

P 1. PATTERNS OF CA19-9 RESPONSE TO NEOADJUVANT CHEMORADIATION FOR PANCREATIC CANCER PREDICT DIFFERENCES IN SURVIVAL

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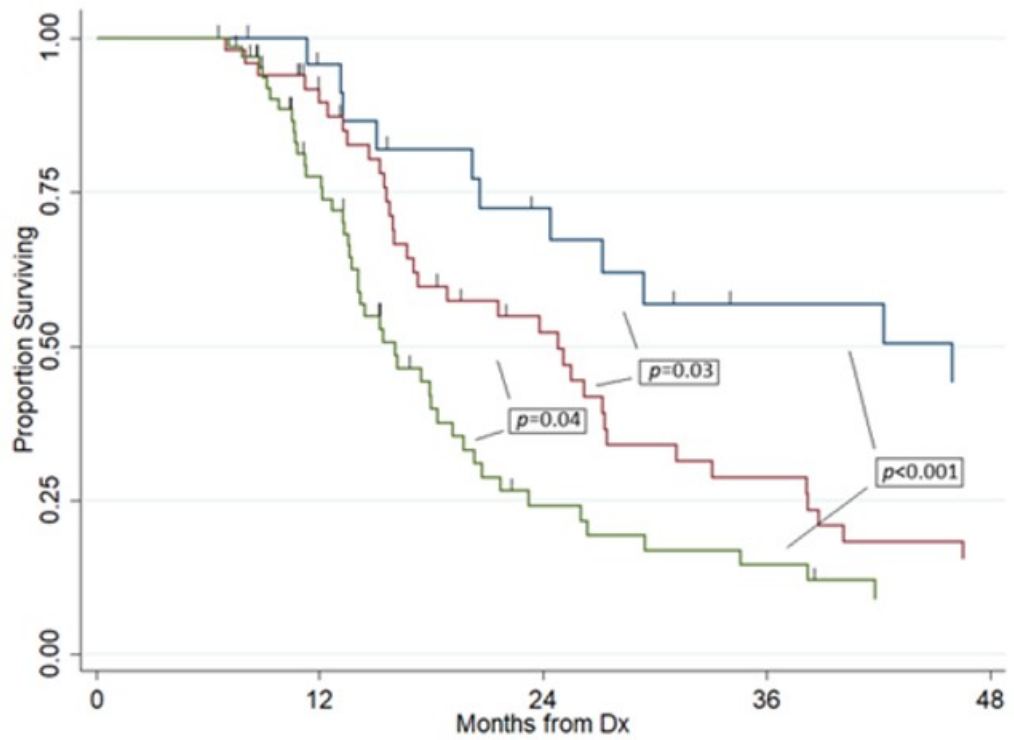
Background: Carbohydrate antigen 19-9 (CA19-9) is a valuable biomarker for pancreatic ductal adenocarcinoma (PDAC) and changes in CA19-9 during therapy may inform subsequent clinical decisions. Patients (pts) with borderline resectable (BLR) PDAC often receive systemic chemotherapy followed by localized radiation (XRT). CA19-9 response pattern during XRT, in the absence of systemic therapy, may help identify pts with radiographically occult metastatic disease.

Methods: Pts with BLR PDAC who had an elevated CA19-9 at diagnosis (with a normal bilirubin) and received neoadjuvant chemotherapy followed by XRT were identified. CA19-9 values were classified as normal or elevated (>35 U/mL). CA19-9 levels were examined at diagnosis, following induction chemotherapy prior to XRT (pre-XRT), and following XRT prior to surgery (post-XRT). Proportional change in CA19-9 during XRT was calculated and categorized as a response ($\geq 50\%$ decrease), stable ($< 10\%$ increase to $< 50\%$ decrease), or increase ($\geq 10\%$ increase).

Results: Of 180 pts, pre-XRT CA19-9 levels following induction chemotherapy were normal in 42 (23%) pts and remained elevated in 138 (77%). Of 138 pts with an elevated pre-XRT CA19-9, the post-XRT CA19-9 was associated with a CA19-9 response in 74 (54%), stable levels in 28 (20%), and an increase in 36 (26%) pts. Normalization of post-XRT CA19-9 was achieved in 25 (34%) of the 74 responding pts, 2 (7%) of the 28 stable pts, and none of the pts with increasing CA19-9 ($p < 0.001$). Completion of neoadjuvant therapy and surgery was achieved in 59 (79%) of the 74 pts with a response, 16 (57%) of 28 pts with stable CA19-9, and 19 (53%) of 36 pts with an increase in CA19-9 ($p = 0.01$). Metastatic disease was found in 11 (15%) of the 74 pts with CA19-9 response, 10 (35%) of the 28 pts with stable CA19-9, and 11 (31%) of the 36 pts with an increasing CA19-9 ($p = 0.04$). Median overall survival (mOS) was 27 mo in the 74 pts with a response, 16 mo in the 28 pts with stable CA19-9, and 15 mo in the 36 pts with an increase in CA19-9 ($p = 0.001$). There were no differences between pts with stable or increasing CA19-9 levels in terms of treatment completion, rates of metastasis, or mOS. Among the 74 pts who had a CA19-9 response to XRT, the mOS for the 25 pts who normalized their post-XRT CA19-9 was 46 mo, compared to 25 mo for the 49 pts with a response but who did not normalize their post-XRT CA19-9. mOS for the 64 pts with a stable or increasing post-XRT CA19-9 was 16 mo ($p < 0.001$; Figure 1).

Conclusion: During neoadjuvant XRT for PDAC, a $\geq 50\%$ decline in CA19-9 is associated with improved mOS and normalization of CA19-9 levels is associated with the greatest survival advantage. Pts with stable or $< 50\%$ decline in CA19-9 levels have similarly poor oncologic outcomes to pts with increasing CA19-9 levels, suggesting a high likelihood of radiographically occult metastasis.

Figure 1: Overall Survival by CA19-9 Response Pattern During Neoadjuvant XRT



Response, normal post-XRT	25	21	14	9	7
Response, elevated post-XRT	49	40	20	11	6
Stable or Rising	64	42	10	6	3



P 2. IMPLICATIONS OF SMAD4 STATUS IN PANCREATIC CARCINOMA TREATED WITH RADIATION THERAPY; A MULTI-INSTITUTIONAL ANALYSIS

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Background: Loss of the tumor suppressor gene SMAD4 is a critical genetic alteration in pancreatic carcinoma (PC). We hypothesized that SMAD4 status in PC is associated with outcomes in patients who received neoadjuvant (NARx) or adjuvant (ARx) radiotherapy.

Methods: PC patients who underwent surgical resection at two high-volume centers following NARx-or those treated with ARx-between 2008-2019 were identified. SMAD4 status was determined based on immunohistochemical staining and classified as preserved (SMAD4+) or lost (SMAD4-). Kaplan-Meier survival estimates and multivariate analysis were used to analyze correlations between SMAD4 status, radiation therapy, and clinical outcomes.

Results: A total of 290 patients (mean age at diagnosis 66 years, 51% female) were identified; 131 (45%) were SMAD4+ and 159 (55%) SMAD4-. Resectable disease was diagnosed in 95 (33%) and borderline-resectable disease in 166 (57%); 29 patients (10%) had locally-advanced disease. NARx was administered in 147 (51%) in combination with chemotherapy while 143 (49%) received ARx; 26 (18%) of which received ARx solely. NARx in SMAD4- PC was associated with a significantly increased incidence of near-complete/complete histopathologic response and lower incidence of none/poor response compared to SMAD4- PC who did not receive NARx (12% vs 2% and 44% vs 19% respectively, $P=0.001$). On adjusted analysis, NARx was a significant predictor of histopathologic response in SMAD4- patients (HR: 3.5, 95% CI 1.6-7.6, $P < 0.001$) while no association was seen for SMAD4+ PC. Neither radiation therapy receipt nor SMAD4 status were associated with overall survival (OS). Yet, SMAD4- PC had a worsened disease-free survival (DFS) compared to SMAD4+ PC (19 vs 16 months, $P=0.03$). This difference persisted even among patients who had received NARx (21 vs 16 months, $P=0.04$) and those with histopathologic treatment response (24 vs 16 months, $P=0.031$). No difference in DFS between SMAD4- and SMAD4+ PC was identified in the ARx group. Lastly, NARx, significantly improved local-recurrence free survival in SMAD4+ PC compared to SMAD4- PC (33 vs 21 months, $P=0.047$).

Conclusion: Outcomes following surgical resection for PC remain primarily driven by SMAD4 status irrespective of radiation therapy timing (NARx vs ARx). However, this analysis suggests that SMAD4 status may help delineate a subset of patients who are most likely to benefit from NARx.

P 3. INDIVIDUALIZED AND DYNAMIC MULTIMODALITY MANAGEMENT OF LOCALIZED PANCREATIC CANCER IMPROVES SURVIVAL: ONE SIZE DOES NOT FIT ALL

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Background: Neoadjuvant chemotherapy (NAC) is increasingly utilized in localized pancreatic carcinoma (PC). Survival correlates with CA19-9 and histopathologic response (PR) following NAC. With several NAC and adjuvant therapy (AT) options now available, we hypothesized that the choice of NAC and AT regimens is best dictated by response to NAC (as measured by CA19-9 and PR), a strategy defined herein as dynamic perioperative therapy (DT). We aimed to evaluate the implications of DT in surgically treated PC.

Methods: Patients with localized PC who received NAC (gemcitabine/nab-paclitaxel or FOLFIRIOX) between 2010-2019 were identified. DT patients were those who remained or switched to an alternative NAC regimen as dictated by CA19-9 response and for whom AT regimen was selected based on CA19-9 and PR. Non-dynamic therapy (NDT) patients were those in whom NAC and AT were selected regardless of CA19-9 and tumoral response. Kaplan-Meier survival estimates and Cox-regression analyses were used to assess outcomes.

Results: Three hundred twenty two patients were identified (mean age 65yrs, 50% females): 216 (67%) underwent DT and 106 (33%) had NDT. The DT group had more CA19-9 normalization (54 vs 38%, $P=0.023$), higher incidence PR (moderate, complete and near complete response 73% vs 55%, $P < 0.001$), lower pathologic tumor size (2.5 vs 2.9cm, $P < 0.027$) and lower incidence of lymph node positive disease (58 vs 74%, $P=0.008$) compared to the NDT cohort. On survival analysis, the overall (OS) and disease-free survival (DFS) were significantly higher in the DT vs NDT group (39 vs 28 months $P=0.014$ and 19 vs 16 months $P=0.048$, respectively). On Cox regression analysis, DT remained an independent predictor of improved OS (hazard ratio (HR): 0.71, 95%CI 0.52-0.97, $P=0.03$).

Conclusion: This is the first study to evaluate the role of DT in localized PC. We demonstrate that selecting NAC and AT regimens based on NAC response is associated with improved OS and DFS. This study supports an individualized and in-vivo assessment of response to perioperative therapy in PC patients.

P 4. INITIAL FOUR YEARS OF THE DUTCH PANCREATIC CANCER AUDIT: DID OUTCOMES IMPROVE IN PANCREATIC SURGERY?

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Background: Clinical auditing is increasingly used but its long-term impact in pancreatic surgery remains unknown. The this study aimed to describe changes in clinical practice and surgical outcomes of pancreatic surgery in the initial four years of the Dutch Pancreatic Cancer Audit (DPCA).

Methods: Consecutive patients who underwent pancreatoduodenectomy or distal pancreatectomy were registered in the mandatory Dutch Pancreatic Cancer Audit (DPCA). Results were analyzed in two time periods (2014-2015 and 2016-2017). Trends in patient, tumor and treatment characteristics and center volume (< or ≥80 pancreatoduodenectomies per period) were assessed using univariable regression analyses. Trends in short-term surgical outcomes, including in-hospital mortality, failure to rescue, and textbook outcome were investigated using multilevel multivariable logistic regression analyses.

Results: Out of 3508 patients 2780 (79.2%) underwent pancreatoduodenectomy and 728 (20.8%) distal pancreatectomy. The median (IQR) hospital volume per period for pancreatoduodenectomy was 80 (67-98), and 23 (20-37) for distal pancreatectomy. Nationwide in-hospital mortality decreased from 3.6% to 2.8% ($p=0.04$; OR 0.65; CI 0.43-0.98). Failure to rescue improved from 12.8% to 10.2% ($p=0.03$; OR 0.61; CI 0.40-0.95). Rates of textbook outcome (59.0%), postoperative pancreatic fistula (ISGPS B/C) (14.8%), readmission (16.7%), and median hospital stay (11 days) did not change significantly. The rate of delayed gastric emptying (ISGPS B/C) increased from 13.8% to 17.5% ($p=0.03$; OR 1.26; CI 1.03-1.53). In the second period, the use of neoadjuvant therapy (5.8% vs 10.4%, $p<0.01$) and minimally invasive pancreatoduodenectomy (6.7% vs 20.5%, $p<0.01$) increased whereas the use of adjuvant therapy (67.3%) did not change significantly.

Conclusion: In the initial four years of the DPCA in-hospital mortality and failure to rescue rates improved whereas textbook outcome remained unchanged. Changes in patient management included increased use of neoadjuvant therapy and minimally invasive pancreatoduodenectomy.

P 5. IMPACT OF G-CSF DURING NEOADJUVANT THERAPY ON OUTCOMES OF OPERABLE PANCREATIC CANCER

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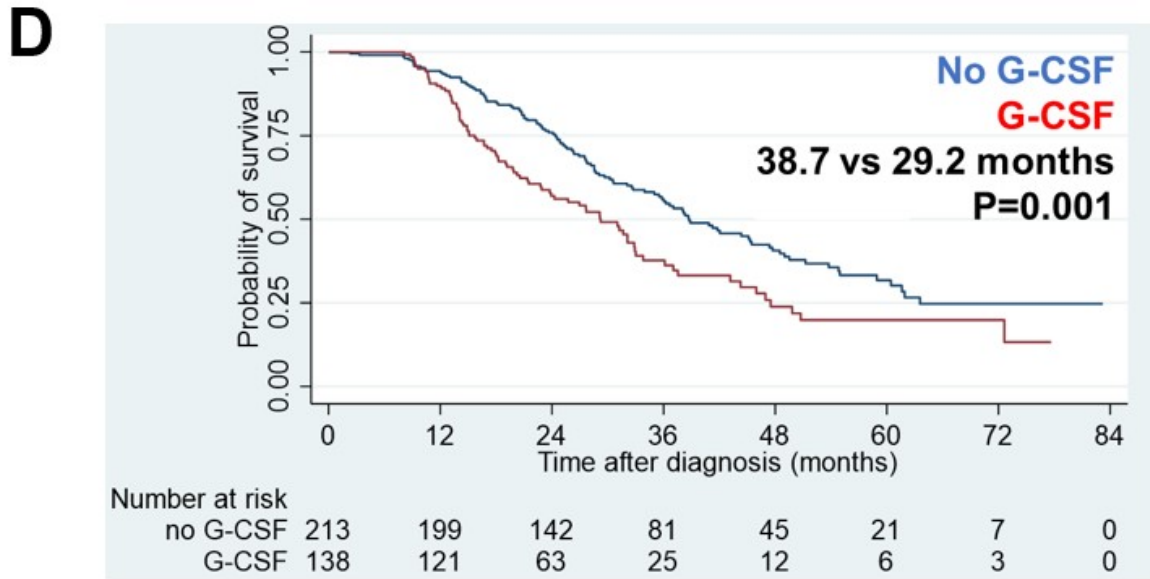
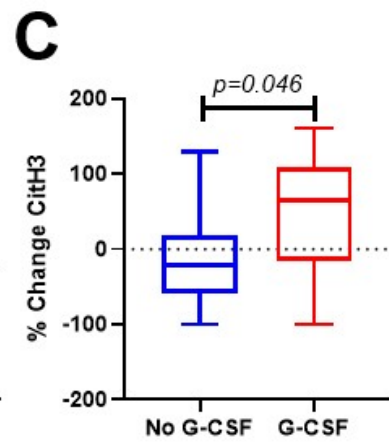
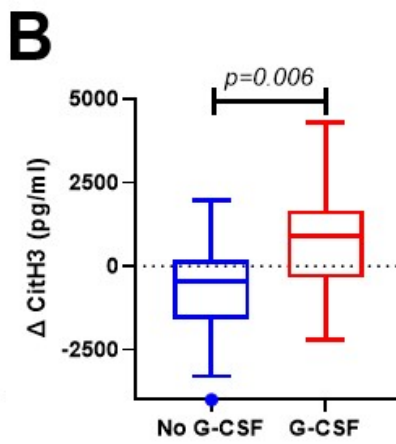
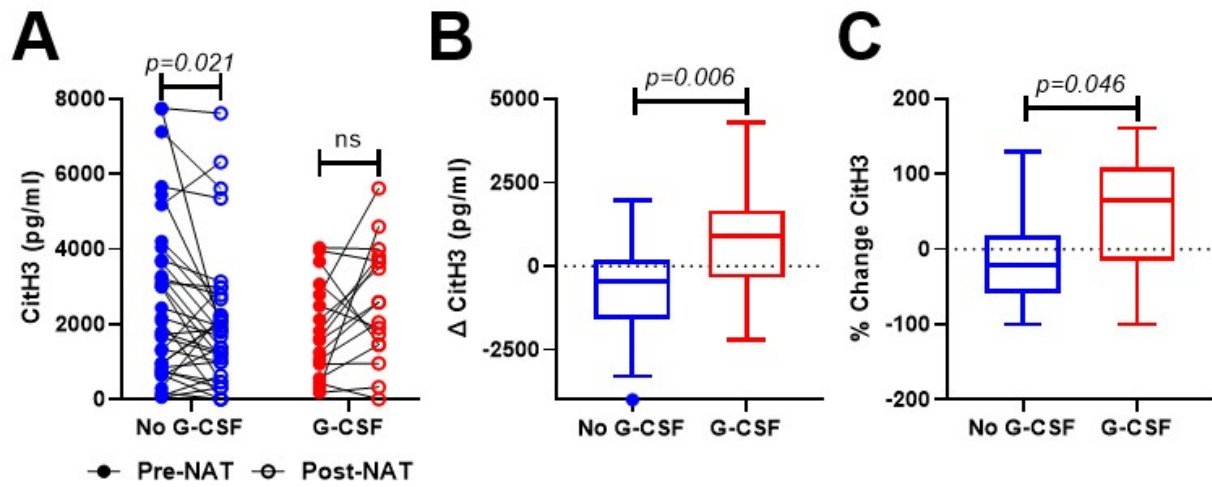
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Background: The interleukin 17 – granulocyte colony stimulating factor (G-CSF) – neutrophil extracellular trap (NET) axis limits adaptive immunity and promotes progression of pancreatic ductal adenocarcinoma (PDAC). Despite frequent utilization of recombinant G-CSF in the management and prevention of chemotherapy induced neutropenia, the long-term effects of G-CSF administration on patients with PDAC is unknown. We sought to evaluate the impact of G-CSF administration during neoadjuvant therapy (NAT) on oncologic outcomes in patients with operable PDAC.

Methods: This retrospective cohort study was conducted on all patients with localized PDAC treated with NAT prior to pancreatic resection at a single institution from January 1, 2014 to December 31, 2019 with a median follow-up duration of 45.8 months. Treatment patterns, changes in blood counts, and surgical-oncology outcomes were assessed by univariate and multivariate analysis. Survival was assessed by Kaplan-Meier analysis, Cox proportional hazards regression models, and inverse-probability-weighted (IPW) estimators.

Results: Pancreatic cancer surgery was completed on 351 patients treated with (n=213 [60.7%]) or without (n=138 [39.3%]) G-CSF during NAT. Patients treated with G-CSF were younger (64.0 vs 66.7, p=0.008), had lower BMI (26.5 vs 27.9, p=0.021), and were more likely to receive 5-FU based chemotherapy (42% vs 28.2%, p<0.0001). No differences were observed in baseline or pathologic tumor staging. Patients receiving G-CSF were more likely to have an elevated post-NAT neutrophil to lymphocyte ratio (45% vs 29.6%, p=0.004). G-CSF treatment was an independent predictor of perineural invasion (HR 2.4, 95 CI [1.08, 5.5], p=0.031) and margin positive resection (HR 1.69, 95 CI [1.01, 2.83], p=0.043). Patients who received G-CSF had decreased overall survival compared to patients who did not receive G-CSF (median OS: 29.2 vs 38.7 months, p=0.0001). G-CSF treatment was an independent negative predictor of overall survival (HR 2.02, 95 CI [1.45, 2.79], p<0.0001). In the IPW analysis of 301 matched patients, the average treatment effect of G-CSF treatment was to reduce overall survival by 10.2 months (95% CI [-16.31, -4.07], p=0.001). In a subset of patients with available pre- and post-NAT serum specimens (n=51), G-CSF administration resulted in an increased number (-619±1516 vs +709±1577, p=0.006) of citrullinated histone H3 complexes following NAT, indicative of enhanced peripheral NET formation.

Conclusion: In patients with localized PDAC receiving NAT prior to surgical extirpation, G-CSF administration is associated with worse oncologic outcomes and should be evaluated in prospective clinical studies.



P 6. LIVER ENDOTHELIUM PROMOTE PANCREATIC CANCER CELL GROWTH IN A PARACRINE FASHION

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Background: Pancreatic ductal adenocarcinoma (PDAC) is the third leading cause of cancer-related deaths in the United States and has the highest mortality rate of all major cancers. More than 50% of PDAC patients develop metastatic PDAC (mPDAC) and the 5-year survival rate for mPDAC patients is 3%. Therefore, it is necessary to develop novel treatment strategies to improve the outcomes of patients with mPDAC. The most common site of PDAC distant metastasis is the liver, which has a unique endothelial cell (EC)-rich microenvironment. Preclinical studies in different cancer types showed that ECs promote cancer cell survival (either cell growth or chemoresistance) by secreting soluble factors in a paracrine fashion. However, the effects of the liver EC environment on mPDAC have not been elucidated. In this study, we will determine the paracrine effects of liver ECs on PDAC cell survival and identify the involved mechanism(s).

Methods: We isolated primary ECs from non-neoplastic liver tissues to recapitulate the liver EC microenvironment. Conditioned medium (CM), which contain EC-secreted factors, were collected after culturing 0.3×10^6 ECs in 3 ml DMEM medium with 1% FBS for 48 hours and centrifuging at 10,000 g. Then, we treated PDAC cells with EC CM to determine the effects of EC-secreted soluble factors on PDAC cells, using CM from PDAC cells as controls. PANC-1, Mia PaCa-2, and BxPC-3 PDAC cells were treated by CM for 72 hours, and cell proliferation was determined by MTT assay. To determine the signaling pathway(s) affected by EC CM treatment, cancer cells were treated by PDAC or EC CM for 30 mins, and phosphorylation of key proteins were determined by Western blotting.

Results: CM from liver ECs activated AKT and significantly increased cell growth in PANC-1, Mia PaCa-2, BxPC-3 cells. Human epidermal growth factor receptor 3 (HER3, also known as ERBB3) was expressed only in BxPC-3 cells (HER3+ve) and blocking HER3 with a humanized antibody, seribantumab, completely blocked EC-induced AKT activation and cell proliferation in BxPC-3 cells. On the other hand, HER3 inhibition had no effect on EC-induced AKT activation and cell proliferation in PANC-1 and Mia PaCa-2 cells without HER3 expression (HER3-ve).

Conclusion: Our results demonstrated that liver ECs promote PDAC cell growth by activating AKT, and HER3 is a key mediator of the EC-induced proliferation in HER3+ve PDAC cells. Our findings suggest a potential for treating mPDAC with HER3 antibodies that are being assessed in clinical trials for other cancer types. The mechanism of EC promoting proliferation in HER3-ve PDAC cells remains unclear and will be determined in future studies.

