0.05$ ), low pre-embolization sFLR(%) ( $p < 0.0001$ ) and high INR ( $p = 0.03$ ) were risk factors for not reaching the cut-off of 30% sFLR after PVE in univariable analysis. In multivariable analysis only low pre-embolization sFLR(%) ( $p = 0.002$ ) and high INR ( $p = 0.03$ ) were associated with not reaching asFLR of 30%.

**Conclusion:** Despite proven success in a large number of patients, PVE fails to induce sufficient growth of the FLR in almost half of the patients in this multicenter cohort. Especially in patients with low pre-embolization sFLR, alternative portal vein manipulation strategies such as ALPPS may be a better approach.

### Natural history of sigmoid diverticulitis: a prospective cohort study

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**Objective:** The natural history of sigmoid diverticulitis is poorly investigated. Relevant information is currently restricted to population-based databases, or retrospective studies. We prospectively assessed the risks of recurrence and complications in a cohort of patients who had a first episode of uncomplicated diverticulitis.

**Methods:** A prospective cohort study of 285 patients who were admitted between January 2007 and December 2011 for a first episode of simple sigmoid diverticulitis documented with CT scan. After successful medical management of the first episode, follow-up was conducted through yearly telephone interviews. A Cox proportional hazard regression was performed to model the impact of various parameters on eventual recurrences and complications.

**Results:** At a median follow-up of 3 years, 83.6% of patients did not present any recurrent attack, and were completely asymptomatic. 46 patients (16.4%) experienced a second episode of diverticulitis: 1- and 3-year recurrence rates were 20%, and 31% respectively. 6 patients (2.1%) developed complicated (Hinchey I-IV) recurrent diverticulitis, and 4 patients (1.4%) underwent emergency surgery for peritonitis (Hinchey III-IV). In multivariate analysis, an elevated serum C-reactive protein (CRP) during the first attack was correlated with the risk of early recurrence: patients with a CRP level >240 mg/L had a 22% recurrence rate, while those with a CRP <240 mg/L had a recurrence rate of 8% at 6 months ( $p = 0.03$ ).

**Conclusion:** This prospective study demonstrates the benign nature of simple sigmoid diverticulitis. Overall recurrence rate in this series is 16%. Patients with CRP >240 mg/L are three times more likely to suffer recurrent episode. The risk to develop a complicated second episode, and for undergoing emergency surgery is less than 2%.

### EpCAM expression varies significantly and is differentially associated with prognosis in the luminal B HER2+, basal-like, and HER2 intrinsic subtypes of breast cancer

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**Objective:** Epithelial cell adhesion molecule (EpCAM) is frequently expressed in breast cancer, and its expression has been associated with poor prognosis. Breast cancer can be subdivided into intrinsic subtypes, differing in prognosis and response to therapy. The aim of our study was to investigate the association between EpCAM expression and prognosis in the intrinsic subtypes of breast cancer.

**Methods:** We performed immunohistochemical studies on a tissue microarray encompassing a total of 1365 breast cancers with detailed clinicopathologic annotation and outcomes data.

**Results:** We observed EpCAM expression in 660 of 1365 (48%) cases. EpCAM expression varied significantly in the different intrinsic subtypes. In univariate analyses for all cases, EpCAM expression was associated with significantly worse overall survival. In the intrinsic subtypes, EpCAM expression was associated with an unfavorable prognosis in the basal-like and luminal B HER2+ subtypes, but associated with a favorable prognosis in the HER2 subtype. Consistently, specific ablation of EpCAM resulted in increased cell viability in the breast cancer cell line SKBR3 (ER-, PR- and HER2+), but decreased viability in the breast cancer cell line MDA-MB-231 (ER-, PR-, HER2-).

**Conclusion:** The differential association of EpCAM expression with prognosis in intrinsic subtypes has important implications for the development of EpCAM-targeted therapies in breast cancer.

#### The impact of graft implantation order on short- and long-term graft survival in simultaneous pancreas-kidney transplants

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**Objective:** The preferred order of revascularization of pancreas and kidney grafts in simultaneous pancreas-kidney transplants has not yet been established. Increased preservation time might have a negative impact on graft function. In particular increased cold ischemia time is associated with a higher risk of technical failure in pancreas grafts. In this study, we investigate the influence of graft implantation order in simultaneous pancreas-kidney transplants on short- and long-term graft survival.

**Methods:** 12,700 simultaneous pancreas-kidney transplants from the Scientific Registry of Transplant Recipients were analyzed. Graft implantation order was determined based on the ischemia times of pancreas and kidney transplants, respectively. Pancreas and kidney graft survival were analyzed depending on graft implantation order at 3 months, 6 months and 5 years using Kaplan-Meier plots. Significance was tested with logrank test and cox regression model.

**Results:** In 8,454 transplants the pancreas was implanted first (pancreas before kidney, PBK) and in 4,246 transplants the kidney was implanted first (kidney before pancreas, KBP). Pancreas graft survival at 3 months was significantly higher in the PBK group (90.6 versus 89.3%,  $p=0.024$ ). Cox regression analysis revealed that graft implantation order as well as time span between pancreas and kidney implantation are significantly associated with pancreas graft survival at 3 months ( $p=0.011$  and  $p=0.010$ , respectively). When kidney graft implantation was delayed by  $>2$  hours from pancreas implantation, difference in graft survival increased to 2.3% (90.1 versus 87.8% pour PAR et RAP,  $p=0.009$ ). Pancreas graft survival at 6 months and 5 years as well as kidney graft survival were similar in both groups.

**Conclusion:** Pancreas graft implantation first in simultaneous pancreas-kidney transplants increases short-term pancreas graft survival. Graft implantation order does not affect long-term pancreas and kidney graft survival.

#### Outcome after neoadjuvant therapy for locally advanced rectal cancer of the upper third

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**Objective:** Neoadjuvant chemoradiotherapy (CRT) is the standard for mid and lower rectal cancer stage II or III. There is a controversy if patients with upper rectal cancer will benefit from CRT. The present study demonstrates perioperative results and morbidity for patients with upper rectal cancer after CRT. 3- and 5-year-disease-free (DFR) and 3- and 5-year-overall survival (OSR) rates were calculated for all patients and separately for responders and non-responders. Results were compared with patients with mid/lower rectal cancer and neoadjuvant CRT.

**Methods:** Patients with rectal cancer stage II or III were treated by CRT with 50.4 Gy and Capecitabine followed by surgery. For staging a standardized protocol was used. Tumor distance was measured by rectoscopy. If tumor

was  $\geq 10$  cm from anal verge it was defined as upper rectal carcinoma. All patients underwent total mesorectal excision with coloanal anastomosis or rectal amputation. Follow-up was documented in our tumor data base.

**Results:** From 5/2005—8/2012 a total of 164 patients with rectal cancer were treated by neoadjuvant CRT, 30 of them had a tumor of the upper third. A major complication was seen in 7% of the upper rectal cancer group and in 8% of the mid/lower group. No anastomotic insufficiency was observed in the upper group, three in the mid/lower group. A complete histopathologic response was seen in 33% of the upper rectal cancer group, compared to 14% in the mid/lower group ( $p < 0.05$ ). The 3- and 5-year OSR were 96% and 60% for upper rectum and 89% and 83% for mid/lower rectum ( $p = ns$ ). The 3- and 5-year DFR were 92% and 76% for upper rectum, 84% and 74% for mid/lower rectum ( $p = ns$ ). For responders to CRT 3-year OSR was 100% (upper rectal group) and 86% (lower rectal group). Results for non-responders were 93% and 87% resp. ( $p = ns$ ).

**Conclusion:** Neoadjuvant CRT for upper rectal cancer is as successful as for rectal cancer located in the mid/lower third. Surgery after CRT can be performed safely with low morbidity (7%). Complete histopathologic response was exceptional high in our collective (33%). Long-term-results are comparable to patients with mid/lower rectal cancer and are excellent for responders to the neoadjuvant CRT.

#### Hepatic resection of noncolorectal, nonneuroendocrine, nonsarcomatous, nonovarian metastases (NCNSO): the Mount Sinai medical center experience

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**Objective:** Hepatic resection is a well-established treatment for colorectal and neuroendocrine tumors. However, its role remains ill-defined and controversial for patients with metastases from other primary sites. The objective of this study is to analyze the outcome of hepatic resection for noncolorectal, nonneuroendocrine, nonsarcomatous and nonovarian (NCNSO) liver metastases and to identify the factors that may predict survival.

**Methods:** Between June 1988 and January 2012, 121 patients underwent liver resection for NCNSO metastases in our Division. We analyzed patient demographics (gender, age), tumor characteristics (site of primary, histology of primary, time of occurrence, presence of extrahepatic disease, size, number, distribution), treatment (extent of the resection, margins), and postoperative outcomes (complications, follow-up, recurrence and survival).

**Results:** We selected 82 patients. We classified them in different categories based on their primary cancer: breast (18), respiratory (11), gastrointestinal (25), endocrine (13) and genitourinary (15). Thirty day postoperative mortality was 0%. The median follow-up was 15 months. Median time for recurrence was 10 months. Overall survival at 1, 3, and 5 years was 98.7%, 67.3%, and 43.5%. Median survival was 37 months. None of the variables analyzed was identified on multivariate analysis as an independent predictor of survival.

**Conclusion:** Resection of NCNSO metastases in this series achieved results comparable to those reported for colorectal and neuroendocrine tumors.

#### Compression anastomoses in colorectal surgery — a prospective audit of 179 patients

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**Objective:** Anastomoses following colorectal resections usually are done in double stapling technique by single use circular stapling devices with titanium staples. Serious risks of anastomotic construction in the colon and rectum include dehiscence and stricture formation. There is a resurgence of interest in sutureless anastomoses formed by pure compression, evoking minimal early inflammatory response whilst maintaining anastomotic integrity. Herein we present our experience using the ColonRing™ in colorectal surgery.

**Methods:** Between October 2008 and October 2012 prospective data of all patients undergoing colorectal resection with rectal reconstruction using a compression anastomotic device at the St. John of God Hospital, Vienna, was collected and analysed.

**Results:** patients (79 female) with a median age of 64.8 years (range = 23–88) underwent surgery for benign (n = 96; 53.6%) and malignant (n = 83; 46.4%) indications. Surgery was performed laparoscopically in 149 (83.2%) cases. There were no technical problems related to the device. All donuts were complete and air test was negative in 99.4%. Diverting stoma was performed in 52 cases. Anastomotic leaks were seen in 6 (3.4%) cases. 30-day mortality was 1.1%. Overall morbidity accounted for 18.6%. 13 (all diverted) out of 53 (24.5%) patients following (ultra-) low anterior resection experienced pain caused by the presence of the ring. All symptoms subsided after ring removal. In non-diverted patients ring passed spontaneously in 98.4%. Two anastomotic strictures (3.3%) were seen during endoscopic follow-up of the initial 60 cases at 6 months.

