

P 1. MEDICAL CABINET ONCOLOGY: DISULFIRAM AND COPPER GLUCONATE SHOW SIMILAR EFFICACY IN PANCREATIC CANCER CELL LINES AND PATIENT-DERIVED XENOGRAFT TISSUE

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Presenter: Jennifer Leiting MD | Mayo Clinic Rochester

Background: Pancreatic cancer remains a difficult malignancy to treat with poor overall outcomes. Disulfiram (DSF) has been previously shown to have anti-cancer effects that are potentiated by copper gluconate (Cu) in other cancer types. We hypothesized that treatment with DSF/Cu would show efficacy in both pancreatic cancer cell lines and patient-derived xenograft (PDX) tissue.

Methods: Two pancreatic cancer cell lines (MIA PaCa-2 and PANC-1), along with dissociated cells from two pancreatic adenocarcinoma (PDAC) PDX tumors (PAX297 and PAX298), were cultured and treated with DSF/Cu. After 24 hours of treatment, cell viability was assessed. Organoids from PAX297 were treated with DSF/ Cu. With IRB and IACUC approval, PAX297 was implanted into NOD/SCID mice and the mice were treated with vehicle or DSF/Cu for four weeks. Treated tumor tissue was used for western blotting to assess for apoptotic protein markers.

Results: When treated with DSF/Cu, MIA PaCa-2 and PANC-1 had a significant reduction in cell viability starting at 0.05 μ M ($p = 0.004$) and 0.1 μ M ($p = 0.016$) respectively (Figure 1A). PAX297 and PAX298 cells had similar responses to DSF/Cu, with significant reductions in cell viability starting at 0.1 μ M ($p = 0.004$) (Figure 1A). Light microscopy reflected these findings (Figure 1B). Organoids cultured from PAX297 were also susceptible to treatment with DSF/Cu, with significant reduction in cell viability beginning at 0.5 μ M ($p = 0.016$) (Figure 1C). Light microscopy shows a loss of organoid structure in the DSF/Cu treated organoid (Figure 1D). In vivo treatment with DSF/Cu resulted in significantly smaller tumors when compared to control (Figure 1E). The DSF/Cu treated tumors showed higher expression of cleaved apoptotic protein markers when compared to control (Figure 1F) suggesting that the mechanism of action for DSF/Cu in these tumors is through apoptotic pathways.

Conclusion: The commonly available drug, DSF, in combination with Cu, is effective against PDAC cell lines, but more importantly, is effective against patient-derived tissue. Further studies are needed to determine its efficacy in additional PDX models, as well a possible role as an adjunct to traditional chemotherapies, but these well-tolerated drugs may be an alternative treatment option for patients with this devastating malignancy.

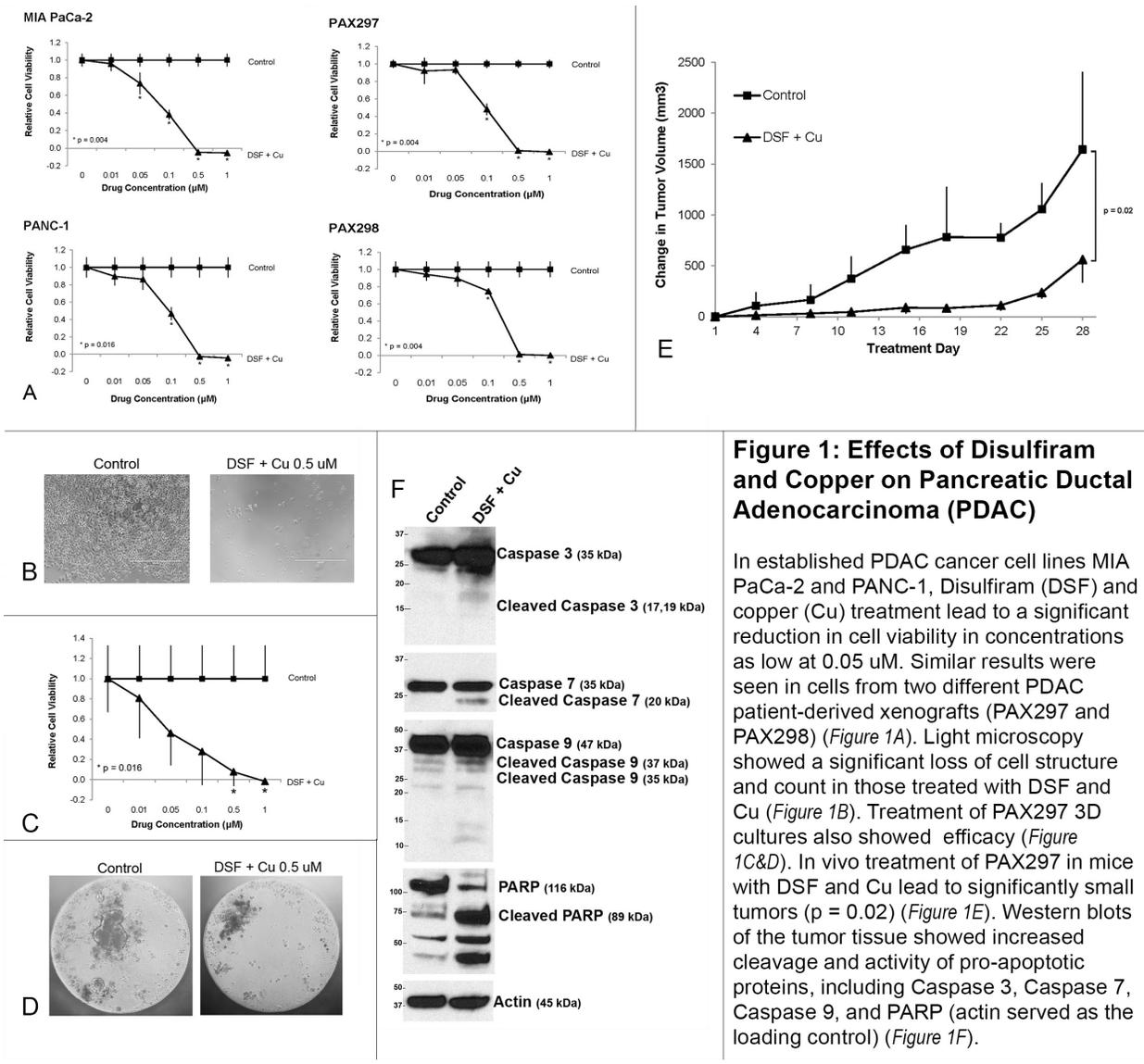


Figure 1: Effects of Disulfiram and Copper on Pancreatic Ductal Adenocarcinoma (PDAC)

In established PDAC cancer cell lines MIA PaCa-2 and PANC-1, Disulfiram (DSF) and copper (Cu) treatment lead to a significant reduction in cell viability in concentrations as low as 0.05 μM . Similar results were seen in cells from two different PDAC patient-derived xenografts (PAX297 and PAX298) (Figure 1A). Light microscopy showed a significant loss of cell structure and count in those treated with DSF and Cu (Figure 1B). Treatment of PAX297 3D cultures also showed efficacy (Figure 1C&D). In vivo treatment of PAX297 in mice with DSF and Cu lead to significantly small tumors ($p = 0.02$) (Figure 1E). Western blots of the tumor tissue showed increased cleavage and activity of pro-apoptotic proteins, including Caspase 3, Caspase 7, Caspase 9, and PARP (actin served as the loading control) (Figure 1F).

P 2. IMPACT OF THE INTRODUCTION OF FOLFIRINOX ON VARIATION IN THE USE OF CHEMOTHERAPY IN PATIENTS WITH METASTATIC PANCREATIC CANCER: A POPULATION-BASED ANALYSIS

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Background: Chemotherapy regimens have shown to cause different survival benefits in patients with metastatic pancreatic cancer. We investigated whether the use of chemotherapy has increased over 10 years, especially since the introduction of FOLFIRINOX and whether this influenced survival.

Methods: A nationwide retrospective cohort study was performed, including patients with primarily metastasized pancreatic ductal adenocarcinoma from the Netherlands Cancer Registration (2007-2016). Regression analyses were performed to assess the association period of diagnosis and type of chemotherapy, and median overall and 1-year survival.

Results: Overall, 7566 patients with metastasized pancreatic cancer were included of whom 62.7% were not treated with chemotherapy. Patients treated with chemotherapy in the post-FOLFIRINOX period had better median overall and 1-year survival than in pre-FOLFIRINOX era (HR for mortality 0.80 95%CI 0.74-0.87); median overall survival was 6.4 months (1-year survival 21%) vs. 5.7 months (1-year survival 14%) respectively. In 2015-2016, 435 patients received FOLFIRINOX (60.6%), 67 patients gemcitabine with nab-paclitaxel (9.3%), 179 patients gemcitabine only (24.9%) and 37 patients received other chemotherapy regimens (5.2%). The percentage of patients receiving FOLFIRINOX increased from 56.1% (206/367 patients) in 2015 to 65.2% in 2016 (229/351 patients) ($p=0.013$). In 2015, 8.4% (31/367) patients received nab-paclitaxel + gemcitabine compared to 10.3% (36/351) in 2016 ($p=0.405$). Patients treated with FOLFIRINOX had a better median overall and 1-year survival than patients with gemcitabine (HR for mortality 0.43 95%CI 0.35-0.53). This also accounted for patients with nab-paclitaxel + gemcitabine (HR for mortality 0.48 95%CI 0.35-0.65).

Conclusion: Current practice on chemotherapy in patients with metastatic pancreatic cancer was highly variable over the last ten years. The percentage of patients with chemotherapy did not increase after the introduction of FOLFIRINOX and gemcitabine + nab-paclitaxel, but patients treated in this period had a better survival. Gemcitabine is still prescribed in a relative large percentage of patients despite little effect on survival. A nationwide strategy to optimize implementation of new therapies should be developed to reduce practice variation with a potential negative effect on patient outcomes.

P 3. FACTORS PREDICTING FAILURE OF PERCUTANEOUS DRAINAGE IN THE “STEP-UP APPROACH” FOR ACUTE NECROTIZING PANCREATITIS: A 10-YEAR RETROSPECTIVE OBSERVATIONAL STUDY WITH A “PROACTIVE” PERCUTANEOUS DRAINAGE STRATEGY

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Background: Image guided percutaneous drainage (PCD) of necrotic collections is currently the first step in the step-up approach for infected pancreatic necrosis. The exact factors responsible for failure of PCD, both before and after drain insertion, remain unclear. Our aim was to determine clinical and radiological factors predictive of failure of PCD as initial intervention in necrotizing pancreatitis.

Methods: Single-center observational study with retrospective analysis of prospectively maintained database of necrotizing pancreatitis was analysed. Patients with severe and moderately severe acute pancreatitis in whom percutaneous drainage was performed as first “step” while patients with mild pancreatitis, acute-on-chronic pancreatitis, those who underwent initial PCD at other hospitals, and those who underwent endoscopic drainage as first intervention. Clinical and radiological parameters prior to first drain placement and details of intervention were studied. PCD success was defined complete resolution of disease with PCD as sole management. PCD failure was defined as need for further step-up i.e. surgical intervention or disease-specific mortality in a patient with PCD. Univariate and multivariate analysis was performed between the two groups. Pre- and post PCD models were calculated and validated.

Results: A total of 304 patients were studied. The mean age was 39.9 ± 12.8 years. There were 228 male and 76 female patients. The underlying etiology was alcohol in 171 (56.3%), gallstones in 77 (25.3%) and others in 56 (19.4%). Number of patients with severe pancreatitis was 221 (72.6%) and moderately severe was 83(27.3%). Median APACHE score at presentation was 9 (IQR 6-12) and at first intervention was 10 (IQR 7-14). PCD was successful in 182 (59.8%) and failed in 122 (40.1%). On univariate analysis, multiple factors were found to be predictive of PCD failure as shown in Table 1. On multivariate analysis of pre-PCD model, multi-organ failure ($p=0.006$), organ failure in first week of illness ($p=0.042$), pancreatic parenchymal necrosis $>50\%$ ($p=0.012$) and positive bacterial blood culture ($p=0.022$) were found to be significant. In post PCD model, left pararenal collection ($p=0.01$), APACHE II score at time of first PCD insertion ($p<0.001$), lack of sepsis reversal within one week of PCD insertion ($p<0.001$) and *Escherichia coli* in initial PCD culture ($p=0.017$) were significantly associated with PCD failure. Both models were internally validated by bootstrap analysis with 5000 resamples and were found to be statistically significant.

Conclusion: Proactive PCD strategy was successful in 59.8%. Pre-PCD factors significantly predicting PCD failure included early-onset organ failure, multiple organ failure, extensive pancreatic necrosis, and bacteremia. Post-PCD factors significantly predicting PCD failure included higher APACHE II score at time of PCD, lack of sepsis reversal within a week post-PCD, left pararenal collection and *E.Coli* in PCD culture.

P 4. A TUG-OF-WAR IN IPMNS MANAGEMENT: A COMPARISON BETWEEN 2017 INTERNATIONAL AND 2018 EUROPEAN GUIDELINES

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Presenter: Stefano Crippa MD, PhD | San Raffaele Scientific Institute

Background: IPMN is a potentially malignant neoplasm of the pancreas with a steadily growing incidence. Multiple guidelines were proposed to identify IPMNs a risk of malignancy. The aim of this study is to compare the 2017 International guidelines (IG) with the 2018 Evidence-based European guidelines (EG) for IPMN management.

Methods: Between 2009 and 2018 the clinical data of 627 resected patients with histologically confirmed IPMNs were prospectively collected at San Raffaele Scientific Institute, Milan, Italy and at Karolinska Hospital Stockholm, Sweden. The criteria of 2017IG and 2018EG were then retrospectively applied in order to evaluate their accuracy in identifying patients with malignant IPMNs (IPMNs with high-grade dysplasia and invasive carcinoma). Since a different role is assigned to EUS in the management flowcharts of IG and EG, we also identified 296 patients who underwent EUS to investigate how often EUS changed the initial surgical indication obtained with magnetic resonance imaging (MRI).

Results: High-risk stigmata (HRS) and worrisome features (WF) of 2017IG are similar to absolute (AI) and relative indications (RI) of EG2018. Accuracy was 69.9% for HRS, 39% for WF, 71% for RI and 36% for RI. Since 2017IG recommend immediate surgery only for HRS and 2018EG for all fit patients with AI but with also RI, we compared the overall accuracy of the two guidelines considering this different approach. Sensitivity (SN) was 99.2% for AI+RI compared with 70.1% of HRS. On the other hand, IG showed higher positive predictive value (PPV) and higher accuracy (PPV: 76.9% IG vs. 59.5% EG; Accuracy: 69.9% IG vs. 59.5% EG). Clinically, applying EG leads to a high number of patients with a benign IPMN undergoing surgery (40.5%). Moreover, the use of EUS based on IG recommendations reduces the number of overtreated patients (12.4%) leading to a potentially higher rate of malignant IPMNs not undergoing immediate surgery (17.7%). 296 (47%) patients underwent EUS, and most of the previously obtained diagnosis (83%) made by MRI were confirmed. Nevertheless, a relevant diagnostic upgrade has occurred in 42 (14%) patients who had WF at MRI that become HRS after EUS.

Conclusion: 2018EG adopt a more surgical aggressive approach compared to 2017IG, determining higher SN for malignancy but with a higher rate of overtreatment. Furthermore, the more conservative approach of 2017IG leads to an increased accuracy with the risk of missing malignant lesions. EUS proved to be very useful in the diagnostic work-up of IPMNs, especially in the subset of patients showing WF at MRI.

P 5. AN EPIGENETIC CLASSIFICATION OF PANCREATIC DUCTAL ADENOCARCINOMA IDENTIFIES UNIQUE SUBTYPES ASSOCIATED WITH CLINICAL OUTCOME

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Presenter: Victoria Aveson MD | New York Presbyterian - Weill Cornell Medical Center

Background: Pancreatic ductal adenocarcinoma features dismal overall survival with heterogeneous outcomes following surgery. Recent research suggests epigenetic changes underlie major steps in pancreatic cancer progression, but studies in human tumors have been limited by the low cellularity of pancreatic tumors and storage methods for surgical samples that interfere with most common methods of epigenetic analysis. As a result, while subtypes of pancreatic cancer have been identified based on gene expression and genomic information, epigenetic subtypes of human tumors have not been well characterized or correlated directly with clinical outcomes

Methods: We employed genome-wide analyses of chromatin accessibility and RNA-sequencing to archival frozen normal and pancreatic tumor tissue. Briefly, flash frozen samples from tumor and normal pancreas of patients with pancreatic ductal adenocarcinoma resected at Memorial Sloan Kettering Cancer Center in 2005 were obtained. Nuclei were isolated by density gradient. Aneuploid nuclei were identified with flow cytometry to enrich for tumor DNA. Tagmentation and amplification of ATAC libraries for sequencing were performed as per our optimized Omni-ATAC protocol. Further enhancement of tumor signal was achieved with computational correction with libraries from matched normal pancreas samples. Clinical data for all patients was evaluated for association between chromatin accessibility subtype and oncologic outcomes, including overall survival, progression-free survival and site of recurrence.

Results: 85 patients were included with a median age of 67 years and 37% were female. The majority of tumors (90.3%) were stage II at resection and moderately differentiated (54.2%) or poorly differentiated (31.3%). All lesions were pancreatic adenocarcinoma or intraductal papillary mucinous neoplasm. Median survival was 722 days and mean survival was 1133 days. Nuclei were successfully isolated from flash frozen samples and viable chromatin accessibility libraries were produced from frozen tissue. Distinct epigenetic signatures were defined, identifying subtypes of disease that do not recapitulate the Collison classical, quasi-mesenchymal and exocrine-like or Bailey squamous, pancreatic progenitor, immunogenic and ADEX schema, nor the TCGA basal/classical or Moffit basal/classical subtyping. Further, a significant association between subtype and risk of early recurrence was identified, suggesting that integration of chromatin accessibility data improves the clinical utility of genomic and transcriptional information.

Conclusion: In our analysis, we developed and refined an epigenetic classification of pancreatic ductal adenocarcinoma using archival snap-frozen tissue. Amplification of tumor signal can be achieved with flow cytometry and computational means, which eliminates the need for costly and potentially confounding xenografts or microdissection. Our epigenetic classification offers information that, when integrated with genomic and transcriptomic characterization, can be predictive of clinical outcomes

P 6. DOES THE MICROBIOLOGY OF BACTIBILIA DRIVE POSTOPERATIVE COMPLICATIONS AFTER PANCREATODUODENECTOMY?

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Presenter: Thomas Maatman MD | Indiana University School of Medicine

Background: The influence of specific bacteria on post-operative outcomes after pancreatoduodenectomy (PD) remains unknown. Preoperative biliary instrumentation and stenting increases the risk of bactibilia; however, the consequences of bile microflora, particularly with broad antimicrobial resistance patterns, are poorly understood. The aim of this study was to determine the influence of the microbiology of bactibilia on postoperative outcomes following PD.

Methods: Intraoperative bile cultures were obtained in 162 study patients undergoing PD between 2015 and 2017; this represents 29% of PD performed during the study period (162/552). Demographic, clinical factors, and all postoperative outcomes were prospectively recorded and retrospectively reviewed. Complications were defined according to the Clavien-Dindo classification. The microbiology of intraoperative bile cultures was analyzed and correlated with short-term outcomes after PD. Where applicable, independent groups t-test and Pearson's correlation or Fisher's exact tests were performed. Statistical significance was defined as p-value of <0.05.

Results: Intraoperative bile cultures grew positive in 89/162 patients (55%). No differences in age, sex, or comorbidities were found between the positive and negative bile culture groups. The bactibilia group had an increased incidence of periampullary cancer (86.5% vs 57.5%, $p=0.001$) and preoperative biliary instrumentation (88.8% vs 24.7%, $p<0.001$). The most common perioperative antibiotic combination was ceftriaxone/metronidazole (93%); antibiotic selection differed only in the event of an allergy. Bactibilia was not associated with increased postoperative complications or mortality (Table 1). When controlling for Fistula Risk Score (FRS), bactibilia was not associated with an increased risk of clinically relevant postoperative pancreatic fistula, POPF (Table 1). The most common bacteria were *Enterococcus* spp. ($n=48$, 53.9%), *Klebsiella* spp. ($n=24$, 27.0%), and *Enterobacter* spp. ($n=17$, 19.1%). *Enterococcus* was associated with higher rates of superficial surgical site infection (OR 6.5, 95% CI 1.2-34.8, $p=0.03$). *Enterobacter* was associated with increased organ space infection (OR 4.9, 95% CI 1.1-22.0, $p=0.03$). No single bacterium was associated with an increased risk of POPF, bile leak, cholangitis, 30- or 90-day mortality. Mortality of the entire cohort was 2.5% and 3.7% at 30- and 90-days, respectively.

Conclusion: Bactibilia, in general, does not increase the risk of developing a postoperative complication following pancreatoduodenectomy; however, specific bacteria within bile influences infectious postoperative complications. *Enterococcus* and *Enterobacter* increase the likelihood of developing superficial and organ space surgical infections, respectively. Knowledge of local bile colonization and antimicrobial resistance patterns is critical for choosing appropriate perioperative antibiotics to decrease surgical site infections.

Outcome	Cohort (n=162)	Sterile (n=73)		Bactibilia (n=89)		p-value
Pancreatic fistula (all)	51 (31.5%)	26 (35.6%)		25 (28.1%)		0.30
Pancreatic fistula (clinically relevant)	18 (11.1%)	11 (15.1%)		7 (7.9%)		0.15
		FRS neg-low FRS mod-high	0/15 (0%) 11/58 (19.0%)	FRS neg-low FRS mod-high	2/43 (4.7%) 5/46 (10.9%)	0.40 0.26
Wound infection	7 (4.3%)	2 (2.7%)		5 (5.6%)		0.37
Cholangitis	1 (0.6%)	0 (0%)		1 (1.1%)		0.37
Organ space infection	9 (5.6%)	3 (4.1%)		6 (6.7%)		0.47
Bile leak	8 (4.9%)	8 (11.0%)		0 (0%)		0.001
Sepsis	2 (1.2%)	1 (1.4%)		1 (1.1%)		0.89
Organ failure	10 (6.2%)	7 (9.6%)		3 (3.4%)		0.10
30-day mortality	4 (2.5%)	3 (4.1%)		1 (1.1%)		0.23
90-day mortality	6 (3.7%)	5 (6.8%)		1 (1.1%)		0.06

P 7. PREOPERATIVE BILIARY STENTING IS ASSOCIATED WITH HIGHER POSTOPERATIVE MORBIDITY AND EQUIVALENT MORTALITY IN PATIENTS WITH MODERATE AND SEVERE HYPERBILIRUBINEMIA - AN ANALYSIS OF THE GERMAN STUODOQLPANCREAS REGISTRY

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Presenter: Louisa Bolm MD | University Medical Center Schleswig-Holstein

Background: The impact of preoperative biliary stenting (PBS) prior to pancreatoduodenectomy (PD) for pancreatic ductal adenocarcinoma (PDAC) in patients with hyperbilirubinemia is controversial.

Methods: Patients undergoing PD in the time period from 2014 to 2016 with or without PBS for PDAC were identified from the German DGAV-StuDoQIPancreas registry. The effects of PBS in patients with and without a history of jaundice were evaluated. Furthermore, the impact of different levels of hyperbilirubinemia and subsequent PBS on postoperative morbidity and mortality were analyzed.

Results: 1133 patients undergoing PD for PDAC were identified from the registry, and 480 patients underwent PBS. 320 patients receiving PBS (66%) had no history of jaundice. In these patients, PBS was associated with higher rates of preoperative cholangio-sepsis (PBS 6% vs. no PBS 2%, $p < 0.001$). In these patients, CDC grade IIIa-IVb complications were more frequent for PBS patients (21% vs. 50%, $p = 0.001$). In patients with serum bilirubin levels of > 20 mg/dl, there was a trend for higher CDC grade IIIa-IVb complications (14% vs 38%, $p = 0.069$). Mortality was comparable in patients undergoing PBS versus upfront surgery for both serum bilirubin cut-off levels.

Conclusion: The majority of PBS procedures were performed in patients with no history of jaundice and lead to a significant increase in perioperative morbidity. Serum bilirubin levels > 15 mg/dl were associated with higher postoperative morbidity and mortality. PBS correlated with higher postoperative complication rates in these patients.

P 8. PHASE II CLINICAL TRIAL USING NOVEL PEPTIDE VACCINE COCKTAIL COMBINED WITH GEMCITABINE FOR SURGICALLY RESECTED PANCREATIC CANCER PATIENTS

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Presenter: Motoki Miyazawa MD, PhD | Wakayama Medical University

Background: The development of effective treatment for preventing recurrence is essential to improve the prognosis of pancreatic cancer. We conducted a multicenter phase II study using peptide vaccine cocktail named OCV-C01 containing epitope peptides derived from KIF20A, VEGFR1, and VEGFR2 combined with gemcitabine with the aim to estimate the disease-free survival and to explore the surrogate biomarker associated with this immunotherapy treatment.

Methods: A single arm phase II study of 30 patients with pancreatic ductal carcinoma who underwent pancreatectomy at the four Japanese high volume centers was performed. Of each 28-day treatment cycles, eligible patients received subcutaneous injection of 1mL of OCV-C01 on days, 1,8,15 and 22 for 48 weeks, and Gemcitabine was administered intravenously at a fixed dose of 1000mg/m² on days, 1, 8 and 15 for 24 weeks. The primary endpoint was disease-free survival and secondary endpoints included safety, overall survival (OS), and immunological assays on peptide-specific CTL activity and KIF20A expression in resected pancreatic specimens.

Results: The median DFS was 15.8 months (95%CI, 11.1-20.6), and the DFS rate at 18 months was 34.6% (95%CI 18.3-51.6). The median OS was not reached and the overall survival rate at 18 month was 69.0% (95%CI 48.8-82.5). The administration of OCV-C01 was well tolerated. In the subgroup analysis of the per protocol set, there was significant differences in DFS between patients with positive CTL responses specific for KIF20A peptides and without them (p=0.027), and between patients with positive KIF20A expression and without them (p=0.014). In addition, all 4 patients who underwent R0 resection with KIF20A expression had no recurrence of pancreatic cancer, and DFS of them was significantly longer than 19 patients who underwent R0 resection without KIF20A expression (p=0.011).

Conclusion: OCV-C01 combined with gemcitabine was tolerable, and DFS was favorably compared with previous data for resected pancreatic cancer. DFS of patients with positive KIF20A expression in resected pancreatic cancer specimen might be prolonged with frequent KIF20A-specific CTL response by receiving this immunotherapy treatment.

P 9. NOVEL PREOPERATIVE PATIENT-CENTERED SURGICAL WELLNESS PROGRAM IMPACTS LENGTH OF STAY FOLLOWING PANCREATECTOMY

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Presenter: Danielle DePeralta MD | Indiana University School of Medicine

Background: Pancreatic resections have the potential for significant morbidity and mortality. Enhanced Recovery After Surgery (ERAS) protocols, while appealing, have been slowly adopted by pancreatic surgeons. An urban, academic medical center created a simple, preoperative, patient-centered, surgical wellness bundle (PWB). This study assessed the impact of this preoperative wellness bundle on patient outcomes following pancreatectomy.

Methods: All pancreatoduodenectomies (PD) and distal pancreatectomies (DP) performed at a single academic medical center from 6/2015-6/2018 were included on study. The PWB consisted of chlorhexidine bath solution, topical mupirocin for the nostrils, an incentive spirometer, immunonutrition supplements, and smoking cessation information, all contained in a sporty red roller bag. In select cases, study staff performed structured patient interviews, observations, and standardized surveys at key intervals throughout the perioperative period. Clinical parameters were obtained from a retrospective review of a prospective clinical database and augmented by institutional ACS NSQIP data, Vizient data and medical records. Chi-Square/Fisher's Exact and Independent-Samples t-Tests were used for univariable analyses; multivariable regression (MVR) was performed.

Results: A total of 669 pancreatectomy patients (411 PD, 258 DP) were enrolled. Of these, 361 patients received the PWB (223 PD, 138 DP). Compliance with individual elements exceeded 60%. Patients that did and did not receive the PWB were similar with respect to age, sex, functional status, presence of comorbidities, and indication for/ extent of surgery. On univariable analysis, patients who received the PWB had a shorter length of stay (8.5 vs. 10.2 days; $p=0.04$). A trend existed for less acute renal failure (0.6 vs. 1.9%; $p=0.185$) and delayed gastric emptying (12.3% vs. 16.7%; $p=0.118$). On multivariable analysis, patients who received the PWB had a shorter length of stay (OR 0.81, CI 0.72-0.91; $p<0.001$).

Conclusion: In an era of slow adoption of ERAS among pancreatic surgeons, implementation of a simple, preoperative, patient-centered, surgical wellness bundle results in a significant reduction in length of stay and may be associated with improved perioperative outcomes.

P 10. DRAIN MANAGEMENT FOLLOWING DISTAL PANCREATECTOMY: CHARACTERIZATION OF CONTEMPORARY PRACTICE AND IMPACT OF EARLY REMOVAL

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Presenter: Laura Maggino MD | University of Pennsylvania

Background: Despite accruing evidence supporting its benefit following pancreatoduodenectomy, early drain removal after distal pancreatectomy (DP) has yet to be explored. The aim of this study was to explore nationwide contemporary drain management practices and examine the impact of early removal following DP.

Methods: The American College of Surgeons' National Surgical Quality Improvement Program (ACS-NSQIP) was queried for elective DPs from 2014-17. When possible, data were linked to survey responses regarding drain management from hepato-pancreato-biliary (HPB) surgeons in the ACS-NSQIP HPB Collaborative conducted in 2017. The independent association between timing of drain removal and patients' outcomes was investigated through uni and multivariable analyses and propensity-score matching.

Results: Of 5581 DPs identified, 4708 (84.4%) patients received intraoperative drains and early removal (\leq POD3) was performed in 716 (15.2%). Drain fluid amylase was recorded on POD1 for 1285 (27.3%) patients who received drains and positively correlated with CR-POPF with an AUC of 0.67. The overall rates of death or serious morbidity (DSM) and clinically-relevant fistula (CR-POPF) were 19.5% and 17.0%. Early removal demonstrated significantly better outcomes when compared to late removal and no drain placement for: DSM, CR-POPF, delayed gastric emptying, percutaneous drainage, length of stay, and readmission (Table). On multivariable analysis, early removal demonstrated reduced odds of developing DSM (OR=0.41, 95% CI=0.26-0.65) and CR-POPF (OR=0.33, 95% CI=0.18-0.61) compared to no drain placement, while late removal displayed increased odds for CR-POPF (OR=2.15, 95% CI=1.27-3.61) when compared to no drain placement. After propensity-score matching, early removal was associated with reduced odds for CR-POPF (OR=0.35, 95% CI=0.17-0.73). One hundred four HPB surgeons responded to the survey, representing a total case-load of 2218 DPs. Among these, 48 (46.2%) replied that they perform early drain removal "Always" or "Frequently" (75-99% of the time). Examining the cases these surgeons performed (N = 995) revealed that just 258 (25.9%) had drains removed early. In the patients whom these surgeons removed drains early, 29.1% did not have a DFA-1 recorded. When this group of surgeons removed drains late, 57.5% did not have a DFA-1 recorded. An additional 41 (39.4%) surgeons responded that their practice was to "Never" or "Occasionally" (1-25% of the time) perform early drain removal. Of the cases that these surgeons performed (N = 921), 108 (11.7%) had drains removed early.

Conclusion: Although not yet widely implemented, early drain removal after distal pancreatectomy is associated with better outcomes. Interestingly, surgeons who were self-professed "early removers" largely did not adhere to this in actual practice. This discrepancy may stem from a lack of confidence in a patient's trajectory, as DFA-1 was not recorded in most cases when these surgeons removed drains late. Conversely, DFA-1 was checked in the majority when these surgeons did adhere to their professed practice. This study demonstrates the potential benefits of early removal and provides a substrate to define best practices and improve the quality of care for DP.

P 11. THE EFFICACY OF THE CDK 4/6 INHIBITOR (ABEMACICLIB) IN PANCREATIC CANCER CELLS

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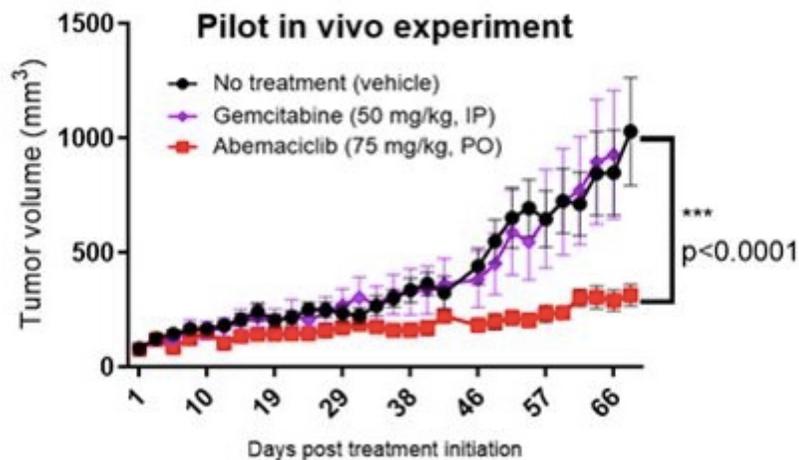
Presenter: Teena Dhir MD | Thomas Jefferson University

Background: Pancreatic Ductal Adenocarcinoma (PDA) is a devastating malignancy with a 9% five-year survival rate and is the third leading cause of cancer-related deaths in the U.S. One common genetic feature in PDA is the loss of the CDKN2A gene expression (p16) which is found in over 90% of tumor samples. P16 inhibits the activity of the cyclin D-CDK4/6 complex leading to a G1 arrest, thus p16 loss leads to unchecked cellular proliferation. We hypothesized that the established FDA approved, CDK4/6 inhibitor, abemaciclib (Lilly, IN), could be a potent targeted strategy by inhibiting this commonly dysregulated pathway in PDA cells.

Methods: We determined the efficacy of abemaciclib, an oral CDK4/6 inhibitor in vitro and in vivo in PDA cell lines. IC50 were calculated in multiple PDA cell lines with known P16 status, along with characterizing abemaciclib's effect on cell cycle progression, apoptosis and senescence. In vivo, athymic female nude mice were engrafted with human PDA, Mia PaCa2 cells and randomized to treatment and control arms.

Results: In vitro, we tested CDK4/6 inhibitors palbociclib and abemaciclib in multiple pancreatic cell lines and found that abemaciclib was more potent with IC50s as low as 100nM and caused significant G1 arrest. Abemaciclib was able to not only induce senescence, but also induce apoptosis in PDA cell lines contributing to its efficacy. In vivo, daily abemaciclib therapy was safe and lead to a statistically significant decrease in tumor volume compared to no treatment ($p < 0.0001$) and gemcitabine ($p = 0.0002$).

Conclusion: Abemaciclib had comparable potency to current chemotherapeutics, inhibited colony formation, lead to G1/S arrest and induced apoptosis and senescence. In vivo, abemaciclib lead to tumor growth inhibition in our pilot study. Future work aims to find synergistic drug combination therapy in PDA in an effort to move this work towards a PDA-specific clinical trial.



P 12. SHOULD DIFFUSE MAIN-DUCT INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS BE TREATED WITH TOTAL PANCREATECTOMY?

AB Blair, RM Beckman, JF Griffin, VP Groot, J Yu, MA Makary, RA Burkhart, MJ Weiss, JL Cameron, CL Wolfgang, J He

Presenter: Alex Blair MD | Johns Hopkins University School of Medicine

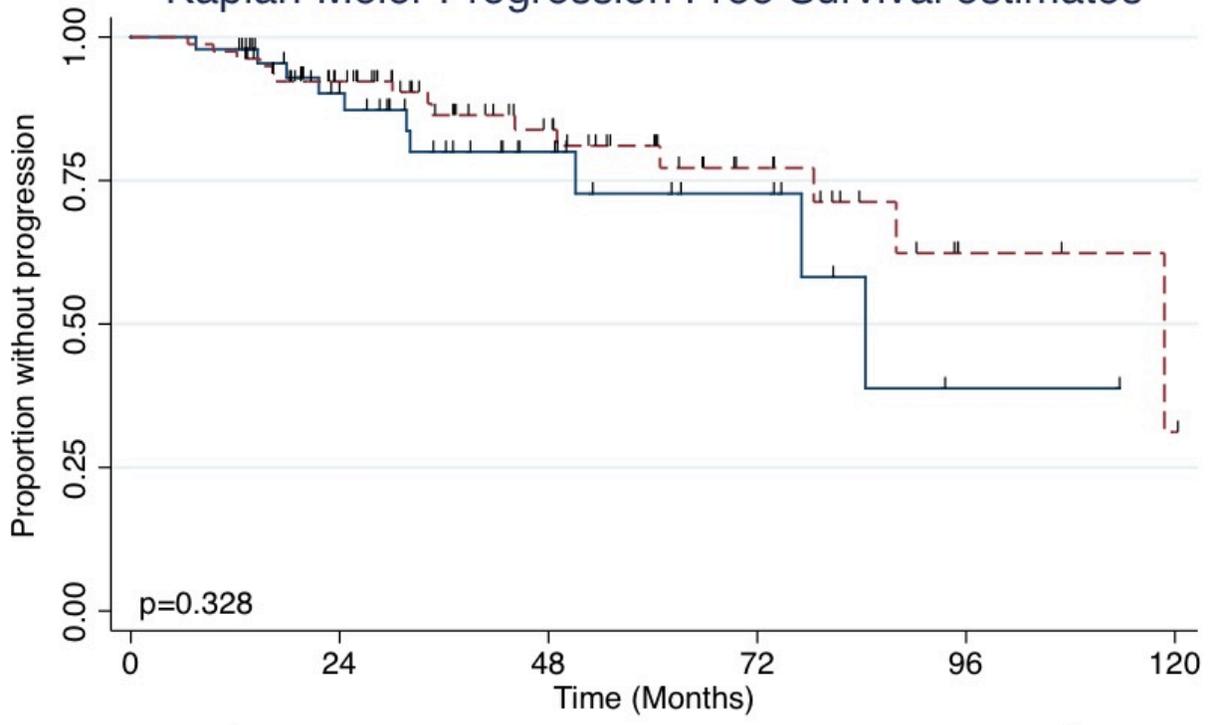
Background: Main-duct (MD) intraductal papillary mucinous neoplasm (IPMN) is associated with a high risk of malignancy. There is a lack of international consensus (partial or total pancreatectomy) when the MD of the whole gland is involved. The fate of the remnant after partial pancreatectomy for benign diffuse MD-IPMN is unclear.

Methods: Consecutive patients with partial pancreatectomy for benign MD-IPMN from 2004 to 2016 were analyzed. Exclusion criteria include any malignancy on final pathology and less than one year of post-operative follow-up. Diffuse MD-IPMN was defined by preoperative imaging as dilation of the MD in the head of the pancreas more than 5mm and involving the whole gland.

Results: Of 127 patients with resected benign MD-IPMN, 47 (37%) had diffuse MD involvement. The majority (96%) underwent pancreaticoduodenectomy and 2 (4%) had distal pancreatectomy secondary to a cyst or larger MD dilatation in the tail. Median age was 73 (IQR: 67-79) with median duct size of 8 mm (IQR 6-13mm). High grade dysplasia (HGD) was observed in 24 (51%), intermediate grade in 21 (45%) and low grade in 2 patients (4%). Two patients had HGD at the resection margin. A median progression free survival (PFS) of 84 months was observed, with 10 (22%) patients developing imaging evidence of progression or new cystic disease in the pancreatic remnant at a median of 25 months. Three of 10 (30%) underwent completion pancreatectomy with no cancer identified in the remnant. A margin positive with intermediate or high grade dysplasia was significantly associated with shorter PFS (HR:4.39, 95%CI 1.05-18.46, p=0.043). When compared to those with focal MD involvement, patients with diffuse MD-IPMN were older (73 vs 67, p=0.009), more likely to receive a pancreaticoduodenectomy (96% vs 56%, p<0.001) and more likely to have high grade dysplasia (51% vs 31%, p=0.025). Nevertheless, MD involvement (diffuse vs focal) was not associated with PFS following surgery (p=0.328).

Conclusion: Partial pancreatectomy is an appropriate surgical approach for diffuse MD-IPMN which are not associated with earlier progression after surgery. Progression in the pancreatic remnant requires ongoing close follow-up.

Kaplan-Meier Progression Free Survival estimates



— Diffuse MD-IPMN - - - Focal MD-IPMN

P 13. PERCEPTION VS. REALITY: A NATIONAL ANALYSIS OF THE SURGERY-FIRST APPROACH FOR PANCREATIC CANCER

JR Bergquist, CL Shubert, CA Thiels, EB Habermann, RL Smoot, ML Kendrick, DM Nagorney, MJ Truty

Presenter: John Bergquist MD | Mayo Clinic Rochester

Background: Surgical resection is necessary for long-term survival in pancreatic adenocarcinoma (PDAC) and is perceived as the optimal initial treatment strategy in patients with "resectable" tumors. However, three critical factors have been repeatedly demonstrated to markedly influence postoperative survival: (A) margin status, (B) CA19-9 levels, and (C) adjuvant chemotherapy. We sought to determine the actual combinatorial frequency of these critical factors and their effect on survival outcomes after a surgery-first approach in localized PDAC using national outcomes data.

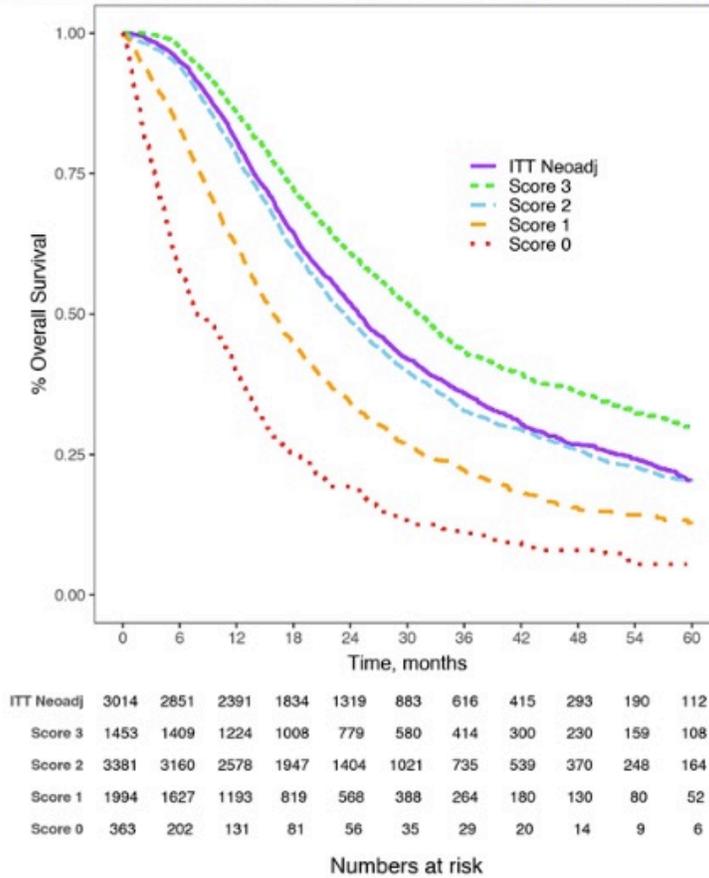
Methods: The National Cancer Data Base (NCDB) 2009-2015 was reviewed for patients with early clinical stage (0/I/II) anatomically resectable PDAC that underwent surgery-first curative intent resection and assessed for: (A) negative margin operation, (B) normal pre-op CA19-9 levels, and (C) receipt of adjuvant chemotherapy. Patients were given a point for the presence (score = 1) or absence (score = 0) of these critical factors as well as various combinations (total score = 0-3) and overall survival (OS) was analyzed by all factor combinations. We then compared these outcomes to equivalently staged patients undergoing neoadjuvant therapy on an intention to treat (ITT) basis, including those patients that did not ultimately undergo curative resection.

Results: 10,205 total patients were included (n = 7,191 surgery-first, n = 3,014 ITT neoadjuvant). Only 20.2% of patients treated with upfront surgery were able to achieve favorable outcomes of all 3 score factors that was associated with greatest survival (median OS = 31.2 months). Unadjusted survival decreased with each failing factor (23.4 months for 2 factors, 14.7 months for 1 factor, and 7.9 months for no factors), and varied by specific factorial combinations (Figure). This decrease in survival persisted after adjustment for other clinically significant variables (age, gender, race, comorbidity score, node status, tumor grade, type of facility). Nearly 1/3rd of patients (32.7%) treated with surgery-first approach had only 1 or none of these survival factors and this was associated with the lowest survival (median OS = 14.7 months). For comparison, the ITT neoadjuvant therapy cohort, including those who did not ultimately undergo resection, were able to achieve survival outcomes (median 24.9 months) superior to 80% of the surgery-first patients (score \leq 2). Over the course of the study, the annual rate of neoadjuvant therapy treatment in the studied population increased from 411 patients (15.6%) of those treated in 2010 to 847 (23.4%) patients of those treated in 2014.

Conclusion: Despite the perceived benefit of a surgery-first strategy in "resectable" PDAC, only 1-in-5 patients will achieve maximum survival. Survival decreases with each failing factor, two of which are not guaranteed prior to attempted resection (margin status, adjuvant therapy). Patients with resectable tumors treated with a surgery-first approach are more likely to have the worst than the best survival outcome. Similarly staged patients undergoing ITT-neoadjuvant therapy achieve survival superior to more than 75% of those treated with surgery-first. Patients should be counseled regarding their probability of actually achieving maximal survival benefit when discussing therapy sequence. Further investigation is needed to critically re-assess the perceived benefit compared to actual outcomes in a surgery-first treatment paradigm for resectable PDAC.

Treatment Strategy	Score Category	% of Pts.		HR, [95% CI], p-value	Median Overall Survival (months)			
Surgery-First	ABC, Score=3	20.2%		Reference	31.2			
	AC Only, Score=2	32.6%	79.8%	1.28, [1.18, 1.39], <0.001	23.9	23.4	19.6	
	AB Only, Score=2	8.5%		1.42, [1.26, 1.60], <0.001	23.3			
	BC Only, Score=2	5.9%		1.48, [1.30, 1.69], <0.001	21.3			
	C Only, Score=1	11.4%		32.8%	1.74, [1.57, 1.93], <0.001	17.5		14.7
	A Only, Score=1	13.9%			2.08, [1.88, 2.30], <0.001	15.2		
	B Only, Score=1	2.4%			2.20, [1.83, 2.65], <0.001	10.4		
	None, Score=0	5.1%			3.32, [2.92, 3.78], <0.001	7.9		
Neoadjuvant (ITT)	-	100%		1.37, [1.25, 1.49]	24.9			

A = Negative Resection Margin, B = Normal Pre-Op CA 19-9, C = Receipt of Adjuvant Chemotherapy



P 14. VISCERAL ARTERY PSEUDOANEURYSM IN NECROTIZING PANCREATITIS: INCIDENCE AND OUTCOMES

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Presenter: Thomas Maatman MD | Indiana University School of Medicine

Background: Visceral artery pseudoaneurysm (PSA) occurs in necrotizing pancreatitis (NP); however, little is known about their natural history. This study aimed to evaluate the incidence, presentation, management, and outcome of PSA at a high-volume pancreatitis center.

Methods: All NP patients treated between 2005 and 2017 were prospectively catalogued into the institution's NP database. Those diagnosed with visceral artery pseudoaneurysm were reviewed for incidence, time from NP onset to PSA development, presenting sign, PSA location, management, and PSA-specific mortality.

Results: Visceral artery PSA developed in 28/647 NP patients (4.3%) between 2005-2017. The most common artery involved was splenic (36%) followed by gastroduodenal (24%), Figure 1. The most common presenting symptom was bloody drain output (32%) followed by incidental CT scan finding (21%). Risk factors for PSA development included age greater than 50 years ($p=0.04$) and the development of any organ failure ($p=0.05$). Median time from onset of NP to diagnosis of PSA was 63.5 days (range 1-957). All patients diagnosed with PSA underwent treatment within 24-hours of diagnosis. Patients were successfully treated with percutaneous angioembolization in 25/28 cases (89%). Three patients required operation (11%): one patient re-bled following embolization and required operative management and two underwent upfront operative management. PSA-specific mortality in the setting of NP was 14% (4/28). All-cause mortality of NP patients with PSA was 25% (7/28); development of PSA was associated with a 4-fold increased risk of death ($p=0.002$).

Conclusion: Visceral artery pseudoaneurysm occurs in 4.3% of NP patients. Percutaneous angioembolization effectively treats most, however mortality of PSA is high (16%). A high degree of clinical suspicion remains critical for early diagnosis of this potentially fatal problem.

P 15. UPDATED ALTERNATIVE FISTULA RISK SCORE TO INCLUDE MINIMALLY-INVASIVE PANCREATODUODENECTOMY: PAN-EUROPEAN VALIDATION

TH Mungroop, S Klompmaker, UF Wellner, EW Steyerberg, A Coratti, M D'Hondt, M de Pastena, S Dokmak, I Khatov, O Saint-Marc, U Wittel, M Abu Hilal, D Fuks, I Poves, T Keck, U Boggi, MG Besselink

Presenter: Timothy Mungroop MD | Academic Medical Center

Background: Minimally-invasive pancreatoduodenectomy (MIPD) may be associated with an increased risk of postoperative pancreatic fistula (POPF) compared to open pancreatoduodenectomy (OPD). The alternative Fistula Risk Score (a-FRS) was developed as a POPF prediction model without blood loss, since (1) Blood loss is currently not registered in several audits (e.g., US-NSQIP), (2) It depends on surgical quality, and therefore a model with blood loss is not suitable for adjusting POPF risk for benchmarking, (3) Blood loss was not a significant predictor in several external validation studies. The a-FRS, however, has not yet been validated specifically for laparoscopic, robot-assisted and hybrid MIPD.

Methods: A validation study was performed in a pan-European cohort of 952 consecutive patients undergoing MIPD (543 laparoscopic, 258 robot-assisted, 151 hybrid) in 26 centers from 7 countries between 2007 and 2017. The primary outcome was POPF (ISGPS grade B/C). Model performance was assessed using the area under the receiver-operating-curve (AUC; discrimination) and calibration plots. Validation included univariable screening for clinical variables that could improve performance. Model improvement was pursued by adding as few predictors as possible while maintaining an adequate AUC, leading to an improved model: the updated a-FRS (ua-FRS). The ua-FRS was externally validated (cross-validation) in the original a-FRS design dataset consisting of 2,479 OPD patients. Finally, a post-hoc validation of the Fistula Risk Score (with blood loss) was performed in the current dataset.

Results: Overall, 202 of 952 patients (21%) developed POPF after MIPD. Before adjustment, the a-FRS performed moderately (AUC 0.68) and calibration was inadequate with systematic underestimation of the POPF risk. Single-row pancreatojejunostomy (OR 4.6, 95-CI 2.8-7.6) and male sex (OR 1.9, 95-CI 1.4-2.7) were identified as important risk factors for POPF in MIPD. Upon testing all univariable significant variables, only male sex, ECOG status ≥ 2 , and single-row pancreatojejunostomy were associated with POPF after adjusting for the original a-FRS predictors. Addition of these factors led to better model discrimination (AUC 0.75 vs. 0.68, $P < 0.001$). After removal of ECOG status model discrimination remained similar (AUC 0.75, 95-CI 0.71-0.79), meaning that ECOG added little to the model accuracy. Single row PJ was removed from the model since this is a modifiable risk factor and results in inferior outcomes. The updated a-FRS, consisting of BMI, pancreatic texture, duct size, and male sex, showed good discrimination (AUC 0.75, 95-CI 0.71-0.79) and adequate calibration. Performance was adequate for laparoscopic, robot-assisted, and hybrid MIPD as well as in OPD (cross-validation showed AUC 0.73, 95CI 0.69-0.78). Of note, discrimination of the original Fistula Risk Score in this dataset showed similar performance compared to the a-FRS before the update (AUC 0.69, 95CI 0.61-0.76).

Conclusion: The updated a-FRS (www.pancreascalculator.com) now includes male sex as a risk factor and is validated for both MIPD and OPD. The significant association between male sex and higher risk of POPF was already found in the a-FRS design study, but this study showed that sex was indispensable in order to achieve adequate performance in all subgroups of MIPD. The increased risk of POPF in MIPD was related to single-row pancreatojejunostomy, which should therefore be discouraged until proven safe.

P 16. SERUM CA19-9 RESPONSE TO NEOADJUVANT CHEMOTHERAPY IS PREDICTIVE OF TUMOR SIZE REDUCTION AND SURVIVAL IN PANCREATIC ADENOCARCINOMA

Al Al Abbas, MS Zenati, CJ Reiser, AB Hamad, JP Jung, AH Zureikat, HJ Zeh III, ME Hogg

Presenter: Melissa Hogg MD | University of Pittsburgh Medical Center

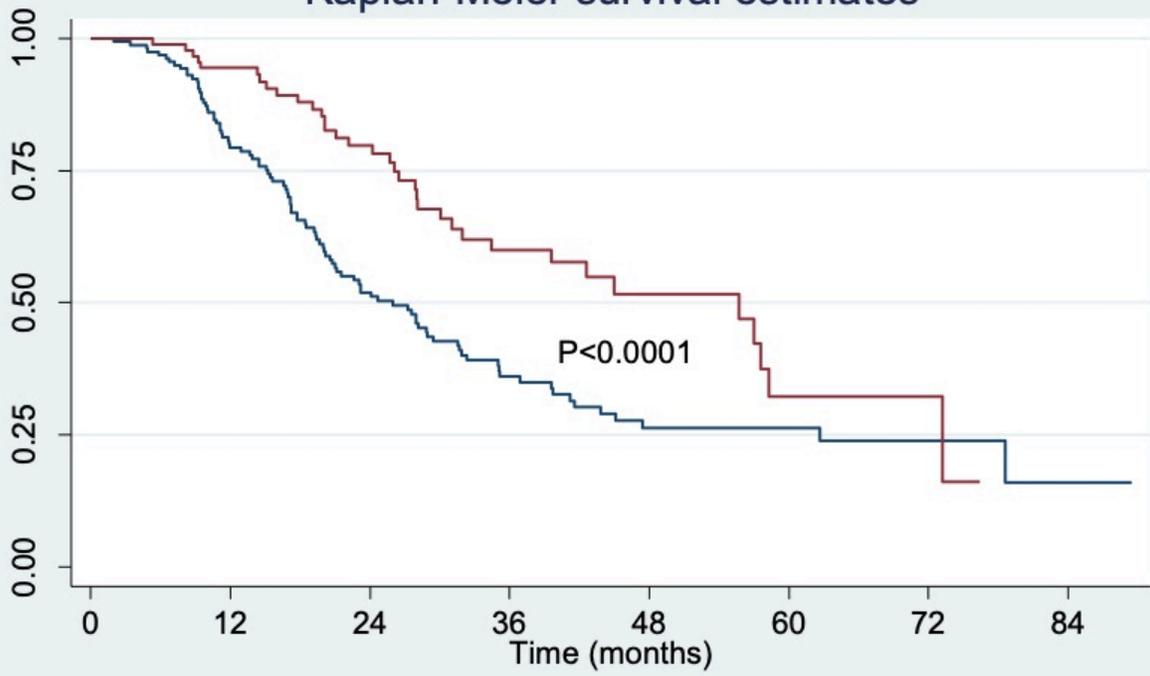
Background: Cross-sectional imaging is a poor predictor of tumor response to neoadjuvant chemotherapy (NT) in pancreatic adenocarcinoma (PDAC). Changes in CA19-9 correspond with resectability, disease-free survival and overall survival (OS), but optimal cut-offs for CA19-9 response are not known. We aim to evaluate serum CA19-9 response to NT and identify thresholds correlating to outcomes.

Methods: Retrospective review of a prospectively collected database of PDAC patients from 2010 to 2017 undergoing resection at a tertiary referral center. Serum CA19-9 measurements were assessed when total bilirubin < 2mg/dL, and cut-offs assessed included normalization and 25-85% response. T-size reduction post-NT was calculated from clinical T-size and pathologic T-size. DFS and OS were analyzed using Kaplan-Meier, and cox hazard regression quantified the effects of different risk factors.

Results: Six hundred and seventy four patients underwent resection: 368 received NT. Non-secretors and patients with total bilirubin elevation were excluded: 250 subjects entered the analysis. Normalization was not associated with improved survival (35.17 [95% CI: 27.27-73.17] vs 29.43 months [95% CI: 24.7-36.87]; p=0.173), but a response \geq 45% was first cutoff associated with improved survival (35 [95% CI: 28.07-42.63] vs 20 [95% CI: 15.6-31.9] months; p=0.018). Response \geq 85% was a strong independent predictor of OS (HR: 0.532 [95% CI:0.358-0.791]; p=0.002). Subjects with \geq 85% response had higher pre-NT CA19-9 (626 [314, 2271] vs. 189 [84, 605], p=0.0001), received more NT cycles (3 [2-6] vs 3 [2-4]; p=0.006) and less adjuvant cycles (4 [3-6] vs 5 [3-6]; p=0.027). There were no significant differences in total cycles received. Patients with an R1 resection with <85% CA19-9 reduction had a greater risk of recurrence (HR=2.73 [95% CI: 1.571-4.742]; p=0.0001) than patients with an R1 resection who had \geq 85% CA19-9 reduction (HR=1.852 [95% CI: 0.865-3.962]; p=0.112) which was not significantly different from the reference. This did not hold true for survival. T-size reduction \geq 25% (56.97 [95% CI: 28.07- *] vs 28.17 [95% CI:22.17-35.17] months, p=0.016) improved survival significantly. Serum CA19-9 response \geq 85% was a strong independent predictor of T-size reduction \geq 25% (HR:2.401 [95% CI:1.268-4.545]; p=0.007).

Conclusion: CA19-9 response \geq 45% is the threshold for predicting survival but optimal at \geq 85%. It is predictive of tumor size reduction and may mitigate the impact of R1 resections on recurrence. Future NT trials should incorporate CA19-9 response as an endpoint.

Kaplan-Meier survival estimates



— CA19-9 Change_85 = 0 — CA19-9 Change_85 = 1

P 17. SMAD4 LOSS IS A PREDICTOR OF NEOADJUVANT TREATMENT RESPONSE IN PANCREATIC DUCTAL ADENOCARCINOMA

R Ramanathan, J Hodges, Al Al-Abbass, A Singhi, H Zeh, ME Hogg, AH Zureikat

Presenter: Rajesh Ramanathan MD | University of Pittsburgh Medical Center

Background: SMAD4 is frequently mutated in pancreatic ductal adenocarcinoma (PDAC). Loss of SMAD4 has been associated with adverse outcomes. This study investigates the association of SMAD4 loss with response to neoadjuvant chemotherapy (NAC) and survival in PDAC.

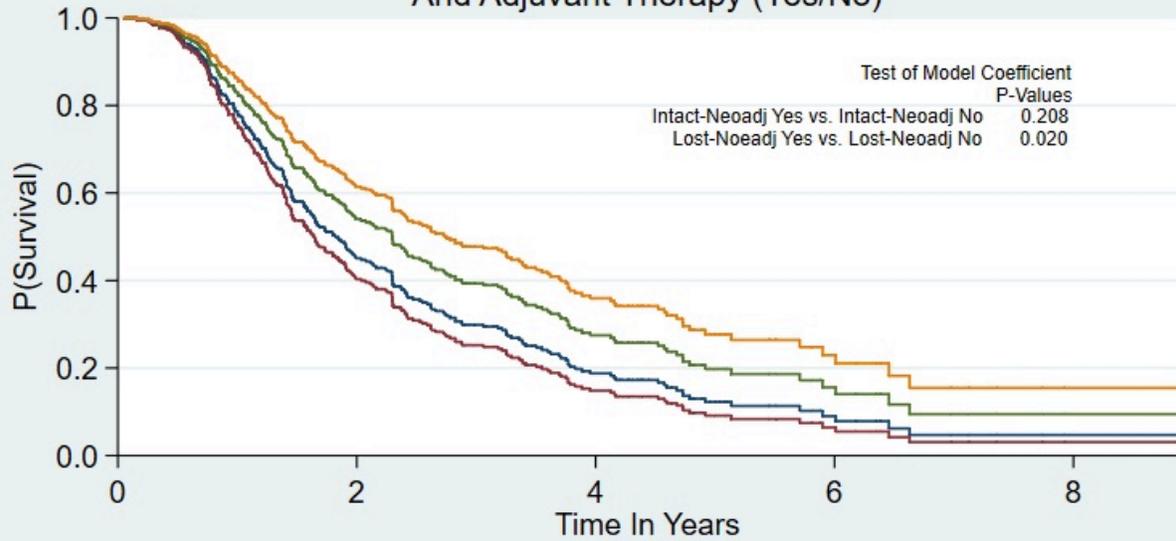
Methods: In patients undergoing pancreatotomy for PDAC between 2008 and 2018, SMAD4 status was classified by immunohistochemistry in resected specimens as preserved, partial loss, or complete loss. For analysis, preserved and partial loss of SMAD4 were categorized as intact, and compared to complete loss. NAC regimens were categorized as 5FU-based and gemcitabine-based (Gem). Response to NAC was assessed by percent change in CA 19-9. Non-secreters of CA 19-9 were excluded.

Results: Of the 470 patients, 139 (29.6%) had loss of SMAD4. 331 had intact SMAD4, with 111 (23.6%) partial loss and 220 (46.8%) preserved SMAD4. 361 patients received NAC: 236 (65.4%) Gem-based regimens, 87 (24.1%) 5FU-based regimens, and 38 (10.5%) with both. Patients with SMAD4 loss had greater median pre-NAC CA19-9 (433.6 vs 295.6 U/mL, $p=0.05$). SMAD4 loss was also associated with larger mean reduction in CA 19-9 compared to intact (71.1% vs. 36.0%, $p<0.01$). 5FU-based NAC was associated with greater reduction in CA 19-9 than Gem (57.8% vs. 52.5%, $p=0.01$). Multivariable analysis adjusting for age, pre-NAC CA 19-9 and tumor size revealed that SMAD4 loss ($p<0.01$) and 5FU-based NAC ($p=0.01$) were independently associated with greater CA 19-9 reduction. Adjusting for age, tumor size and receipt of adjuvant therapy, NAC was associated with improved overall survival (OS) in SMAD4 loss ($p=0.02$), but not in the SMAD4 intact cohort ($p=0.21$) (Figure). Furthermore, 5FU-based NAC was associated with improved OS compared to Gem in SMAD4 loss ($p=0.05$), while no OS difference was observed between chemotherapies in the SMAD4 intact cohort.

Conclusion: Loss of SMAD4 is independently associated with greater CA 19-9 response to NAC, with 5FU based NAC providing the largest reductions in CA19-9. Furthermore, NAC in those with SMAD4 loss is associated with improved OS, with evidence that 5FU-based NAC provides greater survival benefit than Gem-based regimens.

Parametric

Risk Adjusted For Age At Dx, Clinical T-Size,
And Adjuvant Therapy (Yes/No)



P 18. STAGING OF PANCREATIC DUCTAL ADENOCARCINOMA AFTER NEOADJUVANT THERAPY: REAPPRAISAL OF THE PROGNOSTIC ACCURACY OF THE 8TH EDITION OF AMERICAN JOINT COMMISSION ON CANCER STAGING SYSTEM

E Bannone, G Malleo, L Maggino, F Casciani, S Paiella, G Marchegiani, C Bassi, R Salvia

Presenter: Elisa Bannone MD | University of Verona

Background: The 8th revised edition of American Joint Commission on Cancer (AJCC) staging system for pancreatic ductal adenocarcinoma (PDAC) has been modeled and validated on upfront surgery (US) cohorts. However, in recent years an increasing number of patients undergo pancreatotomy after neoadjuvant therapy (NAT). Since NAT significantly affects pathological features of resected PDAC, the prognostic accuracy of the AJCC staging for these patients is unknown.

Methods: All the patients undergoing pancreatotomy for PDAC at a single tertiary care institution from 2002 to 2016 were retrieved from a prospectively maintained database and analyzed retrospectively. Patients were staged according to the 8th edition of the AJCC staging system. Clinical and pathologic characteristics and disease-specific survival (DSS) were compared between patients receiving US and surgery following NAT using standard statistics. Cox-regression modelling was carried out to identify predictors of DSS separately for each group. The predictive accuracy of the AJCC staging system was evaluated using the Harrell's Concordance (C) index in each group.

Results: Among 1330 patients, 252 (18.9%) received NAT. These were younger (60 vs 64 years; $p < 0.001$), and received vascular resections (21.8% vs 12.1%; $p < 0.001$) and total pancreatotomies (10.3% vs 6%; $p = 0.01$) more frequently than US patients. NAT patients displayed a smaller median tumor size (26.9 vs 28.3 mm), and reduced rates of lymph-node involvement (57.9% vs 86%), lymphovascular (70.2% vs 91.2%), perineural (77.0% vs 96.8%) and peripancreatic fat invasion (72.6% vs 91.1%), all $p < 0.001$. T- and N-classes distribution was different, so that early AJCC stages were more represented in the NAT than in the US group (IA 28.6% vs 6.9%; IB 9.9% vs 5.9%; IIA 3.6% vs 1.2%; IIB 29.8% vs 35.4%; III 28.2% vs 50.6%; $p < 0.001$). The median follow-up was 25 months. The median DSS was 31 months, with no significant difference between NAT and US patients (35 vs 31 months; $p = 0.825$). In the US group both the T and N parameters were significantly associated with survival with a sharp segregation between classes (Figure 1.a-b). In the NAT group, this association remained but appeared mainly driven by the difference between T1 and T2-3-4 patients, as well as N0 and N1-2 patients (Figure 1.d-e). The AJCC staging was significantly associated with DSS in both groups. However, while in the US group the survival curves of the various stages were distinct, for patients receiving NAT the main difference was between earlier (IA-B) and more advanced stages (Figure 1.c-f). On multivariable analysis, the AJCC staging was confirmed as an independent predictor of DSS in both groups. Moreover, the performance of the AJCC staging system was similar in NAT as in US patients (C-index of 0.62 and 0.59, respectively).

Conclusion: Patients undergoing surgery after NAT displayed a peculiar representation of the various T- and N-classes, resulting in a different staging distribution, as compared with US patients. However, there was no difference in the prognostic accuracy of the AJCC staging system based on the receipt of US or surgery after NAT, and the AJCC staging was an independent predictor of DSS in both cohorts. These results seem to justify the application of the 8th edition of the AJCC staging system, which has been mainly developed in US cohorts, also to NAT treated patients.

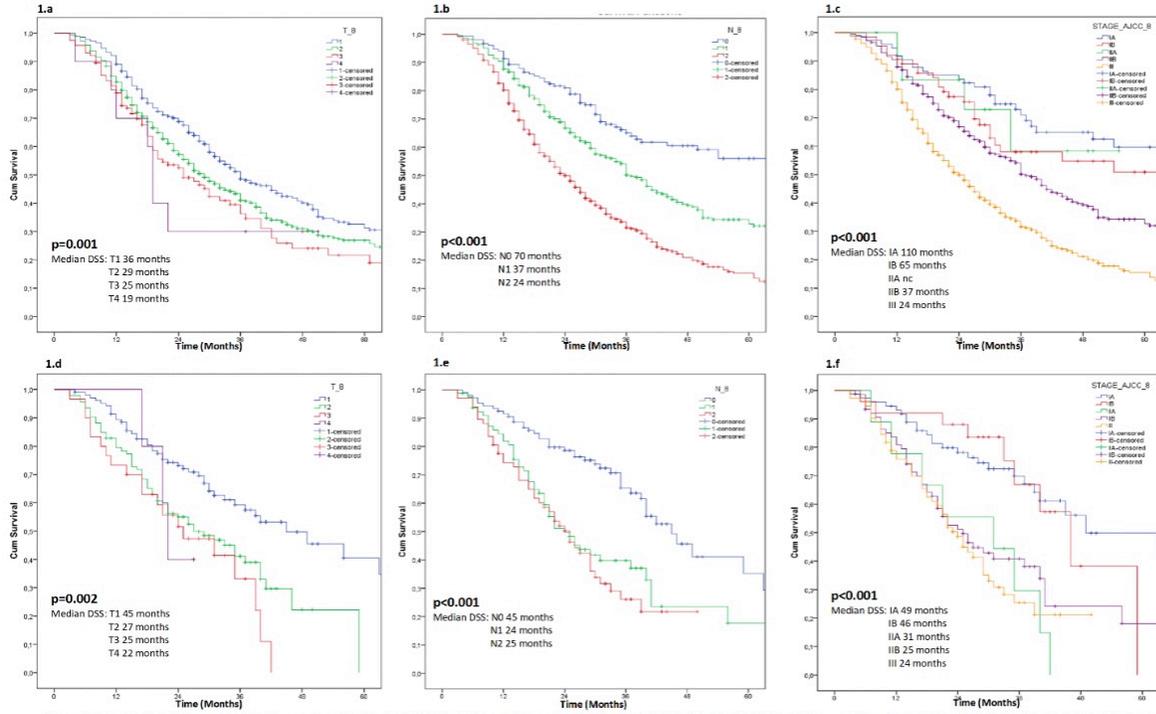


Figure 1: The Kaplan-Meier curves for Disease-Specific Survival (DSS) by T stage of US patients (a) and of NAT patients (d). DSS by N-stage of US patients (b) and of NAT patients (e). The Kaplan-Meier curves for DSS using the 8th edition of AJCC Staging Manual of US (c) and NAT (f) patients. Abbreviations: US: up-front surgery; NAT: neoadjuvant therapy; AJCC: American Joint Commission on Cancer.

P 19. PANCREATIC FISTULA IN THE ERA OF NEOADJUVANT CHEMOTHERAPY IS AN UNCOMMON COMPLICATION BUT MAY HAVE MAJOR IMPACT ON LONG-TERM SURVIVAL

T Hank, M Sandini, CR Ferrone, C Rodrigues, M Weniger, M Qadan, AL Warshaw, KD Lillemoe, C Fernández-del Castillo

Presenter: Thomas Hank MD | Massachusetts General Hospital

Background: Neoadjuvant therapy (NAT) is the standard of care for patients with borderline and locally advanced pancreatic ductal adenocarcinoma (PDAC). The aim of this study was to assess postoperative complications in patients undergoing pancreatectomy following NAT, with a particular emphasis on clinically relevant postoperative pancreatic fistula (CR-POPF) and to compare them with a contemporaneous cohort of patients undergoing upfront resection. We then investigated whether POPF-related morbidity affects long-term outcomes in NAT and upfront resected patients by comparing patients with and without CR-POPF.

Methods: Patients who underwent either NAT followed by surgery or upfront resection for PDAC at the Massachusetts General Hospital between 2007 to 2017 were identified from a prospectively maintained database. Data on demographics, perioperative fistula determinants, pathology and outcomes were collected and analyzed. All postoperative complications and severity were classified and graded according to the Clavien-Dindo Classification and ISGPS recommendations. Follow-up and survival analyses for NAT and upfront resection groups were performed.

Results: 753 patients were identified, of whom 346 (45.9%) received NAT and 407 (54.1%) underwent upfront resection. Patients in the NAT group were younger, had lower BMI and lower CA19-9 levels after completion of NAT than those who underwent upfront resection. NAT was also associated with more favorable post-treatment pathologic findings, including smaller tumor size, lesser frequency of lymph node involvement, lower tumor grade, and higher frequency of negative resection margins. There were no significant differences in overall complications, Clavien-Dindo grade ≥ 3 complications, or 90-day postoperative mortality rates between the two groups. The rate of CR-POPF was 3.6-fold lower in the NAT group compared with the upfront resections (3.8% vs. 13.8%; $p < 0.001$). In addition, the determinants of CR-POPF changed in the NAT group, where only soft pancreatic texture was associated with a higher risk of CR-POPF ($p < 0.001$), and not duct diameter, BMI or intraoperative blood loss. While no differences in survival were seen in patients with and without CR-POPF after upfront resection (26 vs. 25 months; $p = 0.656$), long-term postoperative survival was significantly reduced in the NAT cohort when CR-POPF occurred (17 vs. 34 months; $p = 0.002$). This effect was independent of other established predictors of overall survival on multivariate analysis.

Conclusion: Neoadjuvant therapy is associated with a significant reduction in the rate of postoperative fistula formation. However, once this occurs, it is associated with a significant reduction in long-term survival. Additionally, standard determinants of POPF appear to be no longer applicable following NAT.

P 20. DOES PREOPERATIVE PHARMACOLOGIC PROPHYLAXIS REDUCE THE RATE OF VENOUS THROMBOEMBOLISM IN PANCREATECTOMY PATIENTS?

