BACKGROUND: Intraductal papillary mucinous neoplasm (IPMN) of the pancreas often has distinct pancreatic ductal adenocarcinoma (PDAC) in the same pancreas. Roles of endoscopic retrograde pancreatography (ERP) during the management of IPMN in terms of early diagnosis of concomitant PDAC have not been well documented. The aim of this study was to clarify whether ERP would be useful for the early detection of concomitant PDACs in patients with IPMNs.

METHODS: Medical records of 179 patients who were histologically confirmed to have IPMNs by resected specimens at our department between 1987 and 2011 were retrospectively reviewed. The patients having concomitant PDACs were selected, and then the diagnostic abilities to detect concomitant PDACs of computed tomography (CT), magnetic resonance imaging / cholangiopancreatography (MRI/MRCP), endoscopic ultrasonography (EUS), and ERP were compared between early-stage (stage 0 or I according to the Japanese general rules for pancreatic cancer) and advanced PDACs (stage II, III, and IV). Abnormal findings to suspect the presence of PDAC in CT, MRI/MRCP, and EUS included an irregular solid mass lesion and stenosis/dilation of pancreatic duct, distinct from IPMNs. Abnormalities suspicious of the presence of PDAC in ERP were defined as irregularity of pancreatic duct such as stenosis and obstruction, and/or positive results (class IV or V) of pancreatic juice / brushing cytology.

RESULTS: A total of 23 PDACs developed synchronously or metachronously in 20 patients, and the prevalence of PDACs concomitant with IPMNs was 11.2% (20/179). Sensitivities to detect PDACs of CT, MRI, and EUS in early group (16%, 29%, 29%, respectively) were significantly lower than those in advanced group (87%, 93%, 92%, respectively) (p<0.01). On the other hand, sensitivity of ERP in early group was as high as that in advanced group (86% vs. 82%, p>0.99). Among 7 early PDACs, 3 were diagnosed only by ERP.

CONCLUSION: ERP has an important role in the early diagnosis of distinct PDACs in patients with IPMNs. Further investigation is necessary to clarify the indication and timing of ERP during the management of IPMNs in term of early detection of concomitant PDACs.
40365 ISOLATED PERI-PANCREATIC NECROSIS IS ASSOCIATED WITH BETTER OUTCOMES COMPARED TO PANCREATIC NECROSIS WITH OR WITHOUT PERI-PANCREATIC NECROSIS

**Aim:** There is scant data that isolated peri-pancreatic necrosis (PPN) might be less serious than pancreatic necrosis (PN). We investigated the relationship between PN with/without PPN and isolated PPN with regards to important clinical outcomes in patients with acute pancreatitis (AP).

**Method:** Between 2005-2008, 356 patients with a diagnosis of AP were admitted to our institution and had CT scan. These patients were categorized into three groups based of presence or absence of PN and PPN; Group A (PN-PPN-,#232), Group B (PN-PPN+,#49), Group C (PN+PPN-/+,#75). The persistence organ failure (POF), length of hospital stay (LOS), need for ICU, length of ICU stay (LOICU), need for intervention and mortality were recorded. The clinical outcome were compared between Group A, B and C.

**Results:** For the three groups A, B and C, POF rates were 32(13.8%), 12(24.5%) and 41(54.7%), LOS 8.9 ± 14.2, 22.8 ± 50.3 and 40.1 ± 50.2 days, LOICU 1.5 ± 6.1, 5.0 ± 16.4 and 6.6 ± 16.6 days, need for ICU 45(19.3%), 15(30.6%) and 41(54.6%), need for intervention 0.0(0.0%), 16(32.7%) and 50(66.7%), and the mortality 2.6%, 4.1% and 12.0%, respectively.

LOS, LOICU, need for ICU and need for intervention were significantly different between A and B (P<0.05). All outcomes showed significant differences between A and C (p<0.05). POF, LOS, need for ICU, and intervention showed significant differences between B and C (P<0.05).

**Discussion:** Patients with PN had worse prognosis compared to those with isolated PPN. This finding is very important and may help the recent efforts at revision of Atlanta classification.
High resolution, triple phase, computed tomography (CT) is a standard preoperative test in patients undergoing pancreatic resection. In the context of advances in imaging, we examined the clinicopathologic implications of a range of CT findings. Methods: In the past 5 years, 143 patients with resected pancreatic ductal adenocarcinoma (PDA) and 43 patients with resected non-pancreatic periampullary adenocarcinoma (NP-PA) underwent a pancreas protocol CT at our institution. Imaging findings were analyzed with respect to perioperative data. Vessel involvement was defined as any degree of tumor encasement of major visceral vessels. A mass was identified on CT in 94% of PDAs and 74% of NP-PA. In 50% of patients with PDA, there was a discrepancy of $\geq 1$ cm between the size of the reported mass and the tumor size in the specimen. The mass size was underestimated in 75% of these cases, and overestimated in 25%. CT was particularly inaccurate at imaging distal bile duct cancers, as 47% were undetectable, despite a median pathologic tumor size of 1.8 cm. Enlarged lymph nodes were detected preoperatively on CT in 59% of PDAs. In these patients, 71% had lymph node metastases on pathology. Patients without detectable lymphadenopathy had lymph node metastases in a similar number (73%, $p=1.0$). This observation is seen in the NP-PA group as well ($p=0.8$). Vessel involvement on CT was noted in 23% of PDAs. A vessel resection was necessary in 3% of cases with perceived vessel involvement and 2% of cases without involvement ($p=0.5$). Similarly, there was no difference between the two groups in the rate of a positive uncinate margin (24% vs 27% respectively, $p=0.8$). While pancreas protocol CT is and should remain a key component of the preoperative evaluation, certain radiographic findings should be interpreted with caution. In particular, lymphadenopathy on CT is not associated with true lymph node metastases. Moreover, in patients selected for surgery, a suggestion of major visceral vessel involvement on CT neither predicts the need for vessel resection, nor is associated with a positive uncinate margin.
**40839 DIFFERENTIAL DIAGNOSIS OF PANCREATIC CANCER FROM CHRONIC PANCREATITIS**

**Introduction**
Differential diagnosis of chronic pancreatitis (CP) and pancreatic carcinoma (PDAC) can be difficult. Especially in cases when the carcinoma arises in a chronically inflamed pancreas. The aim of this study was to evaluate the characteristics of the patients’ history, laboratory values and the efficacy of different imaging methods in differentiating between chronic pancreatitis and cancer in focal pancreatic lesions.

**Material and Methods**
Patients with history of chronic pancreatitis and pancreatic cancer (cPDAC) were identified by searching the prospective database of the Department of Vascular, Thoracic and General Surgery of the University Hospital Dresden. Patients were diagnosed with CP on the basis of a typical history and the presence of at least two of the following findings: (1) pancreatic calcification confirmed by computerized tomography, (2) history of alcohol abuse (3) history of CP longer than 12 months or if the diagnosis of CP was histological confirmed prior to operation.

29 Patients with cPDAC were identified, which were operated between 2002 and 2011. Findings of the patients were compared to a control group of patients with PDAC (n= 51) or CP (n= 35) only. For survival analysis we compared cPDAC patients to a bigger cohort of 195 patients with pancreatic head resection for PDAC.

**Results**
In 11 of the 29 cPDAC patients pancreatic carcinoma was only diagnosed intra-operatively. Patients with cPDAC and surgical curative resection had a significantly poorer survival compared with curative resected PDAC patients (35.3 moths vs. 82.6 months, p<0.001). Univariate analysis showed, that history of jaundice, normal exocrine function, negative history of pain and abstinence from alcohol or nicotine were significantly correlated with cPDAC compared to CP. Patients with cPDAC had a significantly shorter history of pain.

Different laboratory values were correlated to cPDAC, namely CA19-9.

CT, US and MRT all could significantly differ between PDAC and CP. However, in the group of patients, that was only diagnosed intraoperatively with cPDAC, all of the imaging modalities failed.

**Conclusions**
We could identify different characteristics in the history of patients with CP that should developed PDAC. All those characteristics should be considered by the clinician in the differential diagnosis of PDAC and CP. The reasons for worse prognosis of cPDAC compared to PDAC without history of chronic pancreatitis remains unclear.
Purpose: The Physiologic and Operative Severity Score for the enUmeration of Mortality and Morbidity (POSSUM) is a predictive scoring system for postoperative morbidity. While numerous studies validate its application to major abdominal surgery, only few exclusively consider pancreatic resections, whose unique complications are costly and problematic. We examined whether POSSUM could accurately reflect clinical outcomes in pancreatic resection.

Methods: 697 consecutive pancreatic head resections (446 classic Whipples, 251 PPPD) were performed between 1993 and 2010. POSSUM score was calculated for each case, and compared to observed morbidity. Binary logistic regression was used to make further statements about the validity of the score.

Results: The POSSUM-predicted morbidity was 50.5%. The observed morbidity was 43.6%. The Hosmer-Lemeshow goodness-of-fit test validated POSSUM as a predictive scoring system for postoperative morbidity. However, the model had a significant poor fit. POSSUM under-predicted actual morbidity in patients who are at low risk, and it over-predicts actual morbidity in patients who are deemed to be at high risk.

Conclusions: POSSUM was statistically shown to be a valid perioperative scoring system for pancreatic surgical outcomes. However, because of the poor fit this scoring system only has little clinical relevance and should not be used to guide management decisions. Modifications of this system might be promising.
40849 NATIONWIDE DIFFUSION OF LAPAROSCOPIC RESECTION IMPROVES QUALITY AND COST MEASURES FOR DISTAL PANCREATECTOMY

BACKGROUND: Laparoscopic distal pancreatectomy (LDP) was first reported in 1996. Since then, all publications evaluating LDP have consisted of institutional case series. We hypothesize that a national database inquiry could offer insight into the application and outcomes of LDP.

METHODS: The Nationwide Inpatient Sample was queried for patients undergoing DP between 1998-2009. Multivariate analyses were performed using logistic regression models, adjusting for age, gender, ethnicity, comorbidities, year of procedure, and hospital settings.

RESULTS: 42,320 open DP (ODP) and 1,908 LDP were performed during this period. The proportion of DPs performed laparoscopically increased from 2.5% to 7.3%. The groups were comparable for gender and Charlson comorbidity index, while LDP patients were 1.5 years older (P=0.002). LDP was associated with significantly lower transfusion requirements (11.0% vs. 17.9%), sepsis rates (0.7% vs. 2.3%), and length of stay (LOS; 8.6- vs. 10.8-days). On multivariate analyses, LDP offered the following statistically significant advantages over ODP: lower mortality (OR 0.36); shorter LOS (1.48-days); lower total charges ($10,909.52); lower sepsis rates (OR 0.246); and fewer transfusion requirements (OR 0.538). There were no differences in complication rates, including fistulae, infections, abscesses, hemorrhage, hematomas, inadvertent organ injuries, wound complications, organ dysfunction, or thromboembolic events.

CONCLUSIONS: The application of LDP has tripled in practice from 1998-2009. We confirmed reports of LDP’s advantages of shorter LOS and lower blood loss. We also identified novel advantages, including lower mortality and sepsis rates, as well as lower total charges. LDP has evolved into a safe and potentially more cost-effective option in the treatment of pancreatic diseases.
Background:
A “step-up” approach is currently the treatment of choice for acute necrotizing pancreatitis (ANP). The aim of this study was to evaluate the outcome of minimally invasive retroperitoneal necrosectomy (MINE) and endoscopic transgastric necrosectomy (ETG) and to compare it to open necrosectomy (ONE).

Methodology:
Patients with acute pancreatitis admitted to our institution from 1998 to 2010 (n > 300) were identified. From these, patients who received either ONE, MINE or ETG were selected for further analysis. Statistical analysis employed two-sided Fisher’s exact test and Mann-Whittney U-test.

Results:
From 2002 to 2010, n = 32 patients were treated by minimally invasive procedures, MINE (n =14) and ETG (n=18) or ONE (n=30) for pancreatic necrosis. Time from onset of symptoms to intervention was shorter for ONE than for MINE or ETG (median, 11 vs. 39 vs. 54 days, p < 0.05) and therefore, the rate of critically ill patients with sepsis or septic shock was highest in ONE (93%) and MINE (71%) compared to ETG (17%; p < 0.05). Problems after ONE and MINE were ongoing sepsis (ONE: 73% vs. MINE: 29% vs. ETG: 11%) and bleeding requiring intervention (ONE: 26% vs. MINE: 21% vs. ETG: 17%). The specific complication of ETG was gastric perforation to the peritoneal cavity during the procedure (28%), requiring immediate open pseudocystogastrostomy. Laparotomy was necessary in 21% after MINE and 28% after ETG, due to specific complications or persistent infected necrosis. Overall mortality was highest after ONE (ONE: 63% vs. MINE: 21% vs. ETG: 6%, p<0.05).

Conclusion:
Morbidity and Mortality remains high in acute necrotizing pancreatitis. Operative procedures should be delayed as long as possible to reduce mortality. Minimally invasive procedures can avoid the necessity of laparotomy but also bear specific complications requiring immediate or secondary open operative treatment. They should therefore only be performed at specialized centers.
40894 EMT IN AMPULLARY CANCER

Background: Ampullary cancer is a relatively rare disease and can frequently be treated by surgical resection. There are two main subtypes, intestinal and pancreatobiliary. Invasion and metastasis of cancer cells has been shown to be promoted by the activation of the 'epithelial to mesenchymal transition' (EMT) program, defined by the loss of epithelial characteristics and the acquisition of a mesenchymal phenotype. ZEB1 (zinc finger E-box binding homeobox 1) is an activator of EMT and cancer stem cell properties in pancreatic cancer.

Materials and Methods: We studied the occurrence and mechanisms of EMT in ampullary carcinoma using immuno-histochemical analysis from human tissue samples and two established human ampullary carcinoma cell lines. For in vitro characterization, expression of EMT and tumor subtype markers, cell growth and inhibition by chemotherapy, matrigel transmigration and tumor sphere formation were employed with two pancreatic cancer cell lines serving as controls.

Results: Immunohistochemical (IHC) analysis of human ampullary cancer tissue showed lymph node metastasis to be associated with tumor budding and loss of CDX2 expression, associated with the pancreatobiliary phenotype. Overall, the degree of EMT was only moderate as Vimentin or ZEB1 expressions were almost never observed in tumor tissue. The two ampullary cancer cell lines displayed a strong EMT phenotype, evidenced by spindle form cell shape, diffuse colony growth pattern, high ZEB1 and Vimentin expression, low levels of E-Cadherin and micro-RNA 200c and strong matrigel transmigration. The intestinal subtype marker CK20 was expressed in all cell lines including pancreatic cancer cell lines, but CDX2 expression was only found at very low levels. Upon knockdown of ZEB1 in vitro, E-Cadherin expression was increased, whereas Vimentin expression, spindle shape and diffuse colony growth pattern, matrigel transmigration as well as tumor sphere formation decreased. The expression of tumor subtype markers did not change with transient ZEB1 knockdown. Treatment with TGF-ß did not further increase the high ZEB1 levels but induced a slight further decrease in E-Cadherin expression and increase of diffuse growth pattern.

Conclusion: Invasion and metastasis of ampullary cancer are associated with EMT. The pancreatobiliary type of ampullary cancer displays more signs of EMT than the intestinal type. High ZEB1 expression levels could not be found in human tumor tissue, but in vitro experiments show that EMT in ampullary cancer cell lines is regulated by ZEB1.
Objective: The aim of this prospective randomized controlled trial was to compare the perioperative outcome of pancreatogastrostomy (PG) versus pancreatojejunostomy (PJ) after pancreatoduodenectomy at our institution with respect to surgical morbidity and primary endpoint pancreatic fistula.

Background Data: Four randomized controlled trials (RCT) have compared PG to PJ, and only the most recent trial did demonstrate a significantly reduced incidence of postoperative pancreatic fistulae with PG.

Methods: We conducted a single-center RCT. Patients were screened and consented preoperatively. Randomization was performed intraoperatively. PG was performed via anterior and posterior gastrostomy with pursestring and inverting seromuscular suture. The control intervention was PJ with duct-to-mucosa anastomosis. The primary endpoint was postoperative pancreatic fistula (POPF) of grade B or C (ISGPN). Results: From 2006 to 2011, n=268 patients were screened and n=116 were randomized to n=59 PG and n=57 PJ. Intention-to-treat analysis did not reveal a statistically significant difference regarding the primary endpoint (PG vs PJ, 10% vs 12%, p=0.775). However, in the subgroup of high-risk patients with a soft pancreas, there was a trend towards a reduction of pancreatic fistula rate with PG (PG vs PJ, 14% vs 24%, p=0.352). The findings from analysis of secondary endpoints validated retrospective data from our group and others demonstrating shorter operation time (404 vs 443min, p=0.005) and reduced hospital stay for PG (15 vs 17 days, p=0.155). On the other hand PG showed increased, however non significant, delayed gastric emptying (DGE, 27% vs 17%, p=0.246) and intraluminal bleeding (7% vs 2%, p=0.364). Mortality was low in both groups (<2%).

Conclusions: Our RCT suggests a reduced POPF rate only in high-risk patients with PG. Retrospective observations suggesting increased rate of DGE, intraluminal bleeding on the one hand and shorter operation time and shorter overall hospital stay with PG on the other hand are confirmed. A larger multicenter trial is needed for generalization and finals answer of these results and currently performed in Germany (RECOPEC).
THE EFFECT OF DEPRESSION ON DIAGNOSIS, TREATMENT, AND SURVIVAL IN PANCREATIC CANCER

INTRODUCTION: Depression has been associated with delayed presentation, inadequate treatment, and poor survival in patients with cancer. Patients with pancreatic cancer have high rates of depression.

METHODS: Using Surveillance, Epidemiology, and End Results (SEER)-Medicare linked data (1992-2005), we identified patients diagnosed with pancreatic adenocarcinoma (N=23,745). ICD-9 codes were used to evaluate depression during the 3-27 months prior to cancer diagnosis. The effect of depression on receipt of therapy and survival was evaluated in univariate and multivariate models.

RESULTS: 7.9% of patients with pancreatic cancer had a diagnosis of depression (N=1,868). Depression was associated with increased age, female sex, white race, single or widowed status, increasing comorbidities, and advanced stage disease (p<0.0001). Patients with depression were less likely to undergo surgical resection, radiation, and chemotherapy, and less likely to see a surgeon or medical oncologist (p<0.0001). In an adjusted model, patients with locoregional disease and depression had 37% lower odds of undergoing surgical resection (OR=0.63, 95% CI 0.52 – 0.76). In a multivariate model without treatment, depression was associated with lower 2-year survival in locoregional disease (HR=1.20, 95% CI 1.09-1.32). After adjusting for surgical resection, this association was attenuated (HR=1.14, 95% CI 1.04–1.26). In patients who underwent surgical resection for locoregional disease, depression was a significant predictor of survival (HR=1.34, 95% CI 1.04-1.73). Patients with distant disease and depression had 21% lower odds of receiving chemotherapy (OR=0.79, 95% CI 0.70–0.90). In a multivariate model without treatment, depression was associated with lower 2-year survival in distant disease (HR=1.08, 95% CI 1.01-1.14). After adjusting for chemotherapy for distant disease, depression was no longer a significant predictor of survival (p=0.3235).

CONCLUSIONS: The decreased survival associated with depression appears to be mediated by a lower likelihood of appropriate treatment in depressed patients. Accurate recognition and treatment of pancreatic cancer patients with depression may improve treatment rates and survival.
Purpose: Front-line, gemcitabine-based chemotherapy for patients with pancreatic cancer has limited efficacy and innovative strategies are urgently needed. In this study we determined the feasibility of its use in combination with non-invasive, non-ionizing radiofrequency electromagnetic radiation (RF) in mouse models of pancreatic adenocarcinoma.

Experimental Design: In vitro, Panc-1 cells were treated with varying doses of gemcitabine with or without RF exposure and examined for cytotoxicity using a flowcytometry-based apoptosis assay. In vivo, mice with established Panc-1 ectopic and orthotopic pancreatic tumors were treated weekly with 70 mg/kg gemcitabine intraperitoneally with or without 10-min RF exposure. Tumor size was measured at the end of experiment. Vital organs were collected for histopathological analysis. Immunohistochemical markers for proliferation (Ki67), apoptosis (cleaved caspase 3), autophagy (LC3B) and angiogenesis (VEGF and CD31) were evaluated. Morphological changes were assessed using high-resolution transmission electron microscopy.

Results: RF treatment significantly enhanced the cytotoxicity of gemcitabine to Panc-1 cells when compared with untreated controls and either therapy alone in in vitro experiments (P<0.001). Immunocytochemical analysis of autophagy marker (LC3B) demonstrated that single RF treatment induced reversible autophagy response lasting 48 hours. Addition of subtoxic doses of gemcitabine to the RF treatment prevented recovery of tumor cells from autophagy, which eventually led to cell death. Consistent with this, a high incidence of autophagosomes was noted in cells treated with combination therapy in comparison with either therapy alone. Addition of RF exposure to gemcitabine treatment in vivo significantly inhibited growth of ectopic and orthotopic Panc-1 tumors in mice (P<0.01 vs untreated group), whereas RF or gemcitabine by themselves showed no effect. Treatment was well tolerated during a 40-day course of therapy. Immunohistochemical analysis confirmed the decline of proliferating, Ki-67 positive tumor cells and an increase in cells undergoing autophagy, LC3B positive cells in the combination therapy group compared with either therapy alone. No significant changes were seen in apoptotic or angiogenic markers.

Conclusions: Exposure to RF induces autophagy in pancreatic cancer cells, which is sustained with a sub-therapeutic dose of gemcitabine eventually causing cell death. RF combination therapy with gemcitabine demonstrated promising anti-tumor efficacy and was well tolerated in mouse models of pancreatic cancer.
Introduction: Although the prognosis in patients with biliary carcinoma remains poor, adjuvant gemcitabine-based chemotherapy after surgical resection for biliary carcinoma has been shown to improve survival. There have been no reports concerning a useful predictive biomarker in patients with cholangiocarcinoma treated with adjuvant gemcitabine chemotherapy. The aim of this study was to evaluate whether the expression of intratumoral human equilibrative nucleoside transporter 1 (hENT1), which is the major transporter responsible for gemcitabine uptake into cells, can predict the survival of cholangiocarcinoma patients treated with adjuvant gemcitabine-based chemotherapy after surgical resection.

Methods: Intratumoral hENT1 expression was investigated immunohistochemically in 105 patients with resected cholangiocarcinoma. The relationship between intratumoral hENT1 expression and prognosis was evaluated statistically. This study was a retrospective analysis on retrospectively collected tissue and data.

Results: Out of 105 patients, 51 (49%) received adjuvant gemcitabine-based chemotherapy. High and low intratumoral hENT1 expression was present in 74 (70%) and 31 (30%) cases, respectively. There were no significant differences in clinicopathological factors between patients with high hENT1 expression and those with low hENT1 expression. Survival of patients with high hENT1 expression was significantly better than that of patients with low hENT1 expression among patients who received adjuvant gemcitabine-based chemotherapy (P = 0.008, Fig 1), but not among patients who did not (P = 0.894). Moreover, a significant difference in survival between patients who received adjuvant gemcitabine-based chemotherapy and those who did not was observed among patients with high hENT1 expression (P = 0.002), but not among patients with low hENT1 expression (P = 0.525). Intratumoral hENT1 expression was only an independent predictive factor for patients treated with adjuvant gemcitabine-based chemotherapy by multivariate analysis (P = 0.027).

Conclusion: High intratumoral hENT1 expression was associated with increased overall survival in patients with cholangiocarcinoma who received adjuvant gemcitabine-based chemotherapy.
INDICATOR FOR PROPER MANAGEMENT OF SURGICAL DRAINS FOLLOWING PANCREATICODUODENECTOMY

Background and Objectives:
Recent reports suggested that early removal of surgical drains following pancreaticoduodenectomy (PD) reduce the postoperative complications including postoperative pancreatic fistulas (POPFs) with decreased hospital stay and costs. However, the indicator for proper drain management still remains unclear. The aim of this study was to identify the indicators for proper drain management after PD.

Methods:
Prospectively collected data from 200 consecutive patients who underwent PD were evaluated. (86 females and 114 males, median age 66 years; range 19-88). The pancreatic anastomosis was reconstructed with a two-layered duct-to-mucosa pancreaticogastrostomy with internal stent. POPF was assessed using the criteria of International Study Group Pancreatic Fistula (ISGPF). The surgical complications were classified according to the Clavien-Dindo (C-D) classification. Predictive clinical factors for clinically relevant POPFs (Grade B and C) were analyzed by logistic regression analysis. Management of surgical drains was also analyzed.

Results:
Of 200 patients, 44 developed pancreatic fistulas; grade A in 29 patients, grade B in 12, and grade C in 3. Thus, clinically relevant POPFs were occurred in 15 (8%). Severe surgical complications (over C-D classification Grade3) were occurred in 17 (9%).
By univariate analysis, drain amylase on postoperative day (POD) 2, 3, 4, 5, the color of surgical drain fluid (dark red) on POD1,3,4, WBC on POD3,4, serum C-reactive protein (CRP) on POD 3,4, and body temperature on POD3,4,5 were found to be significantly associated with clinically relevant POPFs (p<0.05).
By multivariate analysis on POD4, the color of surgical drain fluid (dark red) [p=0.01, Odds ratio 9.8, 95%CI 1.7-58.3] and serum CRP [p=0.03, Odds ratio 1.2, 95%CI 1.1-1.4] were found to be independent predictive factors for clinically relevant POPFs.

Conclusions:
A combination of serum CRP levels and the color of surgical drain fluid on POD4 may be indicators for proper management of surgically placed drains following PD.
40983 YIELD OF CLINICAL AND RADIOGRAPHIC SURVEILLANCE IN PATIENTS WITH RESECTED PANCREATIC ADENOCARCINOMA FOLLOWING MULTIMODALITY THERAPY

Background: The National Comprehensive Cancer Network recommends serial clinical evaluations of patients with resected pancreatic adenocarcinoma (PDAC) to assess for symptoms and to initiate treatment of patients with detected recurrence. We hypothesized that clinical and radiographic surveillance would detect recurrence when it would be most amenable to treatment. We sought to evaluate the diagnostic yield of an intensive surveillance strategy.

Methods: We identified all patients with PDAC who underwent potentially curative pancreaticoduodenectomy at our institution from 1998–2008. We compared clinical factors between patients with symptomatic recurrence and asymptomatic recurrence. Factors associated with post-recurrence overall survival (PROS) were evaluated with multivariate models.

Results: Follow-up was complete for 327/356 (92%) eligible patients; 216 (66%) developed recurrence. Recurrence was symptomatic in 98 (45%) patients and asymptomatic in 118 (55%). The median time between surveillance CT scans did not differ between symptomatic and asymptomatic patients (p=0.33). Symptomatic recurrence was characterized by multifocal disease or carcinomatosis, poor performance status (PS), and low rate of subsequent therapy. The median time to recurrence did not differ between symptomatic and asymptomatic patients (12.3 vs. 14.5 months p=0.38), minimizing lead-time bias. Symptomatic patients had a significantly shorter PROS (5.1 vs. 13.0 months, p<0.001). Treatment was administered more frequently to asymptomatic than to symptomatic patients (91.2% v. 61.4%, p<0.001). At the time of recurrence, preserved PS≤1, administration of further therapy, low CA 19-9, and isolated local or distant (vs. regional or multiple-site) recurrence were independent predictors of longer PROS (p<0.001).

Conclusions: Symptomatic recurrence is associated with poor PS, significant disease burden, and rapid clinical decline, which may preclude further treatment. Intensive surveillance strategies may be useful for detecting patients with preserved PS at recurrence who can tolerate and potentially benefit from further therapy.
41036 TRANSIENT RECEPTOR POTENTIAL ANKYRIN 1 (TRPA1) MEDIATES CHRONIC PANCREATITIS PAIN IN MICE.

**Background and Aims:** Chronic pancreatitis (CP) is characterized by persistent inflammation, fibrosis and destruction of the glandular pancreas. Chronic abdominal pain is a cardinal feature of this disease, but its neurobiology is poorly understood and the mechanisms are largely unknown. We previously showed that the membrane-bound ion channel Transient Receptor Potential Ankyrin 1 (TRPA1) mediates inflammation and pain in acute pancreatitis via the release of Substance P (SP). Here we determined if TRPA1 plays a role in inflammatory pain in a surgical model of CP in mice. **Methods:** CP was induced in C57Bl6 and trpa1-/- mice by retrograde injection of trinitrobenzenesulfonic acid (TNBS) into the pancreatic duct and the mice were monitored for 2-3 weeks. Control groups received vehicle (10% EtOH), or saline (NS) or were sham operated. We assessed the extent of CP by inflammatory endpoints (weight loss, serum amylase activity, pancreas size, histological severity score, fibrosis), behavioral endpoints (spontaneous activity [distance run on a wheel per day], referred mechanical abdominal and somatic pain [measured with Von Frey Filaments in the abdomen and in the hind paw]) and molecular (cyclooxygenase 2 and SP immunoreactivity) endpoints. **Results:** CP mice lost more body weight than controls. CP mice had a robust inflammatory response, with a significant decrease in pancreas size (P<.005 vs NS, <.0001 vs EtOH and Sham) and serum amylase activity (P<.05 vs Sham, <.005 vs NS), accompanied by increased fibrosis (P<.0001 vs EtOH, NS and Sham). Histopathological changes in CP pancreatic tissues included infiltration of monocytes, neutrophils and lymphocytes, necrosis, loss of zymogen, vacuolization and loss of acinar cells with replacement by fat (P<.0001 vs EtOH, NS and Sham). CP mice had decreased spontaneous activity (CP distance was 2-3 folds less than control groups) and increased referred mechanical abdominal (allodynia: P<.0001 vs Sham; hyperalgesia P<.0001 all 3 weeks) and somatic pain (P<.005 vs Sham, all 3 weeks). CP increased cyclooxygenase 2 and SP immunoreactivity in the thoracic levels of the spinal cord that innervate the pancreas. The major differences among experimental groups occurred within the first 2 weeks after CP induction. Thus, to investigate the role of TRPA1, we similarly induced CP in C57Bl6 and trpa1-/- mice and monitored them for 2 weeks. Most of the inflammatory (i.e. amylase P<.05 vs C57Bl6; histopathological changes P<.005) and behavioral endpoints (i.e. abdominal pain P<.05 vs C57Bl6 both weeks; histopathological changes P<.005, both weeks) were significantly decreased in trpa1-/- mice, compared to C57Bl6 mice. Our findings indicate that TRPA1 plays a major role in mediating chronic inflammatory pancreatic pain. **Conclusions:** We have established quantitative measurements characterizing chronic inflammation, visceral and somatic referred pain in a murine model of CP that has histological and behavioral similarities with human disease. These endpoints are applicable to other models of CP to identify novel mechanisms of inflammation and visceral pain. Thus, using these endpoints, we found TRPA1 mediates chronic inflammatory pancreatic pain and is a potential novel therapeutic target.
Background: Chronic pancreatitis (CP) is an inflammatory disease often accompanied by severe, intractable abdominal pain. Such pain lowers quality of life in CP patients, and in many cases is only relieved by total pancreatectomy (TP). To prevent the development of brittle diabetes, autologous islet cell transplantation (AIT) is often used in conjunction with TP for CP patients who have not lost endocrine function. The aim of this study was to evaluate the effectiveness of TP/AIT at reducing pain and improving quality of life in CP patients.

Methods: From 2009 through 2011, twenty-six patients underwent TP/AIT. Twenty-one patients (81%) were evaluated for pain and quality of life pre-transplant; of these, 13 (62%) were re-evaluated one month post-transplant, and 5 (24%) were re-evaluated three months post-transplant. The McGill Pain Questionnaire and the Visual Analog Scale (VAS) were used to evaluate pain, and the Short Form-36 (SF-36) Questionnaire was used to evaluate quality of life. The SF-36 Questionnaire was also administered to 31 healthy controls.

Results: Patients’ VAS and McGill scores decreased post-transplant, with the lowest scores at the 3 months post-operative time point. The mean pre-transplant VAS score was 5.1 on a scale of 0 to 10. Mean post-transplant VAS scores were 3.5 at one month (p = 0.008) and 3.0 at three months (p = 0.189). The mean pre-transplant McGill score was 62.2; mean scores for one- and three-month post-transplant follow-up were 48.2 (p = 0.001) and 40.4 (p = 0.020) respectively. SF-36 scores were slightly lower one month post-transplant with a mean of 97.4, compared to the pre-transplant mean of 100.1 (p = 0.977); however, scores at three months post-transplant were higher than pre-transplant scores (mean = 101.6; p = 0.037). Healthy controls that completed the SF-36 Questionnaire had a mean score of 102.0, which was slightly higher than CP patients at all three time points (p = 0.341; 0.129; 0.920).

Conclusions: CP patients had less pain after undergoing TP/AIT. VAS and McGill scores were significantly lower one month post-transplant than pre-transplant. Although scores decreased from one month to three months post-transplant, this change was not significant. SF-36 scores did not change significantly post-transplant compared to pre-transplant scores. Furthermore, there was no significant difference between the scores of CP patients and those of healthy controls, leading us to conclude that the SF-36 questionnaire is not a powerful tool for assessing quality of life in CP patients.
41160 INDUCTION CHEMOTHERAPY FOLLOWED BY RADIATION THERAPY IS ASSOCIATED WITH BETTER SURVIVAL FOR PATIENTS WITH LOCALLY ADVANCED PANCREATIC CANCER

Background: Advanced pancreatic cancer has a poor prognosis. At diagnosis, 80% of patients are unresectable; and among those unresectable, 40% of those are locally advanced. Currently, the standard treatment for locally advanced pancreatic cancer is not defined. Treatment often starts with radiation therapy in concurrence with low-dose chemotherapy as a radio-sensitizer. Neither the role of standard full-dose chemotherapy nor that of radiation therapy is established; the optimal sequence of full-dose chemotherapy and radiation therapy is also unknown. We performed a retrospective analysis of patients treated at the Johns Hopkins Hospital (JHH) to assess the role of chemotherapy and radiation therapy for locally advanced pancreatic cancer.

Methods: A total of 1433 pancreatic cancer patients were seen at JHH between June 2006 and June 2010 and their medical records were reviewed. After excluding borderline resectable patients and patients who only had consultations at JHH, we identify 67 patients who met the Society of Surgical Oncology diagnostic criteria for locally advanced pancreatic cancer and who were treated primarily at JHH. Clinical information from diagnostic CT scans, chemotherapy and radiation therapy was collected. Overall survival (OS) and progression-free survival (PFS) were compared among different subgroups by Kaplan-Meier analysis.

Results: For the 67 patients (37% female, median age 62y), median OS was 15.7 months, median PFS 7.9 months. Patients who received sequential treatment of full-dose chemotherapy and radiation had a longer PFS than those who received radiation alone (12.0 vs. 4.5 mo, p<0.01) or those who received chemotherapy alone (12.0 vs. 6.8 mo, p=0.08), but there was no difference in their OS. Among patients receiving both therapies sequentially, patients who received chemotherapy first had a significantly longer OS and a trend toward better PFS than patients who received radiation first (OS 18.1 vs. 11 mo, p=0.03; PFS 12.6 vs. 8.3 mo, p=0.15). Patients who received 3 or more cycles of chemotherapy prior to radiation had a trend for better OS than patients receiving less than three cycles of chemotherapy (17.6 vs. 14.6 mo, p=0.06). There was no difference in OS or PFS between patients who received single agent gemcitabine chemotherapy and patients who received a gemcitabine-containing combination (OS 15.8 vs. 18.1 mo, p=0.88; PFS 11.9 vs. 8.7 mo, p=0.41).

Conclusions: Although treatment course including both chemotherapy and radiation therapy is still favored, this study suggests that chemotherapy may play a more important role in the treatment of locally advanced pancreatic cancer. Our results support treating patients with induction chemotherapy for at least 3 cycles followed by consolidation with radiation therapy. These results need to be further validated in prospective clinical studies. Optimal combination chemotherapy regimens still need to be developed.
41185 THROMBOELASTOGRAPHY IDENTIFIES HYPERCOAGULATION IN METASTATIC PANCREAS CANCER: MURINE MODEL

INTRODUCTION: Pancreatic cancer has the highest risk for venothromboembolic events (VTE) of all gastrointestinal malignancies. Furthermore, surgical resection of pancreas cancers has greater than a 50% blood transfusions rate, which increases the risk of VTE. Current diagnostic tests (INR, PTT, PT, platelet count) are unreliable in predicting or preventing VTE. Recently, our lab has demonstrated that Thromboelastography (TEG) is able to better assess coagulation kinetics and direct patient therapy in non cancer patients. We hypothesize TEG will delineate coagulation abnormalities in a murine model of metastatic pancreatic cancer; moreover, we predict blood transfusion will induce hypercoagulability.

METHODS: C57/BL6 mice, age 7-9 weeks, underwent splenic inoculation with 2.5 x 10^5 Pan02 cells. One week after inoculation, mice were randomized to receive blood transfusion via tail vein injection in the amount of 1ml/kg or the equivalent dose of normal saline. Seven weeks after cancer inoculation, blood was collected with citrate in a 10:1 ratio. TEG was obtained via a Thrombelastograph® Hemostasis Analyzer. TEG was compared between mice with metastatic cancer plus blood transfusion, mice with metastatic cancer plus normal saline, and control mice (sham surgery and normal saline). Data were analyzed by ANOVA with p<0.05 used to determine significance.

RESULTS: All mice with metastatic pancreas cancer were found on TEG to have significantly higher maximum amplitude (MA) and G than control mice. The MA reflects clot strength, while G represents clot elasticity. The MA and G elevations indicate a hypercoagulable state.

CONCLUSIONS: TEG is able to delineate hypercoagulability associated with metastatic pancreatic cancer in an immunocompetent murine model. TEG may be a useful tool in identifying pancreatic cancer patients at risk for VTE. Unexpectedly, transfusion did not induce additional hypercoaguability.
Maximum Amplitude

p = 0.013

n ≥ 3
Introduction: In 2010 the WHO adopted a new grading system for neuroendocrine neoplasms (NET) of foregut origin based on proliferation determined by mitotic count and Ki67 index. Using a large single-institution cohort of resected pancreatic NETs (PNETs), we have retrospectively examined the prognostic value of the WHO 2010 classification system, the prior WHO classification system and AJCC stage for well-differentiated neuroendocrine tumors of the pancreas.

Methods: Search of pathology archives identified 114 patients who underwent pancreatic resection for PNETs at UCLA Medical Center from 1991-2009. Retrospective review of medical, surgical, and pathology databases was performed. Correlations between patient survival and various clinicopathologic factors were determined.

Results: By univariate analysis, significant predictors of disease-specific survival (DSS) in PNETs included positive margin status (p=0.019, HR 7.73, 95%CI [1.392-43.01]), and AJCC stage (Stage I, IIA versus IIB, IV, p=0.043, HR 6.87, 95% CI [1.06-37.41]). Individually, tumor size, perineural invasion, vascular invasion and functional tumor status were not significant predictors of DSS in the patient cohort. In our cohort, the new WHO 2010 classification scheme did not significantly predict DSS for well-differentiated PNETs (G1 PNETs versus G2 PNETs, p=0.085, HR 5.35, 95% CI [0.60-48.10]). In contrast, the prior WHO 2000 classification scheme was a significant predictor of DSS (1.0 + 1.1 PNETs versus 2.0 PNETs, p=0.048, HR 6.90, 95% CI [1.12-39.62]). We also examined whether WHO 2010 classification and AJCC staging parameters could be used in combination to better stratify patients into groups of variable prognostic significance. In stratified analysis of those patients with node-positive disease, G1 vs. G2 status showed a non-significant trend towards predicting patient survival after resection (p=0.13, HR 5.2, 95%CI [0.6-43.9]).

Conclusions: Consideration of both AJCC staging parameters and WHO 2010 G grade may be useful for the accurate prediction of DSS in resected, well-differentiated PNET, particularly for those patients with node-positive disease. Our findings in this retrospective analysis of a single institution cohort of PNET warrant further prospective analysis in a larger patient cohort.
Background. Although postoperative adjuvant chemotherapy for pancreatic carcinoma improves survival in some patients, the efficacy varies by individuals, and the results remain unsatisfying. The aim of this study was to clarify which is more useful as a predictive marker of adjuvant gemcitabine-based chemotherapy for pancreatic carcinoma after surgical resection, intratumoral human equilibrative nucleoside transporter 1 (hENT1) or ribonucleotide reductase regulatory subunit M1 (RRM1) expression.

Methods. Intratumoral hENT1 and RRM1 expression were examined by immunohistochemistry in 109 pancreatic carcinoma patients who received adjuvant gemcitabine-based chemotherapy after surgical resection. Relationships between clinicopathological factors, including hENT1 and RRM1 expression, and disease free or overall survival (DFS or OS) were evaluated by univariate and multivariate analyses.

Results. High intratumoral hENT1 and RRM1 expression was observed in 78 (72%) and 44 (40%) cases, respectively. DFS rates for all 109 patients were 59% at 1 year, 42% at 2 years, and 26% at 5 years, and OS rates were 81% at 1 year, 61% at 2 years, and 31% at 5 years, respectively. In univariate analysis, both hENT1 and RRM1 expression were significantly associated with DFS (hENT1: P = 0.004, RRM1: P = 0.011) and OS (hENT1: P = 0.001, RRM1: P = 0.040). In multivariate analysis, the both were identified as independent factors for DFS (hENT1: P = 0.001, RRM1: P = 0.009) and OS (hENT1: P = 0.001, RRM1: P = 0.019). The evaluation of the combination of the both was also identified as a powerful independent predictor for DFS (P < 0.001) and OS (P < 0.001).

Conclusions. Both hENT1 and RRM1 expression is useful as a predictive marker of adjuvant gemcitabine-based chemotherapy for pancreatic carcinoma after surgical resection. In addition, combined analysis of the two is even more useful.
BACKGROUND: Pancreatic stump leak is the major source of morbidity after distal pancreatectomy. We hypothesized that a duct-to-mucosa pancreaticogastrostomy after distal pancreatectomy (DP-PG) can decrease pancreatic fistula (PF) rates when compared to hand-sewn or staple closure. Since 2008, we conducted the nonrandomized cohort study with a prospective DP-PG group, forming our experimental group, and a retrospective control group undergoing hand-sewn closure. The aim of this study is to analyze the safety and efficacy of this method.

METHODS: DP-PG was intended to prevent PF after DP in 30 patients between April 2008 and November 2011. A historical control group was composed of 30 consecutive patients undergoing hand-sewn closure between January 2005 and March 2008. Main outcome measure was incidence of PF which was defined and graded according to the International Study Group on Pancreatic Surgery (ISGPS) classification. Secondary measures were complications which were assessed by the Clavien classification and postoperative hospital length of stay. Two groups were compared using Kruskal-Wallis test or chi-square tests.

RESULTS: Overall, a cohort of 60 patients underwent DP between 2005 and 2011. In the DP-PG group (n=30), none PF was observed in 19 patients (63%), Grade A was 10 (33%), Grade B was 1 (3%), and Grade C was none. In the control group (n=30), none PF was observed in 17 patients (57%), Grade A was 7 (23%), Grade B was 5 (17%), and Grade C was 1 (3%). Therefore the clinically-relevant PF (ISGPS Grade B/C) rate was significantly lower in the DP-PG group (3%) comparing to the control group (20%; P=0.01). Re-operation was required for one patient in both groups, but no one was due to PF. The mortality was zero in both groups. The operative time was slightly longer in the DP-PG group (median, 237 min) comparing to the control group (198min, P=0.05). The Clavien III-V severe complications were observed in 2 patients (7%; none for PF) in the DP-PG group, but in 4 patients (13%) in the control group. Development of a pancreatic leak resulted in prolonged hospital stays: 20 days in the DP-PG group vs. 29 days in the control group (P=0.03). The advantage of this technique is that pancreatic juice leaking from smaller branches on the cut surface which cannot be drained through the remnant main duct directly passes into the stomach and also allows decompress the intraductal pressure through the anastomosis.

CONCLUSIONS: Drainage through the pancreatic stump provided by duct-to-mucosa pancreaticogastrostomy after distal pancreatectomy (DP-PG) appears to have abruptly reduced clinically-relevant PF (ISGPS Grade B/C) rate and hospital stay. The economic impact of lower leak rates is reflected in lower morbidity rate and significantly shorter hospital stays. The results of our study should be validated in a randomized controlled trial.
QUALITY OF LIFE IN PATIENTS AFTER TOTAL PANCREATECTOMY IS COMPARABLE TO QUALITY OF LIFE IN PATIENTS AFTER A PARTIAL PANCREATIC RESECTION.
Background:
Quality of life after total pancreatectomy is perceived to be poor secondary to insulin-dependent diabetes and
pancreatic insufficiency. As a result, surgeons may be reluctant to offer this treatment for benign and premalignant diseases.

Methods:
We retrospectively reviewed a prospectively maintained database of pancreatic operations and identified patients who underwent a total pancreatectomy between 1994 and 2011 at our institution. Presenting features, operative characteristics, and postoperative outcomes were evaluated. Quality of life was assessed using institutional questionnaires and validated general, pancreatic disease-related, and diabetes-related instruments (EORTC QLQ-C30, EORTC-PAN26, ADD-QOL) in patients alive at the time of analysis, and compared with frequency-matched controls, patients after a pancreaticoduodenectomy. Continuous variables were compared using Student’s t-test or ANOVA. Categorical variables were compared using chi-square or Fisher’s exact test.

Results:
Between 1994 and 2011, 77 total pancreatectomies were performed, 39 for benign or premalignant, and 38 for malignant disease. Overall morbidity after total pancreatectomy was 49%, but only 12 (16%) patients experienced a major complication. Perioperative mortality was 2.6%. At the time of this study, 33 (43%) patients were alive and 25 agreed to participate in the survey; final results represent aggregate responses of 15 (10 benign and premalignant, 5 malignant). Mean time between surgery and survey administration was 3.2 years. Scores were compared with 14 matched patients who underwent pancreaticoduodenectomy (10 benign and premalignant, 4 malignant; 8 with postoperative diabetes). There were no statistically significant differences in quality of life in the global health, functional status, or symptom domains of the EORTC QLQ-C30 or in the pancreatic disease-specific EORTC-PAN26 between total and partial pancreatectomy patients, regardless of final pathology. Total pancreatectomy patients had slightly but not significantly higher incidence of hypoglycemic events as compared to partial pancreatectomy patients with postoperative diabetes. The negative impact of diabetes as assessed by the ADD-QOL did not differ between total and partial pancreatectomy patients. Life domains most negatively impacted by diabetes involved travel and physical activity, while self-confidence, friendships and personal relationships, motivation, and feelings about the future remained unaffected.

Conclusions:
While total pancreatectomy-induced diabetes negatively impacts select activities and functions, overall quality of life is comparable to that of patients after a partial pancreatic resection.
Background: Long-term survival after pancreatic surgery has increased gradually due to recent improvements in surgical techniques and experiences; therefore, postoperative evaluation of fat absorption and glucose metabolism disturbances is important. We have been reported that the non-invasive $^{13}$C-mixed triglyceride breath test ($^{13}$C-MTG-T), labelled long chain triglyceride mixture can reliably diagnose pancreatic exocrine insufficiency (Surgery, 2009). In this study, we investigate fat absorptive function in patients status post pylorus preserving pancreatoduodenectomy (PPPD) with pancreaticogastrostomy (PG) reconstruction more than 12 months after the procedure.

Methods: $^{13}$C-MTG-T (200 mg $^{13}$C-MTG, 20 g fat, and breath samples over 7 hours) was performed for 52 patients undergoing PPPD with PG reconstruction and 12 healthy volunteers, forming our control group. Pancreatic exocrine insufficiency was defined as percent of cumulative 7-hour $^{13}$CO2 exhalation (% dose $^{13}$C cum 7h) < 5%, assessed by $^{13}$C-MTG-T. Sections from the surgical pancreatic cut margin were used for histological assessment. The degree of pancreatic exocrine cells was calculated as ratio of the pancreatic exocrine cells area to total area measured in the entire section. We analyze the relationship between $^{13}$C-MTG-T as a measure of pancreatic exocrine insufficiency postoperatively and the degree of pancreatic exocrine cells by histology as well as the development of diabetes mellitus (DM) as a measure of pancreatic endocrine insufficiency.

Results: % dose $^{13}$C cum 7h was significantly lower in patients with PPPD (6.8±4.8%) than in healthy controls (15.5±6.0%; P<0.01). Pancreatic exocrine insufficiency assessed by $^{13}$C-MTG-T (% dose $^{13}$C cum 7h < 5%) was observed in 20 patients (38%) in PPPD group but none in the control group. Of the 52 patients undergoing PPPD, the histological degree of pancreatic exocrine cells was significantly higher in patients with % dose $^{13}$C cum 7h >/= 5% (81.7±5.4%) than those with <5% (67.8±8.5%; P=0.01). Patients with pancreatic insufficiency (% dose $^{13}$C cum 7h <5%) significantly decreased body mass index at 12 months after PPPD comparing to those with % dose $^{13}$C cum 7h >/=5% (-10.9±8.4% vs +0.9±9%; P<010). 6 patients had been diagnosed with DM prior to undergoing the procedure, and, of the remaining 46 patients, 5 (11%) became diabetic after the procedure. Patients with DM demonstrated significantly lower % dose $^{13}$C cum 7h comparing to patients without DM (5.9±4.3% vs. 10.5±5.2%; P<0.01).

Conclusion: $^{13}$C-MTG-T as well as residual pancreatic exocrine cells represented by histological degree of pancreatic exocrine cells at cut margin, reliably show long-term fat absorptive function after PPPD. Glucose metabolism disturbance is also related to post operative fat absorption.
**41493 ACTIVATION OF THE IL6-R/JAK/STAT PATHWAY IS ASSOCIATED WITH A POOR OUTCOME IN RESECTED PANCREATIC DUCTAL ADENOCARCINOMA**

**Introduction:** Inflammation in the form of chronic pancreatitis is an established risk factor for human pancreatic ductal adenocarcinoma (PDAC) development. Furthermore, inflammation has been demonstrated to accelerate pancreatic intra-epithelial neoplasia (PanIN) and PDAC development in Kras murine models. Constitutive activation of inflammation-related signal transducer and activator of transcription (Stat) 3 signalling has been implicated in the development and progression of a number of malignancies, including PDAC. Although, the Janus Kinase (Jak)/Stat pathway is a potential drug target, clinicopathological, molecular and prognostic features of Stat3 activated PDAC remain uncertain.

**Methods:** Using a tissue microarray based cohort of PDAC from 86 patients treated by pancreaticoduodenectomy at a single institution with complete clinicopathological follow-up data we evaluated the expression of activated and non-activated components of the interleukin 6 receptor (IL-6R)/Jak/Stat pathway by immunohistochemistry. IL-6R, Jak, phospho (p)-Jak, Stat3, pStat3\textsuperscript{Tyr705} and pStat3\textsuperscript{Ser727} were assessed in PDAC and PanIN. Protein expression was assessed by means of a modified histoscore. Density of the immune cell infiltrate was also assessed. A Cox regression multivariate analysis model was used to determine factors influencing survival.