P 7. MEDICARE REIMBURSEMENT FOR PANCREATIC RESECTIONS HAS DECLINED OVER THE LAST DECADE

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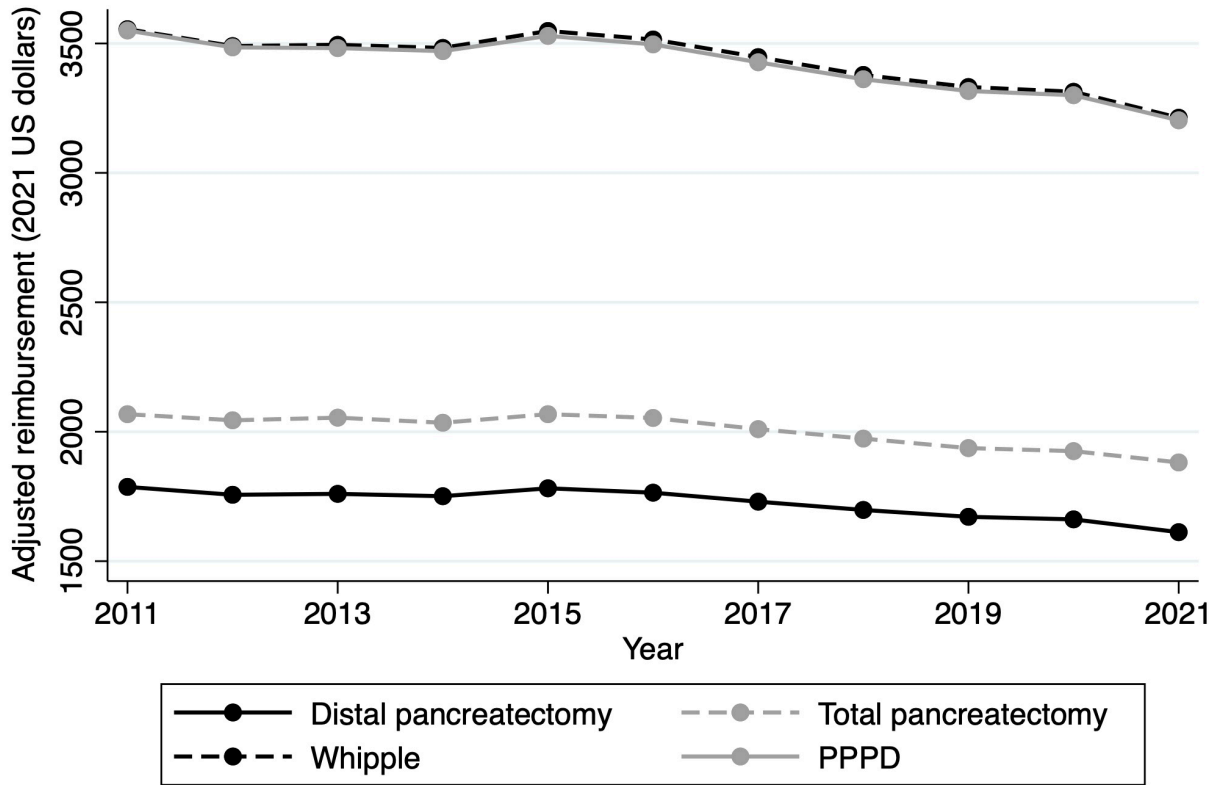
Background: The Centers for Medicare and Medicaid Services (CMS) proposed substantial cuts in reimbursement for operations in 2021. The cuts were mitigated by Congress's approval of a stimulus package allowing for a budget deficit; however, this identified a paucity of literature examining current trends in reimbursement for pancreatic operations.

Methods: National Medicare reimbursement rates were abstracted from the CMS website from 2011-2021 based on Current Procedural Terminology codes. Unadjusted reimbursement rates for distal pancreatectomies (48140), total pancreatectomies (48155), Whipple-type resections (48150), and pylorus-preserving pancreaticoduodenectomies (PPPD, 48153) were analyzed. Reimbursement rates were also adjusted to their value in 2021 based on United States inflation rates reported by the Consumer Price Index. Trends in unadjusted and adjusted reimbursement rates were analyzed using linear regression.

Results: There was no change in work relative value unit (wRVU) for the four included operations over the study period: distal pancreatectomy = 26.32; total pancreatectomy = 29.45; Whipple = 52.84; PPPD = 52.79. Over the study period, the national inflation rate was 16.3%: \$0.86 in 2011 is equivalent to \$1.00 in 2021 (linear coefficient=0.01, R2=0.98, p<0.001). Unadjusted reimbursement rates for all four operations increased modestly from 2011 to 2021: distal pancreatectomy (4.9% increase, linear coefficient=9.7, R2=0.73, p=0.001), total pancreatectomy (5.8% increase, linear coefficient=11.3, R2=0.75, p=0.001), Whipple (5.1% increase, linear coefficient=20.3, R2=0.74, p=0.001), and PPPD (4.9% increase, linear coefficient=19.6, R2=0.76, p<0.001). From 2020 to 2021, unadjusted reimbursement rates for all four operations decreased for the first time in the study period.
All reimbursement rates were then adjusted to 2021 values, based on inflation rates (Figure). The adjusted reimbursement rates for the four pancreatectomies all decreased by a similar amount over the study period: distal pancreatectomy (9.8% decrease, linear coefficient= -15.2, R2=0.80, p<0.001), total pancreatectomy (9.0% decrease, linear coefficient= -17.6, R2=0.81, p<0.001), Whipple (9.6% decrease, linear coefficient= -29.2, R2=0.78, p<0.001), and PPPD (9.8% decrease, linear coefficient= -29.1, R2=0.81, p<0.001).

Conclusion: Since 2011, four of the most commonly performed pancreatic resections have all seen decreases in adjusted reimbursement rates. Decreases in reimbursement are most pronounced in 2021. Awareness of the current downward trends in reimbursement rates should be a priority for surgeons and hospital systems in order to maintain sustainable and accessible surgical subspecialty care among Medicare recipients.

Trends in National Medicare Reimbursement Rates



P 8. OBESITY WORSENS LOCAL AND SYSTEMIC COMPLICATIONS OF NECROTIZING PANCREATITIS AND PROLONGS DISEASE COURSE

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Presenter: Sean McGuire MD | Indiana University School of Medicine, United States

Background: Obesity is epidemic in the United States. Existing evidence suggests that obesity increases the incidence of acute pancreatitis (AP) and worsens AP severity. Limited data exist examining obesity in necrotizing pancreatitis (NP).

Methods: Retrospective review of prospectively maintained database of 571 adult necrotizing pancreatitis patients between 2007 and 2018. Weights closest to disease onset and disease resolution were recorded. Patients were grouped according to body mass index (BMI) at disease onset. Patient characteristics, necrotizing pancreatitis course, and outcomes were compared between non-obese (BMI <30) patients.

Results: Among 536 patients with BMI data available, 232 (43%) were non-obese (BMI <30). Age and sex were similar between groups. NP etiology in the obese group was more commonly biliary (55% vs 46%, $p = 0.04$) or secondary to hypertriglyceridemia (10% vs 2%, $p = 0.02$). 50% pancreatic gland necrosis (27% vs. 19%, $p = 0.02$). The rates of infected necrosis and organ failure were higher among obese patients (Table). NP disease duration was longer in obese patients (Table). Percutaneous drainage was more common in obese patients, but no other differences in NP interventions were observed (Table). The overall mortality rate of non-obese and obese patients did not differ (Table). However, mortality increased with increasing BMI and time to first necrosis intervention decreased with increasing BMI. These results did not achieve statistical significance.

Conclusion: Necrotizing pancreatitis in obese patients is characterized by a prolonged disease course. Obese patients with necrotizing pancreatitis are at higher risk for organ failure, infected necrosis, and the need for early necrosis-related intervention.

	BMI <30 (n=232)	BMI >30 (n=304)	<i>p</i>
CTSI†	6.4 (2.0)	6.8 (2.1)	0.977
Organ Failure (Any)	68 (29%)	134 (44%)	<0.001
Respiratory failure	62 (28%)	117 (38%)	0.004
Renal Failure	39 (17%)	89 (29%)	0.001
Cardiovascular failure	25 (11%)	55 (18%)	0.019
Infected Necrosis	108 (47%)	191 (63%)	<0.001
Disease Duration (d)†	177 (10.6)	212 (12.4)	0.04
Intervention (Any)	198 (85%)	252 (83%)	0.444
Percutaneous drain	63 (27%)	125 (41%)	0.001
Endoscopic	22 (9%)	32 (11%)	0.691
Laparoscopic surgery	16 (7%)	21 (9%)	0.996
Open surgery	158 (68%)	206 (68%)	0.933
Mortality	18 (8%)	31 (10%)	0.332

Table: Necrotizing pancreatitis disease course and outcomes. Data are reported as number of patients (percentage), unless otherwise specified. Results achieving statistical significance are identified in bold.

† Indicates data reported as mean ± SEM

Abbreviations: CTSI- Computed tomography severity index

P 9. PANCREATICODUODENECTOMY FOR BENIGN AND PRE-MALIGNANT PANCREATIC AND AMPULLARY DISEASE: IS ROBOTIC SURGERY THE BETTER APPROACH?

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Presenter: Benedetto Mungo MD | University of Pittsburgh Medical Center, United States

Background: The robotic platform is increasingly being utilized in pancreatic surgery, yet its overall merits and putative advantages – compared to the classic laparotomy approach – remain to be adjudicated. The majority of available comparative analysis focus primarily on pancreatic adenocarcinoma where surgical outcomes are influenced and conditioned by the complex underlying pathology and the need for peri-operative systemic therapy. We hypothesize that the benefits of minimally invasive pancreatic surgery are maximized in pancreatic benign and premalignant disease, in the setting of friable pancreatic tissue and small pancreatic duct.

Methods: Retrospective analysis of a single institution prospectively maintained pancreatic database of all consecutive patients who underwent pancreaticoduodenectomy (PD) for benign or premalignant conditions between 2010 to 2020. Peri-operative outcomes and long-term complications (> 90 days post-PD) were compared between robotic pancreaticoduodenectomy (RPD) and open pancreaticoduodenectomy (OPD). Continuous variables were reported as means and standard deviation or medians and interquartile ranges and compared using two-sided t-test, while categorical variables were reported as frequencies and percentages and compared using Pearson chi-squared ($p < 0.05$).

Results: Two hundred and four ($n=204$) patients met our inclusion criteria, of which 68 were OPD and 136 RPD. Selected histologies included but were not limited to adenoma with dysplasia (any grade), intraepithelial neoplasia, intraductal oncocytic papillary neoplasm, intraductal papillary mucinous neoplasm, pseudopapillary neoplasm, serous cystadenoma and neuroendocrine tumor with no invasive or metastatic features. Findings are summarized in Table 1. There were no significant differences in baseline characteristics between the two groups, exception made for a higher rate of coronary artery disease (24.2% vs. 11%, $p=0.015$) in the OPD group. Patients in the RPD group were more likely to undergo a classic Whipple procedure (84.6% vs. 55.9%, $p < 0.001$) had shorter operative time (387.80 ± 114.11 vs. 453.79 ± 159.18 minutes, $p < 0.001$) and lesser lymph node yield (21 vs. 20, $p=0.011$) when compared to those in the open group. Notable post-operative merits of the RPD included a significantly shorter length of stay (LOS) (7 vs. 10 days, $p=0.004$), fewer grade B pancreatic fistulas (8.8% vs. 32.3%, $p=0.001$) and lower 90-day mortality (0.7% vs. 5.9%, $p=0.025$) as compared to OPD. Finally, rates of long-term complications were comparable between the two groups, exception made for a higher chance of needing surgery for small bowel obstruction in the open group (3.1% vs. 0%, $p=0.039$).

Conclusion: The results of our analysis suggest that robotic pancreaticoduodenectomy has lower 90-day mortality, shorter LOS and lower rates of selected complications when compared to open pancreaticoduodenectomy. While randomized data are needed to strengthen our conclusions, our results make a compelling argument for the prioritization of the robotic platform in the surgical treatment of benign and premalignant pancreatic diseases, in the appropriate patient population.

Table 1: Peri-operative and Long Term Outcomes

	Whole cohort (n=204)	Open Group (n=68)	Robotic group (n=136)	P-value
Clavien-Dindo grade ≥III				0.113
III	26 (12.8%)	7 (10.5%)	19 (14%)	
IV	27 (13.3%)	10 (14.9%)	17 (12.5%)	
V	5 (2.5%)	4 (6%)	1 (0.7%)	
Length of stay (days)	8 (6,12)	10 (7,14)	7 (6,10.5)	0.004
Pancreatic fistula				0.001
A	45 (22.1%)	12 (17.7%)	49 (36.0%)	
B	34 (16.7%)	22 (32.3%)	12 (8.8%)	
C	4 (1.9%)	2 (2.9%)	2 (1.5%)	
Delayed gastric emptying	64 (31.4%)	20 (29.4%)	44 (32.4%)	0.670
Pseudoaneurysm	13 (6.4%)	3 (4.4%)	10 (7.4%)	0.418
GDA	4 (36.4%)	1 (33.3%)	3 (37.5%)	
Hepatic/branches	2 (18.2%)	0 (0%)	2 (25%)	
SMA	4 (36.4%)	2 (66.7%)	2 (25%)	
Other	1 (9.0%)	0 (0%)	1 (12.5%)	
Pseudoaneurysm Treatment				0.179
Embolization	4 (36.4%)	0 (0%)	4 (50.0%)	
Covered stent placement	6 (54.5%)	3 (100%)	3 (37.5%)	
Operative	1 (9.1%)	0 (0%)	1 (12.5%)	
Surgical site infection	21 (11.4%)	11 (16.7%)	10 (8.5%)	0.094
Re-operation	14 (6.9%)	4 (5.9%)	10 (7.4%)	0.695
Re-admission	72 (35.3%)	28 (41.2%)	44 (32.4%)	0.214
30-day mortality	3 (1.5%)	2 (2.9%)	1 (0.7%)	0.217
90-day mortality	5 (2.5%)	4 (5.9%)	1 (0.7%)	0.025
Any Long Term complication(yes)	45 (22.6%)	16 (25%)	29 (21.5%)	0.579
Intervention performed				0.759
Percutaneous	11 (5.5%)	4 (6.3%)	7 (5.2%)	
Endoscopic	19 (9.6%)	6 (9.4%)	13 (9.6%)	
Surgical	27 (13.6%)	7 (10.9)	20 (14.8)	
Bile duct Stricture	20	6 (9.4%)	14 (10.5%)	0.815
Time to Bile duct Stricture	315 (164.5,758)	541 (165,975)	289.5 (164,740)	
Intervention – stricture				0.759
PTC	11 (5.5%)	4 (6.3%)	7 (5.2%)	0.759
ERCP	15 (7.6%)	3 (4.7%)	12 (9%)	0.288
Surgical	2 (1.0%)	0 (0.0%)	2 (1.5%)	0.328
Pancreatitis	16 (8.0%)	7 (10.9%)	9 (6.7%)	0.301
Time to pancreatitis	633 (252.5,925)	666 (552, 1579)	369 (171, 891)	
Small Bowel Obstruction	7 (3.5%)	4 (6.3%)	3 (2.2%)	0.150
Time to SBO	459 (94, 2680)	485.5 (531, 560.5)	171 (94, 2680)	
Surgery for SBO	2 (1.0%)	2 (3.1%)	0 (0.0%)	0.039
Incisional Hernia	36 (18.1%)	11 (17.2%)	25 (18.5%)	0.820
Time to incisional hernia	373 (238, 630)	608 (387, 719)	383 (238, 630)	
Surgery for incisional hernia	24 (12.1%)	5 (7.8%)	19 (14.1%)	0.205
Post-Op Pancreatic Insufficiency	125 (62.8%)	40 (62.5%)	85 (63%)	0.950
Gastrojejunostomy Ulcer	3 (1.5%)	2 (3.1%)	1 (0.7%)	0.197
Time to Ulcer diagnosis	205 (165, 632)	185 (165, 205)	632 (632, 632)	

GDA Gastroduodenal Artery, SMA Superior Mesenteric Artery, PTC Percutaneous Transhepatic Catheter, ERCP Endoscopic Retrograde Cholangiopancreatography, SBO Small Bowel Obstruction.

P 10. PERINEURAL INVASION DETERMINES THE NEED FOR ADJUVANT CHEMOTHERAPY IN SURGICALLY RESECTED PANCREATIC CARCINOMA WITH NODE NEGATIVE DISEASE FOLLOWING NEOADJUVANT THERAPY; A MULTI-INSTITUTIONAL ANALYSIS

A Hammad, J Hodges, S AlMasri, A Paniccia, K Lee, N Bahary, A Singhi, M Aldakkak, DB Evans, S Tsai, A Zureikat

Presenter: Abdulrahman Hammad MBBCh | University of Pittsburgh Medical Center, United States

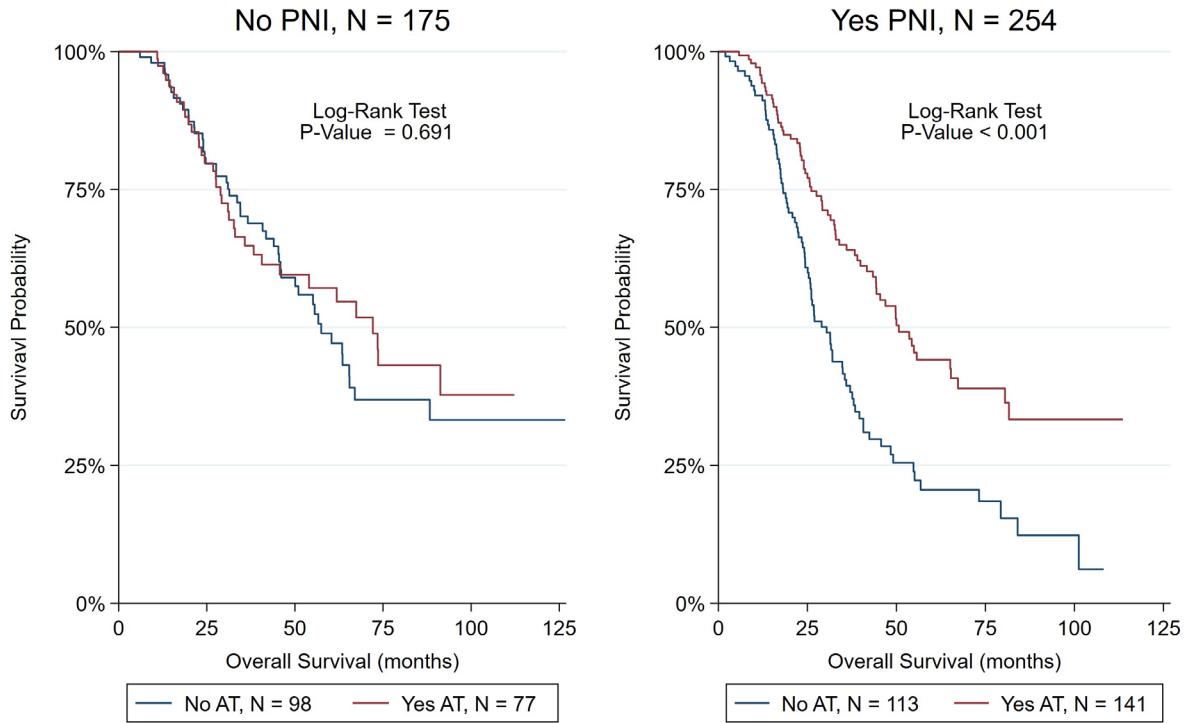
Background: There is growing interest in the potential benefit of neoadjuvant therapy (NAT) for patients with operable pancreatic cancer. NAT is infrequently associated with a complete histologic response in the primary tumor but does result in a robust response in local-regional lymph nodes. Such downstaging of node positive disease to node negative after NAT may have implications for the use of additional postoperative adjuvant therapy (AT). We sought to examine the prognostic implications of AT in node negative patients following NAT and surgery and identify predictors of overall survival (OS).

Methods: Patients treated at two high-volume centers who underwent surgical resection following NAT between 2010-2018 and had lymph node negative disease were identified. Kaplan-Meier survival estimates and Cox-proportion hazard regression were performed to identify predictors of OS.

Results: Four hundred thirty-one patients were included (mean age 65yrs, 51% females). The predominant NAT was gemcitabine-based (45%) and the median duration of therapy was two months (Interquartile range (IQR): 2, 3). Neoadjuvant chemoradiation (NART) was administered to 65% of the cohort. Pancreatoduodenectomy was performed in 72% and 37% required concomitant vascular resection. The median lymph node yield was 26 (IQR: 19, 34) and 254 (59%), 92 (21%) & 87 (20%) of the cohort had perineural invasion (PNI), lymphovascular invasion (LVI) and residual positive margins (R1) respectively. The median follow-up time was 45.9 months (IQR: 40.7, 54.8). On adjusted analysis, poorly differentiated tumors [HR:1.86 (95%CI: 1.14-3.05), p=0.013], LVI [HR: 1.45 (95%CI: 1.04-2.01), p=0.027], and vascular resection [HR: 1.38 (95%CI: 1.06-1.80), p=0.018] were all independent predictors of survival. PNI was associated with worse survival [HR: 1.72 (95%CI: 1.18, 2.51), p=0.005] while NART trended towards an association with better survival although did not reach statistical significance [HR: 0.66 (95%CI: 0.42, 1.03, p=0.065)]. Although AT is associated with prolonged survival in the overall cohort [HR: 0.47 (95%CI: 0.26, 0.85), p=0.013] NART weakens the association [ATxNART interaction; HR: 2.50 (1.40, 4.49), p=0.002] while PNI strengthens the association [ATxPNI interaction; HR: 0.56 (0.32, 0.97), p=0.038].

Conclusion: In patients with node negative disease following NAT, PNI (as assessed in the final resection specimen), was associated with worse survival, especially when NART was not administered. Although – in this select cohort – survival is associated with tumor grade, LVI, PNI, NART, and vascular resection, the current analysis suggests that the presence of PNI may identify a high-risk subset within the group of N0 patients for whom AT may be of benefit.

Association Between Adjuvant Therapy (AT) & Overall Survival Depends On PNI Status



P 12. RADIOGRAPHIC AND SEROLOGIC RESPONSE TO FIRST-LINE CHEMOTHERAPY IN UNRESECTED LOCALIZED PANCREATIC CANCER

G Perri, J Maxwell, N Ikoma, MP Kim, CWD Tzeng, JE Lee, MHG Katz

Presenter: Caitlin Hester MD | University of Texas MD Anderson Cancer Center, United States

Background: A minority of patients with localized pancreatic cancer (LPC) ever undergo pancreatectomy. However, studies evaluating response of LPC to systemic chemotherapy have focused on histopathologic analyses of resected specimens. We have previously shown that changes in tumor volume and CA 19-9 provide a clinical readout of histopathologic response to preoperative therapy. Here, we sought to examine the potential clinical relevance of these simple radiographic and serologic metrics in patients who do not undergo pancreatectomy.

Methods: All patients with LPC who were first treated with chemotherapy between January 2010 and December 2018 and who did not undergo pancreatectomy were evaluated. All radiographic images were re-reviewed by a single observer. Radiographic response to first-line systemic chemotherapy was measured using Response Evaluation Criteria in Solid Tumors (RECIST) 1.1 and tumor volume. To characterize radiographic volume changes, the volume of the primary tumor calculated on pretreatment image review was compared with the posttreatment image review. The % Δ vol was calculated as a percentage of the baseline volume which was stratified into four quartiles (1: 41%). Serologic response was measured using pretreatment and posttreatment CA 19-9 levels. We established three cohorts based on these metrics: 1: Best Responders: patients who experienced a decline in % Δ vol within the top quartile and in CA 19-9; 2: non-responders: patients who experienced an increase in % Δ vol and in CA 19-9; and 3: all other patients.