**Conclusion:** Construction of rectal anastomosis using this novel compression device is feasible and safe and appears to cause only few anastomotic leaks and strictures in the medium term. Discomfort or pain as long as the ring is in place can be observed in a relevant number of patients following (ultra-) low anterior resection.

#### Simplified two-timepoint FDG-PET/CT imaging for pancreatic lesions. Is it helpful in determining pancreatic tumors?

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**Objective:** Predicting the dignity of pancreatic lesions is still a diagnostic challenge. Fusion of FDG-PET/CT with diagnostic computed tomography offers new possibilities, nevertheless the differentiation between benign changes in chronic pancreatitis from pancreatic cancer remains difficult. Therefore the aim of this study was to evaluate, whether early two-timepoint kinetics of pancreatic lesions in FDG PET may be helpful to differentiate pancreatic lesions.

**Methods:** We prospectively analyzed 64 patients (pancreatic cancer n = 45, chronic pancreatitis n = 19) scheduled for two-timepoint FDG-PET/CT scan for pancreatic lesions in our hospital between 2005–2011. Studies were performed 60 and 90 minutes after application of the radioactive substance. Histological samples were collected for all patients, either by resection or by biopsy. Semi-quantitative analysis was performed using the minimal, the maximal and the average standardized uptake value (SUV) from the two different sets of images and a SUV change was calculated as difference between the two measurements in percent. SUV changes of patients with pancreatic cancer and chronic pancreatitis were compared using the student t-test.

**Results:** Mean change of SUVmin. was 12.04% for pancreatic cancer vs. -4.66% for chronic pancreatitis respectively (p = 0.00012). Mean change of SUVavg. was 12.13% for pancreatic cancer vs. -5.65% for chronic pancreatitis respectively (p < 0.0001). Mean change of SUVmax. was 18.18% for pancreatic cancer vs. -4.92% for chronic pancreatitis respectively (p = 0.00026).

**Conclusion:** The present analysis shows a statistically highly significant difference comparing the changes in SUVmin., SUVavg. and SUVmax. in early two-timepoint PET/CT images of pancreatic cancer and chronic pancreatitis. This is one of the first analysis of two-timepoint PET/CT performed as early as 30 minutes after the initial study. The additional time and effort is minimal and fits perfectly into the existing, clinical workflow. Therefore, in patients with suspicious pancreatic lesions the simplified two-timepoint FDG-PET/CT represents an excellent diagnostic option and is helpful in characterizing pancreatic lesions.

#### Quantification of islet loss and graft functionality during immune rejection using iron-labeled islet cells by 3-Tesla MRI in the rat model

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**Objective:** As biological markers are not suitable for early diagnosis of islet graft dysfunction, MRI has been used to study islets that were labeled pre-transplant with superparamagnetic iron oxide nanoparticles (SPION). However, the relation between the graft functionality assessed by glycemia and the MRI signal remains unclear.

**Methods:** We transplanted hyperglycemic Lewis rats intra-portal with ferucarbotran-labeled syngeneic (n = 10) or allogeneic islets (n = 12) with 2500 islet equivalents (IEQ). For xenogeneic transplantations, we transplanted human islets in normoglycemic Lewis rats (5000 IEQ). The graft functionality was assessed by serum human C-peptide level. Images were acquired on a clinical 3-Tesla MRI scanner.

**Results:** When rejection occurred at day 4 and 8 in the xenogeneic and allogeneic recipients, 60% (57/68) and 55% (46/73) of the initial signal remains compared to 93% (71/104) and 82% (59/90) in the syngeneic controls (p = 0.006 and 0.03). Taking a cut-off value of less than 84% at day 4 for diagnosis of rejection, we obtained a sensitivity of 91% and a specificity of 70%. Based on MRI signal at day 4, introduction of anti-lymphocytic serum from day 4 allows graft rescue in 75% of cases.

**Conclusion:** In our model, MRI of pre-transplant SPION labeled islets is suitable for early diagnosis of immune rejection.

## General Surgery and Traumatology

#### Local bone mineral density has no influence on the risk for mechanical failure after angle stable plate osteosynthesis of distal radius fractures in the elderly. A prospective, multicenter cohort study

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**Objective:** There is evidence that osteoporotic bone is a predictor for the risk of treatment complications in elderly patients; this has yet to be substantially evaluated in clinical studies. Our prospective, multicentre observational study set out to evaluate the influence of local bone mineral density (BMD) on the rate of mechanical failure after locking plate fixation of distal radius fractures in the elderly.

**Methods:** Two-hundred and forty-nine patients (age range: 54–88 years) with a closed distal radius fracture were treated with a volar locking plate in 6 different hospitals. Clinical and radiological examinations were scheduled at 6 weeks, 12 weeks, and 1 year. All complications were reported and functional outcome of the upper limb and wrist was evaluated using the Disabilities of the Arm, Shoulder, and Hand (DASH) and Patient Rated Wrist Evaluation (PRWE) questionnaires. Dual-energy x-ray absorptiometry (DXA) measurements from the contralateral distal radius were taken at 6 weeks to assess local cancellous BMD status. For the comparative analysis of BMD and complication status, all patients were categorized as either a “mechanical failure” or “control” based on whether they experienced a defined complication (e.g. loss of reduction, delayed healing, secondary screw loosening) or not during the 1-year period, respectively.

**Results:** The study collective comprised 230 women and 19 men with low BMD (mean = 0.624 g/cm<sup>2</sup>). Of 249, nine patients suffered from a mechanical failure with an estimated risk of 3.6%. The mean BMD for mechanical failure patients (0.561 g/cm<sup>2</sup>) was similar to that for the control group (0.626 g/cm<sup>2</sup>). Functional outcome improved throughout the 1-year period, but DASH and PRWE scores did not return to pre-injury levels indicating some remaining disability for the study population. At 1 year, mechanical failure patients had significantly worse DASH and PRWE scores compared to the control group (p < 0.001).

**Conclusion:** The estimated risk for elderly patients with a volar locking plate-treated distal radius fracture to experience a mechanical failure complication is low, and in line with already published data. No association could be shown between BMD and mechanical failure risk. Other factors than BMD may play a greater role in the occurrence of mechanical failure complications associated with palmar plating of distal radius fractures in the elderly.

### Prophylactic intraperitoneal onlay mesh (IPOM) is feasible and safe and prevents incisional hernias – short-term results of a randomized controlled trial

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**Objective:** Incisional hernias occur in up to 20% of all open abdominal surgeries. This study examines the use of a prophylactic stripe of intraperitoneal onlay mesh (IPOM) to prevent incisional hernia following midline laparotomy.

**Methods:** This prospective, randomized and controlled trial was started in August 2008. Patients undergoing median laparotomy are randomly allocated either to abdominal wall closure according to Everett alone with a PDS-loop running suture (group A) or to the same procedure with an additional stripe of IPOM (group B). The primary endpoint is the incidence of incisional hernias at 2 and 5 years following midline laparotomy. Secondary endpoints are the feasibility and safety of the mesh implantation even in contaminated situations (Alteimer grade I–III), and the identification of risk factors for incisional hernias. Patients with contaminated situation grade IV were excluded from this study. This study is registered on [www.clinicaltrials.gov](http://www.clinicaltrials.gov).

**Results:** Up to date, 246 patients were included in this study, 130 patients in group A and 116 patients in group B. Separated to the different grade of wound contamination the allocation in group A is n=39 grade I; n=29 grade II, n=62 grade III, and in group B: n=34 grad I; n=24 grad II; n=58 grad III, respectively. So far 11/130 in group A and 10/116 in group B died or had a re-laparotomy independent of the mesh and had to be excluded for further analysis. Up to now (median follow-up time 25 months) 17/119 (15%) in group A and 7/106 (7%) in group B had an incisional hernia. In 1/116 patient the mesh had to be removed due to a migration into the subcutaneous tissue. No mesh penetration and no bowel obstruction due to the mesh did occur. One burst abdomen occurred in group A and one in group B.

**Conclusion:** The short-term results indicate that the placement of an IPOM-stripe with prophylactic intention is a feasible and safe procedure and halves the risk for an incisional hernia compared to conventional closure of the abdominal wall.

### The impact of coding systems for the injury severity score (ISS) on the valuation of polytrauma patients

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**Objective:** In order to guarantee a nationwide high-quality trauma management, the Swiss government has decided 2011 to allocate polytraumatised patients to 12 core centers (Level 1 trauma centers). Patients with an injury severity score (ISS) >20 or patients with a traumatic brain injury have to be treated in one of these facilities. The ISS is based on the abbreviated injury scale (AIS). The method of determination of the AIS varies among hospitals. During the coding of the ISS of the patients in our institution in the years 2010 and 2011, we found significant ISS differences depending on the coding method used. These results show the necessity of uniform coding methods in Switzerland to be able to compare different centers.

**Methods:** All trauma patients entering our resuscitation room during 2010 and 2011 were coded by one single resident in order to eliminate inter-observer bias. An abbreviated version of the original AIS manual was used as coding method. The calculated ISS codes were compared to ISS codes that were determined by the emergency team with the use of extended text modules and calculators respectively, used by the Swiss Society of Intensive Care.

**Results:** During the two years period, 396 patients entered our resuscitation room, most of them as polytraumatised patients. The coding of the ISS done by the doctors in charge in the resuscitation room with the aid of the text modules and calculators of the Swiss society of intensive care (Mean 13 points) showed a significant undercoding in two thirds of the patients compared to coding with the AIS manual (Mean 21 points,  $p = 0.002$ ). The median showed 8 ISS-points less coded by the text modules compared to the AIS manual.

**Conclusion:** Depending on the coding method used to assess the trauma severity expressed by the ISS, a significant undercoding can appear. As the ISS is one of the key factors for the comparability and quality control within the 12 level 1 trauma centers in Switzerland, there is a strong need for standardised and uniform coding methods.

### Transumbilical single-port laparoscopic transabdominal preperitoneal repair of inguinal hernia: progress in reducing invasiveness

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**Objective:** Conventional laparoscopic repair of inguinal hernia usually requires 3 ports. Recently, single-port laparoscopic surgery techniques have been developed to further minimize surgical trauma and invasiveness compared to conventional laparoscopic surgery. We want to present our experience in single-port transabdominal preperitoneal (TAPP) repair of inguinal hernia.