**Results:** There appeared to be expression of activated components of the Jak/Stat pathway in PanIN lesions supporting an early role for this pathway in human PDAC. There was a spectrum of tumoral expression with high expression of activated components of the Jak/Stat pathway associated with poorer outcome. High pStat3\textsuperscript{Ser705} expression associated with reduced median overall survival when compared to moderate or low expression (10.3 months versus 21.0 months, \( p = 0.006 \), Log-rank). Similarly, pJak high expression associated with reduced median overall survival when compared to moderate or low expression (11.1 months versus 19.6 months, \( p = 0.022 \), Log-rank). In multivariate survival analysis patients with high pJak tumoral expression experienced a significantly poorer outcome independent of other pathological factors (\( p = 0.036 \), HR = 1.68). Likewise, high pStat3\textsuperscript{Tyr705} expression was a poor prognostic factor independent of lymph node status and tumor grade (\( p < 0.001 \), HR = 2.66). Patients with a combination of pJak\textsubscript{high}/pStat3\textsubscript{Ty705\textsubscript{high}} expression had an especially poor prognosis (median survival 8.8 months, 95% CI: 4.4-13.2). Activation of the Jak/Stat pathway failed to correlate with preoperative serum C-reactive protein levels or with the density of immune cell infiltrate.

**Conclusion:** Recent murine models suggest that Stat3 has an important role in PDAC tumor initiation. We have provided evidence that activation of the Jak/Stat3 pathway via phosphorylation assessed by immunohistochemistry is associated with adverse outcome following resection of PDAC with curative intent. These data support potential roles for pJak and pStat3 as prognostic biomarkers as well as therapeutic targets in the management of PDAC.
Figure: High pStat3$^{\text{Tyr705}}$ expression was associated with poor overall survival following resection with curative intent.
41505 EPIDURAL USE DURING PANCREATICODUODENECTOMY

Introduction: While multiple studies report favorable outcomes with epidural anesthesia and analgesia (EAA) use during major abdominal surgery, there is limited data in regards to EAA use during pancreatic head resection. A recent switch from EAA to narcotic PCA with OnQ pain catheters, allowed us to critically evaluate outcomes in patients undergoing a Whipple procedure with and without an epidural catheter.

Methods: After obtaining IRB approval, a retrospective chart review of 100 pancreaticoduodenectomies (PD) was performed; this included our most recent 50 patients without EAA use, and the last 50 patients with EAA just before we discontinued using this device, with all cases spanning from March of 2008 to July of 2011. Peri-operative and immediate post-operative clinical outcomes were compared.

Results: For obvious reasons, but not without importance, EAA patients had longer time from anesthesia start time to surgery start time (p=0.004). The EAA group had significantly higher rates of intra-operative hypotension (p= 0.001), and revealed a trend towards a higher intra-operative blood transfusion rate (56% EAA vs. 38%, p=0.071). No statistical significance was found between groups in terms of length of surgery, estimated blood loss, or intra-operative fluid administration. Post-operatively, EAA patients had a significant delay in diet initiation (8 days vs 5.6 days, p=0.015), and a higher requirement of post-operative fluid administration on post-op day # 1 (3,983 ml VS. 3,088.1 ml, p=0.001). Although the overall morbidity rate was similar between the two groups, the EAA group had higher rates of urinary tract infections (5/50 VS. 1/50), and intra-abdominal abscess (5/50 VS. 0/50). 10 of 50 (20%) patients in the EAA group had premature discontinuation of epidural catheter secondary to hypotension or inadequate pain control. Length of stay was similar between the two groups (EAA- 17 days VS. PCA- 15.1 days, p>0.05).

Conclusions: In the current study, EAA during PD was associated with a delay in surgery start time, increased episodes of intra-operative hypotension, a trend toward increased intra-operative blood transfusion and a 20% device failure rate. While pain relief may be excellent with EAA, these issues must be considered when selecting a peri-operative pain control strategy.
A FAMILY HISTORY OF PANCREATIC CANCER DOES NOT INCREASE RISK OF MALIGNANY IN IPMN

BACKGROUND: Individuals with a family history of pancreatic ductal adenocarcinoma (PDAC) have a higher risk of developing pancreatic cancer. However, the association between a family history of PDAC and the biologic behavior of IPMN remains unknown.

METHODS: A retrospective review of patients who underwent resection of a pathologically confirmed IPMN at the Massachusetts General Hospital (1990-2011) was conducted. Patients with (PFH) and without (NFH) a family history of PDAC were compared.

RESULTS: 324 patients with resected IPMN were identified, of which, 45 (13.9%) had a family history of PDAC. Of patients with a PFH, 34 (75.6%) had at least one affected first degree relative and the remaining 11 (24.4%) had at least one affected second degree relative. 11 patients (24.4%) had more than one affected first or second degree relative and six (13.3%) had two or more affected first degree relatives. There were no differences in demographic characteristics between the PFH and NFH groups. Extra-pancreatic malignancies (mostly breast cancer) diagnosed prior to the IPMN were more common in the group with PFH (35.6% vs. 20.1%, p = 0.03). There was no difference in tumor size (3.42-cm vs. 2.98-cm), tumor location, proportion of main duct/combined type IPMN (55.5% vs. 54.8%), epithelial subtype, carcinoma in situ/high grade dysplasia (40.0% vs. 44.4%) and invasive carcinoma (15.6% vs. 20.8%) when comparing PFH vs. NFH patients, respectively. Concurrent PDAC (not associated with IPMN) was more common in patients with a PFH (11.1% vs. 2.9%, p = 0.02). The 5-year survival was lower in the group with PFH (73.3% vs. 80%), but the difference was not statistically significant.

CONCLUSION: IPMN occurring in patients with a family history of PDAC are not more aggressive in nature or more prone to progression to invasive carcinoma. These patients, however, do have a higher incidence of extra-pancreatic malignancies and, as expected, a higher incidence of non-IPMN associated PDAC.
BACKGROUND: Acute pancreatitis can be the presenting symptom of IPMN, but its association with a particular morphological subtype or histological phenotype is unknown. We hypothesized that a highly viscous mucin containing MUC2 glycoprotein, which is found in the intestinal phenotype and is more common with main duct involvement, predisposes to development of acute pancreatitis.

METHODS: Demographic and clinical data of 325 cases with resected IPMNs were evaluated. Patients with and without a history of acute pancreatitis were then compared, with emphasis on morphologic and pathologic characteristics.

RESULTS: A history of AP requiring hospitalization was found in 74 patients (23%). Of these, 33 (45%) experienced a single episode, and some patients had as many as 10 distinct attacks; 2 patients presented with necrotizing pancreatitis requiring surgical debridement. The elapsed time between the first attack of pancreatitis and surgery ranged from 1 month to 24 years (median 2 years). IPMNs with a history of acute pancreatitis had a higher proportion of intestinal phenotype (58% vs. 24%, OR 4.51, 95% CI 2.61 - 7.80, p < 0.001) and a higher degree of histologic main duct involvement (66% vs. 52%, OR 1.82, 95% CI 1.06 - 3.14, p = 0.039). No significant difference was observed between the group with a history of AP and the group without AP regarding alcohol use, cholelithiasis, grade of epithelial atypia or presence of invasive carcinoma (16% vs. 21%).

CONCLUSION: Acute pancreatitis is a frequent presentation of IPMN. These patients have a higher likelihood of harboring an intestinal phenotype that involves the main pancreatic duct.
Objective: The objective of the study was to assess the efficacy of two pancreatic remnant closure techniques—stapled/sutured closure versus stapled/sutured closure plus falciform patch and fibrin glue reinforcement—in the setting of a prospective randomized, controlled trial, with the primary endpoint being pancreatic fistula.

Summary and Background Data: Pancreatic stump leak following left sided resection remains common. Despite multiple and varied techniques for closure, the leak rate averages 30%. A retrospective review by Ferrone et al. detected a decreased leak rate in patients receiving a traditional closure buttressed with an autologous falciform ligament patch and fibrin glue.

Methods: Between April 2008 and October 2011, all willing patients undergoing distal pancreatectomy at the authors' institutions, were consented and enrolled at the preoperative office visit. Patients were intraoperatively stratified as “hard” or “soft” glands and randomized to one of two groups: (1) closure utilizing standard stapling, suturing, or both (SS) versus (2) stapled, sutured, or both plus fibrin glue and falciform ligament patch (FF). The trial design and power analysis (α=0.05, β=0.2, power 80%, chi-square test) assumed the FF intervention would reduce the endpoint (pancreatic fistula) from 30% to 15% and yielded an accrual goal of 190 patients. Secondary endpoints included length of stay, mortality, readmission, and ISGPF fistula grade.

Results: The trial accrued 109 patients, 55 in the control group and 54 in the experimental group. Enrollment was closed early, following an interim analysis and futility calculation. Due to insufficient enrollment, patients stratified as having a “hard” gland were excluded (n=8) from analysis, leaving 101 patients in the soft stratum. The pancreatic leak rate was 19.8% (20 patients) for patients with soft glands. Patients randomized to the FF group had a leak rate of 20% as compared with 19.6% in the SS group (p=1.000). Fistula grades in both groups were similar: 1A, 8B, and 1C compared to 1A, 8B and 1C in the FF and SS groups respectively. Complication rates were comparable between the two groups. The median length of postoperative hospital stay was 5 days in both groups. There was a trend towards a higher 30-day readmission rate in the FF group (28% vs. 17.6%, p= 0.243). Based on conditional probability calculations with 52.5% of enrollment, the probability of success of the trial given the current trend fell below 50%, and the trial was ended.

Conclusion: The addition of a falciform ligament patch and fibrin glue to standard stapled or sutured remnant closure did not reduce the rate or severity of pancreatic fistula in patients undergoing distal pancreatectomy. (ClinicalTrials.gov number NCT00889213)
Backgrounds. We have reported that surgical resection following neo-adjuvant chemoradiation therapy (NACRT) can be associated with improved prognosis of pancreatic cancer patients (Pancreas 2009 and 2011 in press). The aim of this study is to explore short-term results of the new regimen of NACRT using S-1 followed by surgical resection in patients with borderline resectable pancreatic cancer.

Patients. Between 2006 and 2010, 17 patients who underwent surgical resection and adjuvant chemotherapy, were classified as adjuvant group, and 23 patients who underwent NACRT followed by surgical resection and adjuvant chemotherapy, were classified as NACRT group. The regimen of NACRT was consisted of S-1 (orally twice daily, 5days in a week, 80mg/m2/day) and concurrent radiotherapy (a total of 50.4Gy). The primary endpoint was the frequency of pathological curative resection (R0).

Results. There was no significant difference in clinical backgrounds between two groups. Other organ resection including vascular resection was done for 14 of 17 patients in adjuvant group and for 16 of 23 patients in NACRT group. The R0 rate in NACRT group was significantly better than in adjuvant group (21/23 vs 7/17, p=0.003). Although there was no significant difference in retrieved number of lymph node, the number of metastatic lymph nodes in NACRT group (1 (0-25)) was significantly lower than in adjuvant group (2 (0-19), p=0.022). The frequency of local relapse in NACRT group was significantly lower than in adjuvant group at 1year after surgical resection (0% vs 35%, p=0.022). There was no significant difference in the frequency of distant organ metastasis between two groups (NACRT 23% vs adjuvant 18%).

Conclusion. NACRT using S-1 can improve the R0 rate, and number of metastatic lymph nodes in patients with borderline resectable pancreatic cancer, resulting in better local control.
41572 AUTOIMMUNE PANCREATITIS (AIP): SHORT AND LONG-TERM OUTCOMES IN PATIENTS TREATED INITIALLY BY PANCREATEICODUODENECTOMY, A COMPARATIVE STUDY

Introduction
Autoimmune pancreatitis (AIP) is a rare, benign inflammatory disease that clinically and radiographically mimics pancreatic adenocarcinoma (PA). When diagnosed, AIP responds well to steroid therapy, but can recur. Inability to accurately distinguish between these two diseases leads many AIP patients to undergo initial pancreateicoduodenectomy. While a 25% disease recurrence rate following steroid therapy in AIP is well established, disease recurrence rates following initial pancreaticoduodenectomy (PD) remains unknown.

Methods
Under IRB authorization, over a 10 yr. period (1999-2009), 10 pts. with histopathologically confirmed AIP treated initially by PD were identified. This group was matched 1-to-1 for operation, surgeon, age, gender, and co-morbidities to two comparison groups of patients with idiopathic chronic pancreatitis (CP) and PA. Clinical presentation, operative variables, and postoperative clinical courses were analyzed. Long-term follow-up, including quality of life (QOL) data utilizing a formal Gastrointestinal Symptom Rating Scale (GSRS) survey given during a structured telephone interview were analyzed. Appropriate statistical tests were applied for nominal and ordinal variables.

Results
The AIP group was 50% male with a mean age of 62 (40-77) yrs. Presenting symptoms were similar between the AIP and PA groups. All groups (AIP, CP, PA) had similar gland morphology on radiographic imaging. Fifty percent of the AIP group had atypia on preoperative FNA biopsy. No patient was diagnosed with AIP preoperatively, and none had a history of autoimmune diseases. No statistically significant differences were found in operative times, blood loss, perioperative morbidity or mortality (90-day) rates between groups. Mean follow-up for the AIP group was 42 (4.5-83.2) months. Three patients (30%) had disease recurrence: 2 with jaundice and 1 with pancreatitis, at a mean time of 7.7 (1.6-12.1) months postop. All 3 were treated with steroids, 2 had an additional recurrences. Six patients (60%) had no recurrence of whom 2 were treated with postoperative steroids. One patient’s recurrence status remains unknown. Long-term rates of diabetes mellitus, pancreatic exocrine deficiency, and GSRS scores [AIP (N=5); 33 (20-59); CP (N=3); 28 (18-45)] were similar between AIP and CP groups.

Conclusion
Preoperative diagnosis of AIP remains uncommon in our experience in patients with a pancreatic head mass and no history of autoimmune disease. PD in AIP is as safe an operation as it is for CP or PA. AIP recurrence following PD is approximately 30%, with similar long-term postoperative QOL as patients with CP.
Background: Patients with pancreatic adenocarcinoma frequently present with depression. Often the depressive symptoms precede the diagnosis of cancer, suggesting that the pathophysiology of depression in pancreatic adenocarcinoma may result from biological changes that are induced by the presence of the tumor itself. We hypothesized that products of the kynurenine pathway, which have been implicated in both depression and tumor-induced immunosuppression, are responsible for this relationship. Specifically, we focused on tryptophan, kynurenine and kynurenic acid, which have both immunomodulatory and neural effects. Methods: Patients with pancreatic adenocarcinoma completed mood questionnaires including the Beck Depression and Beck Anxiety tests and underwent blood testing for kynurenine pathway metabolites. Tumor burden was determined from postoperative pathology reports. Data were analyzed for normality using the Shapiro-Wilks test. For variables that did not satisfy the normality assumption, the nonparametric bivariate Spearman correlation test was performed. We performed multivariate partial correlations on variables found to be significant in the bivariate analysis. Results: We found a significant correlation between the Beck Depression score and the plasma ratio of kynurenic acid/tryptophan ($p=0.008 \rho=-0.617$). Specifically, patients with a higher level of kynurenic acid proportional to their tryptophan level reported better mood. We also found a similar significant correlation between the Beck Anxiety score and the plasma ratio of kynurenic acid/tryptophan ($p=0.029 \rho=-0.5230$); patients with more kynurenic produced relative to their tryptophan level had less anxiety. We found a significant correlation between the plasma kynurenine level and the percentage of lymph nodes positive for metastatic disease ($p=0.034 \rho=0.515$), i.e. patients with higher serum kynurenine levels had more metastatic disease in the lymph nodes. We also found an inverse correlation between the maximal tumor diameter and the plasma level of kynurenine ($p=0.021 \rho=-0.554$). Meaning, as the plasma kynurenine level increased, the size of the primary tumor decreased, likely because these tumors are more aggressive and metastasize earlier in the disease process. The multivariate partial correlation revealed that the correlation between the mood scores and the ratio of kynurenic acid/tryptophan was still significant when controlling for the percent of positive lymph nodes and when controlling for the maximal primary tumor diameter. Conclusion: Both severity of mood symptoms and increased tumor burden in pancreatic cancer appear to be mediated by metabolites of the kynurenine pathway. The information provided by this study clarifies the mechanism of depression in pancreatic cancer patients, and also suggests a role for analysis of serum kynurenine pathway markers in both preoperative staging, and for measuring the success of therapeutic interventions.
Introduction: Periampullary adenocarcinoma (PA) is the most common indication for pancreaticoduodenectomy (PD). The four cancers that comprise the PAs include pancreatic ductal (PDA), ampullary (AA), distal common bile duct (CBDa), and duodenal adenocarcinoma (DA). While PDA has been studied extensively, it is unclear whether these data are applicable to the rarer PAs.

Methods: We queried our institutional PD database for patients treated for PA from November 2005 to October 2011. Out of 650 resections, 390 (60%) patients had PA. Clinicopathologic data were analyzed, and statistical comparisons between PA subtypes were made with respect to PDA, unless otherwise indicated. We aimed to identify the differences in the biology, natural history, and treatment patterns between PAs.

Results: The 390 resected PAs included 293 (75%) PDAs, 48 (12%) AAs, 28 (7%) distal CBDAs, and 21 (5%) DAs. Pre-operative CA 19-9 levels were elevated in 76% of patients with PDA, 56% with distal CBDs (p=0.04), 62% with AA (p=0.071), and 55% with DA (p=0.06). In general, resected PDAs and CBDAs had the more aggressive pathologic features. Specifically, perineural invasion was identified in 92% of PDAs, 93% of distal CBDAs (p=1.0), 51% of AAs (p<0.0001) and 34% of DAs (p=0.0001). Lymph node metastases were identified in 74% of PDAs, 50% of distal CBDAs (p=0.013) 60% of AAs (p=0.05) and 57% of DAs (p=0.1). Documented recurrence patterns were available in a subset of patients (22%) followed at our own institution. Due to the small number of patients, non-pancreatic PAs were analyzed together. The site of first recurrence was the surgical bed in 24% of PDAs and 20% of non-pancreatic PAs. A distant metastasis was identified in 76% of PDAs and 80% of non-pancreatic PAs (p=1.0). With regards to treatment patterns at our institution (N=158 with treatment data), patients with PDA and distal CBDAs are virtually always treated with adjuvant gemcitabine (91%), as compared to the other two subtypes (55%, p<0.0001) which are frequently treated with a 5-FU based regimen. The median and 2-year survivals associated with each PA were (Figure): PDA, 19 months and 39%; CBDa, 18 months and 37% (p=0.8); AA, 43 months and 65% (p=0.002); and DA, median not reached and 67% (p=0.04). After adjusting for lymph node metastases, AA was still more favorable than PDA (hazard ratio=0.73, p=0.01) while DA showed a trend but was not significantly more favorable (hazard ratio, 0.8, p=0.1).

Conclusions: These findings support the notion that PAs are a heterogeneous group. As compared to AAs and DAs, PDAs had more aggressive pathologic features and worse long-term survival. In addition, CA19-9 was a more sensitive test for PDAs than the non-pancreatic PAs. Our practice patterns approach pancreatobiliary cancers primarily with gemcitabine-based treatment, which differs from the approach with the other subtypes.
ENDOSCOPIC ULTRASOUND (EUS) EVALUATION IN THE SURGICAL TREATMENT OF DUODENAL AND PERI-AMPULLARY ADENOMAS.

INTRODUCTION: Precise identification of benign duodenal and peri-ampullary tumors, offers a diagnostic challenge to reliably distinguish adenomas from malignant lesions and render the possibility of trans-duodenal resection. EUS has emerged as a useful technique in assessing tumor depth of invasion and is often employed at our institution when planning endoscopic and surgical resection. We performed a retrospective review of patients with benign duodenal and peri-ampullary adenomas who underwent preoperative EUS to determine the accuracy of this technique in predicting the absence of muscular invasion and also to analyze outcomes associated with endoscopic and trans-duodenal surgical resection.

METHODS: Records of 111 patients seen at our institution over the period of 10 years with post-operative pathological diagnosis of benign ampullary and duodenal adenomas were identified and reviewed. We analyzed information on patient gender, age, tumor location and size, EUS results, type of resection performed, final pathology findings and incidence of local tumor recurrence.

RESULTS: Of the 111 patients with benign ampullary and duodenal adenomas, 47 underwent preoperative EUS for 29 periampullary lesions and 18 duodenal lesions. In 38 (82%) patients, EUS reliably identified absence of sub mucosal and muscularis invasion. In 4 cases, EUS incorrectly predicted the absence of sub-mucosal invasion as proven in the final pathology analysis. However, final pathology showed sub-mucosal invasion. In the other 5 patients, EUS overestimated muscularis invasion in 1 case, 2 cases only demonstrated chronic inflammation, one patient had Brunner’s gland hyperplasia and depth of invasion could not be reliably assessed in the other patient due to tumor location. Type of resection performed included endoscopic resection in 25 cases, partial duodenectomy in 6 cases, transduodenal ampullectomy with sphincteroplasty in 10 cases and pancreaticoduodenectomy in 6 cases. There were 6 local recurrences (median follow-up=20 months) 4 of which were in patients with Familial Adenomatous Polyposis (FAP). The post-operative final pathological results included villous adenoma (n=5), adenoma (n=6), tubulovillous adenoma (n=10), tubular adenoma (n=20), hyperplastic polyp (n=2), dysplasia (n=1), and normal mucosa (n=1). Among the 47 patients who underwent resection, 8 (17%) developed various post-procedural complications which included retroperitoneal hematoma, intraabdominal abscess, wound infection delayed gastric emptying and prolonged ileus.

CONCLUSION: EUS can accurately predict the absence of mucosal invasion in benign ampullary and duodenal adenomas 81% of the time. These patients can safely undergo endoscopic or local resection with acceptable local control rates sparing the need for more radical operations.
41827 CENTRAL PANCREATECTOMY

Background: Central pancreatectomy can be used in the treatment of lesions located in the body of the pancreas, with the advantage of preserved pancreatic parenchyma compared to pancreaticoduodenectomies or distal splenopancreatectomies.

Methods: The central pancreatectomy was performed through a subcostal incision. An intraoperative ultrasound was performed, and the pancreas was divided using electrocautery. The proximal pancreatic duct (PD) was over-sown with layered interrupted U stitches. A pancreaticojejunal anastomosis was performed for the distal PD, using radially oriented sutures over a stent.

Results: A 38 year old female with a family history of pancreatic cancer was found to have an increase in size of a known pancreatic cyst with no history of pancreatitis. Endoscopic ultrasound revealed mural nodules raising the suspicion of a pancreatic cystic neoplasm. She underwent a central pancreatectomy with pancreaticojejunal Roux-en-Y anastomosis. There were no intraoperative or postoperative complications. Final pathology revealed a low-grade pancreatic intraepithelial neoplasia (PanIN1B).

Conclusion: Central pancreatectomy is a viable option for lesions located in the pancreatic body.
41828 LAPAROSCOPIC THREE PORT SPLEEN PRESERVING DISTAL PANCREATECTOMY

Background: Historically, a three-port laparoscopic distal pancreatectomy has been previously described. A three-port spleen-preserving laparoscopic distal pancreatectomy (LSPDP) however has not been previously described. We present a three-port spleen preserving laparoscopic distal pancreatectomy.

Methods: The three-port LSPDP was performed with the patient in a modified left thoracoabdominal position, with a 10mm Hassan in the anterior axillary line, and two 5mm Hassan trocars in the epigastrium and the posterior axillary line. The pancreas was divided using a 3.5mm endo-GIA stapler. The specimen was removed from the 10mm port site.

Results: A 56 year old women underwent the above procedure for a pancreatic tail cystic lesion. OR time was 98 minutes, with an estimated blood loss of 50 mL. The postoperative hospital stay was 3 days. There were no intraoperative or postoperative complications. Final pathology showed intraductal papillary mucinous neoplasm.

Conclusion: A three-port LSPDP is a safe and viable technique. Our early experience suggests a decreased length of hospital stay compared to the open technique, and a comparable operative time and outcome to four or greater ports.
41829 LAPAROSCOPIC LEFT LIVER RESECTION FOR GIANT FOCAL NODULAR HYPERPLASIA

Background: Hepatectomy is used in the treatment of large or symptomatic focal nodular hyperplasia. An open hepatectomy is the standard technique, but laparoscopic hepatectomy is gaining wider acceptance. We present a laparoscopic liver resection of segments 2, 3 and 4.

Methods: The laparoscopic hepatectomy was performed with the patient in a supine position, with two 10mm Hassan and two 5mm Hassan trocars. The liver was resected with a LigaSure device, followed by an endo-GIA stapler across the vascularized pedicles and left hepatic vein. A Pringle maneuver was not performed. There was no evidence of bile leak and hematostatis was assured.

Results: A 30 year old women underwent the above procedure for a large hepatic mass emanating predominantly from segment 3, with imaging findings suspicious for a focal nodular hyperplasia. OR time was 76 minutes, with an estimated blood loss of 300 mL. The postoperative hospital stay was 4 days. There were no intraoperative or postoperative complications. Final pathology showed focal nodular hyperplasia measuring 12 x 9 x 7 cm.

Conclusion: Laparoscopic hepatectomy is a safe and viable technique, with the benefits of decreased blood loss and length of hospital stay compared to the open technique.
Total laparoscopic pancreaticoduodenectomy (TLPD) remains one of the most advanced laparoscopic procedures. With evolution in laparoscopic technology and instrumentation in the last decade, laparoscopic pancreaticoduodenectomy is beginning to achieve wider acceptance.

Data was collected for all patients who underwent a TLPD at our institution from March until July 2011. Preoperative evaluation consisted of CT scan with pancreatic protocol, and selective use of MRI and/or endoscopic ultrasound. The TLPD was done with 6 ports on three patients, and 5 ports on one patient, and included a celiac, periportal, peripancreatic and periduodenal lymphadenectomy. Pancreatic stents were used in all 4 cases, and intestinal continuity was reestablished by intracorporeal anastomoses.

Four patients underwent a TLPD for suspicion of a periampullary tumor. There were 3 females and 1 male with a mean age of 65 years and mean BMI of 30.5. Intraoperatively, the mean operative time was 9 hours and 31 minutes with a mean blood loss of 120 mL. Postoperatively there were no complications with a mean length of stay of 6.5 days. Mean follow up time was 4 months. There was no lymph node involvement in any of the 4 specimens. The pathologies included IPMN in two, pancreatic adenocarcinoma in one (R0 resection), and benign 4cm periampullary adenoma in one.

TLPD is a safe and viable alternative to the standard Whipple procedure. Our early experience suggests decreased length of stay, quicker recovery, and improved quality of life. Complication rates appear to be improved or equivalent.
41831 PANCREATICODUODENECTOMY: 22 YEAR COMPARATIVE OUTCOME ANALYSIS IN A SINGLE INSTITUTION AND THE EFFECT OF ACQUIRING A FELLOWSHIP TRAINED HEPATOPANCREATICOBIILIARY SURGEON

Pancreaticoduodenectomy (PD) outcome prior to and subsequent to acquiring a hepatopancreaticobiliary (HPB) surgeon has not been previously studied. We compared our single-institution data prior to procuring a HPB surgeon, to the data that ensued.

A retrospective review was performed of patients that underwent a PD at our institution between January 1990 and August 2011. Data acquired included demographic data, operative time, blood loss, length of stay, and pathology. A HPB surgeon started in 2003; the data was therefore divided into those performed between January 1990 and December 2002 (Group 1), and those performed between January 2003 and July 2011 (Group 2).

Thirty-nine patients underwent a PD in Group 1, compared to 86 patients in Group 2. The average age was 68.5 vs. 67, the median operating time was 7.5 hours vs. 5.3 hours, median blood loss was 950 vs. 400 mL, median length of stay (LOS) was 21 vs. 10 days, and overall complication rates were 62.5% vs. 22.1% (group 1 vs. group 2 respectively), of which gastric emptying was the most common in both groups. When excluding PDs performed by general surgeons in group 2, 66 PDs (76.7%) were performed by the HPB surgeon, with a median operative time unchanged at 5.3 hours, however median blood loss decreased to 300 mL, median LOS decreased to 9 days, and complication rates decreased to 15.1%.

Pancreaticoduodenectomies performed since acquiring a HPB surgeon were performed more efficiently, with decreased operating time, blood loss, complication rates, and length of stay.
41992 ENDOSCOPIC TRANSLUMINAL NECROSECTOMY IN NECROTIZING PANCREATITIS: A SYSTEMATIC REVIEW

**Background:** Infected necrotizing pancreatitis almost always requires intervention. The historical reference standard is surgical necrosectomy. A promising minimal invasive alternative is endoscopic transluminal necrosectomy (ETN). Various new cohort-studies on ETN have been reported in recent years. We performed a systematic review of the literature on ETN in (infected) necrotizing pancreatitis.

**Methods:** We conducted a systematic literature search in the PubMed, Embase and Cochrane libraries from January 1980 to October 2011 according to the PRISMA guideline. Inclusion criteria were: 1) cohorts of patients undergoing ETN as primary treatment for either infected necrosis or symptomatic sterile pancreatic necrosis; and 2) essential outcomes reported: percentage of infected necrosis, number of ETN sessions, complications and mortality. Exclusion criteria were: 1) cohorts of less than 5 patients; 2) cohorts including only sterile necrosis and 3) cohorts also including chronic pancreatitis, “pseudocysts”, “pancreatic abscesses” unless results of these subgroups were reported separately. The main outcomes of this review were overall success of ETN, number of ETN sessions, definitive treatment with ETN alone, complications and death.

**Results:** After screening 514 papers, 11 papers including 401 patients fulfilled the eligibility criteria. No randomized controlled trials were identified. All studies were retrospective analyses, although 5 studies were post-hoc analyses from prospectively collected databases. Six studies reported on ICU admission before ETN; this occurred in 60/185 patients (32%). Three studies reported on organ failure before ETN, which occurred in 10/34 patients (29%). Average APACHE-II scores and CT Severity Index scores before ETN were reported in 5 and 6 studies and varied from 6 to 11 and 4 to 8 respectively. Infected necrosis was present in 216/401 patients (54%). On average 4.2 ETN interventions were needed per patient. With ETN alone, definitive treatment was achieved in 328/401 patients (82%). Complications occurred in 177/401 patients (44%) and 22/401 patients (6%) died.

**Conclusion:** This systematic review of cohort studies suggest that ETN is promising treatment in necrotizing pancreatitis. However, the percentage of infected necrosis in these cohorts is relatively low and complication rates are significant and comparable to surgical series. Randomized controlled trials are needed to compare ETN with minimally invasive radiological and surgical interventions in patients with infected necrosis.
Background: Infected necrotizing pancreatitis is a potentially lethal disease that almost always requires intervention. A recent randomized trial has shown that a surgical step-up approach with percutaneous drainage followed, if necessary, by video-assisted retroperitoneal debridement (VARD) reduced complications and death from 69% to 40% compared with primary open necrosectomy. These outcomes may further be improved by an endoscopic step-up approach. We describe the design and rationale of a nationwide study called TENSION: “Endoscopic transluminal step-up approach versus surgical step-up approach in patients with infected necrotizing pancreatitis” (Trial registration: ISRCTN09186711).

Methods/Design: The TENSION trial is a randomized controlled, parallel-group, superiority multicenter trial. Inclusion criteria are: 1) suspected or confirmed infection of pancreatic or extrapancreatic necrosis; 2) both endoscopic and surgical step-up approach are possible; 3) age ≥18 years. Exclusion criteria are: 1) previous surgical, endoscopic or percutaneous intervention for necrosis or peripancreatic collections; 2) acute upflare of chronic pancreatitis; 3) indication for laparotomy (i.e., abdominal compartment syndrome, bleeding or perforation of a visceral organ). All candidates for randomization will be discussed by a nationwide expert panel. Patients will be randomized to A) an endoscopic step-up approach or B) a surgical step-up approach. The endoscopic step-up approach consists of endoscopic transluminal drainage followed, if necessary, by endoscopic transluminal necrosectomy. The surgical step-up approach consists of percutaneous (retroperitoneal) catheter drainage, if necessary followed by VARD. If VARD is not possible a laparotomy is performed. Interventions are only performed by specialists with proven adequate skills in these procedures. The primary endpoint is a composite of major complications (i.e., new onset organ failure, bleeding requiring intervention, perforation of a visceral organ requiring intervention, enterocutaneous fistula requiring intervention and incisional hernia) or death within 6 months following randomization. Secondary endpoints include other complications such as pancreatic fistula, pancreatic insufficiency, length of intensive care- and hospital stay, quality of life, and total direct and indirect costs. We assume that endoscopy can reduce the primary endpoint by 26% (from 43% to 17%). With a 2-sided α of 0.05 and 80% power a total of 98 patients will be randomized to demonstrate this effect. Patients will be enrolled in 25 hospitals of the Dutch Pancreatitis Study Group in a 3-year period.

Discussion: The TENSION trial is designed to evaluate if an endoscopic step-up approach is superior to a surgical step-up approach in terms of clinical outcomes and cost-effectiveness in patients with infected necrotizing pancreatitis.
Aging is related to increased intestinal damage and bacterial translocation in acute pancreatitis in rats

Introduction/Background: Acute pancreatitis (AP) in elderly patients in spite of similar occurrence of local complications is followed by a substantial increase in multiple organ failure possibly due to increased bacterial translocation. Intestinal mucosal barrier may be damage with increased permeability promoting bacterial translocation. Intestinal fatty acid binding protein (I-FABP), a 15-kd protein located at the intestinal mucosa may leak out of damaged intestinal mucosal cells to the peripheral circulation. Therefore, plasma levels of I-FABP may be an indication of bacterial translocation. The aim of the present study was to evaluate the effect of aging on intestinal damage, bacterial translocation, and organ failures in AP.

Methods: AP was induced in male Wistar rats by intraductal 2.5% taurocholate injection and divided into 2 experimental groups: GI (n=20): Young (3 month old rats), and GII (n=20): Older (18 month old rats). Two and 24 hours after AP blood were collected for determinations of plasma ileal fatty acid binding protein (I-FABP), and biochemical markers: amylase, AST, ALT, urea, creatinine, and glucose. Pulmonary myeloperoxidase (MPO) activity was also performed. Bacterial translocation was evaluated by bacterial cultures of pancreas expressed in colony-forming units (CFU) per gram.

Results A significant increase in plasma amylase, AST, ALT, urea, creatinine, and I-FABP levels was observed in the older group compared to the young group (p<0.05). Pulmonary myeloperoxidase (MPO) activity was also increased in the older group compared to the young group (p<0.05). Compared to young rats, rate of positive bacterial cultures obtained from pancreas cultures in the older rats was significantly increased.

Conclusion: This study demonstrated that aging is associated to an increased distant organ damaged and bacterial translocation, and that plasma level of I-FABP is an important marker of bacterial translocation.
Introduction/Background: Acute pancreatitis (AP) is associated with bacterial translocation and infection mainly related to the common intestinal microbiota suggesting a possible breakdown of intestinal barrier. Intestinal fatty acid binding protein (I-FABP) is a 15-kd protein localized in intestinal mucosa cells that due to its small size quickly leaks out of damaged cells leading to increase in blood levels. Therefore the plasma levels of I-FABP indicating gut epithelial cells injury during AP may be related to bacterial translocation. The aim of the present study was to evaluate plasma levels of I-FABP and its relationship to bacterial translocation in AP and therefore validate plasma levels of I-FABP as a marker of bacterial translocation in AP.

Methods: AP was induced in 40 male Wistar rats by intraductal 2.5% taurocholate injection. Twenty-four hours after AP blood were collected for determinations of plasma ileal fatty acid binding protein (I-FABP) using standard enzyme-linked immunosorbent assay (ELISA) for rat. Bacterial translocation was evaluated by bacterial cultures of pancreas expressed in colony-forming units (CFU) per gram.

Results: A significant positive correlation between the plasma I-FABP levels and the bacterial translocation was found (r=0.9008, p<0.0001).

Conclusion: Plasma level of L-FABP is a marker of bacterial translocation in acute pancreatitis and may be useful as a guide to antimicrobiotic therapy in this disease.
MUCINOUS CYSTS OF THE PANCREAS: A SAFE APPROACH TO IMAGING SURVEILLANCE FOLLOWING CONSERVATIVE VS. SURGICAL MANAGEMENT

BACKGROUND: Advancement in high resolution abdominal imaging has led to increased incidence of cystic pancreatic neoplasms. For mucin-producing cysts of varying malignant potential, the decision to observe vs. resect is based on the estimated risk of cancer. International guidelines propose that observation with periodic imaging is safe for asymptomatic cysts <3cm without malignant radiographic features. In contrast, surgery is indicated for symptomatic patients with lesions >3cm given the risk of progression. Irrespective of conservative vs. surgical management, yearly imaging to monitor possible progression or recurrence is currently recommended. However, limited data support such recommendations and the management of mucinous cysts remains a challenging dilemma. The aim of this study was to define the optimal frequency of imaging follow-up for mucinous pancreatic cysts and detect the prevalence of recurrence after resection with the intent to determine appropriate management guidelines.

METHODS: We retrospectively analyzed medical records of 375 patients diagnosed with pancreatic cysts from 1992 to 2010. A total of 163 potentially malignant cysts included 116 branch-duct intraductal papillary mucinous neoplasms (BD-IPMNs) and 47 mucinous cystic neoplasms (MCNs). Main-duct IPMNs, which have a high cancer risk, and pseudocysts and serous cystadenomas with a benign natural history were excluded. Patients were observed or treated surgically. Demographics, relevant comorbidities, detailed cyst characteristics, recurrence and time to recurrence were registered. Progression in observed patients and recurrence in surgical patients were evaluated by reviewing follow-up imaging. Progression was defined as 1cm growth in diameter. Kaplan-Meier curves were used to estimate the distribution of time to recurrence and the log-rank test to investigate factors associated with recurrence.

RESULTS: Ninety-two patients with incidentally diagnosed cysts were followed conservatively and 71 underwent surgery confirming non-invasive pathology. The cyst incidence was higher in females (>73%), with the pancreatic head being the most frequent location in observed patients vs. tail in surgical patients. No differences in age and relevant comorbidities were found between observed and surgical patients. Thirty-five % of surgical patients presented with predominant abdominal pain or pancreatitis. Mean cystic size was 1.5cm in observed vs. 3.2cm in surgical patients. Over a median follow-up of 36 months (mean 46, range 0.4–207), none of the observed patients experienced significant lesion growth compared to baseline evaluation. For patients who underwent resection, Kaplan-Meier curves demonstrated estimated probabilities of recurrence of 4% (95%CI:1.1-16.2) at 2 years and 12% (95%CI:5-25.6) at 3 years. The only examined factor significantly associated with recurrence was cyst type, with 9% vs.0% recurrence rates for BD-IPMNs vs. MCNs respectively (p<0.01). Follow-up rates were significantly higher in observed patients than in surgical patients (95% vs.77%, respectively, p<0.01).

CONCLUSIONS: Asymptomatic mucin-producing neoplasms <3 cm in diameter without morphological characteristics of malignancy can safely be treated conservatively with observation. For efficacious use of medical resources while maintaining patient safety, imaging is not necessary until at least 3 years after the baseline evaluation. For resected non-invasive mucinous cysts, follow-up imaging should be performed by 2
years after surgery to detect early recurrence that may require further resection. For these patients, follow-up adherence is necessary.
Background: Intraductal papillary mucinous neoplasm (IPMN) is being diagnosed and resected with increasing frequency, but little long-term data exist to guide postoperative management of surgically treated patients.

Methods: We examined all patients who underwent surgical resection for IPMN between January 1997 and April 2011 at our institution. IPMN was categorized as non-invasive low grade (adenoma and borderline dysplasia), non-invasive high grade (carcinoma in situ), or invasive. Histologic features of primary and recurrent disease were examined and we evaluated predictors of recurrence using Kaplan Meier curves and Cox proportional hazards models.

Results: Two hundred and eight patients underwent resection for IPMN. At presentation, 57% were symptomatic, 20% had a mural nodule or an associated mass, and median cyst size was 1.8cm. Sixty-eight (32.7%) operations for high grade disease were performed, of which 33 revealed invasive carcinoma. Among 165 R0 resections with greater than three months of follow-up we have observed 26 cases of recurrent disease over 502 person-years (median follow-up time 30.8 months). Nine (39%) patients originally diagnosed with invasive carcinoma and 17 (12%) patients originally diagnosed with non-invasive IPMN have recurred. Of the latter, four (23.5%) recurred as invasive carcinoma. Most disease recurred locally (25/26) but three individuals had concurrent metastatic disease at the first observation of recurrence. Median time from initial treatment to recurrence was 18.2 months, but ranged from 3.7 to 126.8 months. Invasive tumors were more likely to recur (HR 3.7, p=0.002) with a median time to recurrence of 13.5 months. Among non-invasive tumors, no single histologic feature—including dysplastic changes at the surgical margin or distant from the primary tumor—meaningfully predicted recurrence. Seven patients had a completion pancreatectomy on average 22.7 months after their initial surgery. Of these, three had low grade or moderate dysplasia on final pathology and have survived greater than 34 months after the second operation, compared with median survival of 14.4 months after diagnosis of recurrent, invasive IPMN.

Conclusions: Invasive IPMN has a high risk of recurrence, but even low grade tumors may recur with high grade disease. IPMN can recur remote from the time of primary surgery and no histologic feature beyond invasion predicts recurrence risk. Most recurrence is local and completion pancreatectomy can be associated with excellent survival if recurrent disease is identified early. We therefore recommend that surveillance of the remnant pancreas continue after primary resection for all tumor types.
Recurrence-free survival among 165 R0 resections for IPMN with at least three months of follow up, stratified by invasive pathology. Non-invasive IPMN includes adenoma (76), borderline or moderate dysplasia (36), and carcinoma in situ (30). Median follow-up was 30.8 months (502 person-years). Invasive IPMN was more likely to recur than non-invasive tumors (HR 3.7, 95% CI 1.7-8.4), with a median time to recurrence of 13.5 months. Of the 17 non-invasive IPMNs that recurred, 4 recurred with invasive disease.
42690 VENOUS INVOLVEMENT DURING PANCREATICODUODENECTOMY: IS THERE A NEED FOR REDEFINITION OF BORDERLINE RESECTABLE DISEASE?

Introduction: The consensus definition of borderline resectable pancreas cancer includes patients with any venous (SMV-PV) or limited arterial (SMA or GDA-CHA) involvement. Recent recommendations suggest that patients with borderline resectable pancreatic adenocarcinoma should receive neoadjuvant therapy to increase the likelihood of achieving R0 resection. It is established that a subset of patients with limited venous involvement can achieve R0 resection by utilizing vein resection. This study compares outcome of patients who underwent pancreaticoduodenectomy with (VR-PD) or without (PD) vein resection, and is unique because none received neoadjuvant therapy.

Methods: A large, multi-institutional database of patients who underwent PD without neoadjuvant therapy was reviewed. Patients who required vein resection due to SMV-PV involvement by tumor were compared to those who underwent PD without vein resection.

Results: Of 492 total patients, 70 (14%) underwent VR-PD and 422 (86%) underwent PD. There was no difference in R0 resection (66% VR-PD vs. 75% PD, p=0.11) or local recurrence rate (18% VR-PD vs. 14% PD, p=0.33), at a median follow up of 16 months (range 3.0 – 129.7). There was no difference in median DFS (10.1 months VR-PD vs. 15.2 months PD, p =NS, HR 1.24 (0.94 – 1.64)). Positive margin, increased EBL, advanced tumor grade, and lymph node involvement, but not vein involvement, were independent predictors of DFS. These same factors, as well as use of adjuvant therapy, predicted OS.

Conclusion: This is the largest modern series examining patients with borderline resectable pancreas cancer due to SMV-PV involvement, none of whom received neoadjuvant therapy. This cohort of patients with vein involvement selected for up-front surgical resection demonstrates that oncologic outcomes, including R0 rate, local recurrence rate, and DFS, were not compromised when vein resection was required. These data suggest that up-front surgical resection is an appropriate option for patients with isolated vein involvement and calls into question the inclusion of SMV-PV involvement within the definition of “borderline resectable disease.”
**DISSECTING SURVIVAL FOR RESECTED PANCREATIC DUCTAL ADENOCARCINOMA IN THE CONTEMPORARY ERA**

**Background:** Survival following resection of pancreatic ductal adenocarcinoma (PDAC) appears to be improving compared to historical benchmarks. Yet, despite advancements in patient selection, surgical technique, and adjuvant therapies, prognosis remains disappointing. We analyze a contemporary experience to better understand current clinical dilemmas and identify those features associated with prolonged survival.

**Methods:** Kaplan Meier and conditional survival analysis was conducted for all 424 PDAC resections performed by five surgeons at two pancreatic surgical specialty programs over a decade (2001-2011). Factors analyzed include patient, operative, and tumor features as well as laboratory results and application of adjuvant treatment. Multivariate analysis was performed to elicit characteristics independently associated with survival.

**Results:** For all patients, median, 1-, and 5-yr survivals were 21.8m, 76%, and 24%, with 30/90-day mortalities of 0.7%/1.7% and an 8d median LOS. Conditional survival escalates with time. With an initial intention-to-treat for cure, patients were categorized by ultimate treatment courses which demonstrate marked survival variation (Table). 76% of patients received adjuvant therapy, primarily gemcitabine based chemoXRT. Patients with Major complications (Clavien IIIb-V; 10%) initiated adjuvant therapy less frequently (21%) and survived 9.5m, while Minor/Total complications had no impact on survival. The median and 5-yr survival for total pancreatectomy was 32.2m/50%; for 90 “favorable biology” cases (R0/N0/M0) was 37.2m/42%; and for IPMN (9% overall) was 62.6 m/54%. Elderly patients (>75 yo) comprised 24% of all the resections and had similar survival to nonelderly patients. Favorable prognostic features include G1/G2 grade, absence of LVI, T1/T2 stage, R0 resection, low LN ratio, absence of weight loss, and receipt of adjuvant therapy.

**Conclusion:** This modern, multi-institutional experience with resected pancreatic adenocarcinoma shows decreasing short-term morbidity and mortality rates along with improving survival, particularly for certain subgroups of patients. Optimal outlook is dependent on pathologic features, complete tumor resection, and successful delivery to post-operative adjuvant therapy.
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<td>25%</td>
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</tr>
<tr>
<td>Classic (73)</td>
<td>18.5</td>
<td>22%</td>
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</tr>
<tr>
<td>Distal Pancreatectomy (61)</td>
<td>19.8</td>
<td>13%</td>
<td></td>
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<tr>
<td>Total Pancreatectomy (22)</td>
<td>32.2</td>
<td>50%</td>
<td></td>
</tr>
<tr>
<td>Therapy Status</td>
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<td></td>
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<tr>
<td>Adjuvant Therapy (324)</td>
<td>23.8</td>
<td>28%</td>
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<tr>
<td>Chemoradiation (248)</td>
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<td>30%</td>
<td></td>
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<tr>
<td>Chemo Only (22)</td>
<td>15.4</td>
<td>18%</td>
<td></td>
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<tr>
<td>Chemo / Radiation Unknown (53)</td>
<td>18.6</td>
<td>9%</td>
<td></td>
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<tr>
<td>No Adjuvant (53)</td>
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<td>22%</td>
<td></td>
</tr>
<tr>
<td>Poor Clinical Outcome (34)</td>
<td>6.0</td>
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<td>&lt;.001</td>
</tr>
<tr>
<td>Therapy Not Elected (19)</td>
<td>62.6</td>
<td>51%</td>
<td></td>
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<tr>
<td>Downstaging Neoadjuvant Therapy (11)</td>
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<tr>
<td>Palliative Chemotherapy (12)</td>
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<td>n/a</td>
<td></td>
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<tr>
<td>Adjuvant Unknown (24)</td>
<td>19.4</td>
<td>17%</td>
<td></td>
</tr>
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<td>Negative (134)</td>
<td>28.8</td>
<td>31%</td>
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<tr>
<td>Positive (290)</td>
<td>19.5</td>
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<td>Margin status</td>
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<tr>
<td>Negative (277)</td>
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<td>Positive (147)</td>
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<tr>
<td>IPMN Status</td>
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<tr>
<td>Arising in IPMN (40)</td>
<td>62.6</td>
<td>54%</td>
<td>0.195</td>
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<tr>
<td>No IPMN (384)</td>
<td>21.5</td>
<td>23%</td>
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RADIOGRAPHIC DOWNSTAGING OF BORDERLINE RESECTABLE PANCREATIC CANCER IS RARE FOLLOWING NEOADJUVANT THERAPY

Introduction: Resection following multimodality therapy for borderline resectable pancreatic cancer is often presumed to require a reduction in tumor size and vascular involvement. The rate of downstaging following therapy using “intent to treat” is unknown.

Methods: All patients with borderline resectable pancreatic cancer per National Comprehensive Cancer Network (NCCN) or MD Anderson guidelines (table 1) staged between 2005 – 2010 and treated with neoadjuvant therapy prior to restaging and potential surgery were identified in our prospectively-maintained database. Radiographic re-review of pancreatic protocol CT scans prior to and following therapy was performed to determine the degree of radiographic response to treatment. Serum CA19-9 was evaluated when bilirubin was ≤ 1.5mg/dl.

Results: 129 patients had borderline resectable anatomy per NCCN guidelines; of these, 77 (60%) were borderline resectable per MD Anderson guidelines. Preoperative chemotherapy was administered to 98 (76%) patients in anticipation of chemoradiation; 31 (24%) received chemoradiation alone. Among restaged patients, 84 (69%) had stable disease, 15 (12%) had a partial response and 23 (19%) had progressive disease by RECIST criteria. Although using either set of radiographic guidelines only 1 (0.8%) patient was downstaged to potentially resectable anatomy following therapy, 85 (64%) patients underwent subsequent pancreatectomy. CA19-9 of 78% of resected patients in whom pretreatment and restaging levels were both evaluable fell following therapy. 81 (95%) resections were R0; 51 (60%) required concomitant vascular resection. The median OS of all 129 patients was 22 (95%CI: 14 – 30) months. The median OS of resected patients was 33 (95%CI: 25 – 41) months and was not associated with radiographic or serologic response (p=0.4).

Conclusion: Although radiographic downstaging of borderline resectable to potentially resectable anatomy occurred in only 1 of 129 patients in this series, favorable survival was observed following multimodality therapy and aggressive use of pancreatectomy.