Results: 329 patients with LPC who received chemotherapy in the first line and did not undergo pancreatectomy were evaluated. In isolation, % Δ vol and change in CA 19-9 were associated with OS ($p \leq 0.1$) but RECIST 1.1 was not. In all, 73 (22.2%) patients were best responders, 42 (12.8%) were non-responders and 214 (65.0%) patients were neither. Best responders lived significantly longer than non-responders and others (median overall survival: 24 vs 12 vs 17 months, respectively, $p < 0.01$, Figure). After adjusting for type of chemotherapy regimen, number of first-line chemotherapy cycles, and whether or not consolidative radiation was administered in a multivariable model, best responders had improved survival relative to the other cohorts (HR 2.90 [1.8-4.8] for non-responders and HR 1.56 [CI 1.1-2.2] for others).

Conclusion: Changes in tumor volume and serum levels of CA 19-9 – but not RECIST 1.1—represent reliable metrics of response to systemic chemotherapy, and here we establish that they can be used as putative predictors of survival in patients with LPC who do not undergo pancreatectomy. Longitudinal, dynamic data analysis could potentially act as a surrogate for pathologic staging in the absence of specimen review, stratify patients by their tumor biology, and guide additional therapies and trial development.

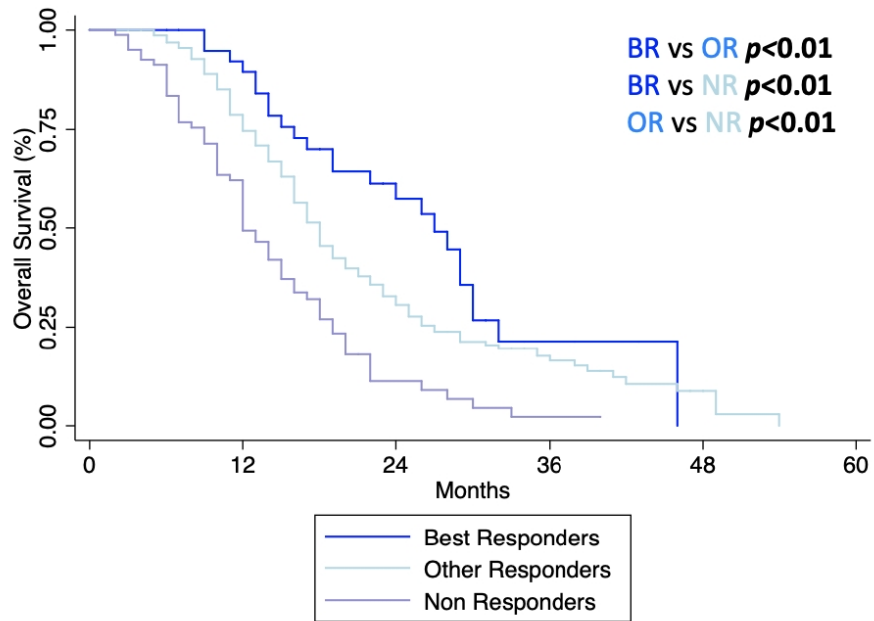


Figure. Response Categories and Survival after Initial Chemotherapy in Unresected Patients with Localized Pancreas Cancer. Median overall survival of patients was 24 months (IQR 16-46), 17 months (IQR 12-26), and 12 months (IQR 9-18) for best responders, mixed responders, and non-responders, respectively.

P 13. REAPPRAISAL OF ANATOMICAL STAGING IN PATIENTS UNDERGOING POST-NEOADJUVANT RESECTION FOR PANCREATIC DUCTAL ADENOCARCINOMA: IMPLICATIONS FOR ADJUVANT TREATMENT

L Maggino, G Malleo, S Crippa, G Belfiori, E Bannone, G Gasparini, S Nobile, C Luchini, P Mattiolo, M Schiavo-Lena, C Doglioni, A Scarpa, C Bassi, M Falconi, R Salvia

Presenter: Laura Maggino MD | University of Verona, Italy

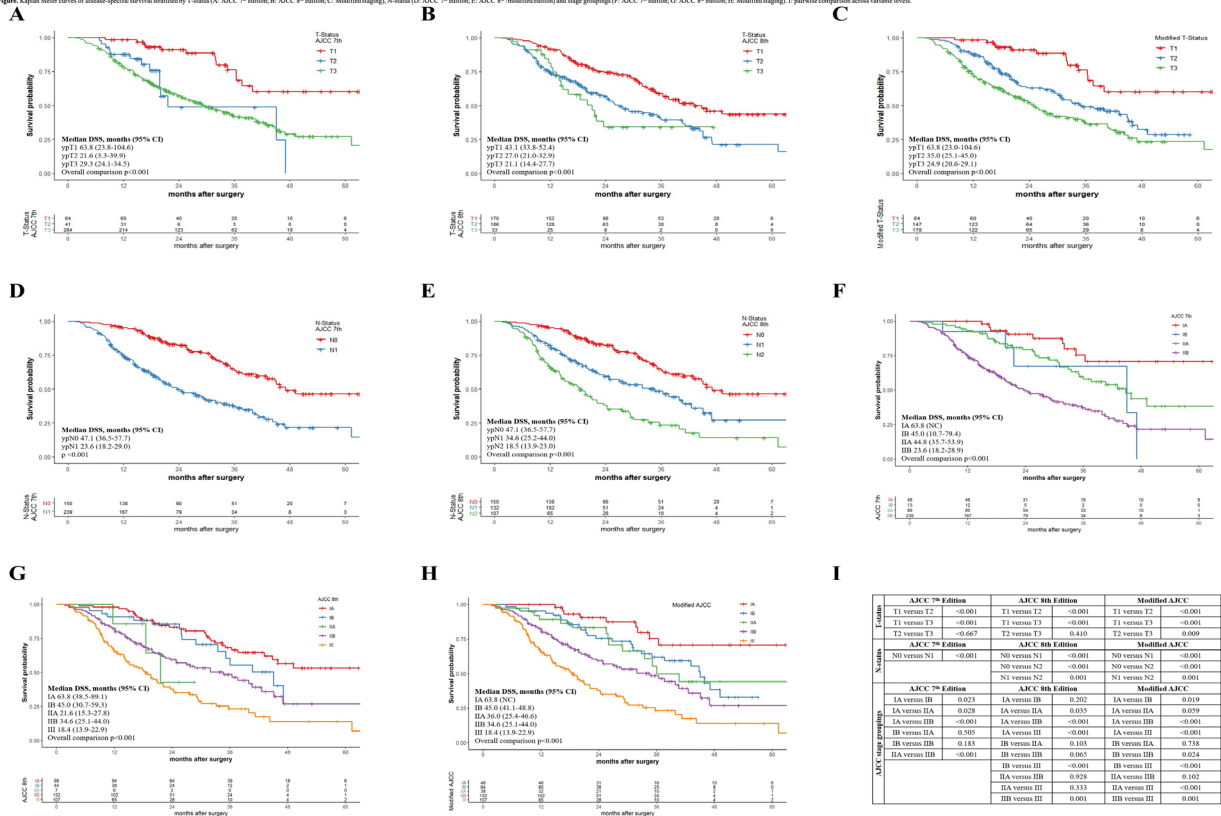
Background: The applicability of pathologic TNM staging to pancreatic ductal adenocarcinoma (PDAC) patients receiving pancreatectomy after neoadjuvant treatment is unclear. Likewise, there is no consensus on whether staging parameters should inform the delivery of adjuvant therapy in this setting. The aims of this study were to: i) evaluate the role of pathologic parameters and different stage groupings in post-neoadjuvant pancreatectomy for PDAC; ii) appraise a modified staging based on a T-status definition combining extrapancreatic invasion and tumor size; iii) investigate the differential impact of adjuvant treatment across the examined staging parameters.

Methods: All patients undergoing post-neoadjuvant pancreatectomy for PDAC at two academic institutions were included (2013-2017). T- and N-classes were assigned per the 7th and 8th editions of the AJCC manual and according to the modified staging (T-status T1: ≤ 2 cm and limited to the pancreas; T2: > 2 cm and limited to the pancreas or ≤ 2 cm with extrapancreatic extension; T3: > 2 cm with extrapancreatic extension; N-status as for the AJCC 8th Edition). Patients were stratified by receipt of adjuvant therapy. The main outcome was disease-specific survival (DSS). This was assessed through pairwise comparisons across levels of staging parameters and stage groupings, prognostic discrimination metrics (C-index, time-dependent ROC curves, Uno's integrated AUC, net reclassification index -NRI), and multivariable interaction analysis of adjuvant treatment with levels of staging parameters and stage groupings.

Results: The study population included 389 patients, with a median DSS of 34.6 months (95% CI 29.8-39.5). The AJCC 7th T-status significantly predicted survival, although survival curves of ypT2 and ypT3 overlapped. The AJCC 8th T-status improved prognostic stratification, yet the significance remained driven by the favorable prognosis of ypT1. The modified T-status was associated with the best prognostic stratification (Figure). N-status was strongly associated with survival in both the AJCC 7th and 8th editions (Figure). Overall, the modified staging system (combining the modified T-status and N-status as per the AJCC 8th edition) displayed the most balanced patient distribution, the best prognostic stratification (Figure), and the highest discrimination (c-index=0.763, 1- to 3-year time-dependent AUC of 0.74, 0.72 and 0.70, Uno's AUC=0.71). Both the AJCC 8th edition and the modified staging system displayed a higher NRI relative to the 7th edition (AJCC 8th: additive NRI=53.23, absolute NRI=23.8%; modified staging: additive NRI=46.24, absolute NRI=25.0%). Overall, adjuvant chemotherapy was administered in 67% of patients. There was no difference in DSS based on the receipt of adjuvant chemotherapy (35 versus 36 months, $p=0.772$). After multivariable adjustment, adjuvant treatment significantly interacted with staging parameters, suggesting a potential survival benefit for its administration in tumors > 2 cm, in those with extrapancreatic extension and/or with nodal metastases (HR for the interaction with the modified stage IIB = 0.152, 95%CI 0.029-0.794, $p=0.025$; stage III = 0.155, 95%CI 0.030-0.805, $p=0.027$).

Conclusion: This study comprehensively appraises staging parameters in post-neoadjuvant pancreatectomy. A modified T-status definition combining extrapancreatic invasion and tumor size is associated with a more balanced patient distribution and better prognostic segregation. Analysis of differential effects of adjuvant treatment across pathologic parameters might provide the backbone for future trials investigating its stage-specific administration following post-neoadjuvant pancreatectomy.

Figure. Kaplan Meier curves of disease-specific survival stratified by T-status (A: AJCC 7th edition, B: AJCC 8th edition, C: Modified staging), N-status (D: AJCC 7th edition, E: AJCC 8th edition and stage grouping), F: AJCC 7th edition, G: AJCC 8th edition, H: Modified staging), I: pairwise comparison across variable levels.



P 14. TARGETING CELLULAR ENERGETICS IN PANCREATIC DUCTAL ADENOCARCINOMA

A Nevler, C Schultz, A Jain, C Yeo, J Brody

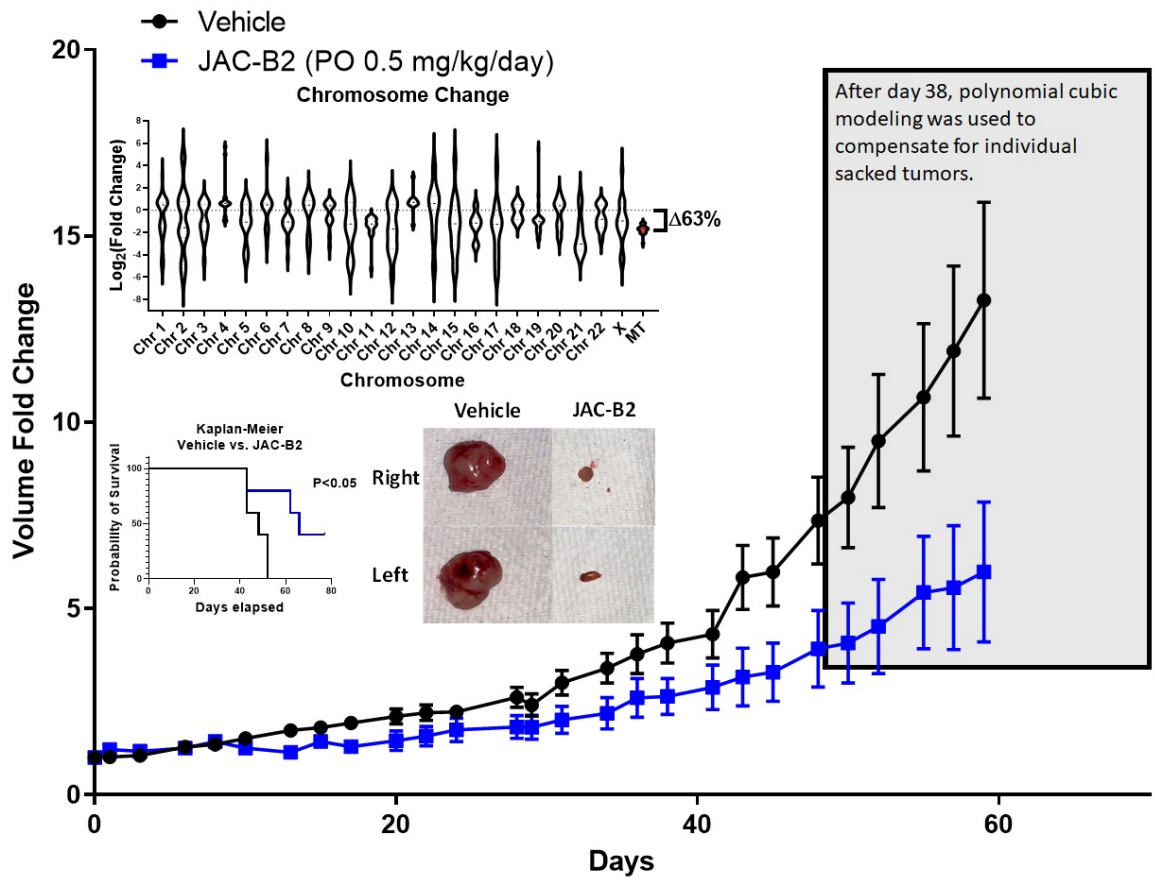
Presenter: Avinoam Nevler MD | Thomas Jefferson University, United States

Background: Pancreatic ductal adenocarcinoma (PDAC) has become the 3rd leading cause of cancer mortality in the U.S., estimated to account for over 60,000 new cases in 2021. Unfortunately, drug therapies for this aggressive and resistant cancer have been slow to advance and overall five-year survival is still only 10%. As the PDAC microenvironment is characterized as a fibrotic, hypoxic and nutrient poor environment, this poses a potentially actionable vulnerability to energy depleting therapies. Mitochondrial inhibitors comprise a part of this exciting new group of anti-cancer compounds. We have been assessing a novel family of lipophilic polymethine compounds, preferentially targeting the mitochondria in PDAC cells. For that end, in-vitro and in-vivo experiments were performed.

Methods: An orally bioavailable mitochondrial inhibitor (JAC-B2, 3'3' Diethylthiadicyanone iodide) was assessed across multiple PDAC cell lines to determine cell viability, ATP production and expression of Electron Transport Chain (ETC) proteins. In-vivo assessment of oral JAC-B2 was performed in two distinct mouse studies using a nude mice/flank xenograft model. In-vitro and in-vivo RNA sequencing was performed to determine gene expression levels and cellular pathway activation patterns. In-vitro metabolomics assessment was performed as well as time-course assessment of mitochondrial gene expression levels.

Results: JAC-B2 IC50s were in the nanomolar range (70nM-120nM). Low glucose conditions representative of the PDAC microenvironment (2mM Glucose) increased cellular susceptibility to the mitochondrial inhibition. JAC-B2 and other known mitochondrial toxins successfully inhibited ATP productions in glucose-free conditions ($P < 0.05$). ETC expression of complexes II, III and IV (and to a limited extent complexes IV and V) was decreased upon 48 hour treatment with JAC-B2. In-vivo treatment with JAC-B2 (2.5mg/kg X thrice weekly) compared with gemcitabine (100mcg/kg once weekly) and vehicle control, showed a JAC-B2 treated tumors to plateau after approximately 25 days of treatment. A second experiment with modified JAC-B2 oral dosing regimen (0.5mg/kg/day) showed significant growth retardation in the JAC-B2 treatment arm with several of the tumors considerably regressing in size (see attached figure). In-vitro and in-vivo gene expression analysis both revealed marked reduction in expression of mitochondrial-encoded genes (92% and 63%, respectively. $P < 0.05$). Cellular pathway analysis showed significant decrease in oxidative phosphorylation, ATP synthesis and varied mitochondrial processes ($P < 0.05$).

Conclusion: Pancreatic cancer and its effect on the tumor microenvironment promote a possible vulnerability to targeting cellular energetics. JAC-B2 is a mitochondrial inhibitor which is orally bioavailable and able to substantially inhibit cancer xenograft growth in in-vivo mouse models. This is most likely mediated through inhibition of mitochondrial gene expression. Importantly, JAC-B2 has been previously approved by the FDA as an antimicrobial drug. As such, it can potentially be more rapidly repurposed for the treatment of PDAC.



P 15. WHEN SHOULD NEUROENDOCRINE TUMORS < 2 CM BE RESECTED: A NATIONAL COHORT ANALYSIS

K Turner, A Delman, A Ammann, S Ahmad, S Patel, G Wilson

Presenter: Kevin Turner MD | University of Cincinnati, United States

Background: Surgical management of small non-functional pancreatic neuroendocrine tumors (PNETs) remains controversial. A significant portion of these tumors exhibit relatively indolent biology, however the risk of lymph node involvement is not insignificant and may push surgeons toward resection in select cases. The aim of this study was to evaluate factors associated with survival in patients with small PNETs.

Methods: The National Cancer Database (NCDB) was queried from 2010-2015 for patients with non-functional, small (< 2cm) PNETs that underwent resection. Only patients with complete data on pathologic node status and mitotic index (count per 10 high power field) were included.

Results: 1,372 patients were included in our study. The median age was 60 years old, with 23.47% (n=322) of tumors in the pancreatic head, 19.90% (n=273) in the body, 3.06% (n=42) in the neck, 42.06% (n=577) in the tail and 11.52% (n=158) in other location/not otherwise specified. Median tumor size was 1.45 cm, with 26.17% (n=359) in the less than 1 cm, 39.43% (n=541) in the 1 – 1.5 cm range and 34.40% (n=472) in the 1.5 – 2cm group. The median number of lymph nodes (LN) examined was 9 (IQR: 4 – 15). Overall rate LN metastatic disease was 12.61% with rates increasing with increasing tumor size: 8.91% in tumors less than 1.0cm, 11.46% of tumors 1 – 1.5cm and 16.74% of tumors 1.5 – 2 cm (p=0.002), despite similar number of lymph nodes examined. The median mitotic index was 0.2 per 10 high power field (hpf), with 83.46% WHO Grade 1 and 15.60% WHO Grade 2 tumors. The rates of WHO grade 2 tumors were 15.04% for tumors 0 – 1cm, 14.23% for tumors 1 – 1.5cm and 17.58% for tumors 1.5 – 2 cm (p=0.230). The rate of lymph node positivity was similar between WHO grade 1 and 2 tumors (11.97% v. 14.95%, p=0.224). On univariate cox proportional-hazards modeling factors associated with overall survival were age, sex, primary site, grade and mitotic index. On multivariate analysis the only factors independently associated with improved overall survival were younger age, low mitotic rate and low grade. (Table 1) On Kaplan-Meier analysis, patients with tumors whose mitotic index was < 2/10 hpf had significantly improved survival compared with those whose mitotic rates ≥2/10hpf (p=0.002); however, there was no difference in survival with positive LN (p=0.096).

Conclusion: Among small resected PNETs, elevated mitotic indexes, not lymph node metastasis, is independently associated with decreased survival. Pancreatic neuroendocrine tumors with elevated mitotic rates should be counseled regarding the risk of LN positivity and possible need for early surgical intervention.

Variable	Univariate		Multivariate	
	OR (95% CI)	P value	OR (95% CI)	P value
Age	1.05 (1.02 – 1.07)	<0.001	1.04 (1.02 – 1.07)	<0.001
Sex		0.012		0.273
Male	Ref.		Ref.	
Female	0.54 (0.33 – 0.88)		0.74 (0.43 – 1.27)	
Primary Site		0.049		0.144
Head	Ref.		Ref.	
Neck	0.56 (0.13 – 2.39)		0.87 (0.19 – 3.87)	
Body	0.36 (0.15 – 0.84)		0.42 (0.16 – 1.08)	
Tail	0.57 (0.32 – 1.01)		0.60 (0.31 – 1.16)	
Other/not specified	1.07 (0.53 – 2.14)		1.29 (0.56 – 2.97)	
Tumor Size		0.217		0.066
0 – 1.0 cm	Ref.		Ref.	
1.1 – 1.5 cm	0.69 (0.39 – 1.21)		0.50 (0.27 – 0.94)	
1.6 – 2.0 cm	0.60 (0.33 – 1.10)		0.52 (0.27 – 1.00)	
Grade		0.001		0.023
Well Differentiated	Ref.		Ref.	
Moderately Differentiated	1.06 (0.43 – 2.58)		0.92 (0.36 – 2.38)	
Poorly Differentiated	5.73 (1.93 – 16.98)		5.21 (1.53 – 17.73)	
Mitotic Index	1.02 (1.01 – 1.03)	0.001	1.02 (1.00 – 1.03)	0.018
Lymphovascular Invasion		0.067		0.826
Absent	Ref.		Ref.	
Present	1.77 (0.99 – 3.16)		1.09 (0.51 – 2.34)	
Regional Nodes Positive		0.138		0.399
Negative	Ref.		Ref.	
Positive	1.62 (0.88 – 2.97)		1.40 (0.65 – 2.98)	

P 16. A COMPREHENSIVE IN SILICO APPROACH TO IDENTIFY GENETIC FACTORS ASSOCIATED WITH ORGAN FAILURE IN ACUTE PANCREATITIS USING GWAS AND TRANSCRIPTOMIC ANALYSES

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Presenter: Apostolos Gaitanidis MD | Massachusetts General Hospital, United States

Background: Patients with acute pancreatitis (AP) develop widely variable severity of organ failure (OF). We hypothesized that genetic factors may influence the development of organ failure in AP. In this study, we identify new candidate genes associated with organ failure in AP using genome-wide association analyses (GWAS) and transcriptomic analyses.

Methods: Subjects enrolled in the Mass General Brigham Biobank were retrospectively queried to determine those with a history of AP. Patients with AP were categorized according to the presence of respiratory or renal failure during the first week of AP. Respiratory failure was defined as the need for mechanical ventilation for >48 hours. Renal failure was defined as elevation of serum creatinine at least 1.5 times over baseline for >48 hours. Patients were further divided into two groups based on the etiology of AP: biliary AP and AP of all other etiologies. A genome-wide association analysis was performed to identify single nucleotide polymorphisms (SNPs) associated with OF in patients with biliary AP. SNPs with $p < 0.001$ were then examined for association with OF in patients with AP of all other etiologies. SNPs that also had $p < 0.001$ in this analysis were kept for further validation using transcriptomic data. We used transcriptomic data from the Gene Expression Omnibus (GEO) database and determined differentially-expressed genes (DEGs) in several inflammatory conditions. Next, we examined whether the closest protein-coding genes to the SNPs identified through GWAS were differentially-expressed in acute pancreatitis, chronic pancreatitis, sepsis and septic shock. Association analysis was performed using PLINK v.1.9 and DEGs were determined using GEO2R.