**Methods:** Since August 2011, data from single-port TAPP interventions have been prospectively collected. Until now, 193 single-port TAPP were performed—51 in patients with bilateral hernia and 142 in patients with unilateral hernia, 10 (5,2%) of them were recurrent hernia. The overall mean BMI was 25 kg/m<sup>2</sup> and mean age was 48.7 years.

**Results:** Median hospitalization period was 2 days, no difference between patients with unilateral and bilateral hernia was observed. Median operation time was 63 minutes for unilateral and 102 minutes for bilateral hernia. Mean fascial incision length was 24.7 mm ( $\pm 9$  mm), median skin incision length was 31 mm ( $\pm 8.5$  mm). In 7.8% one or in 2.1% two additional 5 mm trocars were used due to intraabdominal adhesions, major hernias or technical problems. No additional trocars were placed in patients operated for recurrent hernia. No intraoperative complications were observed. No conversion to open surgery was necessary. Postoperative course was uneventful in most patients, there were two revisions for bleeding resp. Hematoma (one open) and one Single Port revision for small bowel obstruction. Up to now no recurrence was observed.

**Conclusion:** Single-port TAPP represents a safe and generally applicable surgery technique (even for the repair of recurrent hernia). The use of additional trocars is mainly due to improve patient safety. Moreover, it is nearly scarless and minimizes surgical trauma.

### Influence of vanadium 4+ and 5+ ions on the differentiation and activation of human osteoclasts

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**Objective:** Recent research indicates that metal ions and inflammation driven osteoclasts play a crucial role in the pathophysiological mechanisms of implant failure. This study investigated whether vanadium ions induce differentiation of monocytic osteoclast precursors into osteo-resorptive multinucleated cells and influence the activation and function of in vitro generated osteoclasts.

**Methods:** Human monocytes were isolated from peripheral blood monocytic cells (PBMCs). Osteoclasts were generated from PBMCs in the presence of osteoclast differentiation cytokines. The cells were exposed to increasing concentrations (0–3 microM) of vanadium 4+ and 5+ ions for 7 days. The osteoclastic viability, differentiation, and resorptive function were assessed using standard colorimetric cell viability assay 3-(4,5-dimethylthiazol-2-yl)-5-(3-carboxymethoxyphenyl)-2-(4-sulfophenyl)-2H-tetrazolium, inner salt (MTS), fluorescence microscopy, tartrate-resistant acid phosphatase (TRAP) expression (ELF97 and flow cytometry) and functional cell culture resorption assays on bone slide during a period of 21 days.

**Results:** The MTS colorimetric assays showed a significant reduction in cellular viability by vanadium 4+ and 5+ concentrations above 3 microM ( $p < 0.05$ ). Vanadium 4+ and 5+ ions concentrations above 0.5 microM showed a negative effect on osteoclastic differentiation, activation (decrease of TRAP-positive cells) and resorptive function (decreased resorption on bone slide cultures) (all  $p < 0.05$ ) without affecting cell viability. No significant differences were noted between vanadium 4+ and 5+ ions ( $p > 0.05$ ).

**Conclusion:** These results suggest that vanadium 4+ and 5+ ions at concentrations below 3 microM (e.g. released by biocorrosion from orthopedic implants) have a negative effect on osteoclast differentiations and function without affecting cell survival. One can conclude that vanadium-containing implants may reduce bone remodeling by decreasing osteoclast activity. Our results may help developing new metal alloys and/or implants, which may reduce the rate of implant failure.

#### Arthroscopic repair of traumatic isolated subscapularis tendon lesions Lafosse III-IV: a prospective MRI-controlled case series with one year follow-up

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**Objective:** Arthroscopic repair of subscapularis (SSC) lesions is an evolving technique gaining increasing acceptance among shoulder surgeons. However, there are only a few studies available and evidence in the literature is low. To our knowledge there are only two other studies combining a clinical follow-up with MRI/CT arthrography investigations after arthroscopic repair of isolated high grade SSC tendon lesions.

**Methods:** Prospective consecutive case series, approved by the local ethical committee. Between 01/08 and 09/10 eleven patients (9 male, 2 female; median age 43 years, range 32–56) with traumatic isolated SSC tendon lesions Lafosse III-IV underwent arthroscopic repair including long head of biceps tenodesis. All patients were preoperatively assessed by the Constant-Murley score (CMS) and MR arthrography. CMS was obtained regularly until one year. Patient satisfaction was graded between 4 (excellent) and 1 (poor). With the last follow-up a MR-study was performed to assess structural integrity of the repair. The SSC muscle was compared to its preoperative condition regarding fatty infiltration (Goutallier) and size (cross-sectional area).

**Results:** Median time interval from trauma to surgery was 27 days (range 8–400). Arthroscopy revealed 9 grade III lesions (non-retracted) and 2 grade IV lesions (retracted) according to the Lafosse classification. All patients attended their regular clinical follow-ups. MRI was refused by one patient with an excellent clinical outcome (CMS 94). Median CMS improved from 43 (16–80) preoperatively to 93 (51–100) after one year ( $p < 0.001$ ). The functional tests also showed a significant improvement ( $p < 0.001$ ) when compared to the preoperative findings (Belly press: 5 (3–5) vs. 3 (2–3); Gerber lift-off: 5 (3–5) vs. 3 (2–3)). Patient satisfaction was high (4 (2–4)). All tendons showed complete structural integrity. There was a decrease of the fatty infiltration from Goutallier 2 (0–3) to 0.5 (0–2) ( $p < 0.05$ ) and the size of the cross sectional area increased from 1630mm<sup>2</sup> (900–2120) to 2265mm<sup>2</sup> (1370–3080) ( $p < 0.001$ ).

**Conclusion:** Arthroscopic repair of higher grade SSC lesions provides reliable tendon healing accompanied by excellent functional results one year after surgery. In our series, we observed significant decrease in fatty SSC muscle infiltration and an increase of muscular mass.

#### Stabilization of proximal humeral fractures using the multiloc proximal humeral nail

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**Objective:** The optimal operative treatment for proximal humeral fractures is still controversial. The new MultiLoc Proximal Humeral Nail offers several modular proximal locking options to achieve optimal bone anchorage. The central position of the nail provides a shorter leverage arm of the screws compared to plates. Correct nail placement prevents subacromial impingement sometimes occurring in conventional plating. The purpose of this study was to analyze our first results using the MultiLoc Proximal Humeral Nail for stabilization of displaced proximal humeral fractures.

**Methods:** Over a period of 15 months we prospectively collected the data of proximal humeral fractures stabilized with the MultiLoc nail. The patients underwent clinical and radiologic evaluations after 6 and 12 weeks as well as 6 and 12 months postoperatively.

**Results:** 34 patients, 24 women and 10 men, with a mean age of 69 years (range 41–92) were treated with a MultiLoc nail. According to the Neer classification the majority ( $n = 17$ ) were 2-part proximal humeral fractures; eleven 3-part, two 4-part and four proximal humeral shaft fractures were stabilized. We had four losses of follow up, one because of death, three due to comorbidities. So far three implant related complications occurred: one secondary loss of reduction and two interfering proximal screws, all these cases required early implant removal. No other major complications were observed. At three months the average shoulder flexion was 116°, the average shoulder elevation was 106° with no signs of implantation related rotator cuff lesions. So far no signs of delayed fracture healing could be noted.

**Conclusion:** The new MultiLoc nail is a reasonable alternative implant for the stabilization of proximal humeral fractures. Variable screw positioning aiming for optimal bone stock especially in osteoporotic bone provides better stability and less loss of reduction. The multilocking screw heads have to be placed flush with the cortex to prevent subacromial impingement. The early shoulder movement at three months was excellent, still improving one year postoperatively. To outline the difference between nailing and angle-stable plating more long term results and larger series are necessary.

#### Correlation between preoperative nutritional screening tools and postoperative complications

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**Objective:** Preoperative nutrition has been shown to reduce postoperative complications in selected patients at nutritional risk. A multitude of various biological and anthropometric parameters has been suggested along with several scores; the best nutritional screening tool is however still debated.

**Methods:** A recently performed randomized trial on preoperative nutritional interventions (NCT00512213) provided the study cohort of 152 patients at nutritional risk (Nutritional Risk Score  $\geq 3$ ) with detailed prospective documentation of diverse nutritional parameters ( $n = 20$ ) and potential demographic ( $n = 7$ ) and surgical ( $n = 4$ ) confounders. In a first step, risk factors for overall, infectious and severe (Dindo III-V) complications were identified by univariate analysis; significant parameters ( $p < 0.10$ ) were then entered in a multiple logistic regression model.

**Results:** Univariate analysis identified co-morbidity ( $P = 0.010$ ), low hemoglobin level ( $P = 0.071$ ) and upper GI surgery ( $P = 0.065$ ) as risk factors for overall postoperative complications. Severe postoperative complications tended to occur more often in patients with low body mass index (BMI) ( $P = 0.082$ ), lean body mass ( $P = 0.028$ ), and low albumin levels ( $P = 0.097$ ). Non-compliance with the nutritional intervention ( $P = 0.079$ ) was related with postoperative infections. Multivariate analysis identified co-morbidity (OR 6.33, CI 1.75–22.85) and low hemoglobin concentration (OR 2.70, CI 1.16–6.28) as independent risk factors for overall postoperative complications. Compliance with nutritional supplements (OR 0.39, CI 0.16–0.96) was independently associated with decreased infectious complications, while no risk factor was retained after multivariate analysis for severe complications. Interestingly, diverse widely used nutritional parameters did show absolutely no correlation with the postoperative morbidity.

**Conclusion:** No surrogate parameter for malnutrition appeared isolated to be strongly related with overall, severe and infectious complications. Nutritional screening using one single validated instrument is likely enough to select patients for nutritional interventions.

**Prospective, double-blind, randomized controlled single-centre trial: suppression of surgeons skin flora during surgical procedures using a new antimicrobial surgical glove**

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**Objective:** Microbial contamination of a surgical site represents a risk for the development of SSI. Undetected glove perforations are common; their frequency increases with the duration of wear, allowing skin-flora, regrown after pre-operative skin preparation, to contaminate the surgical site. A sterile antimicrobial surgical glove featuring a proprietary complex coating with chlorhexidine as active ingredient on its inner surface has been developed. We hypothesized that antimicrobial gloves might reduce the risk of surgical site contamination in the event of an intraoperative breach of the glove's integrity by suppressing re-growth of skin-flora during the complete course of a surgical procedure.

**Methods:** The study was designed as a clinical, randomized, controlled, double-blind single-centre trial to measure any differences that occur in the bacterial skin population of surgeons' hands during surgical procedures under antimicrobial and non-antimicrobial surgical gloves. This trial was registered with Current Controlled Trials, number ISRCTN71391952.