Table 1. NCCN and MD Anderson Borderline Resectable Anatomic Criteria
<table>
<thead>
<tr>
<th>NCCN Criteria</th>
<th>Potentially Resectable</th>
<th>Borderline Resectable</th>
<th>MDACC Criteria</th>
<th>Potentially Resectable</th>
<th>Borderline Resectable</th>
</tr>
</thead>
<tbody>
<tr>
<td>SMV/PV</td>
<td>No abutment or encasement</td>
<td>Abutment, encasement or occlusion</td>
<td>Abutment or encasement without occlusion</td>
<td>Short-segment occlusion</td>
<td></td>
</tr>
<tr>
<td>SMA</td>
<td>No abutment or encasement</td>
<td>Abutment</td>
<td>No abutment or encasement</td>
<td>Abutment</td>
<td></td>
</tr>
<tr>
<td>CHA</td>
<td>No abutment or encasement</td>
<td>Abutment or short-segment encasement</td>
<td>No abutment or encasement</td>
<td>Abutment or short-segment encasement</td>
<td></td>
</tr>
<tr>
<td>Celiac trunk</td>
<td>No abutment or encasement</td>
<td>No abutment or encasement*</td>
<td>No abutment or encasement</td>
<td>Abutment</td>
<td></td>
</tr>
</tbody>
</table>

Abutment, <180 degrees of vascular circumference; encasement, >= 180 degrees of vascular circumference. SMV/PV, superior mesenteric/portal vein. SMA, superior mesenteric artery; CHA, common hepatic artery.* , 7 patients with celiac abutment were classified as NCCN borderline resectable.
Introduction- As the outcomes from pancreatic resection have improved in recent years, more radical resections are being performed for pancreatic tumors, including those with involvement of additional visceral organs. This study examines the outcomes of extended visceral resection (EVR) for tumors involving the pancreas.

Methodology- This is an IRB approved, retrospective cohort study of patients from Thomas Jefferson University from October 2005 to May 2010. Patients who underwent a pancreaticoduodenectomy (PD) or distal pancreatectomy (DP) along with resection of additional visceral organs, excluding the gallbladder/spleen, were compared to patients undergoing pancreatic resection alone.

Results- Thirty three (33) patients underwent EVR and 659 patients underwent pancreatic resection alone. Both groups had similar demographic characteristics. EVR was performed for a wide variety of primary and metastatic tumors including pancreas, colon, liver, melanoma, lymphoma, and ovarian, among others. There were fifteen (45%) colon, seven (21%) small intestine and adrenal resections, and six (18%) gastric, kidney and liver resections each. Ten (30%) patients had more than one extra-pancreatic visceral organ resected. EVR patients had higher rates of complication (66.7% vs 40.8%; p<0.0001), including increased rates of delayed gastric emptying, wound infection and pulmonary complications (Table). The EVR group had a longer median post-operative hospital length of stay (9 vs 6 days; p<0.0001) and higher readmission rate (30.3% vs 15.5%; p<0.05). Median survival for the EVR group was 25 months, whereas median survival for the pancreatic resection alone group had not been reached. When subdivided by pathology, median survival for patients in the EVR group who had surgery performed for malignant indications was noted to be shorter (12 months vs 27 months, p<0.01).

Conclusion- Pancreatic resection with EVR can be performed safely, though it is associated with a higher post-operative morbidity rate, length of stay, and readmission rate when compared to PD or DP alone.
Introduction: For pancreatic ductal adenocarcinoma (PDAC) several studies have identified differentially expressed genes compared with normal pancreas but there has been a scarcity of gene signatures developed for PDAC that relate to pathological features or prognosis. Our aim was to investigate, using whole-genome oligonucleotide arrays, the gene expression signatures associated with clinicopathological states in patients with PDAC. Furthermore, the identification and validation of a prognostic gene expression signature was attempted.

Methods: Gene expression profiling was performed on fresh-frozen tissue for 48 primary PDACs and 10 matched normal pancreatic samples on Agilent 44K-Human oligonucleotide microarrays to generate signatures of malignant transformation. Patients were treated by pancreaticoduodenectomy between 2003 and 2008 at a single institution with complete clinicopathological follow-up data. Bioinformatic analysis was performed using the Biometric Research Branch tools package.

Results: Gene expression profiles associated with PDAC compared to normal tissue as well as various pathological states including lymph node status, tumor grade and resection margin status were developed. Using a semi-supervised Cox proportional-hazards model, a 107-gene survival profile was identified, which clustered the cohort into long- or short-survival groups (Figure A). The most significant of these genes included TGM2, DUSP5, SELENBP1, CLIC3 and NT5E. The two clusters differed significantly in terms of survival outcome (Figure B). The longer surviving group (23 patients) had a median survival of 30.1 months (95% CI: 12.3–47.8) versus 13.0 months (95%CI: 5.1–20.9, p < 0.001). In multivariate analysis tumor stage, lymph node status and the 107-gene survival profile (HR: 5.36, 95%CI: 2.22–12.9, p < 0.001) yielded independent prognostic value. Validation of the prognostic value of the gene survival profile within two independent microarray cohorts was performed. In validation set one (n = 27), patients in the high-risk group, as determined by the 107-gene survival profile, had a significantly poorer outcome (HR: 4.34, 95%CI: 1.55–12.2, p = 0.005). Integration of a previous prognostic gene set identified five genes shared with our gene survival profile (S100A2, NT5E, PAPPA, LOX and TWIST) with biological plausibility existing for each in PDAC.

Conclusion: A gene signature associated with PDAC has been described, which in addition to confirming previous pancreatic profiling studies, has identified potential tumorigenesis targets. Furthermore, a gene expression signature was described that was associated with poor prognosis independent of clinicopathological parameters and with validated utility in further independent cohorts of PDAC patients. It is hoped that the development of such classifiers will enhance the understanding of PDAC biology, and may lead to the development of more refined prognostic gene signatures.

Figure A: Cluster diagram of genes most associated with survival. The matrix colors represent up- (red) or
down regulation (blue) relative to the median for each gene.

**Figure B:** The Kaplan-Meier survival curves illustrate the divergence in survival between the good (blue) and poor (red) prognosis groups.
CONSERVATIVE RESECTION OF PROXIMAL BENIGN AND BORDERLINE TUMORS OF PANCREAS

INTRODUCTION
Benign and borderline tumors of pancreas encompass different kinds of tumors including cystadenoma, solid-pseudopapillary tumor, islet cell tumor, and intraductal papillary adenoma. Patients with these tumors have good outcomes after complete resection of the tumor. Conservative resections including central pancreatectomy, local resection, and enucleation for tumors of pancreas have been utilized for benign and low grade malignant lesions. Conservative resections for proximal pancreatic tumors especially involving the main pancreatic duct and bile duct have been considered to be dangerous to perform. We hereby present our experience in conservative resection of benign or borderline proximal pancreatic tumors.

METHODS
27 cases with benign or borderline tumors in the head (10), neck and proximal body (16), and ucinate (1) of the pancreas performed conservative resection in our hospital were reviewed. Among the 10 pancreatic head tumors, 8 cases were proved to be close to the main pancreatic duct by preoperative imagings. The pathological diagnosis were serous cystadenoma (11), islet cell tumor(12), and solid-pseudopapillary tumor(4). We attempted enucleation on these patients.

RESULTS
Enucleation was successfully performed in 16 cases, including all the patients had the tumor in the head and ucinate, and 5 cases of the neck and proximal body. Central pancreatectomy was performed in the rest 11 cases who had the main pancreatic duct damaged after enucleation. The main pancreatic duct was damaged and repaired in 3 of the 8 cases had the tumor of pancreatic head close to the duct. pancreatic fistula was found in 11 case, including 8 cases after enucleation and 3 cases after central pancreatectomy. For the 8 patients of pancreatic head tumor close to the main pancreatic duct, 7 cases had pancreatic fistula after enucleation. Severe fistula of over 1200ml per 24 hours occurred in the 3 cases after repair of the pancreatic duct. They were all defined as grade B pancreatic fistula according to the International Study Group of Pancreatic Fistula (ISGPF) clinical criteria because of the occurrence of persistent drainage. The time of drainage keeping was 15-292 days after operation. Two patients with the tumors close to the common bile duct simultaneously underwent cholecystectomy during the operation. One patient was found out to have bile leakage and a T-tube was placed in the common bile duct after the suture of the leakage spot using polypropylene. Delayed gastric emptying was found in 5 cases who also had pancreatic fistula. Postpancreatectomy hemorrhage (PPH) occurred in 1 case and was resolved by conservative treating. After a follow-up of 37.6 months (range 6-100 months), all the patients were alive without signs of tumors recurrence or metastasis. No new-onset diabetes mellitus (DM) or exocrine insufficiency of pancreas was observed.

CONCLUSIONS
Conservative resection including enucleation and central pancreatectomy was adequate for benign and borderline proximal pancreatic tumors even for cases adjacent to the common pancreatic duct. Although pancreatic fistula rate was high after enucleation, enucleation and central pancreatectomy were safe with proper drainage, and were helpful for the preservation of pancreatic function.
Background: The role of regulatory T cells (Treg) in antitumor immune response and tumor growth is incompletely understood. Treg promote pancreas cancer progression in part by inhibition of effector T cell (Teff) function. Interleukin-35 (IL-35), a newly identified member of the IL-12 cytokine family, mediates inhibitory effects of Treg. While IL-35 inhibits Teff proliferation, it promotes Treg proliferation, suggesting the effects of IL-35 may vary by cell type. The effect of IL-35 on pancreas cancer is unstudied. We examined the direct effect of IL-35 on proliferation and apoptosis of a pancreatic cancer cell line, MiaPaCa-2, and the molecular mechanisms involved.

Methods: Clonogenic survival assay, immunohistochemistry (IHC), TUNEL staining, proliferation and caspase-3 activity kits were used to evaluate the effects of IL-35 on cell survival, proliferation and apoptosis of a pancreatic cancer cell line, MiaPaCa-2. We further investigated the possible molecular mechanisms by using RT-PCR, IHC, and Western blot.

Results: We showed that the percentage of colonies, PCNA+ cells and the OD value of SK-Mel-5 cells were significantly increased in the presence of IL-35. TUNEL+ cells and the relative caspase-3 activity were both decreased in the presence of IL-35. The pro-proliferative effect of IL-35 correlated with increased expression of proliferative molecules cyclin B, cyclin D, cdk2 and cdk4. The anti-apoptotic effect of IL-35 correlated with decreased expression of the pro-apoptotic molecule TRAILR1 and increased expression of anti-apoptotic molecules Bcl-2 and survivin.

Conclusions: These results suggest that IL-35 directly enhances pancreas cancer growth by promoting proliferation and inhibiting apoptosis. These findings support a second mechanism by which Treg may promote pancreas cancer growth.
43184 ROLE OF EUS-FNA PRIOR TO NEOADJUVANT CHEMORADIOThERAPY FOR PANCREATIC CANCER PATIENTS. -DOES PREOPERATIVE EUS-FNA PRODUCE DISSEMINATION FOR THREE MONTHS IN PANCREATIC CANCER PATIENTS?- 

BACKGROUND: Neoadjuvant chemoradiotherapy (NCRT) for pancreatic cancer is increasingly being used. Peritoneum dissemination was considered to be a serious problem as complication of EUS-FNA. This study evaluated the safety and utility of EUS-FNA prior to NCRT for pancreatic cancer.

Methods: We retrospectively analyzed patients who received EUS-FNA between April 2006 and October 2010. One hundred forty patients (89 men/51 women) had EUS-FNA of pancreatic lesions (76 head/neck, 49 body, 14 tail). Forty-six patients (31 men/15 women) had EUS-FNA prior to NCRT for pancreatic cancer (32 head/neck, 10 body, 4 tail). Those patients had operation after NCRT. The mean period after EUS-FNA until operation was 99.8 days (70-171).

RESULTS: EUS-FNA had a sensitivity of 92.6%, specificity of 100%, and diagnostic accuracy of 93.6% for pancreatic lesions, respectively.

In potential NCRT 74 cases, EUS-FNA had diagnostic accuracy of 93.2%, clinical decisions were influenced in 19 of 74 (25.7%) patients. There is no tumor seeding after EUS-FNA prior to NCRT in pancreatic cancer. Seven patients (15.2%) showed ascites or peritoneal nodule after EUS-FNA FNA prior to NCRT. Nevertheless there was no significant difference between patients who underwent EUS-FNA and those without EUS-FNA in regard to incidence of ascites or peritoneal nodule.

CONCLUSION: EUS-FNA prior to NCRT is safe, and can help to make surgical decisions regarding pancreatic carcinoma patients.
BACKGROUND:
Autoimmune pancreatitis (AIP) is a rare subtype of chronic pancreatitis that may mimic adenocarcinoma of the pancreas. Although non-operative therapy with glucocorticoids can control AIP, many patients will undergo pancreatic resection when a diagnosis of AIP is in doubt or there is concern for pancreatic malignancy. The aim of this study was to evaluate the short and long-term outcomes of pancreatic resection in patients with AIP.

METHODS:
In this multi-institutional, retrospective cohort study, we identified all patients who underwent pancreatic resection for AIP from 1986 to 2011. Diagnosis of AIP was confirmed by pathology review. Clinical presentation, operative details, and post-operative outcomes were analyzed.

RESULTS:
Seventy-four patients (median age 60, 69% male) with AIP underwent pancreaticoduodenectomy (n = 56, 76%), distal pancreatectomy (n = 15, 20%), and total pancreatectomy (n = 3, 4%). Median follow-up was 58 months (missing, n = 9). Indication for surgical intervention was concern for malignancy (n = 59, 80%), pancreatitis (n = 9, 12%), malignancy on pre-operative biopsy (n = 4, 5%), and unknown (n = 2, 2.7%). Portal/superior mesenteric vein repair or resection was required in 15 (20%) cases. Post-operative complications occurred in 33 (45%) patients with one perioperative death (1%). Clinically relevant (Grade B/C) pancreatic fistula occurred in 2 (3%) patients. Early (< 30 days) reoperation was required in 3 (4%) patients. No patients required operation for recurrent AIP. Late (>30 days after operation) pancreatic and biliary stenting was performed in 3 (4%) patients and 4 (5%) patients, respectively. Recurrent pancreatitis was reported in 20 (27%) patients. Five- and 10-year overall survival were 91% and 76%, respectively. Seventeen (23%) patients required post-operative steroids. Indications for glucocorticoid therapy were inflammatory bowel disease (n = 6, 8%), AIP (n = 4, 5%), rheumatoid arthritis (n = 2, 3%), idiopathic thrombocytopenic purpura (n = 2, 3%), connective tissue disorder (n = 1, 1%), and multiple sclerosis (n = 1, 1%). Extra-pancreatic autoimmune disorders were reported in 19 (26%) patients with 8 (11%) patients developing symptoms after pancreatic resection.

CONCLUSION:
Although we do not advocate pancreatic resection for AIP, operation to rule out malignancy may be indicated in selected patients. Surgical resection resulted in few pancreatic fistulae and a low rate of re-intervention. While nearly a quarter of patients received post-operative steroids, typically for extra-pancreatic autoimmune disorders, steroid therapy specifically for the remnant pancreas was most uncommon (5%).
DEFINING QUALITY FOR PANCREATICODUODENECTOMY: SEVERE ADVERSE POSTOPERATIVE OUTCOMES INCLUDING THOSE REQUIRING MULTIPLE READMISSIONS WITHIN 90-DAYS, PROLONGED OVERALL LENGTHS OF STAY OR MULTIPLE INVASIVE INTERVENTIONS ARE PREDICTABLE

OBJECTIVES Established systems for grading postoperative complications do not change the assigned grade when multiple interventions or readmissions are required to manage the complication. We seek to define a quality outcome for pancreaticoduodenectomy (PD) and identify predictors of poor quality.

METHODS Inpatient and office charts for patients undergoing PD between January 1999 and December 2009 were reviewed to capture all complications and 90-day readmission events. Clavien-Dindo grade IIIb, IV and V complications were classified as severe adverse postoperative outcomes (SAPO). II and IIIa complications requiring either prolonged overall lengths of stay (> three standard deviations beyond the mean for patients without complications) including readmissions or more than one interventional procedure were also classified as SAPOs. All others were considered minor adverse outcomes (MAPO).

RESULTS 490 patients underwent PD. 366 (74.7%) had a complication. 90.4% of PD patients had a complication of low/moderate Clavien-Dindo grade (I, II, IIIa) or no complication. Using our re-classification, however, 29.8% had a poor quality outcome (SAPO) while 70.2% had a high quality outcome (MAPO or no complication). Multivariate logistic regression identified age > 75 years (OR: 2.693, 95% CI: [1.662, 4.362]), intraoperative blood loss > 1500 mLs (OR: 3.024, 95% CI: [1.592, 5.743]) and operative time > 8 hours (OR: 1.912, 95% CI: [1.227, 2.987]) as independent predictors of SAPO. Tumor size, pathology, bilirubin, albumin, cardiopulmonary disease, diabetes and pylorus preservation did not predict outcome.

CONCLUSIONS Generic grading systems underestimate the severity of some complications following PD. Using a procedure specific metric for outcome following PD, we identify advanced age, excessive blood loss and long operative time as predictors of poor quality.
43200 DEFINING QUALITY FOR DISTAL PANCREATECTOMY: DOES THE LAPAROSCOPIC APPROACH PROTECT PATIENTS FROM POOR QUALITY OUTCOMES?

OBJECTIVES Established systems for grading postoperative complications do not change the assigned grade when multiple interventions or readmissions are required to manage the complication. We seek to define a quality outcome for distal pancreatectomy (DP) and determine if laparoscopic distal pancreatectomy (LDP) affords an improvement in quality relative to open distal pancreatectomy (ODP).

METHODS Inpatient and office charts for patients undergoing either ODP or LDP between January 2006 and December 2009 were reviewed to capture all complications and 90-day readmission events. Clavien-Dindo grade IIIb, IV and V complications were classified as severe adverse postoperative outcomes (SAPO). II and IIIa complications requiring either prolonged overall lengths of stay (>2 standard deviations beyond the mean for patients undergoing ODP without complication) including readmissions or more than one interventional procedure were also classified as SAPOs. All others were considered minor adverse outcomes (MAPO).

RESULTS 127 patients underwent DP. 63 (49%) had a complication. 91% of DP patients had a complication of low/moderate Clavien-Dindo grade (I, II, IIIa) or no complication. Using our re-classification, however, 24.8% had what was considered to be a poor quality outcome (SAPO) while 75.2% had a high quality outcome (MAPO or no complication). Of the patients undergoing DP, 77 underwent ODP and 50 underwent LDP. Compared to patients undergoing ODP, patients undergoing LDP were statistically less likely to have ductal adenocarcinoma (4% vs. 26%, p<0.01) and tended to have smaller tumors (3.1±0.36 cm vs. 3.9±0.26 cm, p=0.05). Those undergoing LDP did also demonstrate, however, lower volumes of intraoperative blood loss (234±30.1 mLs vs 752±152.7 mLs, p<0.01), lower rates of postoperative transfusion (2% vs 20%, p<0.01), lower rates of postoperative morbidity (35% vs 58%, P<0.01), shorter initial postoperative lengths of stay (4.1±0.23 vs 8.3±0.7 days, p<0.01), shorter overall lengths of stay including 90-day readmissions (6.1±0.9 days vs. 10.5±0.9 days, p<0.01), and were less likely to have a poor (SAPO) quality outcome (15% vs 31%, p<0.03) than those undergoing ODP. There were no statistical differences between the two groups in regard to age, presenting symptoms, incidence of diabetes, chronic pancreatitis or comorbid cardiopulmonary disease, preoperative albumin, operative time, the rate of readmission or of pancreatic fistula.

CONCLUSIONS Generic grading systems underestimate the severity of some complications following distal pancreatectomy. Using a procedure specific metric for quality following distal pancreatectomy, LDP affords a higher quality postoperative outcome than ODP resulting in shorter initial and overall lengths of stay, a lower incidence of postoperative transfusion and a lower incidence of severe adverse postoperative outcomes.
43202 NEOADJUVANT CHEMORADIATION VERSUS SURGERY FIRST FOR RESECTABLE PANCREATIC HEAD ADENOCARCINOMAAN ECONOMIC AND OUTCOME ANALYSIS

Background The optimal sequence of treating pancreatic cancer with chemotherapy, radiation and surgical intervention remains elusive. Thus, cost should be considered. This study was conducted to compare the cost and outcome of a surgery first approach versus neoadjuvant chemoradiation followed by surgery.

Methods A decision analytic model was constructed to contrast surgery first and neoadjuvant chemoradiation followed by surgery strategies. The National Cancer Data Base (2003-5), ACS National Surgical Quality Improvement Program (2005-9) and surgical literature populated the probabilities and outcomes in the surgery first arm, including immediate operative outcome, complication rate, pathologic stage, adjuvant therapy and stage-specific survival based on adjuvant therapy. Data from the MD Anderson Cancer Center pancreatic cancer database (2002-8) populated the neoadjuvant arm. Cost data were estimated based on Medicare reimbursement (2011 US dollars). Survival, discounted when appropriate, was reported in quality-adjusted life months (QALMs).

Results 164 patients completed neoadjuvant chemoradiation. Of these, 36 (22%) did not proceed to surgery. Failure was due to metastases, 18(50%), prohibitive performance status (PS), 17(47%) and patient choice, 1(3%). 12 patients (7%) proceeded to laparotomy but were deemed unresectable. 116 (71%) patients underwent definitive resection. The surgery first approach cost $46,830 to yield survival of 8.7 QALM, while the neoadjuvant strategy cost $36,583 to achieve 18.8 QALM. This resulted in a savings of $10,247 to achieve 10.1 additional QALM. In the neoadjuvant population, patients not undergoing surgery, those unresectable at laparotomy and those completing surgery demonstrated a cost of $12,401 to yield 7.7 QALM, $20,380 to yield 7.1 QALM and $45,673 to achieve 23.4 QALM, respectively.

Conclusion Treating patients with neoadjuvant chemoradiation identifies those who develop early metastases or a prohibitive performance status and can be spared an ineffectual or prohibitively morbid operation. Our data suggest this approach is associated with improved overall survival at significantly lower cost. Neoadjuvant therapy for resectable pancreatic head adenocarcinoma should be employed more frequently to provide cost-effective care for this lethal disease.
**Introduction:** Various in vivo models of human pancreatic ductal adenocarcinoma (PDAC) have been described but xenograft models offer advantages such as the retention of original primary tumor genetic and growth profiles which potentially can guide post-operative surveillance and treatment. We hypothesized that the growth of xenografts derived from primary PDAC resected for cure could predict recurrence and survival in these patients.

**Methods:** Only patients with PDAC resected for cure and subsequently implanted were analyzed. A portion of human PDAC tumors harvested at the time of resection was subcutaneously implanted into NOD/SCID mice. Xenograft growth patterns and patient clinicopathologic factors were prospectively collected and compared using the Student’s t-test and Fisher’s exact test. Recurrence-free survival (RFS) and overall survival (OS) were determined utilizing the Kaplan-Meier method. A p<0.05 was considered statistically significant.

**Results:** Of 59 patients who had their PDAC resected for cure and utilized for the establishment of a xenograft, 46 (78%) grew into a viable xenograft with those derived from patients who underwent neoadjuvant therapy less likely to grow (p<0.005). Xenograft formation was detected a mean of 136.8 days prior to the detection of clinical recurrence (Fig 1). Xenograft growth was associated with a decreased median RFS and OS (8.6mo and 20.7mo, respectively, p≤0.05) compared to patients without corresponding growth (median not reached, Fig 2). Based on univariate analysis, positive lymph node status (HR 2.2, CI 1.1-4.6, p=0.03) and xenograft growth (HR 2.9, CI 1.4-6, p=0.01) were the only predictors of RFS and xenograft growth was the only predictor of OS (HR 2.8, CI 1.1-7.2, p=0.05).

**Conclusions:** The establishment of patient-derived PDAC xenografts can be performed with a high efficiency and predicts RFS and OS in these patients. Post-operative surveillance and treatment in these patients could potentially be personalized based on the status of a patient’s corresponding xenograft.
**Fig 1.** Comparison of time to detection of xenograft formation after implantation versus detection of clinical recurrence after resection of PDAC.

**Fig 2.** Comparison of overall survival of patients who had corresponding xenograft tumor growth versus those who did not.
43208 PROGNOSTIC IMPACT OF PERIOPERATIVE SERUM CA 19-9 LEVELS IN PATIENTS WITH RESECTABLE PANCREATIC CANCER

Background: Pancreatic cancer is one of the most deadly cancers, and serum carbohydrate antigen 19-9 (CA19-9) level has been reported to be a useful prognostic marker in pancreatic cancer.

Purpose: The purpose of this study was to determine which prognostic factor (preoperative or postoperative serum CA19-9 level) is more useful.

Methods: Pre- and postoperative serum CA19-9 levels were measured in 109 patients who underwent surgical resection for pancreatic cancer between 1998 and 2009, and their relationships to clinicopathological factors and overall survival were analyzed with univariate and multivariate methods.

Results: Preoperative CA19-9 levels were significantly higher in patients with UICC pT3 than in patients with UICC pT1/T2 (P = 0.022). But, there was no significant relationship to other clinicopathological factors. In contrast, postoperative CA19-9 levels were significantly higher in patients with R1 than those with R0 (P = 0.041), and in patients with lymph node metastasis than in those without lymph node metastasis (P = 0.006).

In univariate analysis, tumor location (P = 0.019), postoperative adjuvant chemotherapy (P < 0.001), residual tumor factor status (P < 0.001), UICC pT stage (P = 0.004), lymph node metastasis (P = 0.015) and UICC final stage (P = 0.015) were significantly associated with overall survival. Differences in overall survival were significant between groups divided on the basis of four postoperative CA19-9 cutoff values (37, 100, 200, and 500 U/ml) but not significant between groups divided on the basis of the same four preoperative CA19-9 cutoff values. Pre- to postoperative increase in CA19-9 level was also significantly associated with poor prognosis. In multivariate analysis, postoperative adjuvant chemotherapy (hazard ratio [HR], 1.59; P = 0.004) and postoperative CA19-9 cut-off value of 37 U/ml (HR, 1.64; P = 0.004) remained independent predictors of prognosis.

Conclusion: Postoperative CA19-9 level is a better prognostic factor than preoperative CA19-9 level, and curative surgery for resectable pancreatic cancer should be tried regardless of the preoperative CA19-9 level.
Background: Delayed gastric emptying (DGE) is a major cause of morbidity following pancreaticoduodenectomy (PD), with various factors implicated in its development. The influence of operative technique on the occurrence of DGE is controversial. The impact of a Braun enteroenterostomy (BE) in reconstruction following classic PD was assessed.

Methods: Forty-four consecutive patients undergoing non-pylorus preserving PD from August 2009 to November 2011 by a single surgeon were included in this study. The first twenty patients had a standard antecolic gastrojejunal anastomosis. The subsequent twenty-four patients had an antecolic gastrojejunal anastomosis with the addition of a BE. The groups were compared and complications assessed according to criteria set by the International Study Group of Pancreatic Surgery (ISGPS).

Results: Patient characteristics between the groups were similar as was the extent of surgery and tumour and pancreatic characteristics. The median estimated blood loss was greater in the standard reconstruction group (450 ml (100-1500) vs 325(100-1500 ml) p = 0.04). All other operative factors, including intra-operative blood transfusions were similar between the two groups. The DGE rate in the BE was significantly lower than the standard reconstruction group (1(4%) versus 7(35%); p=0.015). In the standard group, 6 of 7 cases of DGE were Class C in nature. The pancreatic fistula rate in the BE group was similar to the standard reconstruction group (4(21%) versus 5(29%); p=0.706) as was the median length of hospital stay (10 days (7-38) vs 15 (7-45); p= 0.291). On assessing factors associated with DGE, the BE technique was the only significant factor in this study.

Conclusion: The use of BE following non-pylorus preserving PD appears to results in a significant reduction in DGE.
WHAT IS APPROPRIATE BILIARY DRAINAGE IN PANCREATIC CANCER PATIENTS WITH MALIGNANT BILIARY OBSTRUCTION DURING NEOADJUVANT CHEMORADIOThERAPY?

BACKGROUND: Neoadjuvant chemoradiotherapy (NCRT) for pancreatic cancer is increasingly being used. Neoadjuvant regimen in our institution would require 5 weeks of chemoradiotherapy, followed by a recovery period of an additional 4 to 6 weeks before surgery.

Methods: We retrospectively analyzed patients who received biliary plastic stent placement between April 2006 and October 2010. Thirty-four patients (23 men/11 women) with locally advanced pancreatic cancer and biliary obstruction had plastic stent placement (19 cases 8.5 Fr, 15 cases 10 Fr). In 10 Fr stent group, Endoscopic sphincterotomy (ES) was performed before stent placement, 8.5 Fr group received stent placement without ES.

RESULTS: Twenty-two patients (64%) completed neoadjuvant therapy. Stent occlusion occurred in 6 patients (31.5%) in the 8.5 Fr group and 6 patients (40%) in the 10 Fr group. There was no significant difference between two groups in occlusion rate. The difference of the median duration of stent patency was not statistically significant (p=0.30). In 8.5 Fr group pancreatitis developed in 6 patients, whereas pancreatitis occurred in 1 patient in 10 Fr group. One late complication was cholecystitis in 10 Fr group. Complication was managed conservatively.

CONCLUSION: Plastic stents do not maintain patency during the required time for neoadjuvant chemoradiotherapy regimen. This study suggests that the plastic stent size does not affect occlusion rate, the duration of stent patency. Metallic stents placement may be a safer and more effective strategy, larger study are required to confirm the optimal stent during neoadjuvant chemoradiotherapy for pancreatic cancer.
OBJECTIVES: To evaluate if patients with isolated metastatic pancreatic cancer to the lung have better overall survival than patients with other metastatic sites.

METHODS: This is a retrospective review from a prospectively kept pancreatic database. We identified 34 patients as having metastatic pancreatic cancer to the lungs as the only site of distant metastasis. Survival and prognostic factors were analyzed using Kaplan-Meier survival estimators and Cox proportional hazards regressions.

RESULTS: Thirty-four patients were identified as having metastatic pancreatic cancer to the lungs as the only site of distant metastasis, 15 were male (44.1%) and 19 were female (55.9%). The median age at diagnosis was 66 y (range: 59-70). Histologically 33 patients (97.1%) had adenocarcinoma and one patient (2.9%) had a mucinous cystic neoplasm of the pancreas. The tumor was localized to the head in 25 patients (73.5%), to the body in 5 patients (14.7%), and to the tail in 4 patients (11.8%). Twenty-seven (79.4%) patients had a T3 tumor, four had a T2 tumor (11.8%), two had a T1 tumor (5.9%), and 21 patients (61.8%) were N1. Twenty-one patients (61.8%) had a classic Whipple procedure, six (17.7%) had a pylorus preserving pancreatoduodenectomy, six had a distal pancreatectomy (17.7%), and one (2.9%) had an extended central pancreatectomy. Eighty-two percent of patients (n=27) had a R0 resection, 15% (n=5) had a R1, and one (3.0%) had a R2 resection. Ten patients (29%) had neoadjuvant chemoradiation, 29 patients (85.3%) had adjuvant chemotherapy, and 19 patients (55.9%) had adjuvant radiation therapy. Median overall survival (OS) from the time of diagnosis was 26.4 months (range: 17.7-32.4), median disease free survival (DFS) was 17.6 months (range: 14.9-22.3). The median CA 19-9 at diagnosis, at the time of surgery, after surgery, and at recurrence were 306 (85.3-857.2), 189.1 (44.1-429.3), 18.25 (12.8-46.7), 243 (41.5-494.6) respectively. Node negative patients (HR=2.21, P=0.04) and adjuvant radiation therapy (HR=0.43, p=0.02) is associated with better OS. The OS of patients who were node negative was 31.8 months (SE=0.150, 95% CI 0.176-0.718) compared to 21.72 months (SE=0.109, 95% CI 0.257-0.666), and the OS of patients who received adjuvant radiation therapy was 34.5 months (SE=0.117, 95% CI 0.225-0.661) compared to 18.1 months (SE=0.132, 95% CI 0.182-0.667) for the patients that did not receive it. Adjuvant radiation therapy showed improved DFS (HR 0.40, p=0.01) compared to no radiation with a median DFS of 17.9 months (SE=0.114, 95% CI 0.244-0.672) compared to 9.3 months (SE=0.128, 95% CI 0.212-0.687). We identified that a change in CA 19-19 from preoperative and postoperative levels showed and increase hazard of death (HR 29.36, 95% CI 2.34-368.3, p=0.009). At the time of analysis 30 patients (88%) had died.

CONCLUSIONS: Patients with isolated metastatic pancreatic cancer to the lung have better OS than patients with metastatic pancreatic cancer to other sites based on historical controls. Node negative disease and adjuvant radiation therapy are prognostic indicators of better OS. These patients should be stratified in clinical trials and that a search for genomic correlates should be made.
Development and validation of a blood-based biomarker for differential diagnosis of pancreatic adenocarcinoma and chronic pancreatitis

Using the developed technology (MethDet), we analyzed DNA methylation in cell-free circulating DNA isolated from blood of patients with pancreatic adenocarcinoma, chronic pancreatitis, and healthy controls. Twenty four fragments with the most significant differences in methylation among these groups were selected, a qPCR-based clinical-grade test was developed, and a formula for discrimination of these diseases was chosen. In the first set of blinded samples (plasma from patients with pancreatic adenocarcinoma, chronic pancreatitis, and healthy controls) one sample was identified incorrectly and 34 samples – correctly. Results of the second set of blinded samples will be presented.
43222 PANCREATICODUODENECTOMY IN ELDERLY PATIENTS: RESULTS AND COSTS ANALYSIS

Background: It is today accepted that the bad prognosis of pancreatic cancer is life time limiting also in old patients. However, old age is sometimes considered a contraindication for PD due to increased risk of complications and peri-operative costs.

Aim: To analyze short and long-term outcome and peri-operative costs in elderly compared to and younger individuals.

Methods and patients: All patients who underwent PD between 2004 and 2010 at Karolinska University Hospital were retrieved from a prospective data registry and demographics, ASA score perioperative results, length of stay (LOS), costs and survival were analyzed. The cohort was divided by age into elderly (E ≥ 75 years) and younger individuals (Y < 75 years).

Results: In total 367 consecutive PDs (201 males/166 females) were identified (E: n=65; Y: n=302). The two groups were comparable regarding general characteristics except age (mean O 78.7 vs. 61.5 yrs) and pre-operative anesthesiological risk (ASA1+2: E 49.0 vs. Y 65.2 %; ASA 3+4: E 51.0 vs. Y 34.8 %; p=0.02)

Comparing E with Y there were no differences in LOS (E 16 vs. Y 16.7 days), overall post-operative complication rate (E 55 vs. Y 57 %), severe (Clavien score ≥ 3b) complications (E 16.9 vs. Y 16.5 %), re-operation rate (E 6.1 vs. Y 7.9%), mortality (E: 1.5 vs Y 3.3 %) or overall cost (E 30570 vs. Y 32176 Euro). The 1, 3 and 5 year survival rates were comparable between the two groups in patients with pancreatic ductal adenocarcinoma (E: 64.7%, 34.4% and 7.2% vs. Y 71.9%, 31.2% and 22%; p=0.5). In contrast, a significant difference in 1, 3 and 5 year survival rates was found in patients with other periampullary tumors (E: 81.8%, 43% and 32.3% vs. Y: 87.9%, 69.5% and 62%; p=0.01).

Conclusions: The current study shows no major differences in perioperative morbidity, mortality or costs between elderly and younger patients, thus PD can be considered safe in elderly patients. Old age is not “prognostic factor” in pancreatic ductal adenocarcinoma, but a negative one for patients suffering from less aggressive periampullary malignancies. On the basis of these results patients should never excluded from a PD based on age only.
43225 INFECTION OF PANCREATIC NECROSIS IN EXPERIMENTAL NECROTIZING PANCREATITIS INDUCES SUSTAINED BACTEREMIA AND INCREASES PANCREATITIS SEVERITY WHICH IS ONLY PARTIALLY REVERSED BY ANTIBIOTIC THERAPY

**Introduction:** Infection of pancreatic necrosis in necrotizing pancreatitis increases the lethality. This cannot be prevented by pre-emptive antibiotic therapy. To examine the mechanisms underlying this clinical circumstance we used a model of primary infected pancreatic necrosis in taurocholate induced pancreatitis in mice. **Materials and Methods:** Acute necrotizing pancreatitis with sterile necrosis (SN) was induced by retrograde injection of 4% taurocholate in the common bile duct of Balb/c mice. Primary infected pancreatic necrosis (IN) was induced by co-injecting $10^8$ CFU E. coli. For antibiotic therapy 10 mg/kg bodyweight moxifloxacin were administered intravenously prior to pancreatitis induction (AIN). After 6, 12, 24, 48 and 120 hours animals were sacrificed and serum as well as organs related to pancreatitis associated SIRS were examined. **Results:** The intrapancreatic injection of E. coli caused transient bacteremia but did not induce acute pancreatitis. Prolonged bacteremia occurred when infected acinar cell necrosis was induced (24h CFU E. coli in blood; bacteria only not detected, IN 121±63). Infection of pancreatic necrosis with E. coli further increased the pancreatic damage (histology score 24h: SN 17.8±2.6 vs. IN 23.7±2.2; p<0.001) and the systemic complications such as the pulmonary vascular leak (albumin in bronchoalveolary lavage 6h: SN 151.0±57.7 µg/ml vs. IN 219.5±76.2 µg/ml; p<0.05). Additionally, infected necrosis induced impaired hepatic function with reduced serum glucose concentrations (24h: SN 167.0±35.6 mg/dl vs. IN 106.9±12.7 mg/dl; p<0.001). Initial antibiotic therapy did not have an impact on the pancreatic histology or the pulmonary damage induced by infected pancreatic necrosis. However, moxifloxacin treatment reduced the systemic inflammatory response (serum IL-6: IN 330.5±336.6 vs. AIN 38.7±25.5 pg/ml; p<0.001) and restored liver function (serum glucose: IN 105.8±12.7 vs. AIN 155.7±39.5 mg/dl; p<0.001). **Conclusion:** Infection of pancreatic necrosis induces sustained bacteremia. Infected pancreatic necrosis further increases the systemic complications in acute necrotizing pancreatitis. Initial antibiotic therapy reduces the inflammatory response and restores liver function.
Introduction: Hereditary pancreatitis is a very rare cause of chronic pancreatic inflammation. In recent years the genetic mutations leading to hereditary pancreatitis have been characterized. Patients with hereditary pancreatitis present in childhood and, as adults, are reported to have an extremely high risk of pancreatic cancer. However, the rarity of this disorder has resulted in a gap in clinical knowledge. Therefore, the aims of this analysis are to characterize a large series of patients with hereditary pancreatitis and to establish clinical guidelines.

Methods: Pediatric and adult endoscopic, surgical, radiologic and genetic databases were searched from 1994-2011. Patients with chronic pancreatitis and genetic mutations for PRSS-1 or SPINK-1 as well as those with a significant family history of chronic pancreatitis were included. Patients with chronic pancreatitis due to other causes, idiopathic pancreatitis without a positive family history, and familial pancreatic cancer were excluded. Data were gathered on genetic testing, endoscopic and surgical management as well as the occurrence of pancreatic cancer.

Results: Eighty-six patients were identified, and the mean age at presentation was 17 years. Forty-four (51%) were female. Genetic testing confirmed the diagnosis in 38 families (44%) while 48 patients (56%) had a significant family history. In recent years adult patients were counseled to avoid tobacco and alcohol. Eighty patients (93%) with a median age of 15 years were managed endoscopically with sphincterotomy (69%), stone removal (31%) and/or stenting of pancreatic duct strictures (85%). In recent years endoscopic ultrasound was performed in 13 patients (15%) to screen for cancer. Twenty-nine patients (34%) have undergone 35 operations at a mean age of 19 years. Surgery included 15 drainage procedures (lateral pancreaticojejunostomy-9, cystenterostomy-3, Duval-2, sphincteroplasty-1) and 20 resections (proximal-10, distal-9, total-1). Islet transplantation was performed in the one patient who underwent a total pancreatectomy. While 22 patients (26%) were older than 40 years, only one 67 year old man developed pancreatic cancer and died. The remaining 85 patients are all alive and cancer free.

Conclusions: Many children and young adults with hereditary pancreatitis can be managed initially with endoscopic therapy. When surgery is undertaken, the procedure should be tailored to the pancreatic anatomy and the cancer risk. With aggressive endoscopic and surgical management as well as avoidance of cocarcinogens the incidence of pancreatic cancer is surprisingly low in patients with hereditary pancreatitis.
RESECTED PANCREATIC CANCER WITH OPTIMAL PROGNOSIS: FACTORS DRIVING SURVIVAL

Objectives: Despite the generally dismal prognosis of patients with resected pancreatic ductal adenocarcinoma (PDAC), some achieve long-term survival. We sought to characterize an optimal prognosis cohort and identify factors that determine their survival advantage.

Methods: A database containing all resections performed for PDAC at two institutions over a decade (2001-2011) was studied. A “Favorable” cohort of patients was initially defined as R0/N0/M0. For further refinement of this group, univariate and multivariate survival analyses were conducted, applying demographic, pathologic, and perioperative variables. Kaplan-Meier analysis next compared Favorable and Unfavorable cohorts and assessed the impact of adjuvant therapy on each.

Results: Of 412 resections, 90 (22%) were R0/N0/M0. This Favorable group had median and actuarial 5-yr survivals of 37.3m and 42% (versus 19.4m and 20% for the remaining 322 Unfavorable patients; p<0.0001), and contained 46% of all actual 5-yr survivors in the series. Within the Favorable group, multivariate predictors of survival were tumor differentiation, resection type, and 30-day readmission. Using these, Optimal and Sub-Optimal prognosis cohorts were identified within the Favorable group (Table). The majority of Optimal prognosis patients survived five years, whereas Sub-Optimal prognosis patients survived comparably to the Unfavorable group. While adjuvant therapy was associated with significantly improved survival when applied to Unfavorable patients (P<0.001), it afforded no survival benefit in Optimal prognosis patients (p=0.463).

Conclusions: Tumor differentiation, tumor location/surgical resection and effective perioperative care correlate with optimal prognosis for resected PDAC. Current adjuvant therapies do not appear to improve survival in these particular patients.
Table: Survival Analysis of 412 PDAC Patients

<table>
<thead>
<tr>
<th>Group</th>
<th>n</th>
<th>Median surv (m)</th>
<th>5yr surv</th>
<th>Hazard Ratio</th>
<th>P-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Favorable (R0/N0/M0)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td><strong>Optimal Prognosis</strong></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>No: poor differentiation, distal, readmission</td>
<td>39</td>
<td>111.2</td>
<td>55%</td>
<td>0.49</td>
<td>0.031</td>
</tr>
<tr>
<td><strong>Sub-Optimal Prognosis</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any: poor differentiation, distal, readmission</td>
<td>51</td>
<td>28.1</td>
<td>31%</td>
<td>1</td>
<td>-</td>
</tr>
<tr>
<td><strong>Unfavorable</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any N1 or R1 or M1</td>
<td>322</td>
<td>19.4</td>
<td>20%</td>
<td>1.44</td>
<td>0.079</td>
</tr>
</tbody>
</table>

*Comparison with Sub-Optimal group. Cox Proportional Hazards Model
MULTIFOCAL INTRADUCTAL TUBULOPAPILLARY NEOPLASMS WITH EXTENSIVE INVASION OF THE PANCREAS: A CASE REPORT AND REVIEW OF THE LITERATURE

Background: Intraductal tubulopapillary neoplasms (ITPN) of the pancreas are exceedingly rare, accounting for less than 1% of pancreatic exocrine neoplasms and 3% of intraductal pancreatic neoplasms. Most reported cases show high grade dysplasia with only limited invasion, if any. The most common preoperative diagnosis based on imaging is intraductal papillary mucinous neoplasm (IPMN). As a result, these tumors are usually diagnosed only after surgical resection. We report a new case of ITPN with novel features, discuss the clinical findings, management, and outcome of the patient, and review the literature.

Case Report: The patient was a 35 year-old male with no past medical history who presented with epigastric abdominal pain. Abdominal CT showed two enhancing solid masses: a 5.8 cm lesion in the body of the pancreas and a 4 cm lesion in the pancreatic head with duodenal involvement. The patient underwent total pancreatectomy. Grossly there were two well demarcated masses. Histopathology revealed both lesions were ITPN with associated extensive invasive carcinoma. The lesions were composed of tubulopapillary growth with intraductal and extensive invasive components. The tumor cells were cuboidal to columnar with enlarged nuclei and eosinophilic-to–amphophilic cytoplasm. High-grade atypia with frequent mitotic figures were observed throughout the neoplasms. Mucin staining was scant. Tumor cells stained positive for CK7, CK8/18, and negative for CK20. One of three lymph nodes was positive for metastatic disease. The patient is currently receiving adjuvant chemotherapy and has no signs of recurrent disease.

Discussion: The largest reported case series in the literature describes ten patients diagnosed with ITPN over a seven-year period, with the majority of lesions classified as carcinoma in situ. Although some showed limited invasion, none of these patients had metastatic lymph node involvement or extensive invasion. One of the patients in this series died from metastatic liver disease, and another developed a recurrence in the head of the pancreas one year after the lesion in the body was resected. Here we report the first documented case of ITPN with metastatic lymph node involvement and extensive invasion.

Conclusion: Given their infrequency and nonspecific radiologic findings, ITPNs present a diagnostic challenge. Although most reported cases are indolent, some ITPNs can be very aggressive and should enter the differential diagnosis for a well demarcated pancreatic mass. Surgical resection has been the treatment for the majority of patients, but limited data are available for prognosis and optimal therapy for both indolent and aggressive tumors.
THE HEPATOBILIARY SPECIALIZED ACADEMIC PHYSICIAN ASSISTANT; A NEW PARADIGM IN HEALTH CARE

Background: The Physician Assistant profession began in the mid-1960s to help fill the shortage of Primary Care Physicians and has since grown into academic centers to help fill the void of the resident 80 hour work week. The opportunity to define the Hepatobiliary specialized Academic Physician Assistant (HPB APA) reigns strong.

Methods: The Medical University of South Carolina (MUSC) integrated their first HPB APA in March of 2008 to assist the needs of two HPB specialized surgeons. Hospital research and registry databases were retrospectively reviewed to evaluate APA productivity from March 2008, through October 2011.

Results: The HPB APA initiated and facilitated nine studies with the IRB, including the prospectively collected Pancreatectomy with Islet Autotransplant (TPIAT) longitudinal outcome database. The TPIAT program has grown from 25 cases in 2008 to 32 in 2011 (+28%). The HPB surgeons completed 110 pancreas surgeries from March through December 2008, and 128 pancreas surgeries from January through October 2011. In the same timeframe, 3,905 patients were seen in the HPB clinics in 2008 and 3,474 in 2011. The APA has mentored 5 students through hypothesis development, data analysis, and abstract submission. She has co-authored 11 abstracts, one journal article, and presented at three medical conferences. She provides specialized patient care and teaches residents and students on the specific needs of the pancreas population.

Conclusion: The HPB specialized APA allows for consistent quality care of the complex pancreas patient, initiates and facilitates clinical research, and educates general surgery residents and students. This new trifecta will help necessitate future Pancreas Centers of Excellence.
**QUALITY ASSESSMENT IN PANCREATIC SURGERY: WHAT MIGHT TOMORROW REQUIRE?**

**INTRODUCTION:** The Institute of Medicine (IOM) defines healthcare quality across six domains: safety, timeliness, effectiveness, patient centeredness, efficiency, and equitability. Traditional quality metrics in high-acuity surgery (volume and mortality) cannot alone measure or satisfy these domains. We asked experts in pancreatic surgery (PS) whether broader quality metrics are needed, how important they might be, and whether they align to contemporary IOM healthcare quality domains.

**METHODS:** Together with a professional market research firm, we created and distributed a web-based survey to pancreatic surgeons. These experts were identified through PS specialty societies, and verified by survey demographics. Respondents (Rpds) ranked 62 proposed PS quality metrics on level of importance (LoI). Next, Rpds aligned each metric to one or more IOM quality domains (MDA, multi-domain alignment). Descriptive statistics were used to summarize responses. To calculate and rank relative quality scores, points were awarded for LoI (4-Essential, 3-Very important, 2-Somewhat important, 1-A Little important, 0-Not important) and MDA (1 point/each aligned domain). LoI Scores and MDA Scores for a given quality metric were averaged together to render a Total Quality Score (TQS=LoI + MDA/2) normalized to a 100-point scale.

**RESULTS:** 106 surgeons (21%) completed the survey (82% North America and 84% Academic). On average, Rpds and their institutions perform 43 and 114 pancreatic operations per year, respectively. By descriptive analysis, 90% of Rpds indicated a definite or probable need for improved quality metrics in PS. 81% of Rpds indicated a definite or probable value for a “Quality Scorecard” in PS. Of 13 PS quality metrics rated as Essential by >25% Rpds, 10 aligned most strongly to the IOM Safety domain. 22/62 proposed metrics aligned to more than 1.75 IOM Domains, and were rated by >50% Rpds as High LoI (Essential or Very Important). 12 proposed scorecard metrics emerged with the highest TQS, with the highest score assigned to Multidisciplinary Services for Pancreatic Disease. Other high-scoring metrics included those related to mortality, to the rate and severity of complications, and to the rates of readmission. Technical and peri-operative metrics had intermediate TQS. Metrics related to patient satisfaction with care, costs of care, and patient demographics had the lowest TQS. The least represented IOM domains were equitability, efficiency, and patient-centeredness.

**CONCLUSIONS:** We propose a 12-item "Quality Scorecard" for PS based on rank-scoring of quality metrics that PS experts view as both highly important and aligned with more than one IOM healthcare quality domain. While the actual performance thresholds for these metrics require further definition and validation, they may reveal quality to an extent that volume and mortality alone cannot.
**43242 INTERFERONS IN PANCREATIC CANCER**

**Introduction**
Pancreatic cancer (PC) carries a very poor prognosis. Therefore, additional treatment is necessary to improve survival. The antiproliferative agent interferon (IFN) may afford additional effect in the currently used adjuvant therapies. Although several studies have been addressing adjuvant IFN-therapy in PC, it has never been investigated whether or not there is a clear rationale for those IFN-therapies.

**Methods**
We evaluated the anti-tumor activity of IFN-α and IFN-β in 12 human pancreatic adenocarcinoma cell-lines and assessed the correlation between the responsiveness to type-I IFNs and the expression of IFNAR-1 and IFNAR-2c receptors. Furthermore, we measured DNA-fragmentation to evaluate the effect of IFN-α and –β on apoptosis. In addition, we determined the expression of type-I IFN receptors in resected PC tissues by immunohistochemistry.

**Results**
After 7 days of incubation, IFN-α and –β suppressed the growth of most of the cell-lines in a time and dose-dependent manner. The mean maximal inhibitory effect of IFN-α was 25%, for IFN-β this was 75%. All cell-lines expressed IFNAR1 and IFNAR2c mRNA although with great variability, this was also observed at protein level. The expression of IFNAR2c mRNA correlated with the maximal inhibitory effect of IFN-α (r=0.85 p<0.01). At similar concentrations (1000IU/mL) IFN-α and -β were able to induce apoptosis, but the increase in DNA-fragmentation was significantly higher after IFN-β treatment. Both IFNAR-1 and IFNAR-2c receptors were demonstrated in the majority of paraffin embedded PC tissues, although expression levels varied.