Results: Overall, 665 patients were identified, of which 211 had biliary AP (199 mild, 12 severe) and 454 had AP of other etiologies (428 mild, 26 severe). Among SNPs examined for association with SAP among patients with biliary AP, 689 had $p < 0.001$. Among these 689 SNPs, 3 had $p < 0.001$ for association with SAP among patients with AP of all other etiologies (rs62358711: $O_{\text{biliary}} 3.95$, $p_{\text{biliary}} = 8.08e-4$, $O_{\text{Other}} 2.62$, $p_{\text{Other}} = 8.53e-4$, rs79341812: $O_{\text{biliary}} 5.90$, $p_{\text{biliary}} = 3.93e-4$, $O_{\text{Other}} 3.71$, $p_{\text{Other}} = 8.03e-4$, rs72799631: $O_{\text{biliary}} 5.05$, $p_{\text{biliary}} = 2.74e-4$, $O_{\text{Other}} 3.84$, $p_{\text{Other}} = 1.61e-4$). Rs62358711 is located in exons of FYB1 and rs72799631 in exons of CHD9, while rs79341812 is not located in close proximity to a protein-coding gene. Examination of transcriptomic data demonstrated that FYB1 and CHD9 are differentially expressed in acute pancreatitis, chronic pancreatitis, sepsis and septic shock (Table 1).

Conclusion: We identified SNPs located in FYB1 and CHD9 that are associated with persistent OF during the first week of acute pancreatitis. Both FYB1 and CHD9 are differentially-expressed in acute pancreatitis, chronic pancreatitis, sepsis and septic shock and may be involved in the modulation of inflammatory response. These findings can help us better understand the pathogenesis of SAP and identify novel therapeutic targets.

Table 1. Results of DEG analysis in various GEO datasets

GEO Dataset	Source	Comparison groups		<i>FYB1</i> Adjusted P-value	<i>CHD9</i> Adjusted P-value
GSE109227	Mice with cerulein-induced acute pancreatitis	Acute pancreatitis 6 samples	Control 5 samples	0.0051*	0.0006*
GSE41418	Mice with cerulein-induced chronic pancreatitis	Chronic pancreatitis 6 samples	Control 6 samples	0.0007*	0.0001*
GSE131761	Whole-blood RNA from post-surgical pts	Septic shock 81 samples	Control 15 samples	0.3880	<0.0001*
GSE95233	RNA from peripheral WBCs from ICU pts	Septic shock 102 samples	Control 22 samples	0.1876	0.0107*
GSE26378	Whole-blood RNA from children in the ICU	Septic shock 82 samples	Control 21 samples	0.0001*	0.0063*
GSE26440	Whole-blood RNA from children in the ICU	Septic shock 98 samples	Control 32 samples	<0.0001*	<0.0001*
GSE28750	RNA from peripheral WBCs from ICU pts	Sepsis 10 samples	Control 20 samples	0.0070*	0.0007*
GSE64457	RNA from neutrophils from ICU pts	Sepsis 15 samples	Control 8 samples	0.0036*	0.3370

GEO: Gene Expression Omnibus

*denotes statistical significance after adjustment for multiple comparisons

P 18. ARTIFICIAL PANCREAS - BIHORMONAL CLOSED LOOP GLUCOSE CONTROL -VERSUS CURRENT CARE AFTER TOTAL PANCREATECTOMY (APPEL5+): OUTPATIENT RANDOMIZED CONTROLLED CROSSOVER TRIAL

CL van Veldhuisen, AEJ Latenstein, H Blauw, LB Vlaskamp, M Klaasen, MG Besselink, JH de Vries

Presenter: Charlotte van Veldhuisen MD | Amsterdam UMC, Netherlands

Background: Glucose control in patients after total pancreatectomy is problematic due to complete absence of both alpha and beta cells. Recently, a novel bihormonal (insulin and glucagon) artificial pancreas (AP) for closed loop glucose control showed better glucose control compared to standard insulin pump therapy in patients with diabetes type 1. This AP system might also improve glucose control in patients after total pancreatectomy. Therefore, the aim of this study is to assess the efficacy and safety of the bihormonal AP in patients after total pancreatectomy.

Methods: Outpatient randomized crossover trial comparing the fully closed loop bihormonal AP to current diabetes care (i.e. insulin pump or pen therapy) in adults after total pancreatectomy. For safety reasons, since this is a first-in-man-study, the study started with a feasibility phase in two patients. Subsequently, 10 patients were randomized to 7-days treatment with the bihormonal AP (preceded by a 5-day training period) or 7-days treatment using their current care. Hereafter, all 10 patients crossed over. Primary outcome was the percentage of time spent in euglycemia (3.9-10 mmol/L or 70-180 mg/dL).

Results: The time spent in euglycemia was significantly higher in the closed loop bihormonal AP phase (78.30% [IQR 71.05-82.61] vs 57.4% [IQR 52.3-81.4], $p=0.027$), as compared to current care. The time spent in hypoglycemia was also lower in the AP phase (0% [IQR 0.0-0.0] vs 1.6% [IQR 0.8-3.8], $p=0.004$). No serious adverse events related to the AP device were seen.

Conclusion: In patients after total pancreatectomy, the bihormonal closed loop AP is safe and improves time in euglycemia while reducing hypoglycemia as compared to current diabetes care. Larger randomized trials including longer periods of treatment are needed.

Table 1. Primary and secondary endpoints

	Median		
	Closed loop	Open loop	p
Time spent at glucose levels (%)			
Euglycemia	78.30 (IQR 71.05-82.61)	57.38 (IQR 52.38-81.35)	0.027
Hypoglycemia <70 mg/dL (<3.9 mmol/L)	0.00 (IQR 0.00-00.07)	1.61 (IQR 0.80-3.81)	0.004
Hypoglycemia <54 mg/dL (<3.0 mmol/L)	0.00 (IQR 0.00-0.00)	0.62 (IQR 0.00-1.66)	0.016
Hyperglycemia >180 mg/dL (>10 mmol/L)	21.70 (IQR 17.36-28.95)	38.92 (IQR 15.85-45.16)	0.193
Hyperglycemia >250 mg/dL (>13.9 mmol/L)	1.17 (IQR 0.60-3.41)	8.41 (IQR 0.83-18.30)	0.049
Median glucose (mmol/L)	7.95 (IQR 7.71-8.11)	8.55 (IQR 7.78-9.73)	0.430
Glycemic variability			
IQR (mmol/L)	3.05 (IQR 2.76-3.67)	4.05 (IQR 3.15-5.93)	0.027
CV (%)	26.03 (IQR 24.21-30.63)	32.50 (IQR 26.43-41.50)	0.049
LBGI (score)	0.14 (IQR 0.07-0.20)	0.47 (IQR 0.33-0.97)	0.027
HBGI (score)	4.34 (IQR 3.72-5.84)	8.17 (IQR 3.77-11.17)	0.064
BGRI (score)	4.44 (IQR 3.86-6.03)	9.02 (IQR 4.60-11.69)	0.014

IQR: interquartile range, CV: coefficient of variation, LBGI: low blood glucose index, HBGI: high blood glucose index, BGRI: blood glucose risk index. Data are median (IQR).

Bold numbers indicate statistical significance.

P 19. CAN THE COSTS OF THE ROBOT ASSISTANCE DURING PANCREATODUODENECTOMY WITH THE DA VINCI XI BE OFFSET BY CLINICAL ADVANTAGES? A CASE-MATCHED COMPARATIVE ANALYSIS VERSUS OPEN APPROACH

G Di Franco, V Lorenzoni, M Palmeri, N Furbetta, S Guadagni, D Gianardi, M Bianchini, LE Pollina, F Melfi, D Mamone, C Milli, G Di Candio, G Turchetti, L Morelli

Presenter: Luca Morelli MD | University of Pisa, Italy

Background: Robot-assisted pancreaticoduodenectomy (RPD) has shown some advantages over open pancreaticoduodenectomy (OPD) but few studies have reported a cost analysis between the two techniques. We performed a structured cost-analysis comparing PD performed with the use of the da Vinci Xi, and the traditional open approach, in a high-volume multidisciplinary robotic center and considering healthcare direct costs associated to the interventions and those associated to the short-term post-operative course.

Methods: Twenty RPD and 194 OPD performed between January 2011 to December 2020 by the same operator were retrospectively analyzed. Two comparable groups of 20 patients (Xi-RPD-group) and 40 patients (OPD-group) were obtained matching 1:2 the RPD-group with the OPD-group. Perioperative data and overall costs (OC), including overall variable costs (OVC) and fixed costs, were compared. OVC comprised items related to disposable instruments used within each intervention (consumable costs, CCs), operating room personnel (personnel costs, PCs), and hospital stay costs (HCs) which included costs associated to the length of stay, both ICU and general ward, costs of reoperation, and post-operative procedures.

Results: No difference was reported in mean operative time: 428 min for Xi-RPD-group versus 404 min for OPD, $p=0.212$. No differences were reported in terms of overall post-operative complications rate between the two groups: 37.5% in the Xi-RPD-group and 50% in the Xi-RPD-group ($p=0.355$). The incidence of complications with Clavien-Dindo \geq III was similar between the two groups, being 10% in both groups ($p=1.000$). The median overall length of hospital stay was significantly lower in the Xi-RPD-group: 10 days versus 16 days, $p=0.001$. The median PCs were similar between the two groups: €2,115 both for Xi-RPD-group and for OPD-group, $p=0.230$. The comparison of the CCs showed significantly higher costs of Xi-RPD-group with respect to the OPD-group, median values being €6,149 and €1,267 respectively, $p<0.001$. HCs were significantly lower in the Xi-RPD-group with respect to the OPD-group, median values being €5,232 and €8,180 respectively, $p<0.001$. OVCs were not statistically different being €13,483 for the Xi-RPD-group and €11,880 for the OPD-group, $p=0.076$; while OCs including fixed costs were significantly higher for Xi-RPD-group with respect to the OPD-group: €15,311 versus €11,914 respectively, $p=0.003$.

Conclusion: Robot-assisted surgery is more expensive because of higher acquisition and maintenance costs. However, although RPD is associated to higher material costs, the advantages of the robotic system associated to lower hospital stay costs, and the no different personnel costs due thanks to the similar operative time with respect to the OPD, make the overall variable costs of the two techniques no longer different. The higher costs of advanced technology may be offset by clinical advantages, particularly within a high-volume multidisciplinary center for robot-assisted surgery and for pancreatic surgery.

P 20. CHARACTERIZING STROMAL HETEROGENEITY IN PATIENT-DERIVED XENOGRAFT MODELS OF PANCREATIC CANCER

L Bolm, N Petrush, P Finetti, AL Warshaw, C Fernández-Del Castillo, AS Liss

Presenter: Louisa Bolm MD | Massachusetts General Hospital, United States

Background: A dense desmoplastic stroma is a defining characteristic of pancreatic ductal adenocarcinoma (PDAC). This stroma promotes tumor progression and cancer cell invasion. Patient-derived xenograft models have been used to investigate PDAC tumor biology but a systematic characterization of PDAC PDX stroma has not been performed.

Methods: To characterize stromal heterogeneity in patient-derived xenograft models (PDX), RNA sequencing of 41 low-passage PDX models grown in nu/nu mice was performed. By using the species-specific expression of genes in the human cancer and mouse-derived stroma, gene expression in each compartment was defined. Consensus clustering of genes was used to identify differentially regulated genes in the stromal compartment of the PDX models and supervised analysis was performed to define stromal subtypes.

Results: Consensus clustering of identified genes disclosed 1186 genes differentially regulated in the stromal compartment of the PDX models. Supervised clustering analysis revealed four major stromal subtypes. The first stroma subtype, termed "immunogenic", is characterized by genes involved in the production of cytokines and those related to positive regulation of macrophage and negative regulation of dendritic cell differentiation. Furthermore, the MAP kinase and JAK/STAT pathways and their downstream targets, were enriched in this subtype. The second stroma subtype is enriched for genes involved in TGF- β signaling and pathways associated with epithelial-to-mesenchymal transition and has been classified as the "TGF- β /EMT-driven" subtype. The third stroma subtype was termed "invasion-driven" as members of the Rho family of small GTPases and other pathways of cancer cell invasion were enriched in this subtype. The fourth subtype is enriched in genes involved in basic cell metabolism, homeostasis, and osmotic regulation pathways and has been termed "quiescent". While the stromal subtypes were generally associated with a diversity of cancer subtypes, tumors with the invasion-driven stroma were strongly enriched for the squamous subtype of cancer. Of note, the PDX models in this study were implanted into mice with a homogeneous genetic background, implicating the cancer cells in shaping these divergent stromal.

Conclusion: Four distinct stromal subtypes were identified in PDAC PDX models. The stromal diversity of PDX models provides an opportunity to investigate subtype-specific response to stroma-targeted therapies.

P 21. DEFINING AND PREDICTING RECURRENCE IN PATIENTS UNDERGOING PANCREATECTOMY AFTER NEOADJUVANT TREATMENT FOR PANCREATIC DUCTAL ADENOCARCINOMA

L Maggino, G Malleo, S Crippa, G Belfiori, S Nobile, G Gasparini, G Lionetto, C Luchini, P Mattiolo, M Schiavo-Lena, C Doglioni, A Scarpa, C Bassi, M Falconi, R Salvia

Presenter: Laura Maggino MD | University of Verona, Italy

Background: Although the incidence and characteristics of recurrence after upfront pancreatectomy for pancreatic ductal adenocarcinoma (PDAC) have been intensively scrutinized, evidence on patients receiving neoadjuvant treatment (NAT) before the operation is limited. The aim of this study was to investigate incidence, pattern and predictors of disease recurrence after resection following NAT for resectable and borderline resectable (BR) PDAC. In particular, the possible interplay between different radiographic and biochemical parameters in affecting the risk of recurrence was investigated.

Methods: All pancreatectomies after NAT for resectable and BR-PDAC at two academic institutions were reviewed (2013-2017). Resectability was classified according to the NCCN guidelines and only patients who were resectable or BR at diagnosis were included, in compliance with a rigorous definition of NAT. $\Delta\text{Ca19.9}$ was computed as: $(\text{baseline Ca19.9} - \text{post-treatment Ca19.9}) / \text{baseline Ca19.9}$. A minimum p-value approach was used for continuous variables categorization. Standard uni- and multivariable Cox regression models were fitted with recurrence-free survival (RFS) as the primary outcome. The possible interplay between Ca19.9 parameters and between radiological features was assessed including interaction terms in the multivariable Cox models.

Results: The study population consisted of 315 patients, of whom 152 (48.3%) were anatomically resectable at diagnosis. The median postoperative follow-up was 24.9 months overall, 30.8 months in censored cases. The median disease-specific survival was 41.3 months (95%CI 35.0-47.5), with a median RFS of 15.7 months (95%CI 12.7-18.7). Disease recurrence manifested in 215/315 patients (68.3%). The estimated recurrence rates were 19.0%, 41.9%, 51.4%, 63.2%, 69.1% and 24.2% at 6/12/18/24/30/36 months post-pancreatectomy. Isolated local recurrence occurred in 16.7% (n=36), distant metastases in 49.3% (n=106) and combined recurrence in 72 (33.5%) of the cases. Survival outcomes varied depending on the recurrence pattern, with lung-only and multiple-distant sites exhibiting the most and less favorable features, respectively. Differences in RFS between groups were maximized by a threshold of 19 mm in post-treatment tumor size ($p=7.34 \times 10^{-7}$), 53.8% in $\Delta\text{Ca19.9}$ ($p=7.26 \times 10^{-4}$), approximated to 20mm and 50%, respectively. The analysis of RFS predictors is displayed in the Table. When including interactions into the model, that between $\Delta\text{Ca19.9}$ and post-treatment Ca19.9 remained significant (HR 0.551, 95%CI 0.364-0.835, $p=0.005$), suggesting a substantial risk reduction in patients with elevated post-treatment Ca19.9 values, when the $\Delta\text{Ca19.9}$ exceeded 50%.

Conclusion: In patients receiving pancreatectomy after NAT, postoperative recurrence is frequent (>40% at 1-year). Post-treatment Ca19.9 normalization, tumor size < 20mm, and Ca19.9 decrease $\geq 50\%$ are independent predictors of RFS. These results have potential implications for surgical decision-making in patients receiving NAT and might help personalized postoperative prognostication.

Table. Uni- and multivariable analysis of factors associated with recurrence-free survival in the study cohort (n=315)

	Univariable analysis		Multivariable analysis	
	Hazard Ratio (95% CI)	p-value	Hazard Ratio (95% CI)	p-value
Age at diagnosis, years	1.010 (0.996-1.025)	0.154		
Female sex	1.055 (0.806-1.382)	0.695		
Body mass index	1.003 (0.969-1.040)	0.850		
ASA 3-4	1.239 (0.926-1.658)	0.148		
Charlson Age Comorbidity Index \geq 4	1.095 (0.837-0.431)	0.508		
Diabetes	1.022 (0.761-1.371)	0.886		
Symptoms at diagnosis	0.917 (0.658-1.278)	0.609		
Tumor location in the body-tail	1.537 (1.134-2.082)	0.006	1.527 (1.119-2.083)	0.008
Resectability at diagnosis (NCCN)				
Resectable	1 (ref)	-		
Borderline resectable	1.141 (0.872-1.493)	0.335		
Serum Ca19.9 at diagnosis ⁺				
Normal (\leq 37 U/mL)	1 (ref)	-		
Elevated ($>$ 37 U/mL)	1.059 (0.729-1.539)	0.762		
Not expressed	0.603 (0.323-1.127)	0.113		
Tumor size at diagnosis, mm	1.004 (0.995-1.013)	0.364		
MDACC class				
Resectable	1 (ref)	-		
A	1.058 (0.766-1.443)	0.721		
B	1.125 (0.770-1.642)	0.543		
C	1.307 (0.674-2.534)	0.429		
Type of neoadjuvant therapy				
Chemotherapy	1 (ref)	-		
Chemo-radiation	0.929 (0.597-1.444)	0.742		
Chemotherapy regimen				
FOLFIRINOX	1 (ref)	-		
Gemcitabine+nab-paclitaxel	1.142 (0.858-1.520)	0.363		
GEMOX	1.120 (0.685-1.831)	0.652		
Gemcitabine	1.997 (0.874-4.563)	0.101		
Chemotherapy completion	0.937 (0.626-1.403)	0.752		
Number of chemotherapy cycles	1.004 (0.995-1.056)	0.867		
Second-line chemotherapy	1.602 (1.292-1.987)	<0.001	1.768 (1.035-3.020)	0.037
Preoperative resectability (NCCN)				
Resectable	1 (ref)	-		
Borderline resectable	1.176 (0.891-1.553)	0.253		
RECIST response				
Partial response	1 (ref)	-		
Stable disease	1.512 (1.155-1.980)	0.003		
Preoperative Ca 19.9 Serum levels ⁺				
Normal (\leq 37 U/mL)	1 (ref)	-	1 (ref)	-
Elevated ($>$ 37 U/mL)	1.385 (1.048-1.831)	0.022	1.391 (1.049-1.844)	0.022
Not expressed	0.657 (0.376-1.145)	0.138	0.706 (0.404-1.233)	0.221
Delta Ca19.9 ⁺	0.992 (0.985-0.999)	0.023	0.991 (0.984-0.998)	0.018
Delta Ca19.9 \geq 50% ⁺				
No	1 (ref)	-	1 (ref)	-
Yes	0.615 (0.458-0.825)	0.001	0.640 (0.475-0.863)	0.003
Not expressed	0.405 (0.228-0.721)	0.002	0.450 (0.252-0.801)	0.007
Preoperative tumor size, mm [#]	1.037 (1.023-1.052)	<0.001	1.033 (1.019-1.047)	<0.001
Preoperative tumor size $>$ 20 mm [#]	1.929 (1.463-2.542)	<0.001	2.224 (1.603-3.085)	0.021

ASA, American Society of Anesthesiologists; NCCN, National Comprehensive Cancer Network; MDACC, MD Anderson Cancer Center

*non-expressors excluded (n=285); + To avoid collinearity, these variables were analyzed in mutually exclusive multivariable models; # To avoid collinearity, these variables were analyzed in mutually exclusive multivariable models

P 23. KINETICS OF POSTOPERATIVE DRAIN FLUID AMYLASE VALUES FOLLOWING PANCREATODUODENECTOMY: NEW INSIGHTS TO DYNAMIC, DATA-DRIVEN DRAIN MANAGEMENT

AH Zureikat, F Casciani, S Ahmad, C Bassi, CM Vollmer Jr

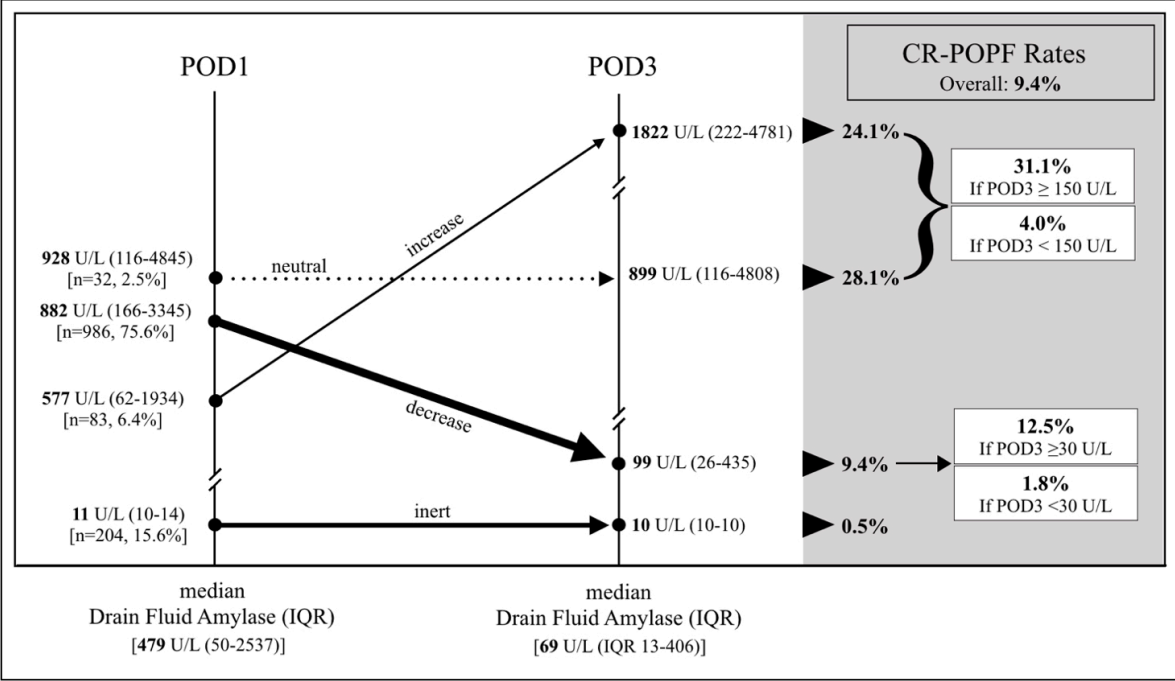
Presenter: Fabio Casciani MD | University of Pennsylvania, United States

Background: Multiple drain fluid amylase (DFA) cutoffs have been proposed as absolute parameters to inform clinically-relevant pancreatic fistula (CR-POPF) prediction and subsequent drain management following pancreatoduodenectomy (PD), with particular emphasis being given to POD1 measurements. However, the usefulness of dichotomous, yet static, POD1 DFA thresholds can be questioned.

Methods: Consecutive PDs performed at two high-volume institutions were accrued. POD1→POD3 DFA trajectories were segregated as increasing or decreasing. When both POD1 and POD3 DFA remained ≤ 20 U/L such variation was considered inert, whereas any other deviations $\pm 10\%$ were defined as neutral. POD1/POD3 DFA measurements and kinetics were correlated to the Fistula Risk Score and CR-POPF occurrence, and predictive capacity of DFA for CR-POPF was assessed by calculating the Area Under the ROC Curve (AUC).