**Results:** For the antimicrobial gloves, the mean cfu/ml count was  $0.28 \pm 0.61$  (median: 0.00; LQ: 0.00; UQ: 0.00); mean  $\log_{10} = 0.02$  (range: 0.00–0.30). For the non-antimicrobial gloves, the mean cfu/ml count was  $65.00 \pm 68.00$  (median: 54.00; LQ: 3.00; UQ: 100.00); mean  $\log_{10} = 1.32$  (range: 0.00–2.39). After a mean of 112 minutes operation time, the  $\log_{10}$  cfu/mL difference was 1.30 and statistically significant ( $p < 0.001$ ).

**Conclusion:** It was demonstrated that a new antimicrobial surgical glove was able to suppress surgeons' hand flora during operative procedures by a magnitude of 1.30  $\log_{10}$  cfu/mL. In the event of a glove breach, this strategy may have the potential to prevent bacterial contamination of a sterile surgical site, thereby decreasing the risk of SSI and increasing patient safety. Further clinical studies are needed to confirm this concept.

**Instant capillary lactates to evaluate bowel ischemia: proof of concept in a porcine model**

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**Objective:** The Edge™ lactate analyzer (ApexBio, Taiwan) is a handheld device that measures lactatemia using test strips equipped with a specific biosensor. Only a small amount of blood (<3  $\mu$ L) which can be obtained by needle-puncturing is required and results are obtained in less than 45 seconds. The aim of this study was to assess the hypothesis that capillary lactates measured on the intestinal serosa may guide the extent of bowel resection, and correct site of anastomosis, in a porcine model of mesenteric ischemia.

**Methods:** Six pigs were included in this study. A 3–4 cm ischemic segment was created in 6 small bowel loops (total=36 loops) by clamping the vascular supply. Duration of clamping ranged from 1 to 6 hours. Five regions of interest (ROIs) were visually identified as the ischemic zone (1), the viable margins of resection (2a-2b) and the normal (3a-3b) zones. ROIs were marked with a surgical pen. Every hour, capillary blood samples were obtained by puncturing the bowel serosa at the ROIs and lactates were measured using the EDGE® analyzer. Accuracy of the analyzer was evaluated by Spearman rho comparing femoral arterial lactatemia, measured with a standard blood gas analyzer, with groin capillary lactates, which are supposed to reflect systemic lactatemia.

**Results:** Spearman rho correlation between systemic arterial and groin capillary lactate per all the time points was 0.9. Mean capillary lactates were statistically significantly higher at the presumed viable margins of resection (2a/2b) than at the normal areas (3a/3b) after 1h of ischemia ( $p = 0.0095$ ). At longer time, there was no difference. Mean capillary lactates (mmol/L) were significantly higher at the ischemic zone (ROI 1) than at the presumed viable

margins of resection (2a/2b) at all the time points but after 5h of ischemia, and higher than at the normal zones (ROIs 3a/3b) at all the time points (Table).

**Conclusion:** Intraoperative measurement with the EDGE™ revealed discordance between visual evaluation and bowel serosa capillary lactate at the presumed viable margins of resection after 1 hour of ischemia. Further studies are needed to establish the optimal threshold and “dynamics” of capillary lactates which ensure adequate intestinal perfusion in more complex surgical situations, such as colorectal resection/anastomoses.

**Is smaller better? - 2.7 mm implants for osteosynthesis of displaced lateral malleolar fractures**

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**Objective:** Displaced lateral malleolar fractures AO 44-A1–C3 are usually treated with open reduction and internal fixation using either 3.5 mm 1/3 tubular plates or 3.5 mm reconstruction plates. In very distal fractures, it can be difficult to place enough screws in the distal fragment to achieve satisfactory stability. Due to thin soft tissue coverage, conventional implants often are bulky and can interfere with soft tissue, especially with the peroneal tendons. New 2.7 mm implants are less bulky and allow placement of more screws over a given distance. Osteosynthesis of lateral malleolar fractures using finer implants can be performed safely and provides good stability.

**Methods:** Retrospective analysis of all lateral malleolar fractures treated operatively at our institution in a two years period between January 2010 and December 2012. Patient reports, x-rays and follow up data were collected and compared regarding wound and fracture healing, rate of infections and implant failures.

**Results:** A total of 339 patients with a displaced lateral malleolar fracture (AO 44-A1–C3, 174 women, 165 men, mean age 49.5 years) with or without an injury of the ipsilateral tibia were treated operatively. 174 patients were treated with a 3.5 mm implant, 134 patients with a 2.7 mm implant and 31 patients with either only screws or other implant combinations.

164 patients in the 3.5 mm group and 111 patients in the 2.7 mm group were treated with a single plate to stabilize the lateral malleolus. 33 patients, mainly those featuring very distal fractures or/and osteoporotic bones, were treated with double plate osteosynthesis.

The two single plate groups showed no difference concerning age, operating time or the anaesthesia technique. More female patients were treated with 2.7 mm plates. Regarding wound and fracture healing, infection rate and implant failure, there was a tendency of less complications in the 2.7 mm group.

**Conclusion:** Smaller and therefore less bulky 2.7 mm implants offer new possibilities and better stability for the treatment of displaced lateral malleolar fractures without increasing implant failure but showing a tendency to less soft tissue irritation and wound complications compared to conventional 3.5 mm implants. In combination with the use of double plate techniques, especially in osteoporotic bone, these implants can be beneficial and may be the preferred implants in the future.

**A radiolucent, carbon fibre reinforced synthetic plate for distal radius fractures: first experience**

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**Objective:** Steel and titanium are widely and successfully used implant metals in traumatology. However, some disadvantages are related to metallic implants: They provoke artefacts in computed tomography (CT) and magnetic resonance imaging (MRI). Also, bone healing might be difficult to monitor in x-ray studies due to the invisibility of the bone underlying the implant. Furthermore, hardware removal still remains an issue, especially with titanium implants. In order to avoid these problems carbon fibre reinforced polyetheretherketone

(PEEK) implant material has been developed. The main advantages of this synthetic material are radiolucency, artefact-free imaging, good fatigue properties and biocompatibility. In spine surgery carbon fibre reinforced PEEK implants have been successfully used and documented for the last few years. Recently palmar plates for distal radius fractures have been developed.

**Methods:** Five consecutive cases of dorsally displaced extraarticular distal radius fracture were stabilized with a palmar semi-rigid carbon fibre reinforced PEEK plate with angular stable screw fixation (icotec AG, Altstätten, Switzerland). Integrated radiopaque tantalum filaments and metallic screw tips allow correct placement of the plate and make the implant visible under image intensifier. A clinical and radiographic follow up was performed at 2 and 6 weeks, and at 3 and 6 months.

**Results:** The range of motion at final follow up was comparable to the contralateral wrist and all patients were pain free. Bony union was achieved in all cases. We did not record any infections, secondary dislocations, tendon ruptures or other complications.

**Conclusion:** We present our first experience on a new carbon fibre reinforced synthetic palmar plate for distal radius fractures. The implant might represent an interesting alternative to metallic implants. Potential advantages are radiolucency, no adherence to surrounding tissues and no artefacts in CT and MR imaging. A disadvantage of the implant is the missing multidirectional screw fixation, making it difficult to use in complex fracture situations.

#### A mass casualty incident - training the entire rescue process at a Swiss level 1 trauma center

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**Objective:** In September 2012, a mass casualty incident (MCI) was trained at the emergency department of a Swiss trauma center (2 resuscitation rooms and 19 places for patients in the emergency room). Neither police, fire department, ambulance service, nor our emergency team were informed in advance. The exercise was monitored by inspectors, documented and carried out under the retention of the real emergency process. The aim was to analyze the procedures by performing the entire process of treatment under true-to-life circumstances. We report our experience.

**Methods:** The scenario simulated a feigned collision between a train and a car with 75 staged casualties. Our institution received 4 major traumas, 5 medium and 7 slightly injured patients. The casualties carried laboratory data, X-ray pictures and medical data on a note. All emergency diagnostics and treatments were processed in real time, including simulated operations. A team, allotted to a certain patient, was not allowed to participate further in the exercise, until the assigned treatment was finished.

**Results:** 14 minutes after the alarm from the scene the MCI-protocol was initiated. The emergency response team (surgeons and specialist nurses, n = 20) was mobilized. The average response time was 30 minutes (15–90). A triage point was set up within 15 minutes. Patients arrived between 22 and 100 minutes (mean: 56). 2 seriously injured patients were simultaneously treated in two resuscitation rooms. A third seriously injured patient could be cared for in an improvised resuscitation room. A fourth seriously injured patient (ISS 15) was managed in the emergency room. The mean resuscitation time was 43 minutes. The mean ISS-score was 30. The other injured patients (n = 12) presented peripheral fractures (5) and trifle injuries (7). Average treatment time in this group was 44 minutes. During the exercise, 8 real patients were admitted. 2 real and 3 staged operations were performed during the exercise. After 192 minutes, the exercise was completed.

**Conclusion:** The emergency procedures during an MCI could be trained and analyzed in this exercise simulating true-to-life circumstances from the place of the accident through the whole rescue chain into the operating theatre. All regular emergency procedures and planned operations were continued during the exercise. The entire patient flow could be mastered by mobilizing additional emergency personnel.

#### Reasons for non-compliance with the protocol in an enhanced recovery program after surgery

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**Objective:** Enhanced recovery after surgery (ERAS) pathways are associated with a significant reduction of complications and hospital stay after colorectal surgery. However, a high compliance with the protocol is essential for a good clinical outcome. We aimed to study reasons for non-compliance with the ERAS pathway.

**Methods:** A consecutive cohort of 26 patients undergoing colorectal resection between August and October 2012 was prospectively analysed with special emphasis on reasons for non-compliance. For each ERAS item, the responsible for the decision to deviate from the clinical pathway - surgeon, anaesthetist, nurse or patient - was determined, and the non-compliance was specified as medically justified or not.

**Results:** During the study period, overall compliance with 22 items in the 26 assessed patients was 75%, ranging from 88% in the pre- and intra-operative period to 66% in the post-operative period. Most of the “problematic” items concerned the postoperative period, such as mobilisation on postoperative day (POD) 0 (48%), Foley catheter removal on POD 1 (48%) and epidural analgesia removal on POD 2 (30%). Decision to deviate from the clinical pathway was taken in 41% by the surgeon, while nurses and patients were responsible in 14% and 20% respectively. Reasons for non-compliance were medically justified in 65%.