ZV Fong, G del Carmen, DC Chang, CR Ferrone, C Fernandez-del Castillo, KD Lillemoe, M Qadan

Presenter: Zhi Ven Fong MD, MPH | Massachusetts General Hospital

Background: It has been proposed that the risk of venous thromboembolism (VTE) may be reduced by preoperative administration of prophylactic unfractionated or low molecular-weight heparin in patients undergoing major abdominal surgery, with the notion that VTE risk begins intraoperatively. However, whether preoperative administration reduces incidence of VTE remains unknown, with practice patterns reflecting substantial variability among surgeons. We hypothesized that timing of heparin administration does not significantly alter the incidence of VTE in pancreatic surgery.

Methods: An analysis was conducted using data from Massachusetts General Hospital's National Surgical Quality Improvement Program from 2012 to 2017. All patients admitted for elective pancreatic resection were included and a manual chart search was conducted to confirm the administration of preoperative heparin. Patients with preoperative VTE's were excluded. The primary outcome was development of VTE. Multivariate regression was performed, adjusting for patient demographics and various clinical factors.

Results: In total, 1,448 patients were analyzed, of whom 1,062 received preoperative heparin (73.34%). Overall VTE rates were low, with 24 (1.66%) patients developing VTE. On unadjusted analysis, there was no statistically significant difference between patients who received preoperative pharmacologic prophylaxis compared with those who did not receive preoperative dosing (1.79% vs. 1.30%, respectively; $p=0.515$). On adjusted analysis, there was still no difference between patients receiving preoperative heparin and no prophylaxis (OR 1.97, 95% CI 0.68-5.71; $p=0.214$). There was an association between prolonged length of hospital stay (>11 days) and development of VTE (OR 4.26, 95% CI 1.22-14.86; $p=0.023$) on multivariable analysis. No additional predictors were identified.

Conclusion: Preoperative heparin administration did not significantly alter the incidence of VTE for patients who underwent elective pancreatic resections. Further exploration of this finding will lead to further refinement of established guidelines and standardization of perioperative care.

Factor	Odds Ratio	95% Confidence Interval	p-value
Clinical Characteristics			
Heparin Administration			
No Pre-Operative Heparin	Reference		
Pre-Operative Heparin	1.97	0.68-5.71	0.214
Hematocrit Level			
<35 HCT	Reference		
35-45 HCT	1.32	0.54-3.27	0.545
Diabetic			
No	Reference		
Non-Insulin	1.80	0.55-5.86	0.330
Insulin	1.91	0.59-6.21	0.28
Length of Stay			
<5 days	Reference		
6-10 days	0.42	0.09-1.92	0.262
>11 days	4.26	1.22-14.86	0.023
Non-Clinical Characteristics			
Age Category			
< 65 age	Reference		
>=65 age	2.02	0.77-5.34	0.155
BMI			
Normal/underweight	Reference		
Overweight	1.56	0.56-4.37	0.398
Obese	0.99	.30-3.29	0.986

P 22. DEVELOPMENT OF RISK PREDICTION PLATFORM FOR PANCREATIC FISTULA AFTER PANCREATODUODENECTOMY USING ARTIFICIAL INTELLIGENCE

IW Han, N Kim, Y Ryu, DJ Park, SH Shin, JS Heo, DW Choi, BH Cho

Presenter: In Woong Han MD, PhD | Samsung Medical Center

Background: Despite advancements in operative technique and improvements in postoperative outcomes, postoperative pancreatic fistula (POPF) is a frequent and potentially life-threatening complication following pancreatoduodenectomy (PD) where it affects nearly one-quarter of patients. There are some reports to predict POPF preoperatively, but the accuracy of those is questionable. Artificial intelligence technology is receiving a lot of attention and is actively being distributed in medical field. However, no studies have been reported on the application of machine learning techniques to outcomes after pancreatic surgery. As a result, this study aimed to develop risk prediction platform for POPF using artificial intelligence model.

Methods: From 2007 to 2016, medical records of 1771 patients at Samsung Medical Center who underwent PD were reviewed retrospectively. A total of 53 variables were inserted into training algorithm. Machine learning algorithms which made risk prediction platform were 'the random forest method (RFM)', 'Neural Network (NN)', and 'Recursive Feature Elimination (RFE)'. Initially, 6 variables (body mass index, preoperative albumin level, pancreatic duct size, sex, ASA score, and location of tumor) which were identified with independent risk factors after multivariate analysis were inserted machine learning algorithm. Afterwards, 48 variables were input the machine learning algorithm with exclusion of high rate of missing values. The area under the receiver operating characteristics curve (AUC) was calculated to examine the discriminative power of the proposed algorithm for POPF prediction.

Results: The number of Clinically-Relevant POPF (CR-POPF) was 222 according to ISGPS definition 2016. Initial AUCs using RFM and NN after 5-folds average using 6 variables were 0.669 and 0.696, which were higher than AUC 0.652 using multivariate analysis. After exclusion of high rate of missing values, AUCs after oversampling were increased as 0.674 and 0.708. The maximal AUC using RFE was 0.756, which variables included were preoperative CA 19-9, CEA level, body mass index, pancreatic duct diameter, histologic type, platelet count, presence of alcoholic history, presence of portal vein resection, DM, presence of pancreatitis, and use of pancreatic duct stent.

Conclusion: Up to now, we think this study is the first report to predict POPF using artificial Intelligence. The performance of new risk prediction platform is reliable as AUC 0.756. After external validation, this new platform could be used for selecting patients who need more intensified therapy, and establishing preoperatively effective treatment strategy.

P 25. ZEBRAFISH EMBRYO AS AVATAR OF PATIENTS WITH PANCREATIC CANCER: PRELIMINARY EXPERIENCE TOWARD A PERSONALIZED MEDICINE

G Di Franco, A Usai, M Palmeri, N Furbetta, D Gianardi, S Guadagni, M Bianchini, E Vasile, S Latteri, A Falcone, V Raffa, L Morelli

Presenter: Matteo Palmeri MD | University of Pisa

Background: In the last years, a new concept of personalized medicine called 'Mouse Avatars' or 'co-clinical trials' has emerged, with the purpose to develop models to study the response of tumor to therapy on an individual basis. A big limitation of xenograft experiments in murine hosts is the requirement of immune-permissive strains and the long duration of time before the detection of human engrafted cells. The aim of this study is to evaluate the usability of Zebrafish embryos (ZE) as avatar and to test the chemosensibility to the different chemotherapy schemes used for the treatment of patients affected by pancreatic cancer.

Methods: For each enrolled patient, a fragment of the tumor, fluorescently labeled with Dil, was xenotransplanted inside the yolk of 2 day post-fertilization ZE. Two hours post-injection (hpi) transplanted ZE were incubated in only E3 media (control-ZE group) or with added standard combinations of chemotherapy (GEMOX, nab-Paclitaxel/Gemcitabine, Gemcitabine, FOLFOXIRI) (treated-ZE subgroups) for 48 hours. Each subgroup was composed by 10 ZE. For each protocol, we used a conversion factor human-to-fish calculated with a toxicity/efficacy study on zebrafish model. A ratio between the tumor mass area at 24 hpi and 48 hpi and the percentages of cell migration through the ZE caudal vein were calculated in the control-ZE and in each treated-ZE subgroup and compared to each other. A $p < 0.1$ was considered statistically significant.

Results: Ten patients with pancreatic cancer were enrolled between January 2018 and November 2018. The first four cases were used for the definition of the protocol for the xenotransplantation and the tests of chemosensibility were not performed. In all cases the tumor cells successfully grafted in the yolk sack of zebrafish embryos. In all cases of the control-ZE group the tumor mass increased at 48 hpi respect 24 hpi in all cases. The mass progression/regression analysis revealed a statistically significant difference of tumor mass progression in the treated-ZE subgroups respect the control-ZE subgroup in 3/6 cases (50%). One chemotherapy scheme was statistically more efficient in 2/6 cases (nab-Paclitaxel/Gemcitabine and FOLFOXIRI, respectively), while two chemotherapy schemes in 1/6 case (nab-Paclitaxel/Gemcitabine and FOLFOXIRI). Cell migration was detected in a percentage of grafted zebrafish embryos of the control-ZE subgroup in 3/6 cases (50%). A significant reduction of the cell migration percentage in the treated-ZE subgroups compared to the control-ZE subgroup was revealed for almost one chemotherapy scheme in 3/3 cases. The reduction of cell migration percentage was revealed for two in 1/3 case, for three chemotherapy schemes in 1/3 case and for all chemotherapy schemes in 1/3 cases.

Conclusion: In our experience, zebrafish embryos could be a used as avatar for oncological patients because in all cases the tumor cells successfully grafted in the yolk sack of zebrafish embryos. Probably the protocol used for the tests of chemosensibility should be improved and the human-to-fish dose should be better defined. Since we have noticed a tendency to inhibit the tumor cells proliferation by the chemotherapy treatments without reaching statistically significance, we have already tried to increase the chemotherapy doses with the intent to reach it. Moreover, a prospective co-clinical trial is under way to evaluate the concordance between the results of tests in zebrafish and the response to chemotherapy in oncological patients.

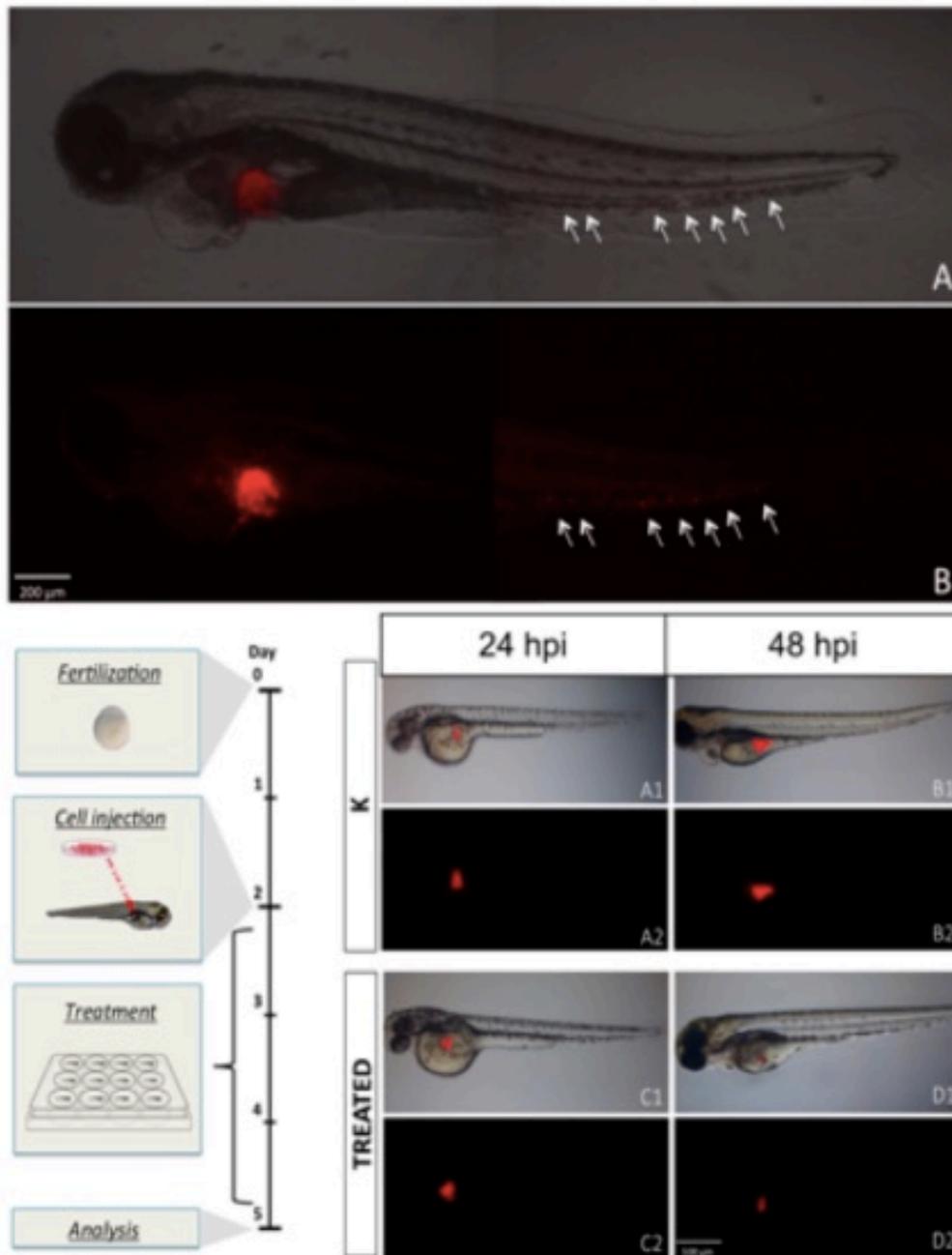


Figure 1 - Representative case of patient's cancer cells spreading through the embryo body. A Overlay of fluorescent and DIC images, and B fluorescence image of the grafted embryo at 1dpi. White arrowheads indicate the migrating cells (DiI stained) in the area of the posterior caudal vein plexus. C Scheme of the *in vivo* experiment carried out by transplanting zebrafish embryos with cancer cells to investigate the efficacy of chemotherapy equivalent dose. At 2 hpi the embryos were exposed to chemotherapy. A representative image of control (A1/2-B1/2) and treated (C1/2-D1/2) embryos after 24 hpi and 48 hpi. Qualitatively images show tumor progression in control group and tumor regression in xenotransplanted embryos treated with chemotherapy.

P 26. CONDITIONAL SURVIVAL IN PATIENTS WITH RESECTABLE PANCREATIC CANCER: A DUTCH POPULATION-BASED STUDY

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Presenter: Stijn van Roessel MD, MSc | Amsterdam UMC

Background: Survival estimates are traditionally calculated from the time of diagnosis until death. Since most patients with pancreatic cancer die within the first year, these survival estimates are an unreliable reflection for patients surviving this first year. These patients and their physicians are left in uncertainty about their prognosis and conditional survival (CS), accounting for time after resection or diagnosis, may be more informative.

Methods: A nationwide retrospective cohort study was performed, including patients with resectable pancreatic adenocarcinoma from the Netherlands Cancer Registration (2005-2016). The Cox proportional hazards model was used to identify risk factors associated with overall survival. Two-year CS (the probability of surviving two additional years after a certain number of years already survived from resection) was stratified by the risk factors found in the multivariable cox regression.

Results: In total, 3085 patients were included with a median age of 67 years (IQR 60-73) and 53% were male. Median overall survival was 17.5 months (95%CI 16.9-18.1 months) with a five-year survival of 14.8%. Two-year CS was 37.6%, 50.4%, 61.1%, 71.1%, 75.3% and 77.4% at 1 to 6 years after pancreatic resection respectively (Table 1). CS showed an opposite trend compared to the Kaplan-Meier survival: 2-year CS at one year after resection was 37.6% and the 3-year overall survival was 24.2%. At four years after resection the 2-year CS increased to 71.1% compared to a 6-year overall survival of 12.8%. In multivariable analyses tumor differentiation grade, T stage, N stage, resection margin status and adjuvant chemotherapy were associated with median overall survival. The 2-year CS per tumor differentiation grade increased per year. It was, almost every year, highest in patients with well differentiated tumors, but the difference compared to other stages decreased over the years. For T stage, 2-year CS one and two years after resection, is especially high in patients with T1 tumors, thereafter it is more similar to the other stages. Two-year CS of patients with nodal metastases increased from 40.3% to 72.1% at respectively two and five years after resection. In patients with N0 stage 2-year CS increased less, from 62.3% to 76.8% respectively. The difference between R0 vs. R1/R2 increased over time from 15.7% difference one year after resection compared 31.5% difference six years after resection. Two-year CS in patients with an R1/R2 resection decreased four years after resection. Two-year CS was higher in the adjuvant chemotherapy subgroup until five years after resection.

Conclusion: In this nationwide study is shown that CS increased over the years and offered a more accurate prognosis for patients with resectable pancreatic adenocarcinoma. After stratification of CS for factors associated with survival, the effect of poor prognostic factors of tumor differentiation grade, T stage and N stage decreased over time.

Table 1. Conditional survival estimates (%) for all patients

Total survival time, y	Years already survived by patient						
	1 y	2 y	3 y	4 y	5 y	6 y	7 y
1 y							
2 y	55.4						
3 y	37.6	67.9					
4 y	27.9	50.4	74.2				
5 y	23.0	41.5	61.1	82.4			
6 y	19.9	35.8	52.8	71.1	86.4		
7 y	17.3	31.3	46.0	62.0	75.3	87.2	
8 y	15.4	27.8	40.9	55.1	66.9	77.4	88.8

Each column represents the years survived from surgery and each row represents the percentage to reach a certain total survival time from that point of survived years. For example, if a patient has survived 3 years after surgery, the probability to survive to year 4 is 74.2% and to survive to year 7 are 46.0%

P 29. MAIN DUCT DILATATION IS THE BEST PREDICTOR OF HIGH GRADE DYSPLASIA OR INVASION IN INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PANCREAS

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Presenter: Ross Beckman MD | Johns Hopkins University School of Medicine

Background: Intraductal papillary mucinous neoplasms (IPMN) of the pancreas may be precursor lesions to pancreatic cancer (PC) and represent a target for early diagnosis or prevention. While there has been much effort to define preoperative risk factors for malignant pathology, guidelines are ever-changing and controversy remains surrounding which patients would benefit most from resection.

Methods: We performed a retrospective analysis of 901 consecutive patients obtained from two tertiary referral centers who underwent pancreatic resection for histologically proven IPMN between 2004 and 2017. Collected data included patient demographic characteristics, preoperative symptoms, radiological findings, and laboratory data.

Results: Main pancreatic duct (MPD) dilatation was the only variable that was significantly associated with increased probability of malignancy (defined high-grade dysplasia or invasion) on both univariate and multivariate analysis. Even middle-range MPD dilatation from 5mm-9.9mm (n = 286) was associated with increased odds of HG-IPMN (OR=2.7; 95% CI= 1.8-4.2) and invasion (OR=4.4; 95% CI= 2.6-7.7). MPD dilatation >10mm (n = 150) had even greater odds of HG-IPMN (OR=6.6; 95% CI = 3.94-10.98) and invasion (OR=15.6; 95% CI=8.21-27.65). A cutoff of 5-7mm MPD diameter was determined to be the best predictor to discriminate between malignant and benign lesions.

Conclusion: In agreement with current IPMN management guidelines, we found MPD dilatation, even low levels from 5mm to 9.9mm, to be the single best predictor of HG-IPMN or invasion, highlighting the critical role that MPD dilatation plays in the selection of surgical candidates.

Figure Legend Figure 1. Predicted probabilities of a different grade of IPMN associated dysplasia as a smooth function of the max diameter of the duct dilatation. Data were fitted with a multinomial logistic regression model using restricted cubic splines with 3 knots at fixed percentiles of the MPD distribution.

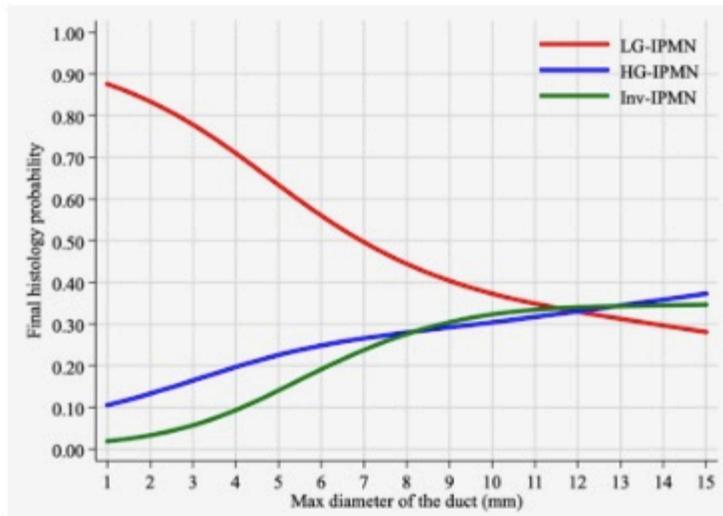
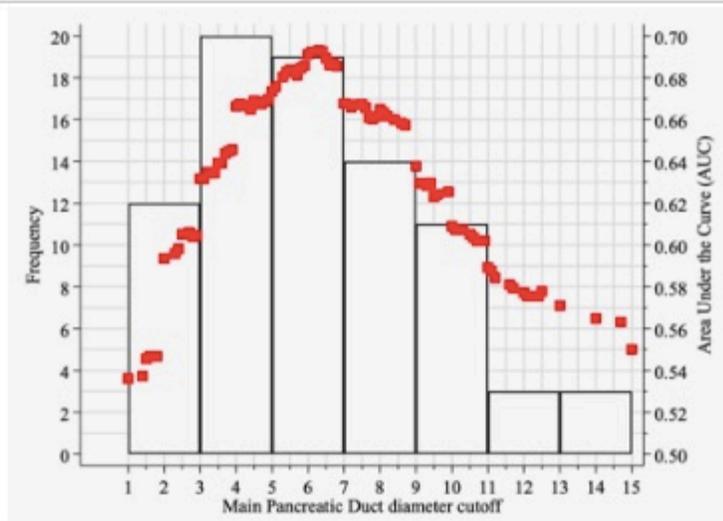


Figure 2: Area under the curve (red squares) associated with every cut-points used to dichotomize max diameter of the duct dilatation as the only predictor of the probability of high grade/invasive IPMN estimated with a logistic regression model. All areas under the curve are estimated on the same number of patients. The observed distribution (percent) of main duct dilatation is shown in the background.



P 30. LAPAROSCOPIC DISTAL PANCREATECTOMY IS ASSOCIATED WITH A COST SAVINGS IN HIGH VOLUME CENTERS

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Presenter: Emanuel Eguia MD, MHA | Loyola University Medical Center

Background: Little is known regarding the impact of minimally invasive approaches to a distal pancreatectomy (DP) on the aggregate costs of care for patients undergoing DP.

Methods: We queried the Healthcare Cost and Utilization Project State Inpatient Database to identify patients undergoing elective laparoscopic (LDP) or open (ODP) distal pancreatectomy in FL, MD, MA, NY, and WA between 2014 and 2016. Multivariable regression (MVR) was used to evaluate the association between surgical approach and rates of postoperative complication, overall lengths of stay (LOS) and aggregate costs of care including readmissions to 90 days following DP. Candidate variables were determined a priori using best variable subsets and included: age, gender, insurance, race/ethnicity, Charlson comorbidity index (CCI), pathology (benign vs. malignant), annual hospital DP volume broken into terciles (low: 41 DP's/year) and overall LOS.

Results: 297 (11%) patients underwent LDP; 2,436 (89%) underwent ODP. On univariate analysis, patients undergoing LDP had higher rates of malignant pathology (53% vs. 39%, $p < 0.001$), shorter overall LOS (6 days, IQR [5-10] vs. 7 days, IQR [5-13], $p < 0.001$) and lower aggregated costs of care (\$22,734 vs. \$26,910, $p < 0.001$) than those undergoing ODP. On MVR adjusted for age, gender, malignant pathology, CCI and hospital volume, LDP was associated with a decreased risk of prolonged LOS (OR 0.47; 95% CI [0.30, 0.74]) relative to ODP. Rates of perioperative morbidity and readmission for patients undergoing LDP were identical to those undergoing ODP. On MVR adjusted for age, insurance, CCI and LOS, and volume, factors associated with being in the highest quartile for aggregate costs following DP included: male gender (OR 1.50; 95% CI [1.24, 1.82]), CCI (OR 1.25; 95% CI [1.19, 1.31]), black race (OR 1.40; 95% CI [1.02, 1.91]), having Medicaid (OR 1.59 95% CI [1.12, 1.25]), malignant pathology (OR 2.10; 95% CI [1.61, 2.74]) and readmissions (OR 5.29; 95% CI [4.35, 6.43]). Patients undergoing LDP had a lower risk of being in the highest quartile for costs (OR 0.52, 95% CI [0.37, 0.74]) than those undergoing ODP. The reduction in risk of being a high outlier for cost was independent of hospital volume but only high-volume centers realized an average lower aggregate cost of care (-\$4,803; 95% CI: [-\$8,341, -\$1,265]) when utilizing LDP. In low (+\$3,606; 95% CI [-\$6,629, \$13,841]) to moderate (-\$3,010; 95% CI [-\$8,008, \$1,988]) volume centers, the aggregate costs of care for LDP and ODP were statistically identical. (Table 1)

Conclusion: Patients undergoing LDP have a lower risk of prolonged overall LOS relative to those undergoing ODP. This association is independent of hospital volume but translates into cost savings in high volume centers only. This finding suggests that high volume centers develop efficiencies of scale that allow them to realize aggregate cost savings when utilizing laparoscopic approaches to DP.

Table 1. Cost of distal pancreatectomy in patients undergoing laparoscopic vs. open approach

	Unadjusted			Adjusted*		
	Cost	95% CI		Cost	95% CI	
Hospital volume, year						
1-5	-\$9,300	-\$26,890	\$8,289	\$3,606	-\$6,629	\$13,841
6-41	-\$9,773	-\$18,425	-\$1,121	-\$3,010	-\$8,008	\$1,988
>41	-\$11,790	-\$19,067	-\$4,512	-\$4,803	-\$8,341	-\$1,265

*Best subsets model adjusted for age, overall LOS, insurance and CCI

P 32. RECEIPT OF ADJUVANT THERAPY AMONG PANCREATIC CANCER PATIENTS WITH A HIGH AREA OF DEPRIVATION INDEX

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Presenter: Susan Tsai MD | Medical College of Wisconsin

Background: Area of deprivation index (ADI) is a geographic-based measurement of socioeconomic deprivation and has been used to study the relationship between social determinants and healthcare quality and outcomes. The impact of ADI on the delivery of postoperative (adjuvant) therapy to patients with pancreatic cancer (PC) is unknown.

Methods: Patients with localized PC who completed all neoadjuvant therapy and surgery were identified from a prospective database at the Medical College of Wisconsin. ADI for all patients was obtained using the ZIP code+4 code. Patients were dichotomized into high and low ADI categories based on the median ADI. Clinicopathologic data, preoperative (neoadjuvant) therapy, surgical outcomes, and the receipt of adjuvant therapy were abstracted.

Results: From 2009-2018, 310 patients with localized, operable PC who completed all neoadjuvant therapy and surgery were identified. If data regarding adjuvant therapy was missing (n=12), these patients were excluded. Of the remaining 298 patients, the median ADI was 97.50 (IQR 17.3); 149 (50%) patients in the high and low ADI groups. There was no difference between groups in age, gender, clinical stage, carbohydrate antigen 19-9 at diagnosis, type of neoadjuvant therapy, or type of operation performed. Pancreaticoduodenectomy was the most common operation performed (n=238; 80%). Grade 3 or higher Clavien complications occurred in 39 (13%) of the 298 patients; 19 (49%) in the low ADI group and 20 (51%) in the high ADI group (p=0.86). Adjuvant therapy was received by 167 (56%) of the 298 patients; 95 (64%) of the 149 patients with low ADI and 72 (48%) of the 149 patients with high ADI (p =0.007). In a multivariable logistic regression, high ADI was associated with a 54% decreased odds of receiving any adjuvant therapy (95% CI:0.27-0.79, p=0.005). Age >65, neoadjuvant therapy consisting of chemotherapy and chemoradiation, and postoperative Grade 3+ complications were also independently associated with decreased odds of receiving adjuvant therapy (Table 1).

Conclusion: Following neoadjuvant therapy and surgery, 56% of patients received any adjuvant therapy. Patients from high ADI neighborhoods were significantly less likely to receive adjuvant therapy independent of other well described risk factors including older age, previous multimodality neoadjuvant therapy, and Grade 3+ postoperative complications. Future studies should examine the challenges to delivery care in high ADI neighborhoods.

Table 1: Predictors of Adjuvant Therapy after Surgery						
Co-variate	Univariable			Multivariable		
	OR	95% C.I.	p-value	OR	95% C.I.	p-value
Age (ref: <65 yr)	0.53	0.33-0.85	0.008	0.44	0.25-0.75	0.003
Male gender (ref: female)	1.30	1.82-2.05	0.27	1.57	0.92-2.69	0.10
Neoadjuvant radiation (ref: chemoradiation)	Ref	Ref	Ref	Ref	Ref	Ref
Chemotherapy	4.82	1.59-14.6	0.005	3.77	1.18-12.11	0.03
Chemotherapy & radiation	0.34	0.20-0.57	<0.001	0.24	0.13-0.43	<0.001
Clavien Grade 3+ complication (ref: no)	0.30	0.14-0.62	0.001	0.25	0.11-0.58	0.001
Elevated postoperative CA 19-9	0.85	0.50-1.42	0.53	0.84	0.46-1.53	0.57
High ADI (ref: low ADI)	0.56	0.35-0.89	0.01	0.46	0.27-0.79	0.005
Operation (ref: pancreaticoduodenectomy)	Ref	--	--	Ref	--	--
Central pancreatectomy	0.71	0.04-11.52	0.81	0.42	0.30-7.00	0.55
Distal pancreatectomy & splenectomy	0.75	0.38-1.48	0.41	0.80	0.36-1.80	0.59
Total pancreatectomy	0.41	0.16-1.09	0.08	0.58	0.19-1.71	0.32

P 34. IMPACT OF PANCREATIC ENZYME REPLACEMENT THERAPY IN THE OUTCOME OF PATIENTS WITH CARCINOMA OF PANCREAS : PROSPECTIVE RANDOMISED STUDY

S Shantanu, R Gupta, S Rana, R Nada, H Singh, S Rana

Presenter: Shantanu Shantanu MS | Postgraduate Institute of Medical Education and Research Chandigarh

Background: Malnutrition in cases of carcinoma of pancreas lead to many negative outcomes, which include quality of life (QoL), increased rates of complications, decreased tolerance to treatment, and increased mortality. The effect of pancreatic enzyme replacement therapy (PERT) on outcomes has been studied in cases of chronic pancreatitis but its effect in cases of adenocarcinoma of pancreas are not well defined.

Methods: The present study is a prospective randomized study conducted between July 2017 to December 2018. Patients with resectable and borderline resectable adenocarcinoma of pancreas were randomized into two arms : arm 1 (PERT arm) and arm 2 (NON-PERT arm). In PERT arm, PERT was started 3 weeks before surgery and then the patients were followed till 12 weeks postoperatively whereas similar looking capsules were administered as placebo to patients in NON-PERT arm. Outcomes in terms of nutritional status by measuring BMI and serum albumin, postoperative complications and QoL (Fact Hep Questionnaire) were compared between two arms. Fecal elastase levels in the preoperative period as compared to postoperative period were also compared in both arms.

Results: A total of 30 patients were enrolled in the study. Mean age of the study population was 55.6 ± 12.3 years in PERT arm whereas was 53.8 ± 10.6 years in NON-PERT arm. 11/15 in PERT arm and 12/15 in NON-PERT arm were males. Thus, there was no significant difference seen between two arms with respect to demographics. Differences in values of BMI between both arms were not statistically significant. The p-values for differences in serum albumin levels in patients in both arms at 3 weeks and just preoperatively were 0.420 and 0.717 respectively and were 0.645, 0.272 and 0.141 at 2, 6 and 12 weeks postoperatively, thus, showing no significant difference. The mean preoperative fecal elastase was similar in both arms (PERT and NON-PERT) with values of 63.7 and 58.3 $\mu\text{g/g}$ of stool respectively. However, postoperatively the mean was 307.1 $\mu\text{g/g}$ of stool in PERT arm and 70.1 $\mu\text{g/g}$ of stool in NON-PERT arm with a p-value of 0.009. This shows that PERT improves the overall exocrine function of pancreas thereby improving fecal fat elastase and thereby fecal fat excretion. Although there was no significant difference seen in terms of postoperative complications, patients who received PERT showed a trend towards decreased complications. There was a significant difference seen in the change of QoL between the two arms. Patients who received PERT had a lower mean score signifying a better quality of life.

Conclusion: PERT improved the fecal elastase of patients thus, signifying improved pancreatic exocrine function. However, it did not make a difference in the nutritional status of patients when compared to control arm. Patients who received PERT had a trend towards decreased postoperative complications and a significantly better quality of life.

Table: Postoperative complications in two arms :

Arm	PERT	NON-PERT	p-Value
PANCREATIC FISTULA	0/8	4/12	0.162
TYPE A	0	2 (16.7%)	
TYPE B	0	2 (16.7%)	
TYPE C	0	0	
DELAYED GASTRIC EMPTING	4/8	6/12	0.432
TYPE A	1 (12.5%)	0	
TYPE B	2 (25%)	4 (33.3%)	
TYPE C	1 (12.5%)	2 (16.7%)	
POSTOPERATIVE BLEED	0	2/12 (16.7%)	0.180
REEXPLORATION	0	1/12(8.3%)	0.254

P 35. ASSOCIATION BETWEEN PREOPERATIVE VASOSTATIN-1 AND PATHOLOGICAL FEATURES OF AGGRESSIVENESS IN LOCALIZED NONFUNCTIONING PANCREATIC NEUROENDOCRINE TUMORS (NF-PANNET)

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Presenter: Valentina Andreasi MD | San Raffaele Scientific Institute

Background: A reliable and accessible biomarker for nonfunctioning pancreatic neuroendocrine tumors (NF-PanNET) is currently unavailable. Chromogranin A (CgA) represents the best-described neuroendocrine biomarker, but its accuracy is low. Vasostatin-1 (VS-1), a fragment derived from the cleavage of CgA, was recently investigated and found to be more accurate as tumor biomarker in a cohort of patients affected by mainly metastatic small intestinal NET. Aim of the present study was to assess a possible association between preoperative VS-1 plasma levels and pathological features of aggressiveness, in comparison to CgA, in a cohort of patients affected by sporadic localized NF-PanNET.

Methods: Patients submitted to surgery for sporadic localized NF-PanNET at San Raffaele Hospital were included in the study. Patients diagnosed with functioning forms or with metastatic disease were excluded, as well as those with tumors classified as pancreatic neuroendocrine carcinoma (PanNEC) G3. Preoperative plasma samples were prospectively collected from May 2015. Circulating levels of total-CgA and VS-1 were retrospectively investigated by sandwich Enzyme-Linked ImmunoSorbent Assays (ELISA).

Results: Overall, 50 patients were included. VS-1 value ($P=0.0001$) was the only preoperatively retrievable factor independently associated with NF-PanNET size. No significant correlation between CgA and tumor diameter was found ($P=0.057$). A VS-1 value of 0.39 nM was identified as the optimal VS-1 cut-off accurately associated with NF-PanNET larger than 4 cm, with a sensitivity of 80% and a specificity of 80%. Patients with VS-1 > 0.39 nM had a significantly higher frequency of microvascular invasion ($P=0.005$) and nodal metastases ($P=0.027$). Global performances of VS-1, expressed as AUC, were 0.712 ($P=0.012$) for identifying the presence of lymph node metastases and 0.763 ($P=0.002$) for predicting the presence of microvascular invasion. Global performances of total-CgA were 0.545 ($P=0.596$) and 0.594 ($P=0.257$) for predicting lymph node metastases and microvascular invasion, respectively. Median VS-1 plasma level was significantly higher in the presence of microvascular invasion ($P=0.001$) and nodal metastases ($P=0.012$). PPI assumption significantly increased total-CgA levels, but not those of VS-1 ($P=0.111$). No significant correlation was found between total-CgA and VS-1 ($P=0.119$).

Conclusion: In localized, non-metastatic NF-PanNET, VS-1 is strongly associated to tumor dimension and its plasma levels are significantly higher in the presence of microvascular invasion and nodal metastases; moreover, VS-1 value is not affected by the PPI use.

P 36. ELUCIDATING THE CAUSES OF IMPROVED SURVIVAL IN RECENT RANDOMIZED ADJUVANT PANCREATIC DUCTAL ADENOCARCINOMA (PDAC) CLINICAL TRIALS

A Alabd, O Bolaji, AG Alabd, J Ammori, J Hardacre, J Winter

Presenter: Andre Alabd BS | Thomas Jefferson University

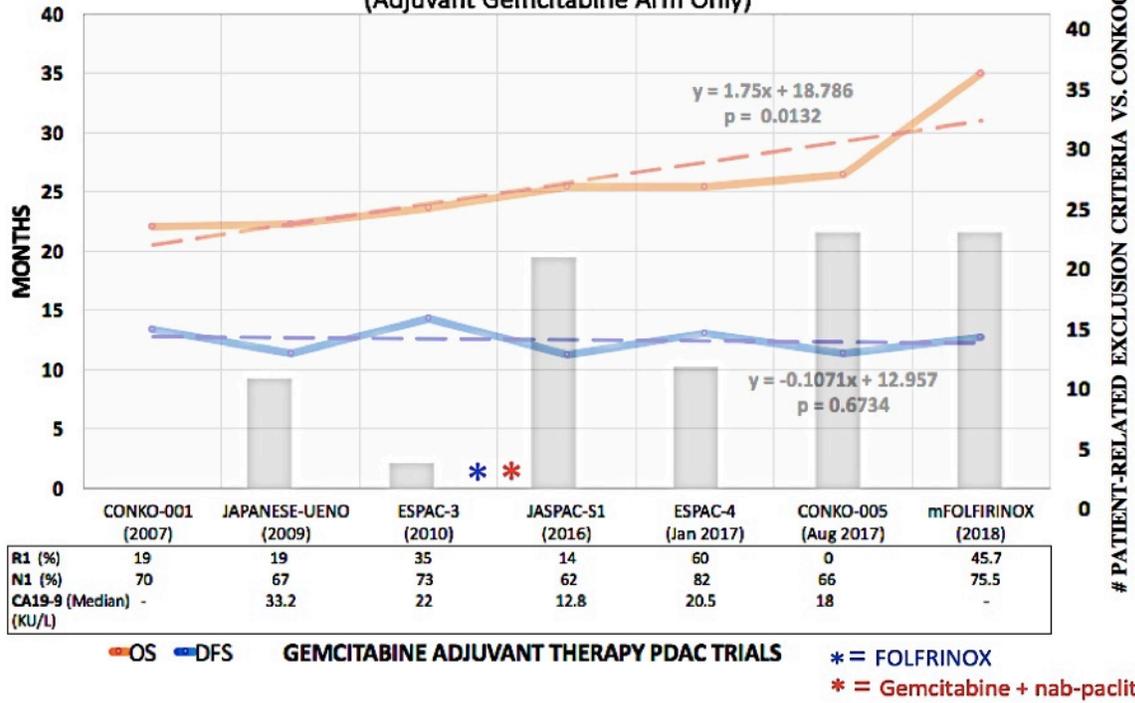
Background: Overall survival (OS) has increased in recent PDAC adjuvant clinical trials, even when the chemotherapeutic agent is constant. While oncologists have taken notice, the root causes have not been examined.

Methods: All phase III adjuvant PDAC clinical trials were screened (n=16), and 7 were identified (2007– 2018) that included gemcitabine mono-therapy treatment arms. Trends in overall survival and disease free survival (DFS) were plotted and analyzed over time using linear regression (quantified by the Y axis, left side of the graph). Eligibility criteria were categorized as: 1) tumor-related factors (CA19-9 levels, pathological criteria) or 2) patient-related factors (medical comorbidities). Eligibility criteria were compared across trials. The number of new or distinct patient-related exclusion criteria in recent trials were compared to the earliest trial (CONKO-001), and quantified (histogram, Y axis on the right side of the graph). Of note, standard-of-care treatment for recurrent PDAC changed to multi-agent chemotherapy in 2011, as indicated by asterisks on the graph.

Results: Overall survival improved over time in patients receiving only gemcitabine (slope=1.75 months, p= 0.01), while disease free survival remained constant (p= 0.7). CA19-9 values were relatively constant, with the exception of the Japanese trials. Pathologic features were also unchanged over time (except CONKO-001 excluding R1 patients). Notably, recent trials had stricter inclusion criteria with respect to patient-related factors (i.e., more patients were excluded for medical reasons)

Conclusion: Overall survival of patients with resected PDAC has significantly improved, irrespective of adjuvant treatment. Consistent disease free survival (12 months) and cancer-related factors indicate that selection bias towards more favorable cancer biology in recent trials cannot account for this observation. However, recent trials included healthier patients, which may have had an effect. More likely, widespread adoption of effective multi-agent chemotherapy after 2011 likely had the greatest impact. These data provide indirect evidence that newer palliative chemotherapy regimens are impacting overall survival following recurrence of resected PDAC.

DFS and OS in Resectable Pancreatic Cancer Trials (Adjuvant Gemcitabine Arm Only)



P 37. IMPACT OF R0 RESECTIONS AFTER NEOADJUVANT TREATMENT AND PANCREATODUODENECTOMY IN PATIENTS WITH PANCREATIC CANCER

S Maeda, A Moore, L Yohanathan, T Hata, MJ Truty, RL Smoot, SP Clearly, DM Nagorney, TE Grotz, EJ Park, MD Girgis, HA Reber, F Motoi, T Masuda, M Unno, ML Kendrick, TR Donahue

Presenter: Shimpei Maeda MD, PhD | Tohoku University Graduate School of Medicine

Background: Resection margin status has been recognized as an independent prognostic factor of overall survival (OS) in patients with pancreatic cancer. However, most studies reporting these findings have been based on data from patients who underwent up-front surgery without neoadjuvant treatment. The impact of margin status on survival in patients who received neoadjuvant treatment remains uncertain.

Methods: We analyzed 305 patients with initially resectable or borderline resectable pancreatic cancer treated with neoadjuvant therapy and subsequent pancreatoduodenectomy (PD) at Mayo Clinic, UCLA, and Tohoku University between 2010 and 2017. Patients found to have metastatic disease at exploratory surgery prior to neoadjuvant treatment or during PD were not included. Positive resection margin (R1) was defined as one or more cancer cells at any surface or margin. Stage information was based on the AJCC 7th edition. OS was measured from the date of surgery until death or last follow-up. A Cox proportional hazard model was used to assess potential predictors of survival.

Results: Among the 305 patients, 99 patients had radiologically resectable pancreatic cancer and 206 had borderline resectable disease. 178 patients received neoadjuvant chemotherapy, while neoadjuvant chemoradiotherapy was administered to 127 patients. The median OS for the entire cohort was 29.8 months. The 1-, 3-, and 5-year OS rates were 79.2%, 44.0%, and 23.5%, respectively. Negative margin resection (R0) was achieved in 275 (90.2%) patients. Patients who received chemoradiation were more likely to have an R0 resection (94.5%) compared with those who did not receive chemoradiation (87.1%, $P=0.032$). The R1 group was associated with higher post-neoadjuvant treatment CA 19-9, higher ypT-stage, lymph nodes metastasis, and perineural invasion. Postoperative CA 19-9 value and receipt of adjuvant therapy were similar between R0 and R1 groups. Patients with an R0 resection had a significantly longer OS than those with an R1 resection (31.3 vs 16.3 months, $P<0.001$). In univariate analyses, OS was associated with age, margin status, histologic grade, ypT, number of lymph nodes involved, perineural invasion, treatment effect, postoperative CA 19-9, and adjuvant therapy. In multivariate analysis, positive margin status, poorly differentiated carcinoma, treatment effect score of 3, postoperative CA 19-9 of 37 U/mL or higher, and lack of adjuvant therapy were predictive of poor OS.

Conclusion: We confirmed that margin status was an independent prognostic factor for OS in patients treated with neoadjuvant therapy and PD, supporting the use of an R0 resection as a surrogate of adequate oncological resection in this setting. Furthermore, our findings may also have significant implications for patient stratification in future randomized trials of adjuvant therapy after neoadjuvant treatment.

P 38. COMPLETION OF ADJUVANT CHEMOTHERAPY FOLLOWING UPFRONT SURGICAL RESECTION FOR PANCREATIC CANCER MAY BE TOO LOFTY A GOAL

AM Altman, K Wirth, SMarmor, K Chang, E Lou, JYC Hui, TM Tuttle, EH Jensen, JW Denbo

Presenter: Keith Wirth MD | University of Minnesota

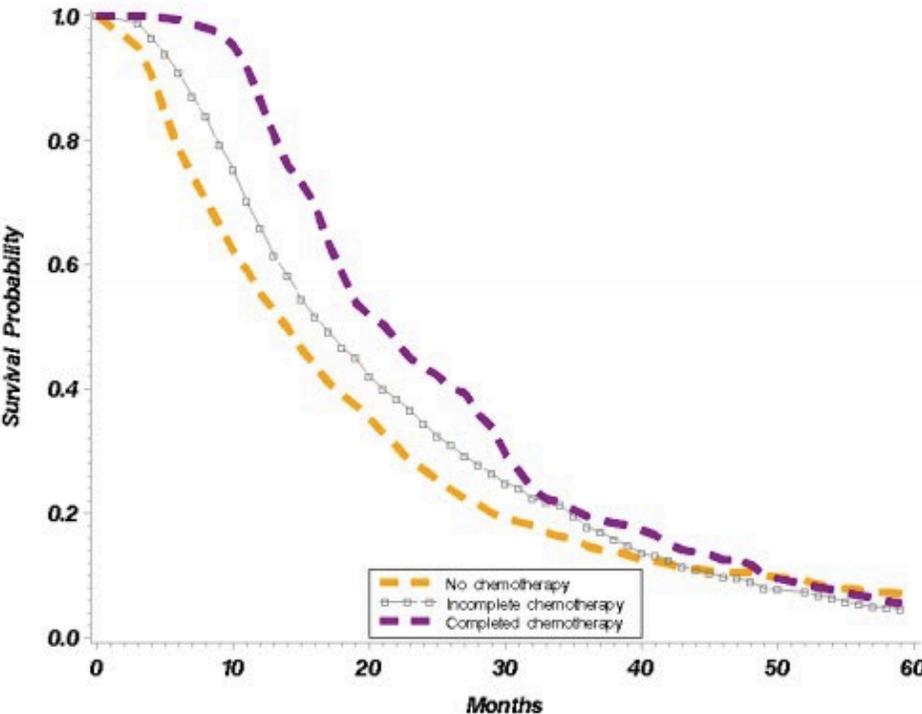
Background: Multiple randomized trials have demonstrated that adjuvant chemotherapy improves survival following upfront surgical resection for pancreatic cancer, but institutional series have reported that many patients do not complete adjuvant chemotherapy. We sought to identify the rate of completion of adjuvant chemotherapy, the factors associated with completion, and its impact on survival in a population-based sample.

Methods: The Surveillance Epidemiology and End Results Medicare-linked data was used to identify patients who underwent upfront surgical resection for pancreatic adenocarcinoma from 2004-2013. Patients were excluded if they had metastatic disease at diagnosis, received preoperative therapy, or postoperative chemoradiation. Complete adjuvant chemotherapy was defined as the initiation of chemotherapy within 12 weeks of surgery and receipt of 6 cycles within 10 months following surgery. Multivariable logistic regression was performed to evaluate factors associated with completion of adjuvant chemotherapy. Overall survival (OS) was evaluated with the Kaplan Meier method and Cox proportional hazard modeling.

Results: A total of 2,518 patients met inclusion criteria. The median age was 74, 46% were male, 79% had Charlson Comorbidity Index (CI) ≤ 1 , 74% were T-stage III, and 58% had nodal metastases. Sixty-six percent of patients did not receive any adjuvant chemotherapy, 27% received an incomplete course, and 7% completed adjuvant chemotherapy. Factors associated with completion of adjuvant chemotherapy were nodal metastases and treatment at a National Cancer Institute Designated Cancer Center ($p \leq .05$). Patients diagnosed more recently (2009-2013) were no more likely to complete chemotherapy than those diagnosed earlier (2004-2008). Patients with CI ≥ 2 were less likely to complete chemotherapy ($p \leq .05$). The median OS for patients who received no, incomplete, and complete adjuvant chemotherapy were 14, 17, and 22 months respectively ($p \leq .05$) (Figure 1). A more recent time-period of diagnosis (2009-2013), increased comorbidities, advanced T-stage (III/IV), nodal metastases, and receipt of no adjuvant chemotherapy were associated with increased hazard ratios for death ($p \leq .05$). Patients with ≥ 15 lymph nodes removed and completion of adjuvant chemotherapy had decreased hazards ratios of death ($p \leq .05$).

Conclusion: In the SEER-Medicare population, completion of adjuvant chemotherapy following upfront surgical resection for pancreatic cancer was independently associated with improved survival; however, only 7% of patients received a complete course of adjuvant chemotherapy. A treatment strategy that utilizes neoadjuvant-intent chemotherapy may improve rates of receipt of systemic therapy in addition to surgery, especially in patients with comorbid conditions.

Figure 1: Kaplan Meier survival curve for patients who underwent upfront surgical resection for pancreatic cancer stratified by receipt of adjuvant chemotherapy.



P 39. PANCREATODUODENECTOMY FOLLOWING ROUX-EN-Y GASTRIC BYPASS: OPERATIVE CONSIDERATIONS AND OUTCOMES

MT Trudeau, L Maggino, BL Ecker, CM Vollmer

Presenter: Maxwell Trudeau BS | University of Pennsylvania

Background: Roux-en-Y bypass (RYGB) has historically been the most applied operation for morbid obesity. Some patients will ultimately require pancreatoduodenectomy (PD) for a spectrum of periampullary pathologies. It is suspected that the altered anatomy of RYGB reconstruction influences intraoperative decisions, and contributes to worse outcomes in patients who subsequently require PD.

Methods: A multi-national (4), multi-center (28) collaborative of 55 pancreatic surgeons who have performed PD following RYGB (2005-2018) was created. Demographics, operative details and perioperative outcomes (including Postoperative Morbidity Index-PMI) from this cohort were analyzed and compared in a propensity-scored matched analysis (Sex, Age, BMI, ASA Class) to a multi-center cohort of 5,533 PDs without prior RYGB. Multivariate regression identified Roux anatomy factors that dictated PD reconstructive variations.

Results: 94 open PDs were performed on RYGB patients (52% MIS; 70% stomach transected from pouch; median-10 years prior/100 lb. weight loss). Pathologic indications between the RYGB anatomy and normal anatomy cohorts did not differ ($p=0.133$; malignancy $\approx 65\%$). Of the 14 distinct reconstructions employed (of 32 options), 4 accounted for 64%, and none demonstrated superior outcomes. The most common reconstruction (25%) removed the remnant stomach, used the original biliopancreatic (BP) limb, and attached the PJ most distally, followed by the HJ. Two-thirds of the cases used the original BP limb for reconstruction - most commonly placed trans-mesenteric (69%). There were no appreciable outcome benefits vs. those where a secondary Roux limb was created for BP reconstitution. The only significant factor driving surgeons to pursue reconstruction requiring a new Roux was a short original BP limb (OR 8.17; 95% CI 1.68-39.60). Remnant stomachs were removed in 45% - paradoxically more often when still in continuity with the Roux pouch ($p=0.046$), with no outcome differences between resected and retained stomachs. Venting G-tubes were used in 36% of retained stomachs without outcome benefits. J-tubes were used infrequently (12%). In the risk-matched analysis, RYGB patients showed no significant differences in major postop outcomes (Table) including: Any/Severe complications, mortality, length of stay, pancreatic fistula, DGE, reoperation and postop disposition. The PMI was equivalent for all patients (0.175 RYGB vs. 0.204 traditional PD; $p=0.255$), and for those suffering complications (0.288 vs 0.327; $p=0.173$). However, ICU use, transfusions, and readmission rates were higher in the RYGB cohort.

Conclusion: PD after RYGB is an infrequently encountered, unique and challenging scenario for any given surgeon. These patients do not suffer higher morbidity than those with unaltered anatomy. Various technical reconstructive options do not appear to confer distinct benefits.

Table 1. A Risk Matched Comparison of Clinical Postoperative Course between RYGB Anatomy and Normal Anatomy for Pancreatoduodenectomy

	RYGB Anatomy	Normal Anatomy	
Clinical Outcome Metric, Frequency, %	N=94	N=93	P-value
Operative Time (min), median (IQR)	353 (258.50-439.50)	334 (285.00-403.00)	0.200
Estimated Blood Loss (ml), median (IQR)	400 (250.00-700.00)	300 (188.00-600.00)	0.266
Any complication (Accordion \geq 1)	57 (60.6)	58 (62.4)	0.808
Severe complication (Accordion \geq 3)	15 (16)	21 (22.6)	0.251
Clinically Relevant Pancreatic Fistula	3 (3.2)	9 (9.7)	0.070
Clinically Relevant Delayed Gastric Emptying	5 (5.4)	2 (12.5)	0.283
Mortality , 90 days	3 (3.2)	2 (2.2)	0.369
Postoperative Morbidity Index, mean (SD)	0.175 (0.22)	0.204 (0.23)	0.255
Length of Stay, median (IQR)	8.00 (6.00-11.00)	8.00 (7.00-10.00)	0.402
Discharge Disposition to Home	65 (69.9)	47 (77)	0.329
Readmission	23 (24.5)	10 (11.1)	0.018
Reoperation	2 (2.1)	3 (3.2)	0.642
Intensive care unit used	44 (46.8)	8 (12.7)	<0.001
TEN or TPN Use	24 (25.5)	15 (23.8)	0.807
Transfusion (Intra-op or Post-op)	32 (34)	12 (19.4)	0.046
Percutaneous Drain Placement	13 (13.8)	8 (8.6)	0.258

P 40. OPTIMAL PANCREATIC SURGERY: ARE WE MAKING PROGRESS?

JD Beane, JD Borreback, AH Zureikat, EM Kilbane, VJ Thompson, HA Pitt

Presenter: Joal Beane MD | University of Pittsburgh Medical Center

Background: Morbidity following pancreatectomy remains unacceptably high. Recent literature suggests that composite measures, benchmarking, and textbook outcomes may more accurately define surgical quality. The ACS NSQIP Hepato-Pancreato-Biliary Collaborative was initiated in January 2015 and aims to improve pancreatic surgery outcomes by providing feedback on risk-adjusted outcomes and disseminating best practices. The objective of this analysis was to assess the delivery of optimal pancreatic surgery and determine whether significant improvements have been made by the collaborative.

Methods: The 2013-17 ACS NSQIP Participant Use Data Files (PUFs) and 2014-17 Pancreatectomy Targeted PUFs were queried to identify patients undergoing elective pancreatoduodenectomy (PD, N=16,222) and distal pancreatectomy (DP, N=7,946). Multiple patient, procedure, process, and 30-day outcome variables were captured and analyzed over time. Optimal pancreatic surgery was defined as the absence of postoperative mortality, serious complications, percutaneous drainage, reoperations, excessive length of stay (>75th percentile), and readmissions. Statistical time-trend analyses were performed, and the threshold for significance was set at $p \leq 0.05$.

Results: The table presents preoperative, intraoperative, perioperative and postoperative factors among PD patients from 2013-17. A greater rate of patients received preoperative chemotherapy ($p < 0.001$) and biliary stents ($p < 0.05$) over time. The number of patients who underwent minimally invasive PD did not change, but the percent undergoing robotic PD increased ($p < 0.001$) while the percent undergoing laparoscopic PD decreased ($p < 0.02$). Fewer transfusions were administered ($p < 0.001$) and mean operative times decreased ($p < 0.05$). The percentage of patients having a drain fluid amylase checked on postoperative day 1 increased ($p < 0.001$). A greater percentage of surgical drains also were removed by postoperative day 3 ($p < 0.001$). Overall morbidity ($p = 0.01$) and mortality ($p < 0.05$) rates decreased, and the mean postoperative length of stay reduced ($p < 0.01$). Finally, the rate of patients who achieved optimal pancreatic surgery increased from 2014-17 for both PD ($p = 0.002$) and DP ($p < 0.001$), while patients with pancreatic cancer (PD: N=7,423, DP: N=1,873) also demonstrated greater optimal pancreatic surgery rates (both $p < 0.01$).

Conclusion: Preoperative, intraoperative, and perioperative pancreatic surgery processes have evolved from 2013-17, resulting in improved postoperative outcomes and a greater percent of patients achieving optimal pancreatic surgery.

Table. Preoperative, intraoperative, perioperative and postoperative factors in 16,222 patients undergoing pancreatoduodenectomy from 2013-17.

	2013	2014	2015	2016	2017	P value
Preoperative						
Chemotherapy (%)	NA	15.5	17.3	19.9	21.8	<0.001
Biliary stents (%)	NA	53.3	52.0	56.5	54.5	0.046
Intraoperative						
Laparoscopic (%)	5.8	3.9	4.3	3.7	4.3	0.018
Robotic (%)	2.5	2.9	3.4	4.8	4.2	<0.001
Pylorus preservation (%)	40.9	42.1	41.0	36.7	35.5	<0.001
Mean operative time (min)	375	376	368	371	369	0.042
Perioperative						
Transfusions (%)	21.5	19.2	17.1	15.7	16.3	<0.001
DFA-1*(%)	NA	22.3	29.7	37.1	43.1	<0.001
Drain out by POD 3 (%)	NA	8.9	10.1	12.9	15.1	<0.001
Postoperative						
Mortality (%)	2.1	2.0	1.7	1.5	1.6	0.047
Any complication [†] (%)	NA	48.5	48.2	46.1	45.9	0.014
Superficial SSI (%)	9.0	9.3	7.8	6.8	7.1	<0.001
Sepsis/Septic shock (%)	10.8	10.6	9.7	8.6	9.2	0.003
Percutaneous drainage (%)	NA	13.4	13.5	11.9	11.6	0.005
Mean LOS (days)	10.7	11.0	10.5	10.5	10.3	0.002
Optimal Surgery (%)	NA	53.7	54.0	56.4	56.9	0.002

NA = Not Available, SSI = Surgical Site Infection, POD = Postoperative Day, LOS = Length of Stay

*Drain fluid amylase measured on POD 1

[†]Including clinically relevant postoperative pancreatic fistulas

P 42. COLLAGEN XVII AND VII SIGNALING COMPLEX IN NEOPLASTIC AND STROMAL CROSS-TALK IN PANCREATIC CANCER

A Li, TP Hank, KC Honselmann, DJ Birnbaum, SKS Begg, KD Lillemoe, AL Warshaw, C Fernández-del Castillo, AS Liss

Presenter: Annie Li | Massachusetts General Hospital

Background: Pancreatic ductal adenocarcinoma (PDAC) is characterized by an extensive desmoplastic reaction formed by extracellular matrix (ECM) components and cancer-associated fibroblasts (CAFs). The ECM represents a heterogeneous group of proteins that support soluble and mechanical signaling in the tumor. Despite its importance, little is known about the regulation of ECM expression in PDAC. Here we investigate the regulation of collagen XVII and collagen VII that are key components of an epithelial cell signaling complex.

Methods: The expression of COL17A1 and COL7A1 was examined by qPCR in mono- and co-cultures of PDAC cell lines and immortalized cultures of CAFs. The expression of both COL17A1 and COL7A1 was analyzed in 13 human PDAC samples by RNA-sequencing of laser capture microdissection (LCM). Immunohistochemistry was performed in patient-derived xenograft (PDX) tumors, chronic pancreatitis and untreated murine pancreas to determine the expression patterns of collagen XVII. To further describe the localization of collagen XVII immunofluorescence studies were done on different fixed PDAC and CAF cell lines.

Results: COL17A1 was highly expressed in PDAC cells in comparison to COL7A1, which was almost absent. Conversely, CAFs did not express COL17A1 but expressed high levels of COL7A1. Upon co-culture with CAFs, an upregulation of COL17A1 and robust expression of COL7A1 was observed in PDAC cells. Additionally, COL7A1 expression increased in CAFs after co-culture with PDAC cells; however, CAFs still failed to express COL17A1. Importantly, these co-culture models recapitulate the expression of COL17A1 and COL7A1 observed in tumors. Analysis of human PDAC samples revealed COL17A1 was predominantly expressed in the cancer cells, whereas COL7A1 was more highly expressed in the adjacent stroma. The expression of collagen XVII appears to be unique to pancreatic cancer as immunohistochemistry analyses showed a strong expression of collagen XVII, which was absent in normal and chronic inflammatory pancreatic tissue. In contrast, collagen VII was pre-dominantly expressed in the stromal compartments of PDAC samples and not in the tumor cells. Furthermore, immunofluorescent analysis demonstrated a strong membranous staining of PDAC cells in culture for collagen XVII which was missing in immortalized CAFs.

Conclusion: The present findings highlight the different contribution of PDAC and CAF cells in the production of a collagen XVII and VII signaling complex. Furthermore, the upregulation of collagen XVII or collagen VII upon co-culture with stromal or neoplastic compartments underlines the importance of PDAC-CAF crosstalk in the tumorigenesis of pancreatic cancer.

P 43. MEK INHIBITOR TRAMETINIB IN COMBINATION WITH GEMCITABINE REGRESSES A PATIENT-DERIVED ORTHOTOPIC XENOGRAFT (PDOX) PANCREATIC CANCER NUDE MOUSE MODEL

K Kawaguchi, M Bouvet, M Unno, RM Hoffman

Presenter: Kei Kawaguchi MD, PhD | Tohoku University Graduate School of Medicine

Background: Pancreatic cancer is resistant to treatment and needs precision individualized therapy to improve the outcome of this disease. To accomplish this goal of precision, individualized treatment of cancer patients, our laboratory established the patient-derived orthotopic xenograft (PDOX) nude mouse model employing the surgical orthotopic implantation (SOI) technique, which includes pancreatic cancer. Previously, we demonstrated that trametinib (TRA), a MEK inhibitor, could inhibit a pancreatic cancer PDOX.

Methods: In the present study, we show that gemcitabine (GEM) in combination with TRA was more effective than TRA alone. We implanted a patient pancreatic cancer orthotopically in the pancreatic tail of nude mice to establish the PDOX model. After seven weeks of tumor growth, we divided 32 pancreatic-cancer PDOX nude mice into 4 groups of eight: untreated control; GEM (once a week for 2 weeks); TRA (14 consecutive days); GEM + TRA (GEM: once a week for 2 weeks, TRA:14 consecutive days). We found that treated mice on day 14 had significantly reduced tumor volume in comparison to untreated control.

Results: TRA and the combination of GEM + TRA therapy significantly inhibited tumor development in comparison to GEM alone. However, GEM + TRA inhibited the PDOX tumor growth significantly greater than TRA alone.

Conclusion: These results suggest the clinical potential of the combination of TRA and GEM for pancreatic cancer.

P 44. KRAS-MUTATED CIRCULATING TUMOR DNA PREDICTS EARLY RECURRENCE IN PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA

T Yamaguchi, K Uemura, Y Murakami, N Kondo, N Nakagawa, K Okada, S Seo, S Takahashi, T Sueda

Presenter: Takuro Yamaguchi MD | Hiroshima University

Background: It has been reported that the presence of preoperative KRAS-mutated circulating tumor DNA (ctDNA) could be a powerful predictor of poor overall survival (OS) in patients with pancreatic ductal adenocarcinoma. However, the significance of the presence of postoperative KRAS-mutated ctDNA was an unresolved issue. The aim of this study was to evaluate whether the presence of KRAS-mutated circulating tumor DNA in postoperative plasma sample could predict disease-free survival (DFS), overall survival, and early recurrence after surgery (ER) of patients with resectable and borderline resectable pancreatic ductal adenocarcinoma (PDAC) in the head of the pancreas.

Methods: KRAS-mutated ctDNA in pre- and postoperative plasma samples obtained from 117 patients with resectable and borderline resectable PDAC was detected by using digital droplet polymerase chain reaction, and its relationship to DFS, OS and ER were analysed with univariate and multivariate methods.

Results: KRAS-mutated ctDNA was detected in 31 patients (27%) preoperatively and 34 patients (29%) postoperatively, respectively. Multivariate analysis showed that lymph node metastasis ($P < 0.001$), pathological differentiation ($P < 0.001$), and the presence of preoperative KRAS-mutated ctDNA ($P = 0.034$), were associated with poor DFS, and lymph node metastasis ($P = 0.020$), pathological differentiation ($P = 0.004$), portal venous invasion ($P = 0.019$), and the presence of preoperative KRAS-mutated ctDNA ($P = 0.006$), were associated with poor OS. It was also shown that residual tumor ($P = 0.019$), distal bile duct invasion ($P = 0.040$), portal venous invasion ($P = 0.020$), and the presence of postoperative KRAS-mutated ctDNA ($P = 0.007$), were independent predictors for ER.

Conclusion: The presence of postoperative KRAS-mutated ctDNA may be a potent predictor for ER and a useful biomarker for patients with PDAC.

P 45. LONG-TERM SEQUELAE OF NECROTIZING PANCREATITIS: A LIFE-LONG DISEASE

TK Maatman, AM Roch, EP Ceppa, MG House, A Nakeeb, CM Schmidt, NJ Zyromski

Presenter: Thomas Maatman MD | Indiana University School of Medicine

Background: Necrotizing pancreatitis (NP) survivors develop long-term sequelae often requiring intervention. Remarkably few data have catalogued these late complications following NP. We sought to identify the types and incidence of long-term sequelae following NP.

Methods: 647 NP patients between 2005-2017 were reviewed. Exclusion criteria included: death before disease resolution (n=57, 8.8%) and patients lost to follow-up (n=12, 1.9%). Descriptive analysis of newly diagnosed conditions was performed.

Results: 578 patients were followed a mean of 44 months (range: 2-165). Figure 1 shows long-term sequelae, including: disconnected pancreatic duct syndrome (285/578, 49.3%), splanchnic vein thrombosis (257/572, 44.9%), insulin-dependent endocrine insufficiency (195/549, 35.5%), exocrine insufficiency (108/571, 18.9%), biliary stricture (90/576, 15.6%), chronic pancreatitis (52/538, 9.8%), chronic pain syndrome (44/575, 7.7%), and gastrointestinal fistula (42/578, 7.3%). Biliary stricture required a mean number of 3.9 interventions in 86 patients (95.6%); stricture resolution was achieved after a median of 6 months (range: 3 days to 8.3 years). Gastrointestinal fistula required a mean number of 3.5 interventions in 36 patients (85.7%); fistula resolution was achieved after a median of 3 months (range: 5 days to 5.5 years). Following NP resolution, a mean number of 2.6 (range 1-14, standard deviation 2.1) pancreatobiliary interventions were required in 230/578 (39.8%) patients.

Conclusion: Long-term sequelae following necrotizing pancreatitis are common. Survivors commonly require invasive pancreatobiliary interventions after acute disease resolution and are affected by life-long degradation of pancreas function.

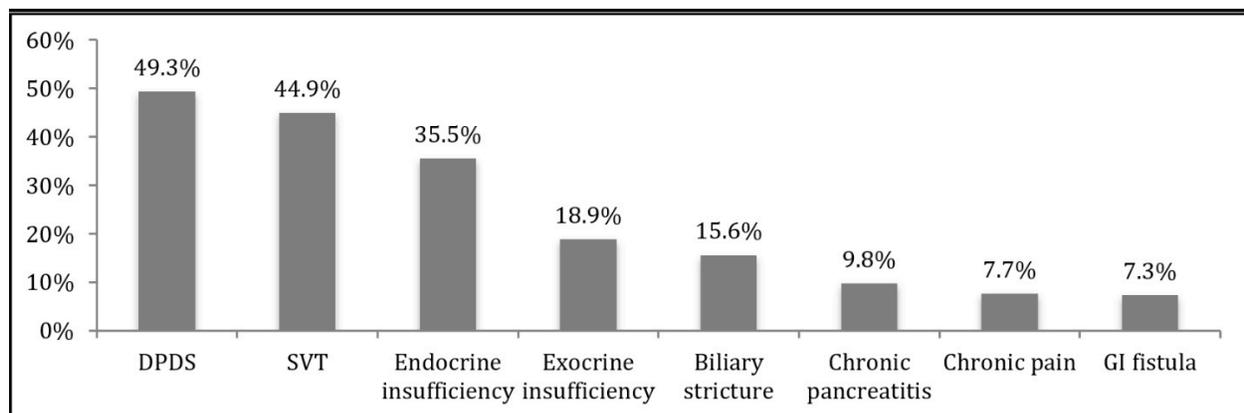


Figure 1: Type and incidence of long-term sequelae following necrotizing pancreatitis.

Abbreviations: DPDS - disconnected pancreatic duct syndrome, SVT – splanchnic vein thrombosis, GI – gastrointestinal.

P 46. NONSELECTIVE B-ADRENERGIC BLOCKADE IMPACTS PANCREATIC CANCER TUMOR BIOLOGY, DECREASES PERINEURAL INVASION AND IMPROVES PATIENT SURVIVAL

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Presenter: Alex Blair MD | Johns Hopkins University School of Medicine

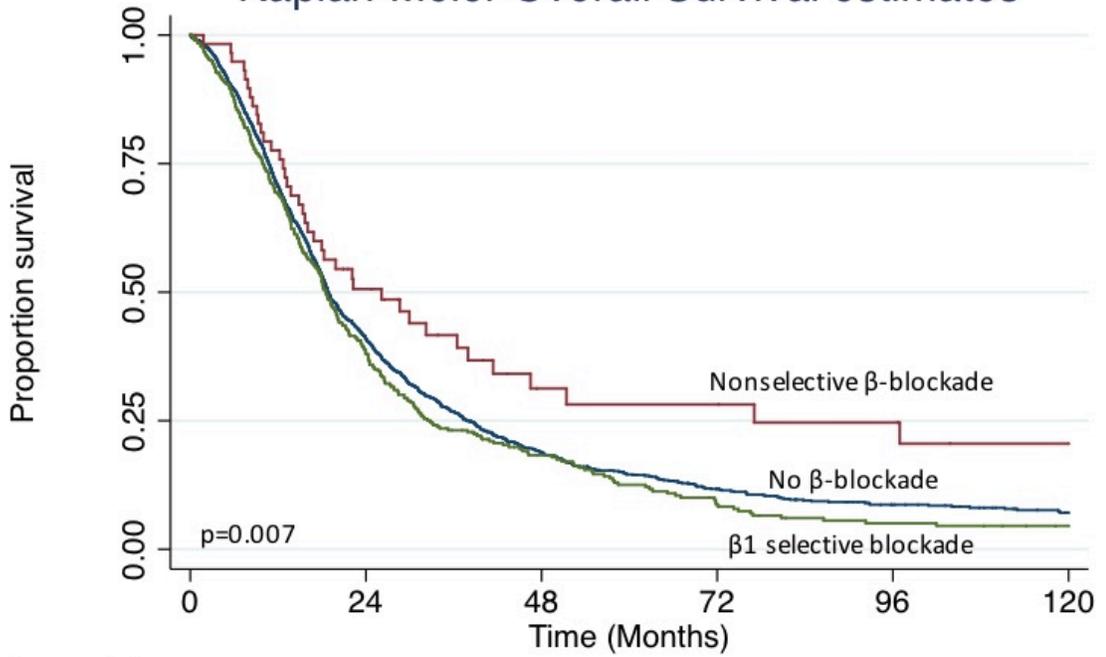
Background: Beta (B) adrenergic signaling mediates progression and invasion in many cancer subtypes. B-blockade, often prescribed for a chronic medical illness such as hypertension, is associated with improved outcomes in breast and prostate cancer. While hypertension is a frequent co-morbid condition found in patients diagnosed with pancreatic ductal adenocarcinoma (PDAC), the impact of B-blockade in this disease remains unknown.

Methods: Clinical data were prospectively collected for patients undergoing pancreatotomy between 2000 and 2016 at a high-volume pancreatic surgery center of excellence. B-blocker use was utilized to stratify patients into independent cohorts and histopathologic and oncologic outcomes data were investigated. Differences between these two cohorts prompted investigations of a proposed mechanism of action of B-blockade on tumor biology in a patient-derived model of PDAC.

Results: In total, 457 of 1,933 patients taken to the operating room for a diagnosis of PDAC were prescribed B-blockade by their primary care physician or cardiologist. Three-hundred and ninety seven were taking B1-selective-blockers and 60 received non-selective B-blockers. When stratified by selectivity, non-selective B-blockade is associated with decreased perineural invasion compared to B1-selective or no B-blockade (NoB) (non-selective=68.3%, B1-selective=84.9%, NoB=85.9%, $p<0.001$). Non-selective B-blockade is also associated with longer overall survival (median: non-selective=26.1 months, B1-selective=18.5m, NoB=18.8m, $p<0.01$). With these data associating B-blockade and perineural invasion, a paracrine mechanism involving noradrenergic hormones was hypothesized. Recapitulating this in-vitro using a human PDAC cell line with norepinephrine administration demonstrated increased cell growth and migration. Co-administration of propranolol successfully abrogated norepinephrine-induced growth and migration.

Conclusion: Non-selective B-blockade is independently associated with decreased perineural invasion and improved overall survival in resected PDAC. In-vitro, norepinephrine stimulates cell growth and migration. While propranolol does not impact cell growth in isolation, co-administration with norepinephrine abrogates the increased growth and migration seen with norepinephrine administration alone. This work highlights the impact of commonly used antihypertensive medications on tumor biology and may elucidate a rationale for the use of common antihypertensive medications as therapeutic adjuncts in PDAC.