Results: 1757 PDs were performed from July 2014-August 2020. After excluding patients with missing DFA values (19.5%) and drain omission/removal before POD3 (6.3%), 1305 PDs were analyzed. As CR-POPF occurred in 123 patients (9.4%), the AUC of DFA for CR-POPF was 0.798 on POD1 and 0.831 on POD3. When analyzing POD1→POD3 DFA kinetics, 75.6% (n=986) decreased (median -83%). Conversely, a DFA increase occurred in 6.4% (n=83; median +115%), whereas 2.5% displayed neutral DFA variation. Finally, DFA were inert for 204 patients (15.6%). DFA trajectories did not correlate with POD1 and POD3 values, with the increasing DFA cohort displaying the lowest median POD1 DFA ($p=0.018$), but the highest POD3 DFA ($p<0.001$). Moreover, the inert variation was the most frequent DFA trajectory in the Negligible Risk Zone (FRS 0: 48.1%), whereas decreasing DFA was prevalent to these extents within the Low (FRS 1-2: 64.9%), Intermediate (FRS 3-6: 75.1%) and High (FRS 7-10: 85.1%) Risk Zones. Finally, a comparable number of patients in each zone displayed increasing DFA ($\approx 6\%$). CR-POPFs occurred 2.5X as often when DFA increased versus decreased (24.1 vs 9.4%; Figure), while the grade C rate was 4X as high (3.6 vs 0.9%; both $p<0.001$). Conversely, for the inert group, CR-POPF was almost nil (1/204; 0.5%). Given their comparable CR-POPF rates, the neutral and increasing DFA groups were combined as one cohort (n=115; overall CR-POPF rate 25.2%). A POD3 DFA cutoff of 150 U/L yielded the highest Negative Predictive Value (NPV) in such a composite cohort (96.6%), with patients below this threshold (n=25, 21.7%) demonstrating an eight-fold CR-POPF reduction (4.0 vs 31.1%; $p=0.004$). Finally, within the decreasing DFA cohort, the POD3 DFA cutoff with the highest NPV (98.2%) was 30 U/L, with the 282 patients (28.6%) below this threshold displaying a seven-fold CR-POPF reduction (1.8 vs 12.5%; $p<0.001$).

Conclusion: While being associated with significantly different fistula rates following pancreatoduodenectomy, unique POD1→POD3 DFA trajectories are independent of both underlying risk and POD1 measurements. Therefore, a dynamic DFA assessment adhering to kinetics identification represents a more sensible, yet simple, framework for postoperative fistula forecasting compared to static POD1 values. Moreover, trajectory-derived POD3 DFA cutoffs allow identification of patients eligible for safe, and more certain, early drain removal, irrespective of the surgeon's usual comfort level for POD1 DFA.



P 24. MARGIN STERILIZATION WITH STEREOTACTIC BODY RADIOTHERAPY IN LOCALIZED PANCREATIC ADENOCARCINOMA IMPROVES LOCAL CONTROL

C Hill, S Sehgal, JJ Meyer, JM Herman, AK Narang

Presenter: Colin Hill MD | Johns Hopkins University School of Medicine, United States

Background: Borderline resectable (BRPC) or locally advanced pancreatic cancer (LAPC) patients are at high risk of margin positive resection. Stereotactic body radiation therapy (SBRT) may help increase the proportion of patients that can be resected with negative margins. We report long-term outcomes of BRPC/LAPC patients treated with upfront primarily multi-agent chemotherapy (CT) followed by 5-fraction SBRT (SBRT) prior to surgical exploration.

Methods: Consecutive BRPC/LAPC patients diagnosed from 2011-2019 who were treated with upfront CT followed by 5-fraction SBRT were retrospectively reviewed. Pathological endpoints and patterns of failure are descriptively reported. One-sided and two-sided T-Test were used to compare covariates of interest with p -value ≤ 0.05 . Kaplan-Meier method was used to analyze survival outcomes.

Results: Of 274 patients, 156 patients (57%) had BRPC and 118 patients (43%) had LAPC. The median follow-up was 25.3 months (range: 6.6 – 88.4) from diagnosis and 18.9 months (1.5 – 81.9) from SBRT. For induction CT, FOLFIRINOX (FFX) was administered in 203 patients (74%) and gemcitabine and nab-paclitaxel (GnP) was utilized in 91 patients (33%). 29 patients (11%) received a different multi-agent regimen or single agent gemcitabine. 45 patients (16%) received more than 1 line of CT prior to SBRT. The median total duration of CT was 4.2 months (range: 0.5-18.0), which was followed by SBRT to a median dose of 33 Gy (range: 25-40 Gy). After SBRT, 250 patients (91%) were surgically explored, and 226 patients (83%) were successfully resected. In resected patients, 208 (92%) had negative margins (R0), 137 (61%) were node-negative, and 17 (8%) had a pathological complete response (pCR). Perineural invasion occurred more frequently in R1 compared to R0 resections (83% vs. 55%, respectively, $p=0.035$). Of the 156 BRPC patients, 112 (72%) were explored, with 104 (67%) undergoing complete resection and 98 (94%) undergoing R0 resection. Of the 118 LAPC patients, 138 (89%) were surgically explored, with 122 (78%) undergoing complete resection and 110 (90%) undergoing R0 resection. Patients experienced significantly better median overall survival (mOS) if they were resected (28.0 mo) vs. those who were not explored (10.0 mo, HR 3.14, $p<0.001$) or aborted (10.1 mo, HR 3.35, $p<0.001$). In BRPC patients, the first type of failure was distant in 43 (20%), followed by synchronous in 31 (15%), and locoregional failures in 15 (7%) patients. In LAPC patients, distant failure occurred first in 57 (27%), followed by locoregional in 30 (14%) and synchronous failures in 26 (12%) patients. From SBRT, local progression-free survival was 24.8 mo. R0 patients had significantly better LPFS, with median LPFS of 36.4 mo versus 16 mo in R1 patients (HR 0.51, $p=0.029$).

Conclusion: In a large cohort of BRPC/LAPC patients treated at a single high-volume institution with SBRT following multi-agent chemotherapy, a high proportion of patients underwent successful resection (>80%), of which a high proportion of resections were margin negative (>90%). Patients who underwent resection experienced significantly improved survival and local control. However, despite aggressive local therapy with SBRT and resection, local failure remained not insignificant, highlighting opportunity to continue to refine radiation therapy for this disease.

P 25. MORPHOMETRIC AND CLINICAL ANALYSIS OF PRION PROTEIN OCCURRENCE IN PANCREATIC DUCTAL ADENOCARCINOMA

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Presenter: Luca Morelli MD | University of Pisa, Italy

Background: Recent evidences have shown a relationship between prion protein (PrPc) expression and pancreatic ductal adenocarcinoma (PDAC). Indeed, PrPc could be one of the markers explaining the aggressiveness of this tumor. However, studies investigating the specific compartmentalization of increased PrPc expression within PDAC cells are lacking, as well as a correlation between ultrastructural evidence, ultrastructural morphometry of PrPc protein and clinical data. These data, as well as the quantitative stoichiometry of this protein detected by immuno-gold, provide a significant advancement in understanding the biology of disease and the outcome of surgical resection.

Methods: Between June 2018 and December 2020, samples from pancreatic tissues of 45 patients treated with pancreatic resection for a preoperative suspicion of PDAC at our Institution were collected. Western blotting was used to detect, quantify and compare the expression of PrPc in PDAC and control tissues, such as those of non-affected neighboring pancreatic tissue of the same patient. To quantify the increase of PrPc and to detect the subcellular compartmentalization of PrPc within PDAC cells, immune-gold stoichiometry within specific cell compartments was analyzed with electron microscopy. Finally, an analysis of quantitative PrPc expression according to prognostic data, such as recurrence of the disease at 12 months after surgery and recurrence during adjuvant chemotherapy was made.

Results: The amount of PrPc within specimen from 38 out of 45 patients was determined by semi-quantitative analysis by using Western blotting, which indicates that PrPc increases almost three-fold in tumor pancreatic tissue compared with healthy pancreatic regions (242.41 ± 28.36 OD vs 95 ± 17.40 OD, $P < 0.0001$). Quantitative morphometry carried out by using immuno-gold detection at transmission electron microscopy confirmed an increased PrPc expression in PDAC ductal cells. The number of immune-gold particles of PrPc was significantly higher in PDAC cells respect to controls, when considering the whole cell (19.8 ± 0.79 particles vs 9.44 ± 0.45 , $P < 0.0001$). Remarkably, the increase of PrPc was higher in the nucleus than cytosol of tumor cells, which indicates a shift in PrPc compartmentalization within PDAC cells. In fact, the increase of immuno-gold within nuclear compartment exceeded at large the augment of PrPc which was detected in the cytosol (nucleus: 12.88 ± 0.59 particles vs 5.12 ± 0.32 , $P < 0.0001$; cytosol: 7.74 ± 0.44 particles vs 4.3 ± 0.24 , $P < 0.0001$). In order to analyze the prognostic impact of PrPc, 24 patients with a mean follow-up of 16.8 months were considered. Immuno-blot analysis revealed a significantly higher expression of PrPc in patients with disease recurrence at 12 months after radical surgery (360.71 ± 69.01 OD vs 170.23 ± 23.06 OD, $P=0.023$), also in the subgroup of patients treated with adjuvant CT (368.36 ± 79.26 OD in the recurrence group vs 162.86 ± 24.16 OD, $P=0.028$), revealing a possible higher chemo-resistance.

Conclusion: Expression of PrPc is significantly higher in PDAC cells compared with normal ones, with a shift concerning the protein placement from the cytoplasm to the nucleus, where the increase is much more pronounced. Preliminary clinical data confirm the correlation between PrPc expression and a poorer prognosis.

P 26. NEOADJUVANT THERAPY AND THE EFFECT OF NODAL DOWNSTAGING IN PANCREATIC ADENOCARCINOMA

M Altimari, J Abad, A Chawla

Presenter: Marc Altimari | Northwestern Medicine, United States

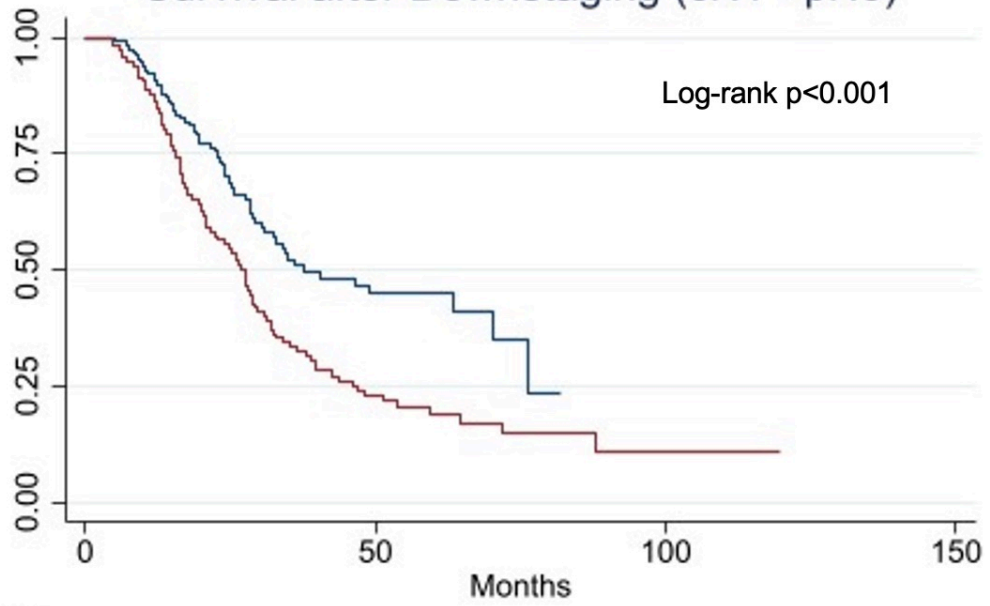
Background: Neoadjuvant chemotherapy and radiation have been shown to enhance resectability in patients with pancreatic adenocarcinoma. However, its role in downstaging remains poorly understood. This study aims to compare the effect of neoadjuvant chemotherapy and chemoradiation on lymph node downstaging in patients with pancreatic adenocarcinoma.

Methods: The National Cancer Database (NCDB) Pancreas Participant User File from 2004-2016 was used to identify patients who underwent surgery for a confirmed diagnosis of non-metastatic pancreatic adenocarcinoma. Fisher's exact test, ANOVA, and log-rank were used in analysis. Multivariate logistic regression was used to identify predictors of nodal downstaging. Patients who underwent neoadjuvant chemotherapy and chemoradiation and surgical resection were included in the study

Results: Of the 45,059 patients who underwent surgical resection for pancreatic adenocarcinoma, 3,311 received neoadjuvant chemotherapy alone and 1,226 received neoadjuvant chemoradiation. We identified 38,008 who did not undergo neoadjuvant therapy. Roughly 28% and 25% of chemotherapy and chemoradiation patients, respectively, were clinically staged as having node-positive disease. After surgery for clinically node-positive disease, 23.3% of patients who received neoadjuvant chemotherapy alone and 41.31% of patients who received chemoradiation were downstaged to node-negative disease on pathology ($p < 0.001$). Younger age and lower comorbidity index were found as independent predictors of nodal downstaging. Additionally, 68.8% of patients who received chemotherapy alone and 46.2% of patients who received chemoradiation were not downstaged and still had node-positive disease on pathology ($p < 0.001$). Median survival in patients who were downstaged was better in patients who received neoadjuvant chemotherapy only versus chemoradiation (37.5 vs. 27.5 months, log-rank $p < 0.001$, Figure 1). There was no difference in survival between these treatment groups in patients who were clinically node-positive and not downstaged.

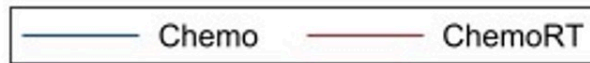
Conclusion: Careful selection of patient factors, particularly patient age and comorbidity status is important when determining the optimal neoadjuvant therapy regimen for pancreatic adenocarcinoma. Although neoadjuvant chemoradiation may help to decrease rates of nodal positivity, it may not confer a survival benefit, suggesting that disease survival is determined by systemic burden of disease.

Survival after Downstaging (cN1 - pN0)



Number at risk

Chemo	157	22	0	0
ChemoRT	117	21	2	0



P 27. PANCREATIC CANCER AND PRECANCERS IN LARGE VOLUMES WITH SUBCELLULAR RESOLUTION

AL Kiemen, AS Braxton, LD Wood, PH Wu, RH Hruban, D Wirtz

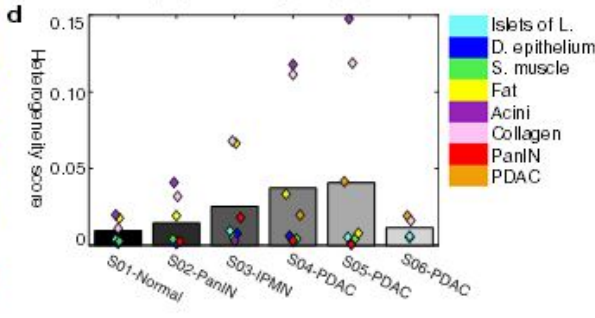
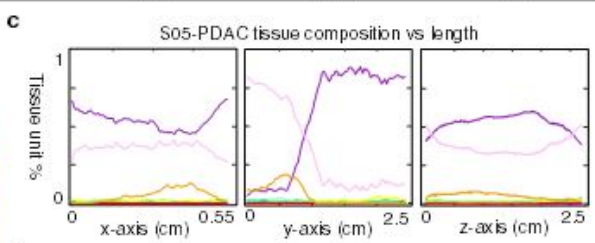
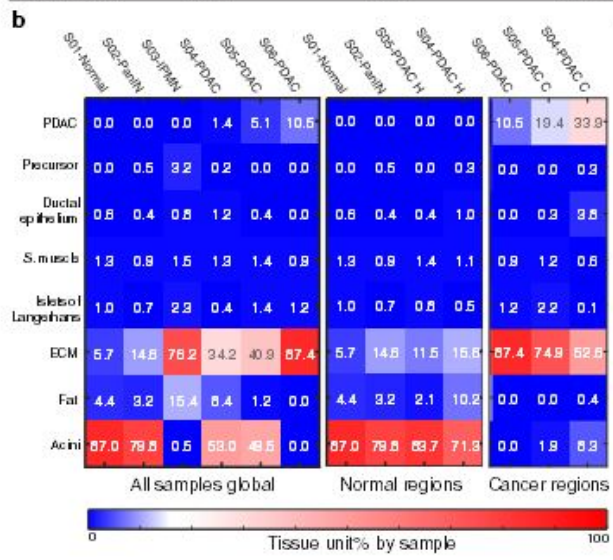
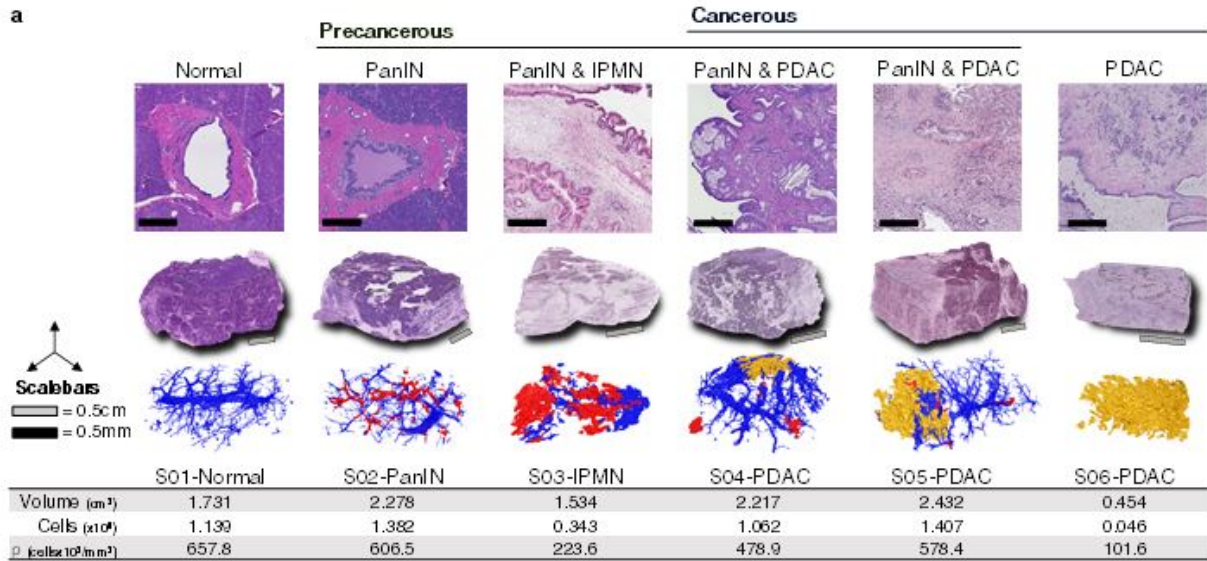
Presenter: Ashley Kiemen MS | Johns Hopkins University School of Medicine, United States

Background: The growth of invasive cancer and its spread into microenvironments containing complex vasculature, stromal, and ductal structures is best understood through accurate three dimensional (3D) representations. As pancreatic ductal adenocarcinoma (PDAC) is predicted to become the second leading cause of cancer death in the US, a better understanding of the spatial complexity of the human tumor microenvironment is necessary for an improved design of in vitro and in vivo model systems. PDAC arises from well-characterized precursor lesions in the pancreatic ducts, is surrounded by an immunosuppressive microenvironment and desmoplastic stroma, and has a propensity for vascular invasion and metastasis to the liver. These phenomena are classically studied in two dimensions (2D) via tissue sectioning and histological staining, where 3D information such as connectivity, tumor morphology, and spatial relationships are lost. While many surrogates for studying tumorigenesis in 3D have been developed in vitro and in vivo, quantitative 3D study of naturally occurring cancers in human tissues, or cancer in situ, is generally lacking.

Methods: Our group has developed CODA: a pipeline for building large (cm-scale) models of PanIN and PDAC to inform understanding of how tumors progress in 3D. We reconstructed serially sectioned hematoxylin and eosin (H&E) stained human pancreatic tissue volumes of up to 3x3x0.7cm³ each. To quantify the tumor microenvironment, we developed a convolutional neural network (CNN) that labels eight tissue components in H&E images with 96% accuracy: lipid, collagen, blood vessels, normal ductal epithelium, islets of Langerhans, acini, PanIN, PDAC cells, and lymphocytes, creating 3D cm scale tumor maps at subcellular resolution.

Results: Using digital maps of normal, precancerous, and cancerous pancreas tissue, we assessed changes to the pancreatic microenvironment in large 3D samples. We characterized the extent, 3D structure, and cellularity of pancreatic cancer precursors (which were found to vary from 30mm³ in volume), quantified periductal collagen alignment in a 3D landscape, and explored aligned collagen as vasculature as structures utilized by pancreatic cancer to invade far from the bulk tumor.

Conclusion: CODA is a powerful tool for the quantitative study of large tissue samples and allows high-detail insights into normal pancreas architecture and changes during precancer and cancer development.



P 28. PANCREATODUODENECTOMY: DOES THE METABOLIC SYNDROME ALTER OUTCOMES?

V Gazivoda, A Greenbaum, M Beier, C Davis, A Kangas-Dick, R Langan, M Grandhi, D August, HR Alexander, H Pitt, T Kennedy

Presenter: Victor Gazivoda MD | Rutgers Cancer Institute of New Jersey, United States

Background: Patients with the Metabolic Syndrome (MS) are a high-risk patient population who may have increased perioperative morbidity and mortality. Whether the MS is associated with worse outcomes after pancreatoduodenectomy (PD) remains unclear due to conflicting results in the literature. The aims of this analysis were to investigate the association of MS with mortality, serious morbidity, and pancreatotomy specific outcomes in patients undergoing PD.

Methods: Patients with the MS who underwent PD were selected from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) including the pancreatotomy specific PUF's from 2014-2018. MS was defined as having obesity (BMI ≥ 30 kg/m²), diabetes mellitus (DM), and hypertension (HTN). Patients with missing variables for height, weight, DM, HTN, postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE), and variables that constitute serious morbidity were excluded. Serious morbidity was defined as deep surgical site infection, organ space infection, dehiscence, pneumonia, unplanned intubation, pulmonary embolism, ventilator dependence, acute renal failure, cerebral vascular accident, cardiac arrest, myocardial infarction, sepsis, and septic shock. Demographics and outcomes were compared by χ^2 and Mann-Whitney tests. Additionally, adjusted odds ratios (aOR) were generated from multivariable logistic regression to assess the association between MS and primary outcomes adjusted for clinically relevant baseline characteristics.

Results: Of the 19,054 patients undergoing PD who met inclusion criteria, 7.3% (n = 1,388) had the MS. Patients with the MS had increased cardiac and respiratory comorbidities as well as an ASA Classification \geq III compared to patients without the MS. No significant differences in pancreatic duct size, pancreatic texture, or malignant vs benign pathology were found between MS and control patients. On univariable analysis, patients with the MS had significantly worse outcomes (p < 0.05), including 30-day mortality (3% vs 1.8%), serious morbidity (26% vs 23%), re-intubation (4.9% vs 3.5%), pulmonary embolism (2.0% vs 1.1%), acute renal failure (1.5% vs 0.9%), cardiac arrest (1.9% vs 1.0%), DGE (18% vs 16.5%), and failure to rescue (10% vs 6.7%). On multivariable analysis, 30-day mortality and serious morbidity were significantly increased in patients with the MS (Table 1).

Conclusion: The Metabolic Syndrome is associated with increased morbidity and mortality in patients undergoing pancreatoduodenectomy. Patients with the MS undergoing PD may benefit from being medically optimized prior to surgery. Preventive strategies with respect to thrombosis prophylaxis, fluid management, and cardiac protection should be employed in the perioperative management of patients with the MS given the increased risk for pulmonary embolism, renal failure, and cardiac arrest.

Metabolic Syndrome	aOR	95% CI	p value
30-Day Mortality	1.58	(1.12, 2.17)	< 0.01
Serious Morbidity	1.13	(1.00, 1.29)	= 0.05

Table 1. Multivariable analysis of outcomes related to the Metabolic Syndrome

P 29. PRESENCE OF LYMPH NODE METASTASIS HAS A GREATER IMPACT ON SURVIVAL IN BLACK PATIENTS WITH PANCREATIC CANCER: AN EFFECT OF TUMOR BIOLOGY OR A DISPARITY IN TREATMENT?