**Conclusion**
IFNAR1 and IFNAR2c receptors are expressed in human PC tissue (figure 1).

![Figure 1. Interferon receptor expression in human pancreatic cancer tissue.](image)

IFN-β is a significantly stronger growth inhibitor in PC cell-lines than IFN-α and is more potent in inducing apoptosis. The expression of type-I IFN receptors can be of predictive value in the responsiveness to IFN treatment. Considering the fact that IFN-β induces already at low concentrations a stronger growth inhibitory effect, this agent seems more promising than IFN-α.
Background: Pancreaticoduodenectomy (PD) with pancreaticojejunal anastomosis to a normal pancreas with small duct reflects an increased risk for development of pancreatic fistula (PF) and overall morbidity, particularly in overweight patients. Pancreas-preserving duodenectomy (PPD) for pre- or low-malignant duodenal tumors, where pancreas is normal, could be a safer alternative to high-risk PD (HR-PD).

Aim: To compare the postoperative outcome after PPD and HR-PD.

Methods: All patients who underwent PPD and HR-PD in the same period at Karolinska University Hospital were retrieved from a prospective data registry. The demographics, length of stay (LOS), and postoperative morbidity and mortality were analyzed.

Results: Forty patients operated with HR-PD and 20 with PPD were identified. The patients in the PPD group were younger compared to the HR-PD group (50yrs vs 64.4yrs; p=0.0003). No differences in mean BMI was found comparing the two groups (25.32 vs 24.69; p=0.5). No differences were found in the overall morbidity rates and surgical related complication rate. However PPD patients showed less post-operative PF (15% vs 37.5%; p=0.08), fewer severe (Clavien grade ≥3b) complications (20% vs 30%), less ICU stay (5% vs 20%), less reoperation rate (15% vs 25%), lower mortality (0 vs 2.5%), and shorter post-operative stay (16.5 days vs 26.08 days), but the numbers were too small to reach statistical significance. PPD was performed with shorter operative time than HR-PD (296 min vs 422 min; p<0.0001) and with less intra-operative blood loss (521 ml vs 1027 ml; p=0.003).

Conclusions: PPD can be performed with shorter operative time, less intraoperative blood loss and with comparable, if not slightly better, postoperative outcome than HR-PD in this small series. Hence, PPD is the preferable surgical alternative for resection of pre- and low-malignant duodenal lesions.
Background: Human equilibrative nucleoside transporter 1 (hENT1) is the major transporter responsible for gemcitabine uptake into cells. Previous studies reported that intratumoral hENT1 expression was associated with an increased survival for patients receiving gemcitabine after pancreatic cancer (PC) surgery, suggesting that hENT1 is predictive of response to gemcitabine. Furthermore, we have already reported that intratumoral hENT1 expression in resected specimens was an independent strong prognostic factor as well as R0 resection in 55 PC patients treated with gemcitabine-based chemoradiotherapy (Gem-CRT) (HR, 95%CI: 3.15, 1.35–7.37, p=0.008). This study aimed to evaluate if hENT1 is available to predict the prognosis using endoscopic ultrasonography-guided fine-needle biopsy (EUS-FNB) samples before the initiation of Gem-CRT.

Methods: From February 2005 to July 2010, 93 PC patients who were proved histologically or cytologically had been enrolled for our Gem-CRT protocol (UICC-T3: 57, T4: 36). Of 55 patients described above, 23 (41.8%) were histologically diagnosed as pancreatic adenocarcinoma by EUS-FNB, the other patients were cytologically diagnosed by endoscopic ultrasonography-guided fine-needle aspiration (EUS-FNA) cytology or pancreatic juice cytology. The intratumoral hENT1 expression was analyzed immunohistochemically in the EUS-FNB samples, and scoring for hENT1 was on the basis of relative intensities of the cancer cells with reference to the normally present hENT1 staining of lymphocytes.

Results: Among the 23 tumors diagnosed by EUS-FNB, the hENT1 expression was positive in 16 patients (69.6%), and negative in 7 (30.4%). The hENT1 expression in EUS-FNB samples was identical in 87% (20/23) with that of resected specimens after Gem-CRT. 16 patients with positive hENT1 expression in EUS-FNB samples had significantly longer overall and recurrence free survival rates than 7 with negative hENT1 expression (2-yr OS and RFS rates: 67.5, 29.2 vs. 35.7, 0%).

Conclusions: Our data provides the evidence that intratumoral hENT1 expression in EUS-FNB samples is available to predict treatment outcome before the initiation of preoperative Gem-CRT. Although improvement of the rate of acquisition of specimen materials by EUS-FNB and further modification of the protocol for assay of hENT1 are needed, this biomarker is a potential predictive tool for outcome in pancreatic cancer patients treated with Gem-CRT before the initiation of treatment.
43246 SELECTIVE REOPERATION FOR LOCALLY RECURRENT OR METASTATIC PANCREATIC DUCTAL ADENOCARCINOMA FOLLOWING PRIMARY PANCREATIC RESECTION

Introduction: Resection of recurrent disease in malignancies such as colorectal cancer has been shown to prolong survival but resection for recurrent pancreatic ductal adenocarcinoma (PDAC) is viewed as futile. We sought to identify factors that may be associated with prolonged survival following resection of recurrent PDAC.

Methods: A retrospective review of a prospectively-maintained pancreatic tumor database identified all patients from 1992-2010 who developed recurrent PDAC after intended surgical cure. The group was screened for those who underwent a second operative procedure with curative intent. Clinicopathologic features were correlated with disease-free interval (DFI) and survival to identify factors that may be associated with prolonged survival in patients undergoing reoperation for PDAC.

Results: Of 700 patients who underwent resection for PDAC, 426 (61%) recurred after a median of 8mo and 21 (5%) of those had a locoregional [pancreas (n=5), other (n=2)] or distant [lung (n=7), liver (n=6), brain (n=1)] recurrence that were selected for a second, potentially curative operation. Those selected had a single, technically resectable lesion, good performance status, and prolonged median DFI compared to patients not selected (22mo v. 8mo, p<0.01). The median DFI from initial resection to recurrence for those with lung (52mo) or locoregional (41mo) recurrence was longer than those with liver recurrence (10.5mo, p=0.03; Figure 1). The median interval between reoperation and second recurrence in patients with lung metastasis (NR) was longer than for liver (6mo) or locoregional recurrence (7.5mo, p=0.02). Patients still alive include 4/7 of lung, 3/7 of locoregional, and 1/6 of liver recurrences with a median follow-up after reoperation of 30mo, 14mo, and 18.5mo, respectively.

Conclusions: Patients who develop a solitary recurrence of PDAC in the lung after a long DFI should be considered for reoperation. Those with recurrence in other sites are likely to re-recur relatively quickly after reoperation regardless of DFI.
Figure 1. Comparison of median DFI after resection of primary PDAC versus reoperation of recurrence based on anatomic location.

Recurrence Location

First DFI defined as time from resection of primary PDAC to first recurrence and Second DFI defined as time from reoperation to diagnosis of second recurrence. Second DFI in patients with resected lung recurrence reported as mean DFI since median has not been reached in this group (*)
Background: Pancreatic ductal adenocarcinoma carries a grave prognosis with the majority of patients presenting with locally advanced or metastatic disease. Patients diagnosed with early stage pancreatic cancer are often candidates for surgical resection and have improved overall 5 year survival. Doublecortin and CaM kinase-like-1 (DCAMKL-1), a microtubule-associated kinase, is a putative intestinal and pancreatic stem cell marker. We have previously demonstrated that DCAMKL-1 is upregulated in multiple cancers. The aims of this study are to determine the plasma expression level of DCAMKL-1 in pancreatic cancer patients by stage, and to measure the tissue expression level of DCAMKL-1 in this patient population.

Methods: Purified plasma samples from controls (n = 10) and stage I (n = 9), II (n=15), III (n = 14) and IV (n = 11) pancreatic cancer patients were subjected to Western blot and ELISA analysis. Surgical cancer specimens and normal pancreas (commercial tissue array) were immunostained for DCAMKL-1. An independent pathologist scored the immunohistochemical staining based on intensity and tissue involvement. Samples of tumor and adjacent normal tissue from pancreatic surgical specimens were homogenized. Real-time PCR was then performed to measure mRNA expression levels.

Results: We observed greater than a 2.5-fold increase in plasma DCAMKL-1 in patients with stage I pancreatic cancer compared to controls by Western blot analysis (p<0.05). We also observed increased DCAMKL-1 expression by ELISA: stage I (3.42-fold, p = 0.07); II (4.1-fold, p<0.05); III (2.06-fold, p>0.05) and IV (1.15-fold, p>0.05). There were similar DCAMKL-1 mRNA expression levels in both stage II and III tumor tissues (n = 8). Interestingly, we found that DCAMKL-1 mRNA levels in adjacent tissues are significantly higher than the respective tumor tissues. DCAMKL-1 mRNA levels were 7-fold higher in the adjacent tissues of stage II patients compared to the respective tumor tissues and approximately 2.7-fold higher in the adjacent tissues of stage III patients compared to the respective tumor tissues. Furthermore, we observed increased DCAMKL-1 immunostaining in all stages of cancer compared to controls. Although there were no significant differences between the stages, we observed increased stromal staining compared to the epithelium within the specimens.

Conclusion: These data suggest that DCAMKL-1 is increased in all stages of pancreatic cancer tissues. Additionally, the higher DCAMKL-1 level in the tissue adjacent to tumor may suggest a premalignant condition in this tissue. Furthermore, DCAMKL-1 is elevated in plasma of stage I and II patients, suggesting that it may potentially be used as a biomarker for the early detection of pancreatic cancer.
Introduction: Early enteral tube feeding reduces morbidity and mortality in patients with severe acute pancreatitis (AP) and is a standard of care. In contrast, patients with less severe disease are traditionally managed by nil-by-mouth (NBM) while they still have pain. And following the introduction of oral food, a proportion of patients have a relapse of pain and possible prolonged hospitalization. It is hypothesized that early enteral feeding in patients with mild and moderate AP would improve tolerance of subsequent oral refeeding, promote intestinal motility and reduce the incidence of ileus. The study aimed to compare the safety, tolerance and efficacy of early nasogastric tube feeding (NGF) versus NBM regimen in patients with mild and moderate AP.

Methods: A pilot randomized controlled trial in patients with mild and moderate AP was conducted between February 2010 and March 2011. The severity of AP was defined on the basis of determinants-based classification of severity. The patients in the intervention group were NBM until NGF was commenced within 24h of hospital admission and continued until the treating team decided to introduce oral food. The patients in the control group were kept NBM until the treating team decided to introduce oral food.

Results: There were 17 patients randomly allocated to NGF group and 18 to the NBM group. At baseline, the two groups did not have any significant differences in terms of demographic, anthropometric, and laboratory data. The visual analogue pain score decreased to a significantly greater extent in the NGF group (from median 9 (range 7–9) at baseline to 1 (0 - 3) at 72h after randomization) compared with the NBM group (from 7 (5 – 9) to 3 (1 - 4)) (p = 0.036). The number of patients not requiring opiates at 48 hours was significantly different (p=0.024) between NGF (9/17) and NBM (3/18). Oral feeding intolerance was observed in 1/17 patient in the ETF group and 9/18 patients in the NBM group (p = 0.004). Time from admission until tolerance of oral food was 5 (4-7) days in the NGF group and 7 (5-9) days in the NBM group (p = 0.162). Time from introduction of oral food until hospital discharge was 3 (1-6.5) days in the ETF group and 4 (2-7) days in the NBM group (p = 0.370). The total length of hospital stay in NGF group was 9 (5-12) days as compared with 8.5 (6-13) days in the NBM group (p = 0.91).

Conclusion: NGF commenced within 24h of hospital admission is safe and well tolerated in patients with mild and moderate acute pancreatitis. Further, when compared with NBM, it significantly reduces the intensity and duration of initial abdominal pain, need for opiates, and risk of oral refeeding intolerance.
BACKGROUND: The mesopancreas, which is a perineural lymphatic layer between the pancreas parenchyma and the superior mesenteric artery (SMA), is focused on because of the primary site for positive resection margins of the pancreas head adenocarcinoma. Although antegrade en bloc pancreaticoduodenectomy including mesopancreas is appropriate for invasive pancreatic head malignancies, this technique is not easy to perform because the end-point of deep vertical resections cannot be controlled.

METHODS: A tape for guidance was passed in a space behind the pancreatic parenchyma and above the SMA, followed by sagittal resection of the pancreas parenchyma with the splenic vein and dissection of the exposed anterior plexus above SMA. Another tape was passed behind the lateral plexus between the pancreas head and the roots of the celiac and SMA. Mesopancreas was dissected close to the SMA resulting in completion of total mesopancreatic excision.

RESULTS: This technique was applied in 11 patients with borderline resectable (n=10) and resectable (n=1) pancreas head cancer based on NCCN guideline 2010. Eight of them (72.7%) underwent chemoradiotherapy using gemcitabine before surgery. All cases were needed to undergo reconstruction of the portal vein. Two of them were needed to remove right colon because of tumor invasion to mesocolon. The mean duration of surgery and intraoperative blood loss were 544±57 min and 783±216 ml, respectively. There was no major morbidity and mortality in these patients. Pathological findings of the resected specimen revealed that the ratio of R0 resection was 91%. The median follow up time was 11 months (2-24) after surgery and 12.5 month (2-24) after initial treatment. All of them are alive without any recurrence.

CONCLUSIONS: Plexus hanging maneuver is an appropriate technique to obtain complete resection of mesopancreas, resulting in the increase R0 resection ratio for pancreatic head cancer.
Improved perioperative outcomes after resection of pancreatic cancer (PaCa) and advances in multimodal treatment might suggest the inclusion of patients with locally advanced or even limited metastasized PaCa as candidates for resectional surgery.

Methods: Since 1995 347 patients underwent resection for PaCa (79% PD, 14% distal, 7% total pancreatectomy) at our institution. 30% (n=103) of the operations were performed with additional portal/superior mesenteric vein resection (group PVRes), 14% (n=49) with resection of one or more further organ other than pancreas or vein (multivisceral resection; group OrganRes; in part with vein resection, splenectomy during distal pancreatectomy not considered), and 56% of the operations were terminated without vein or further organ resection (group LimRes). Perioperative (all 347 patients) and oncological outcome data (n=324) were compared by retrospective analysis of our prospective pancreatic database.

Results: The 3 groups did not differ significantly regarding age, grading, nodal disease (overall 67%) or margin status (positive margins 29%), but tumors in the LimRes group were smaller (p<0.001). Mortality was significantly higher in the OrganRes than in the LimRes or PVRes-groups (8.2% vs 5.1% / 0%; p=0.03). Patients with OrganRes had higher rates of any complication (68% vs 49% in LimRes/PVRes; p=0.02) and of surgical complications (48% vs33%; p=0.04). After OrganRes more patients required a relaparotomy (23% vs 8%; p<0.01). Actuarial 5-year survival (5-ys) was 18% in the entire group. In multivariate (Cox) survival analysis long term outcome was worse in patients with positive nodes (p<0.02; RR 1.5), positive margins (p<0.001; RR 1.7) and after pancreatic resection with OrganRes (p<0.01; RR 1.8). As compared to the group with LimRes, patients with additional PV-resection had comparable mortality, morbidity and survival rates.

Conclusion: In our series multivisceral resections of pancreatic cancer were associated with worse postoperative and long term outcomes. This poor long-term outcome did not directly correlate with node or margin positivity. Patients with PaCa probably requiring multivisceral resection, therefore, should be well selected and/or considered to undergo intensified multimodal treatment.
**43271 GRANULOCYTE MACROPHAGE COLONY STIMULATING FACTOR (GM-CSF) PANCREAS TUMOR VACCINE IN COMBINATION WITH BLOCKADE OF PD-1 IN A PRECLINICAL MODEL OF PANCREATIC CANCER**

**Introduction:**
Our phase I/II human clinical trials utilizing a GM-CSF secreting allogeneic pancreas tumor vaccine (GVAX) have been shown to be safe and effective in inducing anti-tumor immune response in pancreatic adenocarcinoma (PDA) patients. GVAX treated patients have demonstrated infiltration of PD-1+ T cells which is a major immunosuppressive mechanism in the tumor microenvironment. We hypothesized that the use of a PD-1 blocking antibody and GVAX will improve vaccine therapy and pancreatic cancer survival.

**Methods:**
Mice were orthotopically transplanted with $2 \times 10^6$ Panc02 pancreatic tumor cells to form liver metastases by a hemisplenectomy technique on day 0. Following tumor transplantation, wild-type or PD-1 knockout mice were treated subcutaneously with a mouse GM-CSF secreting pancreatic tumor vaccine (mouse GVAX) in combination with anti-PD-1 antibodies or IgG isotype control. GVAX was given subcutaneously to mice on days 4, 7, 14, and 21 following tumor transplantation, together with a single low-dose of Cytoxan on day 3. Anti-PD-1 antibodies or IgG were administered twice weekly starting post-operative day 3 (Figure 1).

**Results:**
PD-1 knockout mice challenged with pancreatic liver metastases had a significant survival advantage over wild-type mice ($p=0.0002$). Wild-type mice showed improved survival both with anti-PD-1 antibody alone ($p=0.008$) or in combination with vaccine ($p<0.0001$) versus IgG controls. GVAX in combination with anti-PD-1 antibodies versus anti-PD-1 antibodies alone shows a statistically significant improved survival ($p<0.05$) (Figure 1).

**Conclusions:**
PD-1 blockade through monoclonal antibodies or genetic knockout in combination with vaccine result in a synergistic anti-tumor effect in a preclinical model of pancreatic cancer versus treatment with PD1 alone. Anti-PD-1 blockade antibody is currently being tested in phase II clinical trials for treating chemotherapy-refractory solid tumor patients. Our study provides a strong rationale for combining PD-1 antibody with GVAX therapy for pancreatic cancer treatment.
Figure 1: PD-1 antibody, administered alone or given in combination with GVAX and cyclophosphamide leads to increased survival in mice challenged with Panc02 liver metastases.  
A) Kaplan Meier survival curve comparing survival of PD-1 alone, PD-1 given with cyclophosphamide and Panc02 GVAX compared with PD-1 & IgG isotype control.  
B) Experimental design for the administration of cyclophosphamide, GVAX given subcutaneously and PD-1 antibody or its isotype IgG control given twice weekly until death.
43274 CHANGING TRENDS OF SURGICAL MANAGEMENT FOR PANCREATIC DISEASE AT A SINGLE HIGH VOLUME INSTITUTION

Introduction:
Laparoscopic pancreatic surgery has been slow in gaining acceptance. Pancreatic resection is associated with 40% morbidity, the largest component being wound complications (18%) which can significantly delay recovery. We examine the changing trend towards minimally invasive pancreatic surgery at a high volume institution which has implications in the training of future pancreatic surgeons.

Methods:
This is a single institution retrospective review from a prospectively collected database from June of 2006 to December of 2011. Main outcome measures include operative time, length of hospital stay, lymph nodes resected, and tumor size.

Results
One hundred thirteen totally laparoscopic pancreatic resections were performed. Eighty-nine were laparoscopic distal pancreatectomies (LDP), 20 laparoscopic whipples (LW), 3 enucleations, and 1 central pancreatectomy. LDP mean operative time was 258 minutes. Average length of stay was 5.9 days, and 37% of the LDPs were spleen preserving. Mean tumor size was 2.3 cm and an average of 11.4 lymph nodes were harvested. LW mean operative time was 454 minutes, average length of stay was 11.7 days, and mean tumor size was 2.7 cm with an average of 19 lymph nodes harvested.

The number of laparoscopic pancreatic resections has progressively increased over this five-year period, from 3 cases in 2006 to 43 in 2011 (Figure 1). Pancreatic leak and delayed gastric emptying are lower with the laparoscopic technique but are not statistically significant. The average wound infection rate of 18% seen with open resections drops down to 2% in the laparoscopic approach (p<0.05).

Conclusion
Totally laparoscopic resections can be done safely while maintaining oncologic principals. Minimally invasive technique allows for an improvement in morbidity, primarily with wound infections. This has led to a shift at our institution with the progressive increase of laparoscopic resections from 2006-2011. Surgical training will need to evolve by making a concerted effort to emphasize advanced laparoscopic skills in the education of tomorrow’s pancreatic surgeon.
Laparoscopic Pancreatic Resections
Background: Fear of Cancer Recurrence (FCR) is well documented among survivors of breast, colon and prostate cancer. Incurable recurrence is common following resection of pancreatic and periampullary neoplasms. The incidence and significance of FCR in this population is unknown. We hypothesized that FCR represents an important source of psychosocial distress following resection of pancreatic neoplasms.

Methods: We conducted a cross-sectional study of patients with non-recurrent pancreatic ductal (PDAC), periampullary adenocarcinoma or pancreatic neuroendocrine tumor (PNET) treated with potentially curative surgery 1991–2011. We assessed 7 discrete dimensions of FCR using the Fear of Recurrence Inventory (FCRI) and evaluated quality of life (QOL) and psychosocial distress using the Functional Assessment of Cancer Therapy-Hepatobiliary Questionnaire and Hospital Anxiety and Depression Scale. Participants completed these validated instruments by mail.

Results: 188 (53%) of 355 eligible patients completed at least one instrument, a median of 49 months (range, 6–222 months) following potentially curative resection. Participants included 73 (39%) patients with PDAC, 55 (29%) with periampullary adenocarcinoma, and 60 (32%) with PNET. The median FCR severity score was higher than a previously established cutoff for clinical significance in 55%, 51% and 63% of patients with PDAC, periampullary adenocarcinoma and PNET, respectively. Older age, male gender, periampullary adenocarcinoma, negative lymph nodes, and longer interval since operation were clinical factors associated with lower total FCR score (all p<0.05). In multivariate analysis, only age (p=0.01) and gender (p=0.03) were independently associated with severity of FCR. A higher total FCR score was significantly associated with higher anxiety (r=0.64), depression (r=0.41) and lower QOL (r =-0.53), all p<0.001.

Conclusion: Fear of cancer recurrence is pervasive following resection of pancreatic neoplasms, regardless of survivors’ histopathologic diagnosis, disease severity, or time since resection. Given its association with anxiety, depression and lower QOL, FCR represents a critical therapeutic target.
43276 DIAGNOSIS OF INFECTED PANCREATIC FISTULA AFTER DISTAL PANCREATECTOMY: SIGNIFICANCE OF CT ATTENUATION VALUE OF FLUID COLLECTION SITE

Introduction: Although pancreatic fistular (PF) is the most common complication after distal pancreatectomy, it is very important to diagnose whether PF is infected or not when we decide to perform interventional treatment such as percutaneous drainage. However, there is no concurrent consensus to diagnose infected PF. Therefore, the present study was performed to clarify that CT attenuation value of the fluid collection site can predict infected PF.

Patients and methods: The studied subjects were the 76 consecutive patients who underwent distal pancreatectomy from January 2005 to July 2012, at our institution. PF was defined and graded (grade A/B/C) based on the criteria of the International Study Group on Pancreatic Fistulas (ISGPF). In this study, postoperative complications were graded according to Clavian classification (Grade I to V). We assessed drain amylase levels (D-amy), inflammatory reaction including body temperature, white blood counts (WBC) and C-reactive protein (CRP), and CT attenuation value (HU) of the fluid collection site post operative day (POD).

Results: In the 76 patients, the relationship between Clavian classification and PF grade was found as follows: 40 (52.7%) including 6 (7.9%) with Grade A had Grade I complications (median hospital stay: 18 days), 25 (32.9%) including 13 (17.1%) with Grade B/C developed Grade II complications (median hospital stay: 36 days), 9 (11.8%) including 8 (10.5%) with Grade B/C developed Grade IIIa complications, requiring radiological intervention to drainage fluid collection (median hospital stay: 57 days), and the remaining 2 was one of Grade ? and the other of Grade V. In the 9 patients with Grade ?a complications, the diagnosis of fluid collection based on amylase level and bacterial culture of drainage fluid was infected PF in 4, non-infected PF in 4, and abscess in 1. Comparing CT attenuation values of the fluid collection site before drainage, 3 (75%) of the 4 patients with infected PF showed more than 25 HU, while all 4 patients with non-infected PF showed less than 25 HU. In the 13 patients with Grade B PF who did not require drainage procedure, 11 (74.6%) had CT values of less than 25 HU. There was the tendency of negative correlation between the fluid volume and CT value. No significant differences in inflammatory reactions on POD 6 and 13 were not detected between Grades ? and ? complications.

Conclusion: It is suggested that CT attenuation value of the fluid collection help to determine the necessity of drainage procedure and to discriminate between infected PF and non-infected PF.
43277 CONTINUOUS GLUCOSE MONITORING (CGM)- A NEW TOOL FOR EVALUATION OF β-CELL FUNCTION IN CLINICAL ISLET AUTOTRANSPLANTATION

Objective: Total pancreatectomy (TP) and clinical islet autotransplantation (IAT) should be considered prior to exhaustion of β-cell mass in patients with unremitting pain of severe chronic pancreatitis (CP). We compared hemoglobin A1C (HbA1C) and continuous glucose monitoring (CGM) values as indicators of islet β-cell function in patients evaluated for pancreatectomy with or without clinical islet autotransplantation.

Methods: Measurements on patients and normal controls using CGM and HbA1C were correlated. CGM measurements used were percentage of time being above normal upper limit of glucose (> 120 mg/dl), below normal lower limit (< 65 mg/dl) and associated areas, in addition with the average glucose level. A stepwise nonparametric discriminant analysis was applied to identify factors which distinguish the control group from the CP patients.

Results: Data was available for 32 patients with CP; 12 were male and 20 females. Additionally, CGM data were available for 8 controls. The HbA1C was below 6.5% in 24/32 (75%) of the CP patients (median 5.6%, range 4.7% - 13.0%) and in all controls (median 5.3%, range 5.3% - 5.6%). Very few hypoglycemic episodes were noted in the CP patients. The discriminant analysis only identified the relative duration above 120 mg/dL out of all the different CGM measurements as significant between controls and CP patients. HbA1C was no discriminator. All controls were classified as normal (100%) and 94% of CP patients as belonging to the CP group. 22 out of 24 CP patients with normal HbA1c were classified as abnormal (92%). Figure 1 shows the distribution between relative duration above 120 mg/dL and HbA1c for both groups.

Conclusion: CGM should be implemented as an evaluating tool for patients suffering from intractable pain of CP and being considered for TP/IAT to evaluate β-cell mass and function. HbA1C alone is a poor predictor of remaining β-cell mass in this patient population.
Postoperative hemorrhage is a serious complication and one of the most common causes of mortality after pancreaticoduodenectomy. We report two cases of post-pancreaticoduodenectomy hemorrhage treated by transcatheter arterial embolization (TAE). The first patient was a 66-year-old man with middle bile duct cancer. He underwent pylorus-preserving pancreaticoduodenectomy. We observed hemorrhage from a drain 12 days after surgery. He underwent emergency angiography. The angiogram demonstrated that the site of hemorrhage was located in jejunal artery. TAE was performed, and complete hemostasis was obtained. The second patient was a 74-year-old man with duodenal cancer. He underwent pylorus-preserving pancreaticoduodenectomy. We observed hemorrhage from a drain 15 days after surgery. He underwent emergency angiography. The angiogram demonstrated that the site of hemorrhage was located in right gastric artery. TAE was performed, and complete hemostasis was obtained. Their post-TAE course was uneventful. TAE is a useful method for postoperative hemorrhage after pancreaticoduodenectomy.
Introduction/Background
Pancreatoduodenectomy (PD) is the only potentially curative treatment for patients affected by periampullary cancer. Resection margin involvement (R1) after PD ranges from 14% to 75% and it has been demonstrated to significantly affect survival. It has been recently supposed that the reason of this difference is the lack of consensus on the method used to manage the specimen. The results of recent studies indicate that the use of a new technique to manage the specimen determines a significant increase of R1 resection rate up to 75%. We report the results of a case control study that evaluated the impact of this new technique in a series of 25 patients undergoing PD for cancer.

Material and Methods
From October 2004 through October 2010 at our Institution surgical specimens after PD were analyzed by the pathologist according to international approved guidelines (Rosai and Ackerman’s – Surgical Pathology ninth edition (2004) 2953-2954). From November 2010 this method was replaced by a different technique (Verbeke CS et Al. in Br. J. Surg. 2006; 93; 1232–1237) that included:
1) introduction of the concept of “circumferential margins”
2) multicolour inking of six margins:
   a. pancreatic transection margin
   b. biliary transection margin
   c. anterior surface of the pancreatic head
   d. posterior surface of the pancreatic head
   e. bed of the superior mesenteric vein
   f. bed of the superior mesenteric artery
3) axial slicing of the specimen
4) the following definition of R0 resection: tumor at a distance of at least 1 mm from the margin
From November 2010 through November 2011 we utilized the new method to manage 25 consecutive specimens after PD.
In order to analyze the results of the new method we planned a case control study focusing the following parameters.
1) Rate of R1 resections
2) Average number of examined blocks
3) Average number of examined lymphnodes
4) Lymphnodal status

Results
Statistical analysis of the two groups of patients showed no significant epidemiological, pathological and clinical difference.
1) The rate of R1 resections was: 72% (new method) and 16% (control group) (p<0.0001)
2) The average number of examined blocks was 56 (new method) and 25 (control group) (p<0.005)
3) The mean number of examined lymphnodes was 35 (new method) and 10 (control group) (p<0.005)
4) Metastatic lymphnodes were found in 92% (new method) and in 56% (control group) (p<0.001)

Discussion
Our results confirmed that the new method allows a statistically significant increase of R1 resections if compared with the results obtained with the conventional method. This evidence confirms recently published data showing that “conventional technique” underestimate the rate of R1 resections. As a consequence, we can assume that R0 resection for periampullary cancer is performed only in a minority of cases. If confirmed, this evidence will impact clinical management of pancreatic cancer.
**43285 KRAS MUTATION ANALYSIS IN ATYPICAL/INDEFINITE ENDOSCOPIC ULTRASOUND FINE NEEDLE ASPIRATION OF Pancreatic SOLID LESIONS**

**Introduction**

Endoscopic Ultrasound-guided Fine Needle Aspiration (EUS-FNA) is a safe and effective technique in the diagnosis of pancreatic solid lesions with high rate of sensitivity and specificity. However, differential diagnosis between pancreatic ductal adenocarcinoma (PDCA) and pseudotumoral forms of chronic pancreatitis remains difficult, frequently resulting in an atypical/indefinite cytopathological diagnosis at FNA examination. According to the data from the literature, an atypical/indefinite diagnosis after EUS-FNA of solid pancreatic lesions is done in approximately 25% of cases. KRAS gene mutations have been found in 75-90% of infiltrating PDCA and such a frequency seems sufficiently high to deserve diagnostic application. However the relevance of these data is severely hampered by the fact that KRAS mutations have been reported also in non-neoplastic pancreatic diseases such as chronic pancreatitis. Aim of the present study was to investigate the feasibility and reproducibility of combined cytopathological examination and KRAS analysis in improving the diagnostic accuracy on atypical/indefinite pancreatic FNA samples.

**Material and Methods**

From January 2009 through November 2011, 155 consecutive patients with solid pancreatic lesions underwent EUS-FNA at our Institution. In 29 cases (18.7%) an atypical/indefinite cytopathological diagnosis was done. The clinical follow-up showed that 23 patients (79.3%) were affected by an histologically documented PDAC, while chronic pancreatitis was the final diagnosis in 6 (20.7%). As controls, KRAS mutation analysis was also performed in histological samples from patients with chronic pancreatitis (n = 10) and pancreatic adenocarcinoma (n = 10). Moreover, in the latter group, mutation analysis was performed also in areas of chronic pancreatitis collected at a distance from the tumour.

**Results**

The preliminary analysis in the Control Group showed highly significant different (p<0.0001) KRAS expression of PDAC vs. non-PDAC tissues. This analysis also showed the following results:

1) all tumor samples were mutated, with an allele frequency of mutation ranging from 7% to 36% (median 27.2%; IQR 14.7-30.9%).

2) allele frequency of mutation in pancreatitis samples ranged from 0% to 5% (median 0.65%; IQR 0.07%-1.9%), and in pancreatitis associated with carcinoma from 2% to 4.5% (median 3.45%; IQR 2.9%-4.0%).

On this basis, 6% of allele frequency of KRAS mutation was defined as an adequate cut-off to distinguish neoplastic from non-neoplastic lesions.

The KRAS mutation analysis of the 29 FNA cases with atypical/indefinite cytopathological diagnosis showed:

1) KRAS mutation rate was constantly <6% (median 1.45%; IQR 0.3-2.9%) in all patients with a final diagnosis of chronic pancreatitis.

2) In patients with final diagnosis of PDCA the mutation rate ranged between 0 to 38.7% (median 6.8%; IQR 2.3-23.4%).

3) 13/23 (56%) patients with final diagnosis of PDCA the mutation rate was >6% (median 22.6%; IQR 13.4-25.4%).

**Conclusion**
Our preliminary data suggest that in case of atypical/indefinite diagnosis on EUS-FNA of pancreatic solid lesions, KRAS mutation analysis may be useful in strongly suggesting a diagnosis of PDCA.
43286 FAILURE TO RECEIVE ADJUVANT THERAPY FOLLOWING RESECTION FOR PANCREATIC CANCER: PATTERNS AND IMPLICATIONS

Introduction: Although adjuvant therapy optimizes the prognosis for resected pancreatic ductal adenocarcinoma (PDAC), literature indicates that this approach is not consistently applied. We sought to identify the frequency, reasons, and predictors of unutilized post-operative adjuvant therapy in a multidisciplinary, specialty setting.

Methods: A database containing PDAC resections performed at two institutions over a decade (2001-2011) was studied. Eligible patients who did not undergo adjuvant therapy were identified and categorized based on the rationale for not receiving treatment. Demographics, perioperative features, tumor characteristics, and surgical risk scores were analyzed by univariate and multivariate methods.

Results: Of 413 resected PDAC patients 336 (81%) received postoperative treatment, while 53 (including 90d mortalities, N=7) did not. Treated patients had median, 1- and 5-year survivals of 23.7m, 81% & 26%, compared to 9.4m, 43% & 22% in the Untreated group (p<.001). Twenty-four patients with unknown treatment status exhibited equivalent survival to the treated cohort (19.3m; p=.290). Characteristics of the Untreated cohort were advanced age, complications, lack of jaundice, and IPMN. Four reasons for unutilized therapy were identified (Table). These segregated into two disparate groups – Poor Clinical Outcomes (≈2/3rds) and Therapy Not Elected (≈1/3rd), which demonstrated a marked median survival difference (6.0m vs. 62.6m respectively; p<0.001). The Therapy Not Elected group was characterized by favorable tumor biology. The Poor Clinical Outcome group contained two-thirds of all Major complications (Clavien 3b-5) in this series. The factors associated with this group by multivariate analysis were older age and COPD, and this cohort could not be discriminated by preoperative risk scoring systems.

Conclusions: This series demonstrates that the vast majority of PDAC patients can receive post-operative adjuvant therapy. There are various reasons for non-utilization, not all of which represent inadequate care. Pre-operative prediction of patients with poor outcomes that prevent adjuvant treatment, using current risk assessment models, remains elusive.
EXTENDING THE CRITERIA FOR SURGERY ON UNRESECTABLE PANCREATIC CANCER

Introduction: Resection criteria for pancreatic malignancies have gradually expanded in the past three decades, to the point where vascular resection, multivisceral resection and even total pancreatectomy are considered selectively acceptable. However, locally advanced tumors and metastatic disease are still widely considered as contraindications. In this study, we assess the perioperative outcomes and ultimate survival of patients who received resection despite these indications of advanced disease.

Methods: A database containing 424 resections performed for pancreatic ductal adenocarcinoma at two institutions over a decade (2001-2011) was studied. Twenty patients were identified with advanced disease: locally advanced tumors (LA; n=9), metastases (M1; n=10), or both (n=1). LA patients, initially with inoperable vascular involvement, were resected if there was demonstrable tumor response to preoperative downstaging chemoradiation therapy. All M1 disease was unsuspectedly discovered at laparotomy, indicative of limited tumor burden. Kaplan Meier survival analysis and descriptive statistics were employed using physiologic, operative, postoperative, and tumor features to compare these advanced disease resections to all others.

Results: Advanced disease patients had no 90d mortalities and demonstrated similar survival compared to all others (17.8m v 22.1m; p=0.15). M1 patients had features of less demanding operations (short OR times, limited EBL, no vascular resection), no major complications, and survived 17.8m (3.8 - 47.6m). Hepatic/omental disease fared better than peritoneal spread. LA patients survived 16.6m post-resection, but 28.1m from diagnosis. Despite only one vein resection, they had higher EBL (1350mL v 400mL, p<0.001), more transfusions, and more major complications (30%). Final pathology revealed 10% N1, 60% R1, and 90% T3, with only one complete response. There was no survival segregation based on margins or tumor grade, nor were there any 5-yr survivors.

Conclusion: These data suggest selected resection of pancreatic cancer with advanced locoregional disease (Metastatic disease with low burden, hepatic/omental sites, and decreased operative complexity; Downstaged locally advanced tumors) can be performed safely and may contribute to real survival gains compared with historical cohorts of unresectable locally advanced and metastatic disease.
Purpose: To review treatment toxicity for patients with pancreatic and ampullary cancers treated with oral capecitabine and proton therapy at our institution.

Materials and Methods: From March 2009 through December 2011, 20 patients were treated with proton therapy and concomitant capecitabine (1000mg PO twice daily) for resected (N=5); marginally resectable (N=5); and unresectable (N=10) biopsy-proven pancreatic (19) or ampullary (1) adenocarcinoma. Two patients were excluded from the analysis for reasons unrelated to treatment. Proton doses ranged from 50.40 cobalt gray equivalent (CGE) to 59.40 CGE.

Results: Median follow-up for surviving patients was 10 months. No patient demonstrated any grade 3 toxicity during treatment or during the follow-up period. 3 patients experienced acute grade 2 gastrointestinal (GI) toxicity during treatment although no patient treated with a plan that avoided anterior and left lateral fields (associated with reduced small bowel and gastric exposure) experienced grade 2 GI toxicity. Average weight loss during treatment was 3.92 lbs (range: loss of 21.2 lbs to gain of 14.1 lbs) for all patients but only 1.87 lbs (range: loss of 11.0 lbs to gain of 14.1 lbs) for patients treated without anterior and left lateral fields.

Conclusion: Proton therapy which avoids the use of anterior and left lateral fields allows for significant sparing of the small bowel and stomach and is associated with virtual elimination of radiation related gastrointestinal toxicity. Although long-term follow-up will be needed to assess efficacy, we believe that protons may allow for radiotherapy dose escalation, chemotherapy intensification and possibly increased utilization of preoperative neoadjuvant radiotherapy.
THE POOR SURVIVAL OF RESECTED EARLY STAGE PANCREATIC ADENOCARCINOMA IS CONSISTENT WITH THE GENETIC EVOLUTION OF THE DISEASE.

BACKGROUND: The poor prognosis of pancreatic adenocarcinoma (PA) is in part due to advanced stage at diagnosis. Recent genetic work demonstrates that the metastatic potential of PA develops around 10 years from the time of tumor initiation. Based on this finding it would appear that even early clinical stage PA is diagnosed beyond the time of the development of metastatic potential. In order to test this theory, we compared the clinicopathologic characteristics and outcome of resected “early state” PA to that of later stages.

METHODS: Among 2,034 patients with pathologically proven typical PA who underwent pancreatectomy with curative intent between 1970 and 2011, 1,580 patients whose pathologic data are available were selected in this study. Clinicopathologic data of T1 patients (n=79) were compared with those of T2-4 patients (n=1,501), and survival outcome of T1 patients was analyzed.

RESULTS: In comparison with T2-4 patients, T1 patients were significantly associated with lower incidence of jaundice (T1 vs. T2-4: 35.4% vs 50.6%), poor tumor differentiation (19.7% vs. 43.2%), lymph node metastasis (22.8% vs. 78.7%), vascular invasion (24.0% vs 58.7%), perineural invasion (57.9% vs 91.8%) and positive resection margin (6.3% vs.26.6%), and lower CA 19-9 level (48.1% vs. 19.3%). The 5-year survival rate of T1 patients was 28.5%, which showed a significant difference compared to that of T3 (13.5%) and T4 (15.8%) patients, but was not significantly different from that of T2 (27.8%) patients (p=0.159). On univariate analyses for survival of T1 patients, history of neoadjuvant therapy, tumor grade, and resection margin status were significant prognostic factors. On multivariate analysis, only a positive resection margin was associated with worse survival (HR=4.000, p=0.038).

CONCLUSIONS: Despite the relatively good prognostic clinicopathological features of resected T1 PA, the overall survival for this stage is poor. Moreover, difference among the various T-stages, although statistically significant, is modest on a practical level. These finding support the theory that all clinical stages of resected PA exist late in the genetic evolution of this disease. The application of T-stage in its current form may not be applicable in PA like cancers originating from other organs.
43292 THE USE OF THE GOAL DIRECTED THERAPY IMPROVES CLINICAL OUTCOME AFTER PANCREATIC SURGERY

Introduction
Peri-operative fluid management is a relevant matter of concern in patients undergoing pancreatic surgery. It has been shown that Goal-Directed fluid Therapy (GDT) guides fluids infusion and determines the preservation of oxygen delivery with improvement of clinical outcomes. The FloTrac/Vigileo is a minimally invasive monitoring system used to perform the GDT. Balanced, plasma adapted solutions reduce hyperchloremic acidosis, with normal Base Excess (BE) and influence patients’ outcome. The present case control study evaluated the preliminary results of a prospective protocol including GDT and infusion of balanced plasma adapted solutions.

Materials and Methods
From April 2011 through November 2011 12 patients undergoing pancreatic surgery were enrolled at our Institution in a prospective protocol of intraoperative management that included:
1) Introduction of the concept of GDT
2) The use of FloTrac/Vigileo
3) The use of balanced plasma adapted solutions
To analyse ongoing results of the protocol we realized a case control analysis with a group of patients managed from January 2010 through March 2011 with a standardized strategy not including GDT. The analysis focused:
1) Acid-base data
2) Electrolytes values
3) Amount of infusion
All the parameters were systematically evaluated 2 hours after surgery was started (T1), at the end of operation (T2) and 4 hours after surgery was ended (T3). Perioperative morbidity was also investigated. The local Ethics Committee approved the study.

Results
1) Acid-base: at T2 and T3 time pH and Chloride values resulted in the physiologic range in a significantly higher number of cases in the GDT group if compared with control group (p value always < 0,05)
2) Electrolytes values: at T1, T2 and T3 BE and Calcium values resulted in the physiologic range in a significantly higher number of cases in the GDT group if compared with control group (p value always < 0,05)
3) Amount of infusion resulted significantly (p<0,05) lower in the GDT group
4) Perioperative morbidity: GDT: 42,2%; control group: 65,2% (p: n.s.)

Discussion/Conclusion
It is well established that hyperchloremia causes metabolic acidosis, splanchnic and renal vasoconstriction. Balanced plasma adapted solutions helps to avoid hyperchloremic acidosis and reduces BE amount. Both over- and under-hydration can result in adverse outcomes. Fluids overload causes splanchnic edema and reduces mesenteric blood flow possibly favouring anastomotic leak. Fluids restriction can result in decreasing
venous return and cardiac output with reducing tissue perfusion. In our experience the use of GDT let to steadily maintain normal pH, Chloride and BE values and prevented hyper- and hypo-volemia. It can be supposed that GDT also allows a relevant increase of tissue perfusion of perianastomotic tissues. This data is supported by our results that showed a significant reduction of intraoperative infused liquids in the GDT group. Finally, based on our preliminary results we can hypothesize that GDT is able to improve clinical outcome.
43296 PREDICTORS AND EFFECT OF BLOOD TRANSFUSION ON MORBIDITY FOLLOWING PANCREATICODUODENECTOMY

Background: While mortality rates have improved, morbidity remains high after pancreaticoduodenectomy (PD). Few have examined the factors associated with increased rates of transfusions and what effects this may have on complications.

Aim: To determine predictors and effects of blood transfusions in patients undergoing PD.

Methods: Patients undergoing PD by a single surgeon from 2005-2010 were retrospectively reviewed and scored using the Charlson co-morbidity index and the Clavien classification of surgical complications. Univariate and Multivariate analyses were performed.

Results: 332 consecutive patients (52% female, mean age 62 years) underwent PD for both malignant (57%) and benign disease. Median length of stay was 8 days and overall morbidity and mortality rates were 65.9% and 2%, respectively. Mean estimated blood loss (EBL) was 340 mL and the intraoperative transfusion rate was 9%. Through multivariate analysis, the strongest predictor of morbidity (Clavien 1 – 5) was transfusion (OR = 5.6, 95% CI 1.3 – 25.0, p < 0.02). Predictors of transfusion were age > 65 (14.2% v. 4.9%, p < 0.01), malignancy (12.6% v. 4.2%, p < 0.01), EBL > 400 mL (17.4% v. 6.1%, p < 0.01), hemoglobin < 11g/dL (23.2% v. 6%, p < 0.01), and Charlson > 5 (11.7% v. 5.2%, p < 0.04). Those undergoing transfusion were more likely to experience any morbidity (93% v. 63.2%, p < 0.01) with the most common being pneumonia (16.7% v. 3.0%, p < 0.01) and ileus (10% v. 2.6%, p = 0.03). Hemoglobin < 11 g/dL (OR = 3.29, 95% CI 1.4 – 7.8, p = 0.01), EBL > 400 mL (OR = 3.27, 95% CI 1.4 – 7.6, p < 0.01), and Age > 65 (OR 3.26, 95% CI 1.3 – 8.4, p < 0.01) were independent predictors of transfusion through multivariate analysis.

Conclusion: Pancreaticoduodenectomy is done safely although the majority of patients will undergo morbidity. In our series, blood transfusion is the strongest independent predictor of complications after PD. Preoperative anemia, advanced age and high intraoperative blood loss are independent predictors of the need for transfusion. These factors should be assessed and followed to help reduce and predict morbidity after PD.
Obesity correlates with morbidity after gastrointestinal operations and more specifically pancreaticoduodenectomy (PD). A Hounsfield Unit (HU), routinely applied to computed tomography (CT), measures tissue density. The purpose is to determine whether lower HU score, which refers to less dense tissue and a higher degree of steatosis, predicts complications.

Methods: Patients undergoing PD from 2005-2010 were analyzed according to the Clavien complication and the International Study Group on Pancreatic Fistula (PF) classification systems. Noncontrast CT HU of normal tissue from representative sample of patients were measured by a blinded assessor. Univariate and multivariate analyses were performed.

Results: Three hundred thirty-three patients underwent PD for malignant (57%) and benign disease. Mean blood loss (EBL) was 340mL, 19% underwent a transfusion, and median stay was 8 days. Overall complication and PF rate was 66% and 20%, respectively. Patients with BMI>25 had a higher rate of PF (32%, p<0.01) as well as any complication (73%, p<0.01). Patients were more likely to develop any complication as HU decrease for pancreas (p=0.04), muscle (p<0.01), spleen (p<0.01), and liver (p<0.01). Multivariate analysis of CT measurements for muscle (p=0.02), liver (p=0.04), and spleen (p<0.05) remained independent predictors of complications when adjusting for BMI, age, gender, EBL, and transfusion (Table 1).

Conclusion: Post-operative complications remain prevalent and imaging characteristics are independent predictors of morbidity after PD. A higher degree of steatosis of tissues correlates with complications and surgeons should consider CT characteristics as adjunctive predictors along with patient factors when discussing morbidity with patients regarding PD.

<table>
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</tr>
<tr>
<td>Overall</td>
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</tr>
<tr>
<td>CT</td>
<td>(noncontrast HU mean)</td>
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<tr>
<td>Spleen</td>
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<td>Muscle</td>
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</tr>
<tr>
<td>Liver</td>
<td>50.0</td>
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</tr>
<tr>
<td>-----------------------</td>
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<td></td>
<td>19%</td>
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<td></td>
<td>0.40</td>
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<td>67%</td>
</tr>
<tr>
<td></td>
<td>33%</td>
</tr>
<tr>
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<td>&lt;0.01</td>
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<tr>
<td>BMI &gt; 25</td>
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</tr>
<tr>
<td></td>
<td>62%</td>
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<td></td>
<td>0.01</td>
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<tr>
<td>EBL &gt; 250 mL</td>
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<td>15%</td>
</tr>
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**43298 SPLENIC VEIN THROMBOSIS IS ASSOCIATED WITH INCREASED PANCREAS SPECIFIC COMPLICATIONS AND REDUCED SURVIVAL IN PATIENTS UNDERGOING DISTAL PANCREATECTOMY FOR PANCREATIC DUCTAL ADENOCARCINOMA**

**Introduction:** Distal pancreatectomy and splenectomy (DPS) is the procedure of choice for the surgical treatment of pancreatic ductal adenocarcinoma (PDA) localized to the pancreas body and tail. Due to a lack of early symptoms, patients with distal pancreatic lesions can present at advanced disease stages, occasionally with direct tumor invasion or peri-tumoral inflammation leading to splenic vein thrombosis (SVT). Little is known regarding the implications of SVT in patients with PDA. This study documents our institution’s experience with SVT in these patients.

**Methods:** In this retrospective cohort study, we queried our pancreatic surgery database to identify patients who underwent DPS for PDA from 2005-2011. These cases were evaluated for preoperative SVT through clinical records and imaging studies. Perioperative outcomes for patients with and without SVT were compared.

**Results:** A total of 284 DPS were performed during the study period. Of these, 70 were for patients with PDA, 27 (39%) who had preoperative SVT and 43 (61%) who did not. The median estimated blood loss was significantly higher in the SVT group versus the non-SVT group (675mL vs. 250mL, p<0.001). The group with SVT also had significantly higher rates of pancreas specific complications, such as pancreatic fistula (33% vs 7%, p<0.01) and delayed gastric emptying (15% vs 0%, p<0.05). The T3 tumor stage (67% vs 56%, p=NS), median postoperative length of stay (6 days), and readmission rates (30% vs 28%, p=NS) were similar between groups. Neither group had a perioperative mortality, however, one-year survival for patients with SVT was reduced compared to the non-SVT group (52% vs 76%, p = 0.08), a difference that approached statistical significance.