Kaplan-Meier Overall Survival estimates



Number at risk						
No β -blockade	1481	537	191	87	48	26
Nonselective β -blockade	60	26	10	9	7	4
β 1 selective blockade	392	128	45	20	10	5

P 47. EVALUATION OF CIRCUMFERENTIAL RESECTION MARGINS FOR PANCREATIC HEAD CANCER: A PROSPECTIVE STUDY WITH COMPARISON OF 0MM VERSUS 1MM RULES FOR R1 RESECTION

Y-S Yoon, H Kim, Y Lee, H-S Han, S Ahn, J-Y Choe, Y Lee

Presenter: Yoo-Seok Yoon MD, PhD | Seoul National University Bundang Hospital

Background: Although microscopic residual disease (R1 resection) has been reported as an independent prognostic factor for pancreatic ductal adenocarcinoma (PDAC), the prognostic significance of R1 resection for PDAC has varied in the literature for the following reasons; 1) a lack of consensus on the definition of R1 resection (1mm rule versus 0mm rule), 2) a lack of consensus on the definition of various resection margins and surfaces (e.g. anterior, posterior, superior mesenteric vein/portal vein (SMV/PV) and superior mesenteric artery (SMA)), and 3) various grossing techniques in the pathology laboratory for pancreaticoduodenectomy specimens.

Methods: We performed a prospective clinicopathological analysis of 119 PDACs, resected by pancreaticoduodenectomy specimens with (n=49) or without (n=70) venous resection between March 2014 and December 2016 at Seoul National University Bundang Hospital. All circumferential margin/surfaces of the pancreas (anterior, posterior, SMV/PV groove, SMA), the pancreatic neck margin, bile duct margin and intestinal margins were painted with standardized ink color codes, and were sectioned by the axial slicing method. The entire pancreatic head was submitted for histopathological mapping and the safety margins for all margin/surfaces were recorded in millimeters. The patients were followed up for up to 51 months (median: 17 months), and the margin status was correlated with the patient outcome, including overall survival (OS), and disease-free survival (DFS).

Results: Of the 199 specimens, 39 (32.8%) cases were R1 by the 0mm rule while the R1 rate increased to 100 (84.0%) by the 1mm rule. When each circumferential margin was analyzed by the 0mm and 1mm-rules, the anterior surface was involved in 7 (5.9%) and 42 (35.3%) cases, the posterior surface was involved in 10 (8.4%) and 53 (44.5%) cases, the SMV/PV groove was involved in 22 (18.5%) and 71 (59.7%) cases, and the SMA margin was positive in 12 (10.1%) and 43 (36.1%) cases, respectively. Involvement of the anterior surface by the 0mm rule was associated with significantly decreased OS, DFS and distant metastasis-free survival (DMFS) ($p < 0.001$, all); however, when the 1mm rule was applied, only OS was decreased in anterior surface-positive cases ($p = 0.044$). Similarly, posterior surface involvement by the 0mm rule was significantly associated with decreased OS ($p = 0.048$) and DFS ($p = 0.037$). In contrast, involvement of the SMA margin was correlated with decreased OS, DFS and local recurrence-free survival (LRFS) when both 0mm and 1mm rules were applied ($p < 0.05$, all). SMA margin status had no influence on DMFS. For SMV/PV groove status, involvement by the 0mm rule was associated with significantly decreased OS, DFS, LRFS and DMFS ($p < 0.05$, all), and when the 1mm rule was applied, LRFS was still decreased ($p = 0.007$) while there was a tendency for decreased OS ($p = 0.072$) and DFS ($p = 0.090$).

Conclusion: A "positive margin" by the 1mm rule was significantly associated with adverse outcome for SMA margin and SMV/PV grooves, while involvement of the anterior and posterior surfaces by the 0mm rule was a poor prognostic factor. In addition, although anterior and posterior surfaces are technically not "margins" because they are not surgically dissected, involvement of these surfaces by tumor is significantly associated with adverse outcome and therefore should be reported.

P 48. TUMOR BUDDING MORPHOMIC ANALYSIS REVEALS EMT AND PROGNOSTIC INFORMATION IN PERIAMPULLARY CANCER

UF Wellner, E Kocsmar, A Kiss, G Lotz, M Hoerner, E Petrova, S Timme, A Csanadi, M Werner, T Keck, P Bronsert

Presenter: Ulrich F. Wellner MD | University Medical Center Schleswig-Holstein

Background: Tumor budding (TB), published in 1949 by Imai et al., describes a prognostic histological feature of cancer and a first rudimentary grading system. Tumor buds are defined as cohesive complexes of up to five tumor cells, and often regarded as a morphological sign of epithelial mesenchymal transition (EMT). Interestingly, quantitative data describing the amount of cells defining a TB, but also direct quantitative correlations to EMT are lacking. Here we apply the concept of cohesive cell clusters, using a quantitative morphomics approach to periampullary adenocarcinomas.

Methods: A cohort of 180 patients with resected periampullary cancers (111 pancreas / 38 ampulla / 9 duodenal / 22 distal bile duct) was included. Serial slides were stained for eCadherin (eCad). Size and number of cohesive cell clusters (from 1 cell to 50 cohesive cells) and pattern of E-Cadherin staining (membranous, cytoplasmatic, mixed) were quantified. These morphomic features were subjected to unsupervised clustering and elastic net regression to test for prognostic relevance and correlations to tumor biology.

Results: Unsupervised as well as supervised analysis of the tumor budding morphome revealed a prognostic tumor budding signature: increased numbers of small tumor buds were associated with pancreatobiliary type cancers, intracellular shuttling of E-Cadherin from membranous to cytoplasmic, and worse prognosis, while the reverse was true for large tumor cell clusters. The tumor budding signature was able to stratify patients into three prognostic categories and constituted an independent prognostic factor in addition to standard histopathology parameters.

Conclusion: A tumor budding signature could provide independent prognostic information in periampullary adenocarcinomas and correlated with histopathological features of EMT.

P 49. FACTORS ASSOCIATED WITH DISEASE PROGRESSION OR PERFORMANCE STATUS DECLINE IN PATIENTS UNDERGOING NEOADJUVANT CHEMOTHERAPY FOR LOCALIZED PANCREATIC HEAD ADENOCARCINOMA

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Presenter: Alessandro Paniccia MD | University of Pittsburgh Medical Center

Background: Neoadjuvant chemotherapy (NT) is increasingly administered to patients with localized pancreatic head adenocarcinoma (PDAC). However, a significant portion of NT patients do not undergo resection either due to disease progression or performance status decline. We sought to identify predictors of disease progression or performance status decline during NT.

Methods: All consecutive patients with localized PDAC who received NT at a tertiary referral center were identified. Univariate and Cox multivariate (MVA) analysis were performed to identify factors associated with disease progression (on imaging or at time of anticipated resection) or performance status decline preventing surgical resection.

Results: Between 2005 and 2017, 479 patients diagnosed with PDAC underwent NT; 69.3% proceeded to surgery, 27.8% had disease progression, and 7.1% experienced performance status decline without disease progression on imaging. Median overall survival was 27.9 (95%CI 23.2-32.3), 12.8 (95%CI 11.2-14.1), and 6.9 (95%CI 4.9-11.2) months for the resected, disease progression and performance status decline groups, respectively ($p < 0.0001$). On MVA, predictors of disease progression were EUS tumor size (OR 1.83, 95%CI 1.03–3.26), unplanned change in NT regimen (OR 3.05, 95%CI 1.19–7.80), hospital admission during NT (OR 2.75, 95%CI 1.54–4.92), CA19.9 response (OR 0.26, 95%CI 0.14–0.47) and biliary stent placement prior to NT initiation (OR 0.42, 95%CI 0.22–0.78). On MVA, predictors of performance status decline during NT were increasing age (OR 1.07, 95% CI 1.01 – 1.14), presence of diabetes (OR 4.58, 95% CI 1.53-13.73), EUS tumor size (OR 10.36, 95% CI 1.49 – 71.72), and hospital admission during NT treatment (OR 20.15, 95% CI 4.26 – 95.29).

Conclusion: This analysis identifies several predictors of disease progression and performance status decline during NT for PDAC. These data provide further insight into which factors can be leveraged in order to successfully pursue various treatment strategies for localized PDAC.

P 51. EXTREMES OF BMI ARE ASSOCIATED WITH A HIGHER RISK OF PANCREATIC FISTULA FOLLOWING PANCREATICODUODENECTOMY: AN ANALYSIS USING THE NSQIP DATABASE

S Leonard-Murali, T Ivanics, A Tang, CP Steffes, RA Shah, DS Kwon

Presenter: Shravan Leonard-Murali MD | Henry Ford Hospital

Background: Elevated body-mass index (BMI) is a well-described risk factor for postoperative complications. Specifically, the impact of BMI on pancreatic fistula rates following pancreaticoduodenectomy (PD) has been inconsistent. The aim of this study was to investigate pancreas-specific morbidity following pancreaticoduodenectomy for patients with extremes of BMI using a large national database.

Methods: The National Surgical Quality Improvement Program database (NSQIP) was queried for patients undergoing PD between 2014-2016. BMI was classified according to the WHO classification as underweight (UW) (< 40). Univariate and multivariable logistic regression models were used to evaluate the effects of BMI on pancreas-specific morbidity. Stepwise selection was performed and adjustments were made for comorbidities, operative factors and pancreas-specific variables. Postoperative pancreatic fistula was classified into biochemical leak (BCL), Grade B and Grade C as per the International Study Group for Pancreatic Surgery (ISGPS) 2016 definition. $P < 0.05$ was considered statistically significant. All analyses were done in SAS 9.4 (SAS Institute, Cary, NC).

Results: 10,526 patients were included in the analysis (UW n=302, NW n=3,721, OW n=3,678, OBI n=1,779, OBII n=653, OBIII n=363) (Table 1). On univariate analysis elevated BMI (OB I-III) was associated with pancreatic fistula development compared to normal weight patients. This difference persisted on multivariable analysis for OBI and OBIII (OBI vs. NW OR=1.55 (1.13-2.12); $p=0.007$) (OBIII vs. NW, OR=1.86 (1.08-3.21); $p=0.026$). The difference did not persist for OBII (OBII vs. NW OR=1.53 (0.96-2.24); $p=0.08$). Similarly, patients with higher BMI (OBI-III) had a lower odds of a lower grade pancreatic leak compared to NW patients. This difference persisted on multivariate ordinal logistic regression analysis for OBI and OBIII but not for OBII (OB I vs. NW OR=0.65 (0.48-0.89); $p=0.008$) (OBII vs. NW OR=0.68 (0.43-1.08); $p=0.099$) (OBIII vs. NW OR=0.53 (0.31-0.90); $p=0.02$). On multivariable logistic regression there was no statistically significant difference for 30-day mortality, readmission rates, morbidity, delayed gastric emptying among the BMI groups.

Conclusion: Elevated BMI increases risk of pancreatic fistula but not mortality or general perioperative morbidity following pancreaticoduodenectomy. Extreme obesity is an independent risk factor for pancreatic fistula and higher fistula grade compared to patients with normal weight. It might be worth considering the incorporation of BMI into the pancreatic fistula risk score.

Variable	All patients (n=10,526)	UW (n=302)	NW (n=3721)	OW (n=3678)	OB I (n=1779)	OB II (n=653)	OB III (n=363)	P-value
Age	64.5 ± 11.7	64.2 ± 11.9	65.5 ± 12.0	65.1 ± 11.5	63.4 ± 11.1	61.8 ± 11.3	59.8 ± 11.5	<.0001
Sex								
female	4868 (46.2%)	209 (69.2%)	1886 (50.8%)	1405 (38.2%)	782 (44.0%)	344 (52.7%)	224 (61.7%)	<.0001
male	5658 (53.8%)	93 (30.8%)	1826 (49.2%)	2273 (61.8%)	782 (44.0%)	309 (47.3%)	139 (38.3%)	
Gland texture								
Hard	3348 (31.8%)	128 (42.4%)	1307 (35.2%)	1137 (30.9%)	514 (28.9%)	159 (24.3%)	90 (24.8%)	<.0001
Intermediate	856 (8.1%)	20 (6.6%)	304 (8.2%)	300 (8.2%)	151 (8.5%)	55 (8.4%)	23 (6.3%)	
Soft	3710 (35.2%)	74 (24.5%)	1182 (31.8%)	1320 (35.9%)	661 (37.2%)	285 (43.6%)	176 (48.5%)	
Unknown	2612 (24.8%)	80 (26.5%)	919 (24.8%)	921 (25.0%)	453 (25.5%)	154 (23.6%)	74 (20.4%)	
Duct size								
3-6 mm	4318 (41.0%)	111 (36.8%)	1588 (42.8%)	1502 (40.8%)	707 (39.7%)	256 (39.2%)	144 (39.7%)	<.0001
<3 mm	2515 (23.9%)	58 (19.2%)	782 (21.1%)	874 (23.8%)	474 (26.6%)	196 (30.0%)	117 (32.2%)	
>6 mm	1397 (13.3%)	65 (21.5%)	561 (15.1%)	489 (13.3%)	184 (10.3%)	51 (7.8%)	38 (10.5%)	
Unknown	2296 (21.8%)	68 (22.5%)	781 (21.0%)	813 (22.1%)	414 (23.3%)	150 (23.0%)	64 (17.6%)	
DGE								
No	8730 (82.9%)	267 (88.4%)	3157 (85.0%)	3008 (81.8%)	1444 (81.2%)	529 (81.0%)	298 (82.1%)	<.0001
Yes	1796 (17.1%)	35 (11.6%)	555 (15.0%)	670 (18.2%)	335 (18.8%)	124 (19.0%)	65 (17.9%)	
SSI								
No	9657 (91.7%)	292 (96.7%)	3428 (92.3%)	3362 (91.4%)	1624 (91.3%)	591 (90.5%)	325 (89.5%)	0.0061
Yes	869 (8.3%)	10 (3.3%)	284 (7.7%)	316 (8.6%)	155 (8.7%)	62 (9.5%)	38 (10.5%)	
OSI								
No	8993 (85.4%)	281 (93.0%)	3288 (88.6%)	3153 (85.7%)	1427 (80.2%)	523 (80.1%)	289 (79.6%)	<.0001
Yes	1533 (14.6%)	21 (7.0%)	424 (11.4%)	525 (14.3%)	352 (19.8%)	130 (19.9%)	74 (20.4%)	
Readmission								
No	8779 (83.4%)	268 (88.7%)	3153 (84.9%)	3048 (82.9%)	1451 (81.6%)	524 (80.2%)	301 (82.9%)	0.0003
Yes	1747 (16.6%)	34 (11.3%)	559 (15.1%)	630 (17.1%)	328 (18.4%)	129 (19.8%)	62 (17.1%)	
Unknown	79 (0.8%)	6 (2.0%)	20 (0.5%)	29 (0.8%)	17 (1.0%)	3 (0.5%)	3 (0.8%)	
30-day Mortality								
No	10350 (98.3%)	297 (98.3%)	3653 (98.4%)	3628 (98.6%)	1739 (97.8%)	643 (98.5%)	354 (97.5%)	0.18
Yes	176 (1.7%)	5 (1.7%)	59 (1.6%)	50 (1.4%)	40 (2.2%)	10 (1.5%)	9 (2.5%)	
Pancreatic Fistula								
No	8556 (81.3%)	265 (87.7%)	3199 (86.2%)	2966 (80.6%)	1364 (76.7%)	479 (73.4%)	256 (70.5%)	<.0001
Yes	1891 (18.0%)	31 (10.3%)	493 (13.3%)	683 (18.6%)	398 (22.4%)	171 (26.2%)	104 (28.7%)	
Unknown	79 (0.8%)	6 (2.0%)	20 (0.5%)	29 (0.8%)	17 (1.0%)	3 (0.5%)	3 (0.8%)	
Pancreatic Fistula Grade								
Biochemical leak only	1234 (11.7%)	22 (7.3%)	330 (8.9%)	442 (12.0%)	251 (14.1%)	109 (16.7%)	74 (20.4%)	<.0001
Grade B POPF	548 (5.2%)	9 (3.0%)	132 (3.6%)	201 (5.5%)	126 (7.1%)	55 (8.4%)	22 (6.1%)	
Grade C POPF	109 (1.0%)	0 (0.0%)	31 (0.8%)	40 (1.1%)	21 (1.2%)	7 (1.1%)	8 (2.2%)	
No	8556 (81.3%)	265 (87.7%)	3199 (86.2%)	2966 (80.6%)	1364 (76.7%)	479 (73.4%)	256 (70.5%)	
Unknown	79 (0.8%)	6 (2.0%)	20 (0.5%)	29 (0.8%)	17 (1.0%)	3 (0.5%)	3 (0.8%)	

Table 1. Demographics, perioperative morbidity, mortality and pancreas specific morbidity stratified by Body Mass Index (BMI)

*UW: underweight BMI<18.5, NW: normal weight BMI 18.5-24.9, OW: overweight BMI 25.0-29.9, OBI: class I obesity BMI 30.0-34.9, OBIII: class II obesity BMI 35.0-39.9, OBIIII: class III obesity BMI =>40, DGE: delayed gastric emptying, SSI=Superficial surgical site infection, OSI= Organ space infection, POPF= Postoperative pancreatic fistula

P 52. TREATMENT SEQUENCING STRATEGIES AND SURVIVAL IN OCTOGENARIANS WITH EARLY STAGE PANCREATIC HEAD ADENOCARCINOMA: A NATIONAL CANCER DATABASE ANALYSIS

T Ivanics, S Leonard-Murali, X Han, C Steffes, R Shah, D Kwon

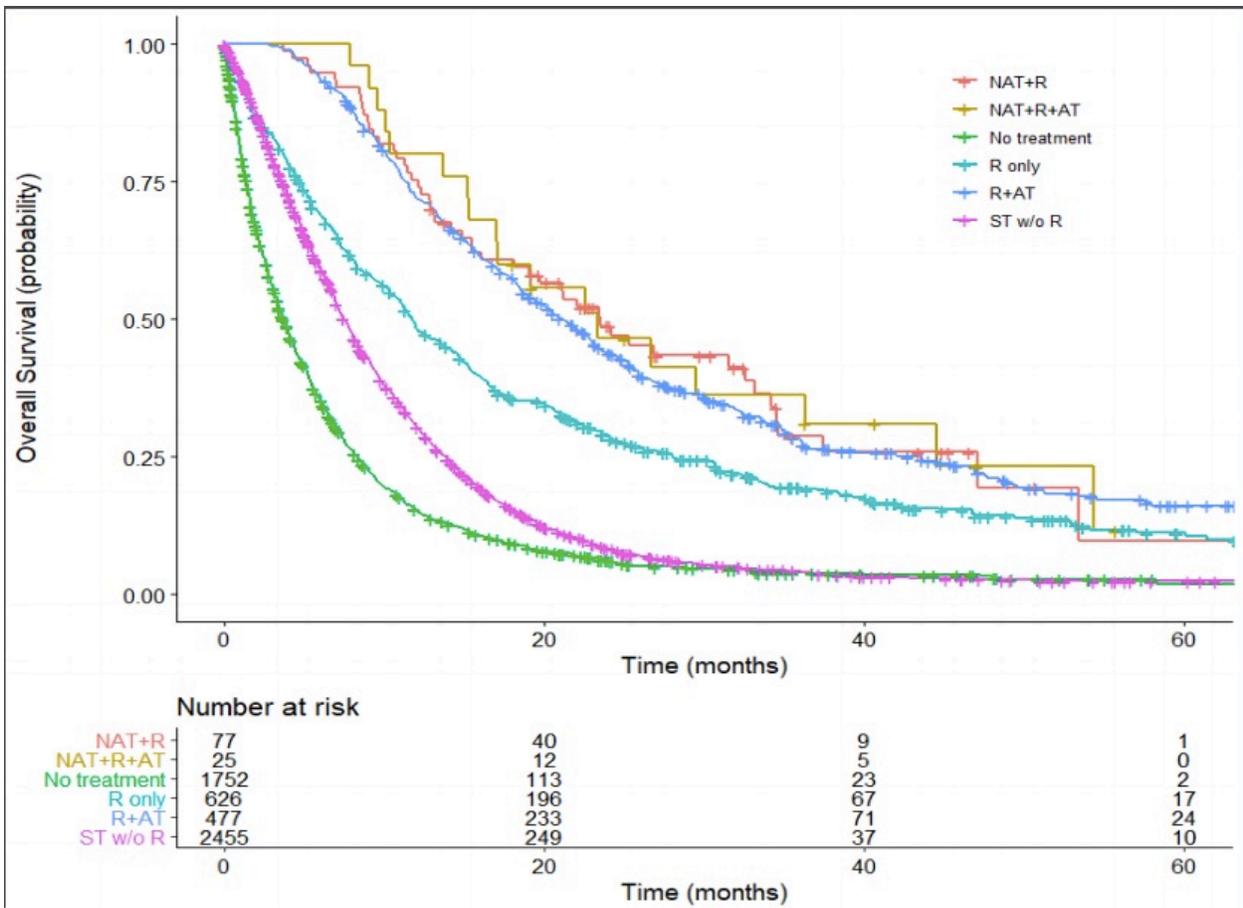
Presenter: Tommy Ivanics MD | Henry Ford Hospital

Background: Multi-modality treatment is essential for optimal outcomes for pancreatic head adenocarcinoma (PDAC), even in the elderly population. Specifically, challenges exist in the octogenarian population due to frailty and associated comorbidities that make multi-modality treatment difficult. Although perioperative mortality associated with pancreaticoduodenectomy (PD) has improved and is safely performed in the elderly, the incidence of perioperative morbidity remains high and may preclude patients from receiving additional therapies essential for improved survival. Oftentimes, frail, elderly patients may not receive all treatment modalities required for optimal outcomes. We sought to describe outcomes of various treatment sequencing strategies in octogenarians with surgically resectable PDAC.

Methods: The National Cancer Database (NCDB) was queried for patients with PDAC from 2010-2015. Patients with Stage I and II disease who were 80-89 years old at the time of diagnosis were included. They were then separated into 6 treatment groups: no treatment (NT), systemic therapy without surgery (ST), resection only (R), neoadjuvant therapy followed by resection (NAT+R), resection followed by adjuvant therapy (R+AT), and neoadjuvant therapy followed by resection and adjuvant therapy (NAT+R+AT). Overall survival was estimated from time of diagnosis using Kaplan-Meier curves and compared using log rank tests. Multivariable cox proportional hazard models were used to compare overall survival among treatment groups, adjusted for demographic and clinicopathologic data. A p-value<0.05 was considered statistically significant.

Results: A total of 5,412 octogenarian patients with stage I (n=2269) and II (n=3143) PDAC were identified between 2010-2015. 32.4% of all stage I and II patients received no treatment, 45.4% of patients received systemic therapy alone, and 11.6% of patients underwent R alone. A low proportion of patients received neoadjuvant therapy sequencing approach (NAT+R: stage I=1%, stage II=1.7%; NAT+R+AT: stage I=0.4%, stage II=0.5%). The R group median survival (11.7 months) was noted to be significantly better than the NT and ST groups (MS 3.7 months, 7.5 months respectively; p<0.001) (Figure 1). On multivariable analysis, multimodal systemic therapy was an independent predictor for survival (Reference: NT, hazard ratios: NAT+R=0.2, NAT+R+AT=0.18, R+AT=0.2; p<0.001 for all three). When patients received multi-modality therapy, there was no survival difference between delivery methods NAT+R, R+AT, or NAT+R+AT (MS 23.5 months, 21.0 months, 23.3 months respectively; p=0.689)

Conclusion: Multi-modality treatment therapy (NAT+R, NAT+R+AT, R+AT) maximized survival in stage I and II PDAC in the octogenarian population and should be considered and discussed when clinically feasible. However, when a single treatment modality was utilized, surgery alone had improved survival benefit versus no resection or systemic therapy alone. Although surgery is technically feasible with low mortality and improved survival rates in the octogenarian population, one must take careful consideration morbidities and quality of life issues that will affect patients clinically when compared to systemic therapy alone.



P 53. NEOADJUVANT THERAPY FOR BODY AND TAIL PANCREATIC ADENOCARCINOMA: PROPENSITY SCORE MATCHED ANALYSIS USING THE NATIONAL CANCER DATABASE

T Ivanics, S Leonard-Murali, X Han, C Steffes, D Kwon, R Shah

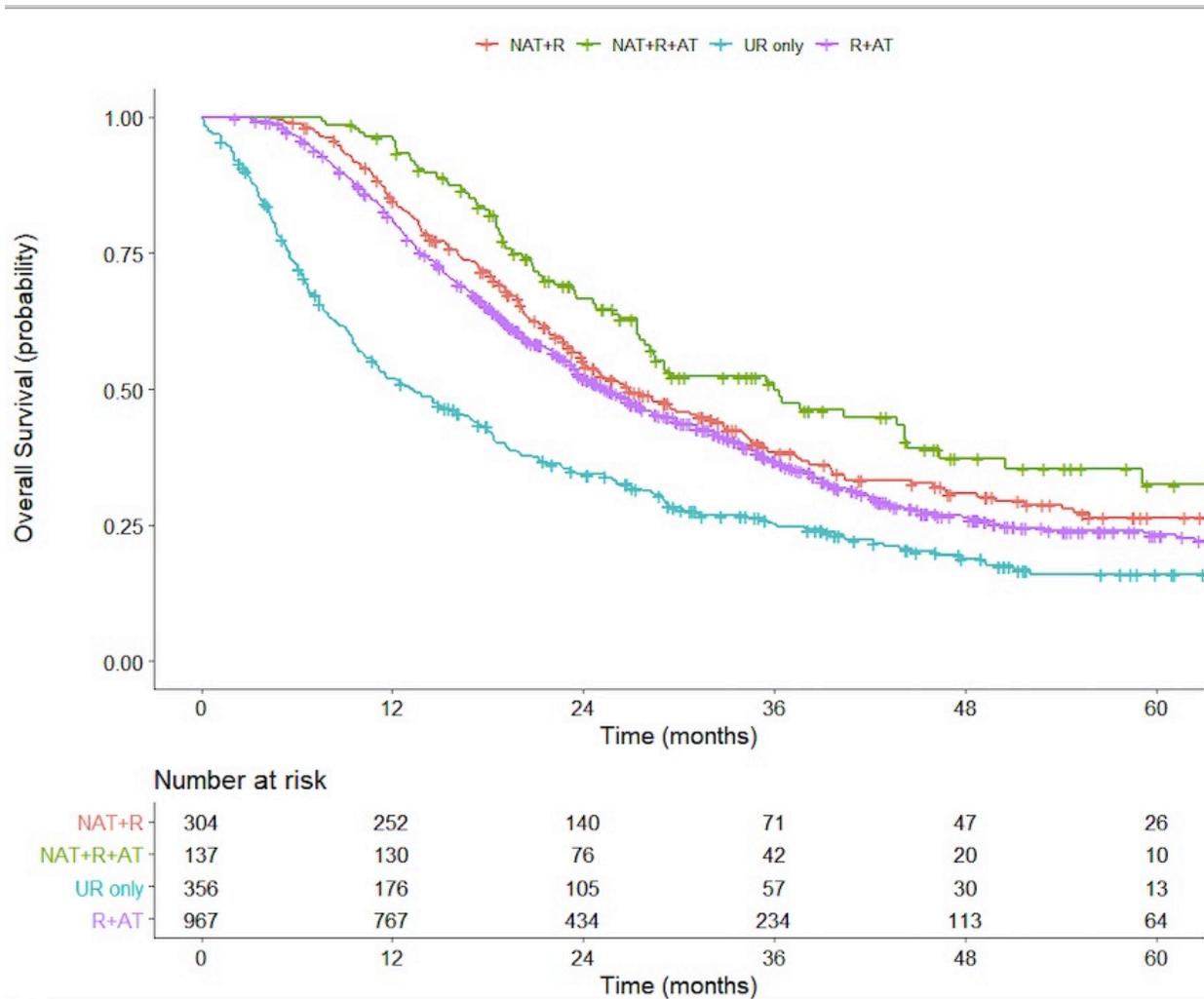
Presenter: Tommy Ivanics MD | Henry Ford Hospital

Background: The role of neoadjuvant systemic therapy in the management of body and tail pancreatic ductal adenocarcinoma (PDAC) is unknown. The aim of our study was to investigate the outcomes associated with neoadjuvant therapy for early stage body and tail PDAC.

Methods: The National Cancer Database (NCDB) was queried for stage I and II body and tail PDAC between 2006-2014. Groups were defined according to treatment sequencing strategies into an upfront resection group (UR), resection followed by adjuvant therapy (R+AT), neoadjuvant therapy followed by resection (NAT+R), and neoadjuvant therapy followed by resection and adjuvant therapy (NAT+R+AT). Patients who underwent neoadjuvant therapy followed by resection were matched by propensity score with patients who underwent upfront resection. Overall survival was compared using Kaplan-Meier method and Cox proportional hazards regression model.

Results: 441 patients received neoadjuvant therapy followed by resection with or without adjuvant therapy compared to 1323 patient who underwent upfront resection with or without adjuvant therapy. NAT+R had lower pathologic stage, lymph node positivity and a higher rate of margin negative resections compared to the matched UR cohort. In the propensity matched cohort, the median survival (MS) was higher in the neoadjuvant (NAT+R/NAT+R+AT) group compared to the upfront resection (UR/R+AT) group (28.6 vs. 22.9 mos; $p < 0.001$). When further stratified by treatment sequencing the MS was longer in a NAT+R+AT cohort compared to the R+AT group (36.0 vs. 25.3 mo; $p < 0.05$) (Fig 1). However, there was no difference in MS between R+AT and NAT+R cohorts. On multivariable analysis, receipt of NAT represented an independent factor for survival (NAT+R+AT HR 0.41, 95% CI 0.32-0.54; NAT+R HR, 0.53, 95% CI, 0.44-0.64; R+AT HR 0.61, 95% C 0.53-0.70).

Conclusion: There appears to be a survival benefit with neoadjuvant systemic therapy in patients with body and tail PDAC. A systemic perioperative treatment sequencing approach (NAT+R+AT) appears to have the greatest survival benefit.



P 55. SURGICAL RESECTION IS ASSOCIATED WITH IMPROVED SURVIVAL FOR SMALL, MODERATE AND WELL DIFFERENTIATED PANCREATIC NEUROENDOCRINE TUMORS

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Presenter: Waseem Lutfi BS | Loyola University Medical Center

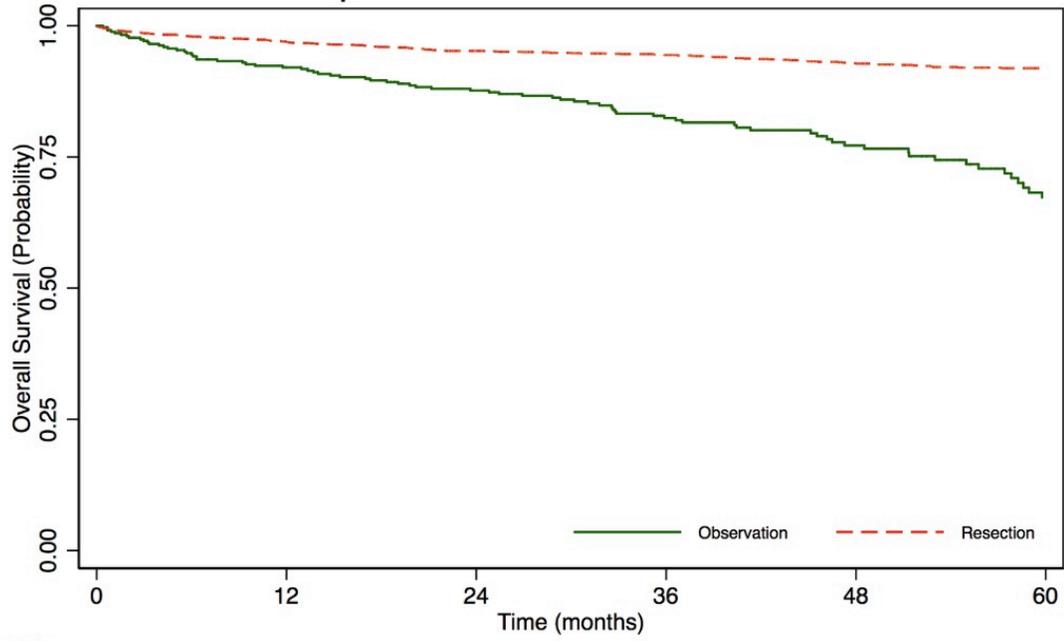
Background: Histologic differentiation has increasingly been recognized to be the most important determinate of long-term outcome in patients with pancreatic neuroendocrine tumors (PNETs). The vast majority of patients undergoing surgical resection for small localized PNETs have well-differentiated tumors with limited malignant potential. The value of resection in these cases remains uncertain.

Methods: The National Cancer Data Base was queried to identify all patients treated for non-metastatic PNETs ≤ 2 cm in size between 2004 and 2013. Kaplan-Meier (KM) analysis stratified by histologic differentiation and treatment (surgery vs. observation), and cox proportional hazard modeling stratified by size and adjusted for age, Charlson-Deyo score, income, insurance, facility type, tumor location and treatment were used to determine the relative importance of surgical intervention on overall survival (OS).

Results: 2,474 patients met inclusion criteria. 374 (15.1%) underwent observation and 2,100 (84.9%) underwent surgical resection. 827 (33.4%) were 1.5-2.0 cm, 944 (38.2%) were 1.1-1.5 cm, 577 (23.3%) were 0.6-1.0 cm and 126 (5.1%) were 0.1-0.5 cm in size. 1,828 (73.4%) were well or moderately-well differentiated, 37 (1.5%) were poorly differentiated, and 609 (24.6%) had unknown histopathology. Median follow up was 46.9 months. Patients undergoing resection were less likely to be ≥ 65 years (32.2 % vs. 50.0%, $p < 0.001$) than those undergoing observation. There were no significant differences between patients undergoing resection and observation with regard to demographics or comorbid disease characteristics. Five-year overall survival (OS) was 91.9% for patients undergoing resection and 67.3% for those undergoing observation ($p < 0.001$). On KM analysis stratified by histologic differentiation, resection was associated with improved OS for patients with well and moderate differentiated tumors (median OS: not reached vs 79.5 months, $p < 0.001$) but provided no survival advantage for patients with poorly differentiated tumors (median OS: 51.6 vs 26.9 months; $p = 0.272$). On risk adjusted Cox analysis, age ≥ 65 (HR 4.86, 95% CI [2.03, 11.61]) and Charlson-Deyo index ≥ 3 (HR 3.99, 95% CI [2.42, 7.11]) were significant predictors of increased risk of death while high income (HR 0.44, 95% CI [0.31, 0.62]), private insurance (HR 0.35, 95% CI [0.18, 0.67]), body/tail tumor (HR 0.65, 95% CI [0.50, 0.84]), and resection (HR 0.36, 95% CI [0.27, 0.47]) were associated with a significant decrease in the risk of death (all $p < 0.050$). On cox analysis stratified by size, resection was a significant predictor of improved OS for tumors 1.6-2.0 cm ($p < 0.001$), 1.1-1.5 cm ($p < 0.001$), and 0.6-1.0 cm ($P < 0.001$) but not for tumors ≤ 0.5 cm ($p = 0.438$).

Conclusion: The vast majority of patients undergoing resection for small PNETs have well differentiated tumors. Surgical resection is associated with improved OS in patients with PNETs 0.6-2.0 cm in size.

Kaplan-Meier survival estimates



Number at risk

Observation	374	300	268	196	126	72
Resection	2100	1969	1840	1510	1080	725

P 57. MANAGEMENT OF SMALL ASYMPTOMATIC NONFUNCTIONING PANCREATIC NEUROENDOCRINE TUMORS: FROM GUIDELINES TO REAL LIFE

M Mazza, S Partelli, M Falconi

Presenter: Michele Mazza MD | San Raffaele Scientific Institute

Background: ENETS guidelines suggest a watchful strategy for small nonfunctioning pancreatic neuroendocrine tumors (NF-PanNET). Aim of this study was to evaluate management and indications for surgery in patients with asymptomatic NF-PanNET \leq 2 cm.

Methods: Patients with asymptomatic, incidental, sporadic NF-PanNET \leq 2 cm without nodal/distant metastases were included in the study. A comparison between active surveillance and surgery groups was performed.

Results: Of the 101 included patients, 72% underwent active surveillance, whereas 28% were surgically treated (2012-2016). Patients submitted to surgery were significantly younger (53 vs 60, $P=0.013$), had higher incidence of positive 18F-FDG PET (18% vs 50%, $P=0.003$) and of cytologically determined G2 tumor (0% vs 14%, $P=0.008$). Conservatively managed patients had a significantly smaller tumor size (16 vs 12 mm, $P=0.0001$). The main reasons determining surgical choice were: patient's anxiety (32%), positive 18F-FDG PET (21.5%), main pancreatic duct dilation (17.5%), cytologically determined G2 tumor (14.5%) and young age (14.5%). At a median follow-up of 40 months, all the 73 patients conservatively managed were alive without evidence of distant metastases and none underwent surgery. Only 5 patients had a tumor growth $>20\%$. The mean tumor size at initial diagnosis was 12 compared to 13 mm at the last follow-up ($P < 0.0001$).

Conclusion: One third of patients with asymptomatic small NF-PanNET \leq 2 cm underwent surgery. Patient's anxiety, initial tumor size and young age were the main determinants of surgical indication. Preoperative diagnostic work-up including 18F-FDG PET and cytological grading seems to be poorly accurate in determining malignant features in these small lesions.

P 58. IS PANCREATIC CANCER DIFFERENT ACCORDING TO THE LOCATION?; A SURVIVAL AND PROGNOSTIC FACTOR ANALYSIS

M Lee, W Kwon, Y Byun, J Kim, H Kim, JY Jang, SW Kim

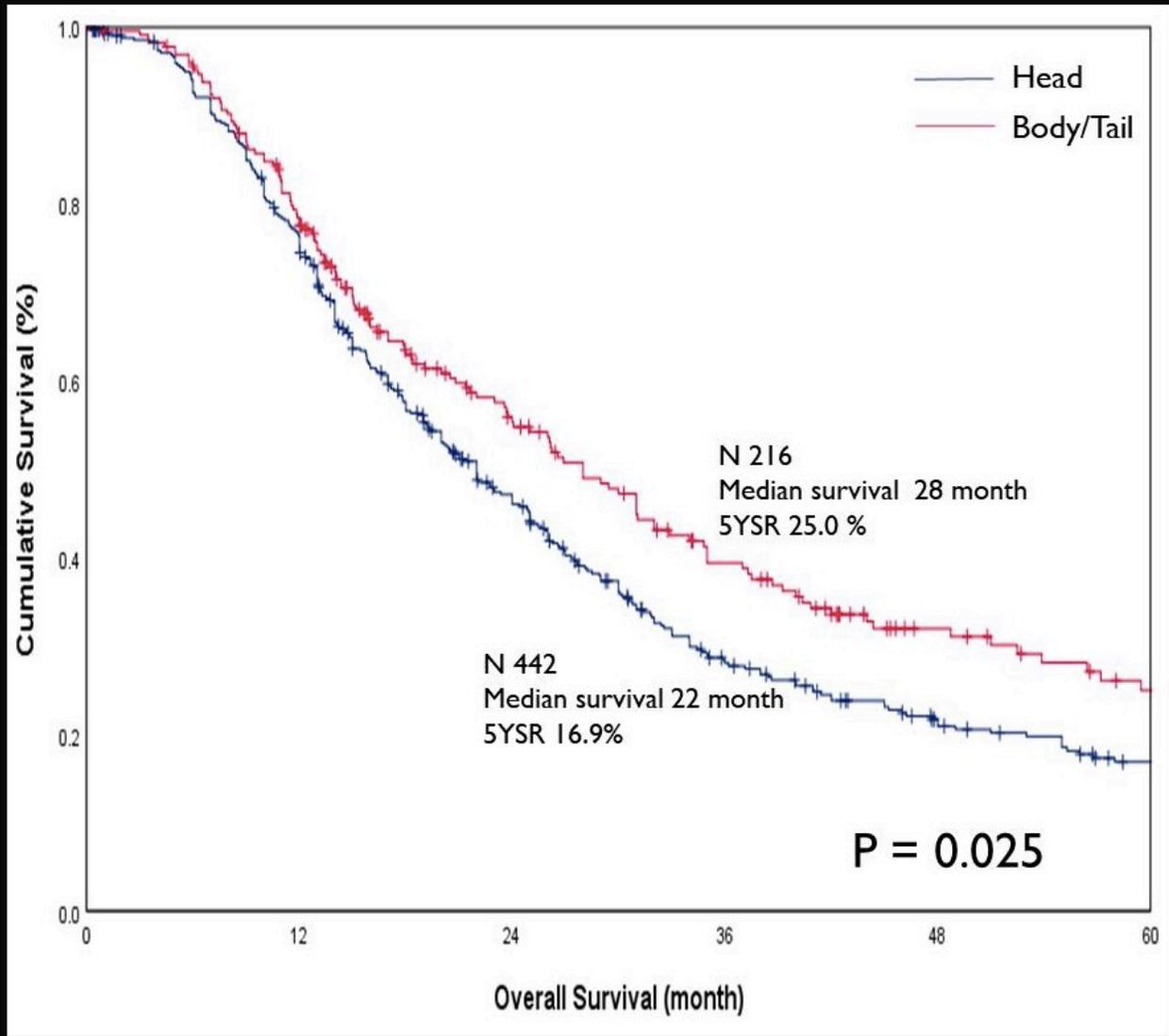
Presenter: Mirang Lee MD | Seoul National University Hospital

Background: The 8th edition AJCC cancer staging system from 2018. Some changes have been witnessed for the pancreatic cancer, but it is applied equally with a single definition without any reference to the location of the tumor as it has been before. However, there are conflicting results regarding whether pancreas head cancer and distal pancreatic cancer have similar prognosis or not. This study aims to investigate whether the staging system is valid for pancreatic cancer in all locations and to compare the survival and prognostic factors of pancreatic cancers according to the location of the pancreatic cancer.

Methods: Patients operated with curative intent for pancreatic cancer between 2005 and 2016 in Seoul National University Hospital were examined. Patients with multiple tumors or those who received neoadjuvant treatment were excluded. Data on 658 eligible patients were collected from prospectively collected database. Demographics, clinicopathologic, and survival data were retrieved for analysis. Survival analysis was performed using Kaplan-Meier method and log-rank test. Univariate and multivariate analyses were done using Cox regression analysis.

Results: Tumor was found in the head (including uncinata process) portion in 442 patients (67.2%), and in the body/tail in 216 (32.8%). R0 was achieved in 84.0%, R1 in 15.8%, and R2 in 3.8%. Adjuvant treatment was given to 78.4% of the patients. Patients were classified into T1, T2, T3, T4 in 14.1%, 65.8%, 17.0%, 3.0%, respectively. 38.1% were N0, 41.8% N1, and 20.1% N2. Comparing clinicopathologic features of head and body/tail cancers, there were no differences in terms of R status and receiving adjuvant treatment. Well-differentiated tumors were more frequent in the body/tail ($p=0.015$). The body/tail cancers had more T3/4 tumors (25.9% vs. 17.0%, $p=0.007$) whereas the head cancers had more T1/2 tumors (83.1% vs. 74.1%, $p=0.007$). Head cancers had more nodal metastasis (64.2% vs. 57.5%) but was insignificant ($p=0.100$). In stage validation, the new system demonstrated reasonable performance. It was valid for overall pancreatic cancer and was effective for both head cancers and body/tail cancers. Prognosis-wise, the body/tail cancers showed significantly longer median survival (28 vs. 22 months, $p=0.025$) and higher 5YSR (25.0% vs. 16.9%). Survival comparison across each T/N category, and stage showed no differences except for T2. T2 body/tail cancers displayed significantly better outcome (median survival; 31 vs. 21 months, $p=0.006$) than T2 head cancers. Among documented recurrences, distant metastasis was more frequent than local recurrence in the body/tail compared to the head (91.1% vs. 78.4%, $p=0.013$). Histologic grade, T category, N category, radiotherapy, and preoperative CA19-9 were prognostic factors shared by tumors of both locations. Angiolymphatic and perineural invasion, and chemotherapy were additional prognostic factor in head cancers. Gross type, margin status, and venous invasion were distinctive of body/tail cancers.

Conclusion: The 8th edition AJCC staging system is valid for pancreatic cancer regardless of the location of tumor. However, despite having more of T1/2 tumors, the head cancer demonstrated worse outcome compared to the body/tail cancer. In addition, tumors showed different recurrence patterns. Finally, while they share some common prognostic factors, there are some that are distinctive of the location. Therefore, there may be a need to consider pancreas head cancer and body/tail cancer as cancers of distinct tumor biology.



P 59. IS THE NEW T1 CATEGORY DEFINED BY THE 8TH EDITION AJCC PANCREATIC CANCER STAGING SYSTEM AN IMPROVEMENT? AN EVALUATION BY MULTINATIONAL DATA

W Kwon, J He, R Higuchi, D Son, SY Lee, M Lee, J Kim, SW Kim, CL Wolfgang, JL Cameron, M Yamamoto, JY Jang

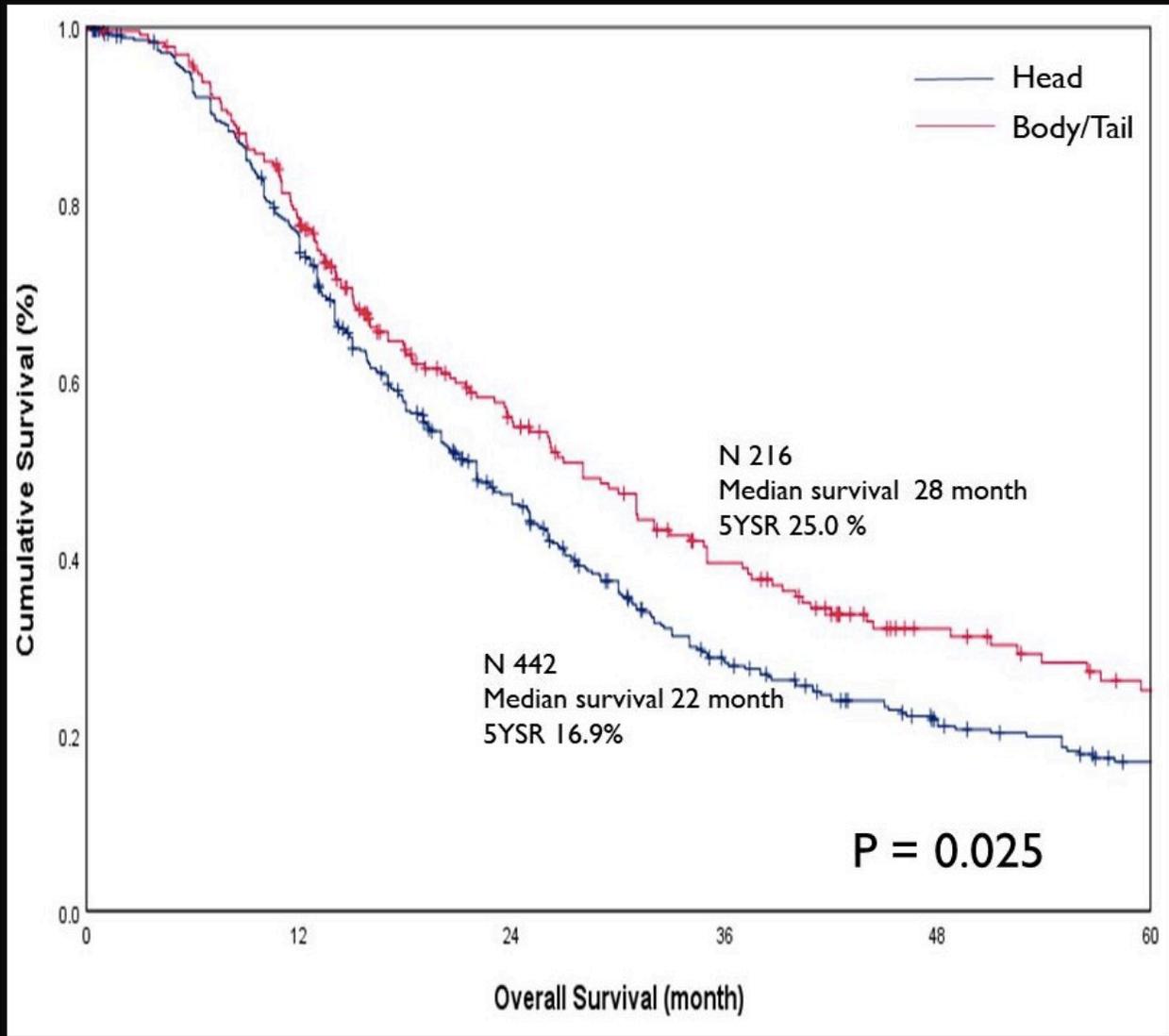
Presenter: Wooil Kwon MD, PhD | Seoul National University Hospital

Background: The new T1 pancreatic cancer by the 8th edition AJCC staging system discards the concept of "extension beyond the pancreas" and focuses on size only. Also, the new T1 is divided into T1a, T1b, and T1c based on size. As the T1 pancreatic cancer is very rare, the feasibility of these changes has not been evaluated. The aim was to evaluate the feasibility of the new T1 definition in the pancreas head cancer cohort.

Methods: Data of 540 patients that underwent surgery with curative intent in 3 tertiary referral centers for T1 pancreatic ductal adenocarcinoma defined by the 8th edition were collected from Korea (n=86), Japan (n=118), and the USA (n=336). The participating centers have multidisciplinary pancreatology specialists and are representative institutions of each nation. Invasive IPMNs and those who received neoadjuvant treatment were excluded. Demographics, operative, pathologic features and survival data were collected. Clinicopathologic features were examined and survival analyses were performed. Max-stat was performed to determine the cut-off tumor size value to subcategorize the patients by the survival outcome.

Results: Of the 540 patients, 181 patients were T1 by the 7th edition and 359 were down-staged to T1 from the former T3 because the concept of "extension beyond the pancreas" have been discarded. R0 was achieved in 82.0%, R1 in 17.4%, and R2 in 0.6%. Despite being T1 cancer, lymph node metastasis was found in 53.0% and 17.8% had more than 4 metastatic lymph nodes. Further, distant metastasis was found during the surgery in 7 cases (1.3%). The 5-year survival rate and the median survival of T1 patients were 30.6% and 27 months, respectively. Comparing tumors that extend beyond the pancreas (new T1) and those confined within the pancreas (original T1), the latter showed significantly longer median survival (43 vs. 24 months, $p<0.001$). The 5-year survival rates were 39.7% for the original T1 and 25.8% for the new T1 implying the prognostic significance of extrapancreatic extension in pancreatic cancer. The median survival of T1a, T1b, T1c were 30, 46, 27 months, respectively. There were no significant differences in survival ($p=0.323$). Furthermore, T1b demonstrated better survival outcome than T1a. Having identified the problematic subcategorization, new subcategorization scheme was investigated. Using max-stat, subcategorizing into 3 groups was not valid. On the other hand, subdividing into 2 groups using 1.1 cm as the cut-off value yielded significantly discrete prognostic groups ($p<0.001$). The new T1a had median survival of 53 months and the new T1b 26 months.

Conclusion: The new T1 definition may be more practical, but the implication of the concept of "extension beyond the pancreas" should be re-investigated. Further, the subcategorization of T1a/b/c does not seem to be adequate. New and more feasible subcategorization needs to be explored. As the incidence of T1 pancreatic cancer will inevitably increase in the future, acquiring in-depth understanding and knowledge of T1 pancreatic cancer is important.



P 60. WHERE IS THE APPROPRIATE BORDERLINE? THE POOR PROGNOSIS IN RESECTABLE PANCREATIC CANCER WITH HAZY DENSITY

T Kato, D Ban, T Ogura, K Ogawa, H Ono, Y Mistunori, A Kudo, M Tanabe

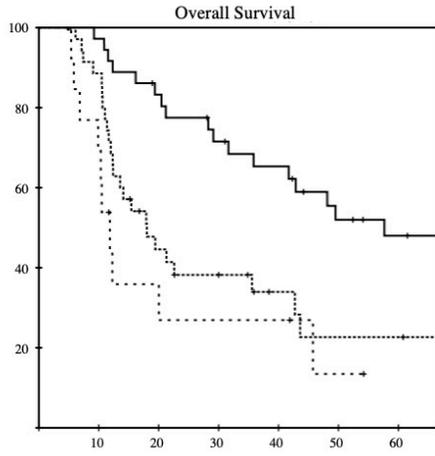
Presenter: Tomotaka Kato MD | Tokyo Medical and Dental University

Background: Treatment policy of pancreatic cancer is decided by resectability based on computed tomography(CT) findings. Relationship between soft tissue and major arteries is particularly important, and it directly affects treatment policy. Cases without contact between soft tissue and main arteries are judged to be resectable, but there are some cases difficult to judge because hazy density is surrounding the main artery. We attempted a retrospective analysis of hazy density about the influence on prognosis. Moreover, in order to clarify what kind of histological findings the hazy density reflects, comparison of CT images and pathological findings were conducted.

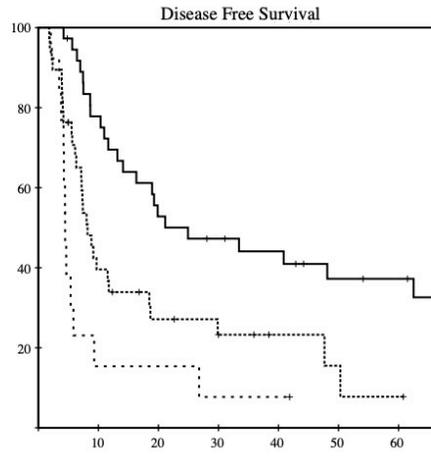
Methods: From 2004 to 2017, patients with resectable and borderline resectable(BR) pancreatic head cancer who underwent surgery without preoperative treatment at our hospital were included in the study. Cases with/without hazy density among resectable pancreatic cancer were classified as Hazy group/non-Hazy group, and BR cases were classified as BR group. Overall survival(OS) were the primary study endpoints, and prognostic factors predictable before surgery was analyzed. In addition, to quantify and consider hazy density, analysis about CT number in the extrapancreatic nerve plexus area (PLX) and comparison of CT findings with pathological findings were conducted.

Results: There were 91 cases satisfying the conditions. 39 cases were Hazy group, 39 cases were non-hazy group, and 13 cases were BR group. For the patient background including the clinical staging, no significant differences was observed between Hazy and non-Hazy group. In Hazy group, the CT number in PLX was significantly higher than non-Hazy group ($p = 0.014$; HR 2.21) were independent prognostic factors. The OS of the Hazy group(18.0months) was significantly poorer than non-Hazy group(57.6months, $p < 0.001$), and not statistically inferior to BR group (11.9months, $p = 0.238$). In the pathological analysis in PLX, Hazy and BR group showed significantly strong fibrotic stroma as compared with non-Hazy group, but there were no significant differences about extrapancreatic infiltration.

Conclusion: Hazy density findings are due to fibrotic stromal spread rather than cancer cell infiltration. Nevertheless, prognosis of cases with hazy density is comparable to BR cases, and it is the strongest prognostic factor predictable before surgery in resectable pancreatic cancer. Preoperative treatment should be considered for cases with hazy density as well as BR cases.



non-Hazy Group }
 Hazy Group } p<0.004 } p<0.001
 Soft Group } p<0.238 }



non-Hazy Group }
 Hazy Group } p=0.002 } p<0.001
 Soft Group } p=0.043 }

— R Group
 Hazy Group
 - - - Soft Group

P 61. FUNCTIONAL OUTCOMES AFTER EXTRAHEPATIC TRANSPLANTATION OF ISLETS IN A PILOT COHORT OF TOTAL PANCREATECTOMY WITH ISLET AUTOTRANSPLANTATION (TPIAT) PATIENTS

KR McEachron, GJ Beilman, TL Pruett, TB Dunn, S Chinnakotla, MD Bellin

Presenter: Kendall McEachron MD | University of Minnesota

Background: Total pancreatectomy with islet autotransplantation (TPIAT) is a treatment for chronic pancreatitis designed to relieve pancreatic pain while mitigating the severity of resultant pancreatogenic diabetes. The traditional process of islet autotransplantation involves infusion of islets through the portal vein for engraftment in the liver. However, if portal pressure rises during infusion, the remainder of islets can be transplanted to an extrahepatic site. In a pilot cohort of patients undergoing extended metabolic testing after TPIAT, we compared measures of beta cell engraftment and function in those with extrahepatic transplantation of some or all islets to those who had exclusively intrahepatic islets.

Methods: At three months post-TPIAT, a cohort of 26 TPIAT patients underwent a mixed-meal tolerance test (MMTT), intravenous glucose tolerance test (IVGTT) and potentiated arginine stimulation test (AST). Insulin use and incidence of severe hypoglycemic events (SHE) were documented at three and twelve months. From this cohort, we compared surgical complications, metabolic parameters, and functional outcomes for patients who had at least a portion of their islets transplanted in an extrahepatic site (n=9) with those receiving only intrahepatic islets (n=17).

Results: Patient demographics were similar including age, BMI, years of pancreatitis pain, and total IEQ transplanted. There was a larger proportion of females in the alternate site group (p=0.03). The islet mass transplanted (IEQ) correlated with islet function, as measured by the area under the curve for C-peptide (AUC-CP) from MMTT (R²=0.28, p=0.008), acute C-peptide response to glucose (ACR_g) from the IVGTT (R²=0.37, p=0.0009), and the glucose-potentiated C-peptide response to arginine (ACR_{pot}) from the AST (R²=0.47, p=0.0003). When transplant site was accounted for, these correlations between IEQ and function remained significant, while transplant site was not significant (p≥0.2 in all models). The AUC-CP, ACR_g, and ACR_{pot} adjusted for IEQ were similar between groups. One patient received all islets in the peritoneal cavity (14 y/o F with hepatic fibrosis, 168,000 IEQ); this patient had graft function but did not achieve insulin independence (insulin dose at 1 year = 0.89 unit/kg/d). Clinical outcomes were similar between the groups, including 90-day surgical complications, one-year insulin dose, and one-year occurrence of SHE (Table 1).

Conclusion: Transplantation of a portion of islets to an alternate site did not increase number of surgical complications. When adjusted for IEQ, diabetes and functional outcomes were similar for TPIAT patients with traditional versus alternate site transplant. Insulin use and occurrence of SHE were also no different. Notably, this included a patient with exclusively extrahepatic islets, indicating that hepatic fibrosis or other liver conditions may not be contraindications to TPIAT.

Variable	All islets intrahepatic (n=17)	Alternate site (n=9)	p-value
Demographics			
--Age (y)	33.3 ± 15.8	27.4 ± 17.1	0.38
--Sex (F), n (%)	8 (47%)	8 (89%)	0.03
--IEQ transplanted (total)	307,823 ± 189,955	361,811 ± 136,245	0.45
--IEQ transplanted intraportal	307,823 ± 189,955	232,361 ± 125,519	0.29
Islet Function at 3 months, Adjusted for Islet Mass Transplanted			
--AUC CP (ng/mL*min) per 100k IEQ	58.4 ± 34.5	74.6 ± 40.4	0.34
--AIRg (mIU/mL*min) per 100k IEQ	2.8 ± 2.2	2.4 ± 2.0	0.67
--ACRpot (mIU/mL) per 100k IEQ	0.66 ± 0.51	0.51 ± 0.37	0.48
Clinical Outcomes			
--90-day Surgical Complications, n (%)	8 (47%)	5 (55%)	0.69
--1-year Insulin Dose (u/kg/d)	0.26 ± 0.23	0.17 ± 0.33	0.44
--1-year Severe hypoglycemic episodes (SHE), n (%)	1 (7%)	3 (33%)	0.09

P 62. PREOPERATIVE SERUM LEVELS OF PHOSPHORUS PREDICTS OCCURRENCE AND SEVERITY OF POST-OPERATIVE PANCREATIC FISTULA AFTER PANCREATODUODENECTOMY

S Iacopi, N Napoli, C Lombardo, F Menonna, EF Kauffmann, C Cacace, A Natali, M Miccoli, U Boggi

Presenter: Niccolò Napoli MD | University of Pisa

Background: Post-operative pancreatic fistula (PoPF) occurs frequently after pancreaticoduodenectomy (PD). In recent years, several predictive scores for PoPF have been proposed and validated. Although these scores can be used to implement mitigation strategies and/or to adapt management to individual needs, they cannot be calculated until after surgery and they cannot be used to modify the risk of PoPF. Nutritional parameters, instead, can be estimated beforehand and can be modified. In this study we investigate the role of pre-operative phosphorus level (PPL) on the incidence of post-operative complications (PoCs) occurring after PD, with special reference to PoPF.

Methods: Patients were considered eligible for this study if PPL were available, before any intravenous therapy or oral supplementation. Data were extracted from a prospectively maintained database and analyzed retrospectively. All PoCs occurring within 90 days were graded according to the Clavien–Dindo classification. PoPF was defined according to the ISGPS 2004 definition. To allow comparison with established, and validated, scores the fistula risk score (FRS) was also calculated. Jarque-Bera test was performed to verify the normality of distributions. T test was used to compare PPL values. Logistic regression was used (evaluating the OR) to study the influence of the PPL on PoCs. Post-hoc power analysis was carried out to estimate the sample sizes. Analysis was performed using the IBM SPSS Statistics.

Results: PPL were available for 225 PD (81 robotic; 36%) (144 open; 64%) performed between May 2011 and February 2018. There were 116 males and 109 females, with a mean age of 65.4 ± 11.5 years, and a mean BMI of 24.8 ± 3.8 kg/m². ASA score was 3 or 4 in 64.9% of the patients. Thirty patients (13.4%) required associated surgical procedures and 67 patients (29.8%) a vein resection. Based on FRS (calculated in 200 pts) 17% of the patients were classified at high risk, 63.5% at intermediate risk, 15.5% at low risk and 4% at negligible risk. PoCs of any severity occurred in 88% of the patients: 16% grade I, 48% grade II, 18% grade III 3.1% grade IV and 3.1% grade V. Overall, severe PoCs (\geq grade III) occurred in 24% of the patients. PoPF (of any grade) occurred in 74 patients (32.9%). When PPL were compared between patients with (2.98 ± 0.50 mg/dl) and without (3.34 ± 0.54 mg/dl) PoPF, lower levels of PPL were associated with higher rates of PoPF ($p < 0.0001$, odds ratio 0.27, p value odds ratio < 0.0001 , power analysis 0.996). When the analysis was restricted to 51 (22.6%) patients who developed a clinically relevant PoPF (i.e. grade B+C), higher PPL was associated with fewer PoPF (3.045 ± 0.503 mg/dl versus 3.269 ± 0.561 mg/dl) ($p=0.013$, odds ratio 2.14, a sample power 0.7) Sub-analysis in patients stratified as “intermediate risk” or “high risk” confirmed the strong protective effect of higher PPL (table 1). The protective effect of PPL was independent of magnesium and calcium levels and remained highly significant in multivariable analysis.

Conclusion: In our study PPL predicted occurrence and severity of PoPF, irrespective of FRS category. The value of this observation is at least twofold. First, PPL can be easily obtained before surgery by means of an easy and inexpensive blood test. Second, PPL is a potentially modifiable parameter. As such, and at a difference from available scores, stratifying patients into risk categories based on PPL would not just allow for implementation of mitigation strategies and/or personalization of management but could, and for the first time, provide a therapeutic trigger that could be used to decrease the risk of PoPF in patients otherwise at high risk. Our results, as well as the potential therapeutic effect of phosphate supplementation, should be validated in prospective cohorts.

Table 1 PPL and PoPF

	n. (%)	Mean PPL±SD (mg/dl)	p	OR
PoPF +	74 (32.9%)	2.98 ±0.50	< 0.0001	0.27
PoPF -	151 (67.1%)	3.34 ±0.54		
CrPoPF +	51 (22.6%)	3.045 ±0.503	0.013	2.14
CrPoPF -	174 (77.3%)	3.269 ±0.561		
<i>Intermediate risk (FRS)</i>				
PoPF +	42 (33.1%)	2.97 ±0.46	< 0.0001	0.14
PoPF -	85 (66.9%)	3.46 ±0.54		
<i>High risk (FRS)</i>				
PoPF +	14 (41.2%)	2.87 ±0.44	0.037	0.18
PoPF -	20 (58.8%)	3.24 ±0.49		

Cr: Clinically Relevant

P 63. ASSESSING THE IMPACT OF UNDERLYING LIVER DISEASE ON 30-DAY POSTOPERATIVE OUTCOMES AFTER PANCREATECTOMY: AN ACS NSQIP® ANALYSIS

Al Al Abbas, JD Borrebach, J Bellon, AH Zureikat

Presenter: Amer Zureikat MD | University of Pittsburgh Medical Center

Background: Pancreatectomy remains associated with significant postoperative morbidity despite recent advances. The Model for End-Stage Liver Disease (MELD), derived from readily available serum chemistries, is primarily applied towards liver transplantation recipient selection. It has become increasingly utilized to predict complications in non-transplant surgical populations. Liver disease has been linked to adverse outcomes following gastrointestinal surgery, however studies examining its impact on outcomes following pancreatectomy are limited. Employing the American College of Surgeons National Surgical Quality Improvement Program® (ACS NSQIP®) Participant Use Data File (PUF), we aimed to compare 30-day postoperative outcomes of patients undergoing elective pancreatectomy and stratified by MELD score.

Methods: Elective Pancreatoduodenectomies (PDs) and Distal Pancreatectomies (DPs) were identified from the 2014–2016 Procedure Targeted Pancreatectomy PUFs. MELD scores were calculated using 90-day preoperative serum creatinine, total bilirubin, INR, and serum sodium. Examined 30-day outcomes included mortality, cardiopulmonary complications, prolonged postoperative length-of-stay (defined as >14 days for PDs and >7 days for DPs), discharge not-to-home, intraoperative/postoperative transfusion, any complication, and serious complication. Outcomes were compared between clinically relevant MELD score strata (<11 vs. ≥11) as established by the United Network for Organ Sharing (UNOS). Multiple logistic regression was used to adjust for potential confounders, including patient sex, age, BMI, relevant comorbidities, ASA classification, and histology. Comparisons yielding p-values <0.05 were considered statistically significant.

Results: A total of 7,580 elective PDs and 3,295 elective DPs with evaluable MELD scores were analyzed. Of these, 1,701 (22.4%) PDs and 223 (6.8%) DPs had a MELD score ≥11. PD patients with MELD ≥11 exhibited significantly higher risks for mortality [OR=2.075 (95% CI: 1.429, 3.012), p<0.001], discharge not-to-home [OR=1.256 (95% CI: 1.073, 1.471), p=0.005], and transfusion [OR=1.699 (95% CI: 1.490, 1.936), p<0.001]. DP patients with MELD ≥11 exhibited significantly higher risks for prolonged LOS [OR=1.754 (95% CI: 1.308, 2.354), p<0.001], discharge not-to-home [OR=1.829 (95% CI: 1.158, 2.889), p=0.010], and transfusion [OR=2.780 (95% CI: 2.023, 3.819), p<0.001]. In PD, following risk adjustment, MELD ≥11 was significantly predictive of mortality [OR=1.690 (95% CI: 1.154, 2.475), p=0.007] and transfusion [OR=1.553 (95% CI: 1.356, 1.779), p<0.001]. In DP, following risk adjustment, MELD ≥11 was significantly predictive of prolonged LOS [OR=1.422 (95% CI: 1.043, 1.940), p=0.026] and transfusion [OR=2.299 (95% CI: 1.643, 3.217), p<0.001].

Conclusion: A MELD score ≥11 is associated with a nearly-two fold increase in the odds of PD mortality despite its low prevalence. These findings underscore the importance of preoperative liver disease assessment in stratifying risks of 30-day postoperative complications following pancreatectomy.

TABLE 1. 30-Day Postoperative Outcomes for Pancreatoduodenectomy and Distal Pancreatectomy Stratified by MELD Score

Postoperative Outcome	Risk-Adjusted	Pancreatoduodenectomy		Distal Pancreatectomy	
		MELD \geq 11 OR (95% C.I.)	p-value	MELD \geq 11 OR (95% C.I.)	p-value
Mortality	No	2.075 (1.429, 3.012)	<0.001*	2.421 (0.830, 7.064)	0.106
	Yes	1.690 (1.154, 2.475)	0.007*	2.231 (0.780, 6.382)	0.135
Cardiopulmonary	No	1.133 (0.927, 1.385)	0.224	1.610 (0.981, 2.642)	0.059
	Yes	1.019 (0.826, 1.258)	0.858	1.079 (0.645, 1.807)	0.771
Prolonged LOS	No	1.038 (0.896, 1.203)	0.617	1.754 (1.308, 2.354)	<0.001*
	Yes	0.999 (0.858, 1.162)	0.988	1.422 (1.043, 1.940)	0.026*
Discharge Not-to-Home	No	1.256 (1.073, 1.471)	0.005*	1.829 (1.158, 2.889)	0.010*
	Yes	0.989 (0.834, 1.173)	0.899	1.129 (0.687, 1.854)	0.633
Transfusion	No	1.699 (1.490, 1.936)	<0.001*	2.780 (2.023, 3.819)	<0.001*
	Yes	1.553 (1.356, 1.779)	<0.001*	2.299 (1.643, 3.217)	<0.001*
Any Complication	No	0.964 (0.865, 1.074)	0.501	1.202 (0.914, 1.580)	0.187
	Yes	0.980 (0.876, 1.097)	0.731	1.069 (0.804, 1.419)	0.647
Serious Complication	No	1.026 (0.909, 1.158)	0.677	1.220 (0.889, 1.674)	0.219
	Yes	1.034 (0.911, 1.174)	0.604	1.024 (0.735, 1.427)	0.888

*Statistically significant at $\alpha = 0.05$

P 64. EFFECT OF SILENCING RAB23 GENE WITH SIRNA ON PROLIFERATION AND APOPTOSIS OF PANC-1 CELLS

Y Liu, H Zhou, T Yu, J Zhang, X Zeng

Presenter: Yunjian Liu PhD | Indiana University School of Medicine

Background: Pancreatic ductal adenocarcinoma (PDAC) ranks fourth as a cause of cancer death in the world and is almost universally fatal, with the annual number of deaths equivalent to the number of newly diagnosed cases. Valuable research has revealed genetic aberrations that contribute to PDAC development and progression, with Rab23 being one of the most frequent mutation in more than 50% of patients. However, to date, there are no any reports to directly target Rab23. In the current study, we investigate the effect of silencing Rab23 gene expression with siRNA on the proliferation of tumor cell line PANC-1, pancreatic ductal adenocarcinoma cell lines, to provide the evidence to treat PDAC.

Methods: Human pancreatic cancer cell line PANC-1 was cultured in vitro and transfected with siRNA of Rab23 by lipofectamine2000. The levels of Rab23 mRNA expression before and after transfection were detected by semi - quantitative reverse transcription polymerase chain reaction (RT - PCR). The levels of Rab23 protein expression before and after transfection were detected by western blot. Apoptosis of PANC-1 cells induced by Rab23 siRNA was counted by trypan blue staining. Flow cytometry (FCM) was used to examine the effects of apoptosis of PANC-1 cells.

Results: The level of Rab23 mRNA in PANC-1 cells was inhibited by the specific siRNA. The expression of Rab23 mRNA at 48h after transfection was apparent difference from normal PANC-1 cells and negative control cells ; and the most apparent interfering efficiency developed 72h after transfection; at 96h, the expression restored a little. Western - blot indicated that the expression of Rab23 protein was down regulated in PANC-1 cells after interfered with siRNA. The cell proliferation in RNAi group was significantly lower than that in the negative control and blank control at 16, 24 and 48h and about 28% PANC-1 cells were apoptotic at 48h after Rab23 was silenced by siRNA.

Conclusion: RNA interference can downregulate the level of Rab23 mRNA and Rab23 protein expression in PANC-1 cells, then induce the apoptosis of PANC-1 cells. Rab23 may be used as a gene therapy target on pancreatic carcinoma.