**Conclusion:** High compliance with the ERAS protocol can be achieved in the pre- and intra-operative period. Of note, “Non-compliance” in the post-operative period is mainly a medical necessity and should rather be labelled as outcome measure than deviation from the pathway. However, 35% of true non-compliance is still amenable to improvement.

#### Violence related injuries treated in a Swiss trauma center

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**Objective:** Violence is a worldwide growing problem. Each year, over one and a half million people lose their life due to violent crimes worldwide with a rising trend. In Switzerland, interpersonal violence seems to be an increasing problem as well. The aim of the current study was to describe a comprehensive picture of violence in a Swiss city with regard to medical and social aspects.

**Methods:** A total of 1575 patients injured by violent crimes between April 2004 and January 2011 were enrolled into this study. In addition, a retrospective analysis of medical records using the electronic patient database was carried out.

**Results:** Most of the treated patients were male. There was no relevant increase in patients affected by violent crimes in 2005 compared to 2010 (268 vs. 275 patients). However, the percentage of affected females increased from 7.1% at the beginning- to 11% at the end of the observation period. Most acts of violence occurred on Fridays and Saturdays with a majority occurring during 0:00 and 6:00 o'clock in the morning. Fifty-six percent of the patients were younger than 26 years old. The leading causes of injury were violent assaults (86%), followed by penetrating knife injuries (11%) and gunshot wounds (3%) with no relevant changes during the observation period. The leading affected body region were head injuries with over 60%, followed by lesions of the skin (17%). The need for a hospitalization varied strongly according to the cause of injury and ranged from 35 to 78%. The total costs for hospitalization after an act of violence amounted to more than 3.5 Million Swiss Francs. Two hundred and ninety surgical interventions were necessary during the observation period.

**Conclusion:** No relevant changes regarding the number of patients could be observed. However, the proportion of affected females increased. Especially at the weekend, there is a need for preventive measures to reduce the high number of affected patients and the associated costs.

**Is an ERAS pathway applicable for emergency colectomy?**D. Roulin<sup>1</sup>, M. Muradbegovic<sup>1</sup>, C. Blanc<sup>2</sup>, D. Hahnloser<sup>1</sup>, N. Demartines<sup>1</sup>, M. Hubner<sup>1</sup><sup>1</sup>Department of Visceral Surgery, University Hospital CHUV, Lausanne, Switzerland,<sup>2</sup>Department of Anaesthesiology, University Hospital CHUV, Lausanne, Switzerland

**Objective:** Enhanced recovery after surgery (ERAS) protocols have proven to decrease complications and hospital stay following elective colorectal surgery, and are hence considered standard of care. However, ERAS principles have not been applied yet to emergency surgery. We aimed to compare our emergency and elective colectomies performed within an established ERAS pathway.

**Methods:** Since April 2012, all patients needing an elective or emergency colonic resection were included in an ERAS pathway without exception; our present prospective analysis included consecutive patients operated between April and December 2012. Emergency surgeries were compared to elective procedures with regards to baseline characteristics, compliance with the ERAS protocol, and clinical outcome.

**Results:** Twenty-three patients requiring emergency colectomy (median 59 years, 39% male) were compared to 53 patients undergoing elective colectomy (median 63 years, 40% male). Overall compliance with the ERAS protocol was 60% for the emergency compared to 75% for the elective procedures. The pre-operative compliance was 60% vs. 94%, the intra-operative compliance was 79% vs. 86%, and the post-operative compliance was 51% vs. 65%, for the emergency and the elective resections, respectively. Problematic items for the emergency patients were preoperative carbohydrate drinks (39%), post-operative nausea and vomiting prophylaxis (48%), balanced intravenous fluids on day of surgery (35%), termination of urinary drainage the first post-operative day (35%), mobilisation on day of surgery (30%) and energy from nutritional supplement on day of surgery of more than 300 kcal (22%). Emergency patients passed flatus after a median of 3 days, compared to 2 days for the elective patients ( $p = 0.068$ ). Overall, 12 emergency patients (52%) and 23 elective patients (43%) developed postoperative complications ( $P = 0.652$ ). Median postoperative length of stay was 8 days in emergency compared to 6 days in the elective setting ( $P = 0.097$ ).

**Conclusion:** Most of the intra-operative and post-operative ERAS items can be applied similarly to an elective setting. However, several items connected with the emergency nature remain problematic with a lower compliance. Despite this, routine application of an ERAS pathway for emergency colectomies is feasible, entailing a favourable clinical outcome.

**A new mini-open technique for operative treatment of displaced intraarticular calcaneal fractures**

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**Objective:** Open reduction and internal fixation via the L-shaped extended lateral approach has developed to the gold standard in the treatment of displaced intraarticular calcaneal fractures. However, wound healing complications are reported in up to 25% of the cases and may cause a longer time of hospitalization, need for antibiotic treatment, or revision surgery. To avoid this, a mini-open procedure has been propagated using a subtalar approach and a special wave-shaped plate. We report our first results with this new technique in comparison to a series of patients treated with the extended lateral approach in the same time period.

**Methods:** For the mini-open procedure a subtalar approach was used to visualize the posterior facet and the anterior process including the calcaneocuboidal (cc) joint. Reduction was achieved with percutaneous manipulation using a Schanz pin in the tuber fragment of the calcaneus. The posterior facet and the cc-joint were directly reduced using an elevator. For internal fixation an anatomical wave-shaped plate was inserted. Both conventional or angular stable screws were used. If necessary, off-plate additional cannulated lag screws were placed to stabilize an anatomically reduced joint surface.

**Results:** We treated a number of 35 consecutive patients with intraarticular calcaneal fractures in a period of 24 months. In 24 patients the extended lateral approach (ELA) was performed, 11 patients were treated with the mini-open technique (MOT). Exclusion criteria were non reconstructable fracture patterns, where a primary subtalar arthrodesis was performed. The subtalar approach gave a good overview over the posterior facet and also the anterior

process, so that even Type Sanders IV fractures could be reduced satisfactorily. Valgus/Varus deformity could be well addressed by reduction with the Schanz pin. Operation time decreased by experience of the surgeons and showed no significant difference in comparison to the open procedure. Quality of reduction was comparable in both groups. While 42% of the patients in the ELA group had wound healing complications, all wounds healed uncomplicated in the MOT group.

**Conclusion:** The mini-open technique for the treatment of intraarticular calcaneal fractures is a promising alternative to the extended lateral approach, protecting the soft tissue of the hindfoot and minimizing wound healing complications.

**Importance of the posterior plafond for the outcome after operatively treated ankle fractures**K. Sprengel<sup>1</sup>, D. Rittirsch<sup>1,2</sup>, E. Wanner<sup>1</sup>, C. von der Lippe<sup>1</sup>, C. M. Werner<sup>1</sup>, H.-P. Simmen<sup>1</sup>, G. A. Wanner<sup>1</sup><sup>1</sup>Department of Trauma Surgery, University Hospital Zurich, Zurich, Switzerland,<sup>2</sup>Department of Surgery, Schaffhausen Cantonal Hospital, Schaffhausen, Switzerland

**Objective:** Exact anatomic reduction of articular fractures is mandatory. But there is no consensus if the posterior plafond in ankle fractures should be addressed in any case. Reasons for an operative fixation of the so called Volkmann's triangle are not only anatomic reduction but also biomechanical aspects.

**Methods:** We retrospectively analyzed 107 patients who suffered an ankle fracture with a Volkmann's triangle as a monotrauma in the period of 1997–2009 and were treated by open reduction and internal fixation. We recorded several data and scores like clinical outcome, complications, the AOFAS and the SF-36 Score.

**Results:** We could analyze data of 60 patients just clinically and 47 clinically and radiologically. We found a good result after 6.6 years with an average AOFAS Score of 90.5. Only a high energy trauma showed a significant poorer outcome in the AOFAS Score (90.7 vs. 92.4, Man-Whitney U Test). No significant influence on the outcome (e.g. AOFAS Score, arthrosis, complications) could be proven for the size or grade of dislocation of the posterior plafond, an articular gap in the postoperative x-rays. Even certification of the surgeon or delayed surgery waiting in a cast or external fixator was without statistical significance.

**Conclusion:** The primary hit on the ankle joint by the trauma mechanism has a high influence on the outcome after an operative procedure of ankle fractures. Performing the operation during fellowship under supervision will be safe. We didn't find a significant influence of the size and the grade of dislocation of the Volkmann's triangle on the outcome of those fractures. Therefore we cannot postulate that the exact reduction and fixation of the posterior plafond is always necessary. But the indication for an operative fixation of the Volkmann's triangle should be considered in every single case with special attention to the stability of the ankle joint. Therefore we will analyze the biomechanical effects of an injured Volkmann's triangle on the stability of the ankle joint in further studies.

**Traumatic lower limb amputation versus salvage with Ilizarov external fixation – comparison of outcomes**D. Baschera<sup>1,2</sup>, V. Rajput<sup>2</sup>, M. Wren<sup>2</sup>, R. Zellweger<sup>2</sup><sup>1</sup>Neurosurgery, Insel Hospital, Bern, Switzerland, <sup>2</sup>Orthopedics and Trauma Surgery, Royal Perth Hospital, Perth, Australia

**Objective:** Literature has looked at specific outcomes of amputation and limb salvage patients following severe lower limb trauma but has not differentiated between types of limb salvage in analyses. Through a cohort study design, we aim to compare a wide range of functional outcomes of patients who have undergone either amputation, or limb salvage by Ilizarov external fixation (IEF) in the treatment of severe traumatic lower limb injury.

**Methods:** Postal surveys were sent to 91 patients who had undergone either IEF or amputation at our level 1 trauma centre between January 2004 and December 2009. The SF-12 Health Survey was incorporated in our self-designed questionnaire to measure an objective Physical Component Score (PCS) and Mental Component Score (MCS) for our patients.

**Results:** Sixty-nine out of ninety-one patients (76%) responded to our postal survey. At follow up, amputees had a significantly lesser decline in physical

activity levels than limb salvage patients (65% Vs 79.4%). There was no significant difference identified in MCS and PCS between Amputation and Ilizarov groups. Change in employment status was not significantly altered between groups, while the incidence of depression amongst our patients, although high, also showed no significant difference between groups. Patients with lower MCS were associated with strong opioid use in both groups.

**Conclusion:** Although no significant difference was detected between our groups in overall physical and mental component scores, our results suggest that physical activity levels aren't affected as drastically after amputation. Another key finding was the high rate of mood disorder amongst all our patients after management, and in particular, its association with strong opioid use.