**Conclusions:** DPS for PDA can be performed safely in patients with preoperative SVT, but our findings reveal higher rates of intraoperative blood loss, pancreatectomy-specific complications, and lower long-term survival rates.
<table>
<thead>
<tr>
<th>Table:</th>
<th>Total n (%)</th>
<th>SVT n (%)</th>
<th>without SVT n (%)</th>
<th>p-value</th>
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<td></td>
</tr>
<tr>
<td>Age (years)</td>
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<td>63</td>
<td>68</td>
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<tr>
<td>Male</td>
<td>42 (60%)</td>
<td>18 (67%)</td>
<td>24 (36%)</td>
<td>NS</td>
</tr>
<tr>
<td>BMI</td>
<td>26.1</td>
<td>24.5</td>
<td>26.9</td>
<td>NS</td>
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<td>DM</td>
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<td>7 (26%)</td>
<td>13 (30%)</td>
<td>NS</td>
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<td>13 (48%)</td>
<td>24 (56%)</td>
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<tr>
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<td>2 (7%)</td>
<td>2 (5%)</td>
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<td>Cardiac</td>
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<td>1 (4%)</td>
<td>5 (12%)</td>
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<td>4 (15%)</td>
<td>1 (2%)</td>
<td>NS</td>
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<td>7 (16%)</td>
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<td>C. diff. colitis</td>
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<td>2 (5%)</td>
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<td>DVT/PE</td>
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<td>1 (2%)</td>
<td>NS</td>
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<tr>
<td>Pulmonary</td>
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<td>1 (4%)</td>
<td>5 (12%)</td>
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<td>6</td>
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<td><strong>Pathology</strong></td>
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<td>T3 Stage</td>
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<td>24 (56%)</td>
<td>NS</td>
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<td>14 (52%)</td>
<td>24 (56%)</td>
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<td><strong>Readmission</strong></td>
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<td>12 (28%)</td>
<td>NS</td>
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<tr>
<td><strong>1-year Overall Survival</strong></td>
<td>36 (67%)</td>
<td>11 (52%)</td>
<td>25 (76%)</td>
<td>NS</td>
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</table>

**Note:** EBL = Estimated Blood Loss, SVT = Stress Vascular Thrombosis, P. fistula = Pseudomonas fistula, UTI = urinary tract infection, DGE = delayed gastric emptying, C. diff. colitis = Clostridium difficile colitis, DVT/PE = Deep Venous Thrombosis/pulmonary embolism.

**Note:** Tobacco use data not available for 2 patients, BMI data not available for 4 patients. Total numbers for these variables exclude these patients. **Number of patients with one or more complications. **Only includes patients with date of surgery from 10/2005-5/2011. All values represent median.
43302 RARE BENIGN CYSTIC LESIONS OF THE PANCREAS MIMICKING PREMALIGNANT NEOPLASTIC CYSTS

Introduction: Given the increased use of cross-sectional radiologic imaging in recent years, pancreatic cysts are being diagnosed with greater frequency. Most neoplastic lesions are either intraductal papillary mucinous neoplasms (IPMNs) or mucinous cystic neoplasms (MCNs). Pseudocysts make up the majority of benign cystic lesions, though there are also rare, benign cystic lesions of the pancreas that can mimic neoplastic cysts. This study’s objective was to review our institution’s experience with these rare cysts.

Methods: We conducted a retrospective analysis of all patients who underwent surgical resection for pancreatic lesions from 2005-2011 at our institution. From 947 total resections, we isolated cases performed for benign cystic disease and examined clinicopathological data on these patients.

Results: Of the 170 operations performed for cystic disease, 13 (1.5%) were for non-neoplastic cystic lesions of the pancreas (9 distal pancreatectomies, 4 pylorus-preserving pancreaticoduodenectomies). Preoperative imaging revealed primary lesions in all patients, with 6 found incidentally. Imaging suggested 11 lesions were consistent with mucinous neoplasms and 2 with pancreatic adenocarcinoma. However, postoperative pathology revealed benign findings, detailed in Table 1. Two patients had complications postoperatively, 1 pancreatic fistula and 1 superior mesenteric vein thrombosis, and both resolved with conservative management. All patients remain disease free with median follow up of 2 years post resection.

Conclusion: Rare benign cystic lesions of the pancreas are often indistinguishable from premalignant cystic neoplasms. Although pancreatic resection is safe in these patients, it is not indicated unless the patient is symptomatic. It is important to recognize the existence of these rare benign pancreatic cysts to aid in developing a proper treatment strategy.

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>Preop Symptoms</th>
<th>Preop Imaging</th>
<th>EUS Results</th>
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<td>PPPD</td>
<td>Gauzed Cyst</td>
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<td>DPS</td>
<td>Lymphangioplastic cyst</td>
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</table>

PPPD = Pylorus-Preserving Pancreaticoduodenectomy; DPS = Distal Pancreatectomy w/ Spleenectomy; DP = Spleen-Preserving Distal Pancreatectomy
43303 (POORLY DIFFERENTIATED) NEUROENDOCRINE CARCINOMAS OF THE PANCREAS: IS SURVIVAL REALLY POOR IN THE LONG-TERM FOLLOW-UP?

Introduction/Background: Poorly differentiated neuroendocrine carcinomas (NEC) of the pancreas are rare tumors and they are “historically” associated with very poor prognosis. However, contemporary data regarding their treatment and long-term outcomes are scant. Aim of the study is to evaluate management strategy, clinico-pathological characteristics and survival of patients with NEC.

Methods: Retrospective analysis of patients with histologically-confirmed NEC of the pancreas as defined by the 2010 WHO classification, observed between 1990 and 2011. Duodenal, biliary and ampullary NEC were excluded. Clinical and demographics details, operative procedures, medical treatment, pathology data were assessed. Ki67 proliferative index was measured in all cases, including surgical specimens or biopsy samples for unresected patients.

Results: In the study period 576 patients with pancreatic endocrine tumors were observed. Of these, 49 (8.5%) patients (21% females, median age 56 years, range: 17-78) had NEC. Nearly all the patients had symptoms (94%) at diagnosis, including abdominal pain (84%), weight loss (57%) and jaundice (24.5%). Median radiological size was 50 mm (range: 20-160). 30 patients (61%) underwent surgical exploration, but resection with radical intent (R0/R1 resection) was performed only in 11 patients (22%). Of those, 10 (91%) had nodal metastases. R2 resection rate was 16%. Overall, there were two stage IIIa (4%), 24 stage IIIb (49%) and 23 stage IV (47%) NEC. The median Ki-67 value was 30%. The median overall survival for the entire cohort was 13 months. Patients who underwent radical surgery had a significant better survival (median survival 37 months) compared with those undergoing palliative surgery (median survival 17 months), and those who were not operated (median survival 9 months) (P=0.024). The largest difference in terms of survival was found for a Ki67 cut-off value of 25% although not statistically different (10 versus 17 months, P=0.078). Four patients (8%) underwent neoadjuvant therapy and 3 were eventually radically operated.

Conclusions: Pancreatic NEC is an aggressive disease, with a biological profile that likely resembles pancreatic ductal adenocarcinoma. Surgical resection with radical intent, possibly after neoadjuvant therapy, offers the best chance of cure. Ki67 value may be useful to predict outcomes.
Background: Quality of life studies after pancreatic resection and islet cell autotransplantation have shown improvement and already been published. Mortality rates have improved, but morbidity remains high after pancreatic operations, in particular total pancreatectomy (TP) and pancreaticoduodenectomy (PD). Few studies have evaluated outcomes after pancreatic operations specifically for chronic pancreatitis, with or without islet cell autotransplantation (IAT), and compared these to operations for pancreatic cancer.

Methods: A retrospective review for patients undergoing operation for chronic pancreatitis from 2005-2011 by a single surgeon at an academic center. Morbidity was evaluated to 90 days according to the Clavien Classification (CC). Patients undergoing pancreatic resection with IAT were evaluated as a subgroup. Both groups were compared to those undergoing similar operations for pancreatic cancer. Statistical analysis was applied.

Results: Of the 200 patients (55% men, mean age 49 years), ninety-eight underwent resection alone (65 PD, 27 distal (DP) and 6 TP)), 67 underwent resection with IAT (47 TP, 18 PD, 2 DP), and 22 underwent drainage with lateral pancreaticojejunostomy (LPJ). There was no mortality; however, the overall morbidity rate was 55% (CC 1 – 5) and 29% of these experienced a more severe complication requiring intervention (CC 3-4). Severe complications (CC3 – 4) occurred more commonly after TP (29%) than DP (28%), LPJ (10%), or PD (10%) (p < 0.01). Resections with IAT did not have a higher overall (66% v. 53%) (p > 0.05) nor severe (20% v. 16%) complication rate than those without IAT (p > 0.05). Specifically looking at PD with and without IAT, length of stay (14 v. 10) and complication rate (72% v. 46%) appeared to be higher, but neither reached statistical significance (both p > 0.05). There was no difference in complication rate between TP-IAT and PD-IAT (67% v. 72%) (p > 0.05). Overall (CC1-5) and severe (CC3-4) complication rate was similar when all pancreatic resections with IAT (65% and 20%) and those without IAT (53% and 16%) were compared to those undergoing PD for pancreatic cancer (n = 133, 65% and 20%) (all p > 0.05). Reoperation for bleeding after IAT was not different than after PD for pancreatic cancer (p >0.05). Partial portal vein thrombosis (4%) after IAT and had no long term sequelae.

Conclusions: Operations for chronic pancreatitis are well established and pose no greater risk than resections, specifically PD, for malignancy. Complication rates remain formidable and mortality rates are low. Improvements to quality of life after IAT have been documented; furthermore, the addition of IAT to resections for chronic pancreatitis adds no risk when compared to those for malignancy. At institutions with capability, IAT should be offered to patients during resection for chronic pancreatitis.
Fifty-six years ago at the Annual Meeting of the American Surgical Association, Robert M. Zollinger and Edwin H. Ellison’s described two patients with primary peptic ulcers of the jejunum, gastric hypersecretion of gigantic proportions, and non-specific islet cell tumors, and their hypothesis that, “an ulcerogenic humoral factor of pancreatic islet origin” was responsible. This presentation captured the imagination of pancreas surgeons worldwide.

Zollinger and Ellison, not unlike the Princes of Serendip in the Persian fairy tale, had discovered by accident and sagacity something they were not in quest of—they were looking for a better ulcer operation! The story is remarkable because of a series of events that occurred at the Ohio State University Hospital during a 12-month period in 1954 that lead to the discovery of the Z-E syndrome.

- January—Failed operations for recurrent ulcers in both Dr. Ellison’s and Dr. Zollinger’s patients (CP and JM).
- January—Dr. Ellison’s ongoing study of “jejunal ulcers”.
- January 28—A movie of Dr. Zollinger’s “Dream” ulcer operation for recurrent ulcers, based in part on a principle of fundusectomy by Dr. Gregory Connell of Oshkosh, Wisconsin, was produced for the American College of Surgeons. Interestingly, this concept had been rejected by Zollinger after dog lab experiments performed during his residency in 1933 in Boston, Massachusetts.
- April 20—Dr. Ellison did a total gastrectomy for continued bleeding in his patient (CP). The patient died postoperatively due to fistula, abscess, and sepsis.
- July 30—Dr. Zollinger wrote a letter to H.P. Dr. Jenkins noting that the “Dream” operation had failed, and withdrew the movie.
- August 5—Dr. Jenkins’s return letter to “Dr. Z”: “I had similar patient with jejunal ulcers”, suggests islet cell tumor and hyperinsulinism caused ulcer diathesis.
- October 18—Clinical Pathologic Conference at University Hospital: Dr. Ellison’s patient CP chosen, and Dr. Ellison was the faculty discussant. A previously undetected pancreatic islet cell tumor not seen at surgery or autopsy was now described after histologic review by pathologist.
- November 3—Zollinger’s “Dream” operation patient (JM) has reoperation for ulcers and total gastrectomy done. Islet cell tumor searched for and found in pancreas.
- November 14—Surgical Biology Club presentation by Dr. Ellison: “the problem of jejunal ulcers”.
- December 1—Abstract submitted to American Surgical Association. Accepted for presentation at the Annual Meeting in Philadelphia, April 24, 1955.

This series of events in 1954 and the concept of an “ulcerogenic hormone” stimulated an explosion of new studies and initiated a brotherhood of “Z-E watchers”, all investigating the pathophysiology, diagnostic avenues, and best outcome treatments for this new disease entity, the Z-E Syndrome.

The unique coincidences of Dr. Greg Connell’s and Dr. Robert Zollinger’s early dog experiments regarding
operations to reduce gastric acid secretion, followed by the clinical saga of two patients in 1954, which included recurrent ulcers after numerous operations, set the stage for discovery. Zollinger and Ellison might well be called the Two Princes of Serendip of a more modern era.
Background: Pancreatoduodenectomy (PD) has been associated with high rates of morbidity and mortality. Identification of early predictors of postoperative complications is important to minimize the morbidity of PD. Objective: To assess the usefulness of systemic inflammatory response syndrome (SIRS) as a predictor of major complications after PD. Hypotheses: 1) Early SIRS (postoperative day [POD] ≤ 3) can predict major complications after PD. 2) Late SIRS (POD 4-7) can predict late major complications (≥ POD 8) after PD. Methods: A retrospective cohort study of 527 consecutive patients who underwent PD between 2007 and 2010 was performed. Incidence of SIRS was investigated three times a day (at the nearest point of 8, 16 and 24 o’clock) from POD 1 to POD 7. SIRS was diagnosed based on the standard criteria including body temperature, heart rate, respiratory rate and white blood cell count. A day of SIRS was defined by meeting the criteria of SIRS at two or more points during the same day. Postoperative incidence of SIRS was classified into two groups: Early SIRS (at least one day of SIRS between POD 1 and 3), and Late SIRS (at least one SIRS positive day between POD 4 and 7). The relationship between clinicopathological factors, Early and Late SIRS, and major complications was evaluated by univariate and multivariate analyses. Results: Early and Late SIRS presented in 193 (37%) and 121 (23%) patients, respectively. Major complications were observed in 149 patients (28%) with 72 (13%) patients developing late. Sixty-day mortality was 1.3%. Total number of days with SIRS was associated with severity of complication (P < 0.001). Incidence of Early SIRS was associated with postoperative major complication (P < 0.001) with a sensitivity and specificity of 57% and 71%, respectively. Multivariate analysis demonstrated that the incidence of Early SIRS (HR 2.5, 95% CI 1.6 – 3.9, P < 0.001), soft pancreatic texture (HR 2.4, 95% CI 1.4 – 3.8, P < 0.001), and prolonged operative time (>360 min) (HR1.6, 95% CI 1.1 – 2.5, P = 0.02) were independent risk factors for major complications after PD. For late complications, multivariate analysis demonstrated that Late SIRS (HR 3.6, 95% CI 1.8 – 7.1, P < 0.001), soft pancreatic texture (HR 2.1, 95% CI 1.1 – 4.1, P = 0.01), and male patients (HR, 1.9, 95% CI 1.1 – 3.6, P = 0.02) were identified as independent risk factors. Conclusion: In a large cohort of pancreaticoduodenectomy patients, early postoperative SIRS (POD ≤ 3) was an independent predictor of major complications after PD; and, similarly, Late SIRS (POD 4-7) independently predicted late major complications (≥ POD 8).
43316 INCIDENCE OF SYSTEMIC INFLAMMATORY RESPONSE SYNDROME AFTER TOTAL LAPAROSCOPIC PANCREATODUODENECTOMY - A COMPARISON WITH OPEN PANCREATODUODENECTOMY

Background: Although feasibility of total laparoscopic pancreatoduodenectomy (TLPD) has been established, a large scale study comparing the invasiveness of TLPD with open pancreatoduodenectomy (OPD) has never reported.

Purpose: The purpose of this study was to investigate if TLPD can reduce the postoperative incidence of systemic inflammatory response syndrome (SIRS) compared with OPD.

Methods: A single-institutional retrospective cohort study of all pancreaticoduodenectomy patients between 2007 and 2010 was performed. The incidence of SIRS was measured three times a day (at the nearest point of 8, 16 and 24 o’clock) from postoperative day (POD) 1 to POD 5. The incidence of SIRS on each POD was defined by meeting the criteria of SIRS at two or more points out of the daily three measurement points. Perioperative outcomes including the incidence of SIRS were compared between TLPD and OPD group. The relationship between the clinicopathological factors and the incidence of postoperative SIRS was investigated using univariate and multivariate analyses.

Results: Five hundred twenty-seven consecutive patients (TLPD n = 125, OPD n = 402) were included in study. Six patients (5%) with conversion to OPD were included in TLPD group based on intent-to-treat. The reasons for conversion were the possibility of major venous resection (n = 3), bleeding (n = 1), severe adhesion (n = 1) and expected difficult reconstruction (n = 1). Compared with patients in the OPD group, those in the TLPD group had significantly less preoperative clinical jaundice (42% vs. 53%, P = 0.03), less adenocarcinoma (58% vs. 70%, P = 0.01), and smaller pancreatic duct size (3.7mm vs. 4.2mm, P = 0.002). Median estimated blood loss was less for the TLPD group than the OPD group (200ml vs. 600ml, P < 0.001). However, there were no differences in postoperative complication (62% vs. 67%, P = 0.3) or clinically relevant pancreatic leak (21% vs. 21%, P = 0.8). The incidence of SIRS in the TLPD group was significantly less than that of OPD group on POD 1 (9% vs. 24%, P < 0.001). Within a subset of 179 patients without postoperative complication, the incidence of SIRS in the TLPD group was significantly less than that of OPD group on POD 1 (2% vs. 13%, P = 0.01) and POD 2 (4% vs. 15%, P = 0.03). Multivariate analysis revealed that increased body mass index (> 27) (HR 1.7, 95% CI 1.1 – 2.6, P = 0.005), OPD (HR 1.8, 95% CI 1.1 – 2.9, P = 0.01) and postoperative complication (HR 2.3, 95% CI 1.4 – 3.7, P < 0.001) were independently associated with SIRS on POD 1 and/or 2.

Conclusion: TLPD independently reduced the early incidence of SIRS after pancreatoduodenectomy. The laparoscopic approach to pancreatoduodenectomy appears to provide an advantage of less invasiveness compared with the open approach especially in patients that do not develop postoperative complications.
43317 MAJOR COMPLICATION AND OPEN APPROACH ARE PREDICTORS OF PROLONGED HOSPITAL STAY AFTER PANcreatricoduodenectomy

Introduction: Length of hospital stay is frequently reported to be reduced with laparoscopic approaches. Few studies have accounted for readmission hospital days which may obviate any perceived benefit. The aim of this study was to evaluate the impact of total laparoscopic approach and other clinicopathologic factors on length of index hospital stay, readmission rates and total hospital days after pancreaticoduodenectomy.

Methods: A retrospective review of clinical, pathologic and outcomes data was performed for all patients undergoing pancreaticoduodenectomy from January 2007 through December 2010 at a single institution. Initial hospital stay, readmission rates, and total hospital stay (initial hospital days plus readmission days) were compared between total laparoscopic pancreaticoduodenectomy (TLPD) and open pancreaticoduodenectomy (OPD). The relationship between the clinicopathological factors and total hospital stay was investigated using univariate and multivariate analyses.

Results: A total of 527 patients were identified having undergone TLPD (n=125) or OPD (n=402). There were no differences in mean age, BMI or ASA Score. A malignant diagnosis was more common in patients undergoing OPD (80% vs. 68%, p=0.004), however, there were no differences in overall or pancreas specific postoperative complication rates. Median length of hospital stay was less for the laparoscopic group (7 vs. 10 days, p<0.001). Hospital readmission within 30 days was observed in 16% and was not different between the TLPD and OPD groups (14% vs. 17%, p=0.4). Common diagnoses on readmission included pancreatic fistula (25%), delayed gastric emptying (21%), and abdominal collection or abscess (20%). Of patients requiring readmission, 62% had Clavien grade 3 or 4 complications diagnosed during initial hospitalization or at subsequent readmission. Median length of readmission hospital stay was 5 days for both TLPD and OPD groups. When accounting for readmission days, total hospital days were less for patients undergoing TLPD compared to OPD (8 vs.11, p<0.001). Multivariate analysis demonstrated that Clavien Grade \(\geq 3\) complication (HR 6.9, 95% CI 4.3 – 11.5, P < 0.001) and open approach (HR 2.5, 95% CI 1.5 – 4.4, P < 0.001) were independent predictors of prolonged total hospital stay.

Conclusions: Compared with open approaches, TLPD results in shorter hospital stay, similar readmission rates and less total hospital days. Major complication and open approach are independent predictors of prolonged total hospital stay. Limitations of this study include potential selection bias as noted by a higher incidence of malignancy in the open group. The impact of reduced hospital stay on cost and patient-specific advantages such as improvement in quality of life needs to be evaluated.
43319 PANCREATIC PLASMACYTOMA: A REVIEW COMPARING SURGICAL AND NON-SURGICAL MANAGEMENT

Background: Plasmacytomas are solitary masses of plasma cells, generally of bone marrow, accounting for approximately 10% of hematologic malignancies. Uncommonly, these plasma cell tumors arise entirely outside of the bone marrow, with 80% occurring in the nasal cavity, paranasal sinuses, and upper airways. Incidence of pancreatic involvement based on autopsy studies has been reported at 2.3%, with reports of patients presenting with clinically significant disease, such as obstructive jaundice to be exceedingly rare.

Methods: A systematic literature search was performed using PubMed with the keywords: pancreatic plasmacytoma or pancreatic multiple myeloma. Case reports and case reviews written in English were reviewed and compared with our case. 48 articles were analyzed, of which 7 met the criteria of a primary diagnosis of plasmacytoma based on pancreatic symptoms. In the remaining case reports, a previous diagnosis of multiple myeloma was established and pancreatic manifestations proved to be a disease recurrence. Our case if of a 50 year old previously healthy male who presented with jaundice, pruritis, and dark brown urine. Abdominal CT scan showed a mass at the head of the pancreas, and FNA demonstrated monoclonal plasma cells. Immunohistochemistry staining was diffusely positive for lambda light chain, confirming the diagnosis of plasmacytoma. Initial treatment with bortezomib and dexamethasone has shown good response.

Results: The seven case reports presented with either recurrent pancreatitis or jaundice and mean age at presentation was 58 years old, with a slight male predominance (57%). Flatulence, weight loss, constipation and dark urine were common symptoms. Over half were treated with resection; the remainder were treated with chemotherapy or radiation. Four patients also suffered from intestinal obstruction or GI bleeding caused by tumor involvement. Four patients received surgical treatment, due to intestinal obstruction or GI bleed, with a mean survival of one day to 7 months, and one patient disease free at article submission. Two patients received either chemotherapy or radiation, including our patient, with one patient surviving 6 years and the other disease free at article submission. One patient deteriorated rapidly and ultimately expired before any treatments. From the data, it can be concluded that patients receiving surgical management presented with more advanced disease and had worse outcomes.

Conclusion: Pancreatic plasmacytoma commonly presents with multiple myeloma related symptoms well before obstructive jaundice develops. Clues to the diagnosis of plasmacytoma include a previous diagnosis of multiple myeloma, age and radiologic appearance. Interestingly, some authors have suggested that smooth common bile duct stenosis on ERCP should raise suspicion for plasmacytoma. Although uncommon, extramedullary plasmacytoma should be included in the differential for any patient with a pancreatic mass.
Introduction: Multiple clinical trials have utilized the combination of gemcitabine and external beam radiation (XRT) therapy for pancreatic ductal adenocarcinoma (PDA) and have generated ambiguous conclusions. Further, despite multiple trials, the molecular basis for this therapeutic combination is largely unknown. We have reported that the RNA-binding protein, HuR, critically influences gemcitabine treatment by upregulating the pro-drug metabolizing enzyme, deoxycytidine kinase (dCK). However, XRT therapy has been shown to cause dissociation of HuR from established targets, including dCK mRNA. The objective of this study was to investigate the sequence of events underlying combination therapy (gemcitabine plus XRT) in relation to HuR and its known targets, with the intent to optimize the existing standard of care for this devastating disease.

Methods: Drug sensitivity assays on PDA lines tested: a) gemcitabine (various doses) followed by low-dose (2 Gy) XRT (termed combination therapy), b) reverse order of treatments, c) XRT alone or d) gemcitabine alone. Ribonucleoprotein-immunoprecipitation followed by RT-qPCR was used to assess HuR binding to mRNAs. Finally, our patient cohort (n=32) was stratified into gemcitabine only or combination therapy and assessed the predictive value of HuR in these patients.

Results: Gemcitabine treatment prior to XRT results in a 70% relative reduction in cell survival as compared to XRT first and a 10% relative reduction in cell survival compared to gemcitabine alone. Accordingly, gemcitabine treatment alone and when treated prior to XRT increased HuR-bound dCK mRNAs by over 4-fold. Conversely, XRT alone and XRT treatment prior to gemcitabine exposure decreased HuR-bound dCK mRNAs up to 5-fold. In clinical samples, high cytoplasmic HuR expression was associated with superior survival (median survival = 39 months) in patients treated with gemcitabine alone (p-value 0.03); this association was lost in patients receiving combination therapy (p-value ns; median survival = 27 months).

Conclusion: HuR is central to the interplay of combination therapy given gemcitabine’s reliance on HuR-mediated upregulation of dCK and the disruption of this association by XRT. In vitro, treating cells with gemcitabine prior to radiation therapy yields an increased efficacy of therapy correlating with the molecular model aforementioned. Based on these findings, we propose the paradigm that combination therapy would be optimized by administering gemcitabine before XRT therapy for the treatment of pancreatic cancer patients.
Objective: Clinically-relevant post-operative pancreatic fistula (CR-POPF) is a serious inherent risk of pancreatic resection. Pre-operative CR-POPF risk assessment is currently inadequate and rarely disqualifies patients who need resection. Risk assessment should occur during the operation, be widely applicable, and drive fistula prevention and response measures.

Methods: Recognized ISGPF risk factors for CR-POPF (small duct, soft pancreas, high-risk pathology, and excessive blood loss) were evaluated during pancreaticoduodenectomy (PD). A Risk Score range model was next derived (N=233) and then validated prospectively (N=212). Clinical and economic outcomes were evaluated across four ranges of POPF Risk Scores.

Results: CR-POPF occurred following PD in 13% of patients. The frequency of CR-POPF was greatest with excessive blood loss. Duct size <5mm was also associated with increased fistula rates that rose with even smaller ducts. These factors, together with soft pancreas texture and certain disease pathologies, afforded a highly predictive 10-point CR-POPF Risk Score (points assigned by odds ratios; p < .001). CR-POPFs increased proportionally with Risk Scores, and these scores correlated with clinical and economic outcomes (Table). Notably, patients with scores of 0 (N=73; 16%) never developed a CR-POPF, while fistulae occurred in all patients with scores of 9-10 (n=5).

Conclusion: A simple 10-point Risk Score derived during PD accurately predicts CR-POPF. It can be readily learned and broadly deployed, and can help surgeons anticipate, identify and manage this ominous complication from the point of operation.
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<th>Intermediate Risk</th>
<th>High Risk</th>
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Introduction: Pancreatic neuroendocrine tumors (PanNETs) are often indolent neoplasms without pathological lymph node (LN) metastasis (pN1). Therefore, in patients with low risk of pN1, surgery can be limited and lymphadenectomy could be avoided.

Aim: To construct a model for predicting the risk of pN1 prior to surgical resection.

Methods: The combined prospective databases from the Surgical Department of the University of Verona and the Beaujon Hospital were queried. Clinical and pathological data of all patients with resected (R0 or R1), pathologically confirmed nonfunctioning PanNET between 1993 and 2009 were retrospectively reviewed. Multiple logistic regression analysis was performed.

Results: Data were analyzed for 194 patients. Metastases were present in the dissected LNs of 58 patients (30%). The 5-year disease free survival for patients with pN1 was significantly lower than for those without nodal metastases (66% vs 93%, P<0.0001). Multivariable analysis suggested the significant independent factors associated with pN1 were radiological nodal status (rN) (odds ratio [OR] 5.01, P<0.0001) and the degree of differentiation (G2 vs G1 OR 4.44, P=0.001) (first model). Overall, the 94% of patients with rN0 PanNET-G1 were pN0. When the degree of differentiation was excluded, the radiological size > 4 cm (OR 2.5, P=0.012) was an independent predictor of pN1 (second model). The area under the ROC curve for the first and the second model resulted to be 80% and 74%, respectively.

Discussion: Patients with PanNET-G1, in the absence of radiological node involvement, have a very low risk of pN1. When a preoperative cytological diagnosis is not achieved, the radiological size of the lesion is a powerful alternative predictor of pN1. The analysis demonstrates that the risk of pathological nodal involvement in PanNET patients can be estimated by a clinical predictive model.
43331 ADEQUACY OF LYMPH NODE RETRIEVAL FOR AMPULLARY CANCER AND ITS ASSOCIATION WITH IMPROVED STAGING AND SURVIVAL

Background: To determine the optimal number of lymph node (LN) examined to stage pN0 patients after surgery for ampulla of Vater carcinoma (AVC).

Methods: We reviewed retrospectively 127 patients with AVC who underwent pancreaticoduodenectomy (PD) with radical intent (1990-2008) at our institution (R2 resections were excluded). Data on the total number of LN evaluated were obtained from the pathology reports. Log-rank comparison was performed to determine the most significant survival difference (maximization of the chi-square statistic). Univariate and multivariate analysis was performed.

Results: The median number of LNs examined was 17 (IQR 12;23). Fifty-nine patients (46.5%) where pN0, whereas 68 patients (53.5%) were pN1. Patients with node metastases had a worse 5-year disease-specific survival (DSS) compared to pN0 patients (46% versus 77%, P<0.0001). In the pN0 cohort, the optimal cut-off number of lymph node analyzed was found to be 12. The 5-year DSS for patients with ≤12 LNs was 50% compared with 89% in those with >12 LNs (P=0.001). By multivariable analysis, a LN count >12 resulted as the only independent predictor of poor survival (HR 0.16 CI 95% 0.05-0.53, P=0.003) among pN0 patients. Among pN1 patients, a LN count > 12 was associated with a significant better 5-year DSS (59% versus 22% ,P=0.027). Patients with a LNR > 0.20 had a 5-year DSS of 24% compared with 58% in those with 0<LNR≤0.20 (P=0.038).

Conclusions: A number of more than 12 examined LNs is associated with an improved survival rate after surgery with radical intent for AVC, both in pN0 and pN1 patients, and allows a more precise stratification of patients for adjuvant therapies.
43332 HAND-SEWN CLOSURE TECHNIQUE AFTER DISTAL PANCREATECTOMY LEADS TO A LOW PANCREATIC FISTULA RATE

Introduction
There is still an ongoing discussion about the best closure technique after distal pancreatectomy. The aim is to prevent a clinical relevant pancreatic fistula. The stapler technique seems not to be superior compared with hand-sewn closure of the remnant. For both techniques a fistula rate of about 30% is described1.

Methods and Patients
We retrospectively analyzed our pancreatic left resections between 01/2000 and 12/2010. In all cases the pancreatic duct was over sewn with a separately stitched ligation of the pancreatic duct (4*0 PDS) followed by a single stitched hand sewn closure of the residual pancreatic gland. In all patients a local drain was placed. Postoperative pancreatic fistulas were classified according to the ISGPF criteria. Indications for operations were: cystic tumors (n= 54), neuroendocrine tumors (n=28), adenocarcinoma (n=22), chronic pancreatitis (n=9), metastasis (n=6), and others (n=6).

Results
During the above mentioned period we performed 124 distal pancreatectomies (n=74, n=50). Mean age was 57.5 years (18-82). Resections were performed by four different surgeons. Postoperative pancreatic fistula rate according to ISGPF criteria was: no fistula 54.8% (n=68), grade A 24.2% (n=30), grade B 19.3% (n=24), grade C 1.7% (n=2). Both patients with grade C fistulas had to be reoperated due to complications. No patient died in consequence of a pancreatic fistula. Therefore in 21.0 % (n=26) of the cases a clinical relevant pancreatic fistula occurred. There was no significant difference between the different surgeons. Mean postoperative stay was significantly higher after grade B/C fistula (26.3 days) vs. no/grade A fistula (13.7 days) (p<0.05).

Conclusion
By using a standardized hand-sewn closure technique of the pancreatic remnant after distal pancreatectomy, with separately stitched ligation of the pancreatic duct, a low fistula rate can be achieved.

Background: Neoadjuvant chemoradiation therapy and more aggressive surgery with vascular resection are two strategies to bring patients with locally advanced pancreatic cancer to the operating room for potential cure.

Methods: We reviewed the medical records of all patients with pancreatic ductal adenocarcinoma who underwent pancreaticoduodenectomy (PD) at our institution between March 1992 and March 2011. We identified patients who received neoadjuvant (NA) therapy or required major vascular resection and evaluated demographics, operative characteristics, morbidity, mortality, and survival. Student’s t- or Mann-Whitney U tests and Chi-squared or Fisher’s exact tests were used to compare continuous and categorical variables, respectively. Kaplan-Meier curves and Cox proportional hazards models were used to compare survival.

Results: A total of 600 patients were brought to the operating room for attempted resection. One hundred fifty-four (25.6%) had received NA therapy for initially unresectable disease whereas 446 (74.4%) were explored at presentation. One hundred twenty-four (80.5%) NA patients underwent successful PD compared to 340 (76.5%) non-NA patients. The NA patients were younger (62.7 years vs. 67.5 years, p<0.001), more often had prior resection attempts (26.6% vs. 0.9%, p<0.001), had longer median operative times (390 min vs. 328 min, p<0.001), and had higher median estimated blood loss (1500mL vs. 1000mL, p<0.001) than non-NA patients. There were no statistically significant differences in R0 resection rate (82.3% vs. 78.2%, p=0.34), median length of stay (9 days vs. 10 days, p=0.16), morbidity (50% vs. 49.4%, p=0.91), or mortality (6.5% vs. 2.7%, p=0.09) between the two groups. Sixty-one percent of NA patients versus 18.8% non-NA patients required vascular resection (p<0.001), therefore a subset analysis was performed. PD with vascular resection resulted in increased morbidity (54.9% vs. 33.7%, p<0.001) and mortality (1.8% vs. 6.3%, p=0.008), but similar R0 resection rates (74% vs. 81%, p=0.07) and lengths of stay (10 days vs. 9 days, p=0.07) compared to standard PD. Median survival of resected NA patients was similar to resected non-NA patients (24.9 months vs. 19.3 months, p>0.05) and significantly longer than non-NA patients aborted for locally advanced disease (24.9 months vs. 8.9 months, p<0.05). NA patients who required vascular resection had longer survival than non-NA patients who required vascular resection (23.6 months vs. 14.4 months, p<0.05).

Conclusion: Many patients with locally advanced pancreatic cancer can be brought to resection through NA therapy and vascular resection with acceptable morbidity and mortality. These patients have significantly improved survival over patients deemed locally inoperable by traditional criteria.
PERIOPERATIVE TUMOR CHARACTERISTICS DO NOT PREDICT EARLY RECURRENTCE OF PANCREAS CANCER FOLLOWING PANCREATICODUODENECTOMY.

Background: Early recurrence after potentially curative resection of pancreatic adenocarcinoma remains a clinical problem. As this phenomenon has not been well characterized, we sought to identify peri-operative variables which may predict early recurrence in patients undergoing pancreaticoduodenectomy for adenocarcinoma of the pancreas.

Methods: A retrospective review was conducted of 97 consecutive patients who underwent pancreaticoduodenectomy for adenocarcinoma of the pancreatic head at the University of Cincinnati between January 2000 and December 2010. Patients were evaluated for radiologic or tissue evidence of recurrence. Early recurrence was defined as recurrence of malignancy within 3 months of resection. Multivariate regression analysis was performed to identify factors that could predict risk for early recurrence.

Results: Out of 97 patients, 27 patients (28%) were found to have evidence of early recurrence. Of these patients 30% had locoregional recurrence, 59% had systemic recurrence, and 11% had both local and systemic recurrence. There was no difference in locoregional failure among patients with respect to margin status. The median time to recurrence was 2.4 months (range 1.1-3.3, 95%CI) with a median overall survival of 6.0 months (range 1.1-78.4, 95%CI). There was no difference in gender, need for vein resection, pre-operative stent placement, tumor size, perineural/lymphatic invasion, margin status or operative blood loss. Univariate analysis demonstrated that tumor grade, stage at resection, age at surgery and positive lymph node status were statistically significant between groups. However on multivariate logistic regression only the presence of positive lymph nodes at the time of resection was a statistically significant determinant of early versus late recurrence with an odds ratio of 4.155 (95% CI 1.414, 12.214).

Conclusion: With the exception of positive lymph node status, histopathologic and perioperative factors do not predict risk of early recurrence in patients undergoing pancreaticoduodenectomy for pancreatic adenocarcinoma. Our findings suggest that all patients with adenocarcinoma of the pancreas be evaluated for neoadjuvant therapy in effort to identify patients with aggressive biology. Offering neoadjuvant therapy to patients with peri-tumoral lymphadenopathy identified on CT or EUS may decrease the risk of early recurrence and ultimately improve survival.
Introduction/Methods: Preoperative detection of metastatic disease, which precludes surgical resection, remains a limitation in the work up of pancreatic tumors. Technology in CT imaging has improved dramatically in the past decade. No recent study has assessed the ability of enhanced-resolution pancreatic protocol CT scans (PPCT) to detect metastatic disease. Therefore, the goal of the present study is to evaluate the accuracy of modern high quality PPCT in assessing pancreatic tumors for metastatic disease.

Methods: This is a single institution review of all patients who underwent PPCT and operative exploration for pancreatic adenocarcinoma and neuroendocrine tumors over a 5 year period using 64-slice or higher PPCT with three-dimensional reconstruction. PPCT results were correlated to operative findings.

Results: 823 patients underwent operative exploration after PPCT. 671 patients had adenocarcinoma and 152 had neuroendocrine tumors. For patients with adenocarcinoma, 410 (61.1%) underwent pancreaticoduodenectomy, 101 (15.1%) distal pancreatectomy, 20 (3.0%) total pancreatectomy, 35 (5.2%) palliative bypass, and 105 (15.6%) underwent non-therapeutic laparotomy/laparoscopy. For patients with neuroendocrine tumors, 51 (33.6%) underwent pancreaticoduodenectomy, 82 (53.9%) distal pancreatectomy, 3 (2.0%) total pancreatectomy, and 16 (10.5%) underwent non-therapeutic laparotomy/laparoscopy. The accuracy of PPCT in detecting metastatic disease is shown in the table.

Discussions/Conclusion: Modern PPCT with three-dimensional reconstruction is a highly accurate method to identify metastatic disease in pancreatic tumors prior to planned surgical resection. All patients should undergo PPCT prior to operative exploration for pancreatic tumors. The sensitivity is lower for detecting metastatic disease in patients with adenocarcinoma than in neuroendocrine neoplasms. Since the sensitivity remains relatively low, diagnostic laparoscopy, magnetic resonance imaging, positron emission tomography, or other modalities may be of benefit in selected patients and should be further studied.

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<th>Adenocarcinoma</th>
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<tr>
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<td>31.4%</td>
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<tr>
<td>Specificity</td>
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43344 RON OVEREXPRESSION ACCELERATES TUMORIGENESIS AND INDUCES METASTASIS IN A KRAS MUTANT MOUSE MODEL OF PANCREATIC CANCER

Introduction
The RON receptor tyrosine kinase is increasingly over-expressed during pancreatic cancer progression and has been implicated as a mediator of KRAS oncogene addiction. It remains unclear if RON signaling promotes disease progression or if RON over-expression simply represents an epiphenomenon. The goal of this study was to directly test the hypothesis that over-expression of the RON receptor promotes pancreatic cancer progression.

Methods
To explore the role of RON signaling in pancreatic carcinogenesis, we generated a transgenic mouse which over-expressed wt-RON in a pancreas-specific manner. To drive RON expression, we used Pdx-1, the identical promoter used to drive pancreatic Cre expression in the LSL-KrasG12D/Pdx-1-Cre (KC) strain that develops progressive pancreatic duct neoplasia. RON over-expression was verified via Western blot analysis and IHC. The Pdx-1-RON strain was crossed with the LSL-KRASG12D strain to yield mice (RK), which were then bred with Pdx-1-Cre mice to combine RON over-expression in the presence of oncogenic KRAS (RCK). RCK mice were aged and sacrificed at various time points and histology was compared to KC controls.

Results
Pdx-1-RON mice developed no pancreatic phenotype prior to 12 months. At 18 months, one of 4 animals developed primary pancreatic adenocarcinoma with lung metastasis. RON overexpression in KRAS mutant mice (RCK) led to accelerated PanIN progression compared to KC (p<0.05). In RCK, PanIN’s were visible at 6 weeks, with invasive carcinoma detectable at 6 months compared to KC mice (average latency >1yr). Metastatic disease was visible in RCK mice at 9 months.

Conclusions
RON overexpression alone results in pancreatic cancer at long latency. In the presence of KRAS mutation, RON overexpression markedly accelerates PanIN progression to primary and metastatic pancreatic duct cancer. This data supports a role for RON in pancreatic carcinogenesis and this model may prove useful for investigations regarding the role of the RON receptor in pancreatic cancer biology.
Background: Postoperative pancreatic fistula (POPF) is a major complication following pancreatic resection (PR). The ability to predict and recognize POPFs early may help in prompt treatment of this complication.

Hypothesis: Pancreatic drain amylase level and total daily drain volume on a certain post operative day (POD) is predictive of the presence or absence of a POPF following PR.

Design: A retrospective review of a prospectively maintained data base on PR at a single institution was performed.

Setting: Tertiary care center

Patients and Methods: Data on patient demographics, drain volume, presence of POPF, as well as drain amylase levels every post operative day (POD) were collected. Fistulas were graded according to the classification set forth by the International Study Group on Pancreatic Surgery (ISGSP

Results: A total of 111 consecutive patients who underwent a PR performed by a single surgeon from May 2008 to December 2011 were identified. Of these, the majority, 79 (71%), underwent pancreaticoduodenectomies, the remaining 32 (29%) underwent distal pancreatectomies. There were 52 (47%) males, 59 (53%) females ranging in age from 20 to 88, with a median age of 67 years. A total of 9 (8%) POPFs were identified, of these, 4 were grade A, 4 were grade B, and 1 was a grade C fistula. Total daily drain volume did not correlate with the presence of POPF (p>0.05), while drain amylase level less than or equal to 1000 U/L on POD 3 did correlate with the absence of POPF with a negative predictive value of 100% and a positive predictive value of 90% (p<0.01).

Conclusion: A pancreatic drain amylase of 1000 U/L or less on POD 3 after PR is predictive of the absence of POPF. Total daily drain volume has no correlation with the presence or absence of POPF. Pancreatic drains can be removed on POD 3 safely if drain amylase is 1000 U/L or less. This may potentially decrease drain associated complications in this cohort of patients.
Pancreatic Pseudocysts (PP) are peripancreatic fluid filled cavities covered by fibrotic tissue that affect 15% of acute pancreatitis cases and 40% of patients with chronic pancreatitis.

The spectrum of treatment options includes surgery, endoscopic or percutaneous drainage and conservative management.

Objective

To compare the success rate, complication rate, and mortality among surgical and non-surgical treatment of PP.

Material and Methods

A retrospective file review of all patients with the diagnosis of pancreatic pseudocyst between the year 2000 and 2009 at Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán was performed.

Eighty-three patient files were reviewed and 17 patients were excluded from analysis. Multiple variables were documented in the remaining 66 patients.

Statistical Analysis

Continuous variables were shown using medians and intervals. Categorical variables were expressed with absolute frequencies and percentages. Chi-square test was used in all categorical variables except in those where a frequency of less than five was expected, exact Fisher test was used in this circumstance. A multivariate analysis was performed with the logistic regression method and a p value of <0.05 was considered significant. SPSS V.15 software was used for analysis.

Results:

From the 66 patients included 65% were men. Median age at presentation was 39.5 (range 17-84). Clear etiology of pancreatitis was determined in 83.3%. Biliary disease (40%) and alcohol ingestion (25%) were the most common.
Surgical treatment was preferred in 41 patients (62.1%), 12 patients (18.2%) were treated conservatively, 6 (9.1%) were drained endoscopically and the remaining patients were treated by a percutaneous drainage.

Open surgery was used in 12 patients (29.3%), followed by cyst-gastrostomy in 10 patients (24.4%), laparoscopic cysto-yeyunostomy in 9 patients (22%) and the remaining were treated by a distal pancreatectomy or pseudocyst resection.

The only significant difference was the size of the pseudocyst; with a median of 9.8cm (range 3-21cm) for the surgical group and 7.8cm (range 2-22cm) in the non-surgical group with a 0.009 p value.

When comparing post treatment variables, hospital stay was significantly prolonged in the surgical group with a median of 16 days (range 7-65 days) compared to 12.5 days (range 3-31 days) in the non-surgical group with a p value of 0.023.

EUS was used in 33.3%, 22.7% for diagnosis purpose and 10.6% for drainage. When comparing patients who had an EUS performed with those who didn’t, a significantly higher number of comorbidities (77% vs. 52%) and a significantly smaller cyst size (6.5cm [range 3-15cm] vs. 10cm [range 2-22cm]) was found in the group who had an EUS performed.

Conclusion:

No differences were found in terms of rate of success, morbidity and mortality when comparing the surgical vs. the non-surgical group in the treatment of PP. Pseudocysts in the surgery group were significantly larger and hospital stay was longer when compared to the non-surgical group.
COMBINATION OF TRAIL AND JAK-2 DOWNREGULATION: NOVEL THERAPEUTIC STRATEGY AGAINST PANCREATIC CANCER.

Introduction: TRAIL (Tumor Necrosis Factor-Related Apoptosis Inducing Ligand) is emerging as a promising anti-cancer therapy by virtue of its strong anti-tumor activity in wide range of cancer cells and minimal toxicity to normal cells and tissues. Unfortunately, pancreatic cancer is resistant to TRAIL. Elucidation of the mechanism of resistance to TRAIL-mediated apoptosis will help design strategies to overcome this resistance. JAK-2/STAT-3 is a pro-survival pathway which is up-regulated in a variety of cancer cells including pancreatic cancer. The aim of the current study was to evaluate the role of JAK-2/STAT-3 pathway in the resistance to TRAIL mediated apoptosis and to evaluate the combination of TRAIL and JAK-2 downregulation as a novel treatment for pancreatic cancer.

Methods: Highly aggressive metastatic pancreatic cancer cell lines (S2013, S2VP10) were treated with JAK-2 inhibitors FLLL-31 (0-5µM) or WP1066 (0-5µM), TRAIL (0-40ng/ml) or a combination of JAK-2 inhibition and TRAIL. The effect on viability (MTT) and parameters of apoptosis (annexin V, caspase 3, 8 and 9 activation) was measured. The results were confirmed with specific inhibition of JAK-2 by siRNA.

Results:
1. Even though TRAIL in itself was ineffective in inducing cell death in pancreatic cancer cells, combination of TRAIL and JAK2 inhibitor FLLL-31 induced marked decreased in viability in pancreatic cancer cells (Viability 48h [% of Control, expressed as mean ±SD]. S2VP10: TRAIL 20ng/ml- 114±1, FLLL-31 5µM- 63 ± 22, FLLL31 + TRAIL - 24 ± 11; S2013: TRAIL 20ng/ml- 87 ± 5, FLLL-31 5µM- 47 ± 9, FLLL31 + TRAIL - 21 ± 3).

2. Combination of TRAIL and FLLL-31 also markedly increased annexin positivity as compared to TRAIL and FLLL-31 alone, suggesting that TRAIL and JAK-2 inhibition synergize in inducing apoptosis in pancreatic cancer cells (Annexin [% apoptotic cells, expressed as mean ±SD]. S2VP10: TRAIL 20ng/ml- 10 ± 1, FLLL-31 5µM- 13 ± 2, FLLL31 + TRAIL - 59 ± 11; S2013: TRAIL 20ng/ml- 16 ± 2, FLLL-31 5µM- 30 ± 1, FLLL31 + TRAIL - 92 ± 4).

3. Similarly, combination of TRAIL and JAK-2 inhibition induce significantly more caspase3, 9 and 8 activation when compared to TRAIL or FLLL-31 alone (data not shown).

4. Similar results were observed with the combination of TRAIL and the other JAK-2 inhibitor WP1066 as well as with JAK-2 downregulation by siRNA (data not shown).
**Conclusion:** Inhibition of JAK-2 pathway sensitizes pancreatic cancer cells to TRAIL induced apoptosis and cell death. Combination of JAK-2 silencing and TRAIL has immense potential to emerge as novel therapeutic strategy against pancreatic cancer.
Aim: The development of pancreatic fistula after pancreatoduodenectomy (PD) is often accompanied by bacterial infection, which is rated grade B on the ISGPF. However, the mechanism of bacterial infection is not clear. To elucidate the mechanism, we examined bacteria from postoperative drainage fluid and removed drains. Methods: Subjects were 81 patients who had undergone PD. On postoperative days (POD) 1, 3, 5, and 7, we collected drainage fluid and cultured bacteria from the fluid samples. The extent of bacterial infection was determined by counting the number of bacterial colonies. We also compared bacteria from drains removed before POD 5 and after POD 7. Results: In 25 cases (34.6%), bacterial infection was detected on POD 1 and 3. Isolated bacterial species were Enterococcus faecalis in 20.9%, Enterococcus faecium in 7.4%, Pseudomonas aeruginosa in 11.1%, and Enterobacter cloacae in 8.6%, thus most of detected bacteria were intestinal bacteria. Among these 25 cases, 21 (84.0%) had cephem-resistant bacteria were detected, which were sensitive to the antibiotics ampicillin, imipenem, levofloxacin, and vancomycin. The incidence of grade A and B was 14.8% and 14.8%, respectively. Among grade B cases, 91.7% were positive for bacterial infection on POD 1 and 3, and in all cases, detected bacteria were the same as those isolated after pancreatic fistula. In contrast, only 16.6% of grade A were positive for infection on POD 1 and 3. Thus, there was a significantly lower incidence of grade A (p<0.01) compared with grade B. The amount of bacteria from drains removed after POD 7 was higher than that from drains removed before POD 5. Conclusion: Grade B is caused by leakage of pancreatic juice with early bacterial infection in the ascitic fluid and drain. Therefore, to prevent grade B, it is important to perform early administration of appropriate antibiotics and early drain removal.
43359 IS MESENTERIC LYMPH BACTERIOCIDAL?

**Background**
In severe acute pancreatitis the pancreas can become infected with a range of bacteria. There is clinical and experimental evidence that lymph can act as a conduit for bacteria from the intestine. The mesenteric lymph (ML) draining from the intestine changes dramatically in composition during acute disease states. It is unknown whether these changes inhibit or promote bacterial growth in ML. The objective of this study was to determine the effect of acute and chronic disease-conditioned ML sources on the growth of commonly translocating bacteria.

**Methods**
Under sterile conditions the mesenteric duct was cannulated and disease-conditioned ML sourced from four animal models (n = 5 per group): i) Acute Pancreatitis [AP] (taurocholate ductal infusion model), ii) Hemorrhagic Shock [HS] (reversible 90 min hemorrhagic shock model), iii) Diabetes Mellitus [DM] (Streptozotocin Type I diabetes model of 5-8 weeks duration) and iv) Control [C] (normal lymph). Five bacterial species were studied: E.coli, S. aureus, K. pneumoniae, E.faecalis, and P. aeruginosa. Bacteria were seeded as low and high concentration inoculums into the disease-conditioned or control ML, and bacterial growth assessed after incubation for 4 and 24 hours.