P 65. REPURPOSING THE FDA APPROVED DRUG PYRVINIUM PAMOATE TO TARGET HUR IN PANCREATIC DUCTAL ADENOCARCINOMA

CW Schultz, T Dhir, AO Haber, W Jiang, S Chand, SZ Brown, EF Petricoin, CJ Yeo, JR Brody

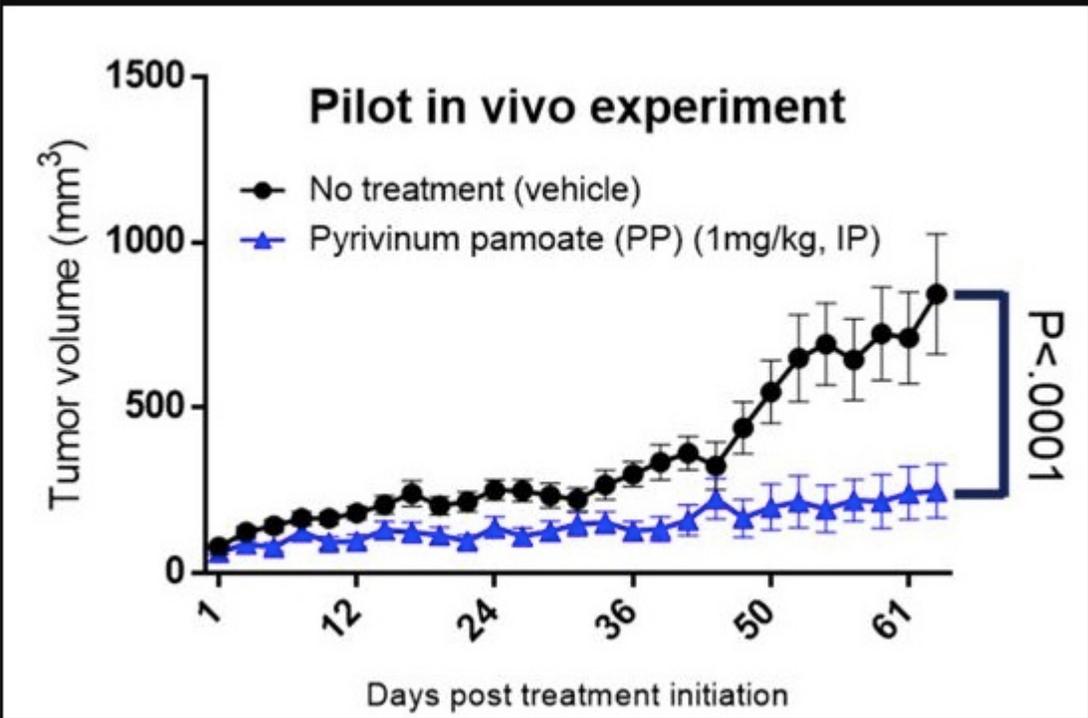
Presenter: Teena Dhir MD | Thomas Jefferson University

Background: Pancreatic ductal adenocarcinoma (PDA) remains a lethal cancer with overall five year survival rates at only 9%. Therefore, there is a dire need for new targeted therapeutics in PDA. HuR (ELAVL1) is an RNA binding protein that upon exposure to intrinsic (low glucose, hypoxia) and extrinsic (chemotherapeutics) stressors translocates from the nucleus to the cytoplasm and binds to a network of pro-survival mRNAs leading to an increase in their stability and translation. HuR is a driver of chemoresistance in PDA and thus a prime target for re-sensitizing PDA cells to current therapies.

Methods: Pyrvinium Pamoate (PP) was approved by the FDA to treat pinworms. In vitro testing with PP was done in Mia PaCa2, HS766T and Panc-1 pancreatic cancer cell lines, and cells were treated and analyzed for immunofluorescence (IF), Western Blotting and phosphoproteomics. In vivo, athymic female nude mice were injected with 5 million Mia PaCa-2 cells per flank, and randomized to treatment arms when tumors reached 100mm³. Mice were then treated with PP intraperitoneally (IP) three times a week, and compared to no treatment. During the course of the experiment animal weights and tumor volumes were recorded three times a week.

Results: We have demonstrated that PP inhibits HuR translocation in PDA cell lines using IF and Western Blotting. By inhibiting translocation PP functionally inhibits HuR binding to target mRNA as demonstrated utilizing RNA immunoprecipitation assays. We have found this HuR inhibition is likely through phosphorylation changes in key HuR effectors as shown through phosphoproteomic screening and Western Blotting. Most chemotherapeutics are most effective when used in combination regimens. In order to determine drugs that PP was likely to synergize with we developed isogenic HuR CRISPR knockout cell lines as we had demonstrated that PP is an HuR inhibitor. We tested these cell lines with commonly used pancreatic cancer drugs, and several targeted therapeutics. We found that HuR knockout cells had significant increases in sensitivity upon treatment with oxaliplatin, olaparib, paclitaxel, gemcitabine, 5-fluorouracil, abemaciclib, palbociclib and irinotecan. We thus expected and then demonstrated that PP as an HuR inhibitor can synergize with various therapeutics in vitro. Lastly, in a small pilot experiment, we show that intraperitoneal administration of PP can inhibit PDA cell growth in vivo. We are currently performing pharmacokinetic studies and larger mouse experiments to determine the bioavailability and efficacy of oral PP. We are also working to test drug combination regimens in vitro and in vivo as well. Reconfirming the relevance of targeting HuR in PDA utilizing a tumor microarray, we found that 79% (n=80) of tumors were positive for cytoplasmic HuR, with no cytoplasmic localization detected in adjacent normal tissues.

Conclusion: PP is potential therapeutic option in pancreatic cancer, as seen both in vitro and in vivo assays. Based on these data, we are in the progress of setting up a clinical trial to determine the safety and bioavailability of PP in PDA cancer patients. In summation we have demonstrated that PP is extremely effective at inhibiting PDA cells in vitro and in vivo, and furthermore that it may be a clinically relevant new therapeutic targeting HuR in PDA.



P 66. FATTY ACID BINDING PROTEIN 4 PROMOTES PANCREATIC CANCER GROWTH VIA ALTERED REDOX SIGNALING

K Wirth, S Kizy, A Sheka, S Ikraumuddin, D Bernlohr, M Yamamoto

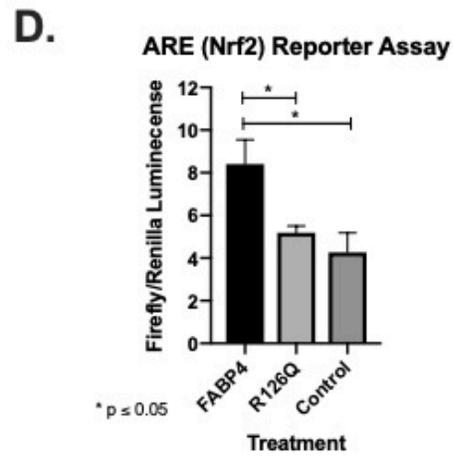
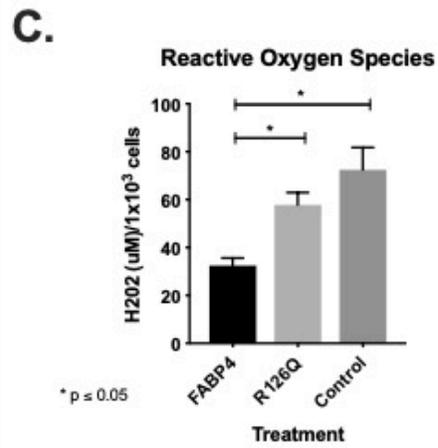
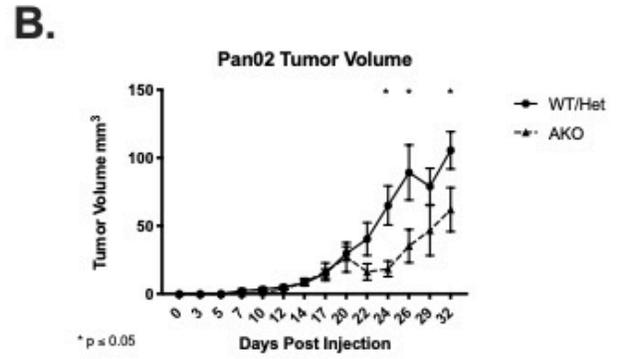
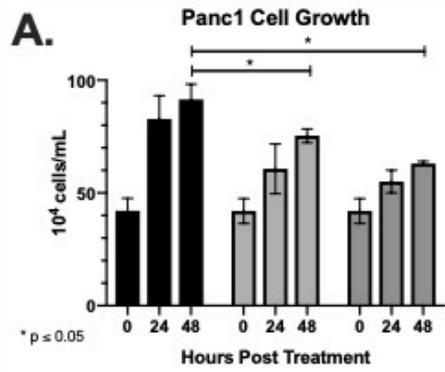
Presenter: Keith Wirth MD | University of Minnesota

Background: Obesity is associated with an increased incidence of pancreatic cancer. Bariatric surgery is the most efficacious treatment of obesity and diabetes mellitus. One protein of interest underlying this effect of bariatric surgery is fatty acid binding protein 4 (FABP4), a lipid transporter and adipokine. FABP4 transcriptional regulation has been linked to cellular redox status, with Nrf2 being a regulator of this balance. Here we investigated the interactions of FABP4 and pancreatic cancer.

Methods: Panc1 pancreatic carcinoma cells were cultured in serum starved media and treated with recombinant FABP4, R126Q (point mutant of FABP4), or vehicle solute (Tris buffer). Cell growth and proliferation was assessed. Endogenous FABP4 intracellular protein levels were assessed with standard western blot. Whole cell reactive oxygen species (ROS) was quantified via Amplex Red assay. Nrf2 activity was quantified with antioxidant response element luciferase assay. C57BL/6J FABP4 knockout (AKO) and littermate wild type (WT) mice were injected with PanO2 cells, a murine pancreatic cancer cell line, subcutaneously in bilateral flanks. Tumor volume and progression was evaluated. All experimental procedures were approved by IACUC.

Results: Panc1 cells treated with recombinant FABP4 demonstrated increased proliferation relative to control and point mutant protein treatment. Intracellular endogenous FABP4 protein levels were increased with FABP4 treatment. ROS levels were decreased and Nrf2 activity was concurrently increased with exposure to exogenous FABP4. Tumor progression, as measured by tumor volume, was significantly decreased in AKO mice.

Conclusion: FABP4 treatment increases pancreatic cancer cell proliferation, and a switch in redox signaling is implicated in this effect. Pancreatic cancer tumor progression is decreased in a murine FABP4 knockout model.



P 67. SYSTEMIC TREATMENT WITH MESOTHELIN-TARGETED ONCOLYTIC ADENOVIRUS SHOWS EFFICACY PATIENT-DERIVED XENOGRRAFT OF PANCREATIC CANCER

M Sato-Dahlman, Y Miura, P Hajeri, H Yoshida, K Jacobsen, C Yanagiba, M Yamamoto

Presenter: Masato Yamamoto MD, PhD | University of Minnesota

Background: Pancreatic cancer is an aggressive malignant disease. Despite extensive efforts, systemic therapies have provided only limited efficacy for patients. Although Oncolytic Adenovirus is a promising cancer therapy agent, when adenovirus vectors are injected intravenously into mice, most of the virus goes to liver and can lead to liver toxicity at high dosage. Because of this, the tumor transduction rate is low, and the in vivo efficacy is limited. Therefore, the improvement of cancer selective transduction and vector distribution to avoid liver sequestration would overcome the obstacles for systemic delivery required for efficient systemic treatment of metastatic lesions of pancreatic cancer.

Methods: To improve the tumor transduction, we have generated the pancreatic cancer-targeted OAd by high-throughput screening of Ad library in mesothelin (MSLN) expressing cells. This virus binds to MSLN protein, which is overexpressed on the surface of pancreatic cancer. After intravenous injection with MSLN-targeted OAd, we analyzed the distribution of the virus in various mouse organs using real-time qPCR. Athymic mice (n = 4) carrying xenograft tumors that were derived from MSLN-positive human cancer cells were intratumorally or intravenously inoculated with MSLN-targeted OAd and untargeted OAd (Ad5 WT virus). The tumor growth was monitored, and adenovirus replication was measured by qPCR and hexon staining. The anti-tumor efficacy of MSLN-targeted OAd was assessed in 2 PDX lines grown as subcutaneous xenografts (4-5 mice per group).

Results: MSLN-targeted OAd showed selective and powerful anti-tumor effect against MSLN-positive xenograft tumor model in both intratumoral (i.t.) and intravenous (i.v.) injection. Importantly, the liver sequestration of MSLN-targeted OAd was lower than untargeted OAd (Ad5 WT virus). By day 7, the viral copy number of MSLN-targeted OAd in the tumor was higher than Ad5 WT virus. These results suggest that systemic injection of the MSLN-targeted OAd showed significantly lower liver sequestration and better tumor accumulation. Next, antitumor effect of MSLN-targeted OAd was assessed in patient-derived xenograft (PDX) model. After intravenous administration, only the MSLN-targeted OAd showed significant antitumor effect compared to the untreated group (p<0.05), while the growth of Ad5 WT virus injected group was same as untreated group.

Conclusion: The systemic injection of MSLN-targeted OAd showed remarkable anti-tumor effect in both systemic and intratumoral injections. Our virus distribution data suggest that systemic injection of the tumor targeted-OAd showed significantly lower liver sequestration and better tumor accumulation. Our results indicated that tumor targeted-OAd can embody efficient systemic treatment for pancreatic cancer which are mostly found with spread or metastatic lesions.

P 68. CAN MORTALITY OF OPERATIVE PANCREATIC DEBRIDEMENT BE PREDICTED ACCURATELY?

AM Roch, TK Maatman, EM Kilbane, EP Ceppa, MG House, A Nakeeb, CM Schmidt, NJ Zyromski

Presenter: Alexandra Roch MD | Indiana University School of Medicine

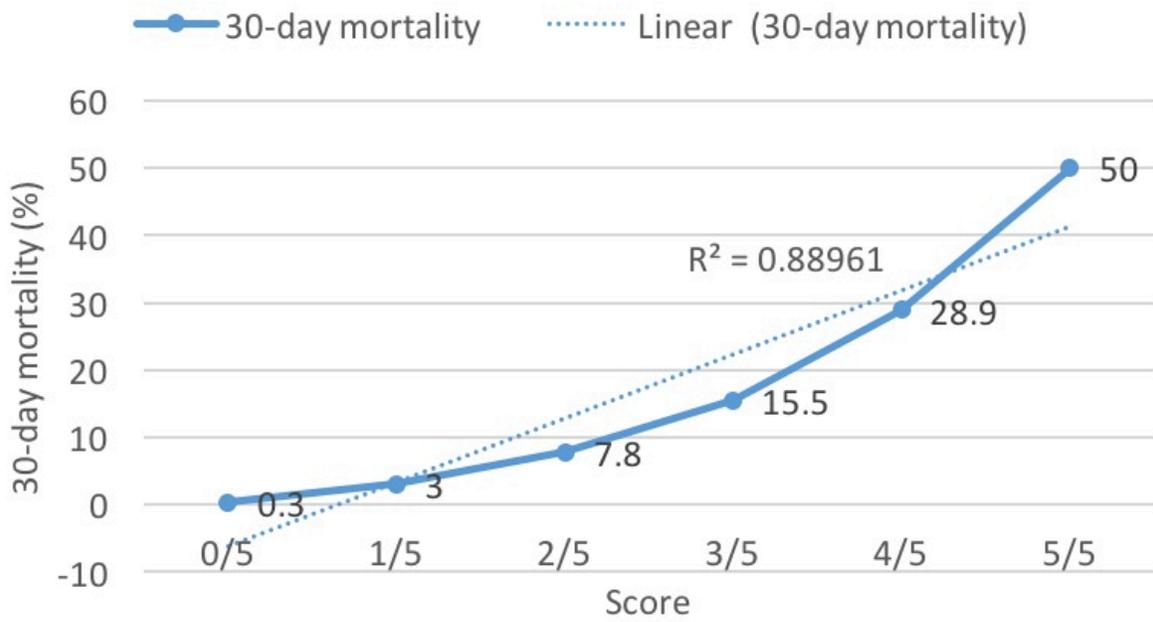
Background: Over the past decade, minimally invasive approaches - percutaneous and endoscopic - have become first line treatment of necrotizing pancreatitis (NP). Surgical debridement is currently applied to select patients refractory to first line approach. Remarkably, no study has to date been able to accurately predict mortality in pancreatic necrosectomy. We hypothesized that preoperative characteristics may predict mortality in open pancreatic debridement.

Methods: The American College of Surgeons National Surgical Quality (ACS-NSQIP) database identified patients undergoing surgical pancreatic debridement (CPT code 48105) from 2007 to 2016. Univariate and multivariate logistic regression determined predictors of 30-day mortality. Receiver operating curves were used with Youden index to evaluate optimal cut-off values for continuous variables.

Results: This study included 1723 patients. Thirty day mortality was 9.1%. Preoperative Mechanical ventilation, Older age (>60.2), Obese with BMI>33.2, Serum creatinine>1.2 and Elevated WBC count>11 were independent predictors of mortality. A scoring system (MOOSE) was created by assigning 0 (absent) or 1 (present) point to each variable. Increase in score was associated with increase in mortality with an excellent correlation ($R^2=0.89$), as shown on graph. Score of 0/5 was associated with 0.3%, 1/5 with 3%, 2/5 with 7.8%, 3/5 with 15.5%, 4/5 28.9% and 5/5 with 50%.

Conclusion: This large NSQIP series shows that an easy and accurate scoring system based on routine preoperative demographic, clinical and biological data accurately predicts mortality associated with surgical pancreatic debridement. This novel tool will help better select surgical candidates and counsel patients with necrotizing pancreatitis.

MOOSE Score and associated 30-day mortality



P 69. INSULIN PROMOTES THE INVASION AND MIGRATION OF PANCREATIC CANCER THROUGH THE EMT PATHWAY

Y Gao, H Gao, G Wang, B Cai, Z Lu, Y Miao

Presenter: Zipeng Lu MD, PhD, MRCS | Pancreas Center, The First Affiliated Hospital with Nanjing Medical University

Background: Pancreatic ductal adenocarcinoma (PDAC) is one of the most deadly cancers in the world. Hyperinsulinemia has been considered to be associated with the risk of pancreatic cancer. Our study is to explore the effect of insulin on the migration and invasion of pancreatic cancer cells and possible mechanism.

Methods: Cell membrane proteins were extracted. According to the expression level of insulin receptor protein, pancreatic cancer cell lines with appropriate expression levels were selected as experimental cell lines. Transwell assay was used to evaluate the effect of insulin on the migration and invasion of pancreatic cancer cells. qRT-PCR was used to detect the expression of functional proteins related to epithelial-mesenchymal transformation (E-cadherin, N-cadherin, Vimentin) at the transcription level. Western Blot was used to detect the expression of the above proteins at the translation level. All experiments were repeated 3 times, and the quantitative data were represented by Mean±SD. T test was used for comparison between the two groups, and the difference was considered statistically significant when P was less than or equal to 0.05.

Results: CFPAC and Capan-2 cell lines were selected as experimental cell lines with moderate expression of insulin receptor. The results of Transwell assay for cell migration and invasion ability showed that the migration ability of CFPAC and Capan-2 cells co-cultured with insulin at 20nM was significantly improved after 48 hours (CFPACins VS CFPACctrl: 354.0 ± 13.5 vs 158.3 ± 9.4 , $p < 0.05$; CAPAN-2ins VS CAPAN-2ctrl: 261.0 ± 13.9 vs 127.7 ± 17.2 , $p < 0.05$). The invasion ability of CFPAC and Capan-2 cells co-cultured with insulin at 20nM was also significantly improved after 48 hours (CFPACins VS CFPACctrl: 229.0 ± 11.0 vs 93.0 ± 11.6 , $p < 0.05$; CAPAN-2ins VS CAPAN-2ctrl: 135.7 ± 10.3 vs 98.7 ± 10.9 , $p < 0.05$). The results of qRT-PCR showed that the expression of E-cadherin decreased at mRNA level after 20nM insulin stimulation of CFPAC, while the expression of N-cadherin and Vimentin were up-regulated, and the relative expression levels were: 0.02 ± 0.10 、 1206.46 ± 162.31 、 50.85 ± 10.98 respectively. After 20nM insulin stimulation of Capan-2, the expression of E-cadherin decreased at mRNA level, while the expression of N-cadherin and Vimentin was up-regulated, and the relative expression levels were: 0.54 ± 0.08 、 5.97 ± 4.33 、 4.00 ± 1.99 , respectively. Western Blot results confirmed the above gene expression changes at the protein expression level, and found that insulin stimulation could up-regulate the expression level of Snail protein.

Conclusion: Transwell assay showed that insulin significantly enhanced the ability of pancreatic cancer cells to migrate and invade. The results of qRT-PCR and Western Blot showed that insulin increased the expression of E-cadherin, decreased the expression of N-cadherin and Vimentin in pancreatic cancer cells, that is, the migration and invasion ability of pancreatic cancer cells were increased through the EMT pathway. Western Blot results suggest that insulin may further affect the expression of E-cadherin by inducing activation of Snail. The mechanism by which insulin triggers the activation of Snail and whether it can affect the ability of pancreatic cancer to migrate and invade through other mechanisms need further experiments.

P 70. WNT/BETA-CATENIN SIGNALING PLAYS MULTIPLE ROLES DURING THE PROCESS OF FIBROTIC REMODELING IN THE EXOCRINE PANCREAS

M Bläuer, M Laaninen, J Sand, J Laukkarinen

Presenter: Anu Aronen MD | Tampere University Hospital

Background: Wnt/Beta-catenin signaling plays vital roles in tissue homeostasis. Dysregulation of the pathway has been implicated in the pathogenesis of cancer and fibrosis in numerous tissues, including the pancreas. We studied the effect of microenvironmental changes related to fibrotic tissue remodeling on the expression of selected Wnt/Beta-catenin pathway-associated proteins in the human exocrine pancreas. The role of acinar-stellate cell interactions on the expression of the proteins in both cell types was examined *in vitro*.

Methods: Pancreatic specimens from patients undergoing pancreatic resection were grouped according to the degree of pancreatic fibrosis. Exocrine tissue areas were analyzed by immunohistochemical means for the expression of β -catenin, Wnt2, Wnt5a and SFRP4. A long-term co-culture system developed in our laboratory was used to elucidate the effect of humoral interactions on the expression of the proteins in mouse pancreatic acinar and stellate cells. The cells were maintained for 4 days in parallel mono- and co-cultures and subjected thereafter to immunocytochemical analyses.

Results: Fibrosis caused redistribution of the studied proteins in and between epithelial and stromal compartments, compared to acinar-rich microenvironment. In non-fibrotic and moderately fibrotic tissue the proteins were only expressed in acinar cells, but resided predominantly in fibroblastoid/stellate cells and macrophages in highly fibrotic tissue. Subcellular changes in the expression of immunoreactive Beta-catenin and Wnt5a were detected in acinar cells, suggesting activation of both canonical and non-canonical regulatory mechanisms in these cells during fibrotic tissue remodeling. The *in vitro* data proposes an involvement of acinar cell/PSC cross-talk in mediating some of the changes observed in tissue specimens.

Conclusion: Wnt/Beta-catenin pathway-associated proteins are abundantly expressed in the exocrine pancreas with distinct changes in their cellular and subcellular distribution alongside increasing levels of fibrosis. The data suggest diverse functions for Wnt/Beta-catenin signaling during the process of fibrotic remodeling in the exocrine pancreas. The *in vitro* data renders our co-culture setting a relevant experimental tool to study Wnt/Beta-catenin signaling in exocrine pancreatic cells.

P 71. PERSONALIZED MEDICINE FOR PANCREATIC FISTULA AFTER PANCREATODUODENECTOMY: TARGETING IMPROVEMENT THROUGH RISK PROFILING

MT Trudeau, BL Ecker, L Maggino, MT Mcmillan, CM Vollmer Jr

Presenter: Maxwell Trudeau BS | University of Pennsylvania

Background: Despite having many technical options, most surgeons employ a “one size fits all” management strategy for preventing pancreatic fistula (CR-POPF) following pancreatoduodenectomy (PD). Yet, the risk of CR-POPF development is different in every patient. The 4-element/10-point Fistula Risk Score (FRS) quantitates that risk, which can be segregated into four discrete zones for comparison (Negligible, Low, Moderate, High). More specifically, 80 unique biologic risk scenarios can be derived by combining the four FRS risk components (gland texture, pathology, duct size, and blood loss). We propose that risk mitigation should be targeted to best practice for the individualized presentation of patient risk.

Methods: FRS profiles and outcomes of 5,323 PDs were accrued from a 17-institution, multinational collaborative (2003-2016). Associations between CR-POPF and varying mitigation strategies were analyzed for both the four defined FRS risk zones and each of the 80 distinct scenarios. Commonly encountered, or highly vulnerable, scenarios were individually investigated using multivariate analysis to derive directed mitigation approaches.

Results: The CR-POPF rate in the overall cohort was 12.9% and varied by FRS zone (Negligible: 0.7%; Low: 5.2%; Moderate: 14.3%; High: 31.6%). The median and mode FRS number was 3. The overall distribution of cases across FRS zones was: Negligible-8.1%; Low-22.6%; Moderate-58.8%; High- 10.5%. Among the overall series, each of the 80 possible distinct FRS scenarios were encountered at least twice. Neither CR-POPF rates, nor severity, necessarily correlate with scenario frequency. For instance, the most common combination was the only Negligible risk (FRS 0) scenario (#1: firm gland, PDAC/pancreatitis pathology, duct \geq 5mm, and \leq 400 mL blood loss), with an 8.1% (n=433) occurrence and just a 0.7% rate, where no specific mitigation strategies are useful. On the other hand, scenario #67 (FRS7), demonstrating the highest CR-POPF rate (50%), was relatively infrequently encountered (n=16). The majority (446/688: 64.8%) of all CR-POPFs actually occurred in the Moderate risk zone – where, notably, the most common scenario (#60) was more vulnerable to fistula occurrence than other scenarios in that zone in a risk-matched analysis (21.1% vs. 14.3%, p<0.001). Fourteen Moderate risk scenarios have higher CR-POPF rates than four high risk scenarios. Overall, 36.3% of CR-POPF encountered come from just five scenarios. Optimal mitigation approaches have been identified for these most prolific situations. For example, for Scenario #60 (soft gland, high risk pathology, 2 mm duct, and \leq 400 mL blood loss), a markedly reduced fistula occurrence (OR 0.22, 95% CI 0.12-0.44) was achieved using a “best-practice bundle” consisting of drain use without applications of stents or octreotide. Table 1 shows the wide heterogeneity of scenarios associated with each important CR-POPF outcome metric.

Conclusion: Through this data a comprehensive catalogue has been created that links specific and unique CR-POPF risk scenarios (based on the biologic interplay of recognized risk factors) to their outcomes. The most commonly encountered case is that of Negligible risk. While High risk scenarios are rare, with high stakes, most fistulas are actually derived from Moderate risk (FRS 3-6) situations. An emphasis on improving management of these particular scenarios should yield the most value in decreasing the problem of CR-POPF. The uniqueness associated with every scenario requires optimal mitigation strategies be utilized at different times. Individualized approaches have been identified for the most common, as well as the most vulnerable, situations that surgeons face during PD.

Table 1: Top 5 (of 80 possible) Fistula Risk Score (FRS) Scenarios for Various Metrics of Clinically-Relevant Pancreatic Fistula (CR-POPF) Occurrence and Burden

Rank	Frequency of scenario occurrence (N; % of 5323 cases)	Number of CR-POPF Contributed (N; % of 688 CR-POPF)	Highest CR-POPF Rate (%)	Grade C Fistula Rate (%)	Average Complication Burden for Fistula (0.00-1.00)	Postoperative Morbidity Index (0.00-1.00)
1st	Scenario #1 FRS 0 n=433 (8.1%)	Scenario #60 FRS 6 n=82 (7.3%)	Scenario #67 FRS 7 n=8/16 (50.0%)	Scenario #77 FRS 9 n=1/3 (33.3%)	Scenario #32 FRS 4 0.607	Scenario #62 FRS 7 0.457
2nd	Scenario #60 FRS 6 n=389 (7.3%)	Scenario #47 FRS 5 n=57 (6.5%)	Scenario #76 FRS 8 n=16/33 (48.5%)	Scenario #67 FRS 7 n=4/16 (25.0%)	Scenario #78 FRS 9 0.527	Scenario #80 FRS 10 0.431
3rd	Scenario #47 FRS 5 n=348 (6.5%)	Scenario #69 FRS 7 n=44 (2.4%)	Scenario #79 FRS 9 n=4/9 (44.4%)	Scenario #62 FRS 7 n=2/10 (20.0%)	Scenario #75 FRS 8 0.507	Scenario #67 FRS 7 0.417
4th	Scenario #20 FRS 3 n=240 (4.5%)	Scenario #20 FRS 3 n=35 (4.5%)	Scenario #62 FRS 7 n=4/10 (40.0%)	Scenario #64 FRS 7 n=3/23 (13.0%)	Scenario #74 FRS 8 0.499	Scenario #72 FRS 8 0.376
5th	Scenario #7 FRS 2 n=232 (4.4%)	Scenario #33 FRS 4 n=32 (2.8%)	Scenario #80 FRS 10 n=4/11 (36.4%)	Scenario #78 FRS 9 n=5/42 (11.9%)	Scenario #10 FRS 2 0.478	Scenario #78 FRS 9 0.358

P 72. PATIENT PERCEPTIONS OF THE POST-PANCREATECTOMY DISCHARGE PROCESS

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Presenter: Rodrigo Calvillo-Ortiz MD | Beth Israel Deaconess Medical Center

Background: Complications after pancreatic cancer resection are frequent and contribute to poor outcome; it has been shown that many develop after discharge. Patients are expected to identify signs/symptoms that can lead to serious complications after discharge, but they may be poorly educated on the harbingers of such complications. The primary aim of this study was to assess the impact of an educational tool on patient perceptions of, and satisfaction with, the discharge process, and its effect on readmission rates.

Methods: A prospective cohort study of patients who underwent pancreatic resection in a high-volume center was undertaken. An iPad-based interactive educational module (iBook) that provided information about the procedure, possible complications, alarm signs, and discharge information was implemented in 2017. Patients lacking English proficiency were excluded. Demographics and clinical characteristics were obtained from chart review. Primary outcomes were readmission (30 and 90 day) and patient satisfaction; readmission rate was compared with patients treated the year prior to implementation of the tool.

Results: There were 100 patients equally divided in the pre- and post-implementation cohorts. Mean age for the total cohort was 65.2 (SD 12.7), 46% were female and 93.3% were white. There were no significant demographic differences between the two groups. In the post-implementation group, 92% were satisfied with the discharge process and well-informed about post-operative expectations (vs 42.4% prior to iBook implementation). 34% used the iBook to answer questions after discharge and more than half found it to be a helpful resource and shared it with family. Overall, 84% reported that the iBook was a good tool and recommended it for other patients. There were no statistical differences in 30- and 90-day readmission rates between patients who received the iBook and those who did not (20% vs. 28% (30d); 32% vs 34% (90d), $p=NS$). Reasons for readmission were similar in both groups at both time points; most commonly, abscess (fistula) and failure to thrive.

Conclusion: An interactive educational module did not impact readmission rates in patients who underwent pancreatectomy in the study period. However, it positively impacted patient satisfaction with the discharge process and resulted in an increased sense of preparedness for the postoperative period, when compared to a previous survey done at our institution. Even without a difference in readmission rate, this additional patient-centered information impacted the overall patient experience and recovery; and facilitated patient comfort with the discharge process.

Demographics	iBook (n = 50)	Non-iBook (n = 50)	p-value
Sex			N/S
Male	62% (n=31)	46% (n=23)	
Female	38% (n=19)	54% (n=27)	
Age at diagnosis	65.9 y	64.4y	N/S
Race			N/S
White	95.45%(n=42)	91.2% (n=42)	
Black	0% (n=0)	6.5% (n=3)	
Hispanic	0% (n=0)	0% (n=0)	
Asian	4.55% (n=2)	2.17% (n=1)	
Education Level			N/S
No schooling	2.32% (n=1)	0% (n=0)	
Middle school	0% (n=0)	0% (n=0)	
Some high school	2.3% (n=1)	4.1% (n=2)	
High School	39.5% (n=17)	43.7% (n=21)	
Associate degree	16.2% (n=7)	22.9% (n=11)	
Bachelor's degree	18.6% (n=8)	6.25% (n=3)	
Master's degree	16.2% (n=7)	18.7% (n=9)	
Doctorate Degree	4.6% (n=2)	4.1% (n=2)	
Marital Status			N/S
Single	34.6% (n=17)	51% (n=25)	
Married	63.4% (n=32)	49% (n=24)	
Type of Cancer			N/S
Pancreatic cancer	70% (n=35)	68% (n=34)	
Periampullary cancer	12% (n=6)	12% (n=6)	
IMPEN	8% (n=4)	8% (n=3)	
Cholangiocarcinoma	4% (n=2)	4% (n=2)	
Duodenal cancer	0% (n=0)	0% (n=0)	
PNET	4% (n=2)	2% (n=1)	
Chronic Pancreatitis	2% (n=1)	4% (n=2)	
Stage			N/S
0	20% (n=10)	14% (n=7)	
I	36% (n=18)	26% (n=13)	
II	42% (n=21)	52% (n=26)	
III	0% (n=0)	8% (n=4)	
IV	2% (n=1)	0% (n=0)	
Surgery			
Whipple	82% (n=41)	66% (n=33)	N/S
Distal	18% (n=9)	34% (n=17)	
LOS			N/S
Mean	9.46 days	12.38 days	
Readmission <30 days	20% (n=10)	28% (n=14)	N/S
Readmission <90 days	32% (n=16)	34% (n=17)	N/S

P 73. PERIOPERATIVE PANCREATIC ENZYME REPLACEMENT THERAPY REDUCES MORBIDITY IN PATIENTS UNDERGOING PANCREATODUODENECTOMY

AS Khithani, TB Cengiz, K El-Hayek, T Augustin, RA Simon, RM Walsh, GJ Morris-Stiff

Presenter: Amit Khithani MD | Cleveland Clinic Foundation

Background: Exocrine pancreatic insufficiency (EPI) is a common entity in patients scheduled for pancreatoduodenectomy (PD) due to obstruction of the pancreatic duct. The treatment for EPI is pancreatic enzyme replacement therapy (PERT) but this is not routinely prescribed in patients undergoing PD. The aim of this study was to examine the effects of perioperative PERT on the incidence of postoperative pancreatic fistula (POPF) and surgical site infections (SSI) in patients undergoing PD.

Methods: Patients undergoing PD from January 2014 to December 2017 were maintained in a database. The EMR was reviewed to determine the presence of symptoms indicative of EPI and the PERT use during the pre- and post-operative periods. The presence of dilated pancreatic duct was ascertained through review of pre-operative cross-sectional imaging. Patients were divided into 3 groups: patients who received preoperative PERT continued into the postoperative period (Preop PERT); patients who received only postoperative PERT (Postop PERT); and patients who did not receive PERT (No PERT). A POPF was defined according to the ISGPF definition and classified as biochemical leaks (A) or clinically significant (B or C). SSIs were classified as superficial, deep, and organ-space. The incidence of SSI and POPF were compared between groups.

Results: Of 327 patients who underwent a PD, 239 (73%) had evidence of EPI, with a dilated pancreatic duct identified in 203 (62.0%) and symptoms of EPI in 142 (43.4%). The rates of POPF were lowest in the Preop PERT group when compared to Postop PERT (9.7% vs. 27.0%; $p=0.001$) and No PERT (9.7% vs. 37.8%; $p=0.0001$) but there was no difference between Post PERT and No PERT (27.0% vs. 37.8%; $p=0.14$). Likewise, clinically relevant POPF were less common in the Preop PERT group when compared to Postop PERT (3.6% vs. 12.5%; $p=0.02$) and No PERT (3.6% vs. 17.4%; $p=0.003$) and there was no difference between Post PERT and No PERT (12.5% vs. 17.4%; $p=0.29$). For SSIs, rates were lowest in the Preop PERT group at 10.9% compared to 18.8% in the Postop PERT cohort, and 25.5% in the No PERT group with a statistically significant difference between the Preop PERT and No PERT groups ($p=0.01$) and a clinically significant difference between Preop PERT and Postop PERT (10.9% vs. 18.8%; $p=0.11$).

Conclusion: Patients who received preoperative PERT had lower rates of POPF both overall and clinically relevant POPF compared to those receiving postoperative PERT or no PERT. The preop PERT group also experienced less SSIs. Routine preoperative use of PERT should be considered in patients undergoing PD.

	Preop PERT (A) (n=82)	Postop PERT (B) (n=159)	No PERT (C) (n=86)	Statistical Significance (p)
POPF All grades	8 (9.7%)	43 (27.0%)	31 (37.8%)	A vs. B = 0.001 A vs. C = 0.0001 B vs. C = 0.14
POPF Grade B and C	3 (3.6%)	20 (12.5%)	15 (17.4%)	A vs. B = 0.02 A vs. C = 0.003 B vs. C = 0.29
SSI	9 (10.9%)	30 (18.82%)	22 (25.5%)	A vs. B = 0.11 A vs. C = 0.01 B vs. C = 0.22

Table 1: Outcomes in patients undergoing Pancreatoduodenectomy based on pancreatic enzyme replacement therapy.

P 74. IMPACT OF BLOOD TRANSFUSIONS ON SHORT-TERM OUTCOMES AND OVERALL SURVIVAL IN PATIENTS UNDERGOING PANCREATIC SURGERY FOR MALIGNANCY

M Chumakova, EA Aleassa, G Morris-Stiff

Presenter: Essa M. Aleassa MD, MSc | Cleveland Clinic Foundation

Background: It has been hypothesized that transfusion of packed red blood cells (PRBCT) has an impact on reducing survival and increasing recurrence in patients undergoing oncologic surgery via a proposed process of immunomodulation. Thus the aim of this study was to evaluate the effects that PRBCTs have on outcomes of patients undergoing oncologic pancreatic surgery.

Methods: Data from the American College of Surgeons National Surgical Quality Improvement (ACS-NSQIP) registry was used to identify patients undergoing pancreatic surgery for a malignant neoplasm at a single institution between January 2011 and December 2016. Transfusion data was obtained from the institutional blood bank database and ACS-NSQIP. Endpoints included post-operative morbidity, operative times (OR), length of stay (LOS) as well as cancer recurrence, 30-day, 1-year and 5-year mortality. Patients were divided into PRBCT and no PRBCT cohorts. PRBCT arm was then further divided into restrictive (transfusion for hemoglobin 7g/dL) groups.

Results: A total of 370 patients were identified, 54.3% were men with median age of 65.7 years. 306 (82.7%) received no PRBCT and 64 (17.3%) received PRBCT. Of those in the PRBCT group, 34 (9.2%) were in the permissive and 30 (8.1%) were in the restrictive PRBCT group. Median survival for the no PRBCT group was 32 months and 22 months for the PRBCT group ($p < 0.001$). 5-year cancer recurrence rates were 27.2%, 35.3% and 73.3% for the no PRBCT, restrictive and permissive PRBCT groups, respectively ($p < 0.001$). 5-year mortality for no PRBCT was 64.7%, whereas 5-year mortality for restrictive and permissive PRBCT groups were 73.5% and 96.7%, respectively ($p = 0.001$).

Conclusion: PRBCT would appear to have a significant effect on outcomes. When unavoidable, restrictive PRBCT should be utilized for patients undergoing oncologic pancreatic surgery as this is associated with an improved survival.

P 75. PROGNOSTIC SIGNIFICANCE OF TUMOR BUDDING IN PANCREATIC CANCER

E Petrova, V Zielinski, L Bolm, J Knief, D Bausch, C Thorns, T Keck, U Wellner

Presenter: Ekaterina Petrova MD | University Clinic Schleswig-Holstein (UKSH) Campus Lübeck, Germany

Background: Tumor budding is associated with aggressive tumor growth. A correlation between tumor budding and epithelio-mesenchymal transition has been shown. In pancreatic cancer tumor budding is a ubiquitous feature. In this study we explored the prognostic value of tumor budding in pancreatic cancer.

Methods: Retrospective analysis of archived embedded tumor tissue was performed. H&E stained slides from the central tumor region were used to quantify the tumor buds. Tumor buds were defined as isolated groups of ≤ 5 cells. The mean number of buds in 3 high power fields (HPF) was calculated. Univariable and multivariable survival analysis with Cox regression was applied. Statistical analysis was performed with the R software.

Results: A total of 137 patients resected for pancreatic ductal adenocarcinoma between 1996 and 2016 at the Department of Surgery, University Clinic Schleswig-Holstein, Campus Lübeck, Germany were included. Tumor budding was present in 85.2 % of cases, in 31.1% the mean number of tumor buds per HPF was higher than 5. Tumor budding with cutoff >5 /HPF was a significant prognostic factor on univariable and multivariable Cox regression analysis. Other significant prognostic factors were nodal status, lymphangiosis, grading and adjuvant therapy.

Conclusion: Tumor budding with cutoff >5 /HPF is an independent prognostic factor for pancreatic cancer.

P 77. NEOADJUVANT THERAPY VERSUS UPFRONT SURGERY FOR RESECTABLE PANCREATIC CANCER: A SYSTEMATIC REVIEW AND META-ANALYSIS

G Nappo, S Bozzarelli, T Comito, F Gavazzi, C Ridolfi, G Capretti, J Galvanin, G Donisi, L Rimassa, A Zerbi

Presenter: Gennaro Nappo MD | Humanitas University

Background: Surgery-first approach is considered the standard of care in resectable pancreatic cancer. Neoadjuvant strategy for borderline and locally advanced pancreatic cancer has been implemented during the last decade. Moreover, recently, more authors advocate the adoption of a neoadjuvant strategy also in the subset of resectable pancreatic cancer. The aim of this study was to perform a meta-analysis of published studies comparing neoadjuvant and surgery-first approach in resectable pancreatic cancer.

Methods: Medline was searched for studies comparing upfront surgery and neoadjuvant approach in resectable pancreatic cancer. The search included all English studies published from January 2007 to June 2018. Evaluated outcomes were: a) resection rate; b) post-operative morbidity and mortality; c) nodal involvement (N+) and microscopic residual infiltration of margins (R1); d) 5-year overall survival. The pooled effect was primarily measured in terms of odds ratio (OR) with 95% confidence interval (CI). Statistical heterogeneity between trials was detected by the I² test. All p values were two-sided and the significance level was set at 5%. Egger's test was performed to rule out any bias from the studies with small patient samples.

Results: In total, thirteen studies were included in qualitative analysis: only 3 of them were randomized controlled trials. Resection rate was significantly lower in neoadjuvant group if compared with surgery-first approach (OR 0.48, 95% CI 0.33-0.69) ($p < 0.001$). Post-operative morbidity and mortality were not significantly different with two approaches (OR 1.28, 95% CI 0.91-1.80 ($p = 0.149$) and OR 1.18, 95% CI 0.71-1.96 ($p = 0.524$) for morbidity and mortality, respectively). A significant reduction in terms of N1 and R1 resection rate in neoadjuvant group was observed (OR 0.32, 95% CI 0.26-0.39 ($p < 0.001$) and OR 0.60, 95% CI 0.51-0.71 ($p < 0.001$) for N1 and R1, respectively). Five-year survival was significantly better in neoadjuvant group if compared with surgery-first approach (OR 0.48, 95% CI 0.26-0.87) ($p = 0.01$).

Conclusion: The evaluation of available literature showed that few and low-quality studies comparing upfront surgery and neoadjuvant approach in resectable pancreatic cancer have been published. However, neoadjuvant strategy seems to be effective: even if some resectable cases become unresectable after neoadjuvant treatment, this approach seems to give advantage in terms of N1 and R1 rate and in terms of 5-year survival, if compared with upfront surgery approach. Other randomized studies are needed in order to confirm these results.

P 78. SOLID PSEUDOPAPILLARY NEOPLASMS OF THE PANCREAS: AN EXTENDED ANALYSIS OF A SINGLE INSTITUTION SERIES AFTER PANCREATIC RESECTION

Y Zhu, T Saunders, L Yin, J Griffin, N Pu, H Hu, RA Burkhart, MA Makary, JL Cameron, MJ Weiss, CL Wolfgang, J He, J Yu

Presenter: Yayun Zhu MD | Johns Hopkins University School of Medicine

Background: Solid pseudopapillary neoplasms (SPNs) of the pancreas often put both patients and clinicians at a surgical dilemma. Few articles are currently available for surgeons to resort to for a convincing evaluation of the value of long-term postoperative follow-up which has been designated for more survival benefits.

Methods: Data concerning relevant demographic, clinical, operative, and pathology were retrospectively collected for all patients with SPN who received surgical resection at the Johns Hopkins Hospital from July 1970 to July 2015. All data collected for this study, including long term survival information, came from the patient medical records and the US Social Security Death index. Perioperative surgical complications and mortalities and post-operative pancreatic were recorded. Statistical analysis was conducted using Standard Student t-test, and chi-squared analysis with IBM SPSS Statistics. A two-sided $p < 0.05$ were considered statistically significant.

Results: A total number of seventy-nine patients with SPN, comprising 66 females (84%) and 13 males (16%) ($p=0.00$). The median age for the total cohort was 33 years (Range: 6-75 years), 31 years and 35 years for females and males respectively. Thirty-two (41%) patients had complications, the most common of which were pancreatitis ($n=11$, 14%), pancreatic fistula/leak ($n=6$, 8%), delayed gastric emptying (DGE) ($n=6$, 8%), abscess formation ($n=3$, 4%), and wound infection ($n=5$, 7%). Malignant characteristics were observed in 11 patients (five in the 13 male patients and six in the 66 female patients, $p=0.018$). Two of the patients presented with liver metastasis, one of which passed away one year after diagnosis and the other survived for 5.6 years. Perineurial invasion was found in six, perivascular invasion in two, and lymph node involvement in three patients. All patients underwent a R0 resection except for three, two of which had R1 resections. The other patient underwent an R2 resection that ended up becoming a complete pancreatectomy. Three patients had lymphatic spread to regional lymph nodes. the median follow-up for the 79 patients is 6 years. Five patients died in the series, two of which died of liver metastasis, one died from Stage IV colorectal cancer at 1.5 years, and two died of unknown causes at 6.8 and 9.7 years respectively. The remaining 74 patients are alive including two patients with R1 resections who have been alive for 15.7 and 27 years respectively.

Conclusion: SPNs are rare pancreas tumors that show predominance in females but are more likely to have malignant characteristics in males. Survival and outcome had no correlations to any preoperative, operative, or postoperative characteristics. This extensive follow up for patients with surgically resected SPNs supports the treatment of surgical resection and gives more insights into the follow up of patients with SPN, especially in males.

P 79. SEPSIS IS THE STRONGEST DRIVER OF AVOIDABLE IN-HOSPITAL COST IN PATIENTS UNDERGOING PANCREATICODUODENECTOMY

E Eguia, PJ Sweigert, M Nelson, F Luchette, M Afshar, MS Baker

Presenter: Emanuel Eguia MD, MS, MHA | Loyola University Medical Center

Background: Few studies evaluate the impact of postoperative sepsis on costs of pancreaticoduodenectomy.

Methods: We queried the National Inpatient Sample to identify patients undergoing pancreaticoduodenectomy between 2012 and 2014. Sepsis was defined using Angus Criteria as infection associated with new-onset organ dysfunction. Costs were inpatient costs for the index hospitalization.

Results: 15,640 patients underwent pancreaticoduodenectomy. 1,975 (13%) had a postoperative complication with 1,760 (11.3%) developing sepsis. Patients who developed sepsis were older (69 vs. 66 years of age; $p < .01$) and had a higher comorbidity index (5 vs. 4; $p = .02$) than those that did not. On multivariable analysis adjusting for age, gender, race, comorbidity, insurance, facility and complication (MI, DVT, PE, CVA, infection without sepsis, sepsis), sepsis had the strongest association with mortality and cost. Patients developing sepsis had an average risk-adjusted cost of care \$25,595 (95% CI [\$20,848, \$30,343]) higher than that for those not developing sepsis and an odds ratio of death of 19.81 (95% CI [7.60, 51.61]). Other factors associated with cost included: Hispanic ethnicity (\$7,230, 95% CI [\$942, \$13,518]), myocardial infarction (MI) (\$16,386; 95% CI [\$7,416, \$25,355]) and infection without sepsis (\$11,815, 95% CI [\$9,212, \$14,418]); those with all-cause mortality included: Medicaid insurance (OR 2.72, 95% CI [1.11, 6.65]), large facility (OR 0.59, 95% CI [0.36, 0.97]), and MI (OR 3.46, 95% CI [1.03, 11.57]). Factors associated with risk of sepsis included: age (OR 1.02, 95% CI [1.00, 1.04]), female gender (OR 0.78, 95% CI [0.62, 0.98]) and gram-negative infection (OR 8.14; 95% CI [5.68, 11.66]). While 5240 patients (33%) underwent PD in small, non-teaching centers, facility type and size were not associated with risk of sepsis, sepsis-related mortality or cost.

Conclusion: Sepsis is the strongest driver of mortality and avoidable cost in pancreaticoduodenectomy. Large, urban, teaching centers do not mitigate risk of sepsis, sepsis-related mortality or cost.

P 80. LYMPH NODE ASSESSMENT INFORMS PROGNOSIS BUT EXTENT OF LYMPHADENECTOMY IS NOT ASSOCIATED WITH SURVIVAL IN PATIENTS UNDERGOING RESECTION FOR PANCREATIC NEUROENDOCRINE TUMORS

E Eguia, P Sweigert, M Afshar, GV Aranha, G Abood, C Godellas, PC Kuo, MS Baker

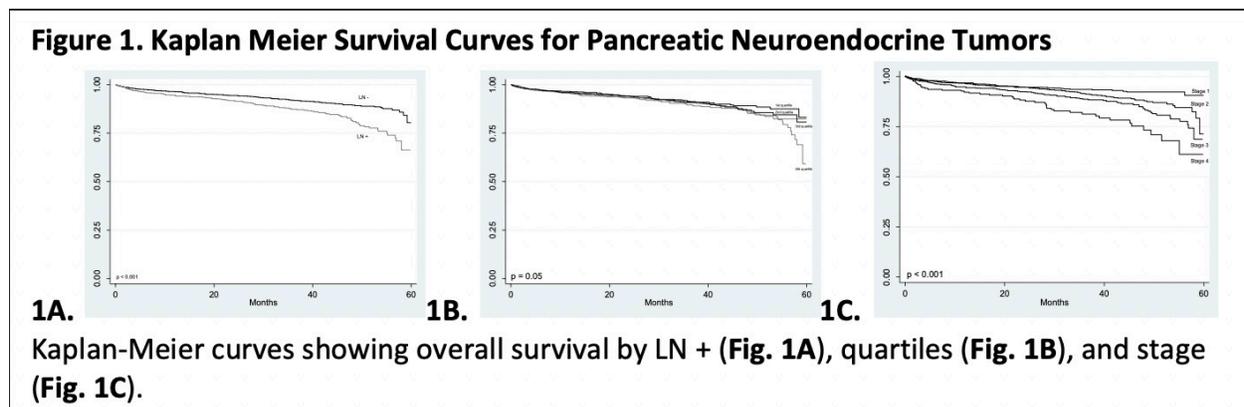
Presenter: Emanuel Eguia MD, MS, MHA | Loyola University Medical Center

Background: Most resected pancreatic neuroendocrine tumors (PNETs) are moderate or well-differentiated tumors with relatively indolent biology. The optimal management of regional lymph nodes in the resection of PNETs has not been definitively determined.

Methods: We queried the National Cancer Database (NCDB) to identify patients undergoing resection for PNET between 2010 and 2014. Patients with poorly differentiated tumors, metastatic disease and those having no nodal assessment were excluded. Parsimonious multivariable (MVR) regression was used to identify factors associated with lymph node involvement (LN+). Cox proportional hazard modeling was used to identify factors associated with overall survival (OS). Candidate variables were chosen a priori and included: age, gender, race, Charlson Comorbidity Index (CCI), insurance status, facility type, procedure, tumor size, histologic grade, margin status, LN+ and number of nodes examined broken by quartiles (1:1-5; 2:6-10; 3:11-16; 4: \geq 17).

Results: 3709 patients met inclusion criteria. 2094 (57%) had tumors 16: OR 2.96; p 70 (HR 2.82; p 16 LN: HR 1.03; p>.05). (Figure 1)

Conclusion: In patients undergoing resection for PNET, lymph node involvement is associated with poor prognosis. The number of nodes examined is itself an independent determinate of identifying nodal metastases, but the extent of regional lymphadenectomy does not impact overall survival.



P 82. IMPACT OF ADJUVANT TREATMENT FOLLOWING SURGERY FOR INVASIVE INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS OF THE PANCREAS

C Rodrigues, D Ciprani, T Hank, M Weniger, M Qadan, C Ferrone, AL Warshaw, KD Lillemoe, C Fernandez-Del Castillo

Presenter: Clifton Rodrigues MD | Massachusetts General Hospital

Background: There is limited data on the utility of adjuvant therapy in invasive IPMN. This study aims to assess the patterns of use of chemotherapy and radiotherapy following surgery for invasive IPMN and its impact on overall survival.

Methods: From a prospectively maintained database at the Massachusetts General Hospital, patients who underwent surgery for invasive IPMN between 1993 and 2018 were included in the study. Data were collected on demographics, comorbidities, type of surgery and pathological characteristics, and compared between patients with and without adjuvant treatment. We evaluated overall survival (OS) using multivariate Cox regression adjusting for age, type of invasive IPMN, tumor and nodal stage.

Results: 110 patients with invasive IPMN were identified; of which 69 were tubular, 35 colloid and 6 oncocytic. 64 patients underwent surgery alone, and 46 underwent surgery followed by adjuvant therapy; of the latter, 13 received chemotherapy alone, 25 chemotherapy and radiation and 8 patients only radiation. Patients who received adjuvant treatment were significantly younger (median: 61.5 vs 74 years; $p < 0.001$), had higher T stage ($p = 0.03$) and N stage ($p = 0.02$). Median follow up was 40.4 months (3.4 - 274 months). Unadjusted median overall survival was 155 months for the surgery alone group and 50.5 months in the adjuvant therapy group, with 5-year OS of 67.8 % and 40%, respectively, $p = 0.001$. Following adjustment for age, invasive type, T and N stage, survival was no longer significantly different between the adjuvant and surgery alone groups, HR of adjuvant therapy 1.575 (0.815-3.034), $p = 0.176$, with a 5-year survival of 66% vs. 51 % in the surgery only and adjuvant therapy group, respectively. N1 and N2 nodal stage and T2 tumor stage were significant predictors of a poor overall survival: N1 vs. N0, HR=3.25 (1.61-6.55), $p = 0.001$. N2 vs N0, HR= 5.88 (2.45-14.14), $p = 0.0001$. T2 vs T1 HR=2.598 (1.312-5.143), $p = 0.006$.

Conclusion: Patients with invasive IPMN receiving adjuvant therapy were younger and had an advanced tumor and nodal stage. Adjuvant therapy did not appear to influence overall survival. The only significant predictors of poor survival following resection were tumor size and nodal metastasis.

P 83. DOES PRACTICE MAKE PERFECT FOR PANCREATIC ADENOCARCINOMA? HIGHER VOLUME CENTERS DELIVERING CHEMORADIATION ARE ASSOCIATED WITH IMPROVED SURGICAL AND SURVIVAL OUTCOMES

LA Bliss, AN Krepline, CA Barnes, KK Christians, B George, PS Ritch, BA Erickson, DB Evans, WA Hall, S Tsai

Presenter: Lindsay Bliss MD, MPH | Medical College of Wisconsin

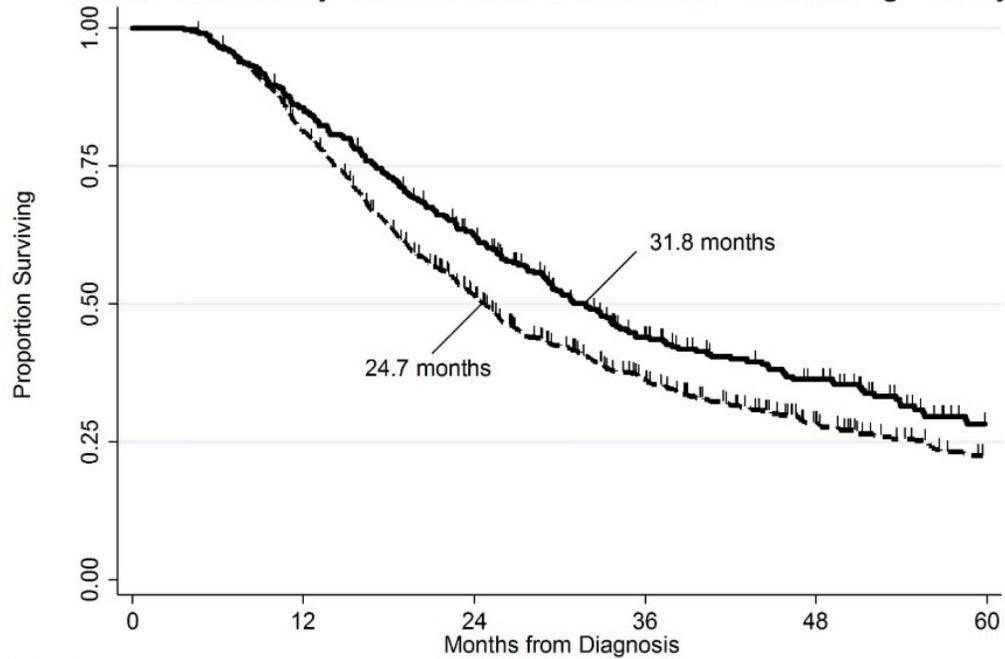
Background: Chemoradiation delivery prior to surgical resection for pancreatic cancer theoretically may improve local control and thereby increase patient survival. Radiation techniques and concomitant chemotherapy regimens vary between centers. Facilities that have a higher patient volume receiving neoadjuvant chemoradiation may have superior radiation planning and delivery as well as supportive care. This study addresses the impact of volume of neoadjuvant chemoradiation on patient outcome.

Methods: Patients with localized pancreatic adenocarcinoma who received neoadjuvant chemoradiation and surgery were identified in the National Cancer Database (NCDB) from 2006 to 2015. Facilities were stratified into low- and high-volume based on number of patients receiving neoadjuvant chemoradiation (cut point = 12). Surgical margin status, lymph node status, readmissions, mortality, and survival were compared between patients at low-volume and high-volume centers as well as patients referred elsewhere for neoadjuvant radiation. Fisher's exact test was used to compare categorical variables between groups. Other than survival time, continuous variables were categorized. Survival was compared using Kaplan-Meier plots and the log-rank test. Cox proportional hazard regression was used to model survival time.

Results: Of the 933 patients identified, 312 (33 %) received treatment at high-volume facilities and 621 (67%) received treatment at low-volume facilities. Over time, a larger portion of patients were treated at low-volume centers (74.10% in 2014-2015 vs 54.65% in 2006-2007, $p=0.05$). Among those treated at high-volume centers, more patients were female (54.17% vs 46.86%, $p=0.037$) and patients were treated at an earlier stage of disease (high-volume: stage I 25.32%, stage II 64.42%, stage III 10.26%; low-volume: stage I 21.7%, stage II 56.20%, stage III 22.06%; $p<0.05$). The percentage of patients age 65 years or greater, burden of co-morbidities, and local income, education and population density levels did not differ from high- and low-volume centers. Patients treated at high-volume chemoradiation facilities were more likely to have negative margins following resection (91.50% vs 84.78%, $p<0.05$). There was no difference in the number of lymph nodes examined, the frequency of node positivity, or the rates of complete pathologic response. Patients treated at high-volume centers had no difference in 30- or 90-day mortality rates. Post-operatively, patients at high-volume centers were more likely to undergo adjuvant therapy (33.65% vs 20.93%, $p<0.05$). The median survival of patients treated at high-volume centers was 31.84 months compared to 24.71 months at low-volume centers ($p<0.05$).

Conclusion: Most patients receiving neoadjuvant chemoradiation therapy do not receive care at facilities frequently providing this service. Patients treated at high-volume centers have increased rates of negative margins at the time of resection as well as improved overall survival. The volume-outcome relationship that has been demonstrated in pancreatic surgery may translate to neoadjuvant chemoradiation, adding even further complexity to the challenge of operationalizing this observation in our current health care environment.

Overall Survival by Volume of Chemoradiation at Treating Facility



Number at risk		0	12	24	36	48	60
Low-volume (<12)	621	499	293	168	104	64	
High-volume (>=12)	312	266	187	107	77	39	

--- Low-volume — High-volume

P 84. IMPLICATIONS OF PERINEURAL INVASION ON DISEASE RECURRENCE AND SURVIVAL FOLLOWING PANCREATECTOMY FOR PANCREATIC HEAD DUCTAL ADENOCARCINOMA

S Crippa, I Pergolini, AA Javed, KC Honselmann, MJ Weiss, F Di Salvo, R Burkhart, CR Ferrone, G Zamboni, J Yu, G Belfiori, M Qadan, C Rubini, J He, KD Lillemoe, C Fernandez-del Castillo, CL Wolfgang, M Falconi

Presenter: Stefano Crippa MD, PhD | San Raffaele Scientific Institute

Background: Although perineural invasion (PI) is described in a number of malignancies, it is a very common feature of pancreatic ductal adenocarcinoma (PDAC) and may be an early event in PDAC progression. The incidence of PI in PDAC is close to 100% in some series, and it is associated with cancer-related pain. However, there is no consensus regarding the prognostic impact of PI following pancreatectomy. The aim of this study is to investigate the role of PI on disease-free survival (DFS) and overall-survival (OS) in a large cohort of patients undergoing surgical resection for PDAC of the head of the pancreas.

Methods: This multicenter retrospective cohort study included patients undergoing pancreaticoduodenectomy or total pancreatectomy for PDAC between 2009 and 2014. Exclusion criteria were: incomplete follow-up or pathological data, lack of data regarding the time of tumor recurrence, and patients with invasive IPMNs. PI was defined simply as present/absent based on the original pathological examination without further sub-classification. R1 resections were defined as tumor cells within the surgical margin or < 1 mm. Survival outcomes were estimated using Kaplan-Meier curves. The association of PI with DFS (primary aim) and OS (secondary aim) was analyzed using Cox proportional-hazards models.

Results: Accurate data were available for 778 patients (52% males, median age: 66 years). 37% of patients underwent neoadjuvant therapy. 70% of patients had nodal metastases while the rate of R1 and PI were 34.5% and 87%. The rate of PI did not differ between patients who underwent neoadjuvant therapy and upfront surgery (88% vs 84%, $p=0.08$). Independent predictors of DFS were N1 status (HR:1.7), CA 19.9 > 37 (HR:1.4), R1 resection (HR:1.2), weight loss (HR:1.3). Although not statistically significant at multivariate analysis (HR:1.3, $p=0.07$), there was a trend toward worst DFS in patients with PI (median DFS: 20 vs 15 months). In order to investigate a prognostic role of PI in "early PDAC", we considered 180 patients with R0 and N0 disease. In this subgroup, PI was the only independent predictor of DFS (HR:2.2). In selected subgroups of patients with R1/N0 or N1/R0 disease, PI was never identified as independent predictor of DFS. Independent predictors of OS in the entire cohort were G3 grading (HR:1.7), N status (HR:1.8), pain (HR:1.3) and PI (HR:1.6). Median OS was 50 months in patients without PI compared with 28 months in those with PI ($p<0.01$). In the subgroup of R0/N0 patients, the only independent predictor of OS was pain (HR:1.9).

Conclusion: This study demonstrates that PI plays an important prognostic role in patients with PDAC of the head of the pancreas. Particularly, PI is the only independent predictor of DFS in patients with N0/R0 PDAC, suggesting that PI may be an early event in PDAC dissemination. Moreover PI is an independent predictor of OS in the entire cohort, while pain, a feature strongly associated with PI was identified as the only independent predictor of OS in N0/R0 PDAC patients.

P 85. PREVALENCE OF PANCREATIC SECRETORY TRYPSIN INHIBITOR GENE MUTATION IN PATIENTS WITH ACUTE ALCOHOL PANCREATITIS COMPARED TO ALCOHOLICS AND HEALTHY CONTROLS

A Nikkola, KH Herzig, K Mäkelä, SJ Mutt, T Lehtimäki, M Kähönen, O Raitakari, I Seppälä, P Paakkanen, H Seppänen, I Nordback, J Sand, J Laukkarinen

Presenter: Anssi Nikkola MD | Tampere University Hospital

Background: Approximately 10% of heavy alcohol users develop acute pancreatitis (AP). This suggests that additional triggers are required to initiate the inflammatory process. Genetic susceptibility contributes to the development of AP and for example SPINK1 mutation is a documented risk factor for the disease. However, only few genetic studies comparing AP patients and heavy alcohol users without pancreatitis exist. Our aim was to study the prevalence of SPINK1 (N34S) mutation in patients with acute alcohol pancreatitis (AAP) compared to heavy alcohol users who had never suffered an episode of pancreatitis.

Methods: For the mutational analysis, we obtained blood samples from patients with the first (n=62) and recurrent AAP (n=43) and from heavy alcohol users who had never suffered an episode of AP (n=93). We compared these findings to a Finnish control population (n=1914). After DNA isolation the prevalence of SPINK1 mutation was determined using suitable primers in PCR.

Results: The N34S mutation was found in 7.6% of the patients with AAP. The prevalence was significantly lower in healthy controls (3.4 %, p=0.034) and very low in alcoholics without pancreatitis (1.0 %, p=0.032).

Conclusion: Our study demonstrates that the prevalence of the SPINK1 mutation is overrepresented in AAP patients as previously studied, but interestingly, very low in alcoholics without pancreatitis. This finding may play a role in the variable susceptibility to AAP found in heavy alcohol users.

P 86. LONG-TERM OUTCOME OF CONVERSION SURGERY FOR INITIALLY UNRESECTABLE PANCREATIC CANCER: A SINGLE INSTITUTIONAL EXPERIENCE

K Wada, K Sano, F Miura, M Shibuya, M Kainuma, K Takahashi, S Kawamura

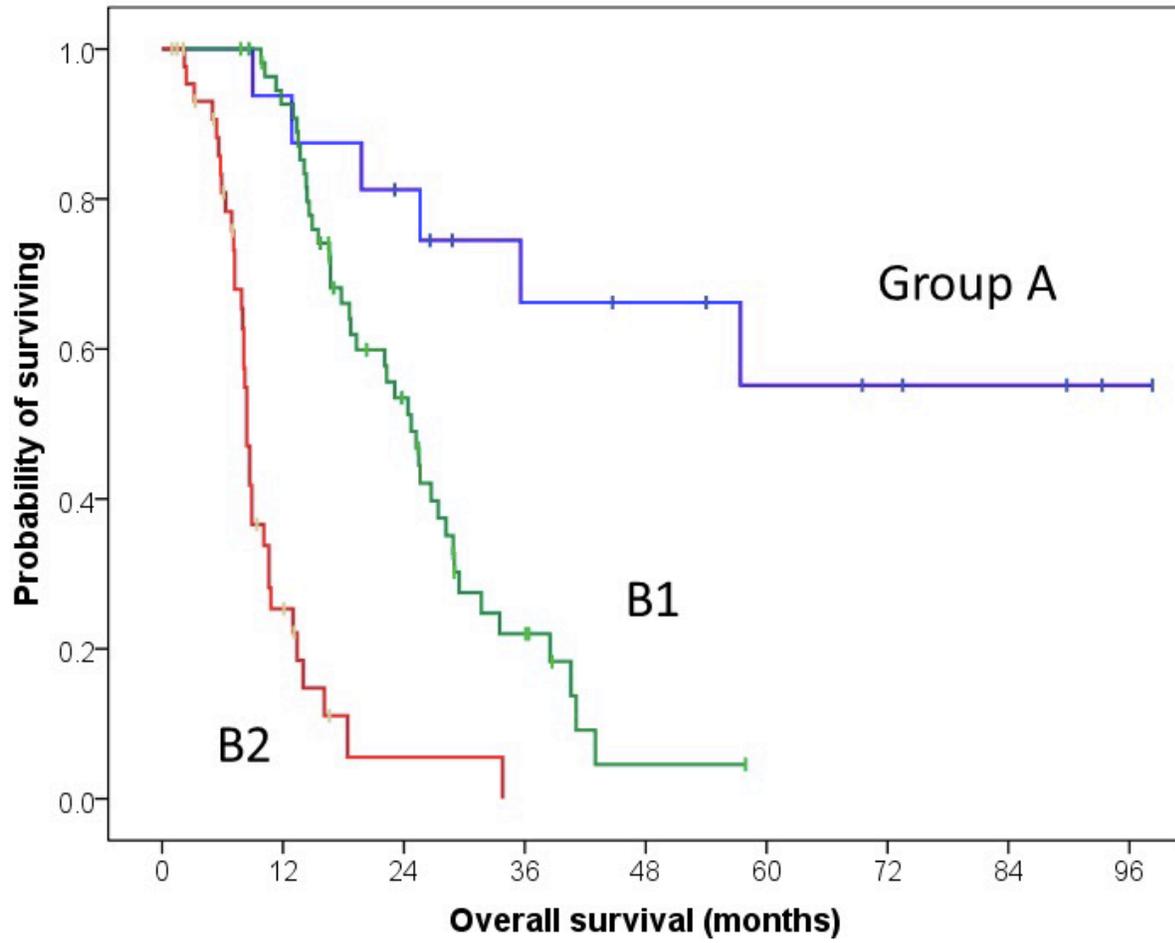
Presenter: Keita Wada MD, PhD | Teikyo University School of Medicine

Background: Owing to recent advances in chemotherapy and radiation therapy for pancreatic ductal adenocarcinoma (PDAC), long-term favorable response can be observed in some patients with unresectable (UR) PDAC. However, it is not clear whether surgical resection, so-called conversion surgery (CS), would further prolong survival for those good responders.

Methods: A retrospective analysis was performed using all PDACs during 2010/6-2016/12 at Teikyo University Hospital. CS is considered if a long-term good response and significant reduction of tumor markers were obtained for longer than 6 months in patients with UR-PDAC. Outcomes were compared between patients who underwent CS (Group A) with those without surgery (Group B). Group B was further subdivided into two groups, "responder" whose disease was controlled at least for 6 months but not underwent surgery (Group B1) and "non-responder" (Group B2).

Results: One-hundred twenty-three UR-PDACs, 58 locally-advanced (UR-LA) and 65 metastatic (UR-M), were included. Palliative chemotherapy using gemcitabine-based combination chemotherapy was the most common first-line treatment in 94 patients (76%). After six months from the initial treatment, 28 (23%) had a partial response (PR) and 45 (37%) had a stable disease (SD) evaluated by the RECIST criteria. Of those, 13 UR-LAs (22%) and 3 UR-Ms (4.6%), were operated with a median time to surgery of 8.5 months (range: 6.0-16.8 months). Surgical procedures included total pancreatectomy in 3, Whipple in 6, distal pancreatectomy in 7, with combined resections of artery (63%), portal vein (56%), and other organs (50%). R0 resection (defined by "zero-mm rule") was achieved in all patients, nodal involvement was observed in 31% with a median number of positive nodes of 0 (0-4). Histologic antitumor effect evaluated by the Evans grade included 50% with grade IIB and 25% with grade III, respectively. Overall survival was significantly better in Group A than B1 and B2 ($p < 0.001$), with an estimated 3- and 5-year survival rate of 66% and 55.2%, respectively. After a median follow-up period of 40 months (range: 9-98 months), with a minimum of 2-years for censored patients, 10 out of 16 patients who underwent CS are still alive, including five actual 5-year survivors with cessation of any anti-cancer treatment. Multivariate analysis showed that modified Glasgow prognostic score (mGPS) of zero (HR=3.4) and RECIST SD or better (HR=6.1) at 6 months after the initial treatment in addition to CS (HR=3.91) were identified as independent prognostic factors, although none of the pre-treatment factors were significant.

Conclusion: Conversion surgery may be beneficial for patients with UR-PDAC as an option in multidisciplinary treatment, if obtaining longer response (RECIST \geq SD) to anti-cancer treatment with maintaining good physical condition (mGPS=0) at 6 months after the initial treatment.



P 87. UNIQUE STEATOSIS PATTERNS ON CONTRAST ENHANCED COMPUTED TOMOGRAPHY AFTER TOTAL PANCREATECTOMY AND ISLET AUTO-TRANSPLANTATION

AJ Coughlan, R Schat, B Spilseth, ME Skube, M Bellin, M Stice, GJ Beilman

Presenter: Alexandria Coughlan MD | University of Minnesota

Background: There is a significantly higher prevalence of steatosis seen on imaging after total pancreatectomy and islet auto-transplantation (TPIAT) compared to the general population (60% vs 15%), and the pattern of steatosis is often atypical. The relationship between steatosis and islet graft function is not clear. Steatosis may correlate with local insulin production by the islet cells, as seen in metastatic insulinomas to the liver. We postulate that different steatosis patterns on contrast enhanced computed tomography (CT) may correlate with islet cell viability and could potentially serve as a marker for graft function.