#### Routine chest radiographs are not mandatory after fluoroscopic-guided totally implantable venous access port devices insertion by vein denudation

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**Objective:** The aim of this study is to evaluate the rates of the three most frequent complications (hemothorax, pneumothorax, catheter migration/malposition) in patients who undertake fluoroscopic-guided totally implantable venous access port devices (TIVAPD) insertion, using procedural post-operative radiographic imaging. We postulate that post-operative chest radiographies are not necessary after TIVAPD placement under fluoroscopic control via the open approach (vein denudation) and does not influence the postoperative course of the patients.

**Methods:** This study consists of a retrospective review of the charts of all patients who undertook an image-guided TIVAPD insertion in an ambulatory and elective setting at the University Hospital of Geneva (n = 936), regardless of the approach (open or percutaneous) or the venous access site (subclavian, cephalic, jugular, others), from July 10, 2009 to April 16, 2012. Access site, number of insertion attempts, peri-operative fluoroscopy results, chest radiograph results, location of the tip of the catheter and immediate complications such as hemothorax and pneumothorax were assessed. Twenty-two patients were excluded (lacking data : 14, failure of implantation : 6, transcathegation of a central venous access : 2).

**Results:** The study group consisted of 914 patients. The total number of complications associated with the placement of the devices and detected by the immediate post-procedural chest radiographs were 1 pneumothorax and 1 migration of the catheter. A single case of hemothorax was found out in the post-procedural chest radiograph in a patient excluded from the study because of a failure to insert the device.

**Conclusion:** The incidence of the immediate complications detected by the post-procedural chest radiographs was very low (1 patient with pneumothorax and 1 patient with an incorrectly positioned catheter's tip in 914 people), letting assume that routine post-procedural chest radiography is not mandatory after fluoroscopic-guided totally implantable venous access port devices (TIVAPD) insertion by open approach. According to recent literature, it should be obtained only in adequation with clinical suspicion of an immediate complication.

## Research

#### Small-for-Size syndrome – overcoming regenerative limits in the liver by tricking organ size control

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**Objective:** Patients left with marginal liver remnants are at risk of developing the Small-for-Size Syndrome (SFSS). Experimentally, SFSS is characterized

by an insufficient recovery of liver mass following resection. Activation of the constitutive androstane receptor (CAR), a nuclear receptor acting in the liver as a xeno/endobiotic sensor, induces spontaneous liver hyperplasia. We investigated the potential of the CAR agonist TCPOBOP (TCP) to ameliorate experimental SFSS.

**Methods:** The effects of TCP on SFSS were assessed in four murine models: 68% hepatectomy (Hx) (100% survival, control), 86% Hx (75% survival), 91% Hx (0% survival), and 30% graft transplantation (0% survival). Serum bilirubin, ALKP, and albumin served as measures of SFSS-like features. Proliferation-associated molecules, including Foxm1b and miR375-dependent pathways, were analyzed.

**Results:** TCP markedly improved survival following 86% Hx, 91% Hx and 30% transplantation. Likewise, SFSS-associated features of bilirubinemia and reduced liver function were normalized by TCP. Furthermore, TCP following 86% Hx reversed the abnormal induction of the Foxm1b/miR375 pathways, normalized upregulated p21 and restored the deficient regeneration.

**Conclusion:** TCP can prevent experimental SFSS. Even when given after extended resection, TCP rescues >40% of otherwise moribund mice. The underlying molecular changes suggest a contribution of pathways promoting cell cycle progression and uncoupling from organ size control. Therefore, TCP appears to override the regenerative deficits of marginal liver remnants. Further assessment is needed to estimate the malignant risk associated with CAR agonism.

#### Rat liver allo-graft rejection promotes cancer clearance: a model of transplantation for hepatocellular carcinoma

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**Objective:** Liver transplantation for hepatocellular carcinoma (HCC) results in a specific condition where the immune response is directed both against allogeneic and cancer antigens. This study assessed the level of anti-cancer immunity during allogeneic rejection after rat liver transplantation.

**Methods:** Dark Agouti-to-Lewis (allogeneic) and Lewis-to-Lewis (syngeneic) rat liver transplantations were performed. The occurrence of a rejection was assessed (survival, histology, liver function tests and mixed lymphocyte reaction). The phenotype, the level of activation and the anti-cancer cytotoxic activity of mononuclear, monocyte/macrophage and NK cells were tested in the peripheral blood, the liver and the spleen.

**Results:** Allogeneic rats experienced rejection as testified by shorter survivals (13 vs. >60 days in syngeneic rats, p < 0.01), the presence of rejection on histology (Banff 8) and increased liver function tests (p < 0.01). Rejection was donor specific as shown by the increased IFN-gamma secretion by recipient peripheral blood mononuclear cells (day 10) after stimulation by donor splenocytes (410 pg/ml). At time of rejection, blood cells demonstrated increased anti-cancer cell cytotoxicity (25.2 vs. 14.7% in syngeneic recipients, p < 0.005). This activity was related to increased blood NK cell frequencies (10.79% vs 4.9%, p < 0.05) and higher blood monocyte/macrophage activation levels (p < 0.01). Similarly in the liver, the number of liver mononuclear cells was increased (16.106 vs. 5.35.106 cells/liver, p < 0.01), as were liver NK cell-specific cytotoxicity (58.8% vs 32% respectively, p < 0.005) and liver monocyte/macrophage activation levels (p < 0.01). The phenotype and the anti-cancer function of spleen cells were not altered.

**Conclusion:** Liver graft rejection is associated to increased peripheral and liver cytotoxicity against cancer cells. This observation supports the use of milder immunosuppression after transplantation for HCC with the idea to improve post-transplant immune clearance of HCC cells.

#### Interleukin-1 receptor antagonist delays progression of liver fibrosis

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**Objective:** Liver fibrosis represents a wound healing response to chronic insults characterized by an excessive accumulation of extracellular matrix

compounds. Interleukin-1beta (IL1beta) has been proposed as an important mediator of inflammation and tissue damage in acute and chronic liver diseases. We aimed to determine whether the modulation of IL1beta signaling through interleukin-1 receptor antagonist (IL-1Ra) up- or downregulation can modulate liver fibrosis.

**Methods:** The contribution of IL-1beta and IL-1Ra was assessed in vitro using human hepatic stellate cells (HSC) and in vivo in a mouse model of liver fibrosis induced by bile duct ligation (BDL). BDL was performed in wild type (WT), IL-1Ra knockouts (KO) and WT mice treated with recombinant IL-1Ra. Hepatic fibrosis, expression of matrix metalloproteinases (MMP) and inflammation were quantified by RT-PCR at 1, 5, 15, and 32 days after BDL.

**Results:** Human HSCs treated with IL-1beta showed an upregulation of IL-1beta, IL-1Ra and MMP-9 mRNA levels that was prevented by addition of recombinant IL-1Ra. Both, IL-1beta and IL-1Ra were strongly up-regulated in serum of WT mice following BDL (6-fold) and IL-1beta was significantly overexpressed in the liver of IL-1RaKO mice compared to WT mice (4-fold). Collagen deposition, macrophage activation, and transaminases levels were significantly increased in IL-1RaKO mice compared to WT mice. Following BDL, IL-1Ra KO mice had a decreased survival compared to WT mice ( $p = 0.044$ ). Other parameters, like expression of MMP-2, 9 and 13, showed increased but similar levels in fibrotic livers of WT and IL-1RaKO mice. IL-1RaKO mice treated with exogenous recombinant IL-1Ra showed a reduced liver fibrosis when compared to IL-1RaKO mice (6.9 vs. 10.6%,  $p = 0.001$ ) and that was similar to WT (6.9 vs. 6.8%,  $p = 0.932$ ).

**Conclusion:** These data indicate that IL-1Ra impede/ delays the progression of BDL-induced liver fibrosis in mice. Modulation of IL-1beta via IL-1Ra is an important regulatory pathway during chronic liver injury.

#### Neural regulation of pancreatic cancer: beta-adrenergic signaling increases primary tumor growth and metastasis

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**Objective:** Pancreatic cancer is the 4th leading cause of cancer-related deaths. New therapeutic strategies to treat pancreatic cancer and to prevent recurrence and metastasis are critically needed. The sympathetic nervous system (SNS) innervates the pancreas and key metastatic target organs such as the lymph nodes and liver and releases stress neurotransmitters in response to activation. In other cancers it has been shown that the SNS plays an important role in tumour progression. However, the impact of SNS signalling on pancreatic cancer progression is currently unknown.

**Methods:** To investigate the effect of SNS signalling, we used an orthotopic mouse model of pancreatic cancer progression and a restraint stress (2 hr daily) to physiologically activate the SNS. To track tumor progression, 1 mm<sup>3</sup> tumor pieces were derived in vivo from luciferase-tagged PANC-1 pancreatic carcinoma cells and then implanted into the pancreatic tail. Bioluminescence imaging was used to track primary tumour growth, metastasis and tumor recurrence after surgical resection.

**Results:** Physiological SNS activation increased primary tumor size by 19-fold ( $p = 0.05$ ). Pharmacological SNS activation with the beta-agonist, isoprenaline increased primary tumor burden by 4-fold. RT-PCR confirmed expression of beta1- and beta2-adrenergic receptors on PANC-1 cells. However, isoprenaline did not modulate tumor cell proliferation in vitro, suggesting that chronic stress accelerated cancer progression through an indirect mechanism. Stress increased metastasis to liver, local regional lymph nodes and adrenal gland. Consistent with beta-adrenergic regulation of metastasis, isoprenaline increased invasion of PANC-1 cells through matrigel by 7.3-fold ( $p < 0.01$ ).

**Conclusion:** Activation of the SNS through chronic stress leads to tumour progression in an orthotopic mouse model. We are now conducting proof-of-principle studies to investigate if blocking beta-adrenergic signalling slows pancreatic cancer progression. These studies will pave the way for new therapeutic interventions that slow or block pancreatic cancer progression by targeting peripheral neural pathways.

#### Aberrant activation of the PI3K/mTOR pathway is associated with a worse prognosis in malignant pleural mesothelioma patients receiving multimodal therapy

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**Objective:** The phosphoinositide-3 kinase (PI3K)/mammalian target of rapamycin (mTOR) pathway is probably one of the most important pathways in cancer metabolism and growth. Here, we sought to investigate the prognostic significance of constituent proteins of the PI3K/mTOR pathway in malignant pleural mesothelioma tumour samples collected prior to and following a multimodality treatment regimen.

**Methods:** A set of pre- and post- induction chemotherapy biopsies from a total of 103 patients diagnosed with malignant pleural mesothelioma uniformly treated within a multimodal context (viz. induction chemotherapy and extrapleural pneumonectomy) were employed for the present study. Expression levels of phosphatase and tensin homologue (PTEN) in addition to phosphorylated forms of mTOR and S6 were evaluated by immunohistochemistry and correlated with overall survival and progression-free survival. For validation purposes a second cohort of independent malignant pleural mesothelioma patients ( $n = 46$ ) was utilized to examine the PTEN expression profile following a similar multimodal therapy regimen. To assess any potential underlying PTEN genomic anomalies, PTEN fluorescence in situ hybridization was performed on a subset of these cases.