**Results**
In all ML groups, after a low concentration inoculation, the concentration of S. aureus, E.faecalis, and P. aeruginosa increased, while E. coli and K. pneumoniae were inhibited by control lymph. After a high concentration inoculation, bacterial growth was promoted in all disease conditioned ML, except that DM- and AP-conditioned ML inhibited the growth of S. aureus and E. fecalis. HS conditioned ML promoted the growth of all bacteria types at both low and high concentration inoculations.

**Conclusions**
There was a complex interaction between inoculum concentration, bacterial species and disease state. Consequently it is not possible to generalise whether disease conditioned ML is bacteriostatic, bacteriocidal, or facilitates bacterial growth. This information is relevant to prophylaxis or empirical treatment for infectious complications in severe disease states.
Introduction

Intravenous fluid therapy (FT) is important in the early management of patients with acute pancreatitis (AP). Current guidelines, variably drawing on available evidence, do not reach the same recommendations. Significant questions remain regarding the type of fluid, the rate of administration and the goal for FT. The aim of this study was to systematically review and grade the quality of current evidence regarding FT in AP.

Methods

A comprehensive literature search was performed using online databases (Medline, Cochrane library and EMBASE). Inclusion criteria were all human studies investigating FT in patients with AP within the last 20 years; not limited by language. The reference lists of identified literature were hand-searched. All current guidelines were summarised. Data was abstracted onto a pro-forma. The quality of the entire body of evidence was then graded according to the GRADE working group guidelines in relation to three key areas: type of fluid, rate of fluid administration and markers used to guide FT.

Results?

The initial search of the databases yielded a total of 410 papers of which there were 88 duplicates. After screening, 309 papers did not meet the inclusion criteria, but 13 did. A further 2 papers were identified from reference lists, giving a total of 15 studies for this systematic review. Grading of the body of evidence concluded that the majority of the evidence is of low to very low quality and the highest quality was only moderate. Only two randomized studies compared types of fluids, one in relation to the requirement for mechanical ventilation and intra-abdominal hypertension and the other in relation to the inflammatory response. Nine studies looked at aggressive versus conservative resuscitation protocols. Four observational studies concluded that an aggressive approach yielded better outcomes. In contrast, five studies (2 randomised and 3 observational) concluded that a conservative approach yielded better outcomes. A wide range of resuscitation markers were used in the studies, making formal analysis impossible. Two studies investigated goal-directed FT using different markers reached different conclusions; one demonstrating benefit and the other no benefit.

Conclusion?

It is an indictment that FT is considered a key to the early management of patients with AP and yet is based on such poor quality evidence. To our knowledge this systematic review is the first to critically appraise and grade the available clinical evidence using the GRADE guidelines. It has demonstrated the equipoise necessary for the design of prospective randomized studies to answer pressing questions relating to the type of fluid, the rate of administration and how FT should be guided.
Infected pancreatic necrosis is a primary determinant of outcome in acute pancreatitis (1) and a target for invasive intervention (2). Elucidating how infection occurs may illuminate some aspects of the pathophysiology and provide new avenues for therapy in severe acute pancreatitis (AP).

This presentation will cover a series of linked experimental studies, which conform to the revised Guiding Principles in the Care and Use of Animals (American Physiological Society (2000), and investigate four questions regarding the role of mesenteric lymph (ML) in the development of infected pancreatic necrosis. (1) Can ML derived from ischaemic small intestine exacerbate the severity of AP? Studies have shown that ML conditioned by mild intestinal ischaemia and delivered systemically to rats with mild AP, increased the histological severity of disease. (2) Could ML impact the pancreas via direct lymphatic connections between the intestine and the pancreas? These studies in the rodent used different direct imaging and infusion methodologies to delineate the lymphatic anatomy and demonstrate that ML can readily and directly enter the pancreas. (3) Can intestinal bacteria enter the pancreas by this route? Labelled bacteria were used to demonstrate that this is possible at physiologic infusion pressures. (4) Does ML protect against bacterial invasion? The effect of normal and AP conditioned ML on the growth and survival of intestinal bacteria were examined in a series of studies which demonstrated species and inoculum specific effects. Together these studies provide evidence suggesting that ML contributes to the development of infected necrosis in AP. It also justifies the investigation of new approaches to treatment, including the delivery of lymphophilic antibiotic therapy.

43365 LAPAROSCOPIC DISTAL PANCREATECTOMY PRESERVING SPLEEN AND SPLENIC VESSELS

Overwhelming postsplenectomy infection (OPSI) is a rare but rapidly fatal infection occurring in individuals following removal of the spleen. The infections are typically characterized by either meningitis or sepsis, and are caused by encapsulated organisms including Streptococcus pneumoniae. The lifetime risk of OPSI has been reported to be 5 percent. Thus, spleen-preserving LDP is a required procedure for laparoscopic pancreatic surgeons, because benign or borderline malignancy is a good candidate for laparoscopic distal pancreatectomy. This can be accomplished by preservation of splenic vessels or the Warshaw’s method. Of the two methods, the splenic vessel-preserving method is ideal in terms of splenic circulation. However, preservation of the splenic vessels is currently not popular in laparoscopic spleen preserving distal pancreatectomy (SPDP) owing to the fact that splenic vessels are often embedded in the pancreatic body. We herein report the lateral approach for laparoscopic splenic vessel-preserving distal pancreatectomy (LA-SVPDP) as the most feasible and reliable method for SPDP.

Patients: Twenty six patients underwent laparoscopic SPDP in single institution from 1999 through May 2011. Of them, twelve patients underwent LA-SVPDP.

LA-SVPDP: The greater omentum was divided toward the lower pole of the spleen while preserving the left gastroepiploic vessels and short gastric vessels. Based on the anatomical feature that the splenic vessels are often embedded in the sinus of pancreatic parenchyma with the exception of the pancreatic tail, separation of the pancreas from the splenic vessels was started from the lateral end of the pancreas. When cutting the branches of the splenic vein and artery, we temporarily occluded the splenic artery by applying a vascular clamp at its root to collapse the splenic vessel and control bleeding. Finally, the pancreatic parenchyma was cut by the use of a linear stapler after complete separation of the splenic vessels.

Results: In the group who underwent LA-SVPDP, no patient was converted to open surgery, nor developed pancreatic fistula. Only one patient suffered from occlusion of the preserved splenic vessels postoperatively. However, gastric varices were not detected by endoscopy.

Conclusion: Vessel-preserving SPDP is an ideal method for SPDP, and our lateral approach may make SPDP easier under laparoscopy.
PLECTIN – A NOVEL MARKER FOR PANCREATIC CANCER

Introduction/Background
The diagnosis of pancreatic ductal adenocarcinoma (PDAC) is often challenging due to its similarity to benign lesions, such as pancreatitis. No single commercially available marker has proven entirely specific for PDAC. Plectin-1 may be such a potential biomarker. It is specific for pancreatic malignancy and not expressed in benign pancreatic disease. However, no data on its use on fine needle biopsies (FNB) is currently available. The aim of this study was thus to determine if Plectin-1 is also capable to detect PDAC in FNB compared to the respective resection specimen.

Material & Methods
FNB and resection samples from formalin fixed primary pancreatic cancer and FNB were stained for Plectin-1 using Immunohistochemistry. For comparison samples from primary colon cancers were also stained. Staining was considered positive if more than 1/3 of the cells were at least moderately or strongly stained. Nerves, which showed strong staining served as internal control.

Results
All of the tumors in the fine needle biopsies and their respective resection samples from PDAC were Plectin-1 positive. In contrast, primary colon cancers only showed diffuse cytoplasmic staining in the tumor cells with only one case considered Plectin-1 positive.

Conclusion
Plectin-1 is a specific diagnostic marker for PDAC in FNB and in resections specimen while the majority of colon cancer does not express the protein. Plectin-1 may thus be useful to evaluate FNB as well as resection margins for the presence of cancer cells in pancreatic cancer.
Background: Unexpected aberrant hepatic artery has an incidence of 10-20% and its importance has been underlined in several reports; we assessed the incidence and type of hepatic artery variants in our series of pancreaticoduodenectomy and we investigated its relationship with the outcome of the surgical procedure. Methods: from January 2010 to November 2011 we realized 95 consecutive pancreaticoduodenectomy for periampullary benign and malignant disease: 36 pancreatic adenocarcinoma, 19 ampullary adenocarcinoma, 23 IPMN (15 with adenocarcinoma), 4 chronic pancreatitis, 5 distal bile duct adenocarcinoma, 6 neuroendocrine tumors, 1 duodenal adenocarcinoma and 1 pancreatic liposarcoma. We retrospectively analyzed operation reports of all cases and compared patients with arterial anomalies (group A) and without (group B).

Results: the group A consisted of 19 patients (20%), while group B of 76 (80%). In the group A we had 2 patients with common hepatic artery originating from the superior mesenteric artery (SMA) (Michels type 9), 16 with replaced right hepatic artery (RHA) arising from SMA (Michels type 3) and 1 with accessory RHA (Michels type 6). Preoperatively examination of CT scan by the surgeon revealed the presence of an arterial anomaly in 60% of cases in group A. Intraoperatively 94.7% of the patients had no injury of the aberrant artery during the dissection of the hepatic pedicle; only the patient with accessory RHA experienced accidental lesion. The characteristics of patients in group A and B were comparable: male to female ratio was about 1:1 in both groups, the mean age was 66±12 years in group A and 67±9 in group B, histological diagnosis were homogeneously distributed in both groups. The intraoperative data were: mean operative time 467±74 minutes in group A and 438±60 in group B (p<0.05), mean blood loss 552±609ml and 409±594ml respectively (p=0.18), average red cells volume transfused 318±711ml in group A and 161±398ml in group B (p=0.10). Surgical complications (37% in group A e 48% in group B) and mortality (1 patient in group A and nihil in group B) were similar in both groups. The histological specimens revealed similar number of lymph nodes harvested in both groups (mean 14±7 in group A and 15±6 in group B) and radicality of resection in case of malignant disease was comparable (14% R1 in group A and 16% R1 in group B). Conclusion: the presence of aberrant hepatic artery is observed in about 20% of cases and pre-operative recognized only in 60% of cases; its preservation significantly prolongs surgical time but doesn’t hamper radicality of resection.
Context: Peripheral myelin protein 22 gene (PMP22) encodes a membrane protein of myelin in the peripheral nervous system, and PMP22 duplication causes the Charcot-Marie-Tooth 1A (CMT1A) phenotype. PMP22 is also capable of delaying the transition from G0/G1 to S phase (Growth Arrest Specific Gene 3, GAS3). However, growth factors involved in PMP22 regulation, such as Insulin-like growth factor-II (IGF-II), are up-regulated after radiation in fibroblast cells, and might influence chemo-radiosensitivity. Since the compound NSC-631570 had a protective effect on human fibroblasts but not human tumour cells against ionizing radiation, and showed beneficial effects in phase II studies in metastatic and locally advanced PDAC patients. Objective: the aim of this study was to evaluate the interaction between PMP22, IGF-II and NSC-631570 in PDAC Primary Cell Cultures (PCCs).

Methods: DNA duplication of PMP22 gene was evaluated by PCR and specific digestion by the endonucleases EcoRI and NsII in 13 PDAC tissues, 2 PCCs and PBMCs from 3 healthy subjects (used as negative controls in genetic tests for the CMT1A syndrome). PMP22 protein expression was evaluated in tissues and cells by ImmunoHistoChemistry (IHC), using a quantitative scoring (eg, 0 absent, 1 low, 2 intermediate and 3 high expression). The PCCs were also exposed to IGF-II, NSC-631570, and their combination. Finally, expression of PMP22 was correlated with cell proliferation index.

Results. The PMP22 duplication was observed in 44% (7/16) of PDAC patients and in both PCCs. PDAC duplicated samples showed significantly higher score of PMP22 protein expression (p=0.0262). PMP22 protein was correlated with decreased cell growth, whereas 400 nM IGF-II reduced PMP22 expression and increased cell proliferation. Conversely, the addition of 1µM NSC-631570 increased PMP22 expression, and overcame IGF-II induced proliferation.

Conclusion. This is the first study reporting PMP22 duplication in PDAC specimens and cells. This duplication was correlated with PMP22 expression. PMP22 protein was inversely related to cell proliferation and its inhibition by IGF-II might explain chemo-radiosensitivity caused by PDAC associated fibroblasts. However, NSC-631570 increased PMP22 expression and might synergize with anticancer treatments against PDAC.
Background: The management of pancreatic cancer continues to evolve. We retrospectively analyzed our experience at a tertiary care center over the past fifteen years with regards to patients who underwent potentially curative resection for pancreatic adenocarcinoma.

Methods: Clinical records of 378 patients who underwent surgical resection of pancreatic adenocarcinoma and were treated at a tertiary care referral center over a fifteen-year period (1994-2009) were analyzed. Information regarding demographics, staging and treatment strategies were collected. Pathologic staging was by the AJCC 7th edition guidelines. Trends over this period were analyzed using linear regression modeling.

Results: A median of 22 patients per year were evaluated (range 7-43). There were no significant changes over time with regards to age at diagnosis, gender, or tumor location. Pre-operative cancer staging was unable to be accurately obtained due to limitations in imaging and interpretation. There was a trend for an increasing proportion of patients with pathologic stage 0 and I cancer (p=0.0001, R2=0.66), and a decreasing proportion of patients with pathologic stage II and III cancer (p=0.008, R2=0.39). An increasing proportion over time received neo-adjuvant chemo-radiation, but this was not significant by linear regression (p=0.09, R2=0.19). However, there was a demonstrated moderate association between the fraction of patients receiving neoadjuvant chemoradiation and the fraction of patients with pathologic stage 0 or I (Spearman correlation coefficient=0.63, CI 95% 0.2-0.86, p=0.009). On further analysis, 63% of patients with pathologic stage 0 or I adenocarcinoma received neoadjuvant chemoradiation compared with 25% of patients with pathologic stage II and III cancer.

Conclusion: Pancreatic adenocarcinoma demographics have remained unchanged over the past fifteen years. With an increasing proportion of patients receiving neo-adjuvant chemo-radiation, there appears to be an increasing proportion of combined patients with pathologic stage 0 and I cancer. It remains to be determined whether this has had an impact on overall survival.
43377 SAFETY AND EFFICACY OF CONTINUOUS WOUND INFUSION OF ROPIVACAINE AS POST-OPERATIVE ANALGESIA AFTER PANCREATIC SURGERY

Background: Continuous wound analgesia (CWA) by pre-peritoneal catheter is used in various surgical settings and several studies had demonstrated a satisfactory pain control, reduction of opioids requirements and earlier return to normal bowel function. The analgesic efficacy of CWA for pancreatic surgery is not widely reported in literature, while epidural analgesia or intravenous morphine infusion are currently used. We evaluate the feasibility of CWA and its efficacy to control post-operative pain versus epidural analgesia (EA) and opioids after elective pancreatic surgery.

Methods: From October 2010 to June 2011 78 patients undergoing elective subcostal laparotomy for pancreatic surgery received post-operative analgesia: 31 with CWA of ropivacaine 2%, 16 with continuous EA of ropivacaine 2% plus fentanyl 3mg, 31 with continuous intravenous morphine infusion. We evaluated: quality of analgesia by static and dynamic VAS, use of rescue drugs, post-operative nausea and vomiting, time of first bowel movement, procedure complications.

Results: We didn’t register statistically significant difference in rest (graphic) or dynamic VAS among the 3 groups. In the first postoperative day, 22% with CWA needed other analgesic drugs, while 43% with EA (p=NS). There wasn’t statistic difference among the 3 groups for nausea and vomiting. The median time of first flatus in CWA group was 64,7±22h, in EA group 78±18h and in morphine group 78,6±27h (p=0.5); CWA allowed a more rapid stool canalization (mean 88 h) than morphine (117 h) and EA (110 h) (p<0.05). In CWA group 9% had therapeutic failure, while 25% of patients with EA. The rate of wound infection and hematoma was similar in the 3 groups. In EA a inferior limb paresthesia was observed. No other specific complication were reported. Conclusion: Local anaesthesia infusion at the fascial plane is an effective analgesia alternative to epidural or opioids infusions. CWA is a safe procedure with a more rapid bowel function recovery that influences the post-operative patient rehabilitation.
Objectives
To evaluate the role of an Absorbable Fibrin Sealant Patch (AFSP) in reducing postoperative pancreatic fistula (POPF) after distal pancreatectomy.

Background
Post-operative pancreatic fistula (POPF) remains the main complication following distal pancreatectomy.

Methods
Open, randomized, prospective, multicenter, parallel-group study. Patients undergoing elective distal pancreatectomy were randomized to receive AFSP. The primary end-point was the incidence of POPF according to ISGPF criteria. Amylase level in drainage fluid, number of days until removal of drain and hospital stay were secondary end-points.

Results
A total of 275 patients were enrolled in 19 Italian centers in a 2-years period: 145 pts received AFSP and 130 pts were the control group. Surgical indication was: pancreatic cancer in 33%, cystic neoplasm/IMPN in 34%, endocrine neoplasms in 22% and other in 11%. Laparoscopy was applied in 20% of patients and spleen preserving resections in 21%. The closure of pancreatic stump was mechanical in 31% and manual in 68% (manual+mechanical in 1%).

The incidence of POPF was 62% in AFSP and 68% in Control Group (p=0.267). Grade A fistula rate was 54% in AFSP and 55% in Control Group; Grade B+C fistula rate was 8% and 14% respectively (p=NS). Drainage amylases level at Day 1 was significantly reduced in AFSP patients (p=0.025). The mean number of days until drainage removal was 10.8 ± 10.9 in AFSP and 13.9 ± 17.1 in Control Group (p=0.077). In Grade A fistula patients, the drainage removal was significantly shortened in AFSP group (p=0.048). The hospital stay was 11.7 ± 5.6 in AFSP and 12.8 ± 7.7 in Control Group (p= 0.184).

Conclusions
The POPF rate was higher than expected when ISGPF criteria were strictly applied even if the majority were biochemical fistulas. There was no significant difference between patients treated or not by AFSP; however the significant reduction of amylases level in drainage fluid suggests a possible role of AFSP as a sealant of the pancreatic remnant.
43380 TISSUE PHARMACOKINETICS OF INTRAOPERATIVE GEMCITABINE INFUSION IN RESECTABLE PANCREATIC ADENOCARCINOMA: RESULTS OF A PILOT CLINICAL TRIAL

Introduction
A distinctive feature of pancreatic adenocarcinoma (PDAC) is inefficacy of systemic therapies. Evidence suggests the significant tumor/stromal barrier in these tumors leads to inadequate drug delivery. Gemcitabine (Gem), a nucleoside analogue first-line agent, has only demonstrated limited responses. Previous clinical trials only measured Gem in peripheral blood mononuclear cells, a surrogate for tissue, and none ever confirmed Gem (or other oncologic drugs) within in-vivo human cancers. Using a novel intraoperative platform and assay that measures Gem incorporation into DNA, we examined tissue Gem levels after intraoperative delivery in patients with resectable PDAC.

Methods
As part of IRB approved trial, untreated patients underwent intraoperative Gem infusion at fixed dose rate (10mg/m2/min) during resection (Figure-1A). Intraoperative methodology was required due to short half-life of Gem. Blood samples were taken for intraoperative pharmacokinetics. Following resection, samples from normal (duodenum, gallbladder, spleen, uninvolved pancreas) and tumor tissue (peripheral and central). Utilizing liquid chromatography-mass spectrometry, relative levels of Gem incorporation within specimen DNA were compared between normal/cancerous tissues. IHC for Gem transporters was performed. Patients followed for hematologic toxicities and surgical related complications for 30 days.

Results
Of 22 patients approached, 12 consented and completed protocol. Asymptomatic, transient grade 2/3 neutropenia developed in 6 patients with no infectious complications. One patient developed venous thromboembolism; otherwise no surgical complications. Assay revealed relative levels of DNA-incorporated Gem did not differ significantly between normal and cancerous tissues (Figure-1B), however there was significant individual patient-tumor variability. IHC for Gem transporters correlated with assay.

Conclusions
Initial experience with this first-in-kind intraoperative platform demonstrates its safety, accrual capabilities, and prospects in drug testing for PDAC. Preliminary analysis of mid-study data suggests individual variability in Gem incorporation into tumor DNA after intravenous delivery, however definitive evidence of tumor/stromal barrier to chemotherapeutics is not supported. Further research is underway to examine mechanisms behind these novel observations.
A.

Serum Samples ↓

Initial Blood Draw

Drug Infusion Start

Infusional Blood Draws

Final Blood Draw

Drug Infusion End

Patient Brought into OR

Patient Intubated and prepped for Surgery

Diagnostic Laparoscopy for occult Metastases

Resectable

Open Incision and Resectability Assessment

Start of Specimen Resection

Specimen Out and Samples Obtained

Operation Complete

Metastatic

Excluded from Study

Unresectable

B.

B.  

<table>
<thead>
<tr>
<th>Specimen</th>
<th>dF/dG(pg/ug)</th>
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<tbody>
<tr>
<td>GB</td>
<td>0.6</td>
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<tr>
<td>SP</td>
<td>0.5</td>
</tr>
<tr>
<td>DM</td>
<td>0.4</td>
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- **Galbladder**: served as negative control as removed before Gem infusion
- **Spleen**: ligated mid Gem infusion
**INTRODUCTION/BACKGROUND:** Pancreatic ductal adenocarcinoma (PDA) is the fourth leading cause of cancer related death in the United States with a 95% five-year mortality rate. Gemcitabine remains the standard of care for first-line systemic therapy despite a median survival benefit of approximately three months over best supportive care. A new class of chemotherapeutic agents, the PARP inhibitors, target DNA damage repair mechanisms. Ubiquitin-Specific Peptidase 11 (USP11) is one member of these DNA repair complexes that functions as a pathway regulator via deubiquitination of BRCA2 and other DNA repair proteins. PARP inhibition has been demonstrated to improve survival in randomized studies in ovarian and breast cancer and investigation into their use in PDA has begun.

**METHODS:** In a systematic high-throughput approach, we biochemically screened 2500 FDA-approved compounds for the inhibition of USP11 enzymatic activity. We then performed in vitro drug sensitivity assays with identified compounds against several PDA cell lines (MiaPaca-2, PL5, ASPC-1, Panc1) utilizing gemcitabine as a control agent. Utilizing these results we narrowed candidate agents to those with effects on PDA cell survival in the nanomolar range. We then used a targeted siRNA oligo to silence USP11 in PDA cell-lines and re-evaluated sensitivity and targeting of candidate compounds including gemcitabine as a control.

**RESULTS:** Our screen identified 6 potent and specific USP11 inhibitors that included sennoside A, sennoside B, and mitoxantrone (an IC50, corrected for quench of 3.15). The latter agent was previously believed to be a type II topoisomerase inhibitor and has been used clinically to treat certain leukemias, advanced breast cancer, prostate cancer and multiple sclerosis. Of the six, only mitoxantrone inhibited PDA cell growth with an IC50 of less than 1000 nM. Across six different PDA cell lines, mitoxantrone (nanomolar range) is 40-20,000 fold more potent than gemcitabine (micromolar range), with increased endogenous USP11 mRNA levels associated with increased sensitivity to mitoxantrone. USP11 silencing in a PDA cell line using targeted siRNA oligos sensitized the cells even further under mitoxantrone exposure, providing further mechanistic evidence. Additionally, USP11 silencing enhanced sensitivity to gemcitabine roughly 10-fold, suggesting synergistic activity between mitoxantrone and gemcitabine.

**DISCUSSION/CONCLUSION:** These data identify USP11 as a ‘druggable’ target in PDA and demonstrate that an available FDA approved agent, mitoxantrone, is a promising and effective USP11 inhibitor in this disease. Moreover, USP11 may prove to be a robust and efficacious predictive biomarker for mitoxantrone and gemcitabine based therapies. Our systematic drug screen provides a logical paradigm for developing and evaluating a targeted therapeutic strategy against critical DNA repair enzymes, demonstrated here with USP11. We strongly believe these studies warrant clinical evaluation for PDA treatment with mitoxantrone as a single agent approach; or more realistically, mitoxantrone in combination with another targeted DNA disrupting agent such as a PARP inhibitor.
Patients identified at surgical exploration with unresectable pancreatic ductal adenocarcinoma (PDAC) go on to receive palliative, not curative therapy. Our hypothesis is that accurate radiographic re-staging, multimodality treatment, and advanced surgical technique offers patients deemed unresectable at previous exploration the possibility of a curative re-operative pancreatectomy.

**Background:**
Patients identified at surgical exploration with unresectable pancreatic ductal adenocarcinoma (PDAC) go on to receive palliative, not curative therapy. Our hypothesis is that accurate radiographic re-staging, multimodality treatment, and advanced surgical technique offers patients deemed unresectable at previous exploration the possibility of a curative re-operative pancreatectomy.

**Study Design:**
Review of a prospectively maintained PDAC database identified patients (1990-2010) evaluated after being deemed unresectable at first exploration elsewhere. Referring hospitals were categorized per National Cancer Data Base criteria (Academic, Community, International). Patients were re-staged using objective imaging (CT) criteria and treated based upon anatomic resectability. Clinicopathologic factors and cancer-related outcomes were assessed.

**Results:**
We evaluated 88 patients who underwent previously unsuccessful resection attempts at Academic (n=50), Community (n=25) and International (n=13) centers. Radiographic re-staging confirmed that 7 (8%) patient tumors were locally advanced and unresectable, but 81 (92%) were resectable (n=61) or borderline resectable (n=20). Using a surgery first (9%) or preoperative chemoradiation (91%) approach, 15 (19%) patients developed metastatic disease prior to re-resection attempt. Successful re-operative pancreatectomy was performed in 66 (81%) of patients. Major vascular resection/reconstruction was required in 30 (46%) patients with 94% receiving R0 resections. Complex revision of previously created palliative biliary/gastrointestinal bypass was required in 61 (94%) of patients. Mean operating time, estimated blood loss, and hospital stay was 543 minutes, 1390 milliliters, and 12 days respectively. The major complication rate was 20% and 3 (4.5%) patients died perioperatively. The median overall survival was 29.6 months for resected patients vs. 10.5 and 5.1 months (p < 0.0001) for locally advanced unresectable patients or those that developed metastatic disease prior to resection, respectively.

**Conclusions:**
In this high-risk cohort, a significant number of patients previously deemed unresectable had anatomically resectable tumors. Accurate radiographic re-staging, a multimodality treatment strategy, and advanced surgical technique may provide an opportunity for cure in a significant proportion of patients previously deemed unresectable at exploration.
Overall Survival Probability %

Unresectable at Referral (n = 7)
Median OS = 10.5 months

Metastasis Identified Prior to Re-resection (n = 15)
Median OS = 5.1 months

Successfully Resected (n = 66)
Median OS = 29.6 months

P < 0.0001
NS
CIRCADIAN GENES IN PANCREATIC DUCTAL ADENOCARCINOMA: ALTERATIONS AND CLINICAL CORRELATIONS

Background: The circadian rhythm regulates various metabolic processes, physiologic homeostasis and behavior. Epidemiologic studies have demonstrated that disruption of the circadian rhythm is associated with cancer development and tumor progression. Several circadian clock genes with tightly connected transcriptional feedback loops have been implicated in loss of cell cycle control, impaired DNA damage repair, and subsequent tumor formation in multiple cancer models. However, the direct links between aberrant circadian clock gene expression and human pancreatic ductal adenocarcinoma (PDA) have not been elucidated. In this study, we investigated the expression profiles of several circadian clock genes in PDA.

Methods: We analyzed the expression of 10 circadian clock genes in matched invasive human PDA (n=62) and surrounding adjacent tissues and in benign lesions (n=10). Quantitative real-time polymerase chain reaction (qPCR) was used to examine the following core clock genes: (BMAL, Clock, Cry1, Cry2, CK1E, Per1, Per2, Per3, Timeless, Timeless-interacting protein). Gene expression levels were correlated with clinicopathologic parameters. Receiver operator curve (ROC) analysis was completed using logistic regression based on individual circadian genes measured in tumor and benign samples, and is reported as area under the ROC curve (AUC). Spearman correlation was used to assess the relationship between circadian genes within tumor samples. Univariable Cox models were completed to assess survival of PDA patients, using the median gene expression level as stratification factor.

Results: In the tumor tissue of PDA patients, compared to their matched adjacent tissue, expression levels of all circadian genes were significantly lower (P<0.05). Benign tissues also expressed significantly (P<0.05) higher levels of all circadian genes when compared to malignant lesions. Spearman correlations of all 10 genes in tumors showed significant correlations of their expression levels ranging from 0.57 to 0.93, p<0.001 in all cases. Univariable survival analysis indicated that Per2 (p=0.004), Per3 (p=0.007), Cry2 (p=0.016), Tim (p=0.016) and CK1E (p=0.024) are significantly related to survival.

Conclusions: Our results reveal for the first time a disturbed transcription of several circadian genes in PDA. Elevation of the gene levels in the benign and matched adjacent tissues may be indicative of their role during the process of tumorigenesis. Altered expression of Per2, Per3, Cry2, Tim and CK1E in PDA provides the basis for future studies to explore their validity as predictive markers of the outcomes and survival in PDA patients.
Background: The prevalence of diabetes mellitus (DM) in patients with pancreatic ductal adenocarcinoma (PDAC) ranges from 20% to 80% at the time of diagnosis. In patients amenable of resection, it is unclear whether DM represents a risk factor for postoperative morbidity. In this study a very large population of patients undergoing pancreatectomy for PDAC was analyzed to address this issue.

Methods: Retrospective analysis of patients with PDAC resected between 2000 and 2010 at the Unit of General Surgery B, University of Verona. A set of pre- and intraoperative variables were analyzed using univariate and multivariate models.

Results: Study population consisted of 631 patients. 130 patients (20.6%) were diabetics. 95/130 patients (73.1%) were classified as having longstanding DM, while 35/130 (26.9%) had a new-onset DM. Diabetics had a greater median age and BMI, but lost more weight unintentionally within 6 months from the diagnosis (all p=0.001). These variables did not differ between patients with a new-onset or longstanding DM. Postoperative morbidity was similar in the two groups, but the rate of pancreatic fistula (PF) was greater in non-diabetics (16.0% versus 7.7%, p=0.034), who were also more likely to have a hard pancreatic texture (p=0.02). Mean postoperative stay was shorter in non-diabetics (12.4 versus 14.5 days, p=0.01). The rate of PF was similar in patients with a new-onset and longstanding DM (7.4% versus 8.6%, p=1). Comparison of variables in patients who did and did not develop PF showed that male sex (p=0.03), higher BMI (p=0.015), DM (p=0.034), unintentional weight loss (p=0.001), pancreatic texture (p=0.001), intra-abdominal collections (p=0.0001), post-operative acute pancreatitis (p=0.0001), post-pancreatectomy haemorrhage (p=0.01), pulmonary complications (p=0.0001), and acute renal failure (p=0.021) were associated with PF. In multivariate analysis DM maintained an independent association with PF, with an odds ratio of 0.460 (95% CI 0.21-0.99, p=0.04). Additional variables associated with an increased probability of a PF formation were male sex (p=0.037), BMI (p=0.043), unintentional weight loss (p=0.003), soft pancreatic texture (p=0.03), intra-abdominal collections (p=0.001).

Conclusion. Preoperative DM is not a risk factor for postoperative morbidity after pancreatectomy for ductal adenocarcinoma. The decreased incidence of PF in diabetics is likely to be a consequence of a harder pancreatic texture, although there was no difference in PF rate or pancreatic texture between patients with a new-onset or longstanding DM.
Introduction
Mounting evidence indicates that Ion Channels and Transporters (ICT) are expressed aberrantly in cancer and underlie many of the hallmarks of cancer. Proving their therapeutic potential, treatments targeting Cl-channels and carbonic anhydrase IX have successfully entered phase II clinical trials in brain and kidney cancer. Thus, proteins involved in membrane transport, long known as important drug targets in other diseases (channelopathies), are a new class of therapeutic and/or diagnostic targets in oncology. In the recent past we demonstrated that, among ICTs, the ether-a-gò-gò-related gene (hERG1) potassium channels are expressed in several types of human cancers. hERG1 has a pleiotropic regulatory effect on cancer (cell proliferation, survival, invasiveness and angiogenesis). Finally, hERG1 is emerging as a novel prognostic marker in acute leukemias and GI tract cancer. We report the preliminary results of a study on hERG1 expression in pancreatic cancer.

Materials and Methods
hERG1 expression was evaluated by immunohistochemistry using Tissue MicroArray (TMA) technology. Arrays were constructed using paraffin blocks of 15 cases of pancreatic ductal adenocarcinoma (PDAC) (median age: 68 aa; M: 7; F: 8) consecutively collected at the Campus Bio-Medico University from March 2007 to December 2007; in each case, two 1mm-diameter cores were punched in a predefined tumor region while two additional cores were punched in an adjacent non-neoplastic area. Follow up was available in all cases but one. Immunohistochemistry was performed using a monoclonal anti-hERG1 antibody raised by us. hERG1 immunostaining was evaluated on the basis of a semiquantitative score system taking into account percentage and staining intensity of tumor cells. To have an insight into the functional significance of hERG1 expression in PDAC, we further analyzed several human PDAC cell lines, using real-time quantitative PCR, western blot, immunofluorescence and patch clamp techniques.

Results
A hERG1 specific immunostaining was observed in Langherans islets, mainly attributable to the expression in beta cells, whereas no expression was detected in normal pancreatic parenchyma. Conversely, a moderate to intense signal was observed in over 50% of tumor cells of 10/15 PDAC. The median overall survival was 18.5 (95%CI: 14.5-26.5) months in hERG1 positive patients and was longer (tending to significance) in patients without hERG1 protein expression (29 months, 95%CI: 28-33.5; p<0.1). In addition, in vitro experiments showed that (1) hERG1 is expressed on the plasma membrane of PDAC cells, where it gives rise to functional potassium currents; (2) hERG1 and integrins form a functional, signaling complex in PDAC cells and (3) such complex regulates PDAC cell motility and invasion.

Conclusion
Our preliminary results suggest that hERG1 might represent a novel prognostic marker and a potential target for therapy in PDAC.
43388 VIDEO: LAPAROSCOPIC PPPD AND LAPAROSCOPIC RECONSTRUCTION VIA PANCREATOGASTROSTOMY

Introduction: Despite of the spread of laparoscopic approaches in GI surgery laparoscopic pancreatic surgery of the pancreas is still only performed in a very limited fashion by very few highly specialized surgeons. On the other hand prophylactic pancreatic surgery for cystic and premalignant lesions has an immense increase and offers a wide spectrum of indications for laparoscopic surgery of the pancreas.

Method: Since 2009 we perform laparoscopic pancreatic resections in our hospital. Since 2010 we performed 15 laparoscopic pylorus preserving pancreatic head resections (Lap-PPPD) with complete laparoscopic resection and reconstruction with hybrid reconstruction via open pancreatogastrostomy. We have now developed our hybrid reconstruction to a total laparoscopic reconstruction via pancreatogastrostomy.

Results: The video demonstrates the laparoscopic PPPD and reconstruction via pancreatogastrostomy. The postoperative histology showed a pT3 N0 (0/18) G1 R0 duodenal cancer. The postoperative course was uneventful. The time for the operation was 436 minutes; the postoperative hospital stay was 10 days. The video demonstrates the surgical technique and possible pitfalls of the laparoscopic pancreatic head resection and a previously non-described technique for laparoscopic reconstruction of the pancreatic remnant. For review the video is posted on http://www.youtube.com/watch?v=g-S5Vw2uc5k&feature=youtu.be

Conclusion: In our video we demonstrate that pancreatic head resections and reconstruction can be safely performed via laparoscopy. The gradual development of a hybrid approach to a complete laparoscopic reconstruction guaranteed in our collective for a safe and standardized reconstruction with no concessions to safety.
Perhaps the greatest challenge to adoption of the laparoscopic radical pancreaticoduodenectomy is the technical challenge of the pancreaticojejunostomy. We present an intussuscepting technique utilizing a running, single layer of absorbable, monofilament suture (5 min video). After the neck of the pancreas is fully mobilized, a 36-cm suture is fashioned by tying two 18 cm 4-0 polydioxanone sutures together. The sutures are positioned to ultimately produce an intussusception of approximately 1 cm. The initial suture is placed tangential to the transected surface of the reconstructive limb on the anti-mesenteric border. The suture is then similarly passed through the cephalad aspect of the pancreas. The next few posterior wall sutures are placed and the suture then parachuted to achieve tissue apposition. Anterior tension is maintained and exposure facilitated during subsequent sutures utilizing a diamond-dust coated instrument. The posterior row is completed at the mesenteric border of the jejunal limb and caudal aspect of the pancreas with tension maintained by the placement of a Lapra-Ty®. The anterior aspect of the anastomosis is completed in an identical fashion. A second Lapra-Ty® is applied allowing knot creation without the challenge of maintaining appropriate tension. In a consecutive series of 21 patients since this technique was adopted in March 2011, the leak rate has been 10.5% (ISGPS criteria) with an average time for the anastomosis being 24 minutes. Only two patient have left the hospital with a drain in place in this series. We conclude that this single-layer, running, intussuscepting technique for pancreaticojejunostomy presents fewer technical challenges and produces acceptable results compared to other techniques.
Background: With increasing scrutiny being placed on the allocation of health care dollars, data supporting the increased time and expense associated with teaching residents in the operating room is lacking. Our hypothesis was that lower post-graduate year (PGY) level is associated with longer procedure times for basic procedures such as laparoscopic cholecystectomy (LC), but not for more complex procedures such as pancreaticoduodenectomy (PD).

Methods: All cases of patients undergoing LCs and PDs at a single institution from July 1, 2006 to July 1, 2011 were analyzed. Demographic data, including patient age, sex, and body mass index (BMI) as well as operative data, including surgical indication, estimated blood loss (EBL), resident PGY level, and total procedure minutes were recorded. LCs were excluded when converted to an open procedure or cholangiogram was required. PDs were excluded if additional procedures were performed. Multiple linear regression was used to evaluate the association between procedure time and PGY year, adjusting for patient age and estimated blood loss.

Results: A total of 236 PDs and 357 LCs were included in the study. For LCs, after adjusting for patient age and estimated blood loss, the association between procedure time and resident PGY was marginally significant (p=0.0519) and suggested an inverse relationship; for every unit increase in resident PGY, there was a 2.66 minute (unit) decrease in OR time. For PDs, however, the association between procedure time and resident PGY did not reach statistical significance (p>0.05). On multivariate analysis, estimated blood loss (EBL) independently predicted longer procedure times for both LC and PD.

Conclusion: These data suggest that for both basic and complex surgical procedures, EBL is an independent predictor of increased procedure time. Resident PGY may affect the length of the procedure for basic procedures such as LC, but not for more complex procedures such as PD.
Introduction: Pancreatic tumors are a diverse group of neoplasms with distinct clinicopathological features and biological behaviors. Over the past four years there has been an explosion in our understanding of the genetics of these neoplasms. Our group has sequenced the exomes of six of the most common types of tumors of the pancreas, including pancreatic adenocarcinoma (PA), pancreatic neuroendocrine tumors (PanNET), intraductal papillary mucinous neoplasms (IPMN), mucinous cystic neoplasms (MCN), serous cystadenomas (SCA) and solid pseudopapillary neoplasms (SPN). We now report here some of the clinical implications of these data.

Method: Using either Sanger or next generation sequencing methods (massively parallel sequencing, Illumina Platform) the whole exome sequence was determined for 24 PA, 10 non-familial PanNET, and 8 of each of the following: IPMN, MCN, SCA and SPN.

Results: 1) exome sequencing of PD lead to the discovery of PALB2 as a familial pancreatic cancer gene (Science 2009). This discovery can be used by genetic counselors as it has implications for breast, ovarian and pancreatic cancer risk, and has therapeutic implications as PA with PALB2 mutations may be more sensitive to DNA cross-linking agents such as mitomycin C (Mol Cancer Ther. 2011). 2) Sequencing of multiple lesions of PA from the same patient helped define the genetic progression of PA and demonstrates the existence of a window of opportunity for the early detection of pancreatic neoplasia (Nature 2010). 3) Sequencing the exomes of PanNETs lead to the discovery of mTOR pathway gene mutations (TSC2, PIK3CA, PTEN) and PanNETs appear to be sensitive to mTOR inhibitors (Science 2011). Sequencing mTOR pathway genes in PanNETs may be a way to prioritize patients for therapy with an mTOR inhibitor. 4) Sequencing of all of the established cancer-associated genes in the cyst fluids of IPMNs led to the discovery of GNAS mutations in IPMNs, suggesting that sequencing of endoscopic sampled of cyst fluid for GNAS and KRAS gene mutations could be used to differentiate an IPMN from a SCA. (Sci Trans Med 2011). 5) Sequencing of the neoplastic epithelium of IPMNs, MCNs, SPNs and SCNs defined a panel of genes that could be used to classify each cyst type (PNAS 2011). SCNs are characterized by mutations in VHL; SPNs by beta-catenin mutations; IPMNs by RNF43, GNAS and KRAS mutations; and MCNs by RNF43 and KRAS gene mutations.

Discussion: The genetic landscape of pancreatic neoplasms been described. The underlying genetic
difference among the neoplasms mirrors their distinct biological differences. The challenge for clinicians will be to take advantage of these discoveries and to use them to improve patient care.
43395 COMPARISON BETWEEN MDCT POST-CONTRASTOGRAPHIC PATTERN AND MICROVASCULAR DENSITY (MVD) IN PANCREATIC NEUROENDOCRINE TUMORS: CORRELATION WITH THE NEOPLASMS NATURE.

At the state of the art, pre-operative suspicion of neuroendocrine pancreatic neoplasms nature arises both from clinical and imaging finding. If clinical criterium generally adopted in order to formulate a diagnosis of benign lesion is related to the presence and the type of secreted hormone, imaging suggestion of lesion nature is based quite only on nodular dimension and on the presence of local and distant spreading. Aim of the study was to determine the nature of neuroendocrine pancreatic neoplasms by analysing lesions enhancement pattern at MDCT (multidetector CT) and by comparing it with histological findings, including the microvessel density (MVD) analysis.

We included 45 patients submitted to surgical resection for pancreatic neuroendocrine tumor. All preoperative CT examinations were performed by a multidetector CT. Post-contrastographic study included 4 phases: early arterial (delay 15-20”), pancreatic (delay 35”), venous (delay 70”) and late phases (delay 180”). Two different patterns of enhancement were defined: pattern A, including lesions showing early enhancement (during early arterial or pancreatic phase) and a rapid wash-out; pattern B, including lesions with wash-in in the early arterial or pancreatic phase with no wash-out nor in the late phase (pattern B1), and lesions showing enhancement only in the venous and/or late phases (pattern B2).

Sixty-six lesions were detected in 45 patients. Of these lesions, 30 (45%) showed a pattern of type A (average diameter at CT-adCT: 11mm), 26 (39%) a pattern B1 (adCT: 32mm) and 10 (16%) a pattern B2 (adCT: 47mm).

At pathology, 28/66 (43%) lesions were classified as adenomas, 14 (21%) as borderline tumors and 24 (36%) as well differentiated carcinomas. In particular, 24/30 (80%) showing pattern A (average diameter at histology-adH: 9mm) resulted to be benign (adH: 9mm), 5 borderline (adH: 15mm) and 1 resulted to be a low grade carcinoma (10mm). Twenty-three out of 36 lesions (64%) showing pattern B resulted to be low grade carcinomas (adH: 41mm), 9 borderline (adH: 16mm) and 4 adenomas (adH:13mm). Among the 26 B1 lesions, 13 (50%) were carcinomas, 9 borderline and 4 adenomas, while all 10 B2 lesions were malignant.

Overall, the pattern A showed a positive predictive value (PPV) of benignancy of 80%, while pattern B showed a negative predictive value (NPV) of benignancy of 89%.

The microvascular density (MVD), expressed by number of vessels/surface unit after CD34 staining, was evaluated in 20/66 lesions (5 adenomas, 4 borderline lesions e 11 carcinomas). We demonstrated significant differences in MVD among the 3 histological subtype (p=0,002) and the 3 enhancement pattern at CT (p=0,04). In particular, malignant lesions demonstrated low MVD, while lesions with pattern A showed high MVD. Moreover, we obtained significant differences between B1 and B2 malignant lesions, by considering metastases (only in B2 carcinomas) and fibrosis (all B2 lesions). The low MVD of B2 lesions, associated with the presence of fibrosis, may justify the delayed enhancement of these lesions. In conclusion, the enhancement pattern at CT is related to MVD and the histological type, thus representing a further criterium for suggesting nature of neuroendocrine lesions.
A NEW SURGICAL TECHNIQUE FOR PANCREATIC HEAD-BODY CANCER WITH SPLENIC ARTERY INVASION: PROXIMAL SUBTOTAL PANCREATECTOMY WITH SPLENIC ARTERY AND VEIN RESECTION (PSP-SAVR)

[Introduction/Background]
Pancreatic adenocarcinoma arising from the head-body region often invades the origin of splenic artery and thus we cannot be able to avoid total pancreatectomy (TP). Although TP can be safely performed, it results in an extreme form of pancreatogenic diabetes: iatrogenic hypoglycemia affects patient’s QOL and prognosis. For such tumors, we developed a new surgical technique of proximal subtotal pancreatectomy with splenic artery and vein resection (PSP-SAVR) usually after preoperative chemoradiotherapy in consideration of the balance between operative radicality and postoperative QOL. Blood flow to the pancreas tail can be obtained by the left gastroepiploic artery and posterior epiploic artery even if we have to resect the left gastric artery combined with total gastrectomy and splenectomy (Mizuno & Isaji, Surgery Today, 2011).

[Method]
From February 2005 to December 2011, we performed proximal pancreatectomy in 56 patients with pancreatic adenocarcinoma: PSP-SAVR in 13 patients (T3:4, T4:9) and pancreaticoduodenectomy (PD) in 43 patients (T3: 30, T4: 13). Most patients were treated by preoperative chemoradiotherapy (45 Gy radiation in 25 fractions with 800 mg/m2 gemcitabine weekly intravenously for 5 weeks including one-week break) or preoperative chemotherapy (S-1: tegafur, gimeracil, oteracil potassium : 60 mg/m2 p.o. b.i.d. from day 1 to 21 and gemcitabine :600 mg/m2 on Day8 and 21). PSP-SAVR group received chemoradiotherapy in 10 and chemotherapy in 2. PD group received chemoradiotherapy in all 43. We compared the two groups with respect to prognosis and postoperative pancreatic function. Prognosis was evaluated by 1- and 3-year survival rate and median survival times (MST). Pancreatic function was measured preoperatively, and at 1, 3, 6 and 12 months postoperatively: glucose control (FBS, HBA1c, insulin therapy), lipid metabolism (cholesterol), nutrition (weight, alb), frequency of bowel movement and amount of pancreatic enzyme supplementation.

[Result]
Overall 1- and 3-year survival rates and MST in PSP-SAVR vs. PD groups were 67.5%, 45% and 23.5 months vs. 64.7%, 40.6% and 24.9 months, respectively (p=0.69). With regard to pancreatic function, glucose tolerance in PSP-SAVR group was significantly impaired, but there were no obvious hypoglycemic attacks and deterioration of QOL. PSP-SAVR group needed large amounts of pancreatic enzymes, but there were no significant differences in lipid metabolism, nutrition and frequency of bowel movement.

[Conclusion]
PSP-SAVR with preoperative chemoradiotherapy or chemotherapy seems to be promising surgical strategy for pancreatic head-body adenocarcinoma with invasion of the origin of splenic artery, in regard to the balance between operative radicality and postoperative QOL.
MICRORNA BIOMARKERS IN PANCREATIC CANCER STRATEGIES TOWARD THE CREATION OF A COMPREHENSIVE AND ACCURATE BIOMARKER PROFILE.

Background: MicroRNAs are small noncoding 20-22 nucleotide RNAs which are stably expressed in tissue and body fluids. To date, no comprehensive molecular pathway-driven miRNA biomarker profile for pancreatic cancer has been created. Previous approaches, including qRT-PCR, can identify known miRNAs only, and cannot be used to assay novel miRNAs or miRNA isoforms (isoMirs). Identification of isoMirs is essential as they can provide insight into gene misregulation due to miRNA polymorphisms, mutations, and modifications, all of which can influence disease formation and progression. High-throughput sequencing of miRNA cDNA libraries offers a tool for the quantification of miRNAs, discovery of novel miRNAs, and detection of isoMirs. Our aim is to report our systematic evaluation of potential pitfalls of miRNA translational research, our solutions, and our preliminary results.

Methods and Results: In order to identify circulating pancreatic-cancer associated miRNAs, after IRB approval and individual informed consent, a prospective cohort of patients with pancreatic cancer as well as noncancer controls was established. For this initial screen and methods development, 130 plasma samples with full phenotypic data available were identified, and divided into 6 groups: cases (unresected pancreatic cancer, resected pancreatic cancer, interval draw on pancreatic cancer patients after-resection), and controls (pancreatic cystic neoplasm, pancreatitis, and healthy volunteers). Steps toward developing a miRNA panel for pancreatic cancer have including the following:
   1) we first identified an inhibitor in miRNA assays, with subsequent elimination of the inhibitor’s confounding effect on miRNA counts; 2) we developed a protocol for reliable and reproducible extraction of RNA from plasma samples; and 3) we conducted screening of miRNA isolated from these plasma samples using qRT-PCR to study levels of 700 miRNAs using available miR-Taqman assays. Finally, 4) we developed a novel streamlined method to isolate and clone miRNA to produce miRNA cDNA libraries. While working towards creation of these libraries, preliminary data shows that our method addresses the lack of sensitivity and sample loss associated with previous small RNA cloning protocols. cDNA libraries from the 6 cohorts described above are currently being created and, from these, we will be able to assess the quantity and identity of circulating miRNAs.

Conclusion: Using a pancreatic cancer cohort and control cohorts, we developed new techniques to mainstream the collection and processing of miRNA from human plasma samples, while allowing for sufficient miRNA volume for analysis. We further mainstreamed miRNA qRT-PCR Taqman assays, and developed a protocol for creation of cDNA libraries from this miRNA. Further studies in larger cohorts are being conducted to expand and validate our preliminary findings.
ACHIEVING AN R0 MARGIN BY INTRAOPERATIVE FROZEN SECTION ANALYSIS DURING PANCREATICODUODENECTOMY HAS A BENEFICIAL IMPACT ON SURVIVAL

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OBJECTIVE: To examine whether re-resection to obtain negative margins after positive intraoperative frozen section analysis imparts a survival benefit after pancreaticoduodenectomy for pancreatic adenocarcinoma.

METHODS: From 1994 to 2006, 1000 consecutive patients with pancreatic adenocarcinoma underwent pancreaticoduodenectomy with systematic analysis of margins (neck, uncinate, proximal duodenum/gastric, bile duct, and vascular groove as indicated). Resections were classified as R0 (margin microscopically negative), R1 (margin microscopically positive), R1→0 (margin microscopically positive initially, re-resected to negative), and R2 (margin grossly positive).