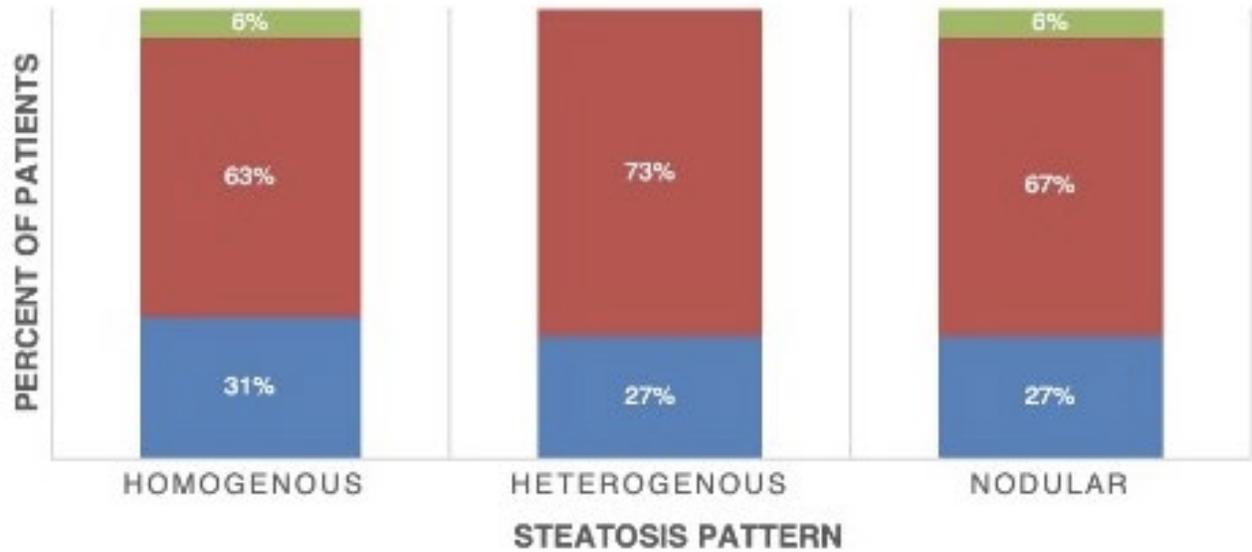
Methods: Patients who underwent TPIAT from 2008-2014 at our institution (n= 366) were reviewed retrospectively for CT exams performed 6-24 months postoperatively (n=82). 78 of these patients (95%) had data regarding islet graft function at one year post-TPIAT. CT scans were read by a radiologist blinded to the clinical status of the patient. Subjective patterns of steatosis were classified as either homogeneous (included diffusely steatotic and non-steatotic livers), heterogeneous, or nodular. Islet graft function was defined as full graft function (insulin independence with hemoglobin A1c < 0.6 ng/ml on mixed meal test), or graft failure (C-peptide level < 0.6 ng/ml). A Fisher's exact test compared graft function amongst the steatosis patterns.

Results: Steatosis patterns on contrast enhanced CT scans included heterogeneous (14%, n=11), homogeneous (67%, n=52), and nodular (19%, n=15). There was an average of 89 days between the one year graft function data entry and the date of CT scan. Distribution of graft function by steatosis pattern can be seen in Figure 1. There were no patients with graft failure in the heterogeneous steatosis pattern compared to the 6% graft failure seen in both the homogeneous and nodular groups. There was no statistically significant difference in graft function based on steatosis pattern ($p = 1$).

Conclusion: We identified a high incidence of unique patterns of steatosis on CT scan after TPIAT (heterogeneous and nodular). Despite this high incidence, pattern of steatosis did not correlate with islet graft function. This finding requires further evaluation including histopathologic correlation and use of other imaging modalities.

ISLET GRAFT FUNCTION RELATED TO PATTERN OF STEATOSIS

■ Full Function ■ Partial Function ■ Graft Failure



Fisher's exact test $p = 1$.

P 88. IDENTIFYING PRETREATMENT PREDICTORS OF NEOADJUVANT CHEMOTHERAPY BENEFIT IN LOCALIZED PANCREATIC HEAD CANCER: A 15-YEAR EXPERIENCE AT A HIGH VOLUME PANCREATIC CANCER CENTER

Al Al Abbas, J Hodges, P Varley, C Bucholz, J Bellon, N Bahary, A Singhi, ME Hogg, HJ Zeh III, AH Zureikat

Presenter: Amer Zureikat MD | University of Pittsburgh Medical Center

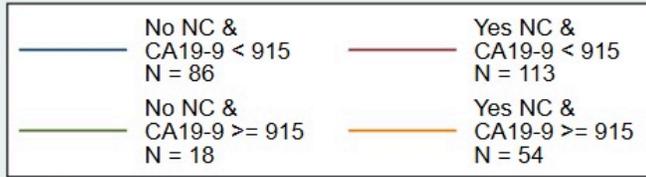
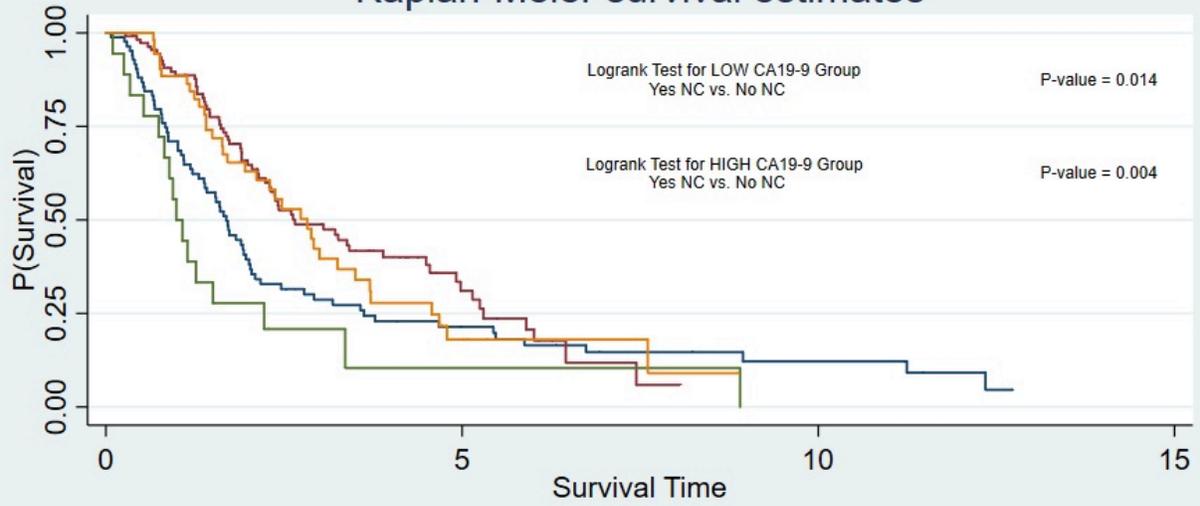
Background: Surgery followed by adjuvant chemotherapy (SF) is the standard approach for localized pancreatic adenocarcinoma (PC). High post-operative morbidity limits adjuvant chemotherapy receipt and affects survival. In addition, there are high rates of early loco-regional recurrence and distant metastasis. As a consequence, more centers are giving neoadjuvant chemotherapy (NC). While this approach has been associated with some benefits, strong indications are lacking. This study aims to identify baseline staging factors associated with greater benefit from NC as compared to SF approach for PC.

Methods: Retrospective review of a prospectively maintained database of all resected localized head PC undergoing NC or SF at a tertiary referral hospital from 2002 to 2018. Baseline staging factors investigated included clinical stage by EUS, CT vessel involvement, and serum CA19-9 after normalization of serum Total Bilirubin (TB <2 mg/dL). Patients with baseline serum CA19-9 <37 IU/dL were excluded from the analysis. Multiple logistic regression was used to adjust for potential confounders, and comparisons yielding p-values <0.05 were considered statistically significant.

Results: Of 390 patients, 198 (50.8%) received NC and 192 (49.2%) had SF. In the overall cohort, lymph node ratio (LNR) was the strongest predictor of overall survival (HR: 6.58, [95% CI: 3.45-12.52]; P<0.001). In the SF cohort, a cut-off of 0.25 for LNR was independently predictive of survival (HR: 2.18, [95% CI: 1.62-2.92]; P<0.001). A logistic regression model using baseline factors predicting LNR ≥ 0.25 included clinical N-stage, serum CA19-9 at diagnosis, and CT vessel involvement, as well as interaction with NC for each predictor. CA19-9 ≥ 915 emerged as the only predictor with a significant interaction with NC (P=0.041). Patients with CA19-9 ≥ 915 experienced a significantly higher reduction in the risk of high LNR (9.26% vs 50 %, P<0.001) compared to those with lower serum CA19-9 (15.9% vs 27.9, p=0.041). Overall survival was significantly improved in patients with CA19-9 ≥ 915 who received NC compared to SF approach (23.34 vs 12.11 months), P=0.004 (Figure 1).

Conclusion: This study identifies a cohort of patients benefiting the most from NC. High baseline serum CA19-9 may serve as the strongest indication for chemotherapy before resection.

Kaplan-Meier survival estimates



NC = Neoadjuvant Chemotherapy

P 90. HEMOGLOBIN A1C AS A MARKER TO STRATIFY DIABETES RISK FOLLOWING PANCREATICODUODENECTOMY

J Bleicher, HM Shepherd, CL Scaife

Presenter: Josh Bleicher MD, MS | University of Utah

Background: The risk for pancreatic endocrine insufficiency following pancreaticoduodenectomy (PD) has not been well described. Evidence supports an association between extended pancreatic resection and the subsequent development of diabetes mellitus (DM) in a small percentage of patients; however, the relationship between patients' preoperative risk for diabetes and the incidence of resulting endocrine dysfunction following pancreatic resection has not been studied. This study describes a cohort of patients who underwent PD and the subsequent incidence of new-onset or worsening DM following resection, stratified by preoperative Hemoglobin A1c (HbA1c) values.

Methods: A retrospective review of patients who underwent PD at an academic-based cancer center from January 2011-December 2017 was performed. Patients without preoperative HbA1c or less than 6 months follow-up postoperatively were excluded. DM was defined as follows: HbA1c value of $\geq 6.5\%$, documentation of DM diagnosis in preoperative history and physical, or treatment with insulin or oral anti-hyperglycemic agents. Patients without a preoperative diagnosis of diabetes but with a HbA1c of 5.5 - 6.5% were considered at risk for diabetes. Worsening DM was defined by an increase in HbA1c level of at least 10% or by an escalation in medical treatment for DM management. Descriptive statistics were calculated to describe new diagnosis of or worsening DM postoperatively. Patients were stratified based on diagnosis and preoperative HbA1c.

Results: A total of 90 patients met the study inclusion criteria. Twenty patients were diagnosed with DM prior to evaluation. There were 7 patients with a HbA1c $\geq 6.5\%$ preoperatively with no known diagnosis of DM. Another 35 patients (38.8%) were at risk for DM preoperatively. In the group of patients with known DM prior to evaluation, 6 (30%) had worse DM postoperatively. Of the 35 patients at risk for DM preoperatively, 5 (14.3%) were diagnosed with DM postoperatively. The median time to diagnosis was 12 months following resection, with 2 of these patients receiving a diagnosis over 2 years following surgery. Only 1 patient was diagnosed within 30 days of surgery. The majority (80%) of patients with newly diagnosed DM had a diagnosis of pancreatic adenocarcinoma. Only 1 patient (3.6%) of the 28 patients with preoperative HbA1c $< 5.5\%$ was diagnosed with DM following resection. This diagnosis was made 22 months following resection by a rise in HbA1c from 5.3 to 10.8. This patient underwent PD for a benign cystic lesion of the pancreas. In all groups, there was no significant difference in newly diagnosed or worsening DM when stratified by underlying pancreatic diagnosis.

Conclusion: Current literature varies on the risk for development of DM following PD. Many studies are limited by short follow-up (< 30 days), lack of HbA1c as a preoperative baseline test for DM, and small patient numbers. This study demonstrates the importance of HbA1c as a marker for risk stratification. This cohort showed similar rates of DM development following PD as other published reports in patients at-risk for DM preoperatively based on HbA1c; however, those with preoperative HbA1c $< 5.5\%$ were extremely unlikely to develop DM following PD. HbA1c is a useful marker in preoperative evaluation to help stratify patients' risk for development of DM postoperatively and can aid in preoperative counseling for patients undergoing PD.

	Patients	DM Diagnosis Pre-op	New DM	Worse DM
No Risk (HbA1c < 5.5%)	28	0	1 (3.6%)	-
At Risk (HbA1c 5.5 – 6.5%)	35	0	5 (14.3%)	-
DM (HbA1c >6.5% or known diagnosis)	27	20	-	6 (30%)

P 91. DIAGNOSTIC POTENTIAL OF CT TEXTURE ANALYSIS FOR PANCREATIC CYSTIC LESIONS

VR Rendell, AM Awe, BM Hanlon, N Marka, PJ Pickhardt, MG Lubner, ER Winslow

Presenter: Victoria Rendell MD | University of Wisconsin

Background: Accurate pre-operative diagnosis of pancreatic cysts is challenging. Invasive tests such as endoscopic ultrasound and fine needle aspiration or biopsy are limited in their ability to differentiate mucinous from non-mucinous cysts and to identify the presence of high-grade dysplasia (HGD) or malignancy. Radiomic tools like texture analysis, which are used to evaluate lesion heterogeneity, hold promise for improved accuracy in a noninvasive fashion, but have not been widely studied in pancreatic cysts. We aimed to identify CT texture features associated with mucinous cysts and the presence of HGD or malignancy.

Methods: Surgical and pathology records at our institution from 1995-2017 were queried for resected non-pseudocyst pancreatic cysts. Texture analysis of cysts identified on contrast-enhanced computed tomography (CT) within 1 year prior to resection was performed using HealthMyne, a novel lesion analytic software. Volumetric segmentation was performed to obtain 5 first order (pixel histogram parameters) and 13 second order Grey-Level Co-Occurrence Matrix texture features. Bivariate logistic regression identified texture features associated with mucinous cysts and HGD/malignancy. A stepwise selection model identified predictive features in a training set of 2/3 of all cysts, and performance was assessed in the remaining test set. Stratified random sampling ensured the same proportion of mucinous to non-mucinous cysts between datasets. A stepwise model for mucinous cysts identified texture features predictive of HGD/malignancy.

Results: A total of 77 resected pancreatic cysts were included (mean size 3.4 ± 2.2 cm), of which 59 (77%) were mucinous, and 18 (23%) were non-mucinous. Mucinous cysts included 17 mucinous cystic neoplasms (29%), 41 intraductal papillary mucinous neoplasms (IPMN) (69%) and 1 unspecified mucinous cyst. Nine of the mucinous cysts (15%) had associated invasive malignancy. Of the mucinous cysts where the pathology report commented on grade of dysplasia ($n=46$), 15 (33%) had associated high grade dysplasia. On univariate analysis, two first order features (skewness and mean gray level intensity) were significantly correlated with a mucinous (vs non-mucinous) pathology, while no second order texture features were significantly correlated. The average skewness for mucinous cysts was 0.46 ± 0.78 vs -0.004 ± 0.43 for non-mucinous cysts, and the average mean for mucinous cysts was 32 ± 18 Hounsfield units (HU) vs 47 ± 23 HUs for non-mucinous cysts ($p=0.02$ and <0.01 , respectively). The stepwise regression model found skewness alone to be significantly predictive of mucinous cysts in the training set (Odds Ratio (OR) 14.3, 95% CI 1.7-118, AUC 0.77), and the model demonstrated overall accuracy of 76%, sensitivity of 95% and specificity of 17% in the test set. For mucinous cysts with HGD/malignancy vs not, univariate analysis found the first order feature mean gray level intensity to be significant (43 ± 22 HU vs 27 ± 15 HU). Mean remained significant in the stepwise model (OR 1.04, 95% CI 1.0-1.1) with accuracy of 71%, sensitivity of 35% and specificity of 93% (AUC 0.72) (Figure 1).

Conclusion: Two first order texture features identified mucinous cysts and the presence of HGD/malignancy with good accuracy. Textural analysis of pancreatic cysts may provide a non-invasive means of differentiation of mucinous cysts from non-mucinous ones. Further, the identification of texture features associated with pre-invasive and invasive cancer within cysts may better inform pre-operative decision-making. This promising area of radiomics deserves further study.

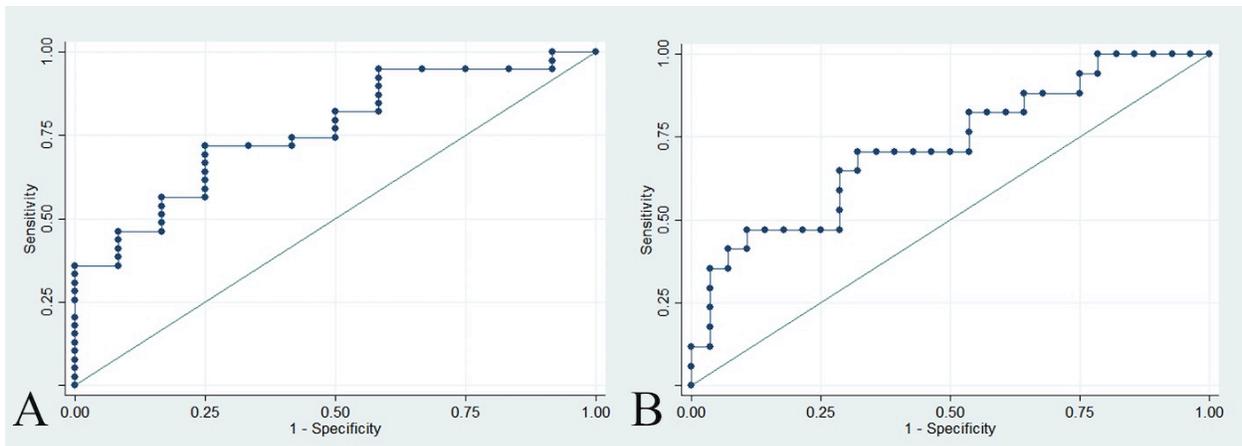


Figure 1. Receiver operating characteristic (ROC) curves demonstrating differentiation of pathologically-confirmed mucinous cysts and mucinous cysts with or without high grade dysplasia (HGD) or malignancy using quantitative first order CT imaging texture characteristics. (A) A stepwise selection model identified that skewness, a first order texture feature, differentiated mucinous from non-mucinous cysts in the training set with an area under the curve (AUC) of 0.77 ($\sigma = 0.05$). **(B)** A stepwise model identified the first order texture feature mean gray level intensity identified the presence of HGD or malignancy in mucinous cysts with AUC of 0.72 ($\sigma = 0.05$).

P 92. INTENSIVE PERIOPERATIVE REHABILITATION IMPROVES SURGICAL OUTCOMES AFTER PANCREATICOUDENECTOMY

Y Kitahata, M Kawai, S Hirono, K Okada, M Miyazawa, R Kobayashi, H Yamaue

Presenter: Yuji Kitahata MD, PhD | Wakayama Medical University

Background: Although the mortality rate for pancreaticoduodenectomy (PD) has decreased to around 2.8–5% in high-volume centers, postoperative complications are still common in 30–50% of cases. Preoperative exercise, called “prehabilitation,” has been recently reported to reduce the frequency of complications after surgery. This study aims to evaluate the impact of the intensive perioperative rehabilitation on improvement of surgical outcomes for patients undergoing PD.

Methods: Between 2003 and 2014, 576 consecutive patients underwent PD in Wakayama Medical University Hospital. Of these, 331 patients received perioperative rehabilitation combined with prehabilitation and postoperative rehabilitation between 2009 and 2014. Previously, 245 patients underwent PD without perioperative rehabilitation between 2003 and 2008. We compared surgical outcomes between the patients undergoing PD with and without perioperative rehabilitation to evaluate the efficacy of our rehabilitation program. Results

Results: The frequency of pulmonary complications was significantly lower in patients undergoing PD with perioperative rehabilitation than those without (0.9% vs. 4.3%, $P = 0.011$). There were no significant differences in other complication or mortality rates. Length of hospital stay was also shorter in patients receiving perioperative rehabilitation than that of those not receiving it (16 vs. 24 days, $P < 0.001$).

Conclusion: Intensive perioperative rehabilitation might reduce postoperative pulmonary complications and shorten postoperative hospital stay after PD. Therefore, we suggest that perioperative rehabilitation should be included as part of enhanced recovery after surgery for patients undergoing PD, although further large-scale studies are necessary to confirm our results.

P 95. IMPACT OF PERIOPERATIVE HYPERGLYCEMIA ON POST-OPERATIVE MORBIDITY AND OVERALL SURVIVAL IN PATIENTS UNDERGOING ONCOLOGIC PANCREATOBILIARY SURGERY

M Chumakova, EA Aleassa, G Morris-Stiff

Presenter: Essa M. Aleassa MD | Cleveland Clinic Foundation

Background: Postoperative hyperglycemia is a common finding in surgical patients and has been implicated in multiple adverse outcomes. The aim of this study was to examine the effects of postoperative hyperglycemia on patient outcomes following pancreatic resection for malignancy.

Methods: Data from the American College of Surgeons National Surgical Quality Improvement (ACS-NSQIP) registry was used to identify all patients undergoing pancreatic resection for a malignancy (proximal, distal, or total pancreatectomy) at a single institution between January 2011 and December 2016. Data analyzed from the ACS-NSQIP database included patient demographics, and co-morbidities and details of operative procedures. Average post-operative blood glucose levels were obtained from the patient electronic record. Primary endpoints included post-operative morbidity and overall survival.

Results: 370 patients were identified; 54.3% were men with median age of 65.7 years. 221 (59.7%) patients were found to have average post-operative blood glucose 160mg/dL. Of those with hyperglycemia, 113 (30.5%) had levels of 160-250mg/dL, and for 36 (13.3%) glucose level was >250mg/dL. Myocardial infarction (MI) was found in 0% of those with blood glucose 250mg/dL ($p=0.044$). The average survival durations were 47, 24 and 17 months for those with post-operative blood glucose of 250mg/dL respectively (95% CI).

Conclusion: The data would suggest that poor post-operative blood glucose control may have significant long as well as the well documented short-term effects. Aggressive blood glucose control should be employed in the post-operative period in order to minimize morbidity and increase overall survival.

P 98. COMPARISON OF PANCREATIC ADENOCARCINOMA LIVER METASTASIS DETECTION BETWEEN COMPUTER TOMOGRAPHY AND MAGNETIC RESONANCE IMAGING

A Rosales, A Stoylen, A Wallace, H Asbun, L Tsamalaidze, JA Stauffer

Presenter: Armando Rosales MD | Mayo Clinic Florida

Background: Majority of patients with pancreatic adenocarcinoma (PDAC) have metastatic disease, especially of the liver or peritoneum. Proper staging is critical to avoid non-therapeutic operations or futile resections. Imaging studies are important to determine resectability yet occult metastatic disease remains a major problem. Computerized Tomography (CT) is the most common modality to assess this, however, magnetic resonance imaging (MRI) can detect liver metastasis or peritoneal disease not appreciated by CT. Pancreatic protocol MRI is used for staging of PDAC at our institution. We reviewed our experience with MRI staging to determine the utility of this imaging modality in comparison to CT.

Methods: With IRB approval, we retrospectively reviewed the charts of all patients seen in our institution with diagnosis of PDAC between 2007 and 2017 that had both an abdominopelvic CT and MRI within one month between studies. All patients who did not have these imaging studies were excluded. Images studies were either from outside or our institution. Image studies were reviewed by the surgeon and radiologist.

Results: Overall, 302 patients [male: 156 (52%), female: 146 (48%)] met inclusion criteria. Of these, 26 (8.6%) had a CT without evidence of liver metastasis, yet were found to have hepatic lesions by MRI. Two patients (0.7%) had concomitant peritoneal carcinomatosis only identified by MRI. Overall, 122 (40%) patients were taken for curative surgery (pancreaticoduodenectomy: 77, distal pancreatectomy: 42 and total pancreatectomy: 4). At the time of surgery, two patients (0.7%) had peritoneal carcinomatosis not previously identified by either CT or MRI. There were no patients found to have unrecognized liver metastases. Two patients (0.7%) that initially were reported to have liver metastasis by CT were identified by MRI to have no evidence of liver metastases.

Conclusion: Accurate preoperative staging is imperative for patients diagnosed with PDAC. Both CT and MRI are excellent tools to determine tumor-vascular interface to determine local resectability. However, MRI has significant advantages over CT to identify and establish the presence or absence of liver metastases and peritoneal involvement for PDAC.

P 99. PORTOMESENERIC VENOUS COMPLICATIONS FOLLOWING PANCREATIC RESECTION: TOWARD DEVELOPMENT OF A CLINICAL SCORING SYSTEM TO PREDICT INCIDENCE, SEQUELAE AND MANAGEMENT

L Yohanathan, SM Thompson, WS Harmsen, RL Smoot, MJ Truty, TE Grotz, SP Cleary, DM Nagorney, JC Andrews, ML Kendrick

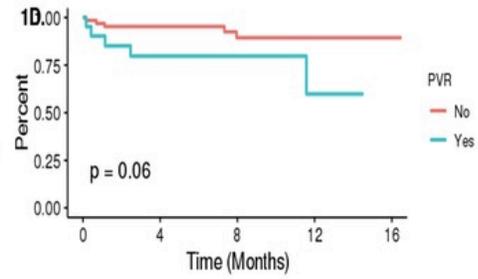
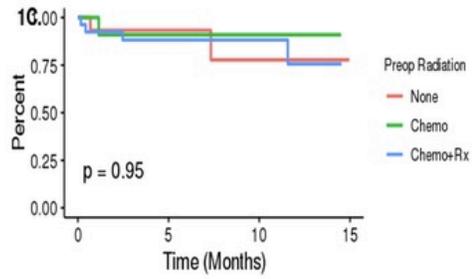
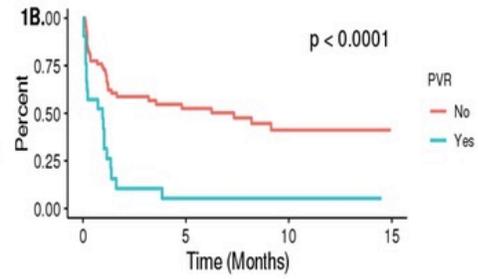
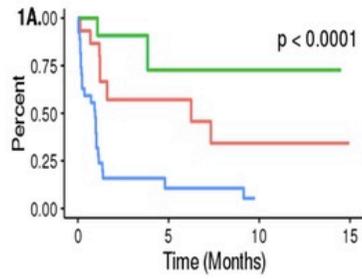
Presenter: Lavanya Yohanathan MD | Mayo Clinic Rochester

Background: Borderline resectable and locally advanced pancreatic adenocarcinomas are commonly encountered in our practice. This leads to increasing utilization of neoadjuvant chemoradiotherapy and need for vascular (arterial and venous) resection and reconstruction. The occurrence of portomesenteric venous complications after pancreatic resection appears to be increasing. However, factors predicting the incidence of venous complications such as portal vein thrombosis/occlusion or superior mesenteric vein thrombosis/occlusion are not well established. We sought out to evaluate the incidence, natural history and identification of potential risk factors that lead to portomesenteric venous complications following a Whipple procedure.

Methods: Single site, retrospective review of patients who underwent a Whipple operation between 2015-2017. Clinical data, including patient demographics, preoperative therapy details (upfront resection, versus neoadjuvant chemotherapy versus neoadjuvant chemoradiotherapy), operative details, pathology details and postoperative portomesenteric venous complications were recorded based on retrospective data analysis. All imaging studies were independently reviewed by a radiologist to assess the incidence of portomesenteric venous narrowing as well as portomesenteric venous thrombosis following operation over the time period that each patient underwent imaging at our institution

Results: 105 patients that underwent pancreaticoduodenectomy were identified. Mean age was 64 yrs. 51 patients (48.6%) underwent neoadjuvant chemotherapy, 42 patients (40%) underwent neoadjuvant radiation. At surgery 24 patients (23%) underwent vein resection and 5 patients (5%) underwent arterial resection. 46 patients (49%) had a postoperative fluid collection of which 12.5% were pancreatic fistula. On postoperative surveillance, portal vein (PV) narrowing was present in 18 patients (19.1%), 8 of which resolved, and 4 required stenting. Superior mesenteric vein (SMV) narrowing was present in 38 patients (40%), 15 of which resolved and 4 required stenting. PV thrombosis was associated with presence of a postoperative fluid collection ($p < 0.03$). SMV narrowing was associated with postoperative fluid collection ($p < 0.001$), neoadjuvant radiation ($p < 0.02$) and vein resection ($p < 0.0001$). Stenting of the PV and SMV were associated with vein resection ($p < 0.01$ and $p < 0.05$). In a univariate model patients who received neoadjuvant chemoradiotherapy compared to neoadjuvant chemotherapy alone were at a significantly higher risk of postoperative PV narrowing ($p < 0.001$) with a HR=11.4, 95% CI 2.7-48.9. A patient who had upfront resection, relative to a patient with neoadjuvant chemotherapy alone was at a non-significant increased risk of postoperative PV narrowing ($p = 0.13$) with a HR=3.3, 95% CI 0.7-15.6. In the same model, patients undergoing portal vein resection had a significantly increased risk of post-operative narrowing ($p < 0.001$) with more than 3-fold increased risk, HR=3.3, 95% CI 1.9-5.9.

Conclusion: Preliminary data suggest that neoadjuvant radiation, vein resection and postoperative fluid collection may be risk factors for portomesenteric venous complications following pancreaticoduodenectomy. The need to define and identify these patients is of utmost significance to evaluate the natural history of PV narrowing and thrombosis, to assist in our understanding of which patients benefit from stenting and the timing to stent.



1A: Percent free of PV narrowing by receipt of neoadjuvant chemotherapy or chemoradiation

1B: Percent free of PV narrowing by portal vein resection

1C: Percent free of PV thrombus by receipt of neoadjuvant chemotherapy or chemoradiation

1D: Percent free of PV thrombus by portal vein resection

P 100. ACINAR CELL CARCINOMA OF THE PANCREAS: A HISTOLOGICALLY AND EPIDEMIOLOGICALLY DISTINCT ENTITY

JA Yonkus, JR Bergquist, T Ivanics, TR Halfdanarson, RL Smoot, SP Cleary, DM Nagorney, ML Kendrick, MJ Truty

Presenter: Jennifer Yonkus MD | Mayo Clinic Rochester

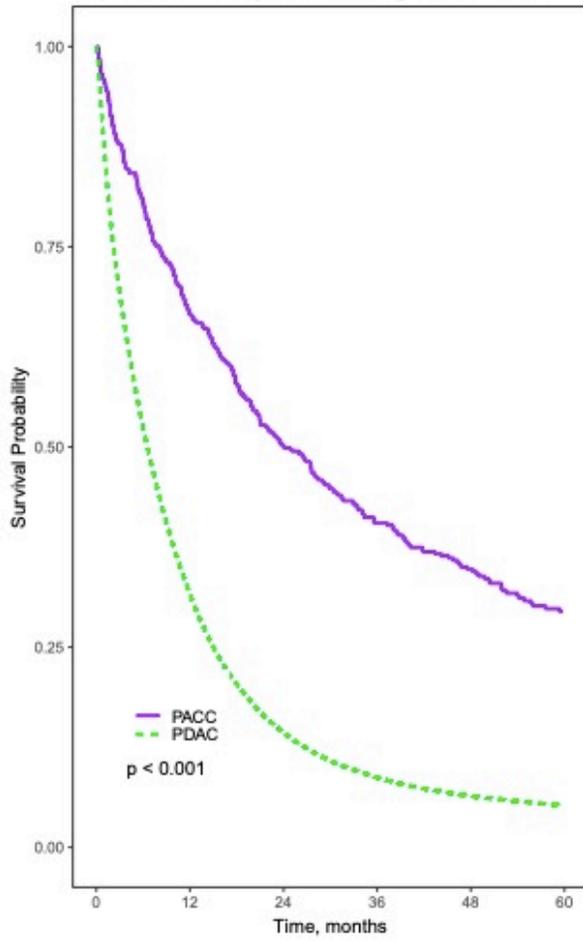
Background: Pancreatic Acinar Cell Carcinoma (PACC) is a rare primary pancreatic exocrine malignancy and is histologically distinct from pancreatic ductal adenocarcinoma (PDAC). Limited previous studies have evaluated the differences between PACC and PDAC; however there have been no recent population database updates specifically assessing incidence, treatment, and outcome trends over time.

Methods: Data from the Surveillance Epidemiology and End Results (SEER) and National Cancer Data Base (NCDB) were collected for patients with histologically proven PDAC and PACC of a contemporary cohort from 2004-2015. Parametric univariate analyses were performed to compare patient characteristics, tumor types and outcomes. Incidence trends were determined relative to the US standardized population and were calculated using SEER data. Unadjusted and adjusted Kaplan-Meier Survival analyses were performed using the NCDB database. P value for all reported comparisons is <0.01 , unless otherwise noted.

Results: We identified 121,001 patients with PDAC and 547 with PACC. Incidence of PACC increased by 73% over the twelve year study period. Stage-specific survival was found to be significantly better for all stages of PACC when compared to PDAC (Figure) with the greatest difference in survival probability difference in Stage I patients. Patients with ACC were more likely to be male (66.2% vs 50.5%) and to have significantly larger tumors (65.29 cm vs 41.95 cm) at the time of diagnosis. The proportion of patients with localized disease was 37.8% in PACC vs. 25.5% in PDAC. The minority of patients with localized PDAC underwent surgical resection compared to localized PACC (18% vs 44%). Among resected patients, those with PDAC were more likely to receive adjuvant systemic chemotherapy (66.4 vs. 54.2%) and radiation (39.2 vs. 28.5%) than those with PACC. A minority of patients treated with neoadjuvant systemic chemotherapy (21.2% PDAC and 16.1% PACC). PACC was more likely to be lower grade and less likely to demonstrate histopathologic lymphovascular invasion. Negative margins were obtained more often after resection for PACC than with PDAC (32.5% vs 11.8%). Among resected patients, after adjustment for clinically relevant factors (stage, grade, node status, margins, radiation and chemotherapy), PDAC histology remained the strongest independent predictor of mortality hazard (HR 2.33, 95% CI 1.95-2.78).

Conclusion: PACC is a rare histologically and biologically distinct exocrine pancreatic cancer with a rising incidence in the modern era. Independent of disease stage, PACC has better overall survival in both unadjusted analysis and after adjustment for other clinically relevant predictors of mortality. Despite its presentation with larger tumor size, PACC demonstrates less aggressive features than its PDAC counterpart.

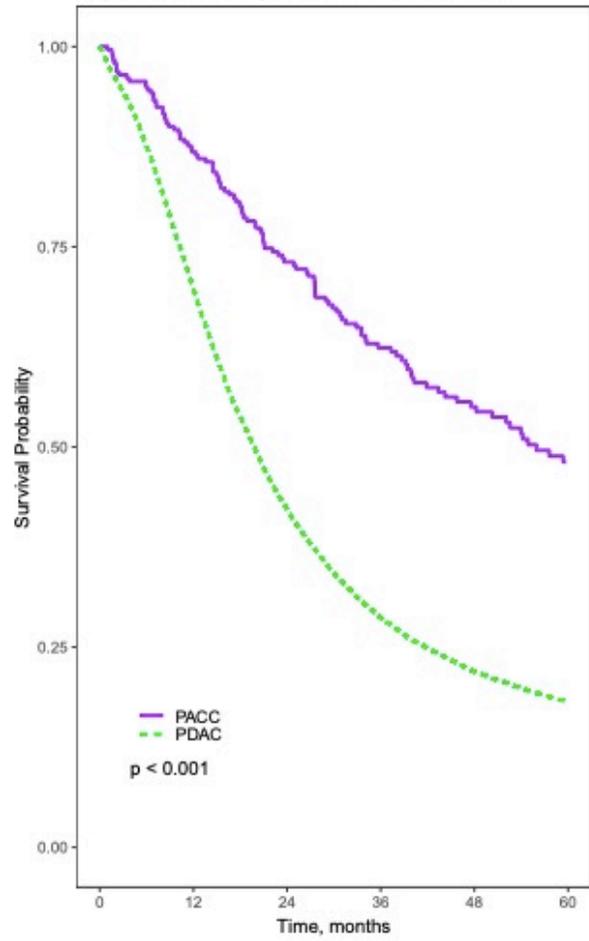
Kaplan Meier Analysis for All Stages Combined



PACC	547	355	246	169	121	88
PDAC	120986	37110	15252	7675	4573	2949

Numbers at risk

Kaplan Meier Analysis for Resected Patients



PACC	253	215	170	121	87	66
PDAC	22253	15191	8531	4956	3187	2148

Numbers at risk

P 101. IMPACT OF AREA OF DEPRIVATION INDEX ON HOSPITAL READMISSIONS AFTER SURGERY FOR PANCREAS CANCER

AN Krepline, J Mora, M Aldakkak, S Misustin, KK Christians, CN Clarke, B George, PS Ritch, WA Hall, BA Erickson, N Kulkarni, AH Khan, DB Evans, S Tsai

Presenter: Ashley Krepline MD | Medical College of Wisconsin

Background: Area of deprivation index (ADI) is a validated metric used to quantify socioeconomic disadvantages by neighborhood. The ADI is composed of 17 educational, employment, housing, and poverty measures abstracted from the US Census Long Form and the American Community Survey; higher ADIs signify a more disadvantaged neighborhood. We sought to examine the impact of ADI on readmission rates after surgery among patients with pancreatic cancer (PC).

Methods: Patients with resectable and borderline resectable PC treated at the Medical College of Wisconsin from 2009 to 2018 were identified. The ADI for all patients was obtained using the zip code+4 code. Patients were dichotomized into low and high ADI categories based on the median ADI. Demographic, clinicopathologic, and readmission data for patients were abstracted.

Results: Neoadjuvant therapy and surgery was completed in 310 patients with resectable and borderline resectable PC. The median ADI was 97.32 (IQR 17.7), 155 (50%) with low ADI and 155 (50%) with high ADI. No differences were observed between groups in demographic characteristics, clinical stage, baseline carbohydrate antigen 19-9, or type of neoadjuvant therapy received. In addition, no differences were observed between low and high ADI groups in the types of operation performed, need for vascular reconstruction, hospital length of stay, or pathologic stage. Of the 310 patients, 66 (21%) had a readmission within 90 days of surgery; 26 (17%) of the 155 patients with a low ADI and 40 (26%) of the 155 patients with high ADI ($p=0.049$). Among the low and high ADI groups, the most common reasons for readmission were procedure-related complications ($n=16$ (10%) vs. 23 (15%) patients, $p=0.30$) and failure to thrive ($n=7$ (5%) vs. 13 (8%) patients, $p=0.25$), respectively. For patients with low vs. high ADI, readmission occurred at a median of 19 days (IQR 14) and 27 (IQR 24), respectively ($p=0.02$). In a multivariable logistic regression, high ADI was associated with 1.80-fold increased odds of 90-day readmission (95% CI:1.02-3.16, $p=0.04$).

Conclusion: ADI was not associated with more advanced clinical or pathologic stage or operation performed. However, patients with high ADI were at increased risk for 90-day readmission. Additional studies are needed to identify modifiable factors associated with readmissions in this high-risk group.

P 102. THE IMPACT OF SURGICAL RESECTION AFTER INITIAL CHEMORADIOOTHERAPY FOLLOWED BY SYSTEMIC CHEMOTHERAPY FOR LOCALLY ADVANCED PANCREATIC ADENOCARCINOMA

M Kishiwada, A Hayasaki, T Fujii, Y Iizawa, H Kato, A Tanemura, Y Murata, Y Azumi, N Kuriyama, S Mizuno, M Usui, H Sakurai, S Isaji

Presenter: Masashi Kishiwada MD, PhD | Mie University School of Medicine

Background: NCCN2018 guideline recommend systemic chemo(radio)therapy as a first-line therapy for locally advanced pancreatic adenocarcinoma (PDAC) and consider resection as second-line therapy for good PS and disease response patients if feasible. However, the impact of surgical resection after preoperative therapy is unknown. Our institution has been performing initial chemoradiotherapy (CRT) followed by chemotherapy for locally advanced PDAC. At the time of reassessment, we determined that curative-intent resection was possible when the following findings on MDCT were observed: no stenosis or change of shape in the CA and SMA, the absence of metastatic lesions in other distant organs, down stage case.

Methods: The 345 consecutive patients with cytologically/histologically proven PDAC from February 2005 to December 2017 had been enrolled for our protocol of CRT regimen. CRT regimen: radiation therapy (total dose, 45 to 50.4 Gy, 25 to 28 fractions) with chemotherapy, which include G-CRT (2005.2-2011.10, n=128): gemcitabine (800mg/m², day1,8,22,29) and GS-CRT (2011.11-2017.12, n=217): gemcitabine (600mg/m², day8,22,36,50)+ oral S-1 (60/m², day1-21 and day 29-49). These patients were retrospectively classified into Japan Pancreas Society (JPS) resectability based on MD-CT. After CRT, systemic chemotherapy had been performed by evaluating disease status every 3 months. The patients underwent curative-intent resection after serial re-evaluations. We evaluated survival rates, R0 resection, biological factors (CA19-9 levels before CRT) and conditional factor (Performance status: PS) in locally advanced PDAC.

Results: The re-evaluated 320 patients were classified as R in 70 patients, BR in 90 and UR-LA in 160. The 25 patients were excluded because they were not re-evaluated due to CRT incompleteness (n=10), rejection (n=11) and no come-back to the hospital (n=4). In locally advanced PDAC, the 75 patients (46.9%) were precluded from surgery due to distant metastasis and no improvement of local status at the time of restaging and the 73 patients (45.6%) underwent surgical resection. The rate of R0 resection was 63.2%. Median survival time (MST) in enrolled patients was 18.0 M. There was significant different survival between resected patients (n=73) and no resected patients (n=87), 24.3M vs.13.9M, P=0.0008. High CA19-9 level patients (>500) was significantly shorter survival time: CA19-9<500(n=109) vs CA19-9 (n=52); MST:21.4 M vs 13.8 M (P<0.001). Poor PS was significantly shorter survival time: PS 0-1(n=151) vs PS 2-3 (n=10); MST:19.3 M vs 7.6 M (P<0.001).

Conclusion: Our CRT protocol for locally advanced PDAC Patients with good PS and low CA19-9 level can select the patients who are likely to benefit from aggressive resection.

P 103. A RETROSPECTIVE COHORT STUDY OF 4,739 PATIENTS WITH PANCREATIC NEUROENDOCRINE TUMORS IDENTIFIES PROLONGED SURVIVAL AFTER SURGICAL RESECTION EVEN IN ADVANCED STAGES

BD Powers, A Kumar, JB Fleming MD, JR Strosberg, DA Anaya

Presenter: Benjamin Powers MD | Moffitt Cancer Center

Background: The management of patients with PNETs according to clinical stage and tumor grade remains controversial. The new AJCC Staging Manual attempts to address this through a new staging system for PNETs that excludes poorly-differentiated and undifferentiated tumors (neuroendocrine carcinoma). In this study, we assess surgical utilization and impact on survival in patients with well- and moderately-differentiated PNETs using AJCC 8th criteria and measure outcomes for stages I, II/III, and IV disease.

Methods: Using data from the NCCDB (2004-2013) we included patients 18 years or older with pancreatic tumors (C25.0 to 25.9); tumor histology codes for PNETs; and well-differentiated and moderately-differentiated tumors. Poorly or undifferentiated neuroendocrine tumors and carcinomas, patients who received treatment at a site other than the reporting center, patients with multiple cancers, and patients with incomplete staging data were excluded. This identified 4,739 patients. 8th edition staging for based on clinical TNM data was used for univariate and multivariate logistic regression models to evaluate clinicodemographic factors associated with receipt of surgery. 8th edition staging for based on pathological TNM data was used for univariate and multivariate Cox regression models to evaluate clinicodemographic factors associated with overall survival.

Results: 3,866 patients (81.6%) underwent surgical resection. Drivers of surgical utilization varied significantly by stage. For clinical stage I and II/III patients, surgery was more likely for patients with body or tail tumors relative to pancreatic head tumors. For stage II/III, and IV patients, community facility type predicted decreased odds of surgery. Predictors of overall survival also varied by stage. For stage I patients, receipt of surgery, tumor location and community facility type were not associated with survival. However, for stage II/III and IV patients, surgery was associated with decreased mortality. Community facility type was associated with increased mortality for stage II/III patients but not for stage IV patients.

Conclusion: When staged according to the 8th Edition of the AJCC manual, surgical resection of the PNET was associated with improved survival in patients of all stages except stage I. Tumor location in the body/tail predicted increased receipt of surgery however neither surgery or tumor location were associated with survival. These observations suggest that local control of the primary PNET through surgical resection drives outcomes even in advanced stage and should be considered in the multidisciplinary management of PNETs.

	Hazard Ratios [95% CI]							
	Overall (n=3,211, events=658)		Stage I (n=689, events=36)		Stage II/III (n=1,912, events 243)		Stage IV (n=901, events=426)	
	Univariable	Multivariable	Univariable	Multivariable	Univariable	Multivariable	Univariable	Multivariable
Surgical Resection (ref: none)	0.14 [0.12-0.17]	0.23 [0.17-0.30]	0.51 [0.18-1.44]	0.74 [0.25-2.19]	0.17 [0.12-0.22]	0.23 [0.17-0.31]	0.27 [0.22-0.35]	0.29 [0.23-0.38]
Community facility type (ref: academic)	1.71 [1.47-1.99]	1.29 [1.10-1.51]	2.26 [1.15-4.44]	1.77 [0.88-3.59]	1.74 [1.34-2.25]	1.56 [1.20-2.03]	1.58 [1.29-1.92]	1.14 [0.93-1.40]

Overall multivariable model was adjusted for age, sex, year of diagnosis, grade, stage, tumor location, comorbidities, insurance status and facility type.

P 104. SUB-ADVENTITIAL DIVESTMENT TECHNIQUE FOR ARTERY-INVOLVED PANCREATIC CANCER: SAFETY AND ONCOLOGICAL EFFICACY

Y Miao, B Cai, Z Lu, K Zhang, L Yin, Y Gao, K Jiang

Presenter: Kuirong Jiang MD, PhD | Pancreas Center, The First Affiliated Hospital with Nanjing Medical University

Background: Artery involvement is the major obstacle of curative operation for non-metastatic pancreatic cancer patients. Here we present the sub-adventitial divestment technique (SADIT) in therapeutic procedures for artery involved pancreatic cancer(ai-PC).

Methods: From April 2014 to June 2016, a total of 73 consecutive ai-PC patients identified with contrast-enhanced CT and surgical exploration received curative pancreatectomies with SADIT were included as the study group (SADIT group). To evaluate safety of SADIT, 247 concurrent pancreatic cancer patients without artery involvement who received curative pancreatectomies served as control (CTRL group). Uni- and multi-variate analysis of demographic and clinical data was performed to reveal risk factors of prognosis. Propensity scored matching (PSM) analysis was performed with independent risk factors to compare the median overall survival (MOS) between two groups of patients. Another 13 T4NxM0 patients who received palliative chemotherapy alone without resection (PALLI group) were further introduced and compared with SADIT group to evaluate oncological efficacy of SADIT.

Results: Gender, age, preoperative CA19-9 and serum albumin showed no difference between two groups. SADIT group tend to have more major vein resection and reconstruction, combined organ resection and extended lymph node dissection. Longer operation time was shown in SADIT group (SADIT vs CTRL: 265.4±101.4 min vs 228.7±90.2 min, p=0.003) without significant increase of estimated blood loss (SADIT vs CTRL: 347±323 mL vs 283±315 mL, p=0.131). Over-all morbidity, incidence of ISGPS post-operative pancreatic fistula, delayed gastric emptying and re-operation rate were of no difference between two groups, while SADIT group had more post-operative hemorrhage (SADIT vs CTRL: 16.4% vs 6.5%, p= 0.016). More 90-day post-operative mortality was observed in SADIT group, though statistically insignificant (SADIT vs CTRL: 6.8% vs 2.0%, p= 0.052). Pre-operative CA19-9, tumor grading, tumor size and nodal status were independent risk factors for survival of resected pancreatic cancer patients and were further utilized in PSM analysis. A PSM analysis was finally carried out in 58 (SADIT group) vs 58 (CTRL group), and revealed no statistical difference in MOS between T4 SADIT group and T1-3NxM0 CTRL group (SADIT vs CTRL: 13.5 months vs 15.1 months, p=0.775). Furthermore, T4NxM0 patients had significantly longer MOS after resection with SADIT technique followed by adjuvant therapy in comparison with those only treated with palliative chemotherapy (SADIT+Chemo vs Chemo: 18.0 months vs 12.4 months, p=0.003).

Conclusion: SADIT is generally safe in surgery for ai-PC. However, the higher risk of post-operative hemorrhage and 90-day post-operative mortality should be noticed and the procedure should be performed in large-volume center. Resection with SADIT provided MOS benefit of 6 months to ai-PC patients with chemotherapy. With similar tumor biology defined by CA19-9, tumor grading, tumor size and nodal status, pancreatectomy with SADIT could offer similar prognosis for ai-PC patients (T4NxM0) comparing to T1-3NxM0 cases. Valid prediction method for tumor biology is warranted to provide more precise strategy for PC and guide the selective utilization of SADIT.

P 105. CLINICAL IMPLICATIONS OF AN UNPLANNED CONVERSION (UC) DURING MINIMALLY INVASIVE PANCREATODUODENECTOMY (MIPD) – REVIEW OF AMERICAN COLLEGE OF SURGEONS NATIONAL SURGICAL QUALITY IMPROVEMENT PROGRAM (NSQIP) DATA FROM 2014 - 2016

AM Schneider, E Alonso, ES Tang, ST Chiu, ML Babicky, PH Newell, PD Hansen

Presenter: Andreas Schneider MD | Providence Portland Medical Center

Background: With the increasing use of minimally invasive techniques during pancreaticoduodenectomy (PD) for benign and malignant diseases, unplanned conversions to an open procedure are occurring more frequently. Conversion has been associated in other gastrointestinal diseases with increased complications and worse outcomes but the short term impact on patients undergoing MIPD remains unclear.

Methods: We conducted a retrospective review of the American College of Surgeons National Surgical Quality Improvement Program (NSQIP) and Procedure Targeted Data set (PTD) from 2014-2016. Patients who successfully underwent totally laparoscopic or robotic PD were included, as were those that experienced an unplanned conversion to an open procedure. Uni-variant and multi-variant analysis was performed between the groups. Emergent cases and patients who underwent hand assisted, open or hybrid procedures were excluded.

Results: Overall 10790 PDs were performed during 2014- 2016, of these 862 underwent minimally invasive resections. Inclusion criteria were met in 684 patients, of these 506 (74%) patients successfully underwent MIPD. Robotic PD was performed in 320 patients (62%) and 186 patients (37%) underwent laparoscopic PD. ($p < 0.0001$). Unplanned conversion to open was performed in 178 patients (26%) and was more common in patients initially planned for laparoscopy resection (72%) ($p < 0.0001$). Preoperative chemotherapy, small pancreatic duct size, soft pancreatic gland texture and benign disease were more commonly seen in those who successfully underwent MIPD. Major vascular resection was more frequent in the conversion group, 32% vs. 8% ($p < 0.0001$). Unplanned conversion was associated with higher post-operative complications (33% vs. 23%), increased rates of percutaneous drainage and clinically relevant pancreatic fistulae (18% vs. 11%). Unplanned returns to the operating room, readmission and death rates were comparable between both groups.

Conclusion: Unplanned conversion comes with a cost to the patient as it is associated, in our study, with an increase in post-operative morbidity and pancreatic fistula rate. Reoperation, readmission and death rates though are not affected. Traditional high risk features such as soft gland, benign disease and small pancreatic duct were not associated with conversion, nor was pre-operative chemotherapy, tumor size, lymph node status or metastasis. Major vascular resection was seen more frequently in patients with an unplanned conversion. Patients undergoing robotic resection were more likely to complete the procedure without conversion.

Table1 Demographic variables and risk factors

Variables		MS N=506		Conversion N=178		P-value
		N	%	N	%	
Laparoscopic and robotic	Laparoscopic	186	37	128	72	<0.0001
	Robotic	320	63	50	28	
Gender	Female	242	48	69	39	0.0988
	Male	264	52	109	61	
Race	White	411	81	146	82	0.9718
	Non-White	56	11	32	18	
Diabetes	No	399	79	134	75	0.3229
	Yes	107	21	44	25	
ASA class	1-No Disturb	2	0	0	0	0.4162
	2-Mild Disturb	134	23	39	22	
	3-Severe Disturb	368	73	127	71	
	4-Life Threat	20	4	12	7	
Preop jaundice	No	323	64	102	58	0.1566
	Yes	182	36	76	42	
Preop stent	No	259	52	82	48	0.3955
	Yes	239	48	88	52	
Preop chemo therapy	No	405	80	156	88	0.0174
	Yes	100	20	21	12	
Preop radiation	No	480	95	171	97	0.391
	Yes	25	5	6	3	
Pancreatic Duct Size	<3 mm	151	30	35	20	<0.0001
	3-6 mm	189	37	63	35	
	>6 mm	75	15	13	7	
	Unknown	91	18	67	38	
Pancreatic Gland Texture	Hard	133	26	53	30	0.0088
	Intermediate	31	6	19	11	
	Soft	236	47	59	33	
	Unknown	106	21	47	26	
Major vascular resection	Artery	10	2	8	5	<0.0001
	Vein	22	4	37	21	
	Vein and artery	6	1	11	6	
	Not performed	461	92	118	68	
Malignant Disease	No	461	92	118	68	<0.0001
	Yes	38	8	56	32	
Benign Disease	No	116	22.92	32	17.98	0.168
	Yes	390	77	146	82	
Benign Tumor Size	<2 cm	284	56	140	79	<0.0001
	>2 cm	222	44	38	21	
Benign Tumor Size	<2 cm	28	5.5	4	2.2	0.0627
	2-5 cm	64	12.6	14	7.8	
	>5 cm	14	2.7	4	2.2	
T STAGE	T0	5	1	1	0.5	0.5245
	T1	50	9.8	13	7.3	
	T2	54	10.6	23	12.9	
	T3	243	47.9	98	55	
	T4	30	5.9	8	4.5	
	Tis	5	1	0	0	
	Tx	3	0.6	0	0	
N STAGE	N0	163	32.2	44	24.7	0.0686
	N1	219	43.3	97	54.5	
	Nx	2	0.4	0	0	
M STAGE	M0/Mx	322	63.6	101	56.7	0.0661
	M1	6	1.2	3	1.7	

P 108. SMALL PANCREATIC NEUROENDOCRINE TUMORS: RESECT OR ENUCLEATE

JD Beane, JD Borreback, AH Zureikat, HA Pitt

Presenter: Joal Beane MD | University of Pittsburgh Medical Center

Background: Debate continues regarding the best management for small pancreatic neuroendocrine tumors (PNETs). Those who recommend observation claim that the risk of malignancy is low and that the complications of resection are high. An alternative strategy to formal resection or observation is parenchymal sparing enucleation. Small series have compared resection with enucleation, but this comparison has not been performed at the continental level. The aim of this analysis is to compare the outcomes of resection and enucleation of small PNETs in North America.

Methods: The 2014-17 American College of Surgeons-National Surgical Quality Improvement Program Procedure-Targeted Pancreatectomy Participant Use File was queried. Patients with nonfunctional pancreatic neuroendocrine tumors classified as less than 2 cm in size and those classified as T1 or T2 were included. Patients undergoing either distal pancreatectomy (DP, N=712) or pancreatoduodenectomy (PD, N=297) were included in the resection cohort. During the same time, 127 patients (11%) had small PNETs enucleated. The resection and enucleation cohorts were compared for multiple demographic, comorbidity, and operative variables as well as postoperative outcomes. The threshold for statistical significance was set at a p-value ≤ 0.05 .

Results: The resected and enucleated cohorts were similar with respect to mean age (59 years in both), gender (53% vs 51% male), BMI (30 vs 31), tobacco use (14% vs 12%), diabetes (21% vs 20%), hypertension (53% vs 54%), COPD (3% vs 6%), and ASA class (2.67 vs 2.60). A minimally invasive (MIS) operative approach did not differ between the resected (48%) and enucleated (46%) patients. DP patients were more likely than those undergoing PD to have MIS (72% vs 10%, $p < 0.001$). Operative time was longer ($p < 0.01$) and perioperative transfusions were required more frequently in resected patients ($p < 0.01$) (Table). Clinically relevant postoperative pancreatic fistulas did not differ between resected and enucleated patients. Overall morbidity was higher in resected patients ($p < 0.01$, Table). Fifteen patients who underwent resection died postoperatively (1.5%) while all 127 enucleated patients survived surgery ($p = 0.058$). Mean postoperative length of stay was shorter in enucleated patients ($p < 0.01$). These findings remained statistically significant when DP and PD cohorts were compared to enucleations separately. In addition, patients who underwent a PD were more likely to develop any surgical site infection (13% vs 25%, $p < 0.01$), sepsis or septic shock (4% vs 12%, $p < 0.01$), delayed gastric emptying (6% vs 20%, $p < 0.001$), require percutaneous drain placement (13.4% vs 22.4%, $p = 0.03$), serious morbidity (17 vs 35%, $p < 0.001$), and mortality 0 vs 2.7%, $p = 0.016$).

Conclusion: In North America, only 11% of the operations performed on patients with small pancreatic neuroendocrine tumors (PNETs) are enucleations. Enucleation of PNETs takes less time and requires fewer transfusions than resection. Overall morbidity is lower and hospital stay is shorter with enucleation. Enucleation of small PNETs is an underutilized strategy.

Table. Comparison of resected and enucleated PNET patient outcomes

Outcome	Resected* (N=874)	Enucleated (97)	P Value
Operative Time (min)	260	170	<0.01
Transfusions (%)	7	2	<0.01
Overall Morbidity (%)	49	36	<0.01
Serious Morbidity (%)	24	17	0.08
CR-POPF (%)	15	14	NS
Mortality (%)	1.5	0	0.06
Length of Stay (days)	6.3	5.8	<0.01

CR-POPF: clinically relevant-postoperative pancreatic fistula

*Pancreatoduodenectomy + distal pancreatectomy

P 109. FACTORS ASSOCIATED WITH DELAYED GASTRIC EMPTYING AFTER PANCREATICODUODENECTOMY IN THE NATIONAL SURGICAL QUALITY IMPROVEMENT DATABASE

RA Snyder, JA Ewing, AA Parikh

Presenter: Rebecca Snyder MD, MPH | University of South Carolina School of Medicine-Greenville

Background: Delayed gastric emptying (DGE) is a common complication after pancreaticoduodenectomy (PD). However, findings regarding the incidence and risk factors for DGE have been difficult to interpret due to a lack of standardized definition of DGE across surgical centers. In 2014, the American College of Surgeons National Quality Improvement Program (ACS-NSQIP) initiated a pancreatectomy specific module to collect data specific to pancreatic resections including DGE. The primary aim of this study was to identify preoperative and intraoperative factors associated with the development of DGE using the standard ACS-NSQIP definition across a national, multicenter cohort of patients undergoing PD.

Methods: A retrospective cohort study of patients who underwent PD from 2014-2016 within the ACS-NSQIP pancreatectomy targeted module was performed. Demographic, clinical, and intraoperative variables were compared among patients with and without DGE. Multivariable (MV) logistic regression models were constructed using variables selected a priori to determine independent preoperative or intraoperative factors associated with the development of DGE.

Results: A total of 10,249 patients were identified, of which 16.6% developed DGE. Patients with DGE were older (65.3 vs. 64.3 years, $p < .001$) [OR 1.22 (95% CI 1.06-1.40)], ASA class ≥ 3 [OR 1.24 (95% CI 1.08-1.42)], pylorus preservation [OR 1.08 (95% CI 1.02-1.14)], and longer operative time [OR 1.26 (95% CI 1.13-1.40)] remained independently associated with DGE (Table). Preoperative chemotherapy, but not preoperative radiation, was independently associated with a decreased likelihood of development of DGE [chemotherapy: OR 0.77 (95% CI 0.64-0.93), radiation: OR 0.89 (95% CI 0.68-1.16)].

Conclusion: In this national, multicenter cohort of patients undergoing PD, 16.6% of patients developed delayed gastric emptying as determined by a standardized definition. Specific patient factors, including increased age, male sex, obesity, ASA class were independently associated with increased risk of DGE, as was increased operative time and pylorus preservation. However, preoperative chemotherapy was independently associated with decreased risk of DGE. Given these findings, further research is warranted to improve the preoperative prediction of patients likely to develop DGE and to identify opportunities to reduce DGE via preoperative rehabilitation strategies and treatment.

Table. Multivariable analysis of factors associated with pancreaticoduodenectomy (PD).

	Odds Ratio (95% Confidence Interval)	
Age	Reference	
<65	Reference	
≥65	1.259	(1.127, 1.408)
Sex	Reference	
Female	Reference	
Male	1.536	(1.377-1.715)
Pathology	Reference	
Benign	Reference	
Malignant	0.927	(0.803, 1.072)
Preoperative Jaundice	Reference	
Absent	Reference	
Present	0.829	(0.739, 0.93)
Diabetes Mellitus	Reference	
Absent	Reference	
Present	0.918	(0.81, 1.039)
ASA Class	Reference	
1-2	Reference	
≥3	1.238	(1.083, 1.418)
Body Mass Index (BMI)	Reference	
<25	Reference	
25-30	1.163	(1.024, 1.321)
30+	1.223	(1.064, 1.404)
Smoking Status	Reference	
Non-smoker	Reference	
Smoker	0.819	(0.705, 0.949)
Preoperative Weight Loss	Reference	
Absent	Reference	
Present	0.972	(0.836, 1.127)
Preoperative Chemotherapy	Reference	
No	Reference	
Yes	0.774	(0.643, 0.927)
Preoperative Radiation	Reference	
No	Reference	
Yes	0.891	(0.681, 1.158)
Anesthesia Technique	Reference	
General Anesthesia	Reference	
General and Epidural Anesthesia	1.067	(0.943, 1.206)
Operative Time	Reference	
< Median (356 minutes)	Reference	
> Median (356 minutes)	1.257	(1.126, 1.403)
Operative Technique	Reference	
Standard PD	Reference	
Pylorus preserving PD	1.076	(1.019, 1.137)
Operative approach	Reference	
Open	Reference	
Minimally Invasive	0.991	(0.812, 1.201)
Vein/Artery Resection	Reference	
No	Reference	
Yes	1.124	(0.972, 1.298)

P 110. COMPARISON OF SHORT- AND LONG-TERM OUTCOMES BETWEEN ANATOMICAL SUBTYPES OF RESECTED BILIARY TRACT CANCER IN A WESTERN HIGH-VOLUME CENTER

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Presenter: Marin Strijker MD | Amsterdam UMC

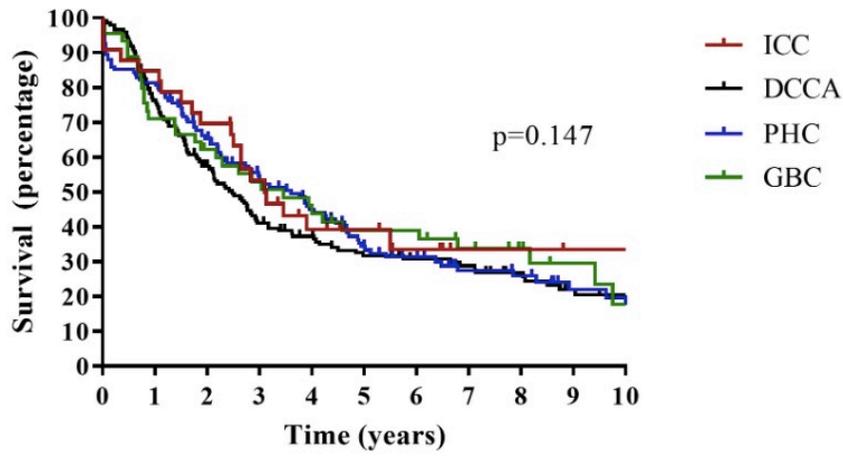
Background: In studies on long-term outcome and prognosis of resected biliary tract cancer (BTC), outcomes for the different anatomical subtypes - intrahepatic, perihilar and distal cholangiocarcinoma (ICC, PHC, DCC) and gallbladder carcinoma (GBC) - are often combined. However, variations in histopathological parameters and long-term outcome are unclear, hampering interpretation of combined outcomes. Therefore, the aim was to compare clinicopathological characteristics and outcomes between the anatomical subtypes of BTC in a Western high-volume center.

Methods: All patients who underwent resection for pathology proven ICC, PHC, DCC or GBC (2000-2016) were retrospectively selected from a prospectively maintained database. Clinicopathological characteristics and outcomes were compared between the four subtypes of BTC.

Results: Overall, 361 patients with resected BTC were included (33 ICC, 135 PHC, 148 DCC, 45 GBC). Higher disease stage (III-IV) was found in 33%, 29%, 55% and 11% of patients with ICC, PHC, DCC and GBC ($p < 0.001$). Perineural growth and angioinvasion were seen in 68% and 26%, 91% and 48%, 89% and 62%, and 68% and 48% in ICC, PHC, DCC and GBC, respectively (both $p < 0.001$). In 27%, 33%, 41% and 18% (ICC, PHC, DCC, GBC) R1 resection were seen ($p = 0.013$). Morbidity was 58%, 66%, 60%, 20% ($p < 0.001$), mortality 9%, 15%, 3%, 4% ($p < 0.001$), and median overall survival 37, 42, 29 and 41 months ($p = 0.147$), for ICC, PHC, DCC, GBC, respectively. ECOG performance score and residual disease were independent prognostic factors for overall survival, anatomical subtype was not.

Conclusion: Short-term outcomes vary between subtypes of BTC and some diversity in pathological outcomes between anatomical subtypes of BTC exist. However, a significant difference in overall survival was not detected and anatomical subtype was not an independent prognostic factor. This data support the concept that BTC should be regarded as a diverse group of closely related tumors and highlights the need for molecular data on BTC in order to improve classification.

Figure 1. Overall survival per group



OS		BL	3 months	6 months	1 year	3 year	5 year	10 year
ICC	No. at risk	33	30	29	28	16	8	1
GBC	No. at risk	45	43	40	32	23	18	3
PHC	No. at risk	135	115	115	110	61	33	9
DCCA	No. at risk	148	143	138	113	57	39	13

P 113. TKS5-POSITIVE INVADOPODIA-LIKE STRUCTURES IN PANCREATIC SURGICAL SPECIMENS AND CLINICAL OUTCOMES

KT Chen, YC Chen, M Baik, J Byers, SW French, B Diaz

Presenter: Kathryn Chen MD | Harbor-UCLA Medical Center

Background: Invadopodia, cellular protrusions which are associated with active remodeling of the extracellular matrix, have been demonstrated in in vitro studies to allow cancer cell extravasation and are thought to play a role in metastasis. Tks5 is a protein specific for invadopodia; cancer cells depleted of Tks5 do not elaborate invadopodia, and have decreased invasive ability. Here, we investigate the presence of invadopodia in pancreatic surgical specimens, and the correlation with clinical outcomes.

Methods: Under IRB approval, we evaluated archived paraffin-embedded blocks of 15 patients with pancreatic tumors of varying pathology. Slides were stained for Tks5, and images were captured from regions containing Tks5-positive tumor cells. Clinical data was collected and compared for Tks5-positive vs. Tks5-negative patients.

Results: Microscopic analysis of Tks5-positive samples revealed the presence of Tks5 puncta arranged in a distribution reminiscent of invadopodia identified in cell cultures. Of the 15 samples, there were 6 pancreatic adenocarcinomas, 5 ampullary adenocarcinomas, 3 solid pseudopapillary tumors, and a mucinous cystadenoma evaluated. Tks5 was positive in 8 of 15 patients; of these, four were ampullary adenocarcinomas, three were solid pseudopapillary tumors, and one was an invasive pancreatic adenocarcinoma. There was no correlation with Tks5 positivity with lymph node involvement, stage, tumor grade, perineural invasion or lymphovascular invasion.

Conclusion: To our knowledge, this is the first time the presence of invadopodia-like structures have been identified in human pancreatic tumor samples. Lower-risk tumors, such as pseudopapillary tumors and ampullary cancers, were consistently identified as having these structures; conversely, the majority of invasive pancreatic adenocarcinomas were Tks5-negative. There was no identifiable correlation of Tks5 positivity with a number of clinically adverse factors. Further studies are needed to elucidate the role of invadopodia in pancreatic tumors.

P 114. DRUG RESISTANCE IN INFECTED PANCREATIC NECROSIS: CAUSE FOR ALARM?

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Presenter: Alexandra Roch MD | Indiana University School of Medicine

Background: Necrotizing pancreatitis (NP) occurs in 20% of acute pancreatitis cases and is associated with a 20% mortality. Infected necrosis substantially increases mortality in NP. Though antibiotic prophylaxis has not reduced NP mortality or morbidity, this practice has raised concern for significant adverse effects including multidrug resistance and opportunistic fungal infections. We sought to evaluate the incidence of pancreatic necrosis infection with multi-drug resistant (MDR) micro-organisms and hypothesized that MDR infected necrosis was associated with poorer outcomes.

Methods: We retrospectively reviewed all consecutive necrotizing pancreatitis patients treated at a single academic institution between 2005 and 2017. Microbiology data were recorded, including sensitivities. Descriptive statistics, univariate analysis and binary regression were applied where appropriate. p -value <0.05 was considered statistically significant.

Results: 647 patients with NP were included in this study (gender ratio male/female 1.8, mean age 52 years). Main etiologies for NP were biliary in 49.6%, alcohol in 20.2%, and idiopathic in 15.3%. A total of 355 patients (54.9%) had documented infected pancreatic necrosis, 59.4% from surgical specimen, 33.9% from interventional radiology drainage, and 6.7% from endoscopy. Among the 355 patients with infected necrosis, 181 (51%) had multi-drug resistant infection, and 81 (22.8%) had fungal infection. No difference over time was observed throughout the study period in the prevalence of infections, MDR infections or fungal infections. In multivariate analysis, patients with infected necrosis were more likely to be transferred from an outside hospital (81.4% vs. 72.6%, $p=0.008$), and had poorer outcomes including prolonged renal failure (29% vs. 15%, $p=0.024$), higher readmission rate (82.8% vs. 63.4%, $p<0.0001$), and increased number of readmissions (2.2 vs. 1.2, $p<0.0001$). Although patients with MDR necrosis infection had higher rates of prolonged end-organ failure (respiratory 44.8% vs. 35.6%, $p=0.08$, and cardiovascular 21.5% vs. 14.4%) in univariate analysis, these associations were not seen in multivariate analysis. In-hospital mortality was comparable in patients with MDR (16.7%) and non-resistant (12.1%) organisms ($p = 0.54$). Patients with fungal infections had morbidity and mortality comparable to other infected necrosis patients.

Conclusion: Infected pancreatic necrosis remains a very common complication of NP, occurring in 55% of our population. No changes were seen over time in either incidence of multi-drug resistant or fungal infections. Infection of pancreatic necrosis is associated with worse short term-outcomes including renal failure and readmissions. Patients transferred from an outside institution were more often infected with multi-drug resistant organisms. Multi-drug resistant and fungal infections did not change morbidity or mortality when compared to sensitive bacterial infections.

P 116. DIFFICULTY SCORING SYSTEM IN LAPAROSCOPIC DISTAL PANCREATECTOMY

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Presenter: Takao Ohtsuka MD, PhD | Kyushu University

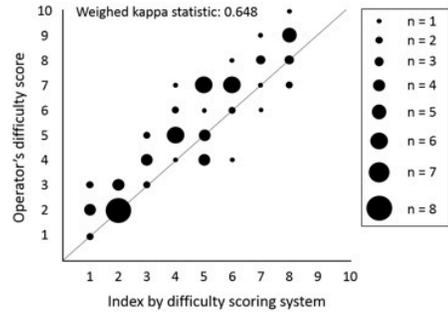
Background: Laparoscopic distal pancreatectomy (LDP) is gaining acceptance as a standard approach for removal of various benign and malignant pancreatic diseases. Several factors affect the level of difficulty of LDP, and it would be advisable to preoperatively identify these factors in order to determine the best surgical strategy. At the same time, understanding the potential difficulty would facilitate the safe, gradual adoption of the laparoscopic approach and assist in creating a plan for training of surgeons. The purpose of this study was to develop a difficulty scoring (DS) system to quantify the degree of difficulty in LDP.

Methods: We collected clinical data for 80 patients including 30 with classic LDP with splenectomy for benign diseases, 20 with laparoscopic spleen and vessel preserving distal pancreatectomy (L-SPDP), and 30 with laparoscopic radical antegrade modular pancreatosplenectomy (L-RAMPS) for pancreatic cancer. A 10-level difficulty index was developed and subcategorized into a 3-level difficulty index; 1-3 as low, 4-6 as intermediate, and 7-10 as high index. Twenty factors such as age, sex, BMI, tumor location and size, diagnosis, operation type, resection line, parenchymal thickness and texture, close proximity of tumor to major vessels, presence of left side portal hypertension/splenomegaly, and tumor extension to peripancreatic tissue, etc. were assessed, and automatic linear modeling statistical tool was used to identify factors that significantly increase level of difficulty in LDP.

Results: There were 25 males and 55 females with a median age of 60 years and median BMI of 21.9kg/m². There was neither conversion case to the open procedure nor mortality case. Based on the operating surgeon's difficulty 10-level index evaluation, 21 cases were clustered to "low", 29 as "intermediate", and 30 as "high" difficulty index. The weighted Cohen's kappa statistic between the operator's 10-level DS and the reviewers' 10-level DS was at 0.869, showing excellent interrater agreement. We identified five factors significantly affecting level of difficulty in LDP; type of operation, resection line, proximity of tumor to major vessel, tumor extension to peripancreatic tissue, and left sided portal hypertension/splenomegaly, and then developed a simpler and more practical scoring system (Figure 1). The operator's 10-level DS concordance between linear modeling index DS and simpler clinical index DS systems were analyzed, and the weighted Cohen's kappa statistic were at 0.729 (good) and 0.648 (good, Figure 1), respectively. Regarding the short-term postoperative outcomes of the cases correlated with the 3-level DS index, median operative time was significantly increased in the high (297 mins) or intermediate (243 mins) difficulty index group than low index (197 mins) ($p < 0.01$). The median estimated blood loss was greatest in the high index group (63 mL), but no statistical significance was observed among groups (intermediate; 50 mL, low; 20 mL, $p = 0.36$). Incidence of postoperative morbidity (Clavie-Dindo classification ≥ 3) and pancreatic fistula (ISGPF $\geq B$) were both 6% (5 of 80 patients) and median hospital stay was 13 days. No statistical difference was seen among groups based on the incidences of postoperative complications ($p = 0.84$) and pancreatic fistula ($p = 0.84$), and length of hospital stay ($p = 0.44$).