HA Fang, A Irfan, SM Vickers, O Gbolahan, GR Williams, TNT Wang, V Dudeja, B Rose, S Reddy

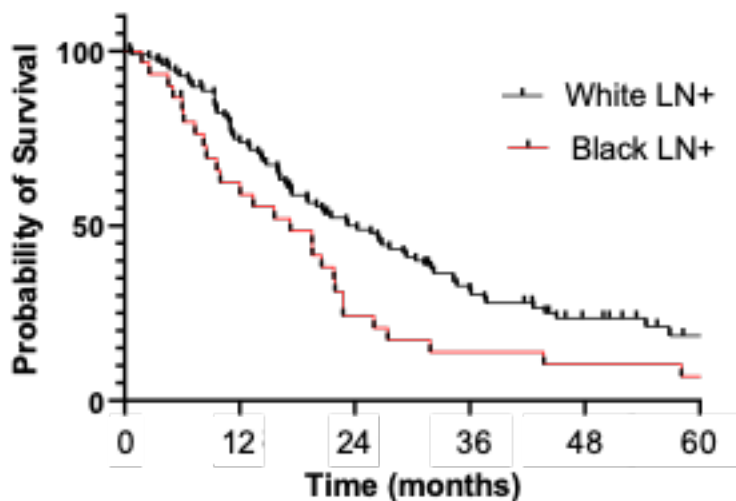
Presenter: Amanda Hua Fang BS | University of Alabama at Birmingham, United States

Background: Despite aggressive surgical care and systemic therapy, patients with pancreatic ductal adenocarcinoma (PDAC) have a poor prognosis. Recent studies show that racial disparity in outcome also exists. We determined the difference in survival between Black and White PDAC patients after resection.

Methods: Retrospective analysis of 226 PDAC patients who underwent resection at a single institution from 2010-2018 was performed with attention to lymph node (LN) metastasis and patient race. The number of patients who received chemotherapy was also evaluated.

Results: 175 (77.4%) PDAC patients were White and 51 (22.6%) were Black. 130 (59.3%) patients had LN metastasis (LN+). LN+ and LN- groups were similar in race ($p=0.93$), sex ($p=0.10$), and age at the time of diagnosis ($p=0.45$). Patients with LN+ disease were more likely to present with larger tumors (3.4 vs. 2.8cm, $p=0.02$) and higher T status ($p=0.001$). White and Black patients had similar rates of LN metastasis (59% vs. 58.8%, $p=1.0$). Median survival for LN- Black and White patients were similar (43.2 vs. 30.2 months, $p=0.82$). LN+ Black patients trended towards receiving more systemic therapy than White LN+ patients (55% vs. 42%, $p=0.10$). Median survival for LN+ Black patients was significantly less than LN+ White patients (17.5 vs. 24.6 months, $p=0.04$, FIGURE)

Conclusion: Black LN+ PDAC patients have an inferior survival rate after resection when compared to their White counterparts. Our disparity in outcome cannot be solely explained by a difference in systemic treatment. Further investigation is warranted to determine racial differences in tumor biology or response to chemotherapy.



P 31. ROBOTIC PANCREATODUODECTOMY: TRENDS IN TECHNIQUE AND TRAINING CHALLENGES

CH Davis, MS Grandhi, VP Gazivoda, AA Greenbaum, TJ Kennedy, RC Langan, HR Alexander, HA Pitt, DA August

Presenter: Catherine Davis MD, MPH | Rutgers Cancer Institute of New Jersey, United States

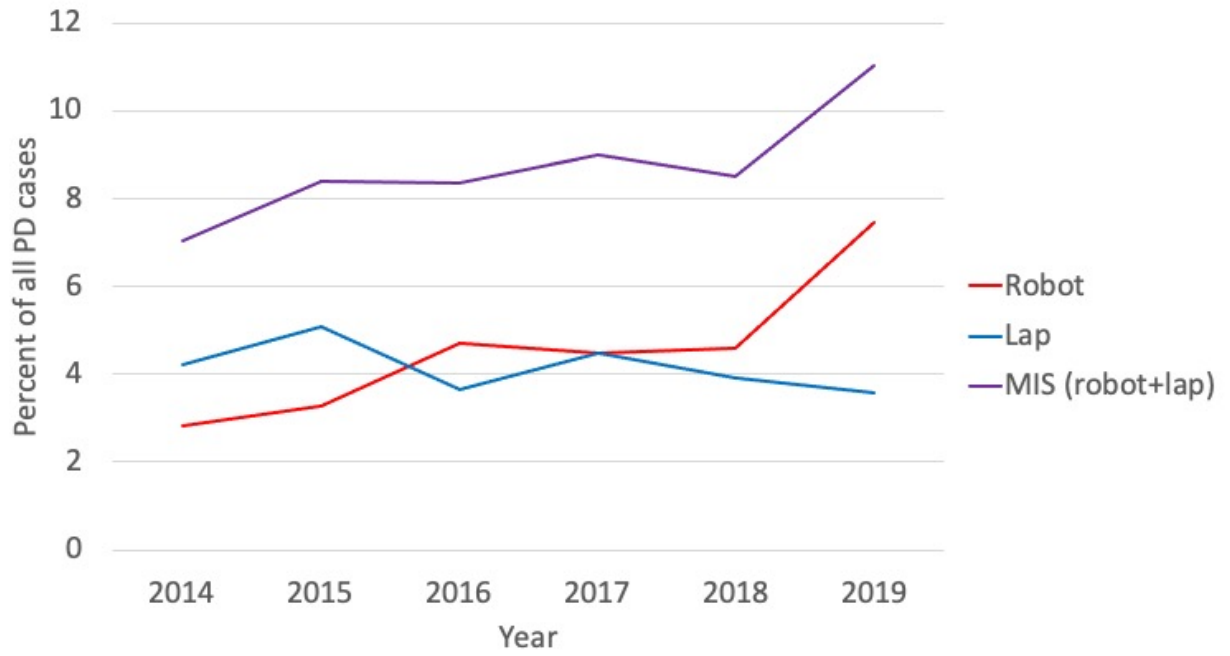
Background: As robot access increases and surgeon experience becomes more advanced, more complex cases are being performed robotically. However, no nationally sanctioned training program currently exists for robotic surgery akin to "Fundamentals of Laparoscopic Surgery." A robotic pancreatoduodenectomy (RPD) curriculum has been developed and is being implemented at a very select number of institutions. However, the learning curve is at least 20-40 cases. This study aims to characterize trends in RPD over time, associated patient outcomes and opportunities for advanced trainees.

Methods: Using the American College of Surgeons (ACS) National Surgical Quality Improvement Program (NSQIP) Procedure Targeted Pancreatectomy database from 2014 to 2019, PD cases were studied, and operative approach (open-OPN, laparoscopic-LAP, robotic-ROB) was characterized. Proficiency was assessed by conversion rates, OR time, and case complexity. Postoperative outcomes were described by year and operative technique. Statistical analysis was performed using Wilcoxon rank sum and Mann-Kendall trend tests. AHPBA, SSO, and ASTS websites were used to determine the number of fellows per year.

Results: During the study period, a total of 24,268 PDs were identified, 71% of which were for malignant disease. The annual number of PD cases increased from 3,137 in 2014 to 4,820 in 2019. An increase was observed in the proportion of cases performed using minimally invasive techniques (LAP+ROB) from 7.0% to 11.0%. The ROB approach increased from 2.8% to 7.5% while the LAP approach decreased from 4.2% to 3.6%. By 2019 ROB accounted for a greater portion of minimally invasive operations (40.0% to 67.7%, $p<0.0001$). (Figure) OR time did not change over time in ROB cases (mean 372 minutes, $p=0.861$). Unplanned conversion increased over time for LAP (27.7 to 40.4%, $p=0.003$) but was unchanged for ROB cases (14.8% to 14.7%, $p=0.257$). No change was observed in the vascular reconstruction rate for patients undergoing robotic PD for malignancy ($p=0.628$). Morbidity increased in OPN PD (35.5% to 36.8%, $p=0.041$) and decreased in ROB PD (38.7% to 30.3%, $p=0.010$). Length of stay (LOS) decreased over time overall as well as by operative approach ($p<0.0001$). Mean LOS was lower in ROB than LAP and OPN (9.51 vs. 10.90, $p<0.00001$). Approximately 100 AHPBA, SSO, and ASTS fellows are being trained each year in North America. In 2019, only 360 RPDs were performed in NSQIP, which accounts for approximately 70% of the PDs. Thus, only about 5 RPDs are available per trainee per year which is far below the learning curve.

Conclusion: Over a six-year period, a gradual, but significant, increase was observed in the use of robotic pancreatoduodenectomy (RPD) without a concomitant increase in conversion rates. RPD was associated with decreased morbidity and length of stay. Despite a shift towards more RPDs, the number of cases being performed in North America is not adequate for all fellows to achieve the learning curve before graduation.

Operative Technique Over Time



P 32. ROLE OF ENDOVASCULAR HEPATIC ARTERY STENTS IN THE CURRENT MANAGEMENT OF POST-PANCREATODUODENECTOMY HAEMORRHAGE

L Finch, M Baltatzis, S Byott, AK Ganapathy, N Kakani, E Lake, R Cadwallader, C Hazar, N de Liguori Carino, S Jamdar, A Siriwardena

Presenter: Louise Finch MPhil, MBChB | Manchester Royal Infirmary, United Kingdom

Background: Post-operative haemorrhage is a potentially lethal complication of pancreatoduodenectomy. This study reports on the use of endovascular hepatic artery stents in the management of post-pancreatectomy haemorrhage.

Methods: This is a retrospective analysis of a prospectively maintained, consecutive dataset of 440 patients undergoing pancreatoduodenectomy over 68 months. Data are presented on bleeding events and outcome and contextualized by the clinical course of the denominator population. International Study Group for Pancreas Surgery (ISGPS) terminology was used for post-pancreatectomy haemorrhage

Results: Sixty-seven (15%) had post-operative haemorrhage. Fifty (75%) were male and this gender difference was significant ($P=0.001$; two proportions test). Post-operative pancreatic fistulas were more frequent in the post-operative haemorrhage group ($P = 0.029$; two-proportions test). The median (IQR) delay between surgery and post-operative haemorrhage was 5 (2 -14) days. Twenty-six (39%) required intervention comprising re-operation alone in 12, embolization alone in 5 and endovascular hepatic artery stent deployment in 5. Four further patients underwent more than one intervention with two having stents. Endovascular stent placement achieved initial haemostasis in 5 (72%). Follow-up was for a median (iqr) of 199 (145-400) days post stent placement. In two patients the stent remained patent at last follow-up. The remaining 5 stents occluded with a median (iqr) period of proven patency of 10 (8-22) days.

Conclusion: This study shows that in the specific setting of post-pancreatoduodenectomy haemorrhage with either a short remnant GDA bleed or a direct bleed from the hepatic artery, where embolization risks occlusion with compromise of liver arterial inflow, endovascular hepatic artery stent is an important haemostatic option but is associated with a high risk of subsequent graft occlusion.

P 33. SHORT- AND LONG-TERM OUTCOMES OF SURGERY FOR PANCREATIC CANCER IN THE ELDERLY

AC Henry, TJ Schouten, LA Daamen, MS Walma, P Noordzij, MG Besselink, OR Busch, BA Bonsing, K Bosscha, RM van Dam, S Festen, B Groot Koerkamp, E van der Harst, IHJT de Hingh, G Kazemier, MS Liem, VE de Meijer, VB Nieuwenhuijs, D Roos, JMJ Schreinemakers,

Presenter: Anne Claire Henry | Regional Academic Cancer Center Utrecht, Netherlands

Background: Older patients with pancreatic cancer are increasingly being offered resection. Because outcome data on these patients are limited, we sought to investigate the short- and long-term outcomes in an unselected, nationwide patient cohort.

Methods: Data from the prospective Dutch Pancreatic Cancer Audit were analyzed, including all patients with pancreatic ductal adenocarcinoma undergoing resection between 2014 and 2016. Patients were classified into two age groups: < 75 and ≥75 years. 90-day postoperative mortality and major complications (i.e. needing invasive intervention or ICU admission, or causing organ failure) were compared using the Chi-square test. Overall survival (OS) was evaluated using Kaplan-Meier analysis in patients without 90-day complication-related mortality. Factors associated with OS and (neo)adjuvant chemotherapy were identified with multivariable Cox regression and logistic regression analyses.

Results: Of 874 patients, 207 patients were aged ≥75 years (24%) and 667 patients were aged < 75 years (76%). Postoperative mortality (8% versus 5%; $p=0.13$) and major complications (29% versus 27%; $p=0.67$) did not significantly differ. OS was 15 (95%-CI 13-18) months versus 20 (95%-CI 19-23) months ($p<0.01$). (Neo)adjuvant chemotherapy was given in 40% versus 73% of patients ($p<0.001$). Age was not independently associated with OS (HR 1.04 [95%-CI 0.86-1.24]; $p=0.70$). Age was, however, associated with receipt of (neo)adjuvant chemotherapy (OR 0.23 [95%-CI 0.17-0.35]; $p<0.001$). (Neo)adjuvant chemotherapy was associated with improved OS (HR 0.50 [95%-CI 0.41-0.60]; $p<0.001$).

Conclusion: Short-term outcomes after pancreatic resection were not significantly different for older patients. Survival was, however, shorter. This may be explained by the observation that elderly less often received chemotherapy.

P 34. THE IMPACT OF OBESITY AND SEVERE OBESITY ON POSTOPERATIVE OUTCOMES AFTER PANCREATODUODENECTOMY

CM Lattimore, WJ Kane, FE Turrentine, VM Zaydfudim

Presenter: Courtney Lattimore MD | University of Virginia, United States

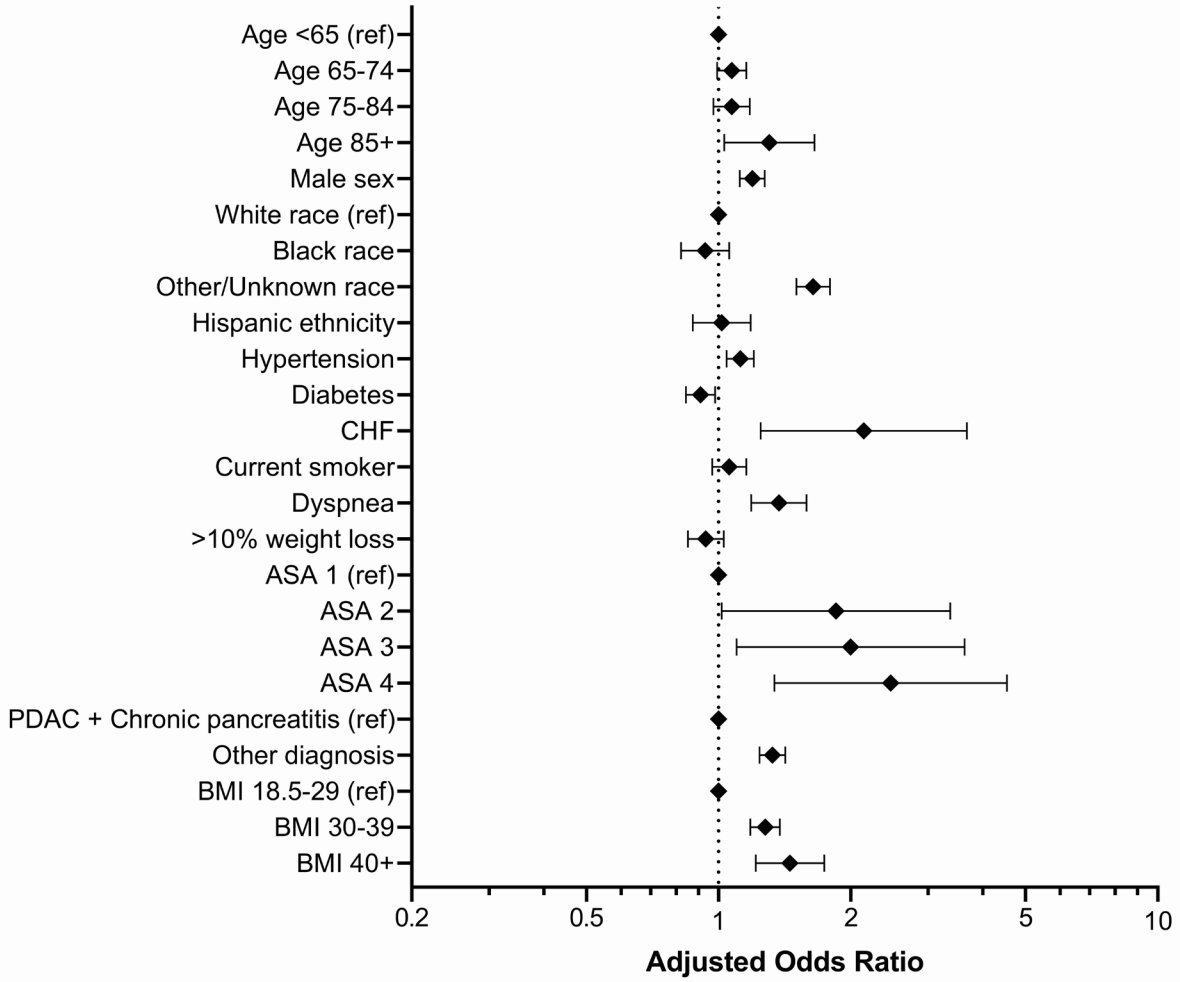
Background: The epidemic of obesity is affecting care delivery and health outcomes across societal strata. The impact of obesity on postoperative outcomes including operation-specific complications, morbidity, and mortality remains understudied for patients undergoing pancreatoduodenectomy for benign and malignant pancreatic disease.

Methods: Patients who underwent pancreatoduodenectomy were abstracted from the 2014-2018 American College of Surgeons National Surgical Quality Improvement Program (ACS NSQIP) Participant Use Data Files and joined with Targeted Pancreatectomy Participant Use Data Files to create the study dataset. Patients were stratified into three BMI categories: non-obese (BMI 18.5-29.9); class 1/2 obesity (BMI 30-39.9); and class 3 severe obesity (BMI>40). Patients with BMI < 18.5, ASA class 5 and emergency operations were excluded. Bivariable analyses tested associations between patient factors and 30-day postoperative outcomes including NSQIP-defined composite morbidity, mortality, delayed gastric emptying (DGE), and postoperative pancreatic fistula (POPF). Multivariable logistic regression models tested independent associations between patient factors and these four outcome measures. Multivariable logistic regression analyses were separately performed in a subgroup of patients with pancreatic adenocarcinoma, including clinically meaningful neoadjuvant chemotherapy and radiation covariates.

Results: 16,823 patients were included: 12,234 (72.7%) non-obese; 4,030 (24%) obese; and 559 (3.3%) with severe obesity. Obesity and severe obesity were associated with younger age and lower rates of smoking (both $p < 0.001$), however greater incidence of preoperative comorbid conditions: hypertension, diabetes, congestive heart failure, dyspnea, and higher rates of ASA class of 3 or 4 ($p \leq 0.008$). Both severe obesity and obesity were associated with a greater likelihood of post-operative complications when compared to non-obese patients, including grade B/C POPF (27.9% vs 21.8% vs 14.5%, $p < 0.001$), DGE (20.2% vs 17.5% vs 15.4%, $p = 0.001$), composite morbidity (41.0% vs 38.2% vs 32.5%, $p < 0.001$), and mortality (1.8% vs 2.2% vs 1.3%, $p < 0.001$). After adjusting for significant covariates, obesity was independently associated with increased grade B/C POPF (OR 1.48, 95% CI: 1.32-1.67, $p < 0.001$), DGE (OR 1.16, 95% CI: 1.05-1.28, $p = 0.004$), composite morbidity (OR 1.28, 95% CI: 1.18-1.38, $p < 0.001$; Figure), and mortality (OR 1.79, 95% CI: 1.36-2.36, $p < 0.001$). Similar associations were observed between severe obesity and increased grade B/C POPF (OR=2.07, 95%CI: 1.62-2.65, $p < 0.001$), DGE (OR=1.50, 95%CI: 1.21-1.87, $p < 0.001$), and composite morbidity (OR=1.51, 95%CI: 1.27-1.81, $p < 0.001$). In a subgroup analysis of 9,560 patients with pancreatic adenocarcinoma, 7,235 were non-obese, 2,063 were obese, and 262 had severe obesity. Obesity was independently associated with increased morbidity (OR 1.28, 95% CI: 1.15-1.42, $p < 0.001$), mortality (OR 1.83, 95% CI: 1.27-2.64, $p = 0.001$), and POPF (OR 1.37, 95% CI: 1.14-1.64, $p < 0.001$). Similarly, severe obesity was associated with increased morbidity (OR 1.40, 95% CI: 1.08-1.82, $p = 0.01$) and POPF (OR 1.57, 95% CI: 1.02-2.41, $p = 0.04$).

Conclusion: Obesity and severe obesity are significantly associated with worse short-term outcomes after pancreatoduodenectomy. Preoperative counseling, individualized weight management strategies, care coordination, and home monitoring programs could improve outcomes in this patient population.

Morbidity



P 35. THE ROLE OF MARGINS AMONG STAGE IIB AND STAGE III PANCREATIC DUCTAL ADENOCARCINOMA PATIENTS ON SURVIVAL

R Ahola, E Zwart, B Kurlinkus, A Halimi, B Yilmaz, G Belfiori, K Roberts, R Pande, GO Ceyhan, J Laukkarinen

Presenter: Reea Ahola PhD | Tampere University Hospital, Finland

Background: The aim of a pancreatic resection for pancreatic ductal adenocarcinoma (PDAC) is a complete tumour removal achieved by R0 resection. Histopathologic slicing technique is one of the factors influencing the proportion of R0. The aim of this study was to analyse the effect of margin widths on survival and disease recurrence among PDAC patients whose specimens were analysed according to a standardized axial method (Leed's protocol).

Methods: Multicentre databases were searched for pancreatic resections performed for pancreatic ductal adenocarcinoma between 2012 and 2017. Patients with a stage IIB disease were included. Patients with M1, R2 resection or who had received neoadjuvant therapy were excluded. The TNM-classification was updated according to the 8th version and stage IIB and stage III were analysed separately. Data on demographics, histopathology and oncologic treatment was recorded from the patient files. Overall survival, time to local recurrence and/or distant metastasis was analysed according to the minimum reported margin (MRM) for cutoffs 0mm, 0.5mm, 1mm and 2mm.

Results: The study population comprised 280 stage IIB and 339 stage III patients. Among stage IIB 84% and among stage III 91% of the patients had undergone pancreatoduodenectomy. A vein resection was more often performed for patients with stage III disease (21% vs. 29%, OR 1.60 (1.10-2.322) p=0.016). Among stage IIB 22% of the patients had an MRM of 0 mm, 66% over 0.5mm, 38% over 1mm and 17% over 2mm. Fifty-five percent of the stage IIB patients received adjuvant therapy postoperatively. In univariate analysis, survival was associated with age, tumour differentiation, MRM over 0mm and adjuvant therapy. In a multivariable analysis, adjuvant therapy and tumour differentiation was associated with survival. Data on local cancer recurrence was available for 88 patients. Time to recurrence was associated with adjuvant therapy and tumour differentiation in the multivariable analysis. Data on distant metastasis was available for 98 patients. Time to distant metastasis was associated with tumour differentiation and tumour size in the multivariable analysis.
Among stage III 35% of the patients had an MRM of 0mm, 54% over 0.5mm, 29% over 1mm and 11% over 2mm. Fifty-seven percent of the stage III received adjuvant therapy postoperatively. In univariate analysis the survival was associated with tumour differentiation, adjuvant therapy and negative vein resection. The multivariable analysis showed that adjuvant therapy was associated with better survival. Data on local cancer recurrence was available for 111 patients. Time to recurrence was associated with adjuvant therapy and preoperative CA19-9 level in a multivariable analysis. Data on distant metastasis was available for 120 patients. Time to distant metastasis was associated with patient age at the time of surgery in a multivariable analysis.