RESULTS: There were 618 (62%) R0, 211 (21%) R1, 94 (9%) R1→0, and 77 (8%) R2 resections. Median overall survival after R1→0 resection was 23 months, which was similar to R0 resection (20 months, P=0.59) and superior to R1 resection (14 months, P=0.002, Figure). Of 94 R1→0 resections, 25 were extended to total pancreatectomy resulting in similar survival compared to re-resections not requiring total pancreatectomy (19 vs. 24 months, P=0.46). Among patients with a positive margin on initial frozen section (R1 and R1→0), the ability to convert to an R1→0 resection was independently associated with improved survival (P = 0.07) after adjusting for tumor grade, nodal metastasis, and vascular invasion.

CONCLUSION: Extending resections to achieve negative margins based on intraoperative frozen section should be standard practice during pancreaticoduodenectomy for pancreatic adenocarcinoma. This strategy confers survival equivalent to R0 resection and superior to R1 resection.
Cumulative Survival

Time (Months)

R0 vs R1, P = 0.59
R1 vs R0, P = 0.002
R1 vs R2, P < 0.001
Background: Pancreatic texture has been identified as one of the most important risk factors for postoperative pancreatic fistula. Texture definition (classically soft/hard) is however subjective and based on intraoperative gland palpation. The aim of this prospective study was to develop a reproducible method to assess pancreatic texture by using elastic module measurement.

Methods: Study population consisted of 140 patients who underwent pancreatic resections at our institution from November 2010 to November 2011. Before pancreatic transection, a calibrated coiled valve was employed to test pancreatic resistance to compression. Texture was expressed by using pancreatic elastic module (Newton/mm²). Measurements were then correlated with a pathologic score (0-100) based on percentage of fibrosis, pancreatic acini and fat infiltration of the resection margin. Furthermore, the pancreas was palpated by an experienced surgeon (blinded to the elastic module measurement) who subjectively assessed texture on a 1-to-10 scale.

Results: There was a significant correlation between pancreatic elastic module and pathologic score (p=0.005). In order to define “soft” and “hard” texture, an arbitrary cut off was set at the 75th percentile for pathological score (Total amount of fibrosis >45%). Mean values of elastic modules for soft/hard pancreas did differ significantly (p<0.001), and – surprisingly – surgeon’s manual evaluation correlated with both elastic module and pathological assessments.

Conclusions: Pancreatic texture can be assessed using elastic module. This is a reproducible method which may represent a common framework for future multicentric studies. The next step of this analysis will be the correlation between pancreatic texture assessed by elastic module and the development of postoperative pancreatic fistula.
Introduction: Aptamers are oligonucleotide ligands that directly bind protein targets and can be used for the dual purpose of identifying novel biomarkers and, simultaneously, reagents to detect them in body fluids.

Methods: We used a positive/negative in vitro selection strategy (Systematic Evolution of Ligands by EXponential enrichment or SELEX) to identify RNAs—modified with 2'-fluoro-pyrimidines for nuclease resistance—that bind to the secretome (prepared from serum-free conditioned media) of the human pancreatic cancer cell line MiaPaCa-2 but not the non-cancerous pancreatic ductal epithelial cell line HPDE-E6E7 (gift of M.S.Tsao, Toronto). Binding activity was measured as fraction of radiolabelled RNA bound to the specified protein mixture and thus retained by a nitrocellulose filter.

Results: Nine rounds of selection resulted in 3 dominant sequences, including one (aptamer M9-5) that demonstrated preferential binding to the cancer secretome over the non-cancer secretome. Aggregate binding values for undiluted serum from 24 pancreatic cancer patients with recently diagnosed, radiographically localized pancreatic cancer were significantly higher than from 24 healthy volunteers (median fraction of RNA bound of 0.25 versus 0.10, P<0.0001). A receiver operator characteristic (ROC) curve was generated with an area under the curve (AUC) of 0.98. If a fraction bound of 0.14 is selected as a threshold—M9-5 has a specificity of 96% and a sensitivity of 92%. Notably, serum CA19-9 levels were normal (less than 40 U/ml) in 10 (41%) of the cancer patients, indicating that M9-5 detects a biomarker that is more sensitive than the best existing serum biomarker for pancreatic cancer. We serially purified the cancer secretome using a variety of biochemical methods and followed the binding activity. This purified fraction was subjected to mass spectrometric analysis, and the binding target was identified as Cyclophilin B (CypB), a secreted protein which has not previously been investigated as a serum biomarker for pancreatic cancer. We used a commercially available enzyme-linked immunosorbent assay (ELISA) kit to measure CypB levels in the same set of cancer patient and healthy volunteer sera that were analyzed using the radioactive M9-5 binding assay. CypB levels were elevated in the pancreatic cancer patient sera as compared to the healthy volunteer sera (median 295 ng/ml versus 60 ng/ml, P<0.0001), and CypB levels by ELISA were significantly correlated with M9-5 binding (r = 0.65, P<0.0001).

Conclusions: We used a novel in vitro selection strategy to identify an RNA aptamer, M9-5, that binds to a secreted pancreatic cancer biomarker, CypB. Serum M9-5 binding activity discriminates between pancreatic cancer patients and healthy volunteers with high sensitivity and specificity, and this biomarker may be useful as a tool for the early detection of pancreatic cancer.
Introduction: Pancreatoduodenectomy is a method of the surgical treatment of tumors located in the pancreatoduodenal field. Pancreatoduodenectomy is one of the most extensive surgical procedures. The aim of this study was to characterize selected intraoperative factors and the operating time in young and elderly patients who underwent pancreatoduodenectomy.

Methods: From 606 patients who underwent pancreatoduodenectomy in years 2001-2010, 210 patients were analyzed in the two groups: group of young (<45) and elderly patients (>70). The statistical analysis was performed by STATISTICAv10

Results: The young group was composed of 89 patients. The mean age was 38± 7 years (range 19 -45 years). The elderly group included 121 patients, the mean age was 74± 3 years (range 70- 81 years). There was a statistically significant difference between age groups in terms of gender: (chi-square 7,37 p<0,01): in the group of young patients women accounted for 35% , whereas in the group of elderly patients 54% were female patients. Statistically significant difference has been presented in terms of the operated tumor size (p<0,01). In the group of young patients the mean size of the tumor was 5,9cm± 3,4 cm (range 1,5 -25cm) and in the group of elderly patients: 3,9 cm ± 2cm (range 1 cm-13cm). In young patients the mean operating time was 5 h ± 1h 35min (range 1h 35 min -10h). In elderly patients the mean operating time was 4h 26 min ± 1h 09min (range 2h -8h 45 min). The operating time presented a statistically significant difference (p<0,01). In young patients the mean BMI was: 22,1± 4,0 (range 12,5 - 33,2) , in elderly patients the mean BMI was 24,7 ± 3,7( range 15,1 -38,5). The BMI presented a statistically significant difference (p<0,01). In terms of the method of digestive system reconstruction after PD there were no statistically significant differences (p>0,05). The most frequent was the Traverso method ( among young patients: 56%, elderly patients: 69%). Statistically significant differences have been observed in terms of the etiology of the tumor; in the group of young patients dominated chronic pacreatitis (66%), whereas in the group of elderly patients malignant neoplastic tumors: pancreatic adenocarcinoma (56%) and ampullary adenocarcinoma (15%). In terms of intraoperative infiltration of the organs no statistically significant differences have been observed (p>0,05) in young and elderly groups (56% and 52% respectively). In terms of intraoperatively analyzed vascular infiltration no statistically significant differences (p> 0.05) in both groups have been observed (in young patients infiltration was present in 21%, in elderly patients in 30%). The necessity of portal vein sewing did not present statistically significant differences in young and elderly groups (8% and 9% respectively).

Conclusions: The difference concerning gender range, the tumor size, the operating time, the BMI and the etiology of the tumor between the age groups have presented statistically significant dissimilarity. The young group can be classified as mostly male patients, with a larger tumor, and due to this, a longer operating time however with a lower BMI and non-neoplastic tumor etiology.
**Background:** Incidental pancreatic cysts are a diverse group of neoplasms that range from completely benign to precancerous or cancerous. The correct classification and management of pancreatic cysts often holds a degree of uncertainty based on current limitations of diagnostic modalities. Improper management may potentially result in unnecessary surgery or under-treatment of a potentially curable malignancy. In light of the known benefit of multidisciplinary cancer management, we sought to determine whether a multidisciplinary program for cystic neoplasms has the potential to improve care for these individuals.

**Methods:** The records of all patients seen at our Multidisciplinary Pancreatic Cyst Program Clinic (MDC) from 01/01/2010 to 12/01/2011 were reviewed, and the clinical, radiologic diagnoses and management recommendations from the patient’s previous treating institution/referring physician were documented and compared to the diagnosis and management plan of the MDC. Alterations in diagnosis and/or management between the previous treating institution/referring physician and the MDC were recorded. Patient outcomes were also assessed.

**Results:** A total of 306 patients (217 female; median age 64, range 20-89) were seen at the MDC. 15 patients were excluded, as no outside records were available. The remaining 291 patients had a diagnosis documented prior to MDC evaluation from either an outside clinic or our own institution. (89 (30.6%) surgeon, 97 (33.3%) gastroenterologist, 21 (7.2%) PCP/internal medicine, 71 (24.4%) radiology, 13 (4.5%) other). 127 patients (43.6%; \( p < 0.001 \)) had a change in diagnosis following review at the MDC. Of those who the MDC evaluation changed the diagnosis, 100 (78.7%) of patients were referred from an outside institution and 27 (21.3%) were internal referrals. The presumptive diagnosis following MDC evaluation was: IPMN (n=204), serous cystadenoma (n=14), pancreatic neuroendocrine tumor (n=6), pseudocyst (n=3), mucinous cystic neoplasm (n=2), adenocarcinoma (n=4), solid pseudopapillary tumor (n=1), and other (n=52). In 5 patients no cyst was present. 283 patients had an outside management plan (89 (31.4%) surgeon, 94 (33.2%) gastroenterologist, 18 (6.4%) PCP/internal medicine, 70 (24.7%) radiology, 12 (4.2%) other, which was altered in 69 individuals (24.4%; \( p < 0.001 \)). Of those who the MDC changed the management in, 76.8% were referred from an outside institution and 23.2% were internal referrals. 36% of those with a diagnosis change also had a treatment change compared to a change in treatment in 16% of those without a change in diagnosis \( p=0.0001 \). Alterations consisted of change to surveillance from surgery in 5 (7.2%), and change from surgery to surveillance in 17 (24.6%). 31 patients underwent surgical resection at our institution. Of these, the pre-operative MDC diagnosis corresponded with the surgical pathology in 26 (83.9%).

**Conclusion:** A multidisciplinary approach significantly alters the diagnosis and management of individuals with pancreatic cysts. To our knowledge this is the first study to report results on the impact of an MDC approach to the management of neoplastic pancreatic cysts. Long-term follow-up will be needed to determine if this approach translates into improved outcomes.
43410 MDCT DETERMINATION OF RESECTABILITY IN LOCALLY ADVANCED PANCREATIC DUCTAL ADENOCARCINOMA: ASSESSMENT OF SURVIVAL PROGNOSTIC FACTORS.

Many efforts have been done in order to extend the indications for curative surgery for patients affected by pancreatic cancer, by applying new surgical techniques such as retroperitoneal tissue cleaning and lymphadenectomy, and vascular resection. Moreover, in order to obtain a pre-operative downstaging in patients with locally advanced disease, chemotherapeutic protocols can be applied before surgery. For these reasons, an adequate pre-operative evaluation is mandatory in order to select resectable patients.

Aim of our study was to evaluate the predictive value of multidetector CT in assessing resectability in patients affected by locally advanced pancreatic ductal adenocarcinoma. The local staging parameters were compared with survival in order to identify possible prognostic factors of survival at preoperative CT.

We included 54 patients with locally-advanced pancreatic adenocarcinoma submitted to surgery with vascular resection.

At CT we evaluated the following criteria: vascular involvement (celiac trunk arteries, superior mesenteric artery, portal-mesenteric venous axis), fat tissue infiltration (mesenteric root and transverse mesocolon root, retroperitoneal fat corresponding to the SMA margin).

On the basis of these findings, patients were divided into 3 groups: resectable, borderline resectable (peripancreatic and venous infiltration liable to resection, likely R0) and palliative resectable (arterial or venous infiltration associated to peripancreatic infiltration, liable to resection likely R+).

All CT findings and the overall resectability judgement were compared to histopathological results.

In order to identify possible prognostic factors, survival was related to size and location of the tumor, length of tumor-vessel contact, type of vessel infiltrated, fat tissue infiltration, judgement of resectability at MDCT and histological SMA margin infiltration.

CT examination considered 67 vessels as infiltrated and 43 vessels as not infiltrated, with an overall judgement of venous infiltration in 24 patients, arterial in 5 patients and artero-venous in 18 patients.

Pathology confirmed the presence of infiltration in 50 vessels.

In the evaluation of vascular infiltration and fat tissue infiltration CT showed diagnostic accuracy of 81% (77% for venous and 85% for arterial infiltration) and 91% respectively.

At CT, 7 patients were judged as resectable, 23 borderline resectable and 24 palliative resectable. At pathology, 7 patients presented findings according to the CT judgement of resectability, 30 of borderline resectability and 17 of palliative resectability, with an overall CT/histology agreement of 72%.

In judging resectability and unresectability, CT showed diagnostic accuracy of 72% and 83% respectively. Survival was 84% and 57% at 6 month and 1 year respectively, and particularly 1 year survival was 100% for patients identified as resectable, 75% for borderline resectable and 28% for palliative resectable.

No statistical correlation with survival existed by considering location of the tumor, size of the tumor at CT and length of tumor-vessel contact.

A significant correlation with survival was obtained by considering type of vessel infiltrated (p=0.03), SMA margin (p=0.03) and mesenteric/mesocolic root (p=0.02) infiltration at CT, histological SMA margin (p=0.03) infiltration and overall judgement of resectability at CT (p=0.0008).

MDCT is accurate in evaluating local staging parameters, that, moreover, can be related to survival, thus confirming the strong contribution of MDCT in the therapeutic planning.
43412 LIMITATION OF SURGERY-FIRST TREATMENT FOR PANCREATIC DUCTAL ADENOCARCINOMA

INTRODUCTION: Our standard practice for potentially resectable pancreatic ductal adenocarcinoma (PDAC) has been “surgery-first” treatment (SFT) which includes surgical resection followed by adjuvant chemotherapy in timely fashion. However, incomplete resection (R1R2) and/or intolerance for adjuvant chemotherapy were sometimes experienced. In order to validate SFT for PDAC we retrospectively reviewed our consecutive series of PDAC during 2001-2009.

METHODS: One hundred sixty-three cases with PDAC were treated by SFT during 2001-2009. Patients were sub-grouped according to the NCCN resectability status (RS), e.g. Resectable(R), Borderline resectable (BR), and Unresectable (UR). Success rate of SFT and factors associated with treatment failure were analyzed. SFT was defined as R0 resection followed by adjuvant chemotherapy that was given within 8 weeks postoperatively and its relative dose intensity was greater than 2/3 of scheduled dose.

RESULTS: Overall success rate of SFT was 53%. Success rate was significantly higher in NCCN-R cases (79%) than in BR (46%) and UR (34%). Reasons for treatment failure of SFT were incomplete resection (25%) and intolerance of adjuvant chemotherapy (30%). Factors associated with treatment failure were NCCN BR/UR (OR=3.2), intraoperative transfusion (OR=2.7), and severe postoperative complication (OR=5.8) by logistic regression analysis. Overall median survival time (MST) for entire cohort was 18.5 months. Survival was significantly better in patients whom SFT was success in every NCCN RS (Table 1).

CONCLUSIONS: “Surgery-first” treatment for PDAC has significant limitations due to low success rate of best practice. Neoadjuvant treatment seems feasible alternative for PDAC.

Table 1

<table>
<thead>
<tr>
<th>NCCN RS</th>
<th>SFT success N (%)</th>
<th>OS (mo)</th>
<th>SFT failure N (%)</th>
<th>OS (mo)</th>
<th>p</th>
</tr>
</thead>
<tbody>
<tr>
<td>R (N=52)</td>
<td>41 (79)</td>
<td>31.7</td>
<td>11 (21)</td>
<td>15.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>BR (N=76)</td>
<td>34 (46)</td>
<td>25.3</td>
<td>42 (54)</td>
<td>10.3</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>UR (N=35)</td>
<td>12 (34)</td>
<td>20.0</td>
<td>23 (66)</td>
<td>11.2</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Total (N=163)</td>
<td>87 (53)</td>
<td>27.0</td>
<td>76 (47)</td>
<td>11.1</td>
<td>&lt;.001</td>
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</tbody>
</table>
Introduction: The Leapfrog Group has stated that outcomes after high-risk procedures, like pancreaticoduodenectomy, are superior at high-volume hospitals. High-volume hospitals are inexorably intertwined to high-volume surgeons; however, high-volume hospitals also have low-volume surgeons. This study was undertaken to determine if outcomes after pancreaticoduodenectomy are different for high-volume vs. low-volume surgeons at high-volume hospitals.

Methods: High-volume hospitals for pancreaticoduodenectomy (defined by Leapfrog as ≥ 12/year) were identified from the State of Florida Agency for Health Care Administration database for a 33-month period ending in October 2010. In these centers, outcomes for high-volume surgeons (undertaking ≥ 12 pancreaticoduodenectomies per year) were compared to those of low-volume surgeons (undertaking < 12 pancreaticoduodenectomies per year). Median data are presented.

Results: 55 surgeons undertook 928 pancreaticoduodenectomies at 6 high-volume hospitals; 10 surgeons were high-volume surgeons. High-volume surgeons in these high-volume hospitals had shorter lengths of stay (LOS), lower in-hospital mortality, and lower hospital costs (p<0.001) than low-volume surgeons (Table).

Conclusions: Within high-volume hospitals, high-volume surgeons have superior outcomes (including decreased lengths of stay, in-hospital mortality, and cost of care) relative to low-volume surgeons. Outcomes after pancreaticoduodenectomy at high-volume hospitals are dependent upon surgeon volume; any “hospital effect” is limited and does not benefit low-volume surgeons.
<table>
<thead>
<tr>
<th></th>
<th># of Surgeons</th>
<th># of PD's</th>
<th>LOS (days)</th>
<th>In-Hospital Mortality</th>
<th>Hospital Charge</th>
</tr>
</thead>
<tbody>
<tr>
<td>High-Volume Hospitals</td>
<td>55</td>
<td>928</td>
<td>11 (15 ± 14)</td>
<td>4.09%</td>
<td>99,409 ($142,578 ± 1)</td>
</tr>
<tr>
<td>High-Volume Surgeons</td>
<td>10</td>
<td>705</td>
<td>10 (15 ± 14)</td>
<td>2.83%</td>
<td>98,848 ($133,218 ± 1)</td>
</tr>
<tr>
<td>Low-Volume Surgeons</td>
<td>45</td>
<td>223</td>
<td>12 (17 ± 14)*</td>
<td>8.07%*</td>
<td>100,289 ($172,166 ± 1)</td>
</tr>
</tbody>
</table>

*p<0.01 vs. Greater with low-volume surgeons then with high-volume surgeons
Introduction: This study was undertaken to evaluate length of stay after pancreaticoduodenectomy, in great detail, in order to reduce length of stay and improve outcomes.

Methods: The hospital courses of 40 consecutive patients undergoing pancreaticoduodenectomy in 2010-11 were reviewed in great depth. Median data are presented.

Results: Patients were 70 years old with a BMI of 26kg/m2. 90% of the patients had severe co-morbidities, 4 per patient: most commonly cardiovascular (70%), diabetes (28%), and COPD (14%). ASA Class was 3. 38% had prolonged preoperative hospitalizations to treat complication of their pancreatic tumor or comorbidities. 48% had complex or extended pancreaticoduodenectomy, including portal vein resections; duration of anesthesia was 259 minutes and blood loss was 400cc. 95% had neoplastic disease; median stage was T3, N1 (AJCC Stage IIB). 35 patients were admitted to the ICU for 3 days. 33% of the patients received blood, 8% received it intraoperatively. 55% of patients experienced complications: most commonly UTI, respiratory failure, surgical site infection, and emesis. Enteral feeding was initiated on postoperative day 6. Two (5%) patients died in the postoperative period: length of stay was 10 days. Three (8%) patients were readmitted within 30 days, 2 for vomiting and 1 for mental status changes.

Conclusions: Pancreaticoduodenectomy is a formidable undertaking, as patients are generally older, deconditioned, and with significant co-morbidities and advanced underlying neoplasia. While duration of length of stay is certainly multifactorial, health support at home, motivation, and expectations play a role. Herein, we document that age, and all that entails, co-morbidities, underlying advanced neoplastic disease, and the occurrence and management of complications are major issues for length of stay after pancreaticoduodenectomy; after pancreaticoduodenectomy, patients are ill and need the support of a tertiary care hospital.
Introduction: Centralization of care improves outcomes after major operations, such as pancreaticoduodenectomy. This study was undertaken to determine if centralization of care for pancreaticoduodenectomy is occurring in Florida, and if so, has it impacted average length of in-hospital stay (ALOS), in-hospital mortality, and hospital costs.


Results: Across the time periods, the number of pancreaticoduodenectomies increased while the number of surgeons undertaking pancreaticoduodenectomies decreased (Table); the number of pancreaticoduodenectomies per surgeon significantly increased (p=0.02) (Table). In-hospital mortality, ALOS, and hospital costs did not improve across the periods (Table). During 2008-2010, the frequency with which surgeons undertook pancreaticoduodenectomy did not generally impact in-hospital mortality, though, relative to the lowest volume surgeons, the highest volume surgeons had significantly improved ALOS, in-hospital mortality, and hospital costs (Table).

Conclusions: Centralization of care is occurring in Florida as fewer surgeons are undertaking more pancreaticoduodenectomies, but without expected improvements in ALOS, hospital costs, and in-hospital mortality. Throughout 2008-2010, surgeons who undertook pancreaticoduodenectomy most frequently have significantly lower ALOS, hospital costs, and in-hospital mortality. With centralization of care over the past 15 years, length of stay, in-hospital mortality, and hospital cost have not improved. However with continued centralization of care, significant improvement in outcomes may become apparent as the number of highest volume surgeons increases, though more attention needs to be given to reducing in-hospital mortality.
<table>
<thead>
<tr>
<th>Study Periods</th>
<th>Number of PD</th>
<th>Number of Surgeons</th>
<th>Number of PD per Surgeon*</th>
<th>ALOS (Days)</th>
<th>In-Hospital Mortality</th>
<th>Hospital Cost (Adjusted to 2010 dollars)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1995-1997</td>
<td>698</td>
<td>282</td>
<td>2.47*</td>
<td>21</td>
<td>5.1%</td>
<td>$104,893</td>
</tr>
<tr>
<td>2003-2005</td>
<td>1314</td>
<td>266</td>
<td>4.94*</td>
<td>16</td>
<td>5.9%</td>
<td>$141,410</td>
</tr>
<tr>
<td>2008-2010</td>
<td>1514</td>
<td>241</td>
<td>6.28*</td>
<td>17</td>
<td>5.8%</td>
<td>$172,688</td>
</tr>
<tr>
<td><strong>2008-2010 Study Period</strong></td>
<td></td>
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<tr>
<td>Lowest Volume Surgeons ≤ 1 PD per year</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Highest Volume Surgeons ≥ 1 PD every 2 months</td>
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<td>ALOS (Days)**</td>
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<td></td>
<td>Hospital Cost**</td>
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<tr>
<td>Lowest Volume Surgeons ≤ 1 PD per year</td>
<td>21</td>
<td></td>
<td>16%</td>
<td></td>
<td></td>
<td>$212,587</td>
</tr>
<tr>
<td>Highest Volume Surgeons ≥ 1 PD every 2 months</td>
<td>15**</td>
<td></td>
<td>5%**</td>
<td></td>
<td></td>
<td>$139,889**</td>
</tr>
</tbody>
</table>

*Greater across study periods, p=0.02  **Less with highest volume surgeons, p<0.0006

PD=Pancreaticoduodenectomies
43417 READMISSIONS AFTER PANCREATICODUODENECTOMY: EFFORTS NEED TO FOCUS ON PATIENT EXPECTATIONS AND NONHOSPITAL MEDICAL CARE

INTRODUCTION: Readmissions after operations are a burden on our health care system and soon may not be covered by insurance providers. This study was undertaken to determine factors predicting readmission after pancreaticoduodenectomy (PD) so that, going forward, we can reduce our readmissions.

METHODS: Since 1991, patients undergoing PD have been prospectively followed. 168 (15%) of 1100 patients were readmitted within 30 days after PD. The causes for readmissions were reviewed in depth. Median data are presented.

RESULTS: All patients had notable preoperative comorbidities: most common were cardiovascular (19%), gastrointestinal (17%), and endocrine (11%). 29% had extended PD, including major vascular resections. The most common reasons for readmission were: nausea and/or vomiting for 42%, pain for 28%, and fever and/or chills for 14%. Gender, BMI, estimated blood loss, transfusion requirements, length of stay, pathology, tumor stage, nodal stage and margin status did not correlate with readmission after PD. Patients being readmitted were younger (65 vs. 69 years, p<0.001), more likely had notable comorbidities (p<0.001), and had longer operations (295 vs. 220 minutes, p < 0.001). Readmission did not impact long-term survival (31 vs. 23 months, p = 0.88).

CONCLUSION: PD are complex operations undertaken with significant risk in patients with notable comorbidities. Readmissions occur frequently after PD. Readmissions after PD are difficult to foresee. However, patients with notable comorbidities and longer operations are at risk for readmission. Readmissions are not due to complications specific to PD, but seem more related to ill health, inaccessible nonhospital post discharge medical care, and a poor understanding of what to expect. Efforts must focus on patient expectations, intermediate care, home health care, and improving medical care after discharge.
43418 INCREASING BMI PORTENDS ABBREVIATED SURVIVAL FOLLOWING PANCREATODUODENECTOMY FOR PANCREATIC ADENOCARCINOMA

Introduction: Obesity is a pandemic with 1.1 billion people worldwide estimated to be overweight. A plethora of epidemiologic evidence exists for a causal link between obesity and development of pancreatic cancer. Visceral fat has been associated with shortened survival in patients with pancreatic cancer. BMI, a common surrogate marker for grading obesity, does not differentiate between metabolically active visceral fat and the relatively inert subcutaneous fat. Moreover, there is no consensus on the utility of BMI in determining the correlation of obesity with perioperative outcomes and survival. This study was undertaken to determine the utility of BMI as a prognostic marker for the impact of obesity on outcomes and survival following pancreateoduodenectomy for pancreatic adenocarcinoma.

Methods: From our database of over 1000 patients who have undergone pancreateoduodenectomy, 228 patients with a diagnosis of pancreatic adenocarcinoma were identified. Demographics including age, sex, BMI, and perioperative parameters including operative time, estimated blood loss (EBL), length of stay (LOS), survival, nodal status, AJCC stage, and readmissions were obtained. Median data are presented.

Results: 192 patients had a BMI $\leq 29$kg/m$^2$ and 36 patients had a BMI $\geq 30$kg/m$^2$ (24 vs 34, p<0.001). Median age was 70 and the majority of the patients (52%) were men; sex and age were not different for patients with BMI $\leq 29$kg/m$^2$ or $\geq 30$kg/m$^2$.

Conclusions: For patients with pancreatic adenocarcinoma undergoing pancreateoduodenectomy, obesity does not impact operative blood loss, length of stay or readmission rates but results in a shortened survival. Therefore, we conclude that BMI is an important prognostic marker that portends an abbreviated survival following pancreateoduodenectomy for pancreatic adenocarcinoma.
<table>
<thead>
<tr>
<th>BMI (kg/m²)</th>
<th>EBL (ml)</th>
<th>LOS (days)</th>
<th>Tumor Size (cm)</th>
<th>Node + (%)</th>
<th>Survival (months)</th>
<th>Readmission (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤29</td>
<td>500</td>
<td>11</td>
<td>3</td>
<td>62</td>
<td>18</td>
<td>26</td>
</tr>
<tr>
<td>≥30</td>
<td>475</td>
<td>10</td>
<td>2.7</td>
<td>69</td>
<td>14*</td>
<td>17</td>
</tr>
</tbody>
</table>

*Less then for patients with BMI ≤ 29 kg/m².*
INTRODUCTION/BACKGROUND: Metabolic transformation towards a glycolytic phenotype is well described in cancer biology and pancreatic tumorigenesis, yet the underlying molecular mechanisms remain largely unknown. To date, cancer literature has focused principally on genetic changes like somatic mutations. However, more likely is that rapid, post-transcriptional regulatory events play a significant role in metabolic adaptive responses given the dynamic nature of conditions in vivo. One element, the RNA-binding protein HuR, directs multiple core signaling pathways under cancer-associated stressors by translocating from the nucleus to the cytoplasm and augmenting target expression. Recently discovered HuR metabolic targets include HIF-1α and the glucose transporter GLUT-1. We hypothesize therefore that HuR is an important post-transcriptional hub of cellular metabolism in pancreatic cancer.

METHODS: First we exposed pancreatic adenocarcinoma (PDA) cell lines to a panel of stressors including known glycolytic inhibitors citrate and hypoglycemia, and α-ketoglutarate agonist and hypoxia mimetic, Dimethyloxalylglycine (DMOG). Western blotting of cytoplasmic extracts and immunofluorescence was used to identify HuR cytoplasmic translocation (i.e. HuR activation). Affects of metabolic stressors on validated HuR mRNA targets (dCK and HIF-1α) were evaluated using quantitative PCR (qPCR). HuR target binding under metabolic stress was confirmed by ribonucleoprotein-immunoprecipitation (RNP-IP) of HuR bound mRNA cargo. Transfection with an HuR silencing siRNA was carried out and glucose utilization over time was evaluated by measuring glucose concentration in culture media. Survival was similarly evaluated in HuR silenced cells under hypoglycemic stress with a picogreen assay. We utilized HuR-bound mRNA from RNP-IP samples in conjunction with qPCR array to identify novel HuR metabolic targets.

RESULTS: Citrate (0.1-10 mM) and DMOG (0.1-1 mM) added to culture media containing PDA cells for 3-24 hours induces HuR activation by western blot and immunofluorescence. Similarly, reducing the glucose in standard media (25mM) to physiologic levels (5mM) and below (down to 0.5 mM) induces HuR activation. qPCR analysis of cell lysates after hypoglycemic stress (1 mM, 6 hours) demonstrates increased levels of established HuR target mRNAs HuR and dCK. Additionally, RNP-IP validated increased binding of HuR protein to these mRNA targets. Silencing HuR increased glucose utilization over time despite decreased cellular survival, especially in hypoglycemic conditions. Finally, a focused qPCR microarray combined with RNP-SEQ data identified approximately 30 new metabolic mRNA targets of the HuR protein including those involved in the first steps of the glycolytic pathway (e.g. glucose-6-phosphate isomerase, isocitrate dehydrogenase 1, and ribose 5-phosphate isomerase A).

DISCUSSION/CONCLUSION: These data are the first demonstrating that HuR is activated to the cytoplasm in PDA cells as a result of physiologic metabolic stress. We also show HuR activation to changes in the metabolic milieu affects not only mRNA levels of known HuR targets, but also novel mediators of metabolic transformation imperative for PDA cell proliferation and survival. Moreover, silencing HuR fundamentally changes cellular metabolism and sensitizes cells to the metabolic stress encountered in vivo. Ongoing studies will evaluate this novel metabolic pathway for ‘druggable’ targeting in the treatment of this devastating disease.
The lymph node (LN)-/N-status is considered as a central prognostic factor in biliopancreatic malignancies after oncologic resection. Recent evidence suggests that the total number and ratio (positive/examined) of dissected LNs significantly enhances prognostic accuracy of the N-status and was subject of our analysis.

Patients and Methods: Out of 278 pancreatic resections performed in our department from 09/2003 to 12/2010 histology revealed ductal pancreatic adenocarcinoma in 105, ampullary cancer in 11, and distal bile duct cancer in 21 patients. Long-term follow-up data were available in 120 patients who represent our study population. Analysis was focused on total LN count, topographic localization (LN compartment 1 and 2), and LN-ratio (< 0.2 vs. 0.2-0.4 vs. > 0.4).

Results: Overall survival was 23 months in N0- (median, range 4-85) and 15 months (range 2-83) in N1-patients (p<0.02). The prognostic accuracy of the N-status was influenced by the total number of LNs examined. A total LN count of at least 12 resulted in a survival of 26 months (median, range 8-85) in N0- and 13 months (median, range 2-76) in N1-patients (p<0.002). Whenever histological analysis was performed separately for the two major LN-compartments (1 and 2) the prognostic value of the N-status was improved. Assessment of the LN-ratio failed to enhance prognostic accuracy compared with the conventional N-status. The R-status was slightly superior to the N-status with a survival of 19 months (median, range 4-85) in R0-resected (53%) versus 13 months (median, range 2-48) in R1-resected (47%) patients (p<0.003).

Conclusions: The total number and compartment-oriented examination of dissected LNs influence the prognostic accuracy of the N-status. These factors should be taken into account by future studies for an improved staging in biliopancreatic malignancies.
ADIPOSE-DERIVED STEM CELLS CONTRIBUTE TO OBESITY-INDUCED INFERIOR ONCOLOGIC OUTCOMES OF PANCREATIC CANCER

INTRODUCTION
Pancreatic cancer is the fourth leading cause of cancer-related deaths in the US. Increased adiposity is implicated in tumorogenesis via adipocyte-induced dysfunctional production of adipocytokines. However, the role of the stromal fraction of fat, containing adipose-derived mesenchymal stem cells (AD-MSC) has not been elucidated. Bone marrow-derived mesenchymal stem cells (BMSC) promote tumor migration in breast cancer cell lines. AD-MSCs have been shown to have similar characteristics to BMSC. Therefore, we hypothesize that obesity with its expanded number of AD-MSCs would potentiate pancreatic cancer cell migration and that AD-MSCs derived from subcutaneous (SubAD-MSC) versus visceral (VisAD-MSC) fat would differentially affect migration.

METHODS
SubAD-MSC and VisAD-MSC were harvested from subcutaneous and visceral fat obtained from obese patients (BMI ≥35) undergoing bariatric surgery. AD-MSCs were then cultured and conditioned media containing only the secreted products of AD-MSCs was obtained. To assess migration, human Panc-1 cells were brought to 70-80% confluence and the scratch test was performed after addition of either control (CTL) media or conditioned media from either SubAD-MSCs or VisAD-MSCs. Migratory cells were counted at 0, 12, and 20 hrs under 100X magnification. Data are mean±SD.

RESULTS
AD-MSCs from both subcutaneous and visceral fat depots increased the migration of Panc-1 cells similarly.

<table>
<thead>
<tr>
<th>Time</th>
<th>CTL media (n=7) (cells/hpf)</th>
<th>SubAD-MSC (n=7) (cells/hpf)</th>
<th>VisAD-MSC (n=8) (cells/hpf)</th>
</tr>
</thead>
<tbody>
<tr>
<td>12 hrs</td>
<td>22±11</td>
<td>43±13*</td>
<td>48±11*</td>
</tr>
<tr>
<td>20 hrs</td>
<td>42±10</td>
<td>76±21*</td>
<td>71±5*</td>
</tr>
</tbody>
</table>

*p<0.001 vs CTL media

CONCLUSIONS
These preliminary data show that 1) adipose-derived mesenchymal stem cells (AD-MSC) amplify migration of human pancreatic cancer cells independent of adipocytes; and 2) AD-MSCs derived from subcutaneous and visceral fat are equivalent in this regard. Therefore, we conclude that the deleterious paracrine effects of numerically increased AD-MSCs may contribute to the poorer oncologic outcomes of pancreatic cancer, in
the setting of obesity.
**43425 TOTAL ROBOTIC PANCREATICODUODENECTOMY: A SINGLE INSTITUTION EXPERIENCE**

**Background:** The enhanced operative abilities of the daVinci surgical system offer an opportunity to verify if pancreaticoduodenectomy (PD) can be safely performed laparoscopically.

**Aim:** We herein report a technique for totally robotic PD developed at a high-volume center of pancreatic surgery, having extensive experience in advanced laparoscopy and robotic surgery.

**Methods:** Between October 2008 and November 2011, total robotic PD was performed in 29 patients. Our technique for robot-assisted PD is unique in several respects:

1. All dissections and reconstructions are carried out robotically;
2. The right colon does not need to be mobilized beyond the right colonic flexure;
3. A total of five ports are used. The specimen is extracted through a suprapubic transverse incision;
4. The camera port is placed along the right pararectal line, to allow optimal view of the uncinate process and retroperitoneal margin;
5. The third robotic arm is placed on the patient’s left side. Being driven by the surgeon’s right hand, this arm can be used for retraction or as the main operative arm. It can also be used to “hang” the duodenum during dissection of the uncinate process;
6. The left sided third robotic arm is also employed to grasp the gallbladder which is used as a handle to retract the liver, thus avoiding the need for a liver retractor.
7. In preparation for dissection of the uncinate process, the first jejunal loop is fully mobilized but it is not sectioned until the specimen is ready for removal. Maintaining intestinal continuity facilitates jejunal passage behind the mesenteric vessels.

**Results:** No patient was converted to open surgery or conventional laparoscopy, despite 2 patients required segmental resection of the superior mesenteric/portal vein and reconstruction using a jump graft. The entire stomach was preserved in 25 patients (86.2%). Mean operative time was 568 minutes (range 420-960 minutes). The mean time spent for instrument changes as well as passing or withdrawing needles was 58 minutes (range 41-81 minutes) representing 10.8% of entire operative time. Thirty-day operative mortality was nil, but a patient died on post-operative day 40. No pseudoaneurysm of the gastroduodenal artery was noted. Despite nearly all pancreas were soft and with small ducts (≤ 3 mm), only three patients developed grade B pancreatic fistulas and none grade C fistulas. Two patients underwent repeat surgery, because of intrabdominal bleeding. Mean hospital-stay was 21.8 days (range 10-60 days). One patient was readmitted on post-operative day 70 because of intestinal obstruction.

Fifty-one percent of the patients were diagnosed with malignant tumors. Overall, the mean number of lymph nodes retrieved was 29.8±16.7. None of the margins was positive.

**Conclusions:** In selected patients total robotic PD is feasible. As compared to hybrid techniques, coupling
laparoscopic dissection with robotic reconstruction, a total robotic procedure spares unnecessary dissections and allows optimal control of large peripancreatic vessels permitting segmental vein resection and tailored reconstruction. Technology refinements and improvement of surgical technique could make robotic PD an appealing alternative to open PD in selected patients.
Introduction: The aim of this study is to improve laparoscopic resection of pancreatic cancer by designing a fluorescence laparoscopic system enabling fluorescence-guided surgical navigation.

Methods: Orthotopic mouse models of human pancreatic cancer were established with the human BxPC-3 RFP pancreatic cancer cell line. Two weeks after implantation, mice were randomized to undergo bright light laparoscopic resection (BLR) or fluorescence-guided laparoscopic resection (FLR). Fluorescence laparoscopy was performed with a 495-nm emission filter and a Stryker L9000 LED light source 24 hours after tail vein injection of anti-CEA-Alexa 488 antibodies. Bright light laparoscopy was performed with a Stryker X8000 xenon light source. Pre- and postoperative images were taken with the Olympus OV-100 Small Animal Imaging System to assess completeness of resection. Postoperatively, whole body images were obtained to assess for recurrence and follow tumor progression. Intravital and ex vivo images were obtained at termination to evaluate tumor burden.

Results: Fluorescence laparoscopy enabled real-time identification and localization of brightly-fluorescent BxPC-3 RFP tumor additionally labeled with anti-CEA-Alexa 488. The red and green fluorophore combination optimized the fluorescence signal of tumor allowing accurate distinction of the tumor margins from normal surrounding tissue without compromising background illumination and thereby enabling adequate visualization for surgical navigation. Tumors were more readily detected and resected under fluorescence guidance (see figure). We achieved a more precise resection in the FLR group, leaving more normal pancreatic tissue behind. At termination, mice in the BLR group experienced a greater metastatic tumor burden compared to mice from the FLR group (26.98 mm$^2$ vs 5.93 mm$^2$). The BLR group demonstrated more metastatic disease to the periportal region, liver, mesentery and pelvis.

Conclusions: The optimal combination of a fluorescence laparoscopy with LED lighting and tumor specific antibody conjugated fluorophores with strong signals resulted in high contrast illumination for surgical navigation enabling greatly improved surgical outcomes.
Background: In the last two decades, laparoscopy has been the greatest innovation in abdominal surgery. The advantages of laparoscopy were so evident that it quickly became the standard for many operations, especially when there was little need for complex intracorporeal reconstructions. The da Vinci surgical system provides the unique opportunity to test whether laparoscopy can improve the outcome of pancreatic resections, especially when complex digestive reconstructions are needed.

Aim: To report on our first 80 consecutive laparoscopic, robot-assisted, pancreatic resections.

Methods: Eighty robotic pancreatic resections were performed between October 2008 and December 2011. There were 23 males (28.7%) and 57 females (71.3%), with a mean age of 58 yrs (range 24-80) and a mean body mass index of 24.6 Kg/m² (range 16.9-35.9).

Thirty patients underwent pancreaticoduodenectomy (PD) (38%), 36 distal pancreatectomy (DP) (45%), 6 total pancreatectomy (7%), 5 tumor enucleation (6%), and 3 central pancreatectomy (4%).

Since our activity spans over a 3-year period, data were analyzed according to the time of surgery, to verify progress in the learning curve: 17 patients were operated on between October 2008 and September 2009, 22 patients between October 2009 and September 2010, and 41 patients during the last 15 months (October 2010-December 2011).

Results: No patient was converted to conventional laparoscopy or open surgery. Mean operative time was 437.8 minutes (range 105-960). Noteworthy, 12.3% of operative time was spent to change robotic instruments as well as to introduce and withdraw needles. During these maneuvers the operation is “paused”, since the surgeon at the console is awaiting the action of the surgeon at the table.

In the first period operative time averaged 512 minutes for PD and 420 minutes for DP. The mean number of lymph nodes examined was 16.8 (range 1-46), 31.2 (range 18-46) for PD and 11.9 (2-24) for DP. Pancreatic fistula, including grade A, occurred in 41% of the patients.

In the second period operative time averaged 596 minutes for PD and 402 minutes for DP. The mean number of lymph nodes examined was 16.7 (range 1-53), 27.2 (range 15-53) for PD and 10.0 (4-23) for DP. Pancreatic fistula, including grade A, occurred in 36.3% of the patients.

In the third period operative time averaged 583 minutes for PD and 288 minutes for DP. The mean number of lymph nodes examined was 28.7 (range 0-74), 36.0 (range 22-57) for PD and 19.1 (0-49) for DP. Pancreatic fistula, including grade A, occurred in 36.6% of the patients.

Fifty-four patients were diagnosed with benign or low-grade tumors, and 26 with malignant tumors. Surgical margins were always negative.

Thirty day post-operative mortality was nil, but a patients died on post-operative day 40 (1/80; 1.2%). Post-operative morbidity was 52%, with a mean length of mean hospital-stay of 16 days (range 5-60 days).

Conclusions: In selected patients laparoscopic robot-assisted pancreatic resections can be safely performed. Despite the existence of a learning curve, experienced pancreatic surgeons are not expected to pay to robotics the same price that they would have been asked for by laparoscopy.
Background: Isolated involvement of an arterial segment in pancreatic and periampullary tumors is exceedingly rare, and does not necessarily mean advanced tumor stage being possibly caused by tumor location rather than by enhanced tumor biology. However, according to the last UICC staging system, all tumors involving a main peripancreatic artery are staged T4 and are deemed unresectable by definition.

Aim: To report on the outcome of a highly selected group of patients undergoing pancreatectomy plus resection of an isolated arterial segment at a single Institution.

Methods: From January 1993 to May 2011, segmental resection of an isolated peripancreatic artery was performed in 26 patients out of 816 undergoing pancreatectomy during the same period of time (3.1%). There were 12 males (46.1%) and 14 females (53.9%), with a mean age of 63.6 yrs (range 37-77 yrs). One patient (celiac trunk resection) was operated by robot-assisted laparoscopy. Only two patients underwent total pancreatectomy (7.7%), while all the others had a partial pancreatic resection, including pancreatectoduodenectomy in 5 patients (19.2%) and distal splenopancreatectomy in 19 (73%). Resected arterial segments were celiac trunk (n=14, 54%), hepatic artery (n=8, 31%), celiac trunk and hepatic artery (n=4, 15%). No isolated resection of the superior mesenteric artery was performed. Reconstruction was required in 6 patients (23%), in whom hepatic arterial flow was reestablished by direct end-to-end anastomosis (n= 1), transposition of the left gastric artery (n= 1), and interposition of a greater saphenous vein jump graft (n= 4). Multivisceral resection was required in 9 patients (34.6%), and included the stomach (n=6), the left adrenal (n=6), and the transverse colon (n=1).

Results: Final pathology disclosed ductal adenocarcinoma (DA) in 18 patients (69.2%), other pancreatic tumor types or periampullary carcinoma in 4 patients, mucinous cystic tumor in 1 patient, and metastatic tumor in 3 patients. Twenty-one DA patients were node positive (85%). Post-operative morbidity and mortality were 55.5% and 3.8%, respectively. The mean follow up time was 111 months (range 5-225 months). Overall actual survival rates at 1 and 3 years were 64% and 20%, respectively. Actual survival at 1 and 3 years in the DA group of DA was 30% and 15%, respectively. These figures favorably compare with an historical cohort of patients with locally advanced pancreatic tumors undergoing palliation without resection. Noteworthy, no patient developed local recurrence, despite none received pre- or post-operative radiation. Consequently, no patient developed intractable pain or required pain medications.

Conclusions: The outcome of patients diagnosed with DA remains poor even in case of seemingly localized tumors. Medical treatments will eventually improve this grim outlook, but currently surgical resection provides the only chance for cure and, possibly, the best palliation. Our experience shows that highly selected patients showing isolated involvement of celiac trunk and/or hepatic artery may undergo pancreatectomy with results similar to patients without vascular involvement and superior to those achieved after palliation or medical therapy alone. Although quality of life was not assessed specifically, lack of local recurrence and intractable pain seems to be relevant addenda when cure cannot be achieved.
**43431 NEAR TOTAL DISTAL PANCREATECTOMY**

**Background:** Total pancreatectomy by inducing brittle diabetes typically worsens post-operative quality of life. Sparing even a small portion of endocrine tissue may mitigate the severity of diabetes, by maintaining some endogenous, servo-regulated, production of insulin which avoids extreme fluctuations in glycemic levels and especially the occurrence of severe hypoglycemia.

**Aim:** To evaluate the outcome of a selected group of patients undergoing near-total pancreatectomy, with or without resection of vascular segments.

**Methods:** A near-total pancreatectomy is defined as the resection of at least 90% of the pancreas. In distal pancreatectomy the resection margin lies well on the right side of the superior mesenteric/portal vein, usually at the level of the gastroduodenal artery. This operation may be indicated for tumors of the neck of the pancreas/proximal body for which sparing a brim of pancreas around the duodenum is thought possible and safe, and avoids the complexity and higher morbidity associated with near-total pancreaticoduodenectomy. From April 2000 to July 2011, near-total pancreatectomy was performed in 25 patients. There were 7 males (28%) and 18 females (72%), with a mean age of 68 yrs (range 40-79 yrs). Twenty-two patients underwent a conventional open resection while in three patients the operation was carried out laparoscopically (2 robot-assisted), Splenectomy was associated in 23 patients (92%) while in two patients there was also a multivisceral resection. Segmental resection of peripancreatic vessels was associated in 4 patients (1 celiac trunk-hepatic artery, and 3 superior mesenteric/portal vein).

**Results:** Sixteen patients were diagnosed with ductal adenocarcinoma (64%), three patients with well-differentiated endocrine neoplasm (12%), three patients with a serous adenoma, one patient with a mucinous cystoadenocarcinoma (4%), one patient with carcinoma on IPMN, and one patient with chronic pancreatitis. Mean operative-time was 330 minutes (range 180-535 minutes). There was no post-operative mortality with a morbidity of 40%. Pancreatic fistula, all low output, was recorded in 8 patients (32%) and was managed conservatively. Thirteen patients developed insulin dependent diabetes mellitus (52%) and 15 developed exocrine insufficiency (60%) requiring enzyme supplementation.

**Conclusions:** Near-total pancreatectomy may be conveniently considered in patients with centrally located pancreatic lesions in whom total pancreatectomy would be otherwise indicated. In selected patients near-total pancreatic resection may also be performed laparoscopically, especially if robotic assistance is available. Careful patient selection and sound experience in pancreatic surgery are crucial to achieve the best results.
ROBOTIC PANCREATIC RESECTIONS FOR PANCREATIC AND PERIAMPUPLULAR MALIGNANCY

Background: Concerns have been raised as to the suitability of laparoscopy to treat high grade pancreatic neoplasms especially in terms of adequate lymphatic clearance and local radicality.

Aim: To report on the outcome of a series of 29 patients undergoing robotic pancreatic resection because of pancreatic or periampullary malignancy.

Methods: Between October 2008 to November 2011 29 patients diagnosed with malignant tumors were selected for laparoscopic, robot-assisted pancreatectomy. Selection criteria became more liberal over time, but patients thought to have tumors involving peripancreatic arteries and/or clearly showing venous adherence/infiltration were not considered for minimally invasive surgery. There were 14 males (48.3%) and 15 females (51.7%), with a mean age of 59.5 yrs (range 24-78 yrs). Sixteen patients underwent pancreaticoduodenectomy (PD) (55.2%), 8 distal pancreatectomy (DP) (27.6%), 3 total pancreatectomy (TP) (10.3%), and 2 to central pancreatectomy (CP) (6.9%).

Results: Final pathology disclosed neuroendocrine carcinoma in 6 patients (20.6%) (3 PD; 3 DP), cancer arising on intraductal papillary mucinous tumor in 6 patients (20.6%) (3 TP; 2 DP; 1 PD), ductal adenocarcinoma in 5 patients (17.2%) (3 DP; 2 PD), distal common bile duct cancer in 5 patients (17.2%) (5 PD), carcinoma of the papilla of Vater in 4 patients (13.8%) (4 PD), solid-pseudopapillary tumor in 2 patients (6.8%) (2 CP), and adenosquamous carcinoma in 1 patient (PD). Resection margins were all negative (R0). A mean number of 29.8 lymph nodes (range 0-74) was retrieved en-bloc with the specimen. Thirteen patients had lymph node metastasis (44.8%) including 3 diagnosed with ductal adenocarcinoma (3/5; 60%), 4 with distal common bile duct cancer (4/5; 80%), 4 with neuroendocrine carcinoma (4/6; 66.6%), 1 with carcinoma on intraductal papillary mucinous tumor (1/6; 16.6%), and 1 with carcinoma of the papilla of Vater (1/4; 25%). Mean tumor size was 2.9 cm for neuroendocrine carcinoma, 2.5 cm for ductal adenocarcinoma, 2 cm for common bile duct cancer, 1.9 cm for carcinoma of the papilla of Vater, and 2.5 cm for solid-pseudopapillary tumor. The adenosquamous tumor measured 3.5 cm in diameter. After a mean follow-up period of 14.1 months (range 1-38) all but two patients are alive and disease-free (93.1%). Two patients had tumor recurrence. One patient, diagnosed with ductal adenocarcinoma developed liver metastasis 13 months after surgery. A further patient developed local recurrence 10 months after surgery.