Conclusion: This novel DS for LDP adequately quantified the degree of difficulty, and can be useful for selecting patients for LDP, in conjunction with fitness for surgery and prognosis.

Type of operation		Tumor close to major vessel	
	Score		Score
DP-S for benign disease	+1	Presence	+2
SPDP	+3	Absence	0
RAMPS	+4	Tumor extension to peripancreatic tissue	
			Score
		Presence	+1
		Absence	0
Pancreatic resection line		Left side portal hypertension and / or splenomegaly	
	Score		Score
Portal vein level	+1	Presence	+5
Pancreatic tail	0	Absence	0



P 121. ROLE OF NEOADJUVANT RADIATION IN DOWNSTAGING PATIENTS WITH LOCALIZED PANCREATIC CANCER - ANALYSIS OF THE NCDB DATABASE

AN Krepline, CA Barnes, M Aldakkak, I Akinola, KK Christians, CN Clarke, B George, PS Ritch, WA Hall, BA Erickson, DB Evans, S Tsai

Presenter: Ashley Krepline MD | Medical College of Wisconsin

Background: Although the acceptance of neoadjuvant therapy for patients with localized pancreatic cancer is growing, there is not an accepted standard therapy. The use of neoadjuvant radiation therapy remains controversial. We sought to examine the role of neoadjuvant radiation on pathologic outcomes.

Methods: Patients with stage I-II PC who received neoadjuvant therapy were identified from the National Cancer Database. Patients were classified by type of neoadjuvant therapy received: chemotherapy (nChemo) or chemotherapy and radiation (nC+XRT). Pathologic nodal status was classified as negative (ypN0) or positive (ypN1/N2). Margin status was classified as negative (ypR0) or positive (ypR1/2). Chi squared test was used to compare categorical variables and median test was used to compare continuous variables. The log rank test was used to compare survival and cox proportional hazards regression was used to model survival time.

Results: Of the 2,132 patients identified, 1,071 (50%) received nChemo and 1,061 (50%) received nC+XRT. Demographic characteristics are summarized in Table 1. Neoadjuvant radiation was associated with a significant decrease in ypN1/N2 pathology (393/1061 patients (37%) vs. 624/1071 patients (58%), $p < 0.001$) and ypR1/2 (138/1061 patients (13%) vs. 188/1071 patients (18%), $p = 0.004$). Adjuvant therapy was administered to 487 (45%) of 1,071 patients who received nChemo and 326 (31%) of 1,061 patients who received nC+XRT ($p < 0.001$). The median overall survival (mOS) was 26 months, 32 vs. 23 months in ypN0 and ypN1/N2 patients, respectively ($p < 0.001$). The mOS for patients with ypR0 disease was 29 months, and 19 months for patients with ypR1/R2 disease ($p < 0.001$). In an adjusted proportional hazards model, ypN1/N2 disease and ypR1/2 disease was associated with a 1.36-fold (95%CI: 1.21-1.52, $p < 0.001$), and 1.68 (95%CI: 1.40-2.02, $p < 0.001$) increased risk of death, respectively.

Conclusion: Patients treated with nC+XRT had higher rates of ypN0 disease and ypR0 margin status than patients treated with nChemo. Since both nodal disease burden and margin status are important prognostic factors, radiation therapy should be incorporated in neoadjuvant treatment regimens.

P 122. MULTIMODALITY NEOADJUVANT THERAPY INCREASES NORMALIZATION OF CARBOHYDRATE ANTIGEN 19-9 (CA19-9) IN PATIENTS WITH PANCREATIC CANCER

AN Krepline, CN Clarke, KK Christians, PS Ritch, B George, AH Khan, N Kulkarni, C Hagen, BA Erickson, WA Hall, M Aldakkak, DB Evans, S Tsai

Presenter: Ashley Krepline MD | Medical College of Wisconsin

Background: We previously demonstrated normalization of CA19-9 levels in response to neoadjuvant therapy is a favorable prognostic marker. We analyzed trends in CA19-9 decline in response to sequential neoadjuvant therapy.

Methods: We identified patients with localized pancreatic cancer who had pretreatment CA19-9 levels >35 U/mL, total bilirubin <2 mg/dL, and received neoadjuvant therapy consisting of 2 months of chemotherapy followed by 50.4 Gy chemoradiation. CA19-9 was assessed after chemotherapy and after chemoradiation (preop) and were classified as normal (nl) or elevated (hi) based on a cutpoint of 35 U/mL. Patients were classified into 4 groups based on CA19-9 response to chemotherapy and chemoradiation: A (nl/nl), B (nl/hi), C (hi/nl), D (hi/hi)

Results: For the 103 patients, Table 1 summarizes changes during neoadjuvant therapy. Following chemotherapy, the median change in CA19-9 was -51% (IQR:49); 26 (25%) patients achieved a normal CA19-9 and 77 (75%) did not. Of 26 patients who normalized their CA19-9 levels after chemotherapy, 16(62%) had a pretreatment CA19-9 level between 35-100. Of the 77 patients with elevated CA19-9 after chemotherapy, 21 (27%) further normalized their CA19-9 levels with chemoradiation (Grp C) and 56 (73%) did not (Grp D). Of 21 Grp C patients, 14 (66%) had a CA19-9 level between 35-100. After neoadjuvant therapy, the median preop CA19-9 was 47 (IQR:112) U/mL. Of 103 patients, 77 (75%) underwent surgical resection, 18 (90%), 5 (83%), 20 (95%), and 34 (61%) in Grp A, B, C, and D, respectively (p=0.003). The preop CA19-9 was higher than the pretreatment CA19-9 in 6 (6%) patients of which 4 (66%) were not resected. In an adjusted logistic regression, elevated preop CA19-9 was associated with an 88% decreased odds of surgical resection (95%CI: 0.03-0.48, p =0.002).

Conclusion: CA19-9 monitoring during neoadjuvant therapy demonstrated normalization in CA19-9 in 20% of patients after chemotherapy and an additional 21% following chemoradiation. Patients with higher CA19-9 are less likely to achieve normalization, and extended neoadjuvant therapy may be an option to augment CA19-9 response.

Group	A N = 20	B N = 6	C N = 21	D N = 56	TOTAL n=103	p-value
CA19-9 after induction chemotherapy	Norm	Norm	Elevated	Elevated		
CA19-9 after chemoradiation	Norm	Elevated	Norm	Elevated		
Median Pretreatment CA19-9 (IQR)	69 (100)	149 (757)	120 (636)	470 (700)	293 (628)	<0.001
Pretreatment CA19-9 range, n (%)						<0.001
35-100	14 (70)	2 (33)	7 (33)	6 (11)	29 (28)	
101-250	3 (15)	2 (33)	6 (29)	8 (14)	19 (18)	
251-750	2 (10)	0	3 (14)	26 (46)	31 (30)	
750+	1 (5)	2 (33)	5 (24)	16 (29)	24 (23)	
Median % change after induction chemo (IQR)	-63 (33)	-90 (28)	-49 (52)	-45 (56)	-51 (49)	0.005
CA19-9 range induction chemo, n (%)						<0.001
Normal (<=35)	20 (100)	6 (100)	--	--	26 (25)	
35-100	--	--	14 (67)	13 (23)	27 (26)	
101-250	--	--	4 (19)	16 (29)	20 (19)	
251-750	--	--	2 (10)	19 (34)	21 (20)	
750+	--	--	1 (5)	8 (14)	9 (9)	
Median % change after chemo & chemoradiation (IQR)	-70 (38)	-55 (34)	-83 (24)	-32 (89)	-51 (44)	<0.001
CA19-9 range after 2 nd therapy, n (%)						<0.001
Normal (<=35)	20 (100)	--	21 (100)	--	41 (40)	
35-100	--	4 (67)	--	26 (46)	30 (29)	
101-250	--	2 (33)	--	14 (25)	16 (16)	
251-750	--	--	--	12 (21)	12 (12)	
750+	--	--	--	4 (7)	4 (4)	
Median Preoperative CA19-9 (IQR)	18 (10)	55 (91)	23 (14)	113 (209)	47 (112)	<0.001
Completed all neoadjuvant therapy and surgery, n(,%)	18 (90)	5 (83)	20 (95)	34 (61)	77 (75)	0.003

P 125. THE EVOLUTION OF POSTOPERATIVE PANCREATIC FISTULA (POPF) SEVERITY ACCORDING TO GRADE B SUB-CLASSIFICATION REFLECTS A STEP-UP MANAGEMENT

V Andreasi, S Partelli, R Ariotti, G Guarneri, M Pagnanelli, G Balzano, S Crippa, M Falconi

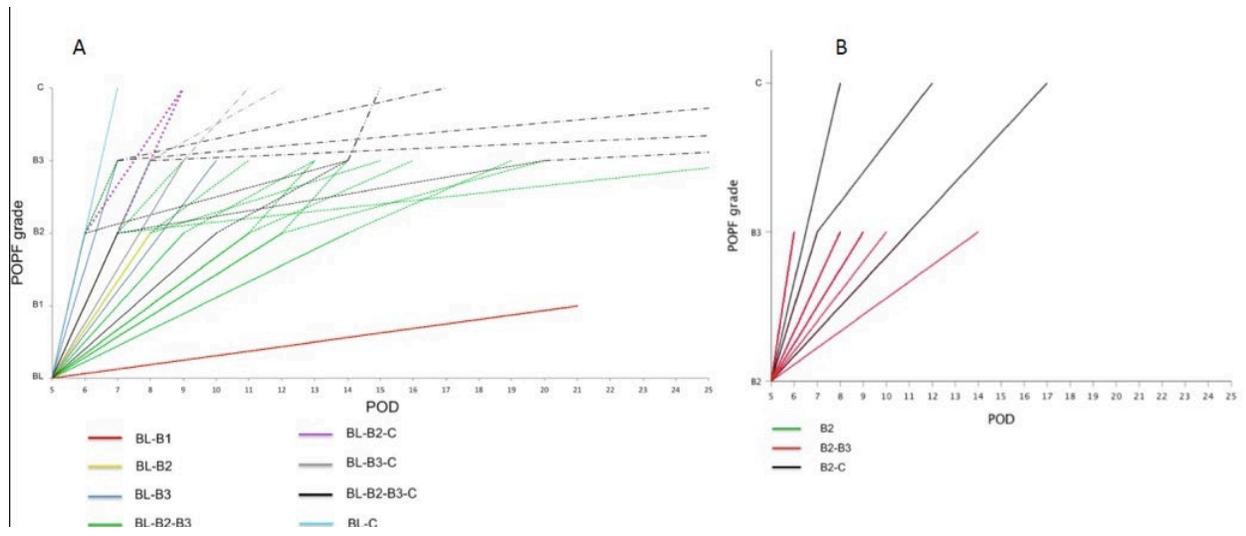
Presenter: Valentina Andreasi MD | San Raffaele Scientific Institute

Background: The current classification aims to distinguish postoperative pancreatic fistula (POPF) by the mere presence of an increased amylase value in drains (AVD) identifying two grades (Grade B and Grade C) according to the clinical burden of POPF. It has been recently proposed a sub-classification of POPF grade B into three categories.

Methods: All the patients who had amylase value in drains (AVD) on postoperative day (POD) 5 > 3 times the upper limit of normal amylase after PD were included. Data regarding POPF classification, timing of diagnostic imaging, and treatment strategy were retrieved. POPF Grade B was further sub-classified into 3 grades.

Results: Overall, 105 patients were included. Of the 67 patients who eventually developed a POPF, 52 patients (78%) had a grade B and 15 patients (22%) had a grade C. Fifty-two patients who had a POPF grade B were further classified into 3 sub-groups: POPF grade B1 (n=5, 10%), POPF grade B2 (n=19, 36%), and POPF grade B3 (n=28, 54%). Patients with a POPF grade B3 had a significantly higher frequency of severe complications as well as a higher median LOS as compared to those who had a POPF grade B1-B2 (29 days [range 20-42] versus 18 days [range 13-23], P=0.001). Looking at evolution of the severity over the time, patients were classified into two groups on POD 5. In the first group, 39 patients (58%) had a biochemical leak whereas, in the second group, 28 patients (42%) had already a POPF B2. In the first group (Figure A) only 1 patient (3%) directly developed a POPF grade C. The remaining 28 patients evolved to a B2 POPF on a median POD of 7.5 (IQR 6-14). Out of those 28 patients, only 2 had directly a POPF grade C. In the second group (Figure B), only 1 patient (4%) who had a POPF B2 directly evolved to POPF C. Of the remaining 18 patients, 5 patients developed a POPF grade B3 and thereafter a POPF grade C whereas 13 patients had eventually a POPF grade B3. On univariate analysis, the only factor that was independently associated with an increased risk of developing POPF grade B3/C was the CRP value on POD5 (210 mg/l, sensitivity: 63%, specificity: 73%, AUC: 0.631, P=0.040).

Conclusion: The clinical burden of POPF grade B is better defined by a sub-classification that should be incorporated in the POPF definition. The progressive worsening in POPF grade proves that this complication represents a dynamic process and it reflects a "step-up" strategy on which was based the POPF treatment in our institution.



P 126. RAPID GROWTH SPEED OF CYSTS CAN PREDICT MALIGNANT INTRADUCTAL PAPILLARY MUCINOUS NEOPLASMS

K Akahoshi, H Ono, M Akasu, D Ban, A Kudo, A Konta, S Tanaka, M Tanabe

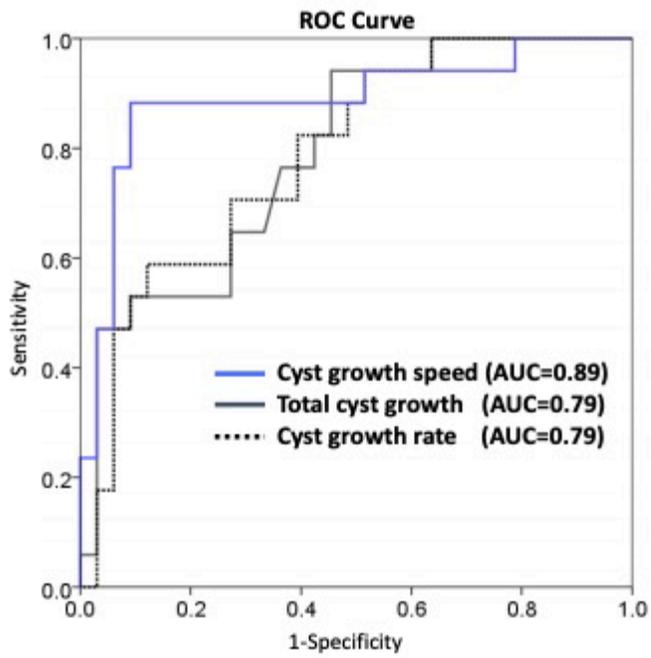
Presenter: Keiichi Akahoshi MD, PhD | Tokyo Medical and Dental University

Background: Branch duct intraductal papillary mucinous neoplasm (BD-IPMN) has the potential for malignant transformation. Current risk factors used to predict malignant transformation, such as mural nodules and cyst size >30 mm, are insufficient. Therefore, we aimed to investigate the predictive significance of cyst growth speed.

Methods: Between 2006 and 2017, 102 patients underwent pancreatotomy for IPMN. Of these, 50 patients with pathologically diagnosed BD-IPMN were selected for cyst growth analysis. Cyst growth speed, total cyst growth, and cyst growth rate were calculated retrospectively using the maximum diameter of the cyst at the first diagnosis and images taken preoperatively.

Results: Of the 50 BD-IPMN cases, 33 were diagnosed as benign (low to intermediate dysplasia) and 17 were malignant (10 high-grade dysplasias and seven invasive carcinomas). While no significant differences were observed in the presence of enhancing mural nodules or cyst size, malignant IPMN grew at a significantly faster speed (5.7 vs 1.6 mm/year; $p < 0.001$), greater amount of cyst diameter (10.1 vs 3.1 mm; $p = 0.015$) and greater percentage of cyst diameter (28.5% vs 9.5%; $p = 0.006$) than those of benign IPMN. Receiver operator characteristic curve analysis indicated that cyst growth speed had the greatest predictive performance among these three factors. Cyst growth speed >3.5 mm/year was demonstrated to predict malignant IPMN with a sensitivity of 88% and specificity of 91%.

Conclusion: Cyst growth speed >3.5 mm/year may be a good predictor for malignant IPMN. It can improve the diagnostic accuracy and optimize surgery for BD-IPMN.



Comparison of three methods to evaluate cyst growth.
Receiver Operator Characteristic (ROC) analysis was performed.
The area under the curve (AUC) was calculated.

P 127. IS THIS THE TIME FOR THE “GOLDEN AGE” OF EARLY PANCREATIC CANCER DETECTION? A NANOPARTICLE-BASED BLOOD TEST

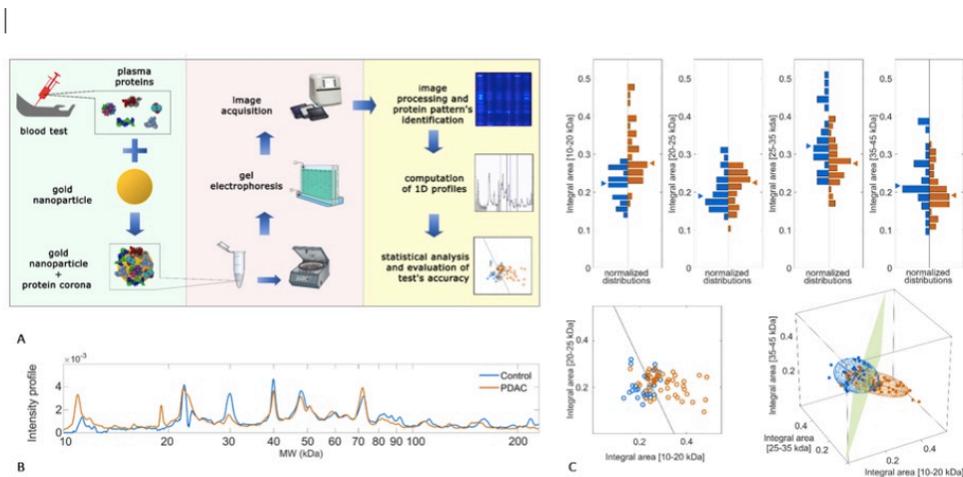
D Caputo, L Digiaco, D Pozzi, S Palchetti, C Cascone, M Cartillone, R Coppola, G Caracciolo
Presenter: Damiano Caputo MD | University Campus Bio-Medico di Roma

Background: To date there is a lack of new cheap, user-friendly techniques for pancreatic ductal adenocarcinoma (PDAC) early diagnosis. Nanoparticles (NPs) are helpful, non-invasive tools for early cancer detection. Interacting with plasma, NPs are covered by a superficial biomolecular corona (BC), whose features and composition depend on NP's physical-chemical properties, molecular source and disease stage. Identification of specific corona molecules could provide an effective way to detect tumors by NP-based blood tests. Previous results supported this idea and suggested that simple combination of gel electrophoresis, image processing and statistical data analysis could be used to develop reliable diagnostic tools for PDAC.

Methods: Plasma samples from cyto-histologically proved PDAC patients and healthy subjects were let to interact with gold NPs. Protein patterns of the resulting BCs were analyzed by monodimensional gel electrophoresis. Gel images were acquired by a ChemiDoc (BioRAD) and processed by custom Matlab scripts. The aim was to distinguish healthy and PDAC samples by molecular weight distributions of the corresponding BCs.

Results: A statistical data analysis over a set of 45 samples was carried out; significant differences between healthy and PDAC patterns, located in specific regions of the electrophoretic profiles (10-20 kDa and 35-45 kDa) were found. Furthermore, a linear discriminant analysis of the experimental data provided an evaluation of the test's sensitivity, specificity and overall accuracy of 85.7%, 76.4% and 82.2% respectively.

Conclusion: If further confirmed on larger series, we envision that different kinds of NPs, larger datasets and more accurate classification of NP-BC based techniques, may improve our knowledge of PDAC biology and offer new diagnostic opportunities.



A. Schematic overview of the experimental workflow. B. Representative electrophoretic profiles of control and pancreatic cancer patients. C. Statistical analysis: distributions of four integral areas within the specified ranges of protein molecular weights; one- dimensional and two-dimensional linear classifications.

P 128. PREOPERATIVE RADIOGRAPHIC MEASUREMENTS CAN PREDICT POSTOPERATIVE PANCREATIC FISTULA FORMATION FOLLOWING PANCREATODUODENECTOMY

EW Box, L Deng, DE Morgan, R Xie, JK Kirklin, S Reddy, TN Wang, MJ Heslin, JB Rose

Presenter: Edmond Box BS | University of Alabama at Birmingham

Background: Postoperative pancreatic fistulae (POPF) are a major contributing factor to pancreatoduodenectomy associated morbidity. Established risk calculators exist to help predict POPF formation, but most rely on subjective or intraoperative assessments. We hypothesized that various objective preoperatively determined computed tomography (CT) measurements could predict POPF as well as validated models and allow for more informed operative consent in high risk patients.

Methods: Patients undergoing elective pancreatoduodenectomies between January 2013 and April 2018 were identified in a prospective database. POPF were defined according to 2017 ISGPS guidelines. Multivariable logistic regression models were generated to predict POPF development. Model performance was tested with receiver operating characteristics (ROC) curves. Pancreatic neck radiodensities (Hounsfield units) were measured in triplicate by pancreatic protocol CT (venous phase, coronal plane) anterior to the portal vein. A pancreatic density index (PDI) was created to adjust for differences in contrast timing by dividing the mean of these measurements by the portal vein radiodensity. Total areas of subcutaneous fat and skeletal muscle were calculated at the L3 vertebral level on axial CT. Pancreatic duct (PD) size was determined by CT.

Results: In the study period 219 patients had elective pancreatoduodenectomies with 35 (16%) developing a POPF of any grade. Multivariable regression analysis revealed that demographics (age, sex, and race) were not associated with POPF, yet patients resected for pancreatic adenocarcinoma or chronic pancreatitis were less likely to develop a POPF (10 vs. 24%; $p=0.004$). We validated a previously established predictive model based on body mass index, PD size, and gland texture (soft vs. non-soft) and obtained an AUC of 0.798. Additional ROC curves were created using various combinations of gland texture, body mass index, skeletal muscle index, sarcopenia, PDI, PD size, and subcutaneous fat area indexed for height (SFI). A model using objective preoperatively determined CT measurements of SFI, PDI, and PD size (AUC 0.803) had equal predictive performance to the established model ($p=0.873$).

Conclusion: A combination of preoperative objective CT measurements can adequately predict POPF and is comparable to established models relying on subjective intraoperative variables. Validation in a larger dataset would allow for better preoperative stratification of high-risk patients and improve informed consent among this patient population.

P 129. PRELIMINARY TOXICITY FOR A PHASE II TRIAL OF ESCALATED DOSE PROTON RADIOTHERAPY WITH ELECTIVE NODAL IRRADIATION AND CONCOMITANT CHEMOTHERAPY FOR PATIENTS WITH UNRESECTABLE, BORDERLINE RESECTABLE OR MEDICALLY INOPERABLE PANCREATIC ADENOCARCINOMA

RC Nichols, CG Morris, D Pham, ME Shaikh, MS Rutenberg

Presenter: Romaine Nichols MD | University of Florida

Background: Report preliminary toxicity for a phase II trial of proton therapy for Patients with Unresectable, Borderline Resectable or Medically Inoperable Pancreatic Adenocarcinoma.

Methods: From 4/2016 through 8/2018, 14 patients were consented and treated on the UFHPTI PC04 protocol. 40.5Gy(RBE) in 18 fractions is delivered to a target volume including gross disease expanded to include the nodal beds in the region of the celiac and superior mesenteric arteries. The gross disease volume is then boosted to a cumulative dose of 63Gy(RBE) in 28 fractions. Patients receive chemotherapy on treatment days consisting of capecitabine at 1000mg PO BID.

Results: Only one patient experienced grade 3 toxicity (outpatient IV fluids for dehydration). 6 other patients experienced transient grade 2 toxicities (abdominal pain, anorexia, fatigue, dermatitis without desquamation, performance status, muscle weakness, oral mucositis, nausea). One patient required a 26 day treatment break due to an unrelated medical event (staph aureus sepsis) but was able to complete proton therapy without further incident. One patient required a 9-day break for paracentesis due to the emergence of non-malignant ascites. No other patient required a treatment break.

Conclusion: Based on the tolerability of this aggressive regimen at the originating institution (University of Florida Health Proton Therapy Institute), in 2019 the trial will be opened nationally through the Proton Collaborative Group (PCG). The trial (currently UFHPTI PC04) will be renamed PAN009-17.

P 131. A PROGNOSTIC SCORE FOR THE SELECTION OF PATIENTS WHO COULD BE CURED BY PANCREATECTOMY WITH SIMULTANEOUS ARTERIAL RESECTION DESPITE LOCALLY ADVANCED DUCTAL PANCREATIC ADENOCARCINOMA

N Napoli, EF Kauffmann, S Iacopi, F Menonna, C Cacace, G Taddei, A Cacciato Insilla, C Cappelli, D Campani, D Caramella, F Vistoli, U Boggi

Presenter: Niccolò Napoli MD | University of Pisa

Background: Following neoadjuvant chemotherapy, pancreatectomy with arterial resection (P-Ar) for locally advanced pancreatic cancer (LA-PDAC) is associated with acceptable survival (J Am Coll Surg, 2018). However, current selection criteria and preoperative prognostic scores are not specific for P-Ar resulting sometimes in poor survival in seemingly optimal candidates. We herein analyze the data from a large series of P-Ar for LA-PDAC with the aim of defining a new pre-operative score to be used in the selection of surgical candidates for these formidable procedures.

Methods: Data from a prospectively maintained database were used to conduct a retrospective cross-sectional study on P-Ar performed for LA-PDAC between March 2000 and July 2017. Disease specific survival (DSS) was calculated using Kaplan-Meier curves. Ninety-day mortality was censored in survival analysis. Univariate proportional hazards regression and multivariate proportional hazards model analyses were used to identify the preoperative prognostic factors that were subsequently used to create a prognostic score (1 point for each factor) aimed at predicting the survival probability of the individual patient. For continuous variable, ROC curves were used to determine a cut-off to be used in the score. We considered the score as positive for values >2. Median survival of patients allocated to different score categories was compared using Tarone-Ware and Log-Rank test.

Results: Sixty-four patients, out of a total of 100 undergoing P-Ar during the study period, met the inclusion criteria. Patients had a mean age of 63.1±9.6 years, a median ASA score of 2 (2-2.8) and included 32 (50%) females. Total pancreatectomy was performed in 53 (82.6%) patients, distal pancreatectomy in 7 (10.9%) patients, and pancreatoduodenectomy in 4 (6.3%) patients. In 57 (89.1%) patients a venous resection was also required. The superior mesenteric artery and the hepatic artery/cealic axis were resected in 29 (45.3%) and 40 (62.5%) patients, respectively. Ten patients died within 90 postoperative days (15.6%). Median DSS was 19.6 (13.3-74) months. Identified preoperative prognostic factors are reported in table 1. Prognostic score was composed by leukocytes level (positive if $\leq 6.3 \times 10^3/\mu\text{L}$), neutrophils level (positive if $\geq 3.3 \times 10^3/\mu\text{L}$), Ca 15.3 level (positive if $\leq 16.4 \text{ KU/L}$), platelets to albumin ratio (positive if ≥ 48857.1), lymphocytes to monocytes ratio (positive if ≥ 4) and type of neoadjuvant chemotherapy (positive if based on FOLFIRINOX). Median DSS was 8.8 (5.6-NA), 16 (12.6-28.3), 23.5 (17.5-NA) and 74 (26.5-NA) months for patients with score values of 0-1, 2, 3 and 4-5, respectively. The median DSS increased along with the score values ($p=0.002$). Positive score was presented in 50% of patients. Median DSS was 25.3 (17.5-74) months in patients with a positive score and 15.7 (12.3-28.3) months in patients with a negative score. Patients with a positive score had a longer survival when compared to patients with a negative score ($p=0.02$).

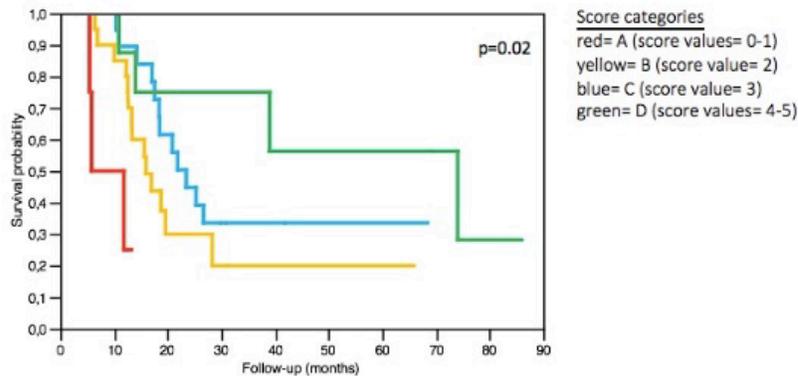
Conclusion: A survival advantage associated with P-Ar performed in the setting of LA-PDAC cannot be reliably anticipated based on currently available selection criteria. Using our single institution database we have created a preoperative score that anticipates post-operative survival. This score would now require external validation, possibly in a larger cohort of prospectively recruited patients. Should this score be eventually validated we would be able to identify a cohort of patients with anticipated long-term survival despite LA-PDAC. Based on our data, some of these patients could be actually cured by induction chemotherapy followed by P-Ar.

Table 1 – Univariate proportional hazards regression and multivariate proportional hazards model for preoperative prognostic factors

	Univariate analysis		Multivariate analysis	
	HR (95% CI)	p	HR (95% CI)	p
Gender (female)	0.42 (0.21-0.84)	0.01		
Leukocytes; n*10 ⁶ /μL	1.17 (1.00-1.34)	0.04	80.58 (6.39-1799.91)	0.0002
Neutrophils; n*10 ⁶ /μL	1.20 (1.04-1.35)	0.02	0.041 (0.0041-0.28)	0.0007
Platelets; n*10 ³ /μL	1.00 (1.00-1.00)	0.03		
Ca 15.3; KU/L	1.05 (1.01-1.08)	0.009	1.10 (1.00-1.20)	0.04
Ca 125; KU/L	1.02 (1.00-1.04)	0.01		
Platelets-to-lymphocytes ratio	1.00 (0.99-1.01)	0.10		
Platelets-to-albumin ratio	1.00 (0.99-1.00)	0.07	0.99 (0.99-0.99)	<0.0001
Monocytes-to-lymphocytes ratio	0.84 (0.68-1.03)	0.09	0.27 (0.11-0.56)	0.0001
Neoadjuvant chemotherapy; (Y)	0.40 (0.20-0.82)	0.01		
Neoadjuvant FOLFIRINOX; (Y)	0.40 (0.18-0.83)	0.01	7.59*e ⁻⁵ (2.59*e ⁻⁷ -0.006)	<0.0001
Neoadjuvant chemotherapy; n° of cycles	0.93 (0.85-1.00)	0.06		

Y= presence of factor; Multivariate model: Chi-squared=66.7, p<0.001

Figure 1 – Kaplan-Meier curves (DSS) for different score categories



P 133. IS THE ROUTINE USE OF SOMATOSTATIN AFTER PANCREATODUODENECTOMY JUSTIFIED? A CASE-MATCHED COMPARISON ACCORDING TO FISTULA RISK SCORE, ASA SCORE AND SURGICAL TECHNIQUE

L Morelli, N Furbetta, S Guadagni, G Di Franco, M Palmeri, D Gianardi, M Bianchini, C D'isidoro, G Caprili, G Di Candio, F Mosca

Presenter: Matteo Palmeri MD | University of Pisa

Background: Pancreatoduodenectomy (PD) is one of the most technically demanding operations. In recent decades, technical evolution and perioperative management improvements have reduced mortality following PD in high-volume centers. Post-operative pancreatic fistula (POPF) still remains the main cause of morbidity, with a ranging incidence from 2% to 42.5% reported in literature. The routine use of somatostatin in prevention of POPF is controversial and several works have shown no beneficial effects in this setting. The aim of this study is to compare the incidence of fistula in patients who underwent PD with the same pancreatojejunostomy technique, with and without the postoperative use of somatostatin.

Methods: 493 pancreatic resections were performed at our General Surgery Unit between October 2008 and October 2018. Among these, 259 were PD of which 152 were carried out with a personal, modified pancreatojejunostomy technique (mPJ), introduced on November 2010. Somatostatin was routinely administered after PD with mPJ (mPJ-PD) between November 2010 and December 2016, while from January 2017 to October 2018, 52 consecutive mPJ-PD without somatostatin (WS) were performed. The WS-group was retrospectively compared with a control (C) group of mPJ in which somatostatin was routinely used. The two groups were matched using a one-to-one case-control design, according to Fistula Risk Score (FRS) and American Society of Anesthesiologists' (ASA) score. The post operative outcomes were compared, with particular attention to POPF.

Results: The study sample consists in 104 patients (52 WS-group versus 52 C-group). In both groups the FRS was graded as following: FRS=0, 3.8%; FRS=1-2, 19.2%; FRS=3-6, 61.5%; FRS=7-10, 15.4%. No difference was found in term of operative time (430.38 ± 79.18 min in C-group versus 413.17 ± 72.28 min in WS-group, p=0.8) and length of hospital stay (18.6 days in c-group versus 19.1 days in ws-group, p=0.7). In the WS-group, POPF was registered in 12 patients: 9 were biochemical leak (BL) and 3 were Grade B fistulas, whereas in the C-group 15 patients developed POPF (11 BL, 3 Grade B and 1 Grade C), without any significant difference between the two groups (p=0.7). No difference was documented for 30-days mortality (2 cases in WS-group versus 3 cases in B-group; p=0.6).

Conclusion: The development of POPF after PD is due to multiple factors including pancreatic texture, pancreatic duct diameter and surgical technique and is not significantly influenced by the post-operative administration of somatostatin. Our results do not support the routinely use of somatostatin for the prevention of POPF after PD.

P 134. PANCREATIC RESECTIONS IN THE ELDERLY: A TERTIARY CARE CENTER ANALYSIS WITH PARTICULAR VIEW ON THE HIGH AMERICAN SOCIETY OF ANESTHESIOLOGISTS' RISK SCORE PATIENTS

L Morelli, G Di Franco, M Palmeri, S Guadagni, N Furbetta, D Gianardi, J Bronzoni, M Bianchini, G Stefanini, G Caprili, G Di Candio, F Mosca

Presenter: Matteo Palmeri MD | University of Pisa

Background: Surgery is the only potentially curative treatment for pancreatic cancer. However, the decision to submit elderly patients to pancreatic surgery still remains controversial. Some authors reported that the risk factor is not represented by the advanced age itself, but rather by the comorbidities associated with it, such as cardiovascular and pulmonary diseases and diabetes, common in the elderly population. The aim of this study is to evaluate the outcome of elderly patients with higher American Society of Anesthesiologists' risk score (ASA 4) who underwent pancreatic resection, compared with younger patients and with elderly patient with lower anaesthesiological risk.

Methods: A consecutive series of 345 patients who underwent pancreatic surgery at our tertiary care centre between 2010 and 2017 was reviewed. We compared three groups based on age at the time of surgery: < 65 years (group A), 65-74 years (group B), and ≥ 75 years (group C). Moreover, group C patients were divided according to the ASA score in two subgroups: patients with ASA score 1-3 (low-medium risk) vs patients with ASA score 4 (high risk). Prospectively collected data regarding pre-, intra-, post-operative course and follow up of patients belonging to these two subgroups were retrospectively analysed and compared.

Results: The group A consisted in 117 (34%) patients, the group B in 128 (37%) patients, and group C in 100 (29%) patients. Group C patients had a significant higher incidence of comorbidities and ASA 4 respect the other two groups ($p < 0.05$). The incidence of the overall post-operative complications was significantly higher in the group C ($p < 0.01$), due to the higher incidence of medical complications. No difference in term of overall surgical complications was reported between the three groups. The reoperation rate was higher in group C (12%) vs group B (2.3%) ($p < 0.001$) but not vs group A (6%) ($p = 0.15$). The mean post-operative length of hospitalization was significant higher in group C (22.4 ± 17.0 days) versus group B (17.9 ± 9.2 days) ($p = 0.02$) and group A (15.9 ± 11.3 days) ($p < 0.01$). No difference was documented for post-operative mortality between the three groups. The mean overall survival was significantly lower for group C ($p < 0.01$), but no difference in mortality for cancer was reported between the three groups. Within Group C, the comparison between patients with ASA score 1-3 and ASA 4 showed no significant differences regarding surgical complications ($p = 0.59$), reoperation rate ($p = 0.45$), mortality ($p = 0.34$) and mean overall survival ($p = 0.53$).

Conclusion: Although elderly patients presented a higher rate of postoperative complications and a lower mean overall survival, they did not show a higher perioperative mortality. Furthermore, mortality due to cancer in operated patients was not different between the three groups. For these reasons, the advanced age should not be considered a reason to preclude the surgical option to elderly patients with pancreatic cancer. Furthermore, no differences were found in short-term and long-term survival in elderly patients with different operative risk factors (ASA score), so the higher anaesthesiological risk in subjects aged ≥ 75 years should not be considered an absolute contraindication to surgical treatment.

P 135. MANAGEMENT OF LIVER METASTASIS IN PATIENTS WITH PANCREATIC NEUROENDOCRINE TUMOR: SURGICAL OR NON-SURGICAL?

E Ghaffarpasand, ASO Carranza, MP Callery, AJ Moser, TS Kent

Presenter: Eiman Ghaffarpasand MD | Beth Israel Deaconess Medical Center, Harvard Medical School

Background: Pancreatic neuroendocrine tumor (pNET) comprise 3% of all pancreatic neoplasms. Patient outcomes of pNETs, like the majority of other solid tumors, depend on tumor grading and local lymph node involvement, along with metastasis- which involves the liver in 80% of cases. There are surgical and nonsurgical modalities for the PNET metastases. In the present study, we compared the survival of patients with pNET liver metastasis to following surgical metastasectomy versus non-surgical systemic and/or ablative therapies.

Methods: In a single-center retrospective pattern, all patients with pNET metastases to the liver were enrolled in the study. Liver metastases were managed either with surgical resection or with other non-surgical therapeutic modalities. Hospital free days (HFD) and the time from diagnosis/treatment to death were compared between two groups using Kaplan-Meier curve. Log-rank test was used to compare the survival distribution of the patients in two groups. Cox Proportional-Hazards Model was used to compare the survival rate adjusted for "primary tumor size" and "number of involved liver segments with metastasis" variables, due to the limited number of metastatic pNET patients. Statistical analysis was performed with STATA version 14, with a statistical significance threshold of P-value less than 0.05.

Results: Forty-three pNET patients with liver metastases were managed surgically (13 subjects, 30%) or non-surgically (30 subjects, 70%) at BIDMC from 2002 to 2018. Among the subjects, 26 (60.5%) were female and the mean age was 57.2 ± 1.8 years. There was no significant difference in age, gender, smoking/drinking history, mean primary tumor size, and the number of involved liver segments between the two groups ($P > 0.05$). Kaplan-Meier curve revealed more "HFD" ($P=0.175$), longer "diagnosis to death" time ($P = 0.015$), and longer "treatment to death" time ($P=0.014$) in patients who were managed surgically rather than those managed non-surgically. Surgical resection of the liver metastases shows HRs of 0.7 (95% CI 0.3-1.7, $P=0.474$), 0.3 (95% CI 0.1-1.3, $P=0.11$), and 0.2 (95% CI 0.1-0.9, $P = 0.04$) for the "HFD", "diagnosis to death" time, and "treatment to death" time, respectively, adjusted for the "primary tumor size" and "number of involved liver segments" variables.

Conclusion: Despite the availability of other modalities including chemoradiotherapy and RFA, surgical resection yielded an improved survival rate in pNET patients with liver metastases in this single-center small sample size. The smaller size of primary tumor and fewer number of involved liver segments are the two main independent identifiers for preference of surgical metastasectomy over other non-surgical approaches in metastatic pNET disease.

Table: Multivariate analysis of the variables associated with survival distribution within the two groups

Characteristics	Hazard Ratio (HR)	95% confidence interval (CI)	P-value (two-sided)
Treatment to first complication			
Surgical treatment	0.7	0.3-1.7	0.474
Primary tumor size	1	0.8-1.2	0.897
Number of involved liver segments	1.3	0.9-1.8	0.169
Diagnosis to death			
Surgical treatment	0.3	0.1-1.3	0.11
Primary tumor size	1.2	0.9-1.6	0.258
Number of involved liver segments	1.9	1.2-3.1	0.009
Treatment to death			
Surgical treatment	0.2	0.1-0.9	0.04
Primary tumor size	0.9	0.7-1.2	0.726
Number of involved liver segments	2.8	1.4-5.5	0.003

P 136. TRENDS AND PREDICTORS OF TIME TO INITIATION OF TREATMENT FOR NON-METASTATIC PANCREATIC CANCER: A NATIONAL CANCER DATABASE ANALYSIS

EM Aleassa, E Brinza, G Morris-Stiff

Presenter: Essa M. Aleassa MD, MSc | Cleveland Clinic Foundation

Background: Time to treatment initiation (TTI) is an important quality metric in oncology and a delayed TTI is believed to negatively influence survival. Trends and predictors of TTI are not well understood in patients with non-metastatic pancreatic cancer. We aim to evaluate trends in TTI and determine predictors of TTI in non-metastatic pancreatic cancer patients.

Methods: Patients and Methods: The National Cancer Database (NCDB) was queried for the period 2004 through 2015 to identify all patients with a diagnosis of pancreatic cancer. Only those patients with a recorded TTI under 365 days were included as were those with non-metastatic pancreatic cancer. Patient, disease, and hospital characteristics were assessed for statistically significant differences in median TTI using Mann-Whitney U and Kruskal-Wallis tests and, where appropriate, assessed for correlation with TTI using Spearman's rho test. Significant variables were then fitted into a zero-inflated negative binomial regression model to determine their significance in predicting TTI. This model was chosen as "0-days" comprised 19.9% of the TTI data element.

Results: A total of 109,627 cases met the study criteria. The median age was 67 years (Interquartile range [IQR] = 58-74 years) with an equal gender ratio and a Caucasian predominance (84.5%). Most patients had Medicare health insurance (53%), attended an academic center for treatment (50.7%), and lived within 10 miles of the center of initial diagnosis (40.8%). The tumors were mainly located within the pancreatic head (61.3%) and of AJCC stage II (43%). Surgical intervention as a single treatment modality was the most common management (26.6%). The median overall TTI was 21 days (IQR = 6-38 days). A significant (<0.001) upward trend in TTI days was noted over the years between 2004 and 2015 from 18 days (IQR = 1-36 days) to 24 days (IQR = 11-40 days) respectively. Univariate analyses of the provided characteristics did show significant differences in relation of TTI, however, the Spearman rho test did not show a correlation with TTI. Furthermore, multivariate analysis using a zero-inflated negative binomial regression model demonstrated that ethnicity, Charlson comorbidity score, insurance status, zip code level of education, living distance from treatment facility, facility type, AJCC cancer stage, and treatment modality had significant differences in TTI ($p<0.05$).

Conclusion: There has been an increase in TTI for PDAC over the period 2004-2015 with a number of significant factors linked to TTI including patient, hospital, and treatment specific characteristics. The only modifiable factor identified is the type of facility with integrated network cancer programs having the lowest TTI and thus choice of facility might reduce TTI and influence outcomes.

P 137. ASSESSING THE ROLE AND DANGERS OF TOTAL PARENTERAL NUTRITION AFTER PANCREATODUODENECTOMY

AM Roch, KA Lewellen, TK Maatman, DK DePeralta, EP Ceppa, NJ Zyromski, CM Schmidt, A Nakeeb, MG House

Presenter: Alexandra Roch MD | Indiana University School of Medicine

Background: Although total parenteral nutrition (TPN) has facilitated nutritional therapy for patients undergoing pancreatoduodenectomy (PD), recent studies suggest that enteral nutrition should be preferred. This study examines the role of TPN in patients requiring nutritional therapy after PD.

Methods: All patients who underwent PD at a single tertiary medical center (2005-2016) were included in a prospective database which was retrospectively queried. Patients who received postoperative TPN were compared to patients who did not for preoperative demographic, clinical, laboratory data, and postoperative outcomes. Univariate and binary regression analyses were performed, with statistical significance set at $p < 0.05$.

Results: 1451 patients had complete data for analysis. Postoperative TPN was initiated in 302 patients (20.8%) based on surgeon's decision at a median of 8.1 days [1-32]. TPN use was continued for a median of 20.6 days [1-16 months]. On multivariate analysis, only delayed gastric emptying was associated with TPN use (31.8% vs. 7.7%, $p < 0.001$). Preoperative weight loss was not an independent predictor for postoperative TPN use (27.8% vs. 25.2%, $p = 0.37$). Postoperative TPN use was associated with significantly increased 90-day mortality (10.6% vs. 2.6%, $p < 0.001$), morbidity (76% vs. 36.8%, $p < 0.001$) and length of stay (19.7 vs. 9.2 days, $p < 0.001$). Postoperative TPN use was associated with complications in 51% of patients: line sepsis 25%, hyperglycemia 20%, transaminitis 5%, thromboembolism 5%. Compared to enteral tube feeding, TPN resulted in a slower rise in serum albumin levels.

Conclusion: TPN is still widely used in high volume centers, without downtrend, despite poorer outcomes and significant morbidity directly associated with its use. TPN should be reserved for very selected patients who are not eligible for enteral routes of nutrition.

P 138. SURVIVAL OUTCOMES OF PANCREATICODUODENECTOMY VERSUS EXTENDED PANCREATICODUODENECTOMY PROCEDURE FOR PANCREATIC HEAD CARCINOMA: A PROPENSITY SCORE MATCHING STUDY

N Pu, W Lou, J Yu

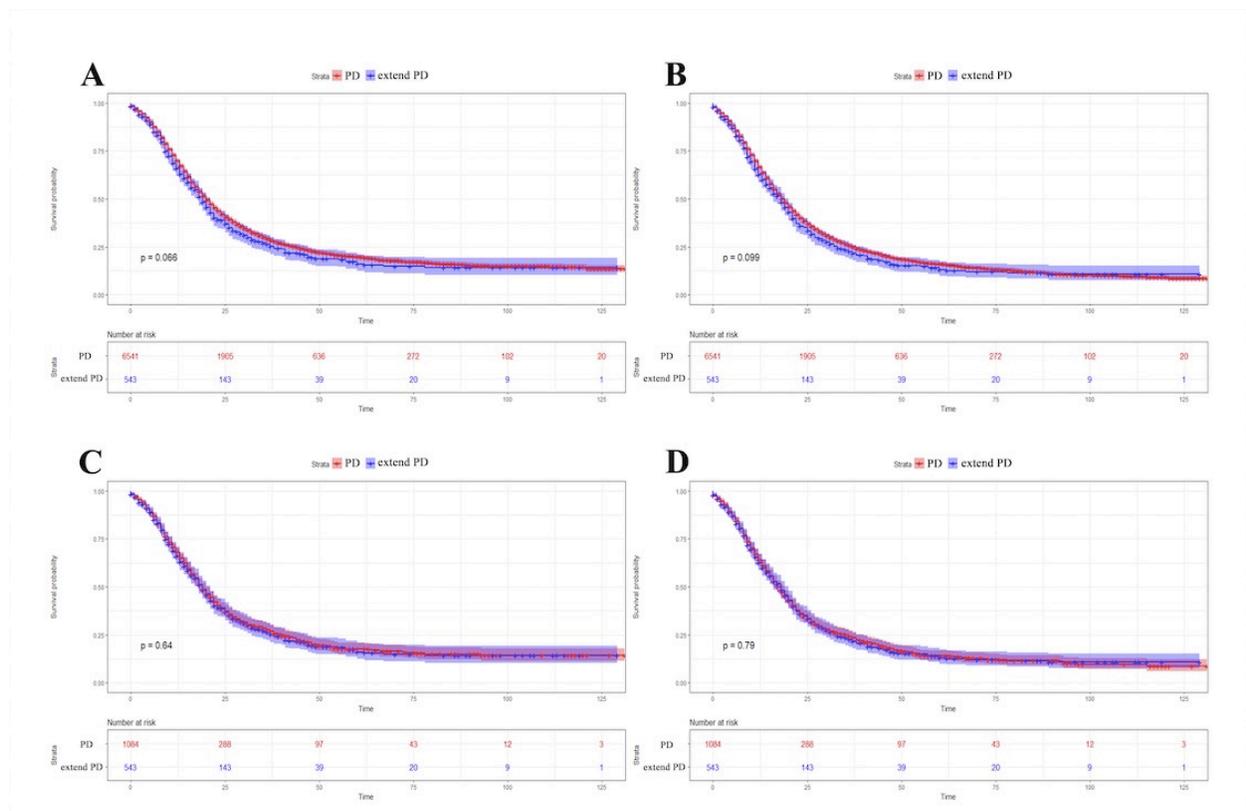
Presenter: Ning Pu MD | Johns Hopkins University School of Medicine

Background: It is unclear if the modified extended pancreaticoduodenectomy (PD) has better outcome superior the conventional PD for patients with pancreatic head carcinoma (PHC). The purpose of this study is to compare the survival outcomes of the classic PD procedure and the modified extended PD procedure for PHC.

Methods: A total of 7,084 resected PHC patients with PD and extended PD procedure from the SEER database from 2004 to 2014 were stratified. With the utilization of propensity score matching (PSM), patient baseline characteristics were balanced to decrease the bias. Overall survival (OS) and cancer-specific survival (CSS) were analyzed in both groups.

Results: Of the 7,084 patients, 6,541 (92.3%) and 543 (7.7%) patients received PD and extended PD surgical procedures, respectively. After 2:1 ratio of PSM, 543 patients with extended PD procedure and 1,084 patients with PD procedure were completely matched. The median CSS and OS for PD and extended PD group were 20.0 months and 19.0 months, and 19.0 months and 18.0 months, respectively. The 5-year CSS and OS rates for PD and extended PD group were 17.5% and 16.1%, and 13.9% and 13.1%, respectively.

Conclusion: There is no distinct difference in survival outcomes between PD and extended PD procedure in patients with PHC.



P 139. RISK FACTOR OF ARTERIAL PSEUDOANEURYSM AFTER PANCREATICODUODENECTOMY AND ITS OPTIMAL MANAGEMENT

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Presenter: Hiroyuki Kato MD | Mie University School of Medicine

Background: Arterial pseudoaneurysm is a rare but fatal complication after pancreaticoduodenectomy (PD), whereas its precise incidence and clinical characteristics are still yet to be clarified. Moreover the optimal management of this lethal complications is not established. As of the cause of pseudoaneurysm, it is well known that pancreatic fistula is mostly associated with the development of pseudoaneurysm. The aim of this study was to clarify the incidence, risk factor and proper treatment of pseudoaneurysm after PD, and also to elucidate the predictors associated with patient death caused by the rupture of pseudoaneurysm.

Methods: Among 401 patients who underwent PD from April 2007 to December 2017, 393 patients in whom risk factor analysis could be conducted, were subjected to our study. Uni- and multivariate analysis were performed to elucidate the perioperative risk factor of pseudoaneurysm, and risk factor analysis for elucidating the patient death was also conducted. Association between the type of interventional treatments and patient death was analyzed.

Results: Out of 393 patients, 21 (5.3%) developed pseudoaneurysm after PD regardless of symptomatic or asymptomatic one assessed by dynamic CT and/or angiography. Median durations from surgery to detection of pseudoaneurysm, were 17.0 (1-50). The primary diseases of these patients were pancreatic ductal adenocarcinoma in 10, bile duct carcinoma in 4, intraductal papillary mucinous neoplasm in 2 and others in 5. The location where aneurysm occurred were hepatic artery in 7, splenic artery in 3, GDA in 3, left or right gastric artery in 2 and others in 6. All pseudoaneurysm were treated with interventional approach using angiography. Univariate analysis revealed that high age, high BMI, large amount of intraoperative bleeding, long operation time, high drain amylase level (POD3-6) were risk factors of pseudoaneurysm, and high age ($p=0.007$) and long operation time ($p=0.040$) were selected as the independent risk factors by multivariate analysis. In fact, only 5 patients had the high drain amylase levels, but other 16 patients who developed pseudoaneurysm showed normal drain amylase levels. Among 21 patients, bleeding occurred in 16 patients (76%) and the 6 patients were dead due to the complications after bleeding. By comparing non-survivors ($n=6$) and survivors ($n=15$), patient age (72 vs.56 year-old, $p=0.041$, cut-off: 65.5, AUC:0.789) and operation time (801 vs. 522 min, $p=0.001$, cut-off: 657min, AUC:0.922) were significantly higher in non-survivor. As for the treatment of pseudoaneurysm, the 9 patients who was treated by transarterial embolization using lipiodol and/or N-butyl-2-cyanoacrylate (Histoacryl) had high mortality rate with compared to the 12 patients treated with coiling of pseudoaneurysm and/or arterial stent. (56%, 5/9 vs. 8%, 1/12, $p=0.042$).

Conclusion: High age and long operation time were recognized as the independent risk factors of pseudoaneurysm after PD and these were significantly associated with patient death. On the other hand, pancreatic fistula was not regarded as the cause of pseudoaneurysm. Thin slice dynamic CT should be performed to detect the aneurysm within 14 days, allowing us to find the unruptured aneurysm and prophylactically treat it with endoarterial coiling and/or stenting into the aneurysm.

P 140. NEUTROPHIL TO LYMPHOCYTE RATIO IS PREDICTIVE OF PATIENT SURVIVAL AFTER RESECTION OF PANCREATIC ADENOCARCINOMA

DT Pointer, DJ Roife, BD Powers, G Murimwa, S Elessawy, PJ Hodul, J Pimiento, JB Fleming, MP Malafa

Presenter: David Pointer MD | Moffitt Cancer Center

Background: White blood cell ratios (neutrophil-to-lymphocyte [NLR] and platelet-to-lymphocyte [PLR] and more recently the lymphocyte-to-monocyte ratio [LMR]) have been associated with pancreatic adenocarcinoma (PDAC) survival. Few studies have examined these inflammatory markers in US surgical cohorts. We sought to evaluate if these ratios predict outcomes and survival in a large US cohort of surgical PDAC patients.

Methods: We used a single institution database of patients who underwent upfront resection for PDAC between 2007 and 2015. This identified 307 patients of whom 277 patients had preoperative lab values to calculate NLR, PLR, and LMR ratios based on prior literature values (NLR, PLR and LMR cutoffs of 5, 150 and 3 respectively). We used Chi squared and Wilcoxon rank sum for statistical analysis. Survival was assessed with univariate and multivariable Cox regression.

Results: Elevated NLR, PLR, and decreased LMR represented 13.7%, 46.9% and 56.3% of the cohort, respectively. Univariate survival analysis showed that high NLR was associated with increased mortality however, high PLR and low LMR were not. On multivariable analysis, after adjusting for sex, comorbidity, insurance, receipt of neoadjuvant and/or adjuvant therapy, node status, margin, lymphovascular invasion, and Clavien grade 3/4 complication, high NLR remained a significant predictor of mortality (See Table). Additionally, more patients with high PLR (46.5%) and NLR (48.7%) and low LMR (47.7%) had borderline resectable PDACs than the total cohort (36.5%).

Conclusion: Our findings confirm using multivariable analysis that a high NLR is a significant predictor of overall survival. However, in contrast to other studies, LMR did not predict survival. The underlying mechanism of inflammatory cells in the tumor microenvironment needs further elucidation to help better clarify the role of predictive biomarkers.

Table 1. Relative Hazard of Death: Univariate and Multivariate Cox Regression

	Hazard Ratios (95% CI)	
	Univariate	Multivariate
Male Sex (Reference: Female)	0.77 [0.58-1.01]	0.88 [0.65-1.18]
Race (Reference: White)		
Black	0.72 [0.33-1.52]	
Other	0.78 [0.35-1.77]	
Age>70	1.56 [1.19-2.05]	
CCI (Reference: 0-3)		
4-5	1.56 [1.09-2.22]	2.09 [1.41-3.10]
≥6	2.44 [1.65-3.62]	2.47 [1.56-3.9]
Insurance Status (Reference: Private)		
Medicare with Private	1.022 [0.73-1.44]	0.66 [0.45-0.98]
Medicare	1.40 [0.97-2.03]	1.02 [0.67-1.55]
Medicaid/Uninsured	1.85 [1.00-3.39]	2.16 [1.14-4.10]
LMR ≤3	0.90 [0.68-1.18]	
PLR ≥150	1.06 [0.81-1.40]	
NLR ≥5	1.81 [1.23-2.67]	2.27 [1.48-3.48]
Neoadjuvant therapy	0.58 [0.43-0.78]	0.61 [0.43-0.87]
Preoperative Resectable	0.58 [0.43-0.78]	
DM	1.02 [0.75-1.39]	
Nodes Positive	1.53 [1.29-1.83]	
Nodes Positive (1-3)		1.80 [1.22-2.65]
Nodes Positive (4+)		1.82 [1.14-2.89]
Margin	1.39 [0.89-2.17]	
LVI	1.74 [1.32-2.28]	1.29 [0.85-1.95]
Perineural Invasion	1.61 [1.15-2.23]	
Adjuvant Failure	2.47 [1.87-3.28]	2.72 [2.00-3.71]
Grade 3-4 Complication	1.59 [1.06-2.39]	1.69 [1.10-2.62]

P 142. TEXTURE ANALYSIS OF CONTRAST ENHANCED CT IMAGING OF PANCREATIC NEUROENDOCRINE NEOPLASMS AND ITS CORRELATION WITH TUMOR GRADING

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Presenter: Zipeng Lu MD, PhD, MRCS | Pancreas Center, The First Affiliated Hospital with Nanjing Medical University

Background: Pancreatic Neuroendocrine Neoplasms are characteristically hypervascular, intensely enhancing lesions in contrast enhanced CT scans. However, necrosis and liquefaction are also fairly common in this kind of solid tumor. Because of different histological components contained, various imaging features could then be detected in dynamic enhanced CT scans. On the other hand, pNENs have different tumor grading, which is related to prognosis. The aim of this study is to perform texture analysis of contrast enhanced CT Imaging of pNENs and investigate the correlation between CT imaging features and tumor grading.

Methods: One hundred and six consecutive patients diagnosed of pNENs by routine pathology and immunohistochemical examination with dynamic contrast enhanced CT scans in the First Affiliated Hospital of Nanjing Medical University were reviewed from from January 2009 to December 2017. Twelve cases were excluded because of no finding of lesions. Texture analysis were eventually conducted in 94 cases in arterial and venous phase imaging of dynamic enhanced CT scans on PACS platform. All imaging texture features and enhanced CT values were detected. Correlation between these different features and tumor grading were analyzed.

Results: Of all the imaging texture features on CT, many characteristics were found correlated to tumor grading with statistical significance, including: tumor size, enhancement CT values, tumor-to-pancreas contrast ratio, enhancement patterns in both arterial and venous phase, iso/low density range in arterial phase, tumor shape, tumor margin, homogeneity, cystic or necrotic component, intratumoral blood vessels, vascular compression or invasion, peripheral tumor or lymph node and common bile duct dilatation. While other features such as peak attenuation time, tumor location, growth pattern, edge enhancement, upstream pancreatic duct dilatation and pancreatic atrophy had no significant correlation with grading. G1 pNENs were much smaller than other types. They usually had less intratumoral blood vessels and better homogeneity on terms of texture. No cases with common bile duct dilatation were found in this type. Nevertheless, cases of G2 showed more cystic or necrotic components in tumors, while G3 tumors had lower enhanced CT values, larger iso/low density range. As the grading increased, lesions tended to be more irregular in shape and more ill-identified in margin. Meanwhile, higher probability of detecting vascular compression or invasion and peripheral tumor or lymph node were eventually showed.

Conclusion: Pancreatic Neuroendocrine Neoplasms are a kind of heterogeneous tumor in not only clinical manifestations and prognosis, but also pathological and radiologic features. High heterogeneity revealed in CT imaging characteristics through texture analysis of dynamic enhanced CT images seems like the heterogeneity in tumor grading. Many imaging texture features suggested to be related to higher grading, such as larger size, more intratumoral blood vessels, more cystic or necrotic components, lower enhanced CT values, larger iso/low density range and poorer homogeneity may be clues of relatively poor prognosis in the future

P 143. PLASMA SUPAR IN DISTINGUISHING A MALIGNANT AND BENIGN PANCREATIC MASS

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Presenter: Anu Aronen MD | Tampere University Hospital

Background: Elevated plasma soluble urokinase plasminogen activator receptor (P-suPAR) is a biomarker associated with different inflammatory conditions and cancers. It predicts severity of first acute alcohol-induced pancreatitis (AAP) (Nikkola et al. *Pancreas* 2017) and 10-year mortality during AAP recovery (Aronen et al., submitted). P-suPAR levels remain low after first AAP during long-term follow-up despite of development of chronic pancreatitis (CP) (Aronen et al., submitted). Serum carbohydrate antigen 19-9 (S-CA19-9) has a relatively low specificity as a pancreatic tumor biomarker, which limits its use. Our aim was to study if P-suPAR could be used to differentiate a malignant and benign pancreatic mass.

Methods: P-suPAR and S-CA19-9 values were preoperatively measured from 46 patients [median age 67 (range 34-84) years, 50% male] who underwent pancreatic surgery because of a malignant-suspicious pancreatic mass. The final histopathological diagnosis was pancreatic cancer (PC) in 25 patients, a premalignant lesion in 14 patients, and the histology was benign in 7 patients.

Results: P-suPAR was significantly higher in patients with PC [median 3.7 (IQR 3.1-4.4) ng/mL] compared to patients with benign [2.1 (1.9-2.7) ng/mL; $p=0.004$] or premalignant [2.2 (1.7-3.8) ng/mL; $p=0.007$] histology. There was no significant difference between P-suPAR values of patients with premalignant and benign histology. ROC-curve in differentiating malignant and benign pancreatic masses resulted in AUC(ROC)=0.93 (95% CI 0.84-1.00); $p=0.001$. A cutoff value of 2.8 ng/mL was yielded using Youden's statistics with sensitivity of 85% and specificity of 86%. S-CA19-9 was 252 (29-384) in PC patients, 10 (7-23; $p=0.075$) in patients with a premalignant lesion and 6 (4-48; $p=0.159$) in patients with a benign lesion, respectively. Despite of the higher median S-CA19-9 levels in the PC group, it was not possible to differentiate malignant from a benign lesion using S-CA19-9.

Conclusion: Unlike S-CA19-9, preoperative P-suPAR is significantly higher in PC patients compared to patients with a benign or premalignant lesion. Thus P-suPAR may be a promising tool to differentiate benign and malignant pancreatic masses.

P 144. QUALITY OF LIFE AND PANCREATIC EXOCRINE AND ENDOCRINE FUNCTION IN THE LONG-TERM FOLLOW-UP AFTER PANCREATODUODENECTOMY

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Presenter: Ismo Laitinen MD | Tampere University Hospital

Background: Pancreatic exocrine and endocrine function is often impaired by a pancreatic tumor. After pancreatic resection, pancreatic function is affected by the volume and condition of the remaining pancreas, as well as by the patency of pancreaticojejunal (PJ)-anastomosis. Earlier we have shown that the Finnish binding pancreaticojejunostomy anastomosis (FBPJ) reduces postoperative pancreatic fistulae (POPF). The aim of this study was to assess the long-term pancreatic function and quality of life (QoL) after pancreatoduodenectomy (PD) using FBPJ.

Methods: 21 patients (14 female; 65 (44-76) yrs) who underwent PD with FBPJ minimum two years earlier and had a preoperative MRCP available, were recruited to the prospective study protocol and gave a written informed consent. Minimum two years after pancreatic resection, pancreatic atrophy, patency of PJ-anastomosis and diameter of pancreatic duct (PD) was studied with secretine-stimulated MRCP (S-MRCP). Pancreatic function was assessed with fasting glucose (fP-gluc), A1c-glycosylated hemoglobin (B-HbA1c) and fecal elastase (F-elast). QoL was assessed using EORTC Questionnaire Core 30 (QLQ-C30) together with disease-specific pancreatic module (QLQ-PAN26). Preoperative pancreatic function and postoperative complications were determined from patient files.

Results: At resection, 76% of the patients had a high-risk pancreas and >40% of acinar cells in the transection line. Grade B-C POPF developed in 24%, PPH in 10% and DGE in 14%. Overall complications according to Clavien-Dindo developed in 23% (Gr II), 4.8% (Gr IIIa), 9.5% (Gr IIIb) and 0% (GrIV) of the patients. All severe complications developed in patients with >40% of acinar cells. Histopathological diagnosis was cancer in 67% and other tumors in 33% of the patients. Preoperatively, MRCP showed atrophic pancreas in 24% and dilatation or stricture of the PD in 57% of the patients. 95% of the patients had pancreatic exocrine insufficiency (PEI) and 52% abnormal glucose tolerance (AGT). At two (range 2-5) years after resection, MRCP showed atrophic pancreas in 71% and dilatation or stricture of the PD in 71% of the patients. 95% of the patients had PEI; F-elast being below measure limit in 81% and <100 µg/g in 14% of the patients. 52% of the patients had abnormal fP-gluc. In EORTC QLQ-C30 reported levels were for physical functioning 80 (13-100; median, range), role functioning 100 (33-100), emotional functioning 92 (42-100), cognitive functioning 100 (33-100), social functioning 100 (33-100) and global QoL 75 (33-100). On symptom scales fatigue was reported 22 (0-78), nausea and vomiting 0 (0-17), pain 33 (0-100), dyspnea 0 (0-67), insomnia 33 (0-100), appetite loss 0 (0-67), constipation 0 (0-67), diarrhea 0 (0-100) and financial difficulties 0 (0-100). In QLQ-PAN26 pancreatic pain was reported 17 (0-75), digestive symptoms 17 (0-83), altered bowel habits 33 (0-83), hepatic symptoms 0 (0-17), altered body image 17 (0-100), sexuality-related symptoms 50 (0-100). Satisfaction with healthcare professionals was 67 (0-100).

Conclusion: At two years after PD, pancreatic dysfunction is extremely common, even in non-cancer patients. Pancreatic atrophy is seen in 71%, PEI in 95% and AGT in 52% of the patients. Despite of this, the QoL is good among these patients.

P 145. PROGNOSTIC FACTORS IN PATIENTS UNDERGOING PANCREATODUODENECTOMY FOR AMPULLARY CANCER - A LARGE MULTICENTER COHORT STUDY OF MORE THAN 200 PATIENTS

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Presenter: Louisa Bolm MD | University Medical Center Schleswig-Holstein

Background: Ampullary cancer (AMPCA) is a rare gastro-intestinal malignancy. We aimed to evaluate long-term overall survival and prognostic factors after pancreatoduodenectomy (PD) in a large multicenter cohort.

Methods: Patients undergoing PD for AMPCA at 4 high-volume surgical centers from 1996 to 2017 were identified from prospectively maintained databases. Patient baseline characteristics, surgical and histopathological parameters, as well as long-term overall survival after resection were evaluated.

Results: A total of 216 patients undergoing PD for ampullary cancer were included. 19.9% had a classical Whipple procedure, 79.2% underwent pylorus-preserving PD and a total pancreatectomy was performed in 0.9%. Median serum CEA was 1.9 (0.0-224.6) while median serum CA 19-9 was 33.85 (0.0-98726.0). 1.4% of the patients underwent neoadjuvant therapy. 47.7% presented with T3-4 tumors, 46.8% were diagnosed N1, and 12.0% had metastatic disease. Positive resection margins were confirmed in 5.1% of the patients. Median overall survival in all patients was 23 months. In univariate survival analysis, CEA (HR 2.239, 95%CI 1.321-3.793, $p=0.003$), CA 19-9 (HR 1.939, 95%CI 1.245-3.018, $p=0.003$), multivisceral resection (HR 4.081, 95%CI 0.985-16.906, $p=0.052$), T stage (HR 3.447, 95%CI 2.193-5.417, $p<0.001$), N stage (HR 0.023, 95%CI 0.003-0.189, $p<0.001$), grading (HR 1.656, 95%CI 1.086-2.525, $p=0.019$) and R status (HR 0.175, 95%CI 0.083-0.368, $p<0.001$) qualified as prognostic parameters. In multivariate analysis, T stage (HR 2.260, 95%CI 1.312-3.891, $p=0.003$) and R status (HR 0.338, 95%CI 0.133-0.859, $p=0.023$) remained independent prognostic factors.

Conclusion: T stage and R status were the strongest prognostic factors for long-term overall survival in AMPCA patients undergoing PD. Consequently, curative resection is warranted in patients with localized disease and careful preoperative evaluation of resectability should be performed.

P 146. RISK STRATIFICATION FOR INTENSIVE CARE UNIT FOLLOWING PANCREATODUODENECTOMY

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Presenter: Louisa Bolm MD | University Medical Center Schleswig-Holstein

Background: In view of limited intensive care unit (ICU) capacities and increasing economic burden, the identification of risk factors could allow for better and more efficient planning. Moreover, a prolonged ICU stay is accompanied with increasing morbidity and lower survival. Therefore, the aim of this study was to assess independent risk factors for the duration of intensive care unit stay after pancreatoduodenectomy.

Methods: 147 patients who underwent pancreatoduodenectomy in the time period from 2013 – 2015 were identified from a prospective database. The primary endpoint was length of time spent in the ICU. A retrograde analysis was performed using univariate and multivariate regression analysis. Pre-, intra- and postoperative risk factors were evaluated.

Results: The median time spent on intensive care unit is 1 day (range 0 – 78 days). The univariate analysis demonstrated smoking, antihypertensive medication, cerebrovascular events, anticoagulation, increased creatinine and CA 19-9 as preoperative predictors, OR time and extended lymphadenectomy as operative and severe postoperative pancreatic fistula (POPF), postpancreatectomy hemorrhage (PPH) delayed gastric emptying (DGE), reoperation and pulmonary complications as postoperative predictor for longer ICU stay. Upon multivariate analysis only antihypertensive medication, OR time, extended lymphadenectomy and severe PPH are significant risk factors for longer ICU stay.

Conclusion: Patients with cardiovascular risk factors and renal insufficiency are at higher risk for a prolonged ICU stay and should therefore be planned as such prior to pancreatoduodenectomy. Risk and benefit of an extended lymphadenectomy should be weighed during the operation. Post-operative pulmonary complications should be avoided in order to keep the stay in the intensive care unit as short as possible. Patients without significant risk factors do not require routine postoperative monitoring in the intensive care unit.

P 147. PROGNOSTIC VALUE OF TP53, CDKN2A/P16 AND SMAD4/DPC4 IN LOCALLY ADVANCED, BUT RESECTED, PANCREATIC CANCER

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Presenter: Niccolò Napoli MD | University of Pisa

Background: The most frequently mutated genes in pancreatic ductal adenocarcinoma (PDAC) are KRAS, TP53, CDKN2A/p16, and SMAD4/DPC4. KRAS is virtually mutated in all patients. These gene mutations affect disease specific survival (DSS) and progression free survival (PFS). Our aim is to evaluate the impact of SMAD4/DPC4, CDKN2A/p16, and TP53 expression on survival of patients who received a pancreatectomy with arterial resection (P-Ar) because of a locally advanced PDAC (LA-PDAC).

Methods: Data from a prospectively maintained database were used to conduct a retrospective cross-sectional study on P-Ar performed for LA-PDAC between March 2000 and July 2017. Post-operative deaths were excluded because the impact of mutated genes on long-term survival could not be evaluated. The status of TP53, CDKN2A/p16, and SMAD4/DPC4 was immunohistochemically assessed. DSS and PFS were calculated using Kaplan-Meier curves. Log-rank test was used to compare survival differences between patient with positive or negative status of TP53, CDKN2A/p16, and SMAD4/DPC4. The relationship between preoperative features and expression of TP53, CDKN2A/p16, and SMAD4/DPC4 was evaluated by using logistic regression. ROC curve was used to identify the cut-off of statistically significant preoperative features.