Conclusion: After analysing MRMs reported using uniform histopathologic slicing technique we conclude that they have only a partial role among other factors in determining survival and disease recurrence among PDAC patients with nodal involvement.

P 37. UPDATED TNM CLASSIFICATION FOR PANCREATIC CANCER: MORE PRACTICAL, BUT ROOM FOR IMPROVEMENT

AM Roch, RC Kim, SL Allen, EP Ceppa, NJ Zyromski, CM Schmidt, A Nakeeb, MG House, TK Nguyen

Presenter: Alexandra Roch MD, MS | Indiana University School of Medicine, United States

Background: The refined 8th edition of the AJCC TNM classification for pancreatic cancer sought to improve staging with a better distribution among T stages. The emphasis shifted from extrapancreatic invasion to tumor size and lymph node number. We hypothesized that the updated classification may result in undertreatment of patients.

Methods: From January 2016 to November 2020, 476 consecutive patients who underwent pancreatectomy for pancreatic ductal adenocarcinoma at a single academic center were included. Survival analysis was performed.

Results: Of the patients who met the inclusion criteria, 53% died over the study period, after a median of 14 months. The 7th AJCC TNM classification categorized 81% as pT3, whereas T stages were more evenly distributed in the 8th edition (T1:22.5%; T2:55.5%; T3:19.7%). T and N staging in either edition failed to predict survival in Cox regression. The newer classification resulted in 14.5% downstaging from stage III to stage I, with 40.5% of down-staged patients not receiving neoadjuvant treatment. Interestingly, however, it yielded the type of pancreatectomy ($p=0.038$), neoadjuvant chemotherapy ($p=0.003$), pathological response ($p=0.017$), grade ($p=0.003$), and extra-pancreatic invasion ($p=0.008$) as independent predictors of longer survival.

Conclusion: The 8th edition of the AJCC TNM staging for pancreatic cancer is easier to use and more reproducible. However, the emphasis on size results in down-staging of some patients and a corresponding decrease in neoadjuvant treatment. A more comprehensive system including extra-pancreatic invasion and grade to reflect tumor biology as in other cancers such as breast, may better impact prognostic accuracy and therapeutic decision making.

P 38. A RISK-ADJUSTED ANALYSIS OF DRAIN USE IN PANCREATICODUODENECTOMY: SOME IS GOOD, BUT MORE MAY NOT BE BETTER

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Presenter: Lisa Brubaker MD | Baylor College of Medicine, United States

Background: Intraperitoneal drain placement is presumed to decrease morbidity and mortality in patients who develop a clinically relevant post-operative pancreatic fistula (CR-POPF) following pancreaticoduodenectomy (PD). It is unknown whether multiple drains mitigate CR-POPF better than a single drain. We hypothesize that multiple drains decrease the complication burden more than a single drain, particularly in cases at greater risk for CR-POPF.

Methods: The Fistula Risk Score (FRS), mitigation strategies (including number of drains placed), and clinical outcomes were obtained from a multi-institutional database of PDs performed from 2003-2020. Outcomes were compared between patients receiving 0, 1, or 2 intraperitoneal drains. A risk-adjusted multivariable regression analysis was used to evaluate the optimal drainage approach.

Results: A total of 4292 PDs utilized 0 (7.3%), 1 (45.2%), or 2 (47.5%) drains with an observed overall CR-POPF rate of 9.6%, which was higher in intermediate/high FRS zone (FRS 3-10) cases compared to negligible/low FRS zone (FRS 0-2) cases (13% vs. 2.4%, $p < 0.001$). The number of drains placed correlated with FRS zone (median of 2 in intermediate/high vs. 1 in negligible/low risk cases). Obviation of drains was associated with increases in mortality regardless of the FRS zone (mortality rate 3% vs. 1.1% vs. 0.4%, $p = 0.017$ for negligible/low risk cases and 14.4% vs. 2.0% vs. 2.1%, $p < 0.001$ for intermediate/high risk cases with 0, 1, or 2 drains, respectively), as well as significant increases in morbidity for the intermediate/high risk cases (Figure 1). In contrast, the use of 1 drain instead of 2 had comparable rates of mortality, CR-POPF, average complication burden attributed to a CR-POPF and reoperations for the intermediate/high risk cases (Figure 1). Further, in a logistic regression model accounting for patient factors, operative details, and alternative risk-reducing strategies, the placement of 1 drain compared to 2 was associated with a lower incidence of CR-POPF (OR 0.59, 95% CI 0.415-0.839, $p = 0.003$) in the intermediate/high risk cases.

Conclusion: For pancreaticoduodenectomy, drain omission is associated with inferior outcomes. In intermediate/high risk zone cases, placement of a single drain appears to mitigate the complication frequency and burden just as well as multiple drains.

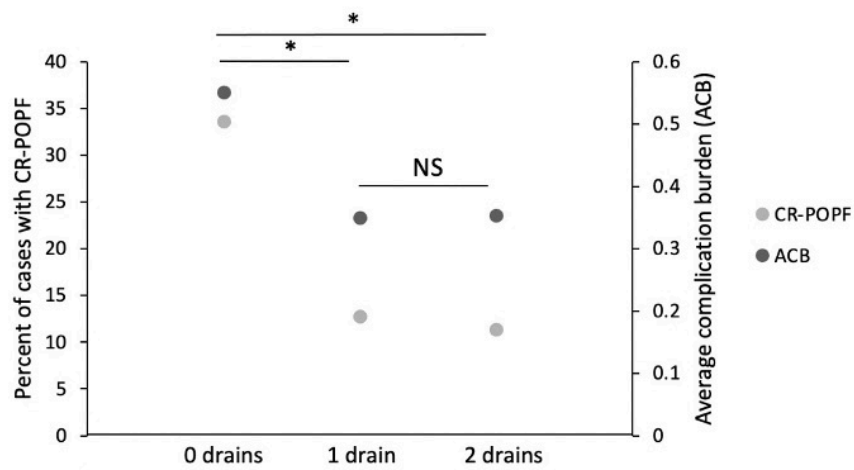


Figure 1: Comparison of clinical outcomes for the intermediate-high risk zone cases (n=2895) stratified by number of prophylactic drains placed. Placement of 0 drains was associated with a significantly higher incidence of CR-POPF and a higher average complication (ACB) burden attributed to the occurrence of a CR-POPF compared to the placement of 1 or 2 drains ($*=p<0.001$). There was no difference in the incidence of CR-POPF or ACB between cases with 1 or 2 prophylactic drains (NS= $p>0.05$).

P 39. AN ASSESSMENT OF PERIOPERATIVE OUTCOMES FOR OPEN, LAPAROSCOPIC, AND ROBOT-ASSISTED PANCREATICODUODENECTOMY IN NEW YORK STATE

M Wach, A Myneni, I Ibrahim-Zada, L Miller, S Schwaitzberg, K Noyes, C Gajdos

Presenter: Michael Wach MD | University at Buffalo, United States

Background: Pancreatic resection is a technically demanding procedure and associated with a high risk of complications. Minimally invasive techniques for pancreaticoduodenectomy (Whipple procedure) are increasing in practice however data remains limited regarding perioperative outcomes. Our study sought to compare patients undergoing Open pancreaticoduodenectomy (OPD) with those undergoing Laparoscopic pancreaticoduodenectomy (LPD) or Robot-assisted pancreaticoduodenectomy (RPD) for malignant and non-malignant conditions.

Methods: Patients who underwent PD during 2016-2018 were identified from the New York State Planning and Research Cooperative System database. Patients were stratified into OPD, LPD, and RPD groups and compared regarding preoperative characteristics, postoperative complications within 30 days (using ICD-10 and CPT codes), length of stay, and mortality. Propensity score weighted logistic regression models were used to examine outcomes.

Results: Of the 1,954 patients identified, 1,708 (87.4%) underwent OPD, 165 (8.4%) underwent LPD, and 81 (4.2%) underwent RPD. The majority of patients were white (36.8%) males (53.3%) with a mean age of 65.4 years. Most patients underwent resection for a malignant tumor (n=1,567, 80.2%) with patients undergoing LPD more frequently having a malignant diagnosis (90.9%) than those undergoing OPD (79.7%) or RPD (74.1%, $p < 0.01$). RPD patients had a lower median Charlson Comorbidity index score (2) than OPD (3) or LPD (3, $p = 0.01$) and were less likely to undergo an operation that involved major vascular resection/reconstruction than OPD or LPD (2.5% vs 12.1% vs 13.3%, $p = 0.01$). The mean annual hospital volume of PD operations performed was comparable among the groups (OPD 42.1 vs LPD 37.3 vs RPD 34.4, $p = 0.74$). After propensity matching, OPD demonstrated a longer length of stay (median 8 days) compared to LPD (7 days) or RPD (7 days, $p < 0.01$). There was no difference between the groups regarding 30-day overall complications, surgical site infections, anastomotic leaks, or mortality ($p = \text{NS}$ for all, Table 1). The severity of complications (Clavien-Dindo classification) was comparable among the groups ($p = 0.25$).

Conclusion: Patients undergoing LPD and RPD may have a shorter length of hospital stay compared to OPD however there was no difference in overall morbidity or mortality in our study.

Table 1. Postoperative (≤ 30 days) outcomes in a propensity score matched sample of patients (n=876) who underwent open/laparoscopic/robot-assisted pancreaticoduodenectomies (Whipple procedure) in New York State (2016-2018)

Outcome/variable	OPD	LPD	RPD	<i>p-value</i>
Sample size	730 (83.3)	73 (8.3)	73 (8.3)	
Length of stay (excludes deaths; n = 859)				
Median (Range)	8 (3–155)	7 (4–27)	7 (4–91)	<0.01
1-5 days	82 (11.5)	8(11.1)	24 (33.3)	<0.01
6-10 days	365 (51.1)	48 (66.7)	34 (47.2)	
>10 days	268 (37.5)	16 (22.2)	14 (19.4)	
Readmissions	144 (15.6)	8 (11.0)	10 (13.7)	0.62
Any postoperative complications (≤ 30 days)	343 (47.0)	32 (43.8)	26 (35.6)	0.17
Cardiovascular complications	39 (5.3)	9 (12.3)	4 (5.5)	0.08
Pulmonary complications	70 (9.6)	3 (4.1)	4 (5.5)	0.19
Sepsis	68 (9.3)	3 (4.1)	4 (4.1)	0.14
Surgical site infection/wound disruption	18 (2.5)	2 (2.7)	0 (0)	0.44
Postoperative abscess	56 (7.7)	3 (4.1)	3 (4.1)	0.43
Anastomotic leak	77 (10.6)	7 (9.6)	9 (12.3)	0.90
Clavien-Dindo classification of postoperative complications				
Mean (SD) (Excluding 0's)	3.1	3.3	3.3	0.25
2	113 (34.2)	9 (29.0)	6 (23.1)	0.27
3	90 (27.3)	4 (12.9)	8 (30.8)	
4	112 (33.9)	17 (54.8)	11 (42.3)	
5	15 (4.6)	1 (3.2)	1 (3.4)	
Death	15 (2.1)	1 (1.4)	1 (1.4)	1.00

P 40. ARTERIAL PEELING VERSUS RESECTION DURING PANCREATECTOMY FOR LOCALLY ADVANCED PANCREATIC CANCER

EF Kauffmann, N Napoli, C Gianfaldoni, M Ginesini, F Asta, C Cacace, F Vistoli, D Campani, U Boggi

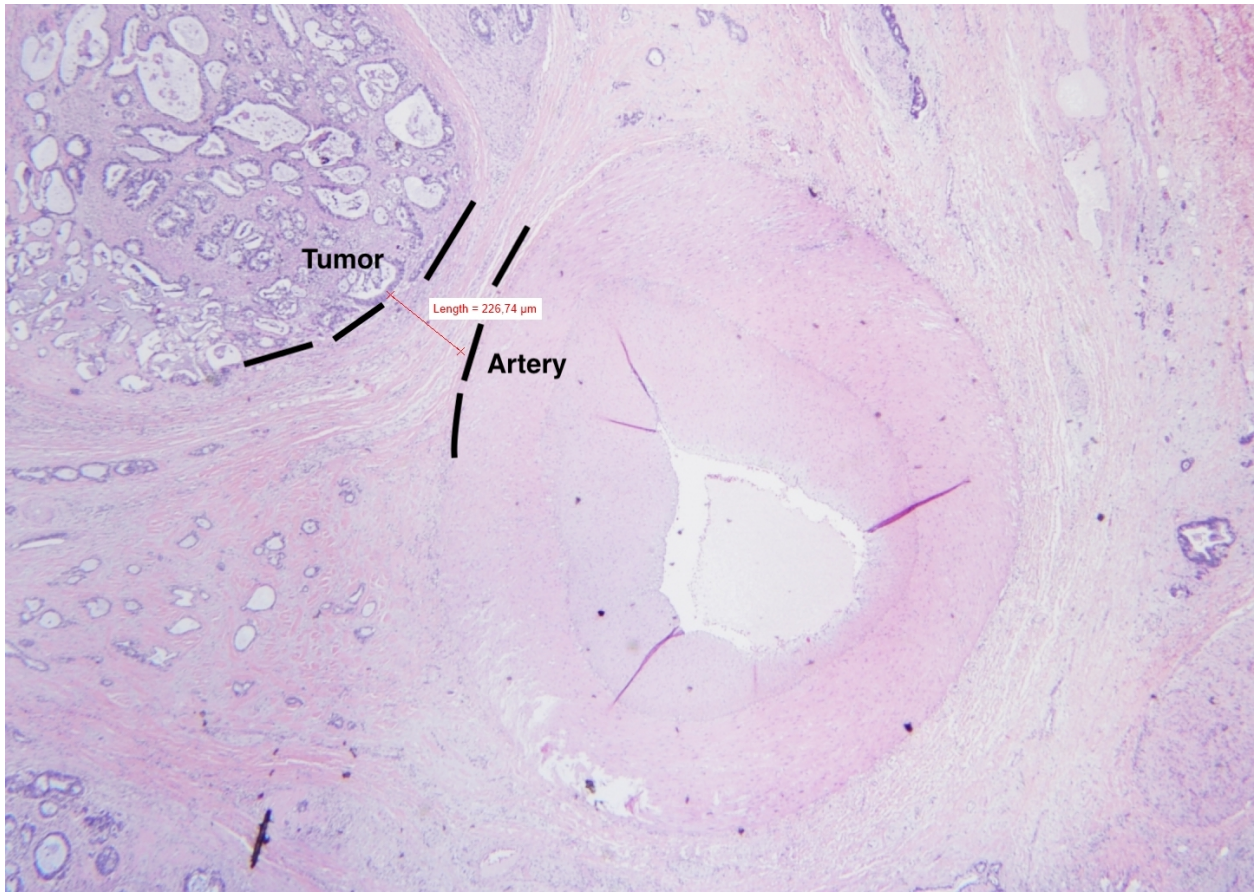
Presenter: Niccolò Napoli MD | University of Pisa, Italy

Background: In the setting of “locally advanced” pancreatic cancer, the development of a fibrotic reaction during neoadjuvant chemotherapy does not allow to intraoperatively understand if the vessels are really infiltrated by tumor or not. The use of intraoperative frozen section allows us to know the vessel status only in a limited area. Therefore, peeling the vessels instead of resection could lead to a higher rate of R1. Thus, the policy of our center is to resect the vessel. The aim of this work was to evaluate the difference in margin status if we had peeled the vessels instead of resecting it.

Methods: We retrospectively analyzed the distance of the tumor from the arterial vessel (figure 1) in patients underwent pancreatectomy plus arterial resection for “locally advanced” pancreatic cancer from August 2004 to May 2020 at our institution. Only patients with R0 margin and artery free from infiltration were considered. The distance of the tumor from hepatic artery (HA), celiac trunk (CT) and superior mesenteric artery (SMA) was evaluated. R1 resection is considered at 1 mm distance.

Results: In this period 119 pancreatectomies with arterial resection were performed. The distance between the tumor and the arterial wall was calculated in 22 patients. CT/HA was resected in 11 (50%) patients, SMA in 8 (36.3%) patients and both in 3 (13.6%) patients. Out of this, 16 (72.7 %) patients underwent neoadjuvant therapies. Pancreatic ductal adenocarcinoma was the main diagnose in 18 (81.8%) patients, in other cases malignant IPMN was present. Two (9.1%) patients died in the postoperative course. Major morbidity (Clavien-Dindo > 2) occurred in 4 (18.2%) patients. The median distance of the tumor was 1525 (371-2569) μm , 526 (150-2094) μm and 935 (335-1670) μm from HA, CT and SMA, respectively. A distance inferior to 1 mm was measured in 4 (40%), in 5 (71.4%) and in 6 (54.5%) patients for HA, CT and SMA respectively. The number of R1 resection in case of arterial peeling would have been 12 (54.5%) instead of 0 (0%).

Conclusion: Arterial resection seems to improve the number of radical resection (R0). Nevertheless, the differences between peeling and resection of the arterial vessels during pancreatectomy in term of morbidity, mortality and long-term survival remain to be established in the setting of multicenter comparative studies from referral centers.



P 41. ASSOCIATION BETWEEN GENETIC POLYMORPHISMS AND THE DEVELOPMENT OF BILIARY ACUTE PANCREATITIS: RESULTS OF A GENOME-WIDE ASSOCIATION STUDY

A Gaitanidis, M Christensen, M Farhat, P Fagenholz

Presenter: Apostolos Gaitanidis MD | Massachusetts General Hospital, United States

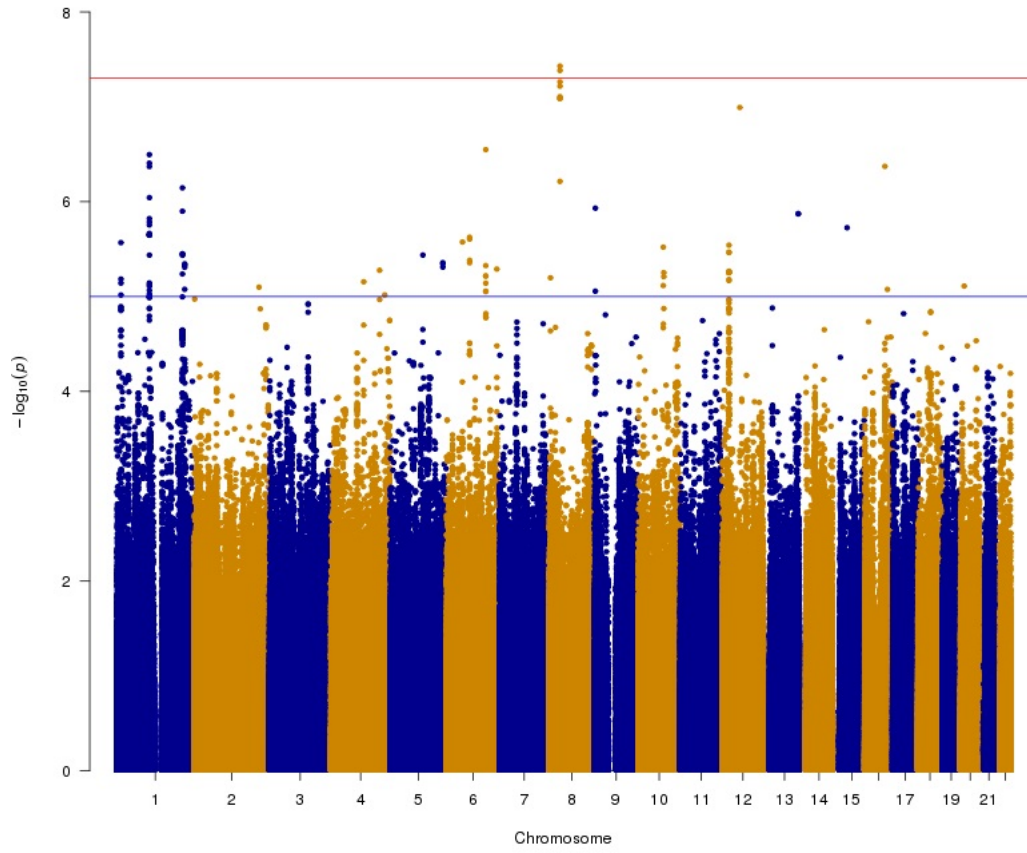
Background: Even though gallstones are the most common cause of acute pancreatitis (AP), only 3-7% of patients with gallstones develop AP. The predisposing factors underlying this discrepancy are not known. We hypothesized that genetic factors may play an important role. In this study, we performed the first genome-wide association study (GWAS) to identify common genetic loci associated with AP in a large US cohort and estimated the heritability of biliary AP.

Methods: Subjects genotyped as part of the Mass General Brigham (MGB) Biobank were examined. All patients with a previous history of biliary AP were identified using comprehensive chart review. The association between single nucleotide polymorphisms (SNPs) and biliary AP was evaluated using a mixed linear model-based analysis with GCTA v.1.91.1, controlling for age, sex, obesity and history of smoking. Only common SNPs were considered, using a minor allele frequency (MAF) cut-off of 0.05. The threshold for significance was set at 5×10^{-8} . The heritability of biliary AP was estimated using restricted maximum likelihood analysis using GCTA v.1.91.1. Functional assessment of the identified SNPs was performed using HAPLOREG v.4.1 in order to identify promoter (H3K4me3) and enhancer (H3K4me1) histone marks.

Results: Overall, 30,046 subjects were included, 176 of whom had a history of biliary AP. A genetic locus at chromosome 8p12 was associated with biliary AP (rs7824631, adjusted OR 1.02, $p=3.72 \times 10^{-8}$). The locus is located in exons of the UNC5D gene. The locus was not associated with cholelithiasis (rs7824631, $p=0.06$). The heritability of biliary AP was estimated at 18.6% (95% CI: 12.9-24.2%). Functional assessment demonstrated that all identified SNPs in 8p12 with $p < 10^{-8}$ were part of regulatory regions in the duodenal mucosa (promoter histone marks [H3K4me3]: rs7844971, rs6983275, rs6996645, rs7820516, rs6998947; enhancer histone marks [H3K4me1]: rs6983275, rs6996645, rs6998947) or the small intestine (promoter histone marks [H3K4me3]: rs113240179, rs16884365, rs7824631).

Conclusion: A region located in the UNC5D gene was found to be associated with biliary AP in a large US cohort. The identified SNPs may be part of promoter and enhancer regulatory regions in the duodenal mucosa and the small intestine, which may suggest implication of differential intestinal gene expression in the pathogenesis of biliary AP. Future studies are needed to better understand the genetic landscape of biliary AP.

Manhattan Plot



P 42. CA19-9 REDUCTION CORRELATES TO HISTOPATHOLOGIC TUMOR RESPONSE FOLLOWING NEOADJUVANT CHEMOTHERAPY IN PANCREATIC ADENOCARCINOMA

S AlMasri, M Zenati, RS Hoehn, AY Hammad, AD Singhi, N Bahary, SG Ellsworth, KK Lee, A Paniccia, AH Zureikat

Presenter: Victoria Kim MD | University of Pittsburgh Medical Center, United States

Background: Neoadjuvant chemotherapy (NAC) using 5FU- or gemcitabine-based regimens is becoming standard treatment for pancreatic ductal adenocarcinoma (PDAC). CA19-9 reduction has been shown to predict NAC response and survival. We aimed to examine the relationship between CA19-9 reduction and pathologic tumor response (pTR) to NAC.

Methods: A retrospective review of PDAC patients who received NAC followed by surgical resection at a high-volume pancreas center was performed. Analysis was limited to patients who did not receive neoadjuvant radiation, had elevated CA19-9 pre-NAC (with normal bilirubin), and repeat CA19-9 post-NAC. CA19-9 response was defined as normalization (50% reduction with NAC. College of American Pathologists score (CAP 3=none/poor, 2=partial/moderate, 1/0=near/complete) or synoptic description was used to determine pTR. Univariate and multivariate analyses identified predictors of progression-free survival (PFS) and overall survival (OS).