Conclusions: After a learning curve, best completed on patients with benign pancreatic diseases, laparoscopic robot-assisted pancreatic resection seems to offer the potential for radical tumor clearance in selected patients without locally advanced tumors. Further experience and longer follow-up are both needed before any final conclusion can be drawn.
43434 PARENTERAL NUTRITION AFTER PANCREATODUODENECTOMY: WHO NEEDS IT?

Background: The impact of proactive nutritional repletion in reducing postoperative morbidity in patients undergoing pancreatoduodenectomy (PD) remains poorly understood. This study analyzes the clinical factors which are associated with the utilization of parenteral nutrition (PN) after PD.

Methods: Between 2005 and 2009, 600 consecutive patients who underwent PD were included in the analysis. The most common indications for PD were adenocarcinoma (n=249, 41%), pancreatitis (n=88, 15%), and cystic neoplasms (n=83, 14%). Two-way statistical comparisons were performed between patients who did (+PN) or did not (-PN) receive postoperative parenteral nutrition within 30 days of PD.

Results: Pylorus-preserving PD was performed in 491 patients (82%), and a classic PD in 109 (18%). Operative mortality occurred in 18 (3%) patients. One hundred twenty-two (20%) patients were prescribed PN at a median of 8 days (range, 1-19) after PD. The median duration of PN usage was 9 days (range, 1-246). There were no differences in age, gender, renal function, operative time, or blood loss between the +PN and –PN groups. Patients requiring PN had lower preoperative (2.80 v. 2.93 g/dl, p=0.03) and hospital discharge (2.05 v. 2.32 g/dl, p<0.001) albumin levels. Higher preoperative total bilirubin levels were associated with postoperative PN usage (2.95, +PN v. 2.14 mg/dl, –PN, p=0.02). Operative outcomes with regards to postoperative PN utilization are listed in the table below. Forty-seven percent of the patients who developed delayed gastric emptying (DGE) required PN. PD was complicated by a pancreatic fistula (all grades) in 13% of patients, 35% of whom required PN.

Conclusions: Postoperative parenteral nutrition is required frequently in patients undergoing pancreatoduodenectomy. Strong associations between poor nutritional parameters, postoperative morbidity, and PN utilization emphasize the crucial role of adequate nutrition in achieving good surgical outcomes. Establishing enteral nutritional access at the time of PD should be considered in patients at risk for postoperative complications.

<table>
<thead>
<tr>
<th>Postop PN</th>
<th>All Complication</th>
<th>Major Complication</th>
<th>Re-operation</th>
<th>Pancreatic Fistula</th>
<th>DGE</th>
</tr>
</thead>
<tbody>
<tr>
<td>No (n=478)</td>
<td>198 (41%)</td>
<td>125 (26%)</td>
<td>20 (4%)</td>
<td>51 (10%)</td>
<td>44 (9%)</td>
</tr>
<tr>
<td>Yes (n=122)</td>
<td>79 (65%)</td>
<td>68 (56%)</td>
<td>18 (14%)</td>
<td>27 (21%)</td>
<td>39 (32%)</td>
</tr>
<tr>
<td>p-value</td>
<td>&lt;0.001</td>
<td>&lt;0.001</td>
<td>&lt;0.01</td>
<td>0.001</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
A 75 year old woman presented with recurring acute pancreatitis. Endoscopy demonstrated a papillary mass arising at the ampulla for which endoscopic resection was performed. Surveillance endoscopy one year later demonstrated recurrence without high grade dysplasia extending proximally into the biliary and pancreatic duct orifices more than 1 cm. The adenoma was resected using a robotic-assisted transduodenal approach with separate reconstructions of the bile and pancreatic duct orifices. Complete excision of the proximal extent of tumor was achieved with negative intraoperative duct margins. The duodenum was closed in two layers transversely using a Connell technique. The patient was discharged home taking a regular diet on the fifth postoperative day. She was completely recovered, pain-free, and with normal liver and pancreatic enzymes at her two week postoperative visit. Robot-assisted ampullectomy retains the technical advantages of open resection for extensive ampullary adenomas using a minimal access approach with less perioperative morbidity.
**43440 INSTRUMENT TRAFFIC DURING LAPAROSCOPIC ROBOT-ASSISTED PANCREATICODUODENECTOMY**

Background. Robotic surgery entails some unique issues that are not present, or are not equally relevant, in open surgery or conventional laparoscopy. Instrument traffic (IT) is one of such issues. IT is the time during which surgery is paused because the surgeon at the console is waiting for instrument change, camera cleaning, and pure laparoscopic action (e.g. introduction/withdrawal of needles). To the best of our knowledge no detailed information is available on robotic IT during robotic pancreaticoduodenectomy (PD).

**Aim.** To analyze IT during laparoscopic robot-assisted PD

Patients and methods. The operative videos of 12 laparoscopic robot-assisted PD were reviewed to measure IT. The analysis included: crude IT time (CITT), relative IT time (RITT) (defined as the percentage of operative time spent for IT), number of robotic instruments changes (RIC), time spent for RIC (TRIC), number of pure laparoscopic actions (PLA), and time spent for PLA (TPLA). Figures were estimated for the entire operation as well as for dissection and reconstruction phases. Details on anastomotic techniques were also noted and related to IT to define their relative impact on operative time.

**Results.** Mean operative time was 517.92 minutes (range 420-600). Mean CITT was 3681.67 seconds (range 2644-4514), giving a RITT of 11.89% (range 8.64-14.42%). Each robotic PD required a mean of 315.75 instrument changes or laparoscopic actions. Each instrument change or pure laparoscopic action paused surgery for 11.83 seconds. Mean RIC was 184.42 (TRIC 2633.83 seconds). Mean PLA was 131.42 (TPLA 1039.50 seconds). Mean dissection time was 326.97 min (range 262-393 min). Mean CITT was 2095.17 seconds (range 1555-2883 seconds), giving a RITT of 10.68% (range 9,89-12,23%). Dissection required a mean of 141.58 instrument changes or laparoscopic actions. Each instrument change or pure laparoscopic action paused surgery for 14,46 seconds. Mean RIC was 105.83 (TRIC 1645.25 seconds). Mean PLA was 35.75 (TPLA 382.58 seconds).

Mean reconstruction time was 177,5 min (range 168-197,9 min).

Pancreaticojejunostomy, always constructed end-to-side in a double layer, was performed by an invaginating technique in 8 patients and by duct-to-mucosa in 4 patients. Duct-to mucosa anastomosis required fewer stitches (26.3 vs. 36.7; p= 0,0182, t-test) but did not affect mean CITT (1812 vs. 1512 seconds; p=NS) or RIC (91,2 vs. 69,43 changes; P= NS)

Hepaticojejunostomy was performed in a double layer using either 4 half running sutures (9 patients) or interrupted external stitches plus inner half running sutures (3 patients). Mean CITT was shorter for the former technique (1527 vs. 1967 seconds; p= 0,07NS, t-test) and was associated with fewer RIC (65 vs. 119 changes; p=0,03, t-test).

**Conclusions.** Some 12% or operative time of laparoscopic robot-assisted PD is wasted because of IT. Since in this series operative time of robotic PD averaged 517.92 minutes, IT prolonged surgery of more than one 1 hour. Technology improvements and/or refinements in surgical technique are expected to reduce IT during
robotic PD.
Background: Reliable biomarkers to predict prognosis are lacking for patients with pancreatic ductal adenocarcinoma (PDAC) who are being considered for appropriate multimodality treatment. The aim of this study was to investigate aberrant hypermethylation of a candidate set of tumor suppressor genes as a potential cancer-specific molecular marker system related to outcomes for patients with resected PDAC.

Methods: Isolated DNA samples from primary PDAC and individually matched adjacent normal tissue from 37 patients who underwent operative resection were analyzed. The methylation status of 6 gene promoters (RASSF1A, MGMT, GSTP1, APC, P16/CDKN2A, and NEFL) was determined by quantitative methylation-specific PCR (QMSP). Promoter site methylation levels were calculated and correlated with clinical, pathologic, and outcome factors.

Results: Hypermethylation of the neurofilament light chain (NEFL) gene was significantly higher in PDAC compared to matched adjacent normal tissue (p<0.01). Promoter methylation levels of APC in PDAC correlated with overall survival, HR = 1.004 (95% CI, 1.001-1.007), and APC gene hypermethylation in matched normal tissue was associated with death within one year after resection (OR 0.073; 95% CI, 0.007-0.724). Promoter methylation of APC in host normal tissue along with APC methylation levels of primary tumors and surgical resection margin status can be used to evaluate the risk of death within one year after resection with a predictive accuracy of 87%.

Conclusion: Hypermethylation of the promoter region of candidate tumor suppressor genes in patients with pancreatic adenocarcinoma treated by operative resection is associated with early recurrence and death. Larger scale studies will be necessary to validate patterns of gene methylation as a potential cancer-specific molecular marker system related to outcomes for pancreatic cancer.
**Introduction:** Inhibitor of differentiation-1 (Id1) demonstrates a role in tumor progression in a variety of tumors but scarce data exists for pancreatic adenocarcinoma. Previously, we demonstrated that nicotine, the addicting component of tobacco, induces Id1 expression through a Src-dependent signaling pathway promoting proliferation, invasion, and chemoresistance in pancreatic cancer cells. Conversely, silencing of Id1 re-establishes gemcitabine sensitivity in acquired and innate gemcitabine-resistant cell lines. Therefore, we determined the role of nicotine and Id1 in tumor progression and chemoresistance in vivo and determined the expression status of Id1 in a large cohort of resected human pancreatic cancer tissues.

**Methods:** Cell lysate analyses (protein analyses, mRNA expression) were determined in a bio-diverse sample of pancreatic cancer cells by western and RT-PCR analyses. Metastatic pancreatic cancer cells were stably transfected with a luciferase expression vector and/or stable short-hairpin RNA silencing of Id1 gene expression with appropriate controls. Orthotopic nude mouse model utilized intraperitoneal injections of nicotine (1mg/kg, M/W/F) and gemcitabine (250 mg/kg, T/Th) with monitoring of in vivo growth and metastases based on luminescent signal concentration weekly. Confirmation of primary tumor growth and metastases was confirmed by H&E staining with corresponding Id1 and phospho-Src levels by immunohistochemical techniques to compare expression levels amongst the tumor and metastatic tumors in each group. Tissue microarrays (TMAs) constructed from 100 resected human pancreatic adenocarcinoma were stained for Id1, phospho-Src, and total Src using immunohistochemistry techniques. Scores based on intensity, percent of positive cells, and pathological grade (1-4) were assigned to each malignant core.

**Results:** In vivo, nicotine significantly promoted tumor growth and metastases in vivo. While gemcitabine reduced the tumor burden in control mice, nicotine abrogated this inhibitory effect and allowed continue tumor growth and metastases. Knockdown of Id1 expression results in a significant decrease in tumor burden with no identifiable liver metastases, regardless of nicotine exposure. Nicotine induced phospho-Src and Id1 expression levels in primary tumors in vivo while having no effect on Id1 expression in tumors originating from cells with stably transfected short-hairpin RNA silencing of Id1. Clinical analyses of resected human pancreatic tumor TMAs demonstrated a statistically significant correlation between Id1 and tumor grade/differentiation (p =0.0368). The correlation of protein levels of Id1 and phospho-Src was also statistically significant (p =0.0024); Comparison of overall survival and tumor grade was also significant (p = 0.05); the correlation between overall-survival and Id1 expression trended toward statistical significance (p =0.06).

**Conclusions:** Id1, through a Src-dependent-Id1 signaling axis, promotes tumorigenesis and chemoresistance in an in-vivo pancreatic cancer model. Id1 expression correlates with phospho-Src levels and tumor differentiation in human pancreatic cancer tissues. These results support the clinical assessment of Id1 expression as a biomarker of prognosis and support investigations toward targeted therapies against Id1 for pancreatic cancer patients.
Introduction: Postoperative complication rates following pancreatectomy remain high in the modern era. Substantial surgical procedures performed with pancreatectomy may result in additional postoperative morbidity and mortality. The aim of this study was to analyze the complications which occur after simultaneous pancreatectomy and colectomy.

Methods: All cases of regional pancreatectomy (P), segmental colectomy (C), and simultaneous pancreatectomy and colectomy (P+C) were reviewed at a single high-volume institution between November 2006 and May 2011. All cases were monitored with complete 30-day outcomes through the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP). Two and three-way statistical analyses were performed among the operation categories.

Results: Twenty patients with a diagnosis of cancer and a median age of 54 yrs underwent P+C. Pancreatoduodenectomy was performed in 9 patients, and distal pancreatectomy in 11. 30-day mortality was 10% for the P+C group (9% distal pancreatectomy, 11% pancreatoduodenectomy, p=NS). Postoperative outcomes for the 3 groups of patients are summarized in the table. Significant differences (*, p<0.01) among the groups are indicated. Superficial surgical site infection occurred in 15% of the P+C patients versus 10% in the P and C groups, p=0.31. The median postop hospital stay was 17 days (range, 6–60 days) for P+C patients compared to 7 and 6 days for P and C patients, respectively (p=0.01).

Conclusions: Extraordinarily high complication rates are observed after simultaneous regional pancreatectomy and colectomy which exceed the cumulative morbidities after each operation separately. Careful patient selection and strategies to prevent and/or control anastomotic leaks are necessary to improve outcomes in these patients.

<table>
<thead>
<tr>
<th>Operation Category</th>
<th># pts</th>
<th>Overall Morbidity</th>
<th>30-day Mortality</th>
<th>Organ space infection</th>
<th>Sepsis or septic shock</th>
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</thead>
<tbody>
<tr>
<td>P</td>
<td>820</td>
<td>33%</td>
<td>3%</td>
<td>10%</td>
<td>17%</td>
</tr>
<tr>
<td>C</td>
<td>356</td>
<td>39%</td>
<td>4%</td>
<td>12%</td>
<td>18%</td>
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<tr>
<td>P + C</td>
<td>20</td>
<td>70%*</td>
<td>10%</td>
<td>45%*</td>
<td>60%*</td>
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</tbody>
</table>
43450 DOES PANCREATIC STUMP CLOSURE METHOD INFLUENCE DISTAL PANCREATECTOMY FISTULA RATE

Introduction: Pancreatic fistula (PF) remains the primary morbidity following distal pancreatectomy (DP). Previous studies have reported specific methods of parenchymal transection and sealing in an effort to decrease the PF rate with highly variable results. The aim of this study was to determine the pancreatic fistula rate following various sealing methods.

Methods: All cases of DP were reviewed at a single high-volume institution between January 2008 and June 2011. Sealing method of the pancreatic stump was used to create operation groups (suture, staple, or saline linked radiofrequency (SLRF)). All cases were monitored with complete 30-day outcomes through the American College of Surgeons-National Surgical Quality Improvement Program (ACS-NSQIP). Two and three-way statistical analyses were performed among the operation groups.

Results: Two hundred and three patients underwent DP over the 42-month period. The most common diagnoses included pancreatitis (32%), adenocarcinoma (19%), and IPMN (13%) which did not differ significantly among the 3 operation groups. The suture, staple, and SLRF groups included 90 (44%), 61 (30%), and 52 (26%) patients, respectively. Operative technique included open (68%) and minimally invasive (32%) approaches and did not differ among the stump sealing groups. Thirty-six patients (59%) within the staple group received staple line reinforcement with bioabsorbable material. Postoperative outcomes for the three groups of patients are summarized in the table. Overall complications and PFs were similar in each group. Operative technique was not associated with the need for carryover outpatient drainage, postoperative interventional drain placement, or hospital readmission.

Conclusions: Postoperative outcomes after distal pancreatectomy are unaffected by the use of SLRF sealing of the pancreatic stump when compared to traditional suture or reinforced stapling techniques. A randomized clinical trial comparing these three operative techniques may not demonstrate a difference that is clinically significant.

<table>
<thead>
<tr>
<th></th>
<th>SLRF, N=52</th>
<th>Staple, N=61</th>
<th>Suture, N=90</th>
<th>p-value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall complications</td>
<td>16 (31%)</td>
<td>23 (38%)</td>
<td>35 (39%)</td>
<td>0.61</td>
</tr>
<tr>
<td>Pancreatic fistula</td>
<td>13 (25%)</td>
<td>16 (26%)</td>
<td>23 (26%)</td>
<td>0.95</td>
</tr>
<tr>
<td>Panc fistula grade B/C</td>
<td>6 (11%)</td>
<td>11 (18%)</td>
<td>15 (17%)</td>
<td>0.60</td>
</tr>
<tr>
<td>Home drain</td>
<td>4 (8%)</td>
<td>10 (16%)</td>
<td>15 (17%)</td>
<td>0.29</td>
</tr>
<tr>
<td>IR drainage procedure</td>
<td>6 (11%)</td>
<td>6 (10%)</td>
<td>13 (14%)</td>
<td>0.71</td>
</tr>
<tr>
<td></td>
<td>SLRF, N=52</td>
<td>Staple, N=61</td>
<td>Suture, N=90</td>
<td>p-value*</td>
</tr>
<tr>
<td>--------------------------</td>
<td>------------</td>
<td>--------------</td>
<td>--------------</td>
<td>----------</td>
</tr>
<tr>
<td>30d hospital readmission</td>
<td>7 (14%)</td>
<td>14 (23%)</td>
<td>17 (19%)</td>
<td>0.44</td>
</tr>
</tbody>
</table>

*Chi-square correlations among all three groups
Margin Distance Is Not an Independent Predictor of Survival After R0 Resection for Pancreatic Adenocarcinoma

Background: Microscopic tumor at the surgical margin is a predictor of recurrence and poor survival for pancreatic ductal adenocarcinoma (PDA). However, the impact of distance between the surgical margin and microscopic tumor on survival remains controversial. We hypothesized that margin distance (MD) would correlate with disease free survival (DFS) and overall survival (OS) in R0 resected PDA.

Methods: Retrospective analysis of 191 resections for PDA. Margin distance was measured (0-1, 1-2, 2-4, 4-10, and > 10 mm) and categorized by location. Parameters including age, gender, BMI, TNM, AJCC stage, lymph node (LN) ratio, vascular and perineural invasion, vein resection, and adjuvant therapy were analyzed. Primary endpoints were DFS and disease specific OS. Univariate analysis was used to estimate factors associated with outcomes. The log rank test was applied to selected group comparisons.

Results: 149 (78%) R0 outcomes were analyzed. 118 (79%) patients received adjuvant chemotherapy, 31 of whom also received XRT. Univariate analysis demonstrated reduced DFS (HR = 1.65, 95% CI = 1.13 – 2.48, p = .009) and OS (HR = 1.52 95% CI = .98 – 2.35, p = .059) among patients with margins ≤ 2mm compared to margins > 2mm. In addition, LN status, LN ratio, tumor size, AJCC stage, vascular invasion, perineural invasion, and adjuvant chemotherapy were found to influence OS on univariate analysis. Adjuvant XRT had no measurable effect on DFS or OS. Following adjustment for covariates in a multivariate model, margin distance >2mm did not correlate with DFS (HR = 1.14, 95% CI = .73 – 1.78, p = .57) or OS (HR = 1.13 95% CI = .69 – 1.85, p = .63), whereas adjuvant chemotherapy and presence of vascular invasion significantly affected OS (P=0.0006 and P=0.008 respectively). The retroperitoneal margin was the margin most commonly in close proximity to tumor (43% of Whipple), although there was no correlation between the closest margin and DFS (p=0.94) or OS (p=0.94).

Conclusion: Margin distance is not an independent predictor of DFS or OS after R0 resection for PDA. Irrespective of margin distance, adjuvant chemotherapy, but not XRT, was associated with improved OS.
MINIMALLY-INVASIVE ROBOT-ASSISTED MODIFIED APPLEBY RESECTION FOR PANCREATIC ADENOCARCINOMA

Selected patients with pancreatic adenocarcinoma involving the celiac trunk may derive prolonged survival benefit from surgical resection. We report two patients who underwent robot-assisted modified Appleby resection after chemoradiation and provide a video depicting the surgical technique. Median age was 82. Operative details are shown in the accompanying video. Median duration of surgery was 374 minutes, median EBL 225 and 11 day length of stay. Surgical margins were negative in both patients. The most severe morbidity was Clavien grade 3 gastric ischemia that resolved with bowel rest. The other patient had an ISGPF grade C pancreatic leak requiring endoscopic drainage. Robot-assisted minimally invasive modified Appleby resection can be completed safely with acceptable morbidity and mortality.
Background: Effective multimodality treatment for localized pancreatic cancer is elusive. We hypothesized that preoperative fixed-dose rate (FDR) gemcitabine (GEM) combined with short-course radiotherapy (RT) and the angiogenesis inhibitor bevacizumab (BEV) would improve margin negative surgical outcomes and complete pathological response rates.

Methods: Multi-site phase II trial evaluating all potentially-resectable pancreatic adenocarcinoma without major arterial involvement or portal venous occlusion. Dual primary endpoints included complete pathological response and margin negative resection rates of 10% and 80%. Subjects received FDR GEM on days 1, 15, and 29 combined with BEV (10 mg/kg IV), followed on day 43 by BEV and concurrent 30 Gy RT (3 Gy/fraction) over 10 days. After restaging, subjects underwent laparoscopy and possible resection after day 85. Stopping criteria required continuous monitoring of serious wound complications.

Results: 58 subjects enrolled, of which 29 (50%) had suspected venous involvement. 57 completed treatment without dose-limiting toxicity or delays in surgery. Two grade 4 (3.4%) and 17 grade 3 toxicities (28.8%) occurred. Four patients progressed before surgery. 54 subjects underwent laparoscopy; ten had unexpected carcinomatosis, and one was unresectable. 43 subjects were resected (74%; 33 pancreatoduodenectomy, 8 distal pancreatectomy, 1 total pancreatectomy, 1 Appleby); 19 (44%) required portal vein resection. Margin negative outcome was achieved in 38 (88%, 95% CI: 75%-96%) with one complete pathological response (2.3%; 95% CI: 0.1%-12%) and seven (6 grade 3; 1 grade 4) wound complications (13%). Median overall survival (OS) was 16.3 months (95% CI: 13.9-22.1) and 21.3 months (95% CI: 15.0-32.9) after resection. Median progression-free survival (PFS) was 5.7 months (95% CI: 3.9-9.1) and 9.9 months (95% CI: 5.7 to 14.1) after resection, with 7 local and 21 distant recurrences.

Conclusions: Combination therapy was well-tolerated and was within statistical design parameters for the primary endpoints despite a significant proportion of borderline tumors.
STEREOTACTIC BODY RADIATION THERAPY AS A NOVEL TREATMENT OPTION FOR
LOCALLY RECURRENT PANCREATIC CANCER AFTER FAILURE OF DEFINITIVE
MULTIMODALITY THERAPY

Introduction/Background: There is currently no standard-of-care treatment option for patients who develop isolated local recurrence of pancreatic ductal adenocarcinoma (PDA) after definitive multimodality therapy. Historically, patients treated with surgical re-resection have a median survival of 11.4 months following the operation. Stereotactic body radiation therapy (SBRT) represents a non-invasive alternative treatment option for this catastrophic scenario. SBRT can accurately deliver a high dose of potentially tumoricidal radiation to an area of local recurrence while sparing adjacent healthy tissue. To date, no study has examined the safety or efficacy of SBRT in treating isolated locally recurrent disease. The purpose of this study is to examine the safety and efficacy of SBRT for isolated local PDA recurrence.

Methods: Retrospective analysis of patients who developed isolated local recurrence of PDA following definitive multimodality therapy and were treated with SBRT in the salvage setting at a single institution from 2009-2011 was performed. Survival was analyzed using Kaplan-Meier statistics and toxicity was assessed using the NCI CTCAE version 3.0.

Results: 6 patients met eligibility criteria (≥18 years of age, ECOG performance status 0-2). Median follow-up was 30.0 months (range, 14.2-61.6), mean age was 59.7 years (SD, 6.3), and 33% were female. All patients had undergone definitive surgical resection (33% margin-positive, 50% T2 and 50% T3, 67% node-positive). 67% of tumors were in the pancreatic head and 33% in the pancreatic body. All 6 patients had progressed despite adjuvant chemotherapy, 5 with gemcitabine-based regimens and 1 with a 5-FU-based regimen. 5 of 6 patients had also received neoadjuvant or adjuvant radiation therapy to the pancreatic tumor bed to a mean dose of 47.4 Gy (SD, 10.0). 5 of 6 patients recurred in the tumor resection bed, while 1 recurred nearby in an aortocaval lymph node. Mean diameter of recurrent disease was 2.4 cm (SD, 1.0). All were treated with salvage SBRT to a mean dose of 25.0 Gy (SD, 3.2) in 5 fractions. Median survival from diagnosis was 27.6 months (95% CI, 8.4-46.7) and median time to local recurrence after surgery was 8.9 months (95% CI, 5.1-12.7). After salvage SBRT, median time to local progression was 10.4 months (95% CI, 3.9-16.9), and median survival was 13.2 months (95% CI, 6.7-27.5). 2 of 6 patients experienced grade 2 acute toxicity. No grade ≥3 acute toxicity was observed and no late toxicities have been reported to date.

Discussion/Conclusion: SBRT appears to be a safe and effective option for achieving local control in patients with isolated local recurrence of PDA after definitive multimodality therapy and may prolong survival compared to historical controls. Although interpretation of these findings is limited by the small cohort size, they support further investigation of SBRT in this scenario through phase I trials.
43458 EFFECT OF CHEMORADIATION-RELATED LYMPHOPENIA ON SURVIVAL IN PATIENTS WITH UNRESECTABLE, LOCALLY ADVANCED PANCREATIC ADENOCARCINOMA

Introduction/Background: Pancreatic ductal adenocarcinoma (PDA) has been shown to elicit antitumor cell-mediated immune responses. In high grade gliomas, treatment-related lymphopenia has been associated with shorter survival. This study was performed to determine if patients with locally advanced PDA treated with definitive chemoradiation therapy (CRT) develop significant lymphopenia and if this affects overall survival (OS).

Methods: Retrospective analysis of patients with locally advanced PDA treated at a single institution with CRT from 1997-2009 was performed. Information relating to known prognostic factors in PDA was obtained from the electronic patient record (EPR) system. Lymphocyte counts were obtained from complete blood counts in the EPR system at baseline prior to CRT and then serially during and following CRT. OS was then analyzed as a function of lymphopenia and known prognostic factors. The Kaplan-Meier method was used for survival statistics and univariate analysis was performed using Cox regression. Significant factors identified in the univariate analysis were selected as covariates to construct a multivariate proportional hazards regression model to estimate the hazard ratio for death attributable to each factor.

Results: 99 patients met eligibility criteria (≥18 years of age, ECOG performance status 0-2, and had baseline and follow-up lab values measured at our institution). Median age was 61 years (range, 35-90), 54% were male, median tumor size was 4.0 cm (range, 1.3-8.0), and 97 had stage III disease. Median pre- and post-CRT CA19-9 values were 241.5 and 105.2 U/mL, respectively. Total lymphocyte counts were normal in 87% of patients prior to RT. Median RT dose was 50.4 Gy (range, 14.0-56.0) and concurrent chemotherapy was 5-FU (67%), gemcitabine (20%), taxotere (7%), or none (6%). Chemotherapy dose reduction was necessary in 9%, and 39% required a radiation therapy break. Total lymphocyte counts fell to <500 cells/mm3 in 51% two months after initiating CRT with a median reduction of 66% from baseline (p<0.0001). Median OS of patients with lymphocyte counts <500 cells/mm3 at 2 months was 8.4 months (95% CI, 7.2-14.0) versus 13.9 months (95% CI, 11.0-16.7) for patients with ≥500 cells/mm3 (HR 1.90, p=0.002). Univariate analysis revealed that among pre-treatment patient characteristics, only age ≥65 was significantly associated with OS (8.8 vs. 11.4 months, HR 1.56, p=0.045). Type of concurrent chemotherapy was not significantly associated with OS (HR 1.30 for gemcitabine versus 5-FU; p=0.34). Multivariate analysis revealed a significant association between survival and lymphocyte count (<500 vs. ≥500 cells/mm3) at 2 months post-initiation of CRT (HR 1.72, p=0.035).

Discussion/Conclusion: Definitive CRT-induced lymphopenia is frequent, severe, and appears to be an independent predictor for OS in patients with locally advanced PDA. Simple, low-risk methods of ameliorating CRT-associated lymphopenia, such as such as drawing blood from patients prior to CRT and re-infusing it back afterwards to achieve immune reconstitution or altering chemoradiation regimens based on degree of lymphopenia (as is currently done for depressed platelet counts and neutropenia), may be worth evaluating in phase I trials.
A STANDARDIZED OPERATIVE TECHNIQUE FOR ROBOT-ASSISTED DISTAL PANCREATECTOMY: MAXIMIZING ONCOLOGIC PRINCIPLES.

Background: Although minimally-invasive distal pancreatectomy reduces postoperative pain and morbidity, there is no consensus about technical factors critical to maximize oncologic outcomes. We evaluated a uniform operative technique for robot-assisted distal pancreatectomy (RADP) which adheres to the important oncologic principles of open radical distal pancreatectomy via minimal access techniques.

Methods: Retrospective analysis (Jan 2008-July 2011) of 41 RADP with the following standard technical components: pancreatic transection over the splenoportal confluence; lymphadenectomy of left gastric and celiac arteries; en bloc excision of the retroperitoneal fascia; splenectomy. Indications for RADP included 9 benign lesions (21.9%) and 32 malignancies: 16 pancreatic ductal cancers and 16 pancreatic neuroendocrine (pNET).

Results: Median operative time was 289 (231-360) minutes with 200 ml (100-300) median estimated blood loss. Conversion to open was required for one (2.4%) benign lesion exceeding 11cm diameter. Four patients required blood transfusion in the first 90 days (9.7%). Pancreatic fistulas (16, 39%) were classified by ISGPF: 7 grade A (17%), 4 B (9.7%), 5 C (12%). Ninety day postoperative morbidity included 22 (53%) minor (Clavien I/II) and 8 (19%) major complications (Clavien III only). Although one patient with PNET (2%) had a positive margin, all PDA achieved margin negative status. Median lymph node harvest was 18 (13-20), median lymph node ratio was 0.015 (0-0.15). Mean hospital stay was 6.7± 2 days. Sixteen patients met eligibility criteria for adjuvant chemotherapy, of which fourteen (87.5%) were treated at a median of 7.5 weeks postoperatively.

Conclusion: Minimally invasive distal pancreatectomy with robotic assistance is safe and feasible. Improved surgical manipulation and visualization with the robotic platform allows for a standardized technique that preserves oncologic principles in a minimal access setting. Multi-institution prospective trials with uniform follow-up are required for meaningful assessment of the comparative effectiveness of open and minimally-invasive surgery for pancreatic tumors.
43462 POLYPHARMACY AFTER PANCREATIC CANCER RESECTION

Background: Patients with resected pancreatic cancer are treated by multiple providers for a number of preexisting and postoperative conditions. The use of multiple medications, while often beneficial, can lead to patient safety issues and adverse medication events. It may also generate significant costs for patients and insurers. Patterns of prescription drug use, the extent of polypharmacy, and the cost implications of prescription drug use in patients with pancreatic cancer have not been well described.

Methods: Pharmacy events were identified for patients in the SEER-Medicare linked database who had undergone pancreatic resection for adenocarcinoma between 5/1/2007-5/1/2008. 116 patients were identified with continuous Part D coverage. The ten most commonly prescribed classes of medications were identified, and the proportion of surviving patients taking each class of medication was calculated in each of three time intervals. The average monthly cost of all prescription medications was calculated for each patient.

Results: The cohort was 64% female and 87% white, with a median age of 74 years. 17% received distal pancreatectomy, with the remainder receiving proximal resection/pancreaticoduodenectomy. Median survival was 25 months. Pharmacy claims were most common in the 60 days following resection, but patients continued to receive multiple medications and incur significant expenses well beyond their resection. After resection, a majority of patients received opiate analgesics, antiemetics, enzyme supplementation, and proton pump inhibitors. Enzyme supplementation generated the highest out-of-pocket expense in all phases of care (median $8-15 per month), followed by PPIs, anticoagulants, and insulin. Among the subset of patients who underwent proximal resections, 67% required enzyme supplementation >60 days after surgery.

Conclusion: Patients with pancreatic cancer receive a multitude of medications of different classes in the postoperative period, and incur significant out-of-pocket expenses. Providers must be cognizant of the potential patient safety, logistical, and financial implications of prescription medications on patients with pancreatic cancer.

<table>
<thead>
<tr>
<th>Medication Class</th>
<th>Preoperative (4 months)</th>
<th>Early Postop (0-60 days)</th>
<th>Late Postop (&gt;60 days)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Opiate analgesics</td>
<td>42.4%</td>
<td>71.6%</td>
<td>62.3%</td>
</tr>
<tr>
<td>Antiemetics</td>
<td>30.2%</td>
<td>56.0%</td>
<td>58.8%</td>
</tr>
<tr>
<td>Enzyme supplements</td>
<td>14.7%</td>
<td>32.1%</td>
<td>57.9%</td>
</tr>
<tr>
<td>Proton pump inhibitors</td>
<td>31.0%</td>
<td>47.7%</td>
<td>57.2%</td>
</tr>
<tr>
<td>Antidepressants</td>
<td>26.7%</td>
<td>20.2%</td>
<td>39.5%</td>
</tr>
<tr>
<td>Insulin</td>
<td>13.8%</td>
<td>23.9%</td>
<td>24.6%</td>
</tr>
<tr>
<td>Non-opiate analgesics</td>
<td>16.4%</td>
<td>10.1%</td>
<td>27.2%</td>
</tr>
<tr>
<td>Medication Type</td>
<td>Oral Hypoglycemics</td>
<td>Anticoagulants</td>
<td>Statins</td>
</tr>
<tr>
<td>-----------------</td>
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<td>---------</td>
</tr>
<tr>
<td>%</td>
<td>24.1%</td>
<td>21.1%</td>
<td>21.9%</td>
</tr>
<tr>
<td></td>
<td>11.9%</td>
<td>20.2%</td>
<td></td>
</tr>
<tr>
<td></td>
<td>25.0%</td>
<td>10.1%</td>
<td>19.3%</td>
</tr>
</tbody>
</table>

| Prescription events per patient per month (Median, IQR) | 3 (1.8-5) | 4.5 (3-6) | 2.6 (1.5-4.9) |

<table>
<thead>
<tr>
<th>Total patient payments (out-of-pocket) per month (Mean)</th>
<th>$88.04</th>
<th>$126.80</th>
<th>$79.04</th>
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<tbody>
<tr>
<td>Total patient payments per month (Median, IQR)</td>
<td>$41.08</td>
<td>$42.88</td>
<td>$39.54</td>
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<tr>
<td></td>
<td>(15.93-71.97)</td>
<td>(12.88-102.80)</td>
<td>(11.20-103.53)</td>
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</table>

<table>
<thead>
<tr>
<th>Total gross drug cost per month (Mean)</th>
<th>$329.90</th>
<th>$399.62</th>
<th>$439.54</th>
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<tbody>
<tr>
<td>Total gross drug cost per month (Median, IQR)</td>
<td>$176.00</td>
<td>$209.69</td>
<td>$185.75</td>
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<tr>
<td></td>
<td>(96.04-352.53)</td>
<td>(109.01-397.84)</td>
<td>(99.09-381.66)</td>
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</table>
43463 TECHNICAL REFINEMENT OF ROBOT-ASSISTED PANCREATICODUODENECTOMY: IMPROVING OUTCOMES AT A SINGLE INSTITUTION

**Background:** Although robot-assisted pancreaticoduodenectomy (RAPD) is safe and feasible at selected centers, technical refinements are required to standardize the operative technique prior to comparing its effectiveness to open or laparoscopic approaches. We analyzed the cumulative effects of surgical experience and procedural refinements on important metrics of RAPD outcome in order to optimize intraoperative techniques.

**Methods:** Retrospective analysis of a prospective database of 76 RAPD divided into two cohorts of 38: early (Oct 2008-May 2010) and late (Jun 2010- Aug 2011).

**Results:** Preoperative characteristics of the two cohorts were equivalent: age, gender, BMI, comorbidities, prior abdominal surgery, frequency of malignancy, and tumor size. Although mean operative duration did not change, the variability in case duration decreased significantly while participation by surgical trainees increased. The rate of pylorus-sparing RAPD increased (11% vs. 74%, p<0.001), estimated blood loss (median 400 vs. 225 ml, p=0.01), probability of blood loss greater than 500 ml (45% vs. 16%, p=0.006) and conversion to open PD (21% vs. 2.6%, p<0.03) decreased significantly. Margin status, lymph node harvest, severity of complications (Clavien scale) and length of stay did not change, although trends toward reduced rates of reoperation (p=0.12) and readmission (p=0.07) were observed. The rate and severity of pancreatic fistula was constant (p=0.15).

**Conclusion:** Outcomes of RAPD achieved technical maturity after approximately forty cases. Lack significant decrease in operating room time in this study is likely confounded by the introduction of the surgical trainee. Well designed studies of the comparative effectiveness of this approach are now appropriate.
HAS THE SURGICAL MANAGEMENT OF NEOPLASTIC CYST OF THE PANCREAS ALTERED OVER TIME? TRENDS IN THE OUTCOME AND PATHOLOGY IN A LARGE SURGICAL SERIES

Introduction: With the widespread use of cross-sectional imaging in the work-up of abdominal conditions the incidental finding of a pancreatic cyst has become commonplace. Indeed, the prevalence of pancreatic cysts identified on imaging has increased over time from 0.21% with transabdominal ultrasound in 1994, to 2.6% with CT in 2006, and 13.4% with MRI in 2010. The aim of this study was to determine if there has been a change in the surgical management and pathological findings of pancreatic cysts over time.

Methods: Consecutive patients who underwent surgical resection for a pancreatic cyst in a tertiary center were identified from our prospectively maintained pancreatectomy database. For purposes of comparison of time-related trends, patients were divided into two groups - 1996-2001 (group 1) and 2006-2011 (group 2). General demographics, pathology and surgical procedure were documented and the prevalence of the resected cysts was compared between the two time periods using Fisher exact and chi-square tests.

Results: From 1996 until 2011 a total of 576 patients underwent resection of a cystic lesion. The pathological findings included: serous cystadenoma (n=87), pseudocyst (n=22), IPMN (n=309), MCN (n=48), solid pseudopapillary tumour (n=34), lymphoepithelial cyst (n=12) and neuroendocrine tumors (n=6). The operations performed included: pancreaticoduodenectomy (n=279), distal pancreatectomy (n=251), total pancreatectomy (n=36) and other (n=10). There were 190 patients (122 female, mean age 62 years (range 15 to 86)) in group 1 and 386 patients (218 female, mean age 62 years (range 12 to 94)) in group 2. There was an increase in the number of IPMN undergoing resection (43.7% to 57.8%; p=0.001) and a decrease in the number of benign cysts being resected (serous cystadenoma 30.5% to 22.5%; p=0.04 and pseudocysts 6.8% to 2.3%; p=0.01) between the two time periods (Table 1). The proportion of resected IPMN with high grade dysplasia did not change over time (25.3% to 21.4%; p=0.47), however, there was a significant decrease in the proportion of IPMN with invasive adenocarcinoma (56.6% to 29.3%; p<0.001) and an increase in the proportion with low or moderate dysplasia (18.1% to 49.3%; p<0.001).

Conclusion: The type of pancreatic cyst undergoing surgical resection has changed significantly over the past 15 years. The ability to identify benign cysts has improved with fewer undergoing resection. The numbers of patients with IPMN undergoing surgical resection has increased, with lesions being removed at an earlier stage of disease. These findings suggest that new tools and guidelines are required to identify those patients with low or moderate dysplasia who could undergo surveillance rather than surgical resection.
<table>
<thead>
<tr>
<th>Type of cyst</th>
<th>Number Resected Group 1 (1996-2001)</th>
<th>Number Resected Group 2 (2006-2011)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudocyst</td>
<td>13 (6.8%)</td>
<td>9 (2.3%)</td>
<td>0.01</td>
</tr>
<tr>
<td>Serous cystadenoma</td>
<td>58 (30.5%)</td>
<td>87 (22.5%)</td>
<td>0.04</td>
</tr>
<tr>
<td>IPMN* - Serous cystadenoma</td>
<td>0</td>
<td>3 (0.8%)</td>
<td>0.55</td>
</tr>
<tr>
<td>IPMN*</td>
<td>83 (43.7%)</td>
<td>223 (57.8%)</td>
<td>0.001</td>
</tr>
<tr>
<td>MCN*</td>
<td>20 (10.5%)</td>
<td>28 (7.3%)</td>
<td>0.18</td>
</tr>
<tr>
<td>Neuroendocrine tumor</td>
<td>2 (1.1%)</td>
<td>4 (1.0%)</td>
<td>1</td>
</tr>
<tr>
<td>SPPT*</td>
<td>11 (5.8%)</td>
<td>23 (6.8%)</td>
<td>1</td>
</tr>
<tr>
<td>Lymphoepithelial cyst</td>
<td>3 (1.6%)</td>
<td>9 (2.3%)</td>
<td>0.76</td>
</tr>
<tr>
<td>Total</td>
<td>190</td>
<td>386</td>
<td>0.01</td>
</tr>
</tbody>
</table>

*SPPT: solid pseudopapillary tumour, MCN: mucinous cystic neoplasm, IPMN: intraductal papillary mucinous neoplasm.
**43470 ANTIOXIDANT STATUS IN ACUTE PANCREATITIS PATIENTS**

**Introduction.** Oxidative stress is an important factor in the pathogenesis of acute pancreatitis. Defining features of oxidative stress in acute pancreatitis patients is necessary for effective treatment.

**Materials and methods.** In 53 patients with acute pancreatitis was measure the blood plasma peroxides levels and total antioxidant capacity.

**Results.** In acute pancreatitis there is a high peroxides level in plasma and reduced total antioxidant capacity, which correlates with the severity of pathology and the development of organ dysfunction. Concentration of peroxides in the admission of patients significantly correlated with the occurrence of organ dysfunction, including respiratory, renal, hepatic, metabolic, and MODS. Levels of total antioxidant capacity likely indirect correlated with the concentration of blood glucose (R=-0.339580, p=0.013782), creatinine (R =- 0.340379, p=0.013547) and C-reactive protein (R=-0.740659, P = 0.002445).

In severe acute pancreatitis antioxidant failure mechanisms clearly correlated with other indicators of the intensity of the inflammatory process.

**Conclusion.** In acute pancreatitis, insufficiency of antioxidant capacity and low coefficient of antioxidant protection may lead to the development of multiple organ dysfunction and death.
43472 ALCOHOL AND SMOKING AS RISK FACTORS IN AN EPIDEMIOLOGY STUDY OF PATIENTS WITH CHRONIC PANCREATITIS

Data derived from the North American Pancreatitis Study 2

Background & Aims: Alcohol has been implicated in the development of chronic pancreatitis (CP) in 60%–90% patients, although percentages in the United States are not known. We investigated the frequency of alcohol-related CP at tertiary U.S. referral centers.

Methods: We studied data from patients with CP (n=539) and controls (n=695) enrolled in the North American Pancreatitis Study-2 from 2000 to 2006 at 20 U.S. referral centers. CP was defined by definitive evidence in imaging or histologic analyses. Subjects and physicians each completed a detailed study questionnaire. Using physician-assigned diagnoses, patients were assigned to the following etiology groups: alcohol (with/without other diagnoses), non-alcohol (any etiology of CP from other than alcohol), or idiopathic (no etiology identified).

Results: The distribution of patients among etiology groups were: alcohol (44.5%), non-alcohol (26.9%), and idiopathic (28.6%). Physicians identified alcohol as the etiology more frequently in men (59.4% in men vs 28.1% in women), but non-alcohol (18% in men vs 36.7% in women) and idiopathic etiologies (22.6% in men vs 35.2% in women) more often in women (P<0.01 for all comparisons). Non-alcohol etiologies were equally divided among obstructive, genetic, and other causes. Compared with controls, patients with idiopathic CP were more likely to have ever smoked (58.6% vs 49.7%, P<0.05) or have a history of chronic renal disease or failure (5.2% vs 1.2%, P<0.01). In multivariate analyses, smoking (ever, current, and amount) was independently associated with idiopathic CP.

Conclusions: The frequency of alcohol-related CP at tertiary U.S. referral centers is lower than expected. Idiopathic CP and non-alcohol etiologies represent a large subgroup, particularly among women. Smoking is an independent risk factor for idiopathic CP.
GREATER VOLUME RESUSCITATION DURING THE FIRST 24 HOURS AFTER ERCP IS ASSOCIATED WITH A LESS SEVERE COURSE OF POST-ERCP PANCREATITIS

Background: Intravenous volume resuscitation (IVR) represents the most important early clinical intervention in pancreatitis to minimize the severity of its course. There are no data correlating volume resuscitation with the severity of post-ERCP pancreatitis (PEP), a unique etiology of pancreatitis in that many patients present earlier in the disease course versus non-iatrogenic etiologies. The aim of this study was to compare early IVR in patients with mild versus moderate to severe PEP.

Methods: We conducted a retrospective cohort study of patients undergoing ERCP between January, 2009 and April, 2011 who were subsequently admitted with PEP within 24 hours to our institution. PEP was defined as new or worsening abdominal pain with elevation in amylase or lipase > 3x upper limit of normal. Mild PEP was defined as hospitalization ≤ 3 days, moderate (4-10 days) and severe (> 10 days). Patients were excluded if IVR data during the pre-, intra-procedure and post-procedure (up to 24 hours after ERCP) periods were unavailable. Patients with acute pancreatitis within 7 days of ERCP, chronic kidney disease and congestive heart failure were also excluded. There are no standard orders for IVR in patients admitted with PEP after ERCP, so the amount of fluid is left to the discretion of the treating physician. In addition to IVR data, medical records were abstracted for known risk factors for PEP and the use of prophylactic PD stents. Variables are presented as medians with interquartile ranges or simple proportions with 95% confidence intervals, with appropriate comparative statistics to determine significant differences.

Results: We identified 70 eligible patients who underwent ERCP and developed PEP prompting admission on the same day as the procedure. Of these, 30 (42.9%) met criteria for at least moderate PEP with median hospital stay of 5 (4, 8) days; 3 of 30 were severe. Sphincter of Oddi dysfunction was the indication for ERCP in 60% of mild and 40% of moderate/severe cases of PEP (p=0.10). Patients with mild PEP were similar to those with at least moderate PEP in terms of known demographic and endoscopic risk factors for PEP (table) except younger age. Patients with mild PEP received significantly greater IVR during the first 24 hours (2892mL) after ERCP compared to those with at least moderate PEP (2147mL, p=0.03). Median pre-procedure and intraprocedure IVR were similar in both groups (table, p=0.72).

Conclusion: In patients with PEP, more aggressive IVR during the first 24 hours after ERCP is associated with a less severe course. This is important preliminary evidence suggesting earlier and more aggressive fluid resuscitation may attenuate the course of PEP, and is consistent with other studies of volume resuscitation in acute pancreatitis. Prospective studies evaluating the impact of IVR on the incidence and severity of PEP are needed.
Background: Solid pseudopapillary tumour of the pancreas is a rare neoplasm with low malignant potential, which affects predominantly young females. Only about 10% to 15% cases of SPTs are malignant. We describe four malignant solid pseudopapillary tumour of the pancreas and retroperitoneum.

Method: One patient had recurrence with multiple liver metastases that could not be resected. Chemotherapy was initiated for this patient. One patient with Virchow's node and liver metastasis received surgery. The other two patients had two recurrences that could be resected. Meanwhile, a literature review was carried out. Some clinicopathological features and strategies of management of malignant solid-pseudopapillary tumour are presented.

Results: In the follow-up of one year, they were all alive except for one died of postoperative abdominal infection.

Conclusion: In general, surgical removal of the tumor even in case of metastases or recurrence offers an excellent prognosis. Chemotherapy and radiotherapy should be taken into consideration in unresectable patients.
Introduction: Surgery in chronic pancreatitis over the past 30 years is dominated by resection types of surgery (Frey, Beger - procedures), the validity of which is extremely controversial and is viewed in isolation from a holistic view of the observed morphological changes in the pancreas (head, body, tail).

Methods: 95 operated patients with chronic pancreatitis with ductal hypertension. Alcoholic chronic pancreatitis was the genesis for 88 (92.7%) of them. Patients with ductal hypertension and dilated Wirsung’s duct over the 5mm in a diameter (82%) had been undergoing a conservative therapy for 3-5 years. For this time, there were many different features of exocrine insufficiency appeared in 68% patients, endocrine insufficiency - in 23%. Resection types of surgery were performed in 49 (49/95, 51.6%) patients (control group), (Frey - 31, Beger - 18). In 46 (46/95, 48.4%) patients (study group) was performed parenchyma-preserving operation type (longitudinal total pancreatowirsungoduodenopapillotomy with longitudinal Roux-en-Y pancreaticojejunoduodenostomy) during which the biopsy material was taken for morphological examination from the head, body and tail of the pancreas. The prevalence of fibrosis and collagen type IV and α-SMA-positive stellate cells, immunocells infiltration of the pancreas were determined by histology and immunohistochemistry (IHCh). In a survey of patients used US, CT, ERCP, intraoperative US, C-peptid, endogenic insulin, paratgormon, CA 19-9, Ig-G, pancreatic fecal elastase-1.

Results: All patients identified completely homogeneous morphological changes in the tail, body and head of the pancreas: a pronounced periductal fibrosis, which occupies a large area with focuses of immunocells infiltration, formation of a thick connective tissue sheath along the Wirsung duct. The activated α-SMA-positive stellate cells were observed in large numbers in all areas of fibrosis of the pancreas, there was a significant expression of collagen type IV. In addition, there was a penetration of α-SMA-positive stellate cells from the area of fibrosis in the interlobular periductal stroma with the formation of fibrous septa between the lobules of varying severity (Figure). In the long term (5 years) in all patients in the control group showed markedly progression of exocrine insufficiency. At the same time after parenchyma-preserving operations in patients with exocrine insufficiency of available severity it hadn’t progressed, and in the absence of exocrine insufficiency before the operation was not observed its development after surgery.

Conclusion: In patients with chronic pancreatitis with ductal hypertension morphological changes in the head, body and tail of the pancreas is completely the same type. This is seriously foregrounds for denial of resection operations. Patients with lasting pain syndrome following ineffective drug management need for parenchyma-preserving operation in time. The direct indications for this operation are dilation of Wirsung’s duct over the 5mm and more, beginning cystic transformation of pancreas parenchyma.
Figure. Homogeneous morphological changes in the tail, body and head of the pancreas in patient with Chronic Pancreatitis