Results: A total of 38 patients were eligible for this study. They had a mean age of 63.5±10 years, a median ASA score of 2 (2-3), and were predominantly males (18; 47.4%). All patients had at least one arterial segment resected. A vein segment was also resected in 35 (92.1%) patients. The superior mesenteric artery was resected in 16 (42.1%) patients and the celiac axis/hepatic artery in 26 (68.4%) patients. Median DSS and PFS were of 25.3 (14.2-74) months and 12.8 (10.3-22) months, respectively. Regarding pathological features, median T status was 3 (3-4), mean number of examined lymph nodes was 71.2±26.2, median number of positive lymph nodes was 3 (1-7), median lymph nodes ratio was 3.2 (1.5-7.5), mean log odds of positive lymph nodes was -1.3±0.4. Arterial and venous infiltration was confirmed in 14 (36.8%) and 18 (51.4%) patients, respectively. R0 resection was confirmed in 33 (86.8%) patients. Abnormal immunolabeling of TP53 was present in 21 (55.2%) PDACs. Loss of p16 and SMAD4 was identified in 23 (60.5%) and 22 (57.9%) PDACs, respectively. DSS and PFS were higher in patient with positive SMAD4 and P53 and negative p16 (table 1). Regarding preoperative features, only preoperative level of Ca 15.3 correlated with the expression of one of these proteins (SMAD4/DPC4; p=0.01). Preoperative Ca 15.3 level higher than 21.7 KU/L was associated with loss of SMAD4 and a worst prognosis (DSS: 17 vs 28.3 months, p=0.24).

Conclusion: Positive SMAD4 and P53 and negative p16 discriminated survival in a cohort of 38 patients with LA-PDAC following P-Ar. A larger number of patients are required to validate our results.

Table 1 – Median disease specific survival and progression free survival in patients with LA-PDAC based on SMAD4/DPC4, CDKN2A/p16, and TP53 status

	SMAD 4/DPC4			CDKN2A/P16			TP53		
	Intact	Loss	<i>p</i>	Positive	Negative	<i>p</i>	Normal	Abnormal	<i>p</i>
DSS	26.7 (20.9-39)	18.6 (13.3-74)	0.43	18.8 (13.3-NA)	25.3 (15.7-74)	0.88	39 (15.7-NA)	18.8 (14-74)	0.37
PFS	16 (10.8-21)	12.7 (8.1-59.6)	0.83	12 (9.9-18.7)	15 (12-22)	0.77	16 (10.8-21.9)	12.7 (10.3-22)	0.58

P 148. ELEVATED BILIRUBIN LEVELS SHOULD NOT INFLUENCE TIMING OF PANCREATIC RESECTION

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Presenter: Guido Alsfasser MD | University of Rostock

Background: Little is known about the effects of hyperbilirubinemia on the rate of complications in pancreatic surgery. Preoperative bile duct drainage increases morbidity in numerous studies and showed increased risk of bleeding complications in earlier studies of our group. German guidelines recommend preoperative stenting only if cholangitis is present. Furthermore, stenting can be considered if the operation needs to be postponed. General opinion strongly suggests early resection in the presence of elevated bilirubin levels.

Methods: Retrospective analysis of prospectively collected data of 578 patients undergoing pancreatic resections at our institution. Rate of cholangitis, preoperative bilirubin levels, amount of general and surgical complications and rate of clinically relevant pancreatic fistula were compared in patients with normal or elevated bilirubin level. Furthermore the cut-off value of 100, 150, 200, and 300 $\mu\text{mol/l}$ bilirubin was evaluated.

Results: Preoperative bilirubin levels of 93% of patients (n=535) were available. Rate of cholangitis was 16% in the entire cohort and 8% of these patients did not receive preoperative biliary drainage. Rate of general complication was 47.5%, rate of surgical complication 59%. Rate of pancreatic fistula was 18.8%. There was no difference in the rate of complications between any of the groups compared (see table 1). Patient with normal bilirubin levels had the same rate of all analyzed complications as patients with elevated levels had. Furthermore, neither high elevated levels of 100 up to 300 $\mu\text{mol/l}$, showed an increase in the rate of complications.

Conclusion: Elevated preoperative bilirubin levels per se do not show any increase in rate of complications in pancreatic resection. Therefore elevated bilirubin levels should not influence the timing of pancreatic resection. To substantiate the conclusion for high range hyperbilirubinemia a multicenter approach is recommended. The need for preoperative biliary decompression should be reserved for patients with cholangitis only.

Table 1: p-values of comparison, chi-square test

Parameter	normal vs. elevated bilirubin	< 100 $\mu\text{mol/l}$ vs. > 100 $\mu\text{mol/l}$	< 150 $\mu\text{mol/l}$ vs. > 150 $\mu\text{mol/l}$	< 200 $\mu\text{mol/l}$ vs. > 200 $\mu\text{mol/l}$	< 300 $\mu\text{mol/l}$ vs. > 300 $\mu\text{mol/l}$
n	372 vs. 163	483 vs. 52	500 vs. 35	519 vs. 16	530 vs. 5
Fistula	0.08	0.56	0.56	0.57	0.67
General complications	0.44	0.34	0.67	0.67	0.43
Surgical complications	0.82	0.78	0.71	0.71	0.41

P 149. PANCREATIC DUCT CALIBER SHOULD NOT BE USED AS THE SOLE JUSTIFICATION FOR SURGICAL SELECTION IN MAIN DUCT IPMNS

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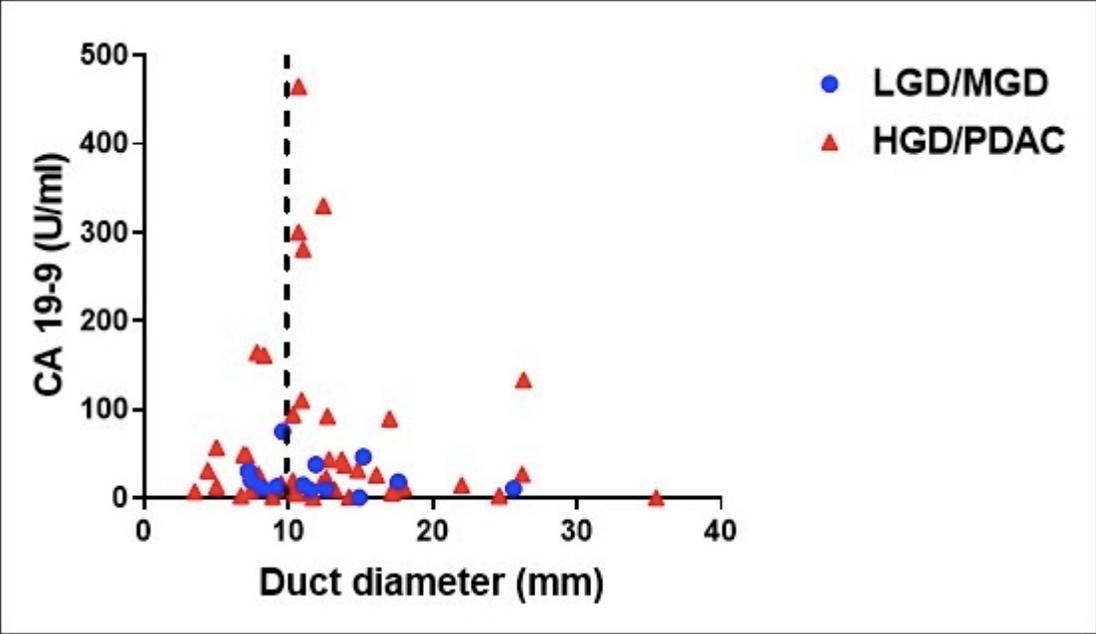
Presenter: Tara Hughes MD | University of Texas MD Anderson Cancer Center

Background: Main duct intraductal papillary mucinous neoplasms (MD-IPMN) are at significant risk for progression into pancreatic ductal adenocarcinoma (PDAC). Previous studies indicate the risk for malignant transformation proportionally increases with the caliber of MD-IPMNs, approaching a >50% incidence of PDAC in MD-IPMNs ≥ 1 cm. For this reason, current guidelines recommend MD-IPMNs with calibers ≥ 1 cm undergo surgical resection. We sought to determine the validity of this recommendation based on our experience at a high-volume, academic center.

Methods: Review of a prospectively maintained, retrospective database identified 71 patients who underwent pancreatic resection for MD-IPMN from 2005-2018. Preoperative MD-IPMN calibers were individually measured on CT or MRI imaging and preoperative CA 19-9 values and radiographic imaging characteristics were recorded for each patient. Patients with MD-IPMNs were grouped based on the presence of LGD/MGD, HGD or PDAC on final pathologic analysis. Student's t-tests were used to test differences in duct caliber, CA 19-9 values and nodule size between patient subgroups and the sensitivities and specificities were calculated for preoperative nodularity/masses to represent PDAC.

Results: Among 71 patients with MD-IPMNs, final pathology revealed LGD/MGD in 13, HGD in 26 and PDAC in 32. Duct caliber was not significantly different between MD-IPMNs with LGD/MGD and HGD (1.2 ± 0.52 cm vs. 1.4 ± 0.78 cm, respectively; $p=0.44$). Moreover, no significant differences were identified in the calibers of MD-IPMNs harboring PDAC (1.26 ± 0.65 cm) relative to LGD/MGD ($p=0.91$) or HGD ($p=0.38$). CA 19-9 levels were not significantly different between MD-IPMNs with LGD/MGD and HGD (23.8 ± 19.8 U/ml vs. 25.8 ± 31.9 U/ml, respectively; $p=0.84$) and approached significance between MD-IPMNs with LGD/MGD and PDAC (23.8 ± 19.8 U/ml vs. 87.3 ± 112 U/ml, respectively; $p=0.05$). A solid nodule or mass was observed on preoperative EUS, CT or MRI in 6/13 patients with LGD/MGD, 16/26 with HGD and 30/32 with PDAC. Collectively, the presence of preoperative nodules/masses had a sensitivity of 93.75% (95% CI 79.2-99.2) and specificity of 43.6% (95% CI 27.8-60.4) for PDAC. Of the patients with a measurable solid component on imaging, There was no significant difference in size of nodules with LGD/MGD compared to HGD (2.42 ± 1.49 cm versus 2.52 ± 1.64 cm, respectively ($p=0.904$)).

Conclusion: Neither pancreatic duct diameter ≥ 1 cm nor elevations in CA19-9 levels consistently correlate with the underlying presence of PDAC in association with MD-IPMNs. Nodularity or masses associated with MD-IPMNs on preoperative imaging were sensitive for the presence of PDAC but inadequate to distinguish premalignant lesions from PDAC. In the absence of biopsy-proven HGD/PDAC, MD-IPMN calibers ≥ 1 cm should not solely be used to justify surgical resection, particularly in high surgical risk patients. Solid nodules >2.5 cm in the setting of MD-IPMNs may confer a higher risk of underlying invasive cancer. MD-IPMN duct caliber should be considered with other high-risk stigmata and/or worrisome features to inform decisions regarding resection of MD-IPMNs.



P 151. ISCHEMIC GASTROPATHY AFTER DISTAL PANCREATECTOMY WITH EN BLOC CELIAC AXIS RESECTION FOR PANCREATIC BODY CANCER

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Presenter: Hiroki Yamaue MD | Wakayama Medical University

Background: Risk factors of ischemic gastropathy (IG) following distal pancreatectomy with en bloc celiac axis resection (DP-CAR) remain unclear.

Methods: Fifty consecutive patients with pancreatic cancer who underwent DP-CAR were retrospectively reviewed for possible risk factors for IG. This study was registered on the UMIN Clinical Trials Registry (UMIN 000028732).

Results: Complications higher than grade 3 were observed in 21 patients (42%), and mortality was 8%. Left gastric artery (LGA) resection ($P=0.046$) and a combination of left inferior phrenic artery (IPA) with LGA resection ($P=0.012$) were risk factors of IG, and an elevated creatine kinase (CK) value ≥ 1005 IU/L ($P=0.025$) was associated with IG. Among prognostic factors, IG (OR, 5.997; 95% CI, 1.543-23.309; $P=0.010$), completion of adjuvant chemotherapy (OR, 0.282; 95% CI, 0.121-0.654; $P=0.003$), longer operative time (OR, 2.261; 95% CI, 1.084-4.714; $P=0.030$), and higher age (OR, 2.212; 95% CI, 1.081-4.524; $P=0.030$) remained independent predictors of survival. Comparison of two and three months post operatively showed nutritional values were higher in patients who underwent LGA-preserving DP-CAR than those with LGA-resecting DP-CAR: total protein (6.65 ± 0.66 vs 7.17 ± 0.56 g/dl, $P=0.007$), albumin (3.43 ± 0.43 vs 4.04 ± 0.45 g/dl, $P<0.001$), and total cholesterol (141.6 ± 27.2 vs 162.3 ± 34.7 mg/dl, $P=0.044$).

Conclusion: The poorer prognosis in patients who underwent DP-CAR may be related to more advanced tumors. A combination of left IPA and LGA resection was a significant risk factor for IG. IG, completion of adjuvant chemotherapy, longer operative time, and higher age remained independent as good predictors of survival.

P 152. RNA-SCOPE TECHNOLOGY AND IMMUNOHISTOCHEMISTRY REVEAL LOW EXPRESSION OF MUC5AC IN METASTATIC PANCREATIC PATIENTS: EPIGENETIC PITFALLS OR A BETTER DISEASE STATUS?

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Presenter: Niccola Funel PhD | University of Pisa

Background: Pancreatic ductal adenocarcinoma (PDAC) patients are in advanced stage of disease and most of them are metastatic (mPDAC) and are not candidate for surgery and clinical treatments remain a palliative. Identification of diagnostic and prognostic biomarkers for mPDAC have been investigated. MUC5AC was identified as high expressed mucin gene in PDAC compared with benign pancreatic pathologies. Its expression, in early pancreatic intraepithelial precursor lesions (PanIN), makes MUC5AC a potential diagnostic and prognostic biomarker. MUC5AC increases during cancer progression, but its role in mPDAC is not well establish. The goal of present study was to investigate MUC5AC expression in mPDAC patients.

Methods: Immunohistochemistry (IHC) and RNA-Scope technology (RST, ACD company) were used to detect both protein and mRNA expression of MUC5AC, respectively. Biomarkers detections were performed on home-made tissue microarrays (TMAs) representing mPDAC patients (52), plus other entities as follows: normal pancreatic (8), hyperplasia of ducts (10), IPMN foci (10) and PDAC cases (30). To highlight the presence of both mRNA and protein of MUC5AC, we used a conventional brown color obtained by peroxidases reaction conjugated with antibodies and RNA probes. In order to verify the pancreatic origin of this lesions, all dots of TMA was stained with AE1/AE3 antibody. IHCs and RST were performed according to automated protocol into a Bound III machine (Leica Microsystems). Positive and negative controls were used to validate the staining.

Results: All TMA cores (100%) representing normal pancreata, pre neoplastic lesions, PDACs and mPDAC showed a strong positivity for AE1/AE3 antigen. While, looking at the MUC5AC immunostaining we found that its presence decreased in linear way according PDAC progression. The hyperplastic lesions had the highest positivity (8/10; 80%), followed by IPMN (7/10; 70%), PDAC (19/30; 66%) and mPDAC (23/52; 44%). We analysed at least 3 cores for each patients and we didn't find heterogeneity for both MUC5AC and AE1/AE3 protein expressions. Indeed, we matched IHC and RST analyse for MUC5AC, in order to verify whether the presence of protein was associated with presence of its RNA. The total of pathological lesions showing positivity for MUC5AC protein expression (49/102; 48%), demonstrated to have a partial or total positivity for mRNA expression of MUC5AC in 92% of cases (45/49). Lesions having mRNA positivity without its protein expression were not observed. Neither protein and mRNA of MUC5AC were detected in normal pancreata.

Conclusion: Genetic analyses revealed MUC5AC as most differently overexpressed mucin in PDAC. The expression of MUC5AC was examined in home-made TMA. Our IHC positivities for both MUC5AC and AE1/AE3 demonstrated similar results comparing them in front of the literature. However, we found a lower percentage (44%) of mPDAC positives for MUC5AC expression. This results were supported by the RNA-Scope technologies validating the presence of MUC5AC mRNA. Indeed, we can have a subcohort of mPDAC patients with a lower aggressiveness disease. It should be remarkable that, to rich the diagnostic and prognostic performance of MUC5AC gene; additional studies combining microRNA (miRNA) by In Situ Hybridization analyses (IHS), with the methodologies used in this study are needed in order to clarify the epigenetic mechanism in PDAC metastatic process.

P 154. DOES CHOICE OF APPROACH TO PANCREATECTOMY AFFECT POSTOPERATIVE OUTCOMES IN PATIENTS UNDERGOING RESECTION FOR CHRONIC PANCREATITIS: A NSQIP STUDY

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Presenter: Essa M. Aleassa MD, MSc | Cleveland Clinic Foundation

Background: Pancreatic resection is the optimal treatment for a subset of patients with chronic pancreatitis (CP). Whilst open and minimally invasive techniques (MIS) are applicable, the optimal approach has not been defined. The aim of the current study was to evaluate the influence of surgical approach (open versus MIS) on outcome in patients undergoing resection for chronic pancreatitis.

Methods: The American College of Surgeons - National Surgical Quality Improvement Program (ACS-NSQIP) Pancreatectomy Targeted Participant Use Data File was queried to identify patients undergoing pancreatoduodenectomy (PD) or distal pancreatectomy (DP) for CP. Patients converted from an MIS procedure were excluded. Surgical site infection (SSI), postoperative pancreatic fistula (POPF), and delayed gastric emptying (DGE) rates were evaluated as were length of stay (LOS), 30-day readmission (30-R), and 30-day mortality (30-M).

Results: From 2014-2016, 1258 patients (DP=396(31.5%); PD= 862(68.5%]) underwent resection. The rates of superficial (1.7%vs.5.4%;p=0.17), deep (0.9%vs.1.8%;p=0.68), and organ space SSI (4.3%vs.13.6%;p=0.007) were less in the MIS-DP cohort as was DGE (1.7%vs6.9%;p=0.038). The rate of POPF was higher after MIS-DP (21.7%vs.18.6%;p=0.48). For PD, the superficial (4.3%vs.8.7%;p=0.42), deep (2.2%vs.1.8%;p=0.59), and organ space SSI (10.9%vs.9.1%;p=0.6) rates were not different by approach as were, DGE (13%vs.14%;p=0.86) and POPF (11.1%vs.12.5%;p=0.78). LOS was less for MIS-DP (5 [Interquartile range, IQR= 4-6] vs. 7 [IQR=7-10] days;p 0.999) and PD (2.2% vs 2%; p=0.61) patients were comparable.

Conclusion: The choice of surgical approach influences the early postoperative outcomes in patients undergoing DP for chronic pancreatitis, favoring an MIS technique. However, the benefits of an MIS approach were not seen for PD except for a shorter length of hospital stay.

P 157. CAN REGIONAL LYMPH NODE METASTASES FROM PANCREATIC CANCER BE PREDICTED WITH CROSS-SECTIONAL IMAGING?

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Presenter: Katelyn Flick MD | Indiana University School of Medicine

Background: Lymph node (LN) metastasis is highly predictive of disease-specific survival for patients with pancreatic cancer. Local and regional LN assessment with cross-sectional imaging may identify patients at risk for early disease progression after resection of pancreatic cancer. The purpose of this study was to compare radiologic characteristics with final histopathologic findings of regional lymph nodes in patients undergoing pancreatoduodenectomy (PD).

Methods: Staff radiologists were blinded to the final histopathology findings for patients undergoing resection for pancreatic cancer. Radiologic interpretations of preoperative CT images were evaluated for the LN status along the celiac axis. Findings were then recorded with regards to the likelihood of nodal metastasis at this level. Two categories of findings were established: benign or suspicious for metastases. Two-way comparisons were performed between radiologic interpretation and final histopathologic findings.

Results: Forty-six cases were assessed. All PD specimens were confirmed as pancreatic ductal adenocarcinoma with the exception two cases of mucinous adenocarcinoma and two of chronic inflammation. Histopathology revealed an average tumor size of 3.3 cm (± 0.16). Among all cases, an average number of 23 LNs were examined, with a mean of almost 5 positive for malignancy. The majority (78%) of cases were staged as pT3N1. Negative surgical margins were achieved in 87% of resections. Metastatic LN disease along the celiac axis was established pathologically in 9 (20%) patients, exclusively at the station 8 LN level. The sensitivity, specificity, negative and positive predictive values of preoperative cross-sectional imaging for pathologic LN staging along the celiac axis was: 44%, 97%, 88%, and 80%, respectively.

Conclusion: Routine preoperative radiologic staging of celiac axis lymph node metastases is inaccurate for patients with pancreatic cancer. Findings of this study do not support further studying the utility of enhanced or functional cross-sectional imaging to detect locoregional LN involvement.

P 159. THE EFFICACY AND SAFETY OF DUODENAL STENT FOR PATIENTS TREATED WITH CHEMORADIO THERAPY FOLLOWED BY SURGERY FOR PANCREATIC DUCTAL ADENOCARCINOMA

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Presenter: Takehiro Fujii MD, PhD | Mie University School of Medicine

Background: Invasion of the duodenum by pancreatic ductal adenocarcinoma (PDAC) is a major cause of failure in preoperative treatments for PDAC because duodenum obstruction causes eating disorder. Duodenal stent placement has been indicated for the alternative palliative therapy to surgical gastrojejunostomy, but few studies have investigated availability of duodenal stent during preoperative treatments for PDAC. Especially, the safety of chemoradiotherapy (CRT) for the patients with duodenal stent has not been elucidated yet, because CRT might increase the risk of duodenal perforation. In this study, we examined the efficacy and safety of duodenal stent placement for duodenal obstruction during CRT for PDAC.

Methods: We included 217 consecutive patients who underwent preoperative CRT for PDAC without distant metastasis from January 2012 to December 2017. Preoperative respectability classification of these patients was resectable in 43 patients, borderline resectable in 66 patients, and locally advanced in 108 patients. CRT completion rate, resection rate of PDAC, incidence of adverse events interrupting CRT and hematological indexes of nutrition (albumin and total cholesterol, and prognostic nutritional index) during CRT were compared between the two groups in the presence or absence of duodenal metallic stent (S vs. non-S group). Among the patients who could undergo pancreaticoduodenectomy (PD), operative time, blood loss and postoperative hospital stay were compared between the two groups.

Results: The 217 patients were classified into S (n=9) and non-S (n=208) groups. Between S and non-S groups, there were no significant differences in CRT completion rate (100% vs. 97.1%), in resection rate (33.3% vs. 55.3%) and in R0 resection rate (66.7% vs. 89.6%). Duodenal stent placement did not increase the incidence of adverse events leading to interruption of CRT. There were no patients who developed perforation of gastrointestinal tract in both groups during CRT, but two patients in S group needed gastrojejunostomy after duodenal stent placement because they developed stent obstruction. The rates of decrease in the nutrition factors during CRT did not differ significantly between the two groups. When the 97 patients undergoing PD after CRT were classified into S-PD (n=3) and non-S-PD (n=94) groups, there were no significant differences in operative time (568±73 vs. 557±120 min) and in blood loss (2372±2427 vs. 1266±1536 ml). Postoperative course was not influenced by duodenal stent placement.

Conclusion: Our results demonstrate the efficacy and safety of duodenal stent placement for duodenal obstruction in the setting of preoperative CRT without increasing adverse events. Duodenal stent commonly used for palliative therapy is a highly potential tool for combined-modality therapy for PDAC.

P 160. IMPACT OF POSTOPERATIVE PANCREATIC FISTULA ON THE PROGNOSIS OF PATIENTS UNDERGOING RESECTION FOR PANCREATIC DUCTAL ADENOCARCINOMA

M Sugimoto, S Kobayashi, S Takahashi, M Konishi, N Gotohda

Presenter: Motokazu Sugimoto MD | National Cancer Center Hospital East

Background: Postoperative pancreatic fistula (POPF) is a major morbidity that can occur after pancreatectomy. However, the impact of POPF on survival outcomes remains unclear. This study aimed to investigate the relationship between perioperative clinicopathological factors and survival outcomes in patients with pancreatic ductal adenocarcinoma (PDAC).

Methods: The study included 366 patients who underwent pancreatectomy for PDAC between January 2007 and December 2016. POPF was defined as grade B or C of the International Study Group of Pancreatic Surgery criteria in 2016. Perioperative clinicopathological data were evaluated for their association with the risk of a shorter disease-specific survival (DSS) and recurrence-free survival (RFS).

Results: Of the 366 patients, the median age was 68, and 232 patients (63%) were male. There were 253 patients undergoing pancreaticoduodenectomy (PD) and 113 patients undergoing distal pancreatectomy (DP). Among 253 PD patients, 33 (13%) developed POPF, while among 113 DP patients, 45 (40%) developed POPF. The median duration of follow-up was 38 months. Independent risk factors for a shorter DSS were lower serum albumin level (hazard ratio (HR) 1.558, $P = 0.015$), greater intraoperative blood loss (HR 1.000, $P = 0.025$), larger tumor size (HR 1.019, $P = 0.009$), lymph node metastasis (HR 1.797, $P = 0.005$), and a lack of adjuvant chemotherapy (HR 2.110, $P < 0.015$). Independent risk factors for a shorter RFS were lower serum albumin level (HR 1.450, $P = 0.020$), greater intraoperative blood loss (HR 1.000, $P = 0.006$), larger tumor size (HR 1.017, $P = 0.002$), lymph node metastasis (HR 1.904, $P < 0.001$), and a lack of adjuvant chemotherapy (HR 2.128, $P < 0.001$). POPF was not associated with DFS (HR 1.077, $P = 0.696$) or RFS (HR 1.115, $P = 0.479$). However, compared with patients without POPF, those with POPF received adjuvant chemotherapy less frequently (68% vs. 79%, $P = 0.037$) and had a longer duration to start adjuvant chemotherapy after surgery (61 days vs. 52 days, $P = 0.001$).

Conclusion: There were no relationship between the occurrence of POPF and survival outcomes in patients who underwent surgery for PDAC. However, because patients with POPF had a smaller chance to receive adjuvant chemotherapy and a longer time to be withheld from adjuvant chemotherapy, POPF might affect on their survival outcomes. Prevention of POPF appears to be important to improve survival outcomes for patients with PDAC.

P 162. LONG-TERM ONCOLOGICAL OUTCOMES AFTER DISTAL PANCREATECTOMY FOR NEUROENDOCRINE NEOPLASMS: A COMPARISON BETWEEN MINIMALLY INVASIVE AND OPEN APPROACH USING PROPENSITY SCORE

V Andreasi, S Partelli, P Rancoita, E Pérez-Sanchez, F Muffatti, M Mazza, G Balzano, R Castoldi, S Crippa, D Tamburrino, M Falconi

Presenter: Valentina Andreasi MD | San Raffaele Scientific Institute

Background: Pancreatic neuroendocrine neoplasms (PanNEN) are ideal entities for minimally invasive surgery. Several series described laparoscopic surgery for PanNEN demonstrating the advantage of this approach compared to open technique in terms of complications, length of hospital stay and cosmetic results. However, scarce data are available on long-term oncological outcomes. Aim of this study was to compare short-term postoperative outcomes, pathological findings and long-term oncological results of minimally invasive distal pancreatectomy (MIDP) and open distal pancreatectomy (ODP).

Methods: Patients who underwent ODP or MIDP for nonfunctioning PanNEN (NF-PanNEN) were retrospectively analyzed. Complications were graded according to the Clavien-Dindo classification. Inverse probability of treatment weighting using propensity score was performed to compare the outcomes of minimally invasive and open approach.

Results: Overall, 131 patients were included in the study: 84 underwent ODP, whereas 47 were submitted to MIDP. Median radiological diameter was 25 mm (interquartile range 18-45). The rate of postoperative complications was significantly lower after MIDP ($P=0.006$, estimated grade of postoperative complication 0 vs 2) and the postoperative length of stay was significantly shorter after MIDP compared to ODP ($P<0.001$, estimated days 8 versus 11). The number of examined lymph nodes was significantly higher after ODP in comparison to MIDP ($P=0.007$, estimated number of examined lymph nodes 13 vs 10). Estimated median follow-up was 77 months (95% confidence interval: 66-85) and overall 22 patients had a recurrence after a median follow-up of 26 months (range 1-92). Similar disease-free survival (DFS) and overall survival (OS) findings were reported for the two groups ($P=0.621$ and $P=0.842$, respectively).

Conclusion: Although MIDP for PanNEN seems to be associated with a lower number of resected lymph nodes, long-term survival is not influenced by the type of surgical approach. MIDP is advantageous in terms of postoperative complications and length of stay, but prospective studies are needed to confirm the overall oncological quality of resection in this group of neoplasms.

P 163. IMPACT OF POST-OPERATIVE PANCREATIC FISTULA ON LONG-TERM OUTCOMES AFTER PANCREATIC RESECTION FOR PERIAMPULLARY ADENOCARCINOMA

JW Bonaroti, MS Zenati, A Al-abbas, C Reiser, AH Zureikat, BA Boone

Presenter: Jillian Bonaroti MD | University of Pittsburgh Medical Center

Background: The short-term morbidity associated with a post-operative pancreatic fistula (PF) is well established, however data regarding the long-term impact of PF are lacking. Limited studies examining outcomes present conflicting data and do not differentiate by PF grade. The goal of this study is to characterize long-term outcomes of PF after pancreatic resection for periampullary adenocarcinoma.

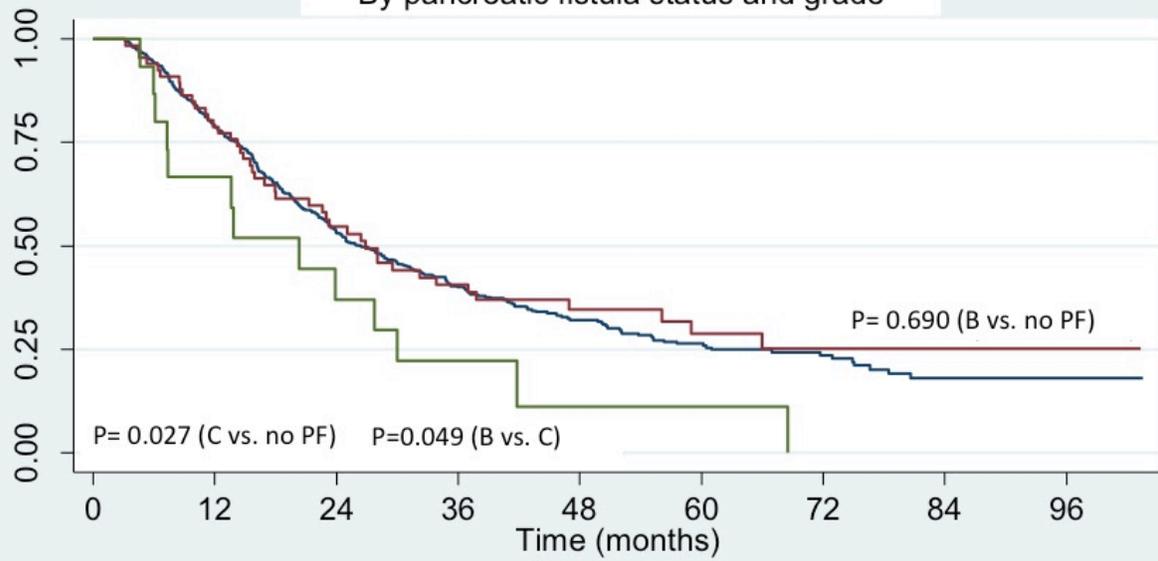
Methods: A single institution study of all pancreatic resections, including pancreaticoduodenectomy and distal pancreatectomy, performed for periampullary adenocarcinoma from 2008 to 2016. PF was defined by ISGPF criteria. Kaplan-Meier survival analysis, logistic regression, and multivariate analysis (MVA) were used to evaluate the impact of PF on overall survival (OS), disease free survival (DFS), time to initiation of adjuvant therapy, and receipt of adjuvant chemotherapy (AC).

Results: 767 patients were included; age 67.2 +/- 10.2 years and 47.5% female. Of those, 82 (10.6%) developed a Grade B (n=67, 82%) or C (n=15, 18%) PF. Patients with a Grade C PF had decreased median OS when compared to no PF (20.33 vs 26.87 months, p=0.027) and compared to Grade B PF (20.33 vs. 26.87 months, p=0.049). PF patients also had a trend towards decreased median DFS when compared to the remaining cohort (9.13 vs 20.3 months, p=0.072). Patients with PF were less likely to receive AC than those without PF (59.5% vs 74.9%, p=0.003) and Grade C PF were less likely to receive AC than all others (26.7% vs 74.2%, p=0.0001). Patients with PF had longer median time to initiation of AC than those without PF (75 vs 61 days, p=0.002), and Grade C had a trend towards longer time to initiation of AC than all others (86 vs 62 days, p=0.083). On MVA, Grade C PF was independently associated with failure to receive AC (OR 0.18, CI (0.05,0.65); p=0.009).

Conclusion: Patients who develop PF are less likely to receive AC and are more likely to have delay in time to receive AC. These factors are exacerbated in Grade C PF and likely contribute to decreased OS. Importantly, these findings validate the clinical significance of the updated ISGPS definitions of post-operative PF.

Kaplan-Meier survival estimates

By pancreatic fistula status and grade



P 164. SIGNIFICANCE OF RADIOGRAPHIC SPLENIC VESSEL INVOLVEMENT IN PANCREATIC DUCTAL ADENOCARCINOMA OF THE BODY AND TAIL OF THE GLAND

JJ Hyun, JB Rose, AA Alseidi, TR Biehl, WS Helton, DL Coy, RA Kozarek, FG Rocha

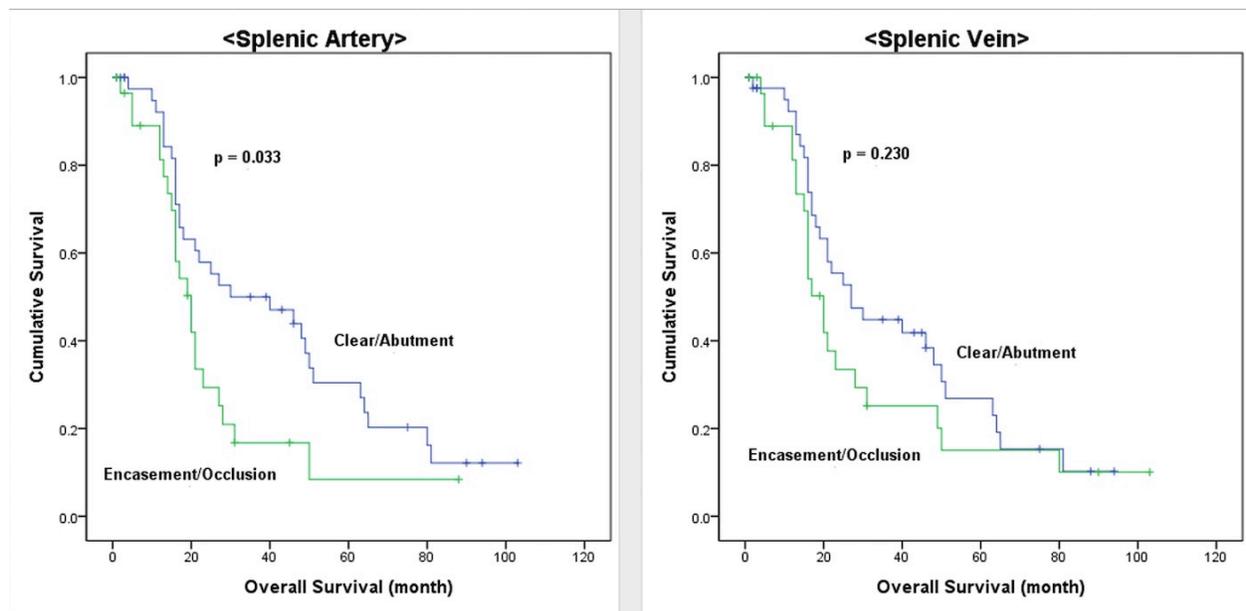
Presenter: Flavio Rocha MD | Virginia Mason Medical Center

Background: Unlike pancreatic head tumors, little is known about the biological significance of radiographic vessel involvement with pancreatic body/tail adenocarcinoma. We hypothesize splenic vessel involvement may be an adverse prognostic factor.

Methods: All distal pancreatectomies performed for resectable pancreatic adenocarcinoma between 2000 and 2016 were reviewed and clinicopathologic data were collected retrospectively. Preoperative computed tomography imaging was reviewed and splenic vessel involvement was graded as none, abutment, encasement or occlusion.

Results: Among a total of 71 patients, splenic artery and vein encasement/occlusion were present in 41%(29/71) of patients, each. There were no significant differences in tumor size or grade, margin positivity, and perineural or lymphovascular invasion. However, splenic artery encasement/occlusion($p=0.001$) and splenic vein encasement/occlusion($p=0.038$) both correlated with lymph node positivity. Splenic artery encasement was associated with a reduced median overall survival(20 vs. 30 months, $p=0.033$). Multivariate analysis also showed that splenic artery encasement was an independent risk factor of worse survival(HR, 2.246; 95% CI, 1.118-4.513; $p=0.023$).

Conclusion: Patients with cancer of the body or tail of the pancreas presenting with radiographic encasement of the splenic artery, but not the splenic vein, have a poorer prognosis and should be considered for neoadjuvant therapy before an attempt at curative resection.



P 165. THE ASSOCIATION BETWEEN SURVIVAL AND LYMPHOCYTE MONOCYTE RATIO AFTER NEOADJUVANT THERAPY FOLLOWED BY PANCREATECTOMY IN PATIENTS WITH BORDERLINE RESECTABLE PANCREATIC CANCER

M Kawai, S Hirono, K Okada, M Miyazawa, Y Kitahata, R Kobayashi, A Shimizu, M Ueno, S Hayami, H Yamaue

Presenter: Manabu Kawai MD, PhD | Wakayama Medical University

Background: The impact of systemic immune inflammatory markers to predict survival in patients receiving neoadjuvant therapy for borderline resectable pancreatic cancer (BRPC) has not been sufficiently investigated. This study aims to evaluate whether systemic immune inflammatory markers after neoadjuvant therapy followed by pancreatectomy become preoperative prognostic factors to predict survival in BRPC patients.

Methods: We retrospectively reviewed 65 BRPC patients who received neoadjuvant therapy followed by pancreatectomy and 58 BRPC patients with upfront surgery between 2010 and 2016. Neutrophil/lymphocyte ratio (NLR), platelet/lymphocyte ratio (PLR), lymphocyte/monocyte ratio (LMR), and prognostic nutrition index (PNI) were assessed before and after neoadjuvant therapy. The association between survival and systemic immune inflammatory markers was evaluated by univariate and multivariate analysis. Regarding the change of LMR before and after neoadjuvant therapy, "increase" indicated that patients who received neoadjuvant therapy had more than a 20% increase in LMR compared with the value before neoadjuvant therapy, and "decrease" was defined as more than a 20% decrease in LMR. Others were defined as "stable".

Results: In univariate analysis, post-neoadjuvant NLR, LMR, and PNI in systemic immune inflammatory markers were associated with survival. Pre-neoadjuvant NLR, PLR, LMR, PNI, and post-neoadjuvant PLR were not associated with survival. In the multivariate cox proportional hazard analysis of the prognostic factors, post-neoadjuvant LMR <3.0 in systemic immune inflammatory markers was detected as an independent prognostic factor (hazard ratio (HR) 2.59; 95% confidence interval (CI) 1.02-6.58; P=0.045). MST among LMR ≥ 3.0 group vs. LMR < 3.0 group vs. upfront surgery group was as follows: post-adjvant LMR ≥ 3.0 group, 31.7 months; post-adjvant LMR < 3.0 group, 14.9 months and upfront surgery group, 13.7 months (Fig. 1-b). Survival in patients with post-adjvant LMR ≥ 3.0 significantly better than that in patients with post-adjvant LMR < 3.0 group (P=0.003) and in patients with upfront surgery (P=0.014). However, there was no significant difference in survival between patients with post-adjvant LMR < 3.0 and those with upfront surgery (P=0.315). Survival of BRPC patients with low LMR after neoadjuvant therapy was poor as with that of BRPC patients with upfront surgery. regarding the association between the change of LMR and survival, of 65 patients, 12 were assigned to "increase" LMR cohort, 37 were assigned to "decrease" LMR cohort, and 16 were assigned to "stable" LMR cohort. Regarding the change in LMR before and after neoadjuvant therapy, survival in patients with increased LMR was as similar as those with stable LMR (MST 25.7 months vs. MST 21.6 months; p=0.776). However, patients with increased LMR had significantly better survival compared to those with decreased LMR (MST 25.7 months vs. MST 14.9 months; p=0.030).

Conclusion: LMR < 3.0 after neoadjuvant therapy and decreased LMR showed useful prognostic information for BRPC patients with pancreatectomy following neoadjuvant therapy. These results might indicate the potential role of LMR to stratify treatment strategy in BRPC patients. Furthermore study of the management during neoadjuvant therapy to prevent low post-neoadjuvant LMR will be required to improve survival in patients with BRPC. Implement adequate nutritional support during neoadjuvant therapy may lead to better survival by improving post-neoadjuvant LMR in patients with BRPC.

P 166. SIGNIFICANCE OF COMPLETE RESECTION OF NERVE PLEXUS AROUND COMMON HEPATIC ARTERY IN PANCREATIC DUCTAL ADENOCARCINOMA

K Okada, Y Murakami, K Uemura, N Kondo, N Nakagawa, S Seo

Presenter: Kenjiro Okada MD | Hiroshima University

Background: The nerve plexus invasion of patients with pancreatic ductal adenocarcinoma (PDAC) is a risk factor for poor survival. In patients with borderline resectable PDAC (BR-PDAC) with contact to common hepatic artery (CHA), the invasion of nerve plexus around CHA (PLcha) is sometimes found. In patients with resectable PDAC (R-PDAC), the complete resection of PLcha is regarded as extended nerve plexus dissection, and the frequency of PLcha invasion and the significance of PLcha resection are still unclear. The aim of this study is to evaluate the rate of PLcha invasion and significance of the complete resection of PLcha in PDAC patients.

Methods: Medical records of consecutive PDAC patients, who underwent R0 or R1 resection at our institution between May 2013 and December 2018, were reviewed retrospectively. Patient characteristics and clinicopathological factors were compared among the R and BR groups, and the rate of PLcha invasion was evaluated in both groups. The relationships between PLcha status and overall survival (OS) were analyzed, and risk factors of PLcha invasion were predicted. For patients with PLcha no invasion by HE staining, microinvasion by immunohistochemical staining of CAM 5.2 monoclonal antibody was also evaluated.

Results: A total of 253 PDAC patients underwent radical pancreatectomy during this study period. Of these 253 patients, 49 patients with PDAC in the tail of pancreas were excluded. Of the 204 patients, 68 patients were also excluded, because PLcha of these patients could not be detected. The eligible 136 PDAC patients were divided into 72 R-PDAC and 64 BR-PDAC patients. All of the R-PDAC patients were received upfront surgery, and 46 patients (72%) of BR-PDAC patients were neoadjuvant chemotherapy. In R-PDAC patients, the rate of PLcha HE-positive was 0%, and the microinvasion by CAM 5.2 was also 0%. On the other hand, in BR-PDAC, the PLcha HE-positive was in 13 patients (20%), and microinvasion was in 5 patients (8%). The median survival time of patients with PLcha invasion (HE-positive and microinvasion) and no invasion were 29.8 and 60.2 months, respectively ($p=.088$). In multivariate OS analysis, elevated preoperative CA19-9 level ($p=.018$), lymph node metastasis ($p=.003$) and lack of adjuvant chemotherapy ($p<.001$) were independent poor prognostic factors. Within a subset of 64 BR-PDAC patients, preoperative CHA encasement ($p<.001$) was the only independent risk factor of PLcha invasion.

Conclusion: In PDAC patients, the rates of PLcha invasion in R-PDAC and BR-PDAC patients were 0% and 28%, respectively. For R-PDAC patients, the complete resection of PLcha may be not important for survival benefits.

P 167. SINGLE INSTITUTION OUTCOMES OF ENHANCED RECOVERY AFTER SURGERY PROTOCOL IMPLEMENTATION IN PANCREATODUODENECTOMY

EM Aleassa, N Anzlovar, G Morris-Stiff

Presenter: Essa M. Aleassa MD, MSc | Cleveland Clinic Foundation

Background: Enhanced recovery after surgery protocols (ERAS) have gained wide acceptance in several sub-specialties, the most notable being colorectal surgery. However, there is to date limited data on its role in major hepatopancreatobiliary, possibly due to the complexity of cases and fear of major morbidity. We aim to present our experience implementing ERP in patients undergoing pancreatoduodenectomy (PD).

Methods: All patients undergoing PD between January 2014 and December 2017 were identified from institutional American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) data. The first elements of ERAS for PD were implemented in January 2016; the cohort was therefore divided by year of procedure into either Pre-ERAS (2014/2015) or ERAS (2016/2017) groups. Data collected includes patients baseline demographics, perioperative data, and outcome measures including 30-day readmissions.

Results: A total of 294 patients underwent pancreatoduodenectomy during the study period. There were 156 (53.1%) patients in the Pre-ERAS group and 138 (46.9%) in the ERAS cohort. The length of hospital stay, calculated from the procedure day to discharge, was 7 (IQR=6-10) and 6 (IQR=5-9) for Pre-ERAS and ERAS groups ($P=0.014$), respectively. The rate of 30-day readmission was 27 (17.3%) and 23 (16.7%) for Pre-ERAS and ERAS groups ($P=0.884$) respectively. While there were three 30-day mortalities in the Pre-ERAS group, there were none in the ERAS group ($P=0.25$).

Conclusion: The institution of an ERAS protocol for patients undergoing PD resulted in a reduced length of stay, and was safe with no increase in 30-day readmission or mortality.

P 168. TRANSDUODENAL AMPULLECTOMY FOR AMPULLARY NEOPLASMS: INITIAL RESULTS FROM A HIGH-VOLUME CENTER

H Fayazzadeh, AT Strong, A Khithani, R Simon, RM Walsh, G Morris-Stiff, T Augustin, KM El-Hayek

Presenter: Hana Fayazzadeh MD | Cleveland Clinic Foundation

Background: When technically feasible, ampullary neoplasms may be resected using an endoscopic approach. Large lesions or those with high-risk features may require transduodenal ampullectomy (TDA), pancreas-sparing duodenectomy (PSD), or pancreaticoduodenectomy (PD). Compared to PD and PSD, TDA may be a less invasive option for large periampullary tumors, especially those with features suspicious for invasive carcinoma as well as for patients with significant comorbidities. Here we report single-center outcomes of TDA with regards to safety, efficacy, and recurrence rates.

Methods: All patients with a diagnosis of ampullary neoplasm undergoing TDA between August 2006 and December 2017 were analyzed. Pre-operative symptoms and comorbidities, surgical details, and perioperative outcomes are reported.

Results: A total of 29 patients underwent TDA during the study period (median age, 63.7 years; age range, 43-85 years; female, 76.0%). The most common pre-operative symptoms included changes in bowel habits (98.3%), nausea (79%), abdominal pain (67.5%), and vomiting (53.3%). Preoperative biopsy was performed in 93% of patients, the majority of which were consistent with adenoma. A minimally-invasive (laparoscopic or robot-assisted) approach was attempted in 21% (n=6) of cases of which 2 converted to open due to technical challenges or presence of adenocarcinoma. When intraoperative adenocarcinoma was identified (n=2), the case converted to PD. A total of 79% (n=23) of cases were initiated and completed through open approach. Median operative time was 240 minutes (range, 140-748 minutes), with a median blood loss of 63 mL (range, 25-1000 mL). Median length of stay was 6 days (range, 3-22 days). A total of 17% of patients developed post-operative complications including atrial fibrillation (7%, n=2), prolonged ileus with surgical site infection (3%, n=1), pancreatitis (3%, n=1), and deep venous thrombosis of lower extremity (3%, n=1). No 30-day mortality was noted. Post-operative pathology showed tubular or tubulovillous adenoma in 76% (n=22), neuroendocrine tumor in 10% (n=3), adenocarcinoma in 7% (n=2), and inflammation of the ampulla in 3% (n=1). Mean follow up duration was 22.4 months, during which only 1 case (3%) had recurrence confirmed by endoscopy.

Conclusion: For endoscopically unresectable ampullary neoplasms and those with suspicion for invasive carcinoma, TDA represents a safe alternative to PD or PSD with the advantage of lower morbidity and post-operative mortality. These patients require longer-term post-operative surveillance to better identify early and late recurrence.

P 170. BARRIERS TO IMPLEMENTATION OF AN ENHANCED RECOVERY PROGRAMME FOLLOWING UNEVENTFUL PANCREATICODUODENECTOMY. A RETROSPECTIVE COHORT STUDY

S Partelli, M Michele, G Guarneri, G Maggi, N Pecorelli, D Tamburrino, S Crippa, R Meani, L Beretta, M Falconi

Presenter: Michele Mazza MD | San Raffaele Scientific Institute

Background: Pancreaticoduodenectomy (PD) is one of the most complex abdominal operation and it represents the only curative option for pancreatic cancer. Despite surgery complexity, the enhanced recovery after surgery (ERAS) pathway has been shown to be feasible and safe. However, low adherence to ERAS items protocol is often reported, mainly related to the high incidence of morbidity after PD. Main outcomes of this study were evaluating patients' compliance to the ERAS items following PD and the impact of ERAS compliance on length of stay (LOS).

Methods: 169 patients with an uneventful postoperative course following PD were considered, in order to reduce the bias related to the occurrence of postoperative morbidity. Patients were classified in low or high risk for developing a post-operative pancreatic fistula (POPF) according to the fistula risk score (FRS). The protocol included 18 ERAS items (11 preoperative and 7 postoperative). Prolonged length of stay and low ERAS items adherence were measured around the median values observed in the cohort.

Results: The median adherence to the ERAS protocol for the entire cohort was 13 items out of 18 items, hence a low adherence to ERAS protocol was defined by the compliance to ≤ 13 items. In the low adherence to ERAS group a higher frequency of patients with $FRS > 2$ was observed ($P=0.011$). ERAS items adherence was significantly lower among those patients who had $FRS > 2$. The rate of patients who had a low adherence to the ERAS protocol following PD was significantly higher in those who had a prolonged LOS (> 7 days). On multivariate analysis, a low adherence to the ERAS protocol was confirmed to be independently associated with a prolonged $LOS > 7$ days ($P < 0.001$).

Conclusion: This study shows that an increased risk of developing POPF is an important barrier to the implementation of an ERAS protocol following uneventful PD and that a decreased ERAS compliance is associated with a significantly longer LOS.

P 171. PREOPERATIVE FACTORS FOR EARLY RECURRENCE OF RESECTED PANCREATIC DUCTAL ADENOCARCINOMA

T Sugawara, D Ban, S Watanabe, T Ogura, K Ogawa, H Ono, Y Mitsunori, A Kudo, M Tanabe

Presenter: Toshitaka Sugawara MD | Toyko Medical and Dental University

Background: Pancreatic ductal adenocarcinoma is a devastating disease, with 5-year survival in patients with stage I cancer as low as 41.2% in Japan. This is attributed to lack of clinical manifestations and powerful examinations for early detection, and up to 70% of patients are diagnosed as unresectable at initial diagnosis. Even after undergoing potential curative resection, early systemic recurrence occur in 80% patients. For these patients, neoadjuvant approach may be a better practice than upfront surgery. We investigated the factors of early recurrence of pancreatic ductal adenocarcinoma.

Methods: Data of a total of 240 patients who underwent pancreatectomy for pancreatic ductal adenocarcinoma between January 2005 and August 2018 were retrospectively reviewed. Patients who underwent neoadjuvant therapy and total pancreatectomy for recurrent pancreatic cancer in the remnant pancreas were excluded. Patients whose follow-up interval were incomplete were also excluded. In this study, the cut-off value of early recurrence was defined as 12 months.

Results: A total of 177 patients were included in the final analysis. The anatomical location of tumors was in the head of pancreas (H) in 109 (61.6%) patients and in the body and tail (BT) in 65 (36.7%) patients. At the point of last follow-up, 122 patients recurred, and 114 patients died from their cancer. Among patients who recurred, 90 (73.4%) recurred within 12 months after surgery: 56 patients were H group and 34 patients were BT group. On univariate analysis, three variables proved to be associated with early recurrence in H group: tumor size ($P=0.016$), invasion to duodenum ($P=0.041$) and resectability of the tumor defined by UICC ($P=0.023$). On the other hand, in BT group, variables associated with early recurrence were tumor size ($P=0.007$), invasion to portal vein ($P=0.023$) and invasion to splenic artery ($P=0.049$). On two separate multivariable logistic regression models, resectability (OR 8.04, 95% CI 2.70–24.0, $P=0.000$) and tumor size (OR 2.22, 95% CI 1.08–4.55, $P=0.030$) were independently significant factors associated with early recurrence in H group and BT group respectively.

Conclusion: The present study shown that resectability was independently associated with early recurrence within 12 months in H group, as well as tumor size was in BT group. Neoadjuvant approach, rather than upfront resection, should be considered for patients with borderline resectable pancreatic ductal adenocarcinoma in the head of pancreas, and with large tumors in the body and tail of pancreas.

P 172. PREOPERATIVE RADIOLOGICAL PARAMETERS PREDICT POSTOPERATIVE PANCREATIC FISTULA IN PANCREATODUODENECTOMY

H Lapshyn, E Petrova, L Bolm, D Bausch, T Keck, UF Wellner

Presenter: Hryhoriy Lapshyn MD | University Medical Center Schleswig-Holstein

Background: Postoperative pancreatic fistula (POPF) remains the achilles heel of pancreatic surgery. Several risk stratification strategies have been described, but rarely these are preoperatively available. We attempted to predict the development of POPF based on preoperative radiological parameters from cross-sectional imaging.

Methods: A cohort of n=254 patients with pancreatoduodenectomy from 2013 to 2018 and available preoperative cross-sectional imaging were included. The following parameters were analyzed: thickness of pancreatic parenchyma at the pancreatic neck, calcifications, diameter of the pancreatic duct, lymphadenopathy, cholestasis, irregularities of the pancreatic duct. A multivariable model was constructed to predict the occurrence of clinically relevant POPF according to ISGPS.

Results: A multivariable model containing four of the radiological parameters was able to stratify patients into three risk categories, low / medium / high, with 5%, 10% and 40% of clinically relevant POPF. Area under the curve (AUC) of this model was 0.79.

Conclusion: Preoperative risk stratification based on cross-sectional radiological parameters is possible in pancreatoduodenectomy.

P 173. "I WILL TAKE GLUE WITH STITCHES": A COMPARISON OF SKIN CLOSURE TECHNIQUES IN PANCREATODUODENECTOMY

KF Flick, RE Simpson, MG House, EP Ceppa, N Zyromski, A Nakeeb, CL Colgate, ML Fennerty, MC Schmidt

Presenter: Katelyn Flick MD | Indiana University School of Medicine

Background: Surgical site complications are one of the most closely monitored and prevalent post-operative problems, occurring in as many as 15 to 28% of patients that undergo pancreaticoduodenectomy. Wound complications not only affect patient recovery and quality of life, but also negatively impact quality metrics like cost and hospital length of stay. With many closure techniques available, we sought to determine if any closure method (subcuticular stitch vs. subcuticular stitch + skin sealant vs. staples) provided a benefit of reduced post-pancreatoduodenectomy wound complications.

Methods: All patients that underwent open pancreatoduodenectomy from June 2015 to June 2018 were reviewed and grouped based on wound closure (subcuticular stitch vs. subcuticular stitch + skin sealant vs. staples). We performed a retrospective review of our institution's prospective ACS-NSQIP database and augmented it through medical record review for wound closure method and superficial surgical site complications (SSSC). These included cellulitis, seroma, abscess, fat necrosis, and other. Closure groups were compared using independent samples t-test/analysis of variance and chi-square test for continuous and categorical variables respectively. Univariable analysis and multivariable regression models were used to examine the effect of wound closure method on the various post-operative outcomes, while controlling for pre-operative and peri-operative covariables.

Results: A total of 418 pancreatoduodenectomies were included on study (N=74 subcuticular stitch, N= 205 subcuticular stitch + skin sealant, N=139 stapled). Operative time did not differ between groups. There was a significant difference in the incidence of SSSC between wound closure methods. Patients with subcuticular stitch + skin sealant (9.8%) were significantly less likely to develop a SSSC compared to patients with stapled closure (20.1%) on univariable ($p=0.009$) and multivariable analyses ($p=0.016$; OR 0.37). A similar though insignificant trend was seen for patients with subcuticular stitch + skin sealant (9.8%) compared to suture alone closure (16.2%) on univariable ($p=0.142$) analysis. Unadjusted length of stay was significantly longer for stapled closure (11.9 days) compared to subcuticular stitch + skin sealant (9.6 days) and subcuticular stitch alone (9.8 days) ($p<0.05$), but did not reach significance on multivariable analysis.

Conclusion: Subcuticular suture with skin sealant after pancreaticoduodenectomy appears to be the preferred method for skin closure to reduce the risk of superficial surgical site complications. A change of practice and prospective study of this technique is warranted in light of this data.

P 174. EX-VIVO HUMAN MODEL OF THERANOSTIC NANODELIVERY SYSTEM FOR PANCREATIC NEOPLASMS - A FEASIBILITY TRIAL

K Chouliaras, L McNally, A Samykutty, E McWilliams, RB D'Agostino, CJ Clark, P Shen

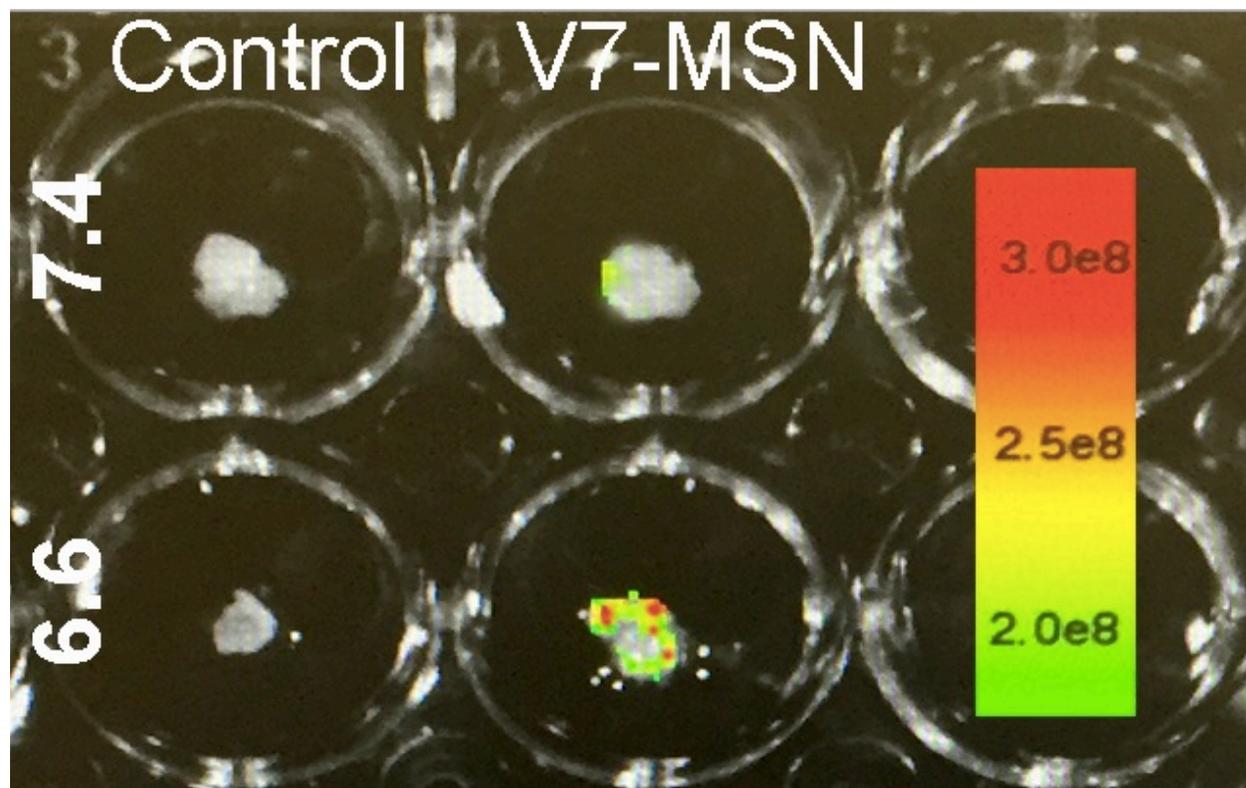
Presenter: Konstantinos Chouliaras MD | Wake Forest School of Medicine

Background: Despite the progress made in the diagnosis and treatment of pancreatic neoplasms, there remains considerable ambiguity and false negative results. Multispectral Optoacoustic Tomographic Imaging (MSOT) has been used in-vitro and in animal models targeting pancreatic cancers showing good affinity. In this trial we sought to demonstrate the affinity of the nanoparticles in human pancreas tumor specimens.

Methods: Patients who underwent resection of pancreatic tumors were prospectively enrolled in the trial. 0.5 x 0.5 x 0.5 cm of fresh tumor and normal tissue (cells and stroma) were obtained during a resection with curative intent. An acidic pH targeted wormhole mesoporous silica nanoparticle, coated with chitosan and targeted with a V7 peptide, was (V7-CWMSN) developed to serve as a contrast agent. The acidic pH targeted particle, V7-CWMSN, containing either IR-780 dye or propidium iodide was evaluated in human pancreatic tumor and normal tissue. Tumor uptake of the particle was evaluated using MSOT with secondary confirmation of V7-CWMSN using near infrared fluorescent imaging (NIR).

Results: Four patients were included in this feasibility trial - 2 underwent Whipple resections and one distal pancreatectomy for pancreatic adenocarcinoma and another patient underwent Whipple for isolated breast metastases to the pancreas. The core mesoporous component of the particle was 33.0 ± 1.94 nm and enlarged to 38.87 ± 1.5 nm upon the addition of the chitosan gatekeeper. The polydispersity index indicated a monodispersed particle at 0.12 over the course of 100 h indicating a lack of particle aggregation. Ex vivo evaluation of particle uptake in resected patient pancreatic tumors at pH 6.6 resulted in 2.3X increased uptake compared to normal tissue at pH 7.4 ($p=0.0023$) as observed using 3D MSOT imaging and 1.9 X increased uptake at pH 6.6 compared to pH 7.4 ($p=0.0076$) using 2D NIR fluorescence imaging.

Conclusion: In this feasibility trial, increased affinity of the mesoporous silica nanoparticle was shown both with MSOT and NIR fluorescence imaging. Further study is needed to confirm the reproducibility of these results.



P 175. INCIDENTAL PANCREATIC TUMORS

CR Medina, E Murrieta, MA Teliz, JA Mier, S Valanci

Presenter: Claudia Medina MD | American British Cowdray Medical Center

Background: With the widespread use of abdominal imaging, the prevalence of incidental pancreatic tumors has increased. Cohort studies in asymptomatic patients revealed unsuspected cysts in 2.4-13.5% of cases and demonstrated a strong correlation with age. The incidental discovery of these lesions opens up an opportunity for early treatment of pancreatic cancers. Because of this, the American college of radiology published in 2017 a guide that takes in to account: anatomy and localization, size, duct communication, growth rate, number of lesions, and high-risk characteristics. The aim of our study was to determine the prevalence of incidentally pancreatic lesions detected by CT scan.

Methods: We performed a retrospective observational study. A team of three surgeons and two radiologists reviewed all CT scans made in university affiliated community hospital in Mexico City (American British Cowdray medical center), between February 2014 and February 2018. Inclusion criteria included all patients with no previous pancreatic known lesions. Patients without follow up or demographic data were excluded. Demographic, clinical and paraclinical data was also collected for correlation purposes. Follow up with image studies and treatment were also collected. Descriptive statistical analysis and correlations were carried out accordingly.

Results: A total of 7420 abdominal and pelvic CT scans were included over a period of 5 years. An unknown pancreatic lesion was spotted in 78 patients (2.1%), 63 patients had solid lesions and 15 had cystic lesions. Of the cystic lesions 73.3% of them (11 patients) are branch duct types and less than 1 cm in diameter. Only 5 follow up CT scans have shown up to date, one of them was within a week of the first CT scan, the first one had showed a solid lesion and the follow up showed hepatic metastasis. The other four were after surgery and showed three with peripancreatic fluid and one hematoma.

Conclusion: Reported international literature reports that 75% of unknown pancreatic lesions are cystic, but in our study 80% of the positive CT scans have demonstrated to be solid. This may be relevant to the behavior of pancreatic lesions in our country and could probably become an early screening method for solid lesions in our population. To our knowledge a study of this size has not been conducted in this population and would require further correlation.

P 177. IMPACT OF PREOPERATIVE BILIARY DRAINAGE AND EXTERNAL PANCREATIC STENTS ON CLINICAL OUTCOME AFTER PANCREATICO-DUODENECTOMY

JA Reza, C Canavan, K Wissinger, M Uwah, P Veldhuis, Y Du, JP Arnoletti

Presenter: Joseph Reza MD | Florida Hospital Orlando

Background: Pancreatic fistula (PF) with associated sepsis is a potentially life-threatening complication following pancreatoco-duodenectomy (PD). Additionally, septic complications are reportedly more frequent in the presence of contaminated bile associated with pre-operative biliary stenting. We analyzed the impact of routine utilization of temporary external pancreatic stents on clinical outcome of PD at our institution.

Methods: We retrospectively reviewed the medical records of 148 consecutive patients undergoing open PD at Florida Hospital between March 2014 and April 2018. The most common indications for surgery were pancreatic ductal adenocarcinoma (PDAC, 50 patients), ampullary cancer (32 patients) and intraductal papillary mucinous neoplasm (27 patients). Patients with indwelling biliary prosthesis were treated with IV antibiotics for at least 5 days post-operatively and the midline wounds, were closed over a wick. All patients underwent pancreatoco-jejunosotomy with a trans-anastomotic external pancreatic stent and placement of a closed suction drain. No somatostatin analogues were utilized. Data were collected from review of the medical record, operative reports, anesthesia records and imaging reports. Continuous and categorical variables were analyzed with students T-test or Chi-square analysis.

Results: Median patient age was 69 years old (\pm 10.3 years). Average operative time was 315 minutes with an average estimated blood loss (EBL) of 249 milliliters. The overall postoperative complication rate was 27%, including infectious, pulmonary and cardiac complications. Peri-operative blood transfusion rate was 11% and the thirty-day postoperative mortality was 2.7% (4/148). The mean length of stay was 10.5 days. The overall postoperative pancreatic fistula incidence rate was 3.4% and there were 5 Type B PF in the non-PDAC patients and 0 Type C in the entire patient group, as defined by 2017 ISGPS guidelines. No PDAC patients experienced Type B fistula. On multivariate analysis, only infected bile was predictive of PF (OR 0.28, 95% CI 0.108-0.744; $p=0.01$) and the presence of a Type A fistula did not predict Type B fistula ($p=0.267$). Overall length of stay was not influenced by PF or biliary contamination. Preoperative biliary stents were more common in patients with PDAC ($p=0.002$). Bacterial contamination of the bile was significantly more common in patients with preoperative biliary stents ($p=0.016$), with gram negative organisms being most the common cultured organism. Despite frequent bacterobilia associated with biliary prosthesis, the overall postoperative wound infection rate was 6%. Infectious complications requiring opening of the wound were infrequent and no difference in incidence could be associated with biliary stent presence (6/78 stented patients vs 3/70 without stent, $p=0.38$). Five patients were re-admitted with superficial surgical wound infection complications and 3 of those required negative-pressure wound device placement. 19% of patients required additional medical care and could not be discharged home after surgery and post-operative complications were predictive of this outcome ($p=0.004$).

Conclusion: Preoperative internal biliary drainage was associated with biliary contamination, but this was not associated with significant increase of postoperative infectious complications among patients who routinely received IV antibiotics with broad gram-negative coverage and had wound closure over a wick. Routine use of external pancreatic stents during PD was associated with low rates of clinically significant PF. The presence of infected bile rather than biochemical pancreatic fistula may be associated with Type B fistula. Despite low intra-abdominal infection rates, postoperative complications are associated with need for additional institutional care after hospitalization.

P 178. EARLY NODE-NEGATIVE INVASIVE INTRADUCTAL PAPILLARY MUCINOUS TUMORS SEEM TO HAVE A BETTER PROGNOSIS THAN NODE-NEGATIVE PANCREATIC DUCTAL ADENOCARCINOMAS

F Gavazzi, G Capretti, C Ridolfi, G Nappo, S Carrara, M Sollai, M Angrisani, A Zerbi

Presenter: Francesca Gavazzi MD | Humanitas University

Background: Pancreatic Ductal Adenocarcinoma (PDAC) and invasive Intraductal Papillary Mucinous Tumor (IPMN) show a different prognosis. The prognosis of invasive IPMNs is generally believed to be more favorable as compared to classic PDAC because IPMN-associated carcinomas are frequently diagnosed at an earlier stage. Exactly the favorable prognosis of invasive IPMNs in respect to PDAC ones is retained lost considering node positive patients. We evaluated a surgical cohort of patients resected for PDAC's and invasive IPMN's early stages and compared these 2 groups.

Methods: We prospectively collected clinical, surgical, postoperative, and histologic data of 76 patients undergone radical pancreatic resection for PDAC's and invasive IPMN's early stages (node negative) at Humanitas Cancer Center Pancreatic Surgery Unit from January 2010 to December 2016. Surgery specimens were re-staged according to American Joint Committee on Cancer (AJCC) 8th edition from our pathologists. Data were illustrated as frequencies, percentages, median and range. Chi-square or Fisher's exact test were used to compare percentages between groups. Medians were compared using the nonparametric 2 sample median test. Overall survival (OS) was estimated using the Kaplan-Meier method and compared by log-rank test. Hazard Ratio (HR) and their corresponding 95% confidence intervals (CI) were calculated by Cox Regression Model. P value was set at 0.05, two sides.

Results: We identified 50 PDACs and 26 invasive IPMNs, 46 (60.5%) men and 30 (39.5%) women. 30.3% of patients were asymptomatic. At diagnosis, only 25% of patients had jaundice. Pancreaticoduodenectomy was the surgical procedure more frequently performed in the cohort (57.9%) and in PDACs (62%), while, total pancreatectomy was above all realized in the IPMNs (38.5%, $p=0.001$). No differences in postoperative course were noted. 89.5% of patients had Clavien-Dindo score ≤ 2 . 54% of PDAC patients had tumor grade ≥ 3 versus 4% of IPMN ones ($p=0.001$). With a median follow-up of 47 months, 84.8% invasive IPMN patients reached 4ys overall survival, while 41.6% PDACs ($p=0.008$). Univariable model found tumor grade ≥ 3 ($p=0.001$), presence of perineural invasion ($p<0.001$), high stage ($p=0.043$) and positive resection margin, R1, ($p=0.002$) to have an adverse prognostic effect on OS. PDAC histological type had 3.6 times higher risk of death (95%CI: 1.4;9.4, $p=0.001$) than IPMN one. Multivariable model confirmed the negative prognostic role of perineural invasion (HR_{yes vs no}: 6.0, 95%CI: 1.8;20.3, $p=0.004$) and of R1 (HRR_{1 vs R0}: 2.7, 95%CI: 1.25;6, $p=0.012$).

Conclusion: The prognosis of early stages of IPMN patients seems to be better than that of patients with node-negative PDAC, but it should be investigated in larger studies.

P 179. PAIN AT DIAGNOSIS AND HIGH ASA ARE NEGATIVE PROGNOSTIC FACTORS IN PATIENTS WITH PANCREATIC CANCER OR INVASIVE IPMN

F Gavazzi, G Capretti, C Ridolfi, G Nappo, S Carrara, P Spaggiari, P Riva, A Zerbi

Presenter: Alessandro Zerbi MD | Humanitas University

Background: Pancreatic Ductal Adenocarcinoma (PDAC) and invasive Intraductal Papillary Mucinous Tumor (IPMN) show several various clinical, radiological and histological features. We want to describe the clinical characteristics of a cohort of radically resected patients comprehended both PDAC and invasive IPMN, possible clinical differences between the 2 histologies and the influence of clinical parameters on overall survival (OS).

Methods: We prospectively collected clinical, surgical, postoperative, and histologic data of 332 patients undergone pancreatic resection for PDAC and invasive IPMN at Humanitas Cancer Center Pancreatic Surgery Unit from January 2010 to December 2016. Metastatic and pTis tumors and neoplasms underwent neoadjuvant therapy were excluded from the analysis. Data were summarized as frequencies, percentages, median and range. Chi square test or Fisher's exact test were used to compare percentages between the 2 groups. Medians were compared using the nonparametric 2 sample median test. OS was estimated using the Kaplan-Meier method and differences between groups were tested by the log-rank test. Hazard Ratio (HR) and their corresponding 95% confidence intervals (CI) were calculated by Cox Regression Model. P value was set at 0.05, two sides.