Results: 222 patients treated between 2009-2019 were analyzed (30.6% CAP 3, 61.7% CAP 2, 4.9% CAP 1/0). Patients with no pTR were older with more comorbidities ($p < 0.05$). Near/complete pTR was associated with higher R0 rates, less neurovascular invasion, and less node-positive disease (all $p < 0.05$). CA19-9 response correlated with pTR (CAP 3=19% vs CAP 2= 39% vs CAP 1/0= 64%, $Rho = -0.201$, Spearman's correlation 0.247, all $p < 0.01$). On multivariate analysis, pTR was predicted by CA19-9 response (OR 2.94, 95%CI 1.44-5.99, $p < 0.05$). CA 19-9 response and pTR were both associated with improved PFS ($p < 0.05$), but only CA 19-9 response was associated with improved OS ($p < 0.05$). On adjusted analysis, CA19-9 response independently predicted improved OS (HR 0.49, 95%CI 0.33-0.72), whereas pTR did not. Combining CA19-9 response with pTR demonstrated an additive effect in predicting OS.

Conclusion: CA19-9 response and pTR correlate among patients receiving NAC for PDAC. pTR is associated with other local tumor characteristics but not survival, while CA19-9 independently predicts progression-free and overall survival.

P 44. COMBINED MULTIAGENT CHEMOTHERAPY AND RADIOTHERAPY IS ASSOCIATED WITH PROLONGED OVERALL SURVIVAL IN PATIENTS WITH NON-OPERATIVELY MANAGED STAGE II-III PANCREATIC ADENOCARCINOMA

K Sugumar, JJ Hue, JM Hardacre, JB Ammori, LD Rothermel, J Dorth, J Saltzman, A Mohamed, E Selfridge, D Bajor, JM Winter, LM Ocuin

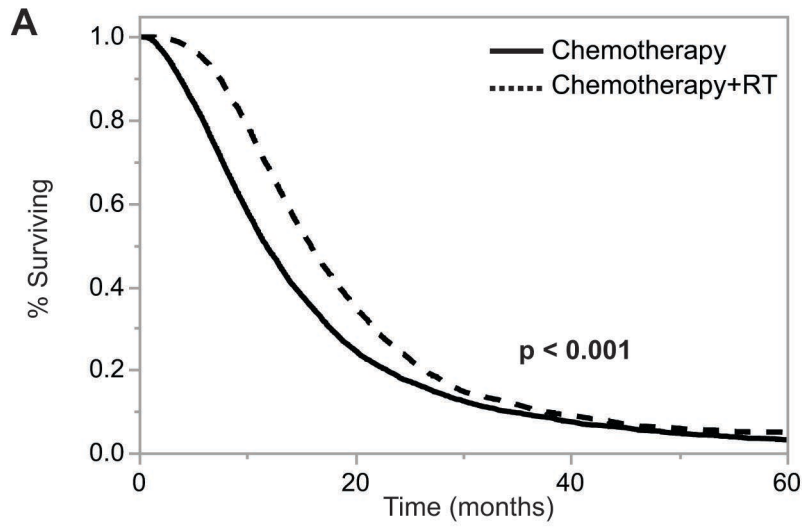
Presenter: Kavin Sugumar MD | Case Western Reserve University School of Medicine, United States

Background: The majority of patients diagnosed with pancreatic adenocarcinoma (PDAC) do not undergo surgical resection. The role of systemic chemotherapy (CT) is well defined, but the role of radiotherapy (RT) in non-operatively managed localized pancreatic adenocarcinoma is unclear. We used a large administrative database to compare survival between patients treated with CT and those treated with CT+RT.

Methods: The National Cancer Database (2010-2016) was queried for patients with clinical stage II-III PDAC who were managed non-operatively and treated with multiagent systemic CT +/- RT. We analyzed for demographic and clinical variables associated with the receipt of RT by multivariable logistic regression analysis. Overall survival was compared, adjusting for demographic and clinical variables by Cox proportional hazards regression analysis.

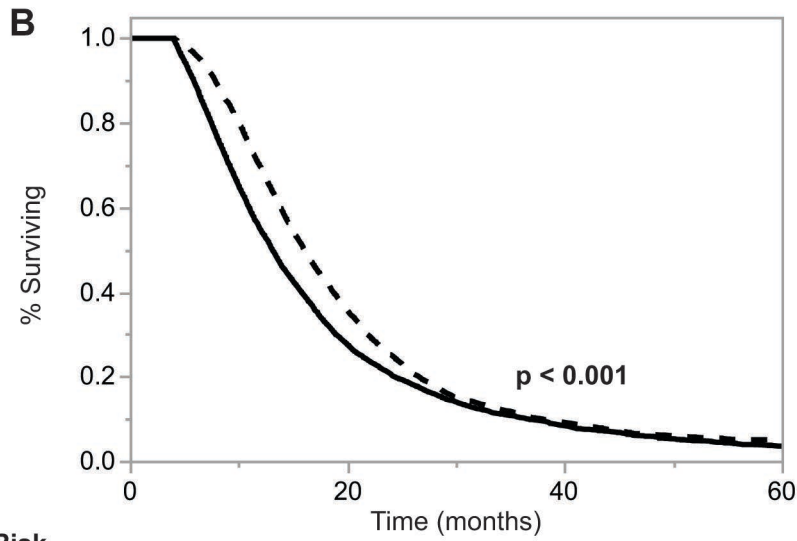
Results: A total of 14,921 patients were included, of whom 9,279 received CT and 5,382 received CT+RT. Patients treated with CT+RT were younger (65 vs 66 years), more often treated at non-academic facilities (48.8% vs 46.7%) and more often had private insurance (40.3% vs 36.5%). Additionally, patients who received CT+RT had a higher proportion of clinical T4 tumors (53.6% vs 48.7%). Median time from diagnosis to start of multiagent CT was similar between patients treated with CT compared to those treated with CT+RT (29 vs 28 days). For patients treated with CT+RT, most patients received external beam radiotherapy (89.3%), median time to start of RT was 129 days, and the median dose was 5000 cGy. On multivariable analysis, factors associated with receipt of RT included age (OR 0.99, 95% CI 0.98-0.99), Medicaid (OR 0.72, 95% CI 0.58-0.88), clinical T4 tumors (OR 1.28, 95% CI 1.04-1.57), clinical N1 disease (OR 0.89, 95% CI 0.80-0.98), and CA19-9 >37 U/ml (OR 0.85, 95% CI 0.77-0.95). CT+RT was associated with longer overall survival (15.9 vs 11.8 months, $p < 0.001$, Figure A), and remained independently associated with survival on multivariable Cox proportional hazards analysis (HR 0.74, 95%CI 0.70-0.78) compared to CT alone. On a 4-month landmark survival analysis, combined CT+RT remained associated with improved overall survival compared to CT alone (16.0 vs 13.1 months, $p < 0.001$, Figure B).

Conclusion: In patients with localized pancreatic adenocarcinoma that do not undergo surgical resection, combined radiotherapy and multiagent systemic chemotherapy is associated with improved overall survival compared to chemotherapy alone.



Number at Risk

Chemotherapy	7046	1468	249	48
Chemotherapy+RT	4443	1415	222	55



Number at Risk

Chemotherapy	6162	1468	249	48
Chemotherapy+RT	4361	1415	222	55

P 45. DOES RACE AFFECT THE LONG-TERM SURVIVAL BENEFIT OF SYSTEMIC THERAPY IN PANCREATIC ADENOCARCINOMA?

A Irfan, HA Fang, S Awad, A Alkashah, SM Vickers, O Gbolahan, GR Williams, MJ Heslin, V Dudeja, JB Rose, S Reddy

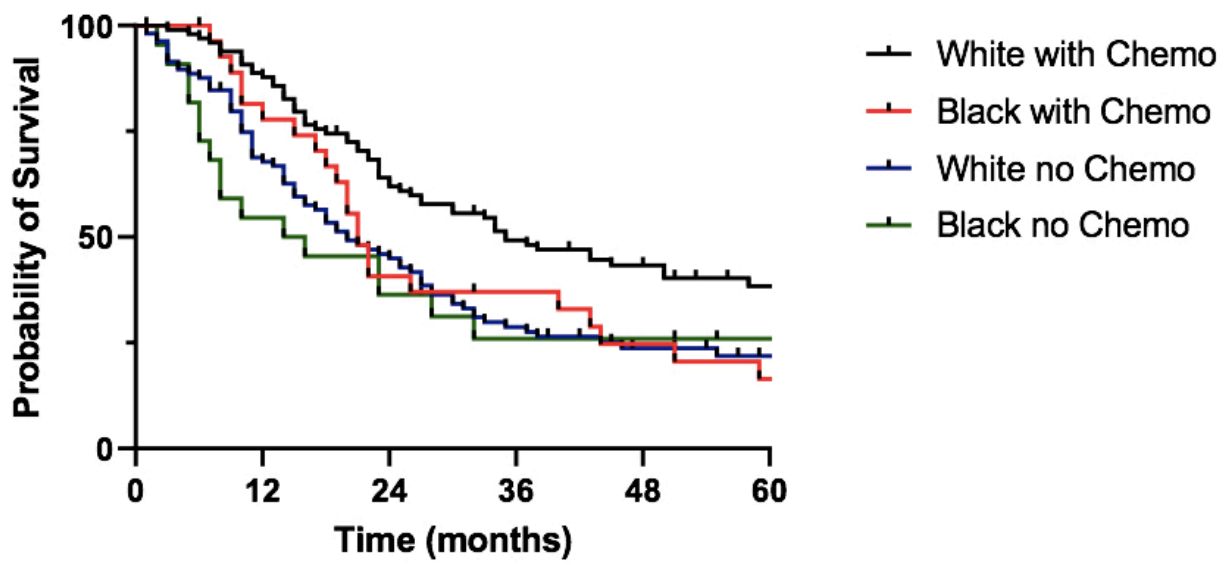
Presenter: Ahmer Irfan MBChB, MRCS | University of Alabama at Birmingham, United States

Background: Pancreatic Adenocarcinoma (PDAC) is increasingly viewed as a systemic disease. There are known disparities in PDAC outcomes by race. As chemotherapy regimens have developed, the use of systemic therapy is now a key component in the management of PDAC, often in combination with surgical resection. As socioeconomic variables have been linked to variations in outcomes in patients with PDAC; we sought to investigate if race impacted survival in patients who underwent systemic therapy in combination with resection for PDAC.

Methods: A retrospective analysis of a prospectively collected database was performed for all patients who underwent surgical resection for a PDAC at a tertiary center over an 8-year period (2010-2018). There was no protocolized administration of adjuvant systemic therapy, and it could be administered at the discretion of individual providers.

Results: 234 patients (183 White, 78.2%; 51 Black 21.8%) were included in our analysis. Black patients were more likely to present at a younger age (62.5 vs 66.3 years, $p=0.03$) but had larger tumors (3.6 vs 3.0cm, $p=0.02$) compared to White patients. The two groups had no differences in tumor T-stage (T1: 11.2% vs 6.3%, T2: 13.5% vs 16.3%, T3: 74.7% vs 72.9%, $p=0.06$), positive resection margins (12% vs 12%, $p=1.0$), lymph node positivity (60.2% vs 58.8%, $p=0.86$), or evidence of lymphovascular (41.1% vs 28.9%, $p=0.14$) or perineural (73.4% vs 76%, $p=0.71$) invasion. Although not statistically significant, Black patients were more likely to receive systemic therapy (54.9% vs 40.7%, $p=0.07$), but there were no differences in specific agents used between the races (gemcitabine ($p=0.37$), 5-fluorouracil ($p=0.39$), protein-bound paclitaxel ($p=0.75$), oxaliplatin ($p=0.18$), cisplatin ($p=1.0$), leucovorin ($p=0.32$), and irinotecan ($p=0.28$)) or number of cycles used (mean, 6.5 vs 6.2 cycles, $p=0.67$). White patients benefited from systemic therapy with longer overall survival (median 35 vs 20 months, $p=0.002$). However, this survival advantage was not present in Black patients who received systemic therapy (median 21 vs. 15 months, $p=0.15$). Black patients who got systemic therapy did experience an early survival advantage over Black patients who did not (1 yr. overall survival, 77.8% vs. 54.5%, $p=0.003$) but this was eliminated later (2 yr. overall survival, 40.7% vs. 36.4%, $p=0.21$, Figure). In fact, Black patients receiving systemic therapy had similar survival as White patients who did not ($p=0.81$).

Conclusion: Black PDAC patients present at younger ages and with larger initial tumors. In our limited population, systemic therapy was more effective in White patients than Black patients. These findings may indicate differences in tumor biology between races. Further prospective studies are planned to investigate this difference.



P 46. FORMAL ROBOTIC TRAINING DIMINISHES THE LEARNING CURVE FOR ROBOTIC PANCREATODUODENECTOMY: IMPLICATIONS FOR NEW PROGRAMS IN COMPLEX ROBOTIC SURGERY

BR Niemann, CR Schmidt, KA Musgrove, P Rao, JW Marsh, AA Thomay, ME Hogg, HJ Zeh, AH Zureikat, BA Boone

Presenter: Britney Niemann MD | West Virginia University School of Medicine, United States

Background: Robotic pancreatoduodenectomy (RPD) is safe with increasing utilization. The learning curve associated with RPD is a hurdle to implementing new programs. Since initial learning curve analyses, robotic training has expanded, and the RPD approach has been refined. The purpose of this study is to examine RPD outcomes for surgeons who implemented a new program after formal RPD training to determine if such training reduces or eliminates the learning curve.

Methods: Patient demographics, pathologic characteristics, and 90-day post-operative outcomes for consecutive patients undergoing RPD at a single tertiary institution from October 2018 to June 2020 were compared to optimal RPD benchmarks from a previously reported learning curve analysis. Exclusion criteria for the robotic approach included the anticipated need for vein resection or extensive prior abdominal surgery. Two surgical oncologists with formal training in RPD performed all operations with one surgeon as bedside assistant and the other at the console.

Results: Consecutive pancreatoduodenectomy operations during the study period were completed using the RPD approach in 40 patients and the open approach in 12. Mean operative time for RPD was 354 ± 54 minutes, and median estimated blood loss was 300 ml (IQR 60-500 ml). Median length of stay was 7 days (IQR 6-10), and a median of 26 lymph nodes were harvested (IQR 16-28). Three RPD patients (7.5%) underwent conversion to an open procedure. Morbidity occurred in 55% of patients with pancreatic fistula (ISGPS grade B/C) noted in 5 (12.5%). Readmission occurred in 12 patients (30%). Operative time was stable over the study period and lower than the previously reported benchmark. These RPD operative outcomes were similar to reported outcomes for surgeons after the usual learning curve.

Conclusion: This study suggests formal robotic training facilitates safe and efficient adoption of RPD for new programs, reducing or eliminating the learning curve. Further study of RPD outcomes from surgeons with formal training is required to validate these single institution findings. Once validated, formal training should be a required standard for complex operations including RPD and similar procedures such as robotic esophagectomy and robotic cardiothoracic procedures.

	Post-Learning Curve Benchmarks* (n=120)	Initial RPDs w/ Formal Training (n=40)	p
Operative time, min	417 ± 78	354 ± 54	<0.0001
Estimated blood loss,ml	250 (150-400)	300 (160-500)	0.10
Rate No. (%)			
Conversion	3.3	7.5	0.37
Transfusion	21.7	12.5	0.35
Pancreatic Fistula (ISGPF grade B/C)	6.9	12.5	0.32
Readmission	29.2	30	0.99
90-Day Mortality	3.3	0	0.57
R0 resection	91.4	92.5	0.99
Clavien-Dindo classification rate (%)			
<3	43.2	32.5	0.26
>3	23.3	25	0.83
Length of stay, days	9 (7-14)	7 (6-10)	<0.0001
Lymph node harvest	26 (19-32)	26 (16-28)	0.11

*Boone, BA, Zenati M, Ho gg ME. Assessment of Quality Outcomes for Robotic Pancreaticoduodenectomy. JAMA Surg. 2015; 150(5):416-422.

P 47. INCIDENCE AND PREDICTORS OF INFECTION IN SYMPTOMATIC PERI/PANCREATIC NECROTIC COLLECTIONS- A PROSPECTIVE STUDY

M Mandal, V Bhargav, SS Rana, M Kang, A Chakrabarti, V Gupta, P Kumar M, R Gupta

Presenter: Meenakshi Mandal MD | Postgraduate Institute of Medical Education and Research, India

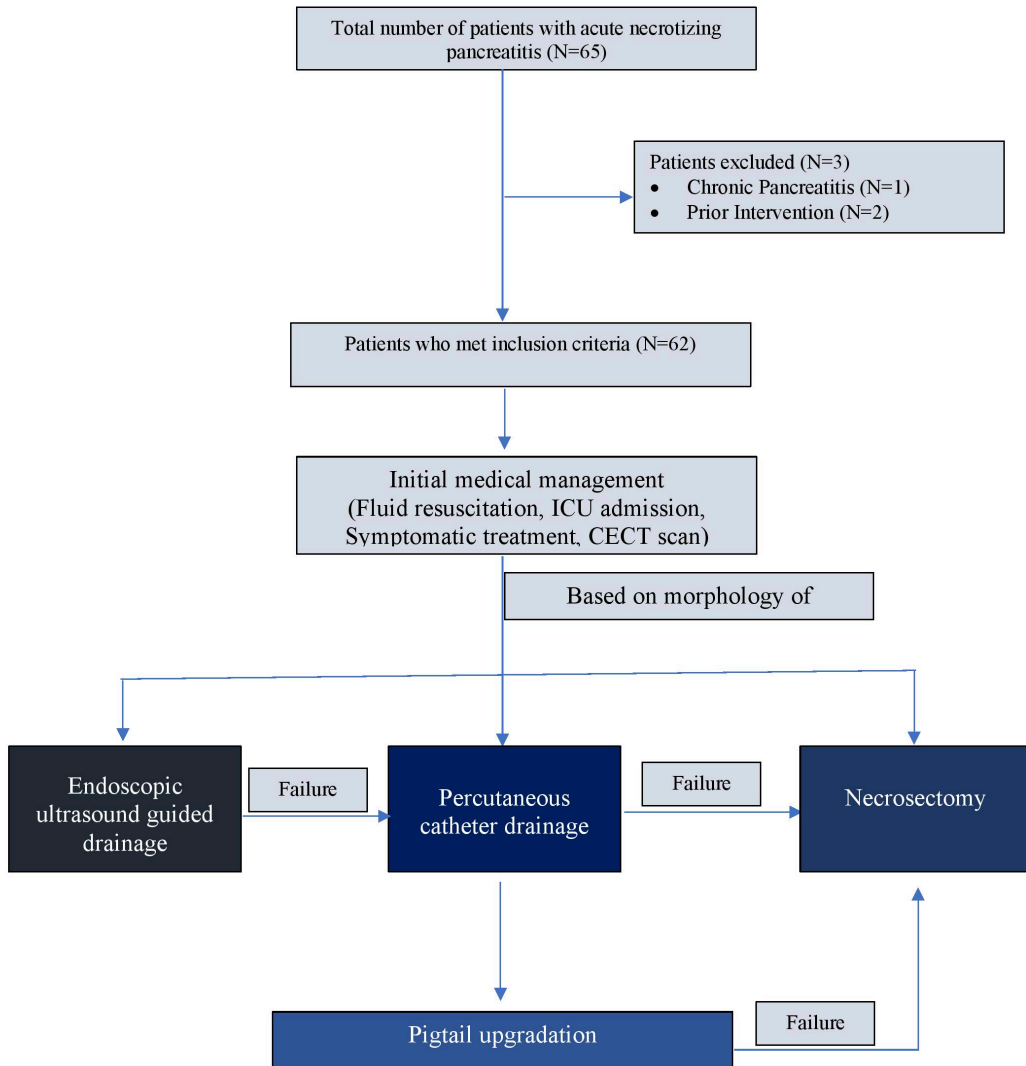
Background: Necrotizing pancreatitis is seen in 15-20% of patients of acute pancreatitis. They can remain sterile or may get infected. Infected pancreatic necrosis (IPN) is associated with poor outcomes. Present study looked at incidence of infection and predictors in symptomatic peri/pancreatic collections.

Methods: Prospective clinical observational study done between July 2019 to October 2020. Symptomatic patients of acute necrotic collections (ANC) and walled off necrosis (WON) of pancreas requiring drainage were included. Demographic parameters and radiological findings were noted. Necrotic fluid drained during percutaneous intervention, endoscopic drainage, necrosectomy and blood were analysed for bacterial and fungal infection. Data was critically analysed to identify any early predictors of infection.

Results: Sixty-two patients were included, out of which 11 were females and 51 were males. Mean age was 36.8 ± 11.5 years. Commonest etiology of acute necrotizing pancreatitis (ANP) was alcohol (53%). Eighteen patients (29.1%) had sterile necrotic collection while 44 patients (70.9%) had IPN. Twenty-three (37%) patients had infected blood cultures. Patients with IPN had higher APACHE-II score at admission. Other demographic characters were comparable between the two groups. Eighteen patients had splanchnic venous thrombosis (SVT) on initial CECT scan, out of which, 17 developed IPN (94%; $p=0.022$) (PPV=94.4%, NPV=38.6%), and 11 had infected blood cultures (61%; $p=0.027$). On multivariate analysis, SVT was significantly associated with IPN ($p=0.009$) and infection in blood ($p=0.012$) as well as polymicrobial growth in both necrotic fluid aspirate ($p=0.015$) and blood ($p=0.02$). IPN was more likely to be associated with higher MCTSI score ($p=0.034$), multiple organ failure ($p=0.019$), higher chances of surgical necrosectomy ($p=0.048$), longer ICU stay ($p<0.001$) and higher mortality ($p=0.006$) as compared to sterile collection. Commonest organisms isolated from IPN were *Escherichia coli* (40.9%), *Klebsiella pneumoniae* (38.6%), *Acinetobacter baumannii* (22.7%) and *Enterococcus sp.* (15.9%). Blood cultures grew *Staphylococcus sp.* (43.4%) and *Acinetobacter baumannii* (26.08%) as the most common organisms. Patients growing *E. coli* in necrotic collections had higher APACHE-II score at admission ($p=0.030$), more chances of cardiovascular organ failure ($p=0.048$) and higher mortality ($p=0.017$). *E. coli* isolated were most susceptible to amikacin (77.7%), colistimethate (72.2%) and imipenem (50%). Patients with infected blood cultures had longer ICU stay ($p=0.001$) and higher mortality ($p=0.038$). The presence of *Acinetobacter* in blood was associated with a longer ICU stay ($p=0.032$). Overall mortality rate of the cohort was 23%, with no mortality in sterile collection and 31.8% in IPN.

Conclusion: More than 2/3rd of symptomatic peri/pancreatic necrotic collections were infected in our set up and incidence of bacteremia was 37%. Presence of splanchnic venous thrombosis on CECT scan was a significant risk factor for development of IPN, bacteremia and polymicrobial growth in both necrotic fluid aspirate as well as blood. These, in turn, affect outcome, surgical interventions and mortality in these patients. Based on these findings, we propose to add splanchnic venous thrombosis as one more factor in calculating modified CTSI score.

Figure 1: Flowchart of patient selection and management



P 48. IRREVERSIBLE ELECTROPORATION VERSUS CHEMOTHERAPY WITH OR WITHOUT RADIOTHERAPY FOR UNRESECTABLE LOCALLY ADVANCED PANCREATIC ADENOCARCINOMA: A SYSTEMATIC REVIEW AND META-ANALYSIS

K Sugumar, A Hurtado, I Naik, JJ Hue, LD Rothermel, JB Ammori, JM Hardacre, JM Winter, LM Ocuin