**Results:** Kaplan-Meier survival analysis showed that high p-S6 expression in treatment naive biopsies was associated with short progression-free survival. Paired comparison within patients prior and post multimodal therapy revealed that decreased cytoplasmic PTEN expression was associated with a worse overall survival. Additionally, increased cytoplasmic p-mTOR was shown to predict a shorter overall survival in patients. No association between PTEN FISH status and PTEN protein expression level was identified.

**Conclusion:** Our results confirm p-S6 as a prognostic marker for malignant pleural mesothelioma in pre-chemotherapy biopsies. This study also shows that aberrant expression of PTEN and p-mTOR represent additional prognostic factors for malignant pleural mesothelioma patient survival. Together, these data support the growing evidence targeting the PI3K/mTOR pathway in the treatment of malignant pleural mesothelioma.

## Vascular

#### Role of hybrid procedures for multilevel peripheral arterial disease

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**Objective:** Multilevel arterial disease is a challenging disorder. Indeed restricted endovascular or surgical approaches cannot usually overcome the extensive lesions. The one-session hybrid procedures using both techniques could be a good alternative in high risk patients. The aim of the study is to evaluate the results of these procedures in term of patency rates, limb salvage, complications and also quality of life.

**Methods:** Between December 2008 and 2011, 69 hybrid procedures were performed in 64 consecutive patients. Endovascular approach was used to correct the inflow in 20/69 (28.9%) of the cases. The endarterectomy of the common femoral artery was the principal surgical technique in 45/64 (65.2%). We collected retrospectively all the data of the study endpoints concerning the patency, limb salvage, complication and mortality during the follow-up. We called all the patients to fulfil a VasculQol document to assess quality of life and capacity of walking after the procedures. We had finally 38/64 patients that properly answer the questionnaire.

**Results:** Patients (64% male) were a median age of 70 years (interquartile range [IQR], 41–95), 42% had diabetes mellitus, 31% had critical limb ischemia, 59% were scored ASA 3, 53% were taking statin and 88% antiplatelet medication. Median follow-up was 428 days (IQR, 4–1140 days). The 1-year primary patency rate was 68% and 80% for the secondary patency during the same interval of time. Limb salvage was 94% during the follow-up. General complications were observed in 13% and local in 22% of the cases. The 30-day mortality rate is 3%. The hybrid procedures improve the walking distance in 47% of the cases and decreased significantly the leg pain in 61%. Only 31% claimed an improved independence.

**Conclusion:** Hybrid procedures appear to improve walking distance and quality of life in high risk patients with multilevel arterial disease. The patency and limb salvage rate allow selecting this option when critical limb ischemia threatens the leg.

#### Clinical outcomes of symptomatic versus asymptomatic abdominal aortic aneurysm

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**Objective:** Symptomatic abdominal aortic aneurysms (AAA) are believed to represent advanced disease with impending rupture. In addition clinical outcomes could be impaired because, if treated promptly, surgical patient fitness cannot be optimised. Aim was to determine whether symptomatic AAAs were intrinsically associated with worse outcome than asymptomatic AAA.

**Methods:** Out of a consecutive series of patients undergoing intact AAA repair between 2001 and 2010 those presenting with a symptomatic AAA were usually treated within 24 hours and compared to asymptomatic patients regarding procedural and long term survival. Comparisons were adjusted for suspected confounding factors to assess independent influence of symptomatic state. These included age, gender, aneurysm diameter and configuration, type of repair, renal function and body mass index.

**Results:** A total of 823 patients underwent intact AAA repair. Of those 137 (16.6%) presented with aneurysm-related symptoms. Median follow up was 4.17 years (interquartile range 1.8–6.0) and similar between groups. 204 patients (24.8%) received endovascular repair and this was more likely in the asymptomatic group (28.4% vs 6.6%,  $p < 0.001$ ). Thirty day mortality was equal between the groups at 1.2% (1.5% for asymptomatic and 0% for symptomatic AAA, respectively,  $p = 0.383$ ). Actuarial 5-year survival rates did not differ either (confounder-adjusted hazard ratio 1.139, 95%-confidence interval 0.71–1.82;  $p = 0.584$ ).

**Conclusion:** If treated without undue delay, symptomatic state of AAA patients does not imply an additional surgical risk in our series, even though patient fitness could not be optimised preoperatively. Similarly, long term survival is not affected by the clinical presentation of intact AAA.

#### Influence of suprarenal aortic clamping on clinical outcome during open abdominal aortic aneurysm repair

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**Objective:** Open repair of juxtarenal abdominal aortic aneurysm (AAA) is complicated by the need for suprarenal aortic clamping, which could negatively affect procedural and long term survival. The aim was to quantify such a potential effect in a contemporary and consecutive series of patients undergoing open AAA repair.

**Methods:** Patients undergoing juxtarenal AAA repair were identified prospectively between 2001 and 2010 and compared post-hoc to those undergoing infrarenal AAA repair. Comparisons of procedural and long term survival rates were statistically adjusted for suspected confounding factors including age, sex, aneurysm-related symptoms, aneurysm diameter and complexity (including iliac involvement) and renal function.

**Results:** During the study period, 619 patients underwent open repair of intact AAA. Among them 176 (28.4%) presented with a juxtarenal aneurysm and needed supraaortic clamping. Median follow up was 4.0 years (interquartile

range 2.0 to 6.4) and significantly longer in patients with infrarenal AAA (4.6 vs 3.2,  $p < 0.001$ ) indicating that surgical complexity increased over the years. Thirty day mortality was higher in patients with juxtarenal aneurysm both in absolute terms (3.4% versus 0.7%,  $p = 0.019$ ) and after adjustment for confounding factors (odds ratio 5.11, 95%-Confidence Interval (CI) 1.2–22.2,  $p = 0.029$ ). In contrast, adjusted 5 year survival rates were not different between the groups (hazard ratio 1.38, 95%-CI 0.9–2.1,  $p = 0.142$ ).

**Conclusion:** The use of a suprarenal aortic clamp during open AAA repair increased the risk of early postoperative death about five fold. A similar long term prognosis among all study patients suggests an actual short term effect of the additional surgical trauma. Nonetheless, results remained in the same range as the published early mortality of endovascular juxtarenal aortic repair.

#### Current spectrum, decision-making and treatment results in surgical thoracic and thoraco-abdominal aortic disease: experience of a decade

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**Objective:** Prevalence of thoracic aortic repair is steadily increasing while the therapeutic options are evolving rapidly. Thus, thoracic aortic disease appears more and more in daily vascular practice. The aim was to determine the current spectrum of surgical thoracic aortic disease, clinical decision-making and associated results in a contemporary patient series.

**Methods:** Descriptive analysis of a consecutive series of patients undergoing thoracic aortic repair between 2001 and 2010. Clinical presentation, indication for surgery, type of repair and clinical outcomes were all assessed and correlated with patient-related characteristics. The main outcome parameters included short and long term mortality which were assessed using Kaplan Meier survival estimates.

**Results:** During the assessed decade, 369 patients (76.4% men, median age 67, interquartile range 58 to 74) underwent a total of 394 thoracic aortic repairs. Of those, 186 were confined to the thoracic aorta (TA) whereas the remaining 208 dealt with more extensive thoraco-abdominal aortic (TAA) disease according to the modified Crawford classification: I ( $n = 33$ ), II ( $n = 99$ ), III ( $n = 26$ ), IV ( $n = 23$ ), V ( $n = 8$ ) and the suprarenal aorta ( $n = 19$ ). Indication for surgery was intact TA(A) aneurysm or dissection in most cases ( $n = 312$ , 50% symptomatic); and ruptured aneurysm in another 59 cases ( $n = 18$  posttraumatic). In the remaining 13 cases various other entities were treated. Overall, 145 patients (37%) underwent endovascular repair. Overall, 30 day mortality was 9.6% (for elective TA repair 0%, for elective TAA repair 5.9%, respectively). Unsurprisingly, aortic rupture was the main independent predictor of early mortality (OR 15.34, 95% confidence Interval 5.4–43.6;  $P < 0.001$ ). Survivors were followed for a median of 3.9 years (interquartile range 2.2–6.3). At 5 years actuarial survival was not impaired after TAA as compared to TA repair; if anything absolute survival seemed somewhat favourable (69.8% vs 79.0%,  $p = 0.069$ ).

**Conclusion:** The scope of surgical thoracic and thoraco-abdominal aortic disease remained heterogenous in this contemporary series. However, despite the advent of endovascular therapy, 63.2% of all thoraco-abdominal aortic interventions were still performed using open surgical technique. In contrast to abdominal aortic management, a majority of patients are treated for symptomatic disease. Overall, up to date management remains a moving target.

#### Posterior approach to the popliteal vessels after knee joint dislocation

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**Objective:** Every third knee joint dislocation is associated with vascular trauma. With a risk of amputation as high as 10%, urgent revascularisation is often necessary. Usually, a medial approach is preferred, which however implies surgical bypass. Aim was to evaluate local management of the injured vessel via a posterior approach to the popliteal space.

**Methods:** Descriptive post-hoc evaluation of a consecutive case series of patients suffering from vascular trauma in the popliteal segment due to knee joint dislocation between May 2011 and November 2012.

**Results:** A total of six patients was treated after traumatic knee joint (n=2) or knee prosthesis (n=4) dislocation. Two patients suffered from combined arterial and venous, and four from isolated arterial trauma, respectively. After a limited posterior approach three patients received a saphenous vein interposition graft, two underwent arterial resection followed by direct re-anastomosis and in one the arterial defect was reconstructed using a bovine pericardium patch. Traumatized veins were replaced with a saphenous vein conduit or a direct re-anastomosis after local resection, respectively. Orthopedic stabilisation was necessary in five patients. At a median follow-up of 7 months (range 1 to 19) all limbs were preserved and arterial patency was 100% without repeat intervention. One out of two reconstructed veins however had occluded shortly after operation.

**Conclusion:** The posterior approach to the popliteal vessels is feasible and effective after traumatic tissue disruption and, in contrast to the remote medial approach, allows for local revascularisation or short segment bypass surgery. Particularly patients without suitable autologous conduit may be spared an unnecessary prosthetic bypass.

## Thoracic

### Extracorporeal life support as a bridge to lung transplantation: institutional experience

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**Objective:** Extracorporeal life support (ECLS) is the only option for lung transplant candidates who do not respond to maximal ventilator support while waiting for an available donor lung. The study objective was to compare survival in patients requiring pretransplant ECLS with that of patients not requiring ECLS. Institutional experience with ECLS as a bridge to lung transplantation (LuTX) is reported.

**Methods:** Between January 2000 and December 2012, 285 LuTX were performed at our institution. Twenty patients underwent ECLS with intention to bridge to LuTX. Sixteen patients (median age 44.5 years, range 17–65 years) were successfully bridged to LuTX on ECLS. The underlying diagnosis was idiopathic pulmonary fibrosis (n=9), cystic fibrosis (n=6), and emphysema (n=1). The type of ECLS was venovenous extracorporeal membrane oxygenation (ECMO) (n=6), venoarterial (n=3), interventional lung assist (n=2), and stepwise combination of them (n=5). Primary LuTX was performed in 14 and retransplantation in 2 cases. The type of procedure was bilateral LuTX in 9, bilateral lobar LuTX in 5 and unilateral LuTX in 2 patients.

**Results:** Two patients weaned from ECLS and 2 patients died on ECLS while waiting for a donor. Success rate for bridging was 80%. Median duration of ECLS was 17.5 days (range, 1–46 days). Twelve patients required ECMO in the postoperative period (median 2.5 days, range, 1–9 days). Unadjusted 30-day, 1-year, and 2-year survivals were 81%, 66%, and 47%, respectively, for ECLS patients and 95%, 86%, and 80% who were transplanted during the same period without preoperative ECLS (p=0.0001).

**Conclusion:** Extracorporeal life support as a bridge to LuTX is associated with higher perioperative morbidity and mortality. Our data show significantly lower survival in this high-risk group compared to those who were transplanted without preoperative ECLS.

### Adequacy of video-assisted mediastinal lymphadenectomy for stage I non-small cell lung cancer

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**Objective:** The rationale of this study was to compare the efficiency of video-assisted thoracic surgery (VATS) mediastinal lymph node dissection (MLND) and MLND by thoracotomy for stage I NSCLC.

**Methods:** Retrospective study on 50 cases of MLND and lobectomy by VATS for clinical stage I NSCLC and a matched group of patients undergoing open MLND and lobectomy. Total number of resected lymphnodes, resected lymphnodes per station and postoperative outcome were compared between both groups after matching for age, gender, clinical stage of NSCLC and type of lobectomy.

**Results:** Patients median age was 64 years (VATS: 49–86; open: 47–84) and 40% of patients were female. Clinical stage was cT1a in 72% and 68% (VATS: 36; open 34), cT1b in 28% and 32% (VATS: 14; open: 16). 50% of patients underwent right-sided lobectomies and 64% had upper lobectomies (VATS: 30; open: 32). Median numbers of removed lymph nodes were 19.5 (range 6–55) in the VATS group and 18 (range 6–40) in the open group. Right-sided VATS lymphadenectomy resulted at station 2R/4R in 6 (median; range 1–25) (open 5.5; 0–28; ns) at station 7 in 7(2–23) (open 4.5; 1–11; ns) and at station 8/9 in 1(0–4) removed nodes (open 1; 0–4; ns) On the left side VATS lymphadenectomy resulted at station 5 and 6 in 4 (median; range 1–12) (open 4; 1–12; ns), at station 7 in 7(2–21) (open 4.5, range 1–14; ns) and at station 8/9 in 1 (0–6) dissected lymph nodes (open 1; 0–7). Pathological upstaging (pN1; pN2) was found in 9 patients (18%) after VATS MLND, and 8 (16%) after open MLND, respectively.

**Conclusion:** VATS MLND results in an equal number of dissected lymph nodes as compared to MLND by thoracotomy. The implementation of a VATS lobectomy program does not influence the extend of mediastinal lymphadenectomy for stage I NSCLC.

### Perioperative morbidity and mortality after lung volume reduction surgery in an established program

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**Objective:** There is convincing evidence from observational and randomized studies that Lung Volume Reduction Surgery (LVRS) in selected patients with advanced emphysema improves symptoms, pulmonary function, exercise tolerance, quality of life and may even prolong survival in comparison to medical treatment. However, despite these advantages LVRS is not adequately applied worldwide partially due to a misleading notion of prohibitive risks. After establishing selection criteria's and optimized treatment algorithms the aim of this study is to evaluate our current mortality and morbidity.

**Methods:** 252 consecutive patients (64 years (31–84), 111 females) with advanced emphysema FEV1 26% (14–58%), RV/TLC: 0.68 (0.53–0.87); DLCO: 34% (10–71%) (median and range) were treated by video-assisted thoracoscopic LVRS (77 unilateral) and analyzed from our prospective study (started in 1994) over the last 10 years. All types of emphysema morphology including the non-heterogeneous type were accepted.

**Results:** The 90-day mortality was 1.2% (3/252). 2 patients died due to cardiac insufficiencies (elevated cardiac risk profile known preoperatively) and 1 due to respiratory failure. The median drainage time was 6 days (2–43) and hospitalization was 11 days (4–91). Except one patient who developed cardiac insufficiency, none of the patients had intraoperative complications. All were extubated in the operating theatre. Out of the 252 patients 143 (57%) had no complications at all. In 88 (33%) patients pulmonary complications occurred; 60 (24%) had prolonged air leaks (>7 days) with 30 (12%) treated with a reoperation, 6 (2%) with pneumonia, 10 (4%) were temporarily reintubated, 2 (1%) patients with severe adhesions developed a hemothorax). 13 (5.2%) patients had cardiovascular morbidity requiring medical and antiarrhythmic treatment. 6 (2%) had a gastrointestinal complication and 11 (4%) other complications (cerebrovascular incident, urinary tract infection).

**Conclusion:** LVRS in selected high-risk patients with very severe emphysema and impaired lung function is safe in a dedicated and experienced centre when the appropriate selection criteria's are respected. The 90-day mortality with 1.2% is low and the perioperative morbidity is acceptable when the possible gain in quality of life is taken into account.

### Impact of induction therapy on airway complications after sleeve lobectomy for lung cancer

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**Objective:** Sleeve lobectomy is a valid alternative to pneumonectomy for the treatment of centrally located operable non-small cell lung cancer (NSCLC) but concern was evoked regarding a potentially increased risk of bronchial anastomosis complications after induction therapy. This study examines the impact of induction therapy on airway healing after sleeve lobectomy for NSCLC.

**Methods:** Bronchial anastomosis complications were recorded with respect of the induction regimen applied (neoadjuvant chemotherapy vs chemoradiotherapy) in a consecutive series of patients with sleeve lobectomy for NSCLC.

**Results:** Ninety-nine patients underwent sleeve resection, 28 of them after induction therapy. Twelve patients received chemotherapy alone and 16 patients had radio-chemotherapy. There were no significant differences in postoperative 90-day mortality (3.6% vs 2.8%) and morbidity (54% vs 49%) for patients with and without induction therapy. Bronchial anastomosis complications occurred in three patients (10.8%) with neoadjuvant therapy and in two (2.8%) without ( $p=0.3$ ). In the induction therapy group, two bronchial stenoses occurred after radio-chemotherapy and one broncho-pleural fistula after chemotherapy alone. In patients without induction therapy, one bronchial stenosis and one broncho-pleural fistula were observed. All bronchial stenosis were successfully treated by dilatation and both broncho-pleural fistulas occurring after right lower lobectomy were successfully treated by reoperation and completion sleeve bilobectomy with preservation of the upper lobe.

**Conclusion:** Sleeve lobectomy for NSCLC can be safely performed after induction chemotherapy and radio-chemotherapy with similar mortality and incidence of airway complications as observed in non-pretreated patients. The treatment of airway complications does not differ for patients with and without induction therapy.

### Management of postpneumonectomy empyema caused by oesophago-pleural fistula

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**Objective:** Postpneumonectomy empyema (PPE) remains a challenging complication and is often associated with high morbidity and even mortality. One of the rare causes is an oesophago-pleural fistula. We present a case-series

of four patients and applied the accelerated treatment of PPE without Clagett-window.

**Methods:** We evaluated our established surgical concept for accelerated treatment of PPE in patients with an oesophago-pleural fistula into the empty pleural cavity. The fistula was closed by direct suture with reinforcement or indirect closure by an omentum- or latissimus dorsi muscle-flap and the chest cavity closed and debrided in a scheduled manner.

**Results:** Four patients (one female), median age 59.75 years (range 55–65 y.) had a pneumonectomy for lung cancer (2), destroyed lung (1) or emphysema (1). 3 PPE were on the left side. Oesophago-pleural fistula occurred on the 8th d, 64th d, 105th d and 50 months after pneumonectomy. In 2 patients the fistula was covered by omentum flap or omentum- and muscle-flap or mediastinal tissue in one. Scheduled debridement occurred every 18–72 hours and the chest was definitively closed within 14 days in all patients. Discharge was between 17 and 37 days after first revision-thoracotomy. In the follow up (16, 25, 30 and 57 months) no recurrence of fistula or empyema occurred.

**Conclusion:** In all patients the oesophago-pleural fistulas have been successfully closed by local measures and the pleural empyema treated with a closed chest.

### Natural killer cells improve allogeneic lung transplants via depletion of donor dendritic cells

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**Objective:** Natural killer (NK) cells are innate lymphocytes targeting virus infected and tumor cells. Little is known about their ability to limit adaptive immune responses. We here investigated to which extent NK cells can influence lung allograft rejection.

**Methods:** Using an orthotopic lung transplantation (Tx) mouse model, we employed allogeneic strains to induce allo-rejection, stimulated recipient NK cells by IL-15/IL-15Ra complexes for testing the gain of function, while using IL-15Ra deficient and CD11c-DTR mice deficient for dendritic cells recipient mice to test the loss of function. Furthermore, congenic marker CD45.1 to prove the origin of cells, flow cytometry, histology, oxygenation capacity, magnetic resonance imaging, and CD107 degranulation assay were employed.

**Results:** NK cells infiltrated mouse lung allografts prior to T cells and diminished allograft inflammation while NK cell deficiency enhanced allograft rejection. Vice versa, IL-15/IL-15Ra complexes expanded recipient NK cells, resulted in decreased T cell infiltration and improved lung Tx function. These NK cells killed allogeneic dendritic cells (DCs) in vitro and significantly decreased the number of allogeneic DC in transplanted lungs in vivo. Furthermore, DC depleted lung allografts presented with ameliorated signs of rejection.

**Conclusion:** NK cells favor allograft acceptance and promote Tx tolerance by depleting graft derived DCs which otherwise prime alloreactive T cell responses.