Results: We identified 289 PDACs and 43 invasive IPMNs. Comorbidities were present in 66.3% of patients, 237 patients (71.4%) had an American Society of Anesthesiologists (ASA) ≤ 2 . 21.4% of patients were asymptomatic. The more frequent onset symptoms were: jaundice (38.6%), weight loss (17.2%), abdominal pain alone (16.9%). Median Ca19-9 value was 178UI/ml. 81.4% of invasive IPMNs had a pathological history positive for comorbidities versus (vs) 64% of PDACs ($p=0.025$). 44.2% IPMNs had ASA ≥ 3 vs 26.3% PDACs ($p=0.016$). PDAC patients had jaundice at diagnosis more than IPMN ones ($p=0.004$) while IPMNs lost weight more frequently ($p=0.015$). Median Ca19-9 was higher in PDACs ($p<0.001$). With a median follow-up of 47 months, the median OS of the cohort was 26.8 months. Invasive IPMN patients showed a better prognosis of PDAC, reporting a median OS of 76.6 compared to 25.6 months ($p<0.001$). Multivariable model showed that PDAC patients had 1.82 times higher risk of death (95%CI: 1.02;3.24, $p=0.044$) than invasive IPMN ones. ASA (HR3-4 vs 1-2 1.78, 95%CI: 1.32;2.40, $p=0.0002$) was an independent predictor of patients' survival. Pain at diagnosis resulted as a bad prognostic factor for OS, both when unique (HRyes vs no: 1.45, 95%CI: 1.01;2.08, $p=0.042$), and with other symptoms (HRyes vs no: 1.55, 95%CI: 1.03;2.33, $p=0.036$). Considering multivariate analysis for subgroups, PDACs too with pain at diagnosis, alone (HR 1.76, 95%CI: 1.22; 2.56, $p=0.003$) or with other symptoms (HR 1.64, 95%CI: 1.07; 2.51, $p=0.023$), showed a statistically significant shorter survival than PDAC pain-free patients.

Conclusion: Clinical differences are present in PDAC patients and invasive IPMN ones. Patients with a cancer of the pancreas and a severe ASA score had a statistically significant shorter survival than that with mild ASA, as well as patients with pain at diagnosis. In these subjects neoadjuvant treatment should be considered rather than upfront surgery.

P 180. INTERNAL PANCREATICOJEJUNOSTOMY STENTING DECREASES RATE OF PANCREATIC FISTULAS AFTER PANCREATICOUDENECTOMY

AW Elias, JA Stauffer

Presenter: John Stauffer MD | Mayo Clinic Rochester

Background: Despite overall improving outcomes following pancreaticoduodenectomy, pancreatic fistula remains a common cause of morbidity and mortality. Internal or external anastomotic stenting has been proposed as a potential method for limiting the rate of leak from pancreaticojejunostomies following pancreaticoduodenectomy, however data is limited. Herein, we sought to compare the rate of pancreatic fistulas with internal stenting versus without stenting following pancreaticoduodenectomy for a variety of pathologies.

Methods: A prospectively maintained database identified 175 consecutive patients who underwent pancreaticoduodenectomy (Whipple procedure) between July 2011 and December 2017 by a single surgeon at our academic institution. 50 patients who underwent internal stenting of the main pancreatic duct were compared to 125 patients who did not undergo stenting. Demographics (age, operation, gender, body mass index, and comorbidities), clinicopathological characteristics (periampullary adenocarcinoma, pancreatic cystic disease, neuroendocrine, benign stricture/pancreatitis, other), operative outcomes (EBL, open vs. laparoscopic, pancreas texture) and postoperative outcomes (LOS, pancreatic fistula, additional complications) were compared using Fisher's Exact Test for categorical variables and T-test for continuous variables.

Results: 57% of patients were male ($p = 0.47$). Median age was 68.1 ($p = 0.74$). Median BMI was 26.1 ($p = 0.9$). Median main pancreatic duct diameter was 3mm ($p = 1$). Median length of stay was 6 days ($p = 0.3$). Compared to stented patients, unstented patients were healthier (ASA I-II vs. III-IV) pre-operatively ($p = 0.05$). Pancreatic texture did not differ between stented and unstented patients (grade 1-3 = soft vs >3 = firm) ($p = 0.41$). While the majority of cases in both groups were performed for periampullary adenocarcinoma (68%), there was a significantly higher proportion of adenocarcinoma in the stented group (86% vs 61%; $p < 0.01$), and there were significantly more benign strictures/pancreatitis in the unstented group (0% vs 14%; $p < 0.01$). More stented than unstented cases were done laparoscopically (28% vs. 14%; $p = 0.02$). Mean estimated blood loss was significantly higher in the stented group (375 cc vs. 231 cc; $p < 0.01$). While there was not a significant difference in overall complications between groups, there was a significantly lower rate of pancreatic fistulas following stenting (2/50 = 4%) compared to patients who were not stented (17/125 = 14%) ($p = 0.05$).

Conclusion: Internal stenting of the pancreaticojejunostomy during pancreaticoduodenectomy appears to reduce the rate of pancreatic fistulas, even in the setting of sicker patients and higher blood loss. Stenting is able to be performed via open or laparoscopic approach and does not increase the rate of other perioperative complications. Regular practice of internal stenting of the pancreaticojejunostomy should be considered to reduce the morbidity and mortality associated with pancreatic fistulas following pancreaticoduodenectomy.

Table: Demographics and perioperative outcomes

	Total		Stent		No Stent		P-value
	N or median	%	N or median	%	N or median	%	
# Patients	175	-	50	-	125	-	-
Male	99	57	29	58	70	56	0.47
Female	76	43	21	42	55	44	
Age (years)	68.7	-	66.6	-	69.1	-	0.74
BMI (kg/m ²)	26.1	-	25.5	-	26.3	-	0.90
ASA I-II	32	18	5	10	27	22	0.05
ASA III-IV	143	82	45	90	98	78	
Open	144	82	36	72	108	86	0.02
Laparoscopic	31	18	14	28	17	14	
Texture = soft (grade 3 and less)	67	38	18	36	49	39	0.41
Texture = firm (grade 4 and greater)	108	62	32	64	76	61	
Estimated blood loss (cc)	150	-	250	-	150	-	0.002
Main pancreatic duct diameter (mm)	3	-	3	-	3	-	1
Path = Periampullary adenocarcinoma	119	68	43	86	76	61	<0.001
Path = Pancreatic cystic disease	13	7	2	4	11	9	0.23
Path = Neuroendocrine	11	6	2	4	9	7	0.34
Path = Benign stricture/Pancreatitis	17	10	0	0	17	14	0.002
Path = Miscellaneous neoplastic disease	15	9	3	6	12	10	0.38
Length of stay (days)	6	-	6	-	6	-	0.34
Total complications	83	47	20	40	63	50	0.14
• Clavien I-II (Minor)	49	28	13	26	36	29	
• Clavien III-V (Major)	34	19	7	14	27	22	
Pancreatic fistula	19	11	2	4	17	14	0.05
• Fistula Grade A	3	2	0	0	3	2	
• Fistula Grade B	9	5	2	4	7	6	
• Fistula Grade C	7	4	0	0	7	6	

P 181. INFLAMMATORY MARKERS PREDICT SURVIVAL IN LOCALLY ADVANCED PANCREATIC CANCER PATIENTS AFTER CHEMOTHERAPY

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Presenter: Sushanth Reddy MD | University of Alabama at Birmingham

Background: Pancreatic cancer is thought to be the result of a pro-inflammatory state. Authors have previously reported the utility of measuring ratios between inflammatory markers in peripheral white blood cells such as neutrophils (N), leukocytes (L), and monocytes (M) to predict survival in heterogeneous pancreatic cancer populations (including resectable, locally advanced, and metastatic disease). Upfront chemotherapy and radiotherapy are increasingly utilized in pancreatic cancer treatment paradigms. Therefore, we theorized that trends in these inflammatory cells can be used to infer the biology of these tumors and predict long-term survival in a homogenous population of pancreatic cancer patients receiving upfront FOLFIRINOX.

Methods: A retrospective review of all patients who received upfront FOLFIRINOX (with or without subsequent radiation) for locally advanced pancreatic adenocarcinoma was performed exclusively at a single center from 2005 to 2015. Laboratory variables (complete peripheral white blood cell differential count and CA 19-9) were collected prior to and at the completion of chemotherapy. All patients received chemotherapy as their initial treatment. Patients who received any part of their therapy elsewhere were excluded. Ratios of N, L, and M were calculated before initiating and after completing FOLFIRINOX chemotherapy.

Results: Forty-one patients were included in this study. Nearly half (N=21) were male, and 68% (N=28) were Caucasians. The median age was 60 (range 38-81). Patients received a median of 4 cycles of FOLFIRINOX (range 4-14), and half received radiotherapy (N=21). Sixteen patients (39%) went on to surgical resection (10 pancreaticoduodenectomy, 6 distal pancreatectomy). Although not statistically significant, patients who underwent resection received fewer chemotherapy cycles (mean 5.25 vs. 6.48, P=0.17) and were less likely to receive radiation (37.5% vs 60%, P=0.21) as those who did not have a pancreatectomy. The median overall survival of the entire cohort was 26.5 months (range 10.4-92.1 months). Cox proportional hazard analyses only identified an increasing final N:M ratio (as a continuous variable) after completing FOLFIRINOX (HR 1.088, P=0.033) and surgical resection (HR 3.13, P=0.003) as predictive of survival. Changes in the ratios of N, L, and M and CA 19-9 trend during chemotherapy did not correlate to survival. Patients who underwent surgery had improved survival (40.1 vs 21.9 months, P=0.021). Using stepwise logistic analysis, a final N:M ratio cutoff of 4.5 was identified as predictive of survival (29.5 vs. 21.4 months, P=0.04). Patients who underwent surgery did not have a difference in their final N:M ratio (P=0.25).

Conclusion: In this small cohort of locally advanced pancreatic cancer patients receiving FOLFIRINOX chemotherapy, surgical resection has the strongest influence on survival. An aggressive surgical approach should be employed for these patients. The final N:M ratio is a strong predictor of outcomes as well; though the N:M ratio does not alter with chemotherapy. Larger cohorts will be needed to further assess inflammatory states with systemic therapy.

P 182. A NOMOGRAM TO PREOPERATIVELY PREDICT EARLY CANCER-RELATED MORTALITY IN RESECTED PANCREATIC CANCER FOLLOWING NEOADJUVANT CHEMORADIATION THERAPY

HK Hwang, K Wada, MD, HY Kim, Y Nagakawa, Y Hijikata, Y Kawasaki, Y Nakamura, LS Lee, DS Yoon, WJ Lee, CM Kang

Presenter: Ho Kyoung Hwang MD, PhD | Yonsei University

Background: This study aimed to develop a nomogram to predict the 1-year survival of patients with pancreatic cancer who underwent pancreatectomy following neoadjuvant treatment with preoperatively detectable clinical parameters. Extended pancreatectomy is necessary to achieve complete tumor removal in borderline and locally advanced pancreatic cancer. However, it increases postoperative morbidity and mortality rates, and should be balanced with potential benefit of long-term survival.

Methods: The medical records of patients who underwent pancreatectomy following neoadjuvant treatment from January 2005 to December 2016 at Severance Hospital were retrospectively reviewed. Medical records were collected from five international institutions from Japan and Singapore for external validation.

Results: A total of 113 patients were enrolled. The nomogram for predicting 1-year disease-specific survival was created based on 5 clinically detectable preoperative parameters as follows: age (years), symptom (no/yes), tumor size at initial diagnostic stage (cm), preoperative serum CA 19-9 level after neoadjuvant treatment (<34/≥34), and planned surgery (pancreaticoduodenectomy [PD] (pylorus-preserving PD)/distal pancreatectomy(DP)/total pancreatectomy). Model performance was assessed for discrimination and calibration. The calibration plot showed good agreement between actual and predicted survival probabilities; the Greenwood-Nam-D'Agostino goodness-of-fit test showed that the model was well calibrated ($\chi^2=8.24$, $p=0.5099$). A total of 84 patients were used for external validation. When correlating actual disease-specific survival and calculated 1-year disease-specific survival, there were significance differences according to the calculated probability of calculated 1-year survival ($p=0.0441$).

Conclusion: The developed nomogram had quite acceptable accuracy and clinical feasibility in the decision-making process for the management of pancreatic cancer.

P 183. PANCREATIC ADENOCARCINOMA CAUSING NECROTIZING PANCREATITIS: NOT AS RARE AS YOU THINK?

KA Lewellen, TK Maatman, MA Heimberger, EP Ceppa, MG House, A Nakeeb, CM Schmidt, NJ Zyromski

Presenter: Kyle Lewellen BS | Indiana University School of Medicine

Background: Necrotizing pancreatitis presents a unique clinical challenge due to its lengthy disease course, therapeutic complexity, and numerous associated complications. Pancreatic necrosis occurs in 15-20% of acute pancreatitis patients and may result from any etiology of acute pancreatitis. Scattered reports describe pancreatic tumors causing necrotizing pancreatitis; however, the relationship between these disease processes has not yet been fully elucidated. We have treated a number of patients whose necrotizing pancreatitis was caused by pancreatic adenocarcinoma and therefore sought to clarify the clinical outcomes of these patients.

Methods: Review of an institutional database identified necrotizing pancreatitis patients treated between 2008 and 2018. Medical record analysis of those with necrotizing pancreatitis and pancreatic adenocarcinoma included patient demographics, date of diagnosis of necrotizing pancreatitis, date of diagnosis of pancreatic adenocarcinoma, management details, and date of last follow up or death.

Results: Among 647 patients treated for necrotizing pancreatitis during this time frame, seven patients (1.1%; two females, five males) had pancreatic adenocarcinoma contemporaneous with necrotizing pancreatitis. The mean age at diagnosis of necrotizing pancreatitis was 60.6 years (range 49-66). Two patients had post-procedural pancreatitis after cancer diagnosis, the remaining five had pancreatitis caused by adenocarcinoma. The average duration between diagnosis of necrotizing pancreatitis and diagnosis of pancreatic adenocarcinoma was 245 days (range 23-655). For pancreatic adenocarcinoma treatment, three patients received chemotherapy alone, one received palliative radiation therapy, and one died without oncologic management. One patient's treatment plan was unknown. Only one patient underwent operative resection of pancreatic adenocarcinoma. Median survival was 12.0 months (range 0.4-49.9).

Conclusion: These data suggest that pancreatic adenocarcinoma may be a more common cause of necrotizing pancreatitis than previously considered. The long duration between diagnosis of necrotizing pancreatitis and pancreatic adenocarcinoma highlights the diagnostic and therefore therapeutic delay in this patient population. Pancreatic adenocarcinoma should be considered in necrotizing pancreatitis patients of this age group in whom etiology is otherwise unclear. Prompt diagnosis of pancreatic adenocarcinoma facilitates optimal treatment in this extremely challenging clinical situation.

P 184. PANCREATIC METASTASIS FROM RENAL CELL CARCINOMA: ANALYSIS OF 16 CASES

A Rosales, DL Cardoso, H Asbun, JA Stauffer

Presenter: Armando Rosales MD | Mayo Clinic Rochester

Background: Pancreatic metastasis (PM) accounts for 1-2% of all pancreatic tumors. Renal cell cancer (RCC) is the most common primary neoplasia that metastasizes to the pancreas. Approximately 22% of the cases of PM occur in asymptomatic patients older than 70-years and are identified during follow-up for the primary neoplasia. In patients with resectable PM, surgery is accepted as the treatment of choice for long-term survival. This study analyzes outcomes of patients with RCC PM.

Methods: After Institutional Review Board approval, we conducted a retrospective review of patients who were diagnosed with metastatic RCC (mRCC) in our Institution between 2001 and 2018. We included all patients ≥ 18 years with mRCC who underwent surgical resection. The variables studied in this case series include patient demographics and clinical presentation, tumor characteristics, surgical management, and outcome. All patients had a known primary RCC and a pathology report on the pancreatic specimen consistent mRCC. Follow-up information was obtained by office visit, review of records or by contacting the patient directly. Descriptive statistics were performed and results are reported as mean \pm standard deviation or median (range).

Results: There were 16 patients (67 ± 8 years, male eight (50%), BMI 29 ± 5.36 kg/m²). Half of them were asymptomatic. Diagnosis was incidental in nine (56%), the median size of the lesions was 25 mm (12 – 80). Pancreatic resections performed were: pancreatoduodenectomy, distal pancreatectomy and total pancreatectomy in five (31%), 9 (56%) and two (13%), respectively. Median estimated blood loss was 225 ml (15 – 2,200) and operative time was 242 min (63 – 420). Median length of stay was six days (2 – 30). Two (12%) patients had wound infection, and four (25%) had abdominal abscess. New-onset diabetes was detected in 6%. Reoperation occurred in one patient (6%) after pancreatoduodenectomy who required a partial colectomy with end ileostomy for ischemic colon, patient recovered without any sequelae. The median harvested lymph nodes were 18 (4 – 31), and all were negative. All patients underwent R0 resection, and none had lymphovascular or perineural invasion. Three (19%) had recurrence of disease, one in the lung (79 months after disease onset), one had local recurrence (35 months after disease onset), and one on the right adrenal (27 months after disease onset). The median time from surgery to recurrence was three years (2 – 6). The median follow-up was 9 years (0 – 15). Eleven (69%) patients are still alive, of these, six are disease free, one has progression of disease with new peritoneal implants, progression of bone and stable lung mets, two have stable metastatic lesions (n=1 bone, n=1 liver) and two unknown. Three (19%) patients died: one due to gastrointestinal bleeding (17 months after the surgery); one of unknown cause or period after surgery; and one due widespread metastasis.

Conclusion: High index of suspicion and continuous follow-up is important for patients with a history of RCC since PM is possible and may present with no symptoms. Moreover, outcomes of surgical resection are better than that for primary pancreatic adenocarcinoma. In conclusion, long-term survival can be achieved with surgical resection of PM from RCC in selected patients in whom complete resection is possible. Pancreatic surgery outcomes are significantly better in high-volume centers. There is limited understanding of the underlying drivers of RCC metastasis clinical heterogeneity.

P 185. THE ASSOCIATION BETWEEN ELEVATED CA 19-9 AND RECURRENCE, SITE OF RECURRENCE, AND OVERALL SURVIVAL IN UPFRONT RESECTABLE PANCREATIC CANCER

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Presenter: Benjamin Powers MD | Moffitt Cancer Center

Background: Current practice guidelines for pancreatic adenocarcinoma (PDAC) recommend consideration of neoadjuvant therapy for patients with elevated CA 19--9. We sought to assess the association of preoperative elevated CA 19--9 (>1,000 U/ml) with outcomes in a cohort of patients with upfront resectable pancreatic cancer.

Methods: We used a single institution database of patients who underwent upfront resection for PDAC between 2007 and 2015. Patients with a bilirubin above 1.5 after decompression were excluded. A total of 144 resectable patients were analyzed. We used Chi--squared analysis for categorical variables and a Wilcoxon rank sum for continuous variables. Kaplan Meier curves, univariate and multivariate proportional hazards regression models were used to assess survival.

Results: 16 patients (11.1%) had elevated preoperative CA 19--9. There was no difference between elevated CA 19--9 and sociodemographic, pre-, peri-, and post-operative variables, including recurrence and site of recurrence (Table 1). Multivariable Cox regression showed that increased Charlson comorbidity index, increasing number of positive lymph nodes, perineural invasion, grade 3/4 Clavien complication and failure to complete adjuvant therapy were all predictors of increased mortality. CA 19--9 >1,000 (HR 1.30; 95% CI [0.73- 2.34]) did not predict increased mortality in the multivariable model.

Conclusion: While practice guidelines suggest neoadjuvant treatment for anatomically resectable PDAC with elevated CA 19--9, there was no association between elevated CA 19--9 and recurrence, site of recurrence, or overall survival in this cohort. Our findings do not suggest that elevated CA 19--9 alone should drive the decision for neoadjuvant treatment.

Table 1: Characteristics of Resectable PDACs by Pre-Operative CA 19-9 Level (n=144)

	Low CA 19-9	High CA 19-9	p-value
Number	128	16	
Sex			0.584
Female	47 (36.7)	7 (43.8)	
Male	81 (63.3)	9 (56.2)	
Age, y			0.443
<70	69 (53.9)	7 (43.8)	
≥70	59 (46.1)	9 (56.3)	
Race			0.552
White	117 (91.4)	15 (93.8)	
Black	4 (3.1)	1 (6.2)	
Other / Unknown	7 (5.5)	0 (0.0)	
Charlson Comorbidity Index			0.945
0-3	35 (27.3)	4 (25.0)	
4-5	58 (45.3)	7 (43.8)	
6+	35 (27.3)	5 (31.2)	
BMI (mean)	26.4	24.9	0.455
Operation			0.116
Whipple/total pancreatectomy	89 (69.5)	8 (50.0)	
Distal pancreatectomy +/- splenectomy	39 (30.5)	8 (50.0)	
Pathologic T Stage			0.859
1	9 (7.0)	1 (6.2)	
2	11 (8.6)	0 (0.0)	
3	63 (49.2)	9 (56.3)	
4	45 (35.2)	6 (37.5)	
Nodes Examined (mean)	19.5	18.3	0.767
Nodes Positive (mean)	2.8	2.1	0.849
R1 resection			0.639
No	117 (91.4)	14 (87.5)	
Yes	11 (8.6)	2 (12.5)	
Grade 3 / 4 Clavien Complication			0.129
No	107 (83.6)	16 (100.0)	
Yes	21 (16.4)	0 (0.0)	
Recurrence			0.708
No	42 (32.8)	6 (37.5)	
Yes	86 (67.2)	10 (62.5)	
Site of Recurrence			0.366
None	42 (32.8)	6 (37.5)	
Local	17 (13.3)	1 (6.2)	
Liver	30 (23.4)	3 (18.8)	
Lung	12 (9.4)	4 (25.0)	
Multi-site	15 (11.7)	2 (12.5)	
Other	12 (9.4)	0 (0.0)	

P 186. THE STRATEGY OF COMPLETE CLEARANCE AROUND SUPERIOR MESENTERIC ARTERY, CELIAC ARTERY AND ITS TRIANGLE IN RADICAL PANCREATODUODENECTOMY FOR PANCREATIC CANCER

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Presenter: Kuirong Jiang MD, PhD | Pancreas Center, The First Affiliated Hospital with Nanjing Medical University

Background: Local recurrence after pancreaticoduodenectomy generally occurs in residual tissue around superior mesenteric artery (SMA), celiac artery (CA) and the triangle between SMA, CA and portal vein-superior vein (PV-SMV). A thorough clearance in this area may reduce the local recurrence and further improve patients' survival.

Methods: We divided the clearance strategy into four steps, and deliberated the cleaning region in our clinical practice.

Results: We succeeded in performing this four-steps clearance strategy in radical pancreaticoduodenectomy. Step1-Extended Kocher's maneuver, No.16a2, 16b1 lymph nodes and right celiac ganglion dissection was performed, and the orientation of SMA and CA were positioned simultaneously. Step2-Clearance of hepatoduodenal ligament and skeletonization of common hepatic artery, gastroduodenal artery (GDA), proper hepatic artery, left and right hepatic artery, left gastric artery and proximal splenic artery, and hepatic portal vein. After cholecystectomy, common hepatic duct was transected and GDA was detached, neural and lymphatic plexus at the right anterior semi-cycle of CA was dissected at the adventitial layer. Step3-Skeletonization of the left posterior semi-cycle of SMA from left-sided infra-colic approach with artery divestment technique. After blood supply judgement, jejunum and its mesentery was resected and pulled to the right upper quadrant through posterior side of SMV. Right-side approach to skeletonize right anterior semi-cycle of SMA, and then transected the pancreas. Step4-Dissection of all tributaries from PV-SMV to pancreatic head, then PV-SMV could be divided and pulled towards the left side and the head of pancreas towards the right side. Finally, separated former neural and lymphatic tissue along the surface of abdominal aorta from SMA upwards to CA and entire clearance of SMA, CA and its triangle was achieved.

Conclusion: Our four-steps clearance strategy significantly increased the dissection efficiency and quality, which could be applied in clinical routine of radical pancreaticoduodenectomy.

P 187. DOES PLACEMENT OF EXTERNAL PANCREATIC DUCT STENT (EPDS) DURING PANCREATICODUODENECTOMY (PD) REDUCE THE RATE OF CLINICALLY RELEVANT POSTOPERATIVE PANCREATIC FISTULA (CR-POPF) IN HIGH RISK GLANDS?

AM Schneider, E Alonso, ES Tang, ST Chiu, ML Babicky, PH Newell, PD Hansen

Presenter: Andreas Schneider MD | Providence Portland Medical Center

Background: Clinically relevant post-operative pancreatic fistula (CR-POPF) is a known complication after pancreaticoduodenectomy (PD) and major cause of morbidity and mortality. Risk factors for developing CR-POPF, including gland texture, duct size and BMI, have been incorporated into fistula risk scores, to help identify high risk patients. Despite this knowledge, operative strategies to decrease the rate of CR-POPF remain limited. Placement of an external pancreatic duct stent (EPDS) has been proposed to decrease the rate of CR-POPF but its role in high risk patients remains unclear.

Methods: We conducted a retrospective review of patients undergoing PD for benign and malignant conditions involving the pancreatic head. Patients with combined high-risk features of soft gland texture and small duct size (≤ 5 mm) were included. Fistula risk score (FRS) and alternative fistula risk score (A-FRS) were calculated, and comparison was performed between patients without (-) EPDS and with (+) EPDS. Primary endpoint was rate of CR-POPF, Grades B and C, according to International Study Group in Pancreatic Surgery (ISGPS) criteria. Secondary endpoints were rate of percutaneous drainage, reoperation, complications, death and hospital length of stay.

Results: Two hundred eighteen consecutive patients underwent PD at our institution between 2013 and 2017. High risk features were identified in 67 patients and EPDS were placed, at the surgeon's discretion, in 17 cases (25%). Demographics, BMI, operative time, FRS and A-FRS were comparable between groups (Table 1). CR-POPF was detected in 32% (-) EPDS and 18% (+) EPDS (p -value = 0.356). Two grade C fistulas were seen in the non-stented group. Percutaneous drains were placed in 36% (-) EPDS and 18% (+) EPDS of patients (p -value = 0.159). 2 patients in the non-stented and 1 patient in the stented group underwent reoperation. There were 3 mortalities overall, 2 in the non-stented and one in the stented group. Overall complications and length of stay were comparable.

Conclusion: In this retrospective study of patients at high risk for developing a CR-POPF after PD, those who underwent placement of an EPDS had a relative risk reduction for developing a fistula of 44%. Although this did not reach statistical significance in this limited number of patients, these data corroborate recent trials that show the advantages of pancreatic duct stenting in this high-risk group.

Table 1. Clinical summary

		Groups				(p-value)
		Control N=50 (75%)		Stent placed N=17 (25%)		
<i>Age Mean(SD)</i>		62	(14)	58	(18)	0.405
<i>Gender N(%)</i>	Female	22	(44)	10	(59)	0.291
	Male	28	(56)	7	(41)	
<i>BMI Mean(SD)</i>		28	(6)	27	(7)	0.367
<i>Duct Size in mm Mean(SD)</i>		3	(1)	2	(1)	0.129
<i>Estimated blood loss in ml Mean(SD)</i>		611	(614)	488	(291)	0.277
<i>Operative time in mins</i>		476	(126)	466	(120)	0.736
<i>Etiology N(%)</i>	Pancreatic adenocarcinoma	19	(38)	3	(18)	0.225
	Ampullary, Duodenal Neuroendocrine tumor, other	29	(58)	14	(82)	
	Pancreatitis	2	(4)	0	0	
<i>Fistula Risk Score Mean(SD)</i>		5.6	(1.7)	6.2	(1.7)	0.270
<i>Alternative Fistula Risk Score</i>	High	26	(52)	11	(65)	0.363
	Intermediate	24	(48)	6	(35)	
<i>30-day death N(%)</i>	Yes	2	(4)	1	(6)	1.000
	No	48	(96)	16	(94)	
<i>LOS Mean(SD)</i>		15	(10)	19	(10)	0.167

P 189. PREDICTION OF PANCREATIC FISTULA AFTER DISTAL PANCREATECTOMY: IS IT NECESSARY TO PLACE PROPHYLACTIC DRAIN?

K Suzumura, E Hatano, K Iida, H Iwama, Y Kawabata, T Okada, N Uyama, I Nakamura, M Tada, S Hai, H Sueoka, K Toriguchi, A Kurimoto, S Tamagawa, J Fujimoto

Presenter: Kazuhiro Suzumura MD, PhD | Hyogo College of Medicine

Background: The aim of this study was to determine the predictive factors for pancreatic fistula (PF) after distal pancreatectomy (DP) among preoperative and intraoperative parameters, and moreover we considered whether we could exactly choose the patients who did not need to place a drain.

Methods: Between July 2009 and April 2017, 102 consecutive patients underwent DP at Hyogo College of Medicine. The preoperative and intraoperative data were collected, and the predictors for PF after DP were identified.

Results: PF were identified in 35 (34 %) patients. In the multivariate analysis, 3 factors [body mass index (BMI) ≥ 22.4 , contiguous organ resection, and pancreatic thickness ≥ 11 mm] were found to be independently the predictive factors of PF (odds ratio, 5.7; 95 % confidence interval, 1.9-17, $p = 0.002$, odds ratio, 6.7; 95 % confidence interval, 1.6-28, $p = 0.009$, odds ratio, 11.6; 95 % confidence interval, 3.7-36, $p < 0.001$, respectively). A scoring scale for the prediction of PF was developed. BMI ≥ 22.4 (score: 1), contiguous organ resection (score: 1), and pancreatic thickness ≥ 11 mm (score: 2) were included in the scoring scale. The patients with scores of 0 never developed a PF, while PF occurred in all patients with scores of 4.

Conclusion: BMI ≥ 22.4 , contiguous organ resection, and pancreatic thickness ≥ 11 mm were predictive factors for PF after DP. Patients with BMI < 22.4 , no contiguous organ resection, and pancreatic thickness < 11 mm were not developed PF after DP, so it may not be necessary to place the drain for the patients during DP.

**P 190. CENTRAL PANCREATECTOMY FOR EARLY-STAGE PANCREATIC DUCTAL ADENOCARCINOMA:
A SINGLE-CENTER CASE-CONTROL STUDY**

*JS Wei, H Gao, TT Liu, GF Wang, Y Gao, LD Yin, YP Peng, N Lyu, K Zhang, WT Gao, JL Wu,
KR Jiang, Yi Miao*

Presenter: Zipeng Lu MD, PhD, MRCS | Nanjing Medical University

Background: Investigate the role of central pancreatectomy (CP) in the treatment of pancreatic ductal adenocarcinoma (PDAC) in the neck or body of the pancreas.

Methods: Patients who underwent CP at the pancreas center of Nanjing Medical University between 2009 and 2016 were identified. Patients treated by distal pancreatectomy (DP) were matched according to the tumor size, location, and staging. The surgical and survival outcomes were compared between the CP and DP groups.

Results: Nine patients had CP. Five had postoperative complications and two had clinically significant (grade B+C) fistula. No significant difference was found between CP and DP group for the rate of overall morbidity, pancreatic fistula, reoperation, and readmission. Tumor size was smaller in the CP group compared to DP group. The mortality of both groups was zero. The median postoperative survival was similar between the two groups (20.4 months for CP vs 19.4 months for DP, $p = 0.842$).

Conclusion: CP is safe for patients with small PDAC at the neck and body of pancreas. Considering the good preservation of pancreatic endocrine and exocrine functions, CP could be used for small PDAC in the neck or proximal body of the pancreas.

P 191. SELECTIVE USE OF A BLUMGART-TYPE TECHNIQUE FOR PANCREATICOJEJUNOSTOMY FOLLOWING PANCREATICOUDENECTOMY DOES NOT REDUCE CLINICALLY SIGNIFICANT FISTULA RATES

CY Wang, J Lyons, JM Hardacre

Presenter: Catherine Wang | Case Western Reserve University School of Medicine

Background: Pancreatic fistula (PF) remains a major contributor to morbidity and mortality after pancreaticoduodenectomy (PD). Many techniques have been described to create the pancreaticojejunostomy (PJ). Some data have shown that a Blumgart-type anastomosis may reduce the incidence of PF and associated complications after PD. This study examines the selective use of a Blumgart-type anastomosis in high-risk glands.

Methods: This single-surgeon series examines outcomes after 193 consecutive PDs over a nearly six-year period. The first 117 PDs were done utilizing an invaginating PJ. For the subsequent 76 PDs, a Blumgart-type PJ was done selectively based on surgeon assessment of fistula risk, with pancreatic duct diameter (3mm or less) and gland texture driving risk assessment. Data before and after starting the selective use of the Blumgart were compared. The primary outcome was clinically significant PF rates in patients with intermediate/high-risk glands according to the Fistula Risk score as well as surgeon assessment of fistula risk. Secondary outcomes included overall clinically significant PF rates, Clavien-Dindo grade 3 or higher complications, reoperation rates, and length of stay.

Results: The median age of the entire cohort was 66 years, and there was an equal gender distribution. There were 4 deaths (2.1%) within 90 days of surgery, and the overall Clavien-Dindo grade 3 or higher complication rate was 16.6%. The median length of stay was 6 days, and the 90-day readmission rate was 6.2%. The reoperation rate was 4.1%. There were 20 (10.4%) clinically significant PFs (18 B, 2 C) in the entire cohort. There were no differences in the rates of clinically significant PFs in patients with intermediate/high risk anastomoses between groups (10% vs 19.6%, $p = .23$) or in patients with a small duct and soft gland (15.4% vs 31.3%, $p = .31$). In group two, a Blumgart-type anastomosis was done in 31 patients. 26 of the patients had an intermediate/high-risk anastomosis, and the clinically significant PF rate was 19.2% (5/26). 13 of the patients had a small duct and soft gland, and the clinically significant PF rate was 23.1% (3/13).

Conclusion: In this single-surgeon series, the selective use of a Blumgart-type PJ did not lower the incidence of clinically significant PF after PD.

P 193. PREDICTING SURVIVAL OF PDAC PATIENTS BEFORE SURGERY: A MULTI-OMICS APPROACH

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Presenter: Zipeng Lu MD, PhD, MRCS | Pancreas Center, The First Affiliated Hospital with Nanjing Medical University

Background: Although many prognosis systems had been proposed to predict the disease progression and survival in pancreatic ductal adenocarcinoma (PDAC), there is still a lack of tool to predict the survival for PDAC patients, especially to guide the precision treatment strategy for PDAC before surgery. This study aim to evaluate the prognostic value of different “-omics” information before the surgery for the overall survival of PDAC patients after radical resection, and to develop preoperative tools for survival prediction to achieve a better patient selection.

Methods: Survival analysis have been carried out in patients underwent curative intent surgery in our institution, which is a multi-disciplinary, tertiary referral center for pancreatic diseases. Prognostic value of different preoperative variables in clinical parameters, regular lab studies, radiomics and genomics have been co-related with overall survival. We tested a panel of miRNA in the preoperative serum of the patients to represent the genomics information. Uni- and multi-variate Cox and logistic regression was utilized to identify the independent risk factor for long-term survival and death within 1 year after surgery, while LASSO regression were applied for feature selection and radiomics signature construction. An artificial intelligence (AI) platform was further employed to build a survival prediction model and compared with the traditional one.

Results: Multiple preoperative variables from different “omics” panels corelated with the overall survival after radical resection for PDAC patients, and together they can identify patients die within one year after radical surgery. Both prediction model based on multivariate Cox regression and the AI analytic platform can predict the overall survival well.

Conclusion: Overall survival of PDAC patients after radical resection can be predicted with different preoperative “multi-omics” variables, and both of the two models (Cox regression and AI) based on these factors can predict survival well.

P 196. THE IMPLICATION OF INDUCTION CHEMOTHERAPY FOLLOWED BY CHEMORADIOTHERAPY FOR LOCALLY ADVANCED PANCREATIC CANCER, INTENDED CONVERSION SURGERY

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Presenter: Daisuke Ban MD, PhD | Toyko Medical and Dental University

Background: In recent years, options for conducting Conversion Surgery are attracting attention for cases in which chemotherapy and chemoradiotherapy have been successful in locally advanced unresectable pancreatic cancer (UR - LA). Cases in which Conversion Surgery could be performed are expected to have a certain prognosis from the previous report. It seems that there is a possibility that the treatment strategy for UR-LA we are working on and the treatment combined appropriately in the previous report may possibly greatly improve the prognosis, but to show the results is a future issue.

Methods: When judged as SD, PR, CR after performing gemcitabine (GEM) + albumin suspended paclitaxel (nabPTX) therapy or GEM + S-1 as a chemotherapy for locally advanced unresectable pancreatic cancer, After conducting chemoradiotherapy (50 Gy / 25 times, S-1), Conversion Surgery was performed for cases judged to be resectable.

Results: Between 2014 and 2017, 16 cases of locally advanced unresectable pancreatic cancer were attempted by Conversion Surgery and chemotherapy and chemoradiotherapy were performed. GEM + S1 was performed in 4 cases as introduced chemotherapy, and GEM + nabPTX was performed in 13 other cases. In the evaluation after introduction chemotherapy, 6 cases of PR, 8 cases of SD, 2 cases of PD, 13 patients underwent chemoradiotherapy. Seven cases (44%) judged that resection was possible and implemented Conversion Surgery. In addition, 1 case was attempted to do Conversion Surgery, but it result in an exploratory laparotomy due to micro-liver metastasis. Eight patients did not undergo surgery, they continued chemotherapy and became palliative treatment. Pathological R0 resection could be performed in all cases where Conversion Surgery was done. The effect of preoperative treatment was Evans' classification, 2 cases in IIa, 2 cases in IIb, and 3 cases in III. The 2-year survival rate of cases with Conversion Surgery was 75%, and in non-resected cases was 54% ($p = 0.176$). At the present time, we have too short follow-up observation period and too little number of cases to examine the implication of these treatments.

Conclusion: Introduction chemotherapy and radiation chemotherapy designed for Conversion Surgery for locally advanced unresectable pancreatic cancer were feasible in our case with R0 resection rate. Further case accumulation and consideration with a large number of cases are necessary.

P 197. ROBOT-ASSISTED TRANS-GASTRIC TREATMENT OF WALLED-OFF PANCREATIC NECROSIS WITH THE DA VINCI XI

L Morelli, N Furbetta, M Palmeri, G Di Franco, S Guadagni, D Gianardi, M Bianchini, G Caprili, C D'Isidoro, F Mosca, G Di Candio

Presenter: Matteo Palmeri MD | University of Pisa

Background: Walled-off pancreatic necrosis (WOPN) is a late complication of acute pancreatitis which represents a challenging critical problem with still high rate of mortality and morbidity. The management depends on the patient's symptoms and the location of the WOPN. Trans-gastric drainage and debridement of WOPN is a valid surgical treatment option for selected patients. Herein we report the case of a WOPN treated with a robot-assisted trans-gastric drainage and debridement using the da Vinci Xi with the new EndoWrist stapler.

Methods: A 63-years old man with a previous episode of acute severe pancreatitis was referred to our center. We started with medical conservative treatment (total parenteral nutrition), with progressive normalization of pancreatic enzymes. However, the patient developed a walled massive fluid collection, with an extensive pancreatic necrosis, causing obstruction of the gastrointestinal tract. The CT-scan, performed 6 weeks after the acute episode, confirmed the presence of a WOPN that compressed the stomach and the first duodenal portion. The patient was then operated with the use of the da Vinci Xi surgical system. The procedure was successfully completed in 130 min. Firstly, guided by intraoperative US scan, an anterior ideal gastrotomy was performed. The intra-operative US scan was obtained with a dedicated robotic probe using the TilePro function. This technology consents the surgeon to view a 3D rendering of the operative field along with the US exam. Then, through the gastrotomy, the best location for drainage on the posterior gastric wall was again US-guided identified. The anastomosis between the posterior gastric wall and the WOPN wall was carried out with the new EndoWrist stapler with vascular cartridge. Debridement and washing of the cavity through the anastomosis were performed. The Xi platform flexibility was particularly useful in this phase, reducing external conflict between the robotic arms and allowing an easier access to the narrow cavity. Finally, the anterior gastrotomy was closed with three layers of 3-0 V-Lock running sutures and the cholecystectomy was performed. No intra-operative complications occurred. The postoperative course was uneventful and a post-operative CT-scan showed the collapse of the fluid collection.

Conclusion: In selected cases of WOPN the da Vinci Surgical System can be safely used as a surgical treatment option, alternatively to endoscopic approach. The enhanced surgical dexterity allows an extensive debridement in the narrow cavity. The robotic stapler, with its range of 108° of articulation, can facilitate the suture and allows the operator to directly control all the steps of suturing. Furthermore, the stapler is able to detect the suitable thickness of the tissue between the branches and this function, together with the vascular cartridge, reduces the risk of anastomotic bleeding, which is one of the most frequent complications of this operation. Finally the TilePro multi-input display function can superimpose the US imaging on the console screen, eliminating several problems related to hand-eye coordination and interrupted surgical dissection.



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P 198. PANCREATODUODENECTOMY FOR PERIAMPULLARY ADENOCARCINOMA IN A PATIENT WITH A PREPANCREATIC PORTAL VEIN

M Bonds, J Rekman, G Baison, F Rocha

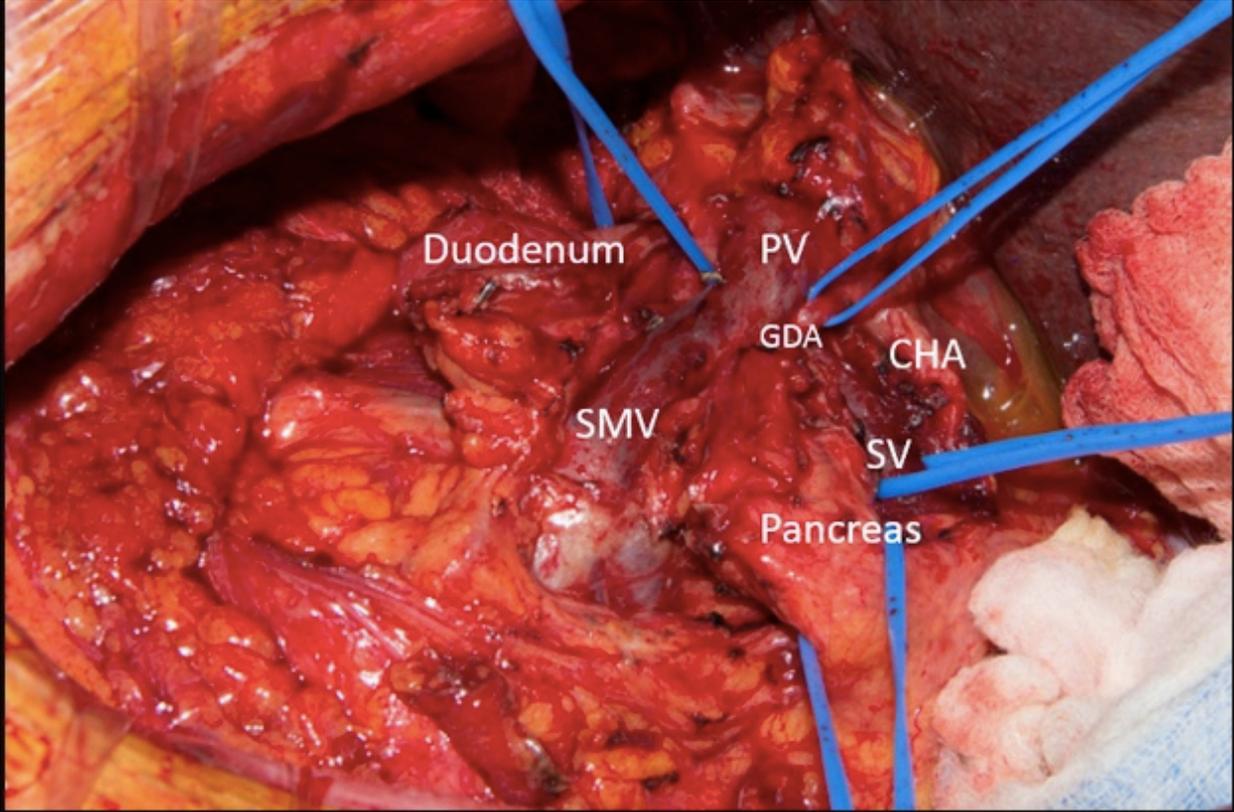
Presenter: Morgan Bonds MD | Virginia Mason Medical Center

Background: Prepancreatic portal vein (PPPV) is a rare congenital anomaly that results in the portal vein coursing anterior to the neck of the pancreas due to aberrant regression of the vitelline veins. The presence of this anomaly can present challenges when planning pancreatectomies, even for experienced surgeons. Previously, distal pancreatectomy and total pancreatectomy of an annular pancreas have been described in patients with PPPV. This case demonstrates that pancreaticoduodenectomy for malignancy can be successfully performed in a patient with a PPPV.

Methods: An 80 year old woman presented with abdominal pain and obstructive jaundice. Endoscopy demonstrated a 2.7 centimeter periampullary mass that invaded the distal common bile duct requiring stent placement. Biopsy of the mass confirmed the diagnosis of adenocarcinoma. On pre-operative pancreatic protocol computed tomography, she was found to have a PPPV without evidence of metastases. Given her good functional status and desire for curative therapy, she was consented for a pancreaticoduodenectomy.

Results: After confirming the tumor was resectable, we created a tunnel around the pancreas to the left of the PPPV. Pancreatic dissection was continued in the standard fashion. The splenic vein was identified coursing behind the common hepatic artery and superior to the pancreatic body; it was followed to identify the take-off of the gastroduodenal artery which was adjacent to the splenic vein-portal vein confluence. After the bile duct and proximal duodenum were transected, the pancreatic neck was divided. The pancreas was freed from the retroperitoneum with Ligasure device, taking extreme care to preserve the superior mesenteric artery at the mesenteric root. The pancreas was adhered to the posterior superior mesenteric vein (SMV); it was able to be removed with ligation of the middle colic vein and controlled creation of a small venotomy in the SMV with less than five minutes of clamp time. Reconstruction was performed in the standard fashion.

Conclusion: PPPV is a rare congenital vascular anomaly. Identification of unusual vascular anatomy is essential prior to undertaking any procedure in the right upper quadrant. Most descriptions of PPPV in the literature are in the pediatric population; there are two pancreatectomies reported in adults for malignancy but neither required a pancreatic anastomosis. We have shown that PPPV does not preclude successful pancreaticoduodenectomy for a malignant process. Pre-operative imaging and planning are essential when approaching any pancreatic procedure in a patient with PPPV.



P 199. KIDNEY TRANSPLANTATION AFTER EXTENDED MULTI-VISCERAL RESECTION FOR PANCREATIC DUCTAL ADENOCARCINOMA

H Lapshyn, L Bolm, E Petrova, D Bausch, T Keck, UF Wellner

Presenter: Louisa Bolm MD | University Medical Center Schleswig-Holstein

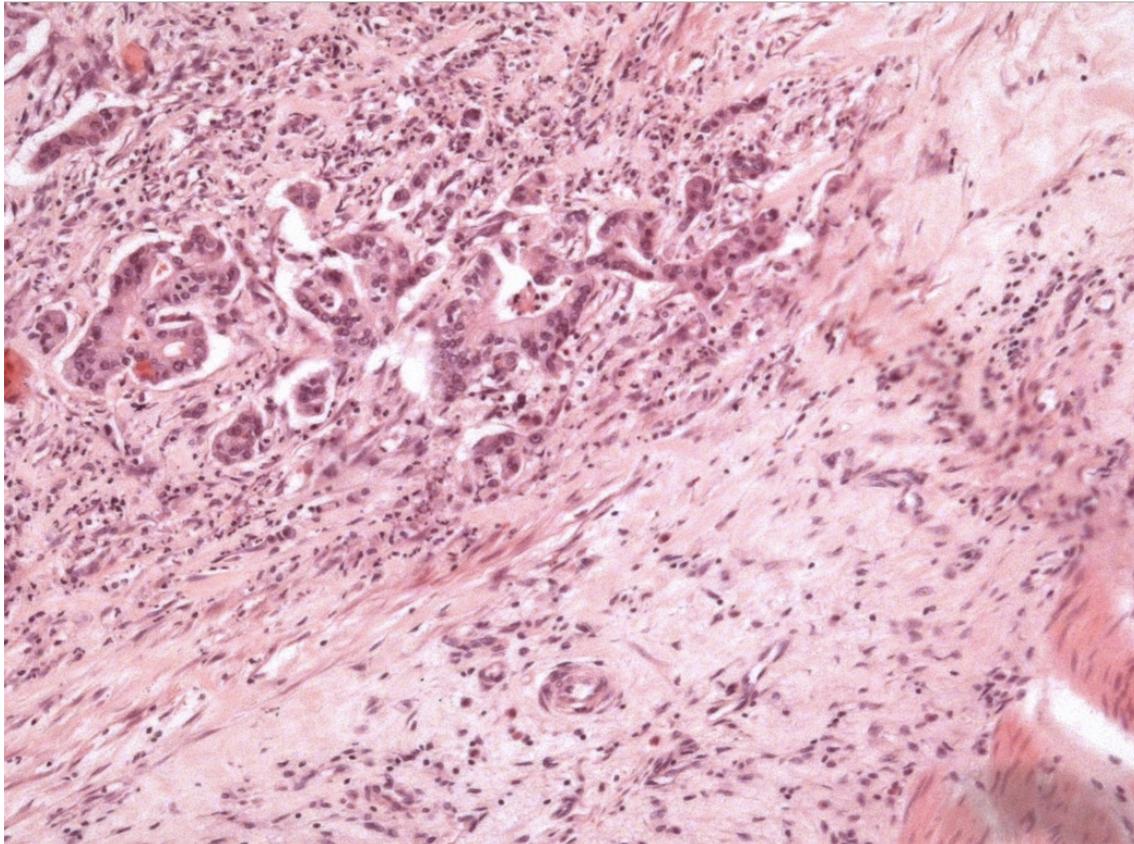
Background: Pancreatic ductal adenocarcinoma (PDAC) is an aggressive cancer with dismal prognosis and few therapeutic options. PDAC is considered the most aggressive solid tumor characterized by early local and systemic tumor cell spread. Complete surgical resection remains the only curative option in PDAC, however, only few patients are eligible for this option. In patients undergoing combined surgical and oncologic treatment including curative resection, 5-year survival increases to 20-30%. As a consequence of dismal prognosis in PDAC patients, solid organ transplantation is usually not considered. This is the first case report of kidney transplantation (KT) in a 57 year old female patient after extended multi-visceral resection for PDAC of the distal pancreas who had developed end-stage renal disease (ESRD) due to toxic kidney damage by adjuvant chemotherapy.

Methods: The patient presented at the clinic in September 2004. At this point of time, the female patient was 46 years old and presented in a good clinical condition. She reported to suffer from progressive abdominal pain also affecting the back since June 2004. An abdominal computed tomography - imaging (CT) disclosed a 5 x 4 cm solid mass of the pancreatic corpus/tail. A complete staging did not show distant metastases or pathologically enlarged lymph nodes. Endosonography confirmed these findings and additionally showed tumor infiltration into the stomach. A tumor biopsy revealed PDAC grade G2. Level of tumor marker carbohydrate antigen 19-9 (CA 19-9) was 2792 kU/l, significantly exceeding the reference range (normal value <37-40 kU/l). Initial renal function was normal. The tumor was considered resectable and the patient underwent radical extended pancreatoco-splenectomy with adrenalectomy, subtotal gastrectomy, radical systematic lymphadenectomy, radical omentectomy, resection of the abdominal wall, tangential transverse colon resection and cholecystectomy in September 2004. Histopathological work-up revealed a pancreatic ductal adenocarcinoma (Figure 1) of the corpus with a diameter of 6.2 cm, tumor infiltration of the gastric and colon wall, localized peritoneal carcinomatosis as well as lymph- and hemangiogenesis. Resection margins were negative. Final histopathological staging was pT3, pN1, pM1, L1, V1, G2-3, R0, UICC-Stage IV.

Results: After the operation CA 19-9 increased to over 10000 kU/l. Following complete resection, the patient received adjuvant chemotherapy with gemcitabine, followed by combined gemcitabine and cisplatin (November 2004 to April 2005) and combined gemcitabine together with mitomycin (five cycles April 2005 to January 2006) at standard dose. Chemotherapy was stopped after normalization of the tumor markers. In May 2006, the patient developed toxic chemotherapy-related end stage renal disease (ESRD) requiring hemodialysis. In December 2012, the patient presented at the Transplant Center of the University of Lübeck (Germany) for KT. Due to PDAC history, the patient underwent extended follow-up examination. Abdominal magnetic resonance imaging (MRI) and positron emission tomography with deoxy-fluoro-D-glucose integrated with computed tomography (FDG-PET-CT), thoracic conventional x-ray, gastroscopy, colonoscopy, gynecological and other examinations as well as measurement of tumor markers (carcinoembryonic antigen (CEA), CA 19-9) disclosed no evidence of local or systemic recurrence. Allogenic KT was performed in March 2015. Cold ischemia time was 17 hours and warm ischemia time was 20 minutes. Intraoperatively, 6 para-iliacal lymph nodes were removed. Histological work-up in fresh frozen section and terminal histology revealed reactive lymphadenopathy with no signs of malignancy. Initial immunosuppression comprised Methylprednisolon, Basiliximab 40 mg, Mycophenolat-Mofetil and Ciclosporin. Kidney function promptly recovered and ultrasonography showed sufficient perfusion of the transplanted kidney without evidence of urine retention. The patient was discharged on postoperative day 17. Due

to the patient's history of malignancy a mechanistic target of rapamycin (mTOR) inhibitor based immunosuppression was considered but declined by the patient [6].

Conclusion: Currently, the patient presents in a good general health condition with sufficient function of the kidney transplant and a normal CA19-9. No local or distant PDAC recurrence has been detected in 36 months of follow-up.



P 200. CLINICOPATHOLOGIC FEATURES OF INTRADUCTAL TUBULOPAPILLARY NEOPLASMS OF THE PANCREAS

J Rekman, R Dorer, M Bonds, G Baison, F Rocha

Presenter: Janelle Rekman MD, MAEd | Virginia Mason Medical Center

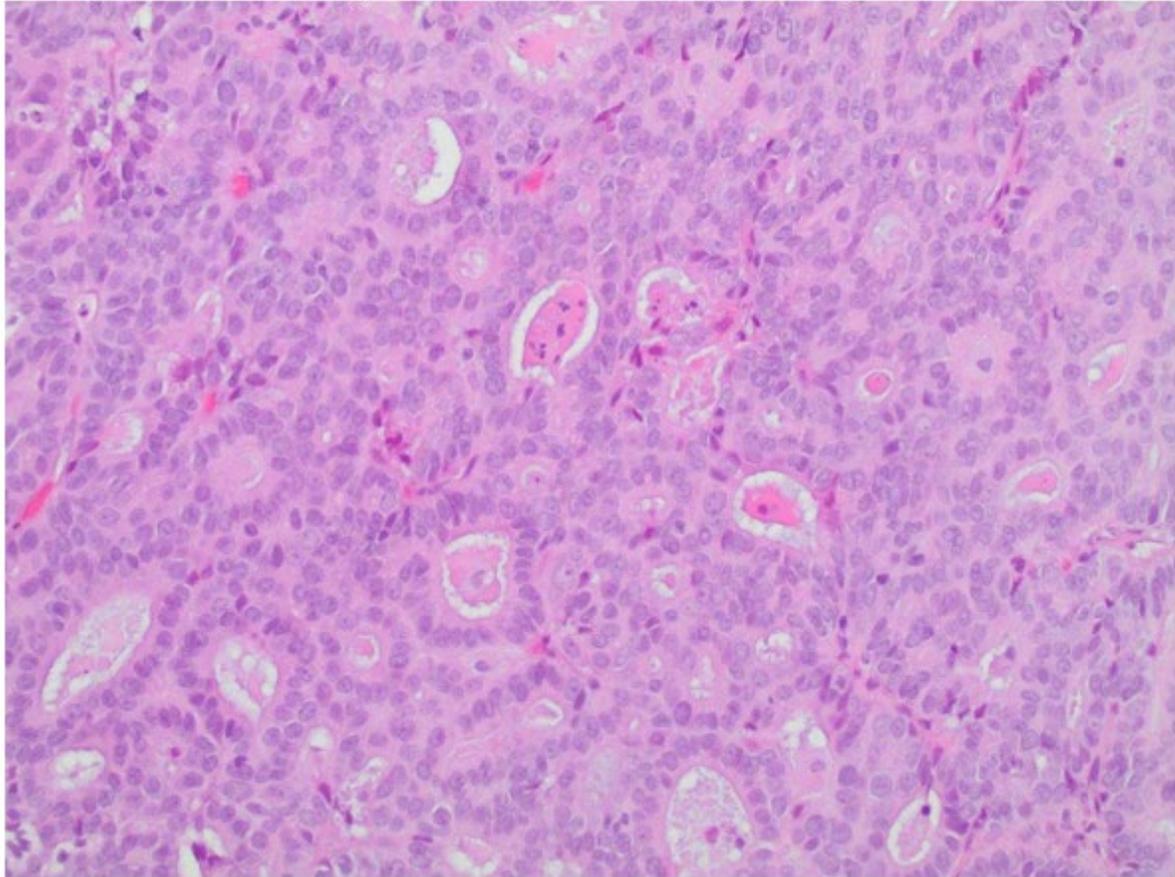
Background: Intraductal tubulopapillary neoplasms (ITPNs) are a newly described entity in the family of pancreatic lesions. They are characterized histochemically with minimal cytoplasmic and luminal mucin and a tubulopapillary growth pattern. Given their rarity, data on their biologic behavior and clinical features are limited. Here we describe a case series of 3 patients diagnosed with ITPN and treated with surgical resection.

Methods: Cases were identified by pathologic review of all intraductal papillary mucinous neoplasms (IPMN) at our institution between 2009 and 2018. Patient demographic data including medical history, presenting symptoms, tumor markers, imaging features, pathologic findings and survival were obtained from the electronic medical record.

Results: On review of pathologic IPMN specimens, 3 were found to have ITPN. The median age at diagnosis was 64. Two of 3 patients presented with weight loss, diarrhea and pancreatitis, and all patients had a history of pancreatitis and epigastric abdominal pain prior to diagnosis. Ca19-9 values were normal. Computed tomography scan found abrupt caliber change of the jaundice, diabetes, or a family history of pancreatic ductal adenocarcinoma. All pre-operative pancreatic duct (PD) at a mass lesion in all 3 patients, with 2 lesions in the head and 1 in the tail of the pancreas. Preoperative biopsies were obtained from all patients and 2/3 contained adenocarcinoma. Following proper staging, 2 patients underwent a pancreaticoduodenectomy while the other had a spleen-preserving distal pancreatectomy. Final pathology revealed an ITPN with a focus of invasive component in 2 patients and high grade dysplasia in the third. None of the patients had positive lymph nodes. The 2 patients who had foci of invasive adenocarcinoma in their specimens received adjuvant chemotherapy. Papillary cells were prominent and no mucin was seen in any of the specimens. Patients were followed for 48, 51, and 12 months respectively. The patients followed for 48 and 12 months are alive with no evidence of disease. The final patient, who had originally had an ITPN in the tail of the gland, developed a second primary adenocarcinoma in the head. While undergoing neoadjuvant therapy for this second primary cancer, the patient was diagnosed with peritoneal metastases and died 60 months after initial surgery.

Conclusion: ITPN patients presented with PD dilatation and abdominal pain, but without jaundice, and their tumors showed significant intraductal components with papillary features and a distinct lack of mucin. Despite foci of invasive carcinoma in 2 of 3 patients, no LN metastases were seen in this series. Malignancy arising in the setting of ITPN may be associated with a more favorable survival compared to conventional pancreatic ductal adenocarcinoma.

Image 1: The ITPN cases showed characteristic histologic features. The ducts were completely filled by a tubule-forming neoplasm comprised of back-to-back glands resulting in enlarged cribriform structures within dilated ducts. The neoplasms contained tubular and solid areas comprised tightly packed glands lined by cuboidal cells with atypical nuclei consistent with high-grade dysplasia.

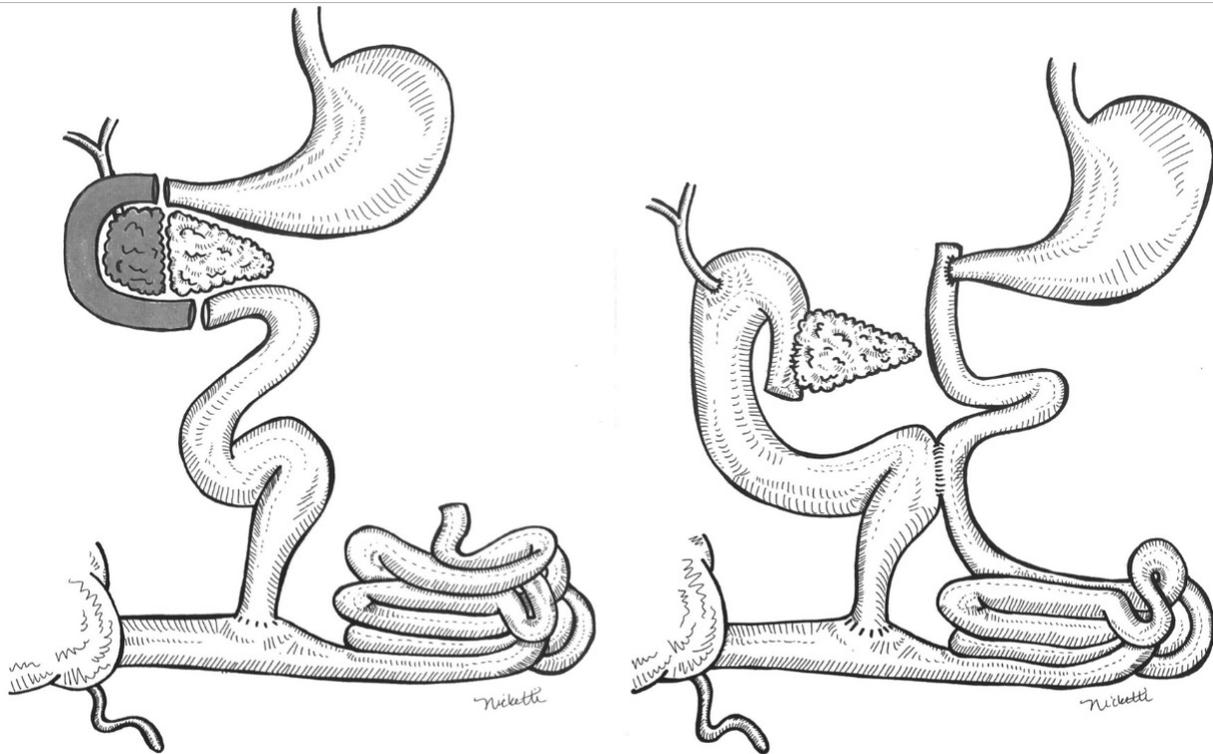


P 201. PANCREATICODUODENECTOMY IN PATIENT WITH JEJUNOILEAL BYPASS

N Handy, L Harmon, FG Rocha

Presenter: Flavio Rocha MD | Virginia Mason Medical Center

Background: A 77yo F with a history of a remote jejunoleal bypass (JIB) for morbid obesity presented with obstructive jaundice, diarrhea and weight loss. Abdominal and pelvic CT showed biliary dilation and a poorly defined mass in the distal bile duct without evidence of metastatic disease as well as several loops of atretic small bowel consistent with JIB. Endoscopy with ERCP revealed a stricture of the common bile duct which was stented and brushings were consistent with adenocarcinoma. On exploration, a dilated proximal jejunum was found anastomosed end to side to the terminal ileum. Following an uncomplicated resection, the pancreatic remnant and common hepatic duct were anastomosed to the dilated, functional jejunal limb. Reversal of JIB and conversion to biliopancreatic diversion were considered. Instead, a duodenojejunosomy was constructed to the previously defunctionalized intestine and a jejunojejunostomy was constructed between the pancreatobiliary limb and the alimentary limb. (See Figure) Final pathology revealed a T3N0 poorly-differentiated adenocarcinoma of the bile duct. Postoperative recovery was prolonged requiring supplemental tube feeding for one month but the patient was eventually nutritionally intact on oral intake alone. Upper gastrointestinal series demonstrated patency of the jejunojejunostomy with antegrade flow through both limbs as well as reflux into the proximal atretic ileum. Resection of pancreatobiliary malignancy following bariatric surgery can be challenging due to restricted reconstruction options. This is particularly true after JIB where most of the functional jejunum is not suitable for an anastomosis. To our knowledge, this is the first description of a successful pancreaticoduodenectomy in a patient with an intact JIB.



P 202. AN UNKNOWN PRIMARY—A CASE OF A MERKEL CELL CARCINOMA IN THE INGUINAL NODES AND PANCREAS

SS Murthy, S Reddy, M Hill, E O'Halloran, J Hoffman, J Farma

Presenter: Shilpa Murthy MD, MPH | Fox Chase Cancer Center/Temple University

Background: This is a case of a 70-year-old diabetic and morbidly obese woman who felt a pulling sensation in her right inguinal area. She felt a mass which started to grow in July 2018. A CT scan of the pelvis demonstrated a 2.4 x 3.8 cm right inguinal lymph node. An ultrasound-guided core needle biopsy showed a high-grade neuroendocrine carcinoma, consistent with Merkel Cell Carcinoma (MCC). She was referred to Fox Chase Cancer Center for further management. On physical examination she had a mobile palpable mass in her right inguinal region. Clinical examination failed to reveal any skin lesions suspicious for a primary site. A PET/CT was performed that demonstrated the inguinal lymph node had enlarged in size to 6.6 x 3.4 cm, it additionally showed a PET avid 2.2 cm right external iliac chain lymph node and a 1.5 cm right pelvic sidewall lymph node. There was also a 1.4 x 1.3 cm mass in the body of the pancreas with minimal FDG avidity and a minimally FDG-avid peri-pancreatic lymph nodes. She had a breast lesion, and a subtle focus of activity in the left lobe of the liver. She underwent a mammogram and ultrasound of her breast which demonstrated benign cysts and a liver MRI was negative. She underwent a right superficial and deep pelvic node dissection with sartorius muscle transposition on 9/2018. Surgical pathology revealed 1/7 right superficial inguinal lymph nodes, 6/8 right external iliac nodes and 1/1 right obturator nodes positive for MCC. She subsequently had an endoscopic ultrasound and biopsy of her pancreatic mass. This demonstrated high grade neuroendocrine tumor consistent with MCC. Her pathologic stage is TxN1bM1c. She is currently being treated with immunotherapy with plans for radiation to the inguinal region and pancreas. The surgical plan following immunotherapy has yet to be determined.

P 203. LUMEN-APPOSING METAL STENTS FOR DRAINAGE OF WALLED-OFF NECROSIS – A CASE REPORT

NHV Coelho, CRF Rodrigues, AB Osvaldt

Presenter: Nelson Coelho MSc | Hospital Moinhos de Vento

Background: Acute pancreatitis is a prevalent and often serious condition associated with high morbidity and mortality. Endoscopic intervention has become the first-line therapy for the management of pancreatic and peripancreatic fluid collections in the setting of acute pancreatitis. Endoscopic drainage of walled-off necrosis requires the creation of a fistula between the gastrointestinal lumen and the pancreatic or peripancreatic fluid collection. In this case report, we present the steps of the procedure and the results of the use of a lumen-apposing metal stent (LAMS) in a large walled-off necrosis.

Methods: A 40-year-old man was admitted to the hospital with the diagnosis of acute pancreatitis that progressed to necrotizing pancreatitis. Simultaneously, he had myocardial infarction, undergoing coronary angioplasty and stent placement. During hospitalization, the patient developed diabetes and a large pancreatic fluid collection of about 12 cm, compromising a large portion of the pancreas, which compressed the stomach causing considerable pain and discomfort to the patient. Control computed tomography (CT) scans were performed. Drainage of the pancreatic fluid collection was performed with placement of a 15-mm LAMS (Hot AXIOS™; Boston Scientific, Natick, MA, USA) under general anesthesia and endoscopic ultrasound (EUS) guidance in the Endoscopy Unit.

Results: Immediately after LAMS deployment, we observed a large amount of brownish viscous liquid draining from the collection to the stomach cavity. Three days later, we introduced a flexible endoscope into the necrotic cavity through the cystogastrostomy (figure 1). The cavity was inspected for identification of viable and non-viable tissue, followed by irrigation and debridement of solid content using a snare-basket device. Debridement and lavage were repeated every 7 days until the cavity was clean, with oozing walls indicating the presence of viable tissue. After 4 weeks, the collection was resolved and the LAMS was removed. The patient progressed well, and a control CT scan was obtained without any signs of residual collection. The patient is currently in good condition almost 12 months after the procedure.

Conclusion: Endoscopic intervention plays an important role in the modern management of pancreatic fluid collection. Endoscopic techniques have been used to treat local complications, such as walled-off necrosis, often in a step-up approach, by which less invasive techniques are preferred initially. The LAMS for endoscopic transmural necrosectomy, as demonstrated in this case, is a new and very effective device for drainage of walled-off necrosis.



P 204. NEEDLE TRACT SEEDING FOLLOWING ENDOSCOPIC ULTRASOUND-GUIDED FINE-NEEDLE ASPIRATION FOR PREOPERATIVE DIAGNOSIS OF STAGE IA PANCREAS HEAD CANCER

H Hisai, T Sakurai, Y Koshihara, K Watanabe, S Ameda, M Sato, R Kawasaki, H Gyobu, N Yoshida

Presenter: Hiroyuki Hisai MD, PhD | Japanese Red Cross Date Hospital

Background: Gastric wall implantation and needle tract seeding, although extremely rare, have been reported as a serious consequence of endoscopic ultrasound-guided fine-needle aspiration (EUS-FNA). Herein, we report a case of needle tract seeding on the gastric wall following EUS-FNA. To the best of our knowledge, this is the first report of a gastric wall implantation of pancreatic head cancer caused by EUS-FNA. A 65-year-old Japanese female with a history of scirrhous carcinoma of the breast (pT2N1M0, pStage IIB) was introduced to our department for the further examination of the main pancreatic duct dilatation. Contrast-enhanced CT (CECT) revealed main pancreatic duct dilatation of the body and tail of the pancreas and no mass could be detected. EUS revealed 20-mm hypoechoic mass with irregular margin in the head of the pancreas. EUS-FNA using 22-gauge needle without side hole was performed with a suction technique using 20 strokes through the duodenal bulb, but adequate specimens were not obtained. Consecutively, EUS-FNA with 25-gauge needle without side hole was performed with the same technique via the gastric antrum. The procedure was completed without complication. The tumor was diagnosed as adenocarcinoma which was strongly positive for CK7 and maspin and negative for CK20, estrogen receptor (ER), progesterone receptor (PgR) and gross cystic disease fluid protein 15 (GCDFP-15) by immunohistochemistry. Pylorus-preserving pancreatoduodenectomy was performed 21 days after EUS-FNA. Pathological findings revealed 18-mm invasive pancreatic ductal adenocarcinoma. There was no vascular or lymphatic involvement, and the resection margins were not involved by malignancy. The stage of the cancer was pT1 pN0 M0, Stage IA. Adjuvant chemotherapy using gemcitabine was administered for 12 months. CECT showed a 40-mm-diameter hypo-vascular mass in the posterior wall of the gastric antrum with minimal ascites at 26 months after surgery accompanied by a rising level of serum CA19-9. We retrospectively reviewed CECT images and noted a 9-mm hypo-vascular mass at 14 months after surgery, even though CECT was performed every 3 months. A second EUS-FNA was performed and the histologic features were consistent with pancreas primary. Positron emission tomography/CT revealed the other small peritoneal metastases. Thereafter, she received 60 cycles of modified FOLFIRINOX followed by 4 cycles of nab-paclitaxel with gemcitabine. Unfortunately, she died from the cancer 68 months after the initial EUS-FNA.

P 206. ANTITUMOR ROLE AND MOLECULAR REGULATION OF HEAT SHOCK PROTEIN 70 AND 90: ACUTE PANCREATITIS AND PANCREATIC DUCTAL ADENOCARCINOMA

A Gulla, K Strupas, GH Su

Presenter: Aiste Gulla MD, MHCM | Vilnius University

Background: Pancreatic ductal adenocarcinoma (PDAC) is one of the deadliest cancers for which few curative therapies are available to date. Acute pancreatitis (AP) is uncommon manifestation of PDAC. Heat shock proteins are important for a dynamic range of cellular processes that include protection against cell stress and inflammation. The inducible heat shock proteins-70 and 90 are anti-oxidative, anti-inflammatory and cytoprotective enzymes, however their upregulating role remains unknown in AP leading to PDAC.

Methods: Acute pancreatitis (n= 50) patients and 25 age-and sex-matched pancreatic cancer patients (n=50) were studied. Peripheral blood samples from pancreatitis and pancreatic cancer patients were collected on admission. Plasma samples were stored -80C. Commercially available ELISA kits were used.

Results: The results are currently being analyzed.

Conclusion: Further studies are now underway to analyze the pancreatic levels of HSP-70 and HSP-90 in acute pancreatitis and pancreatic cancer to determine whether the presence of simultaneous upregulation of these proteins are protective and play anti-tumor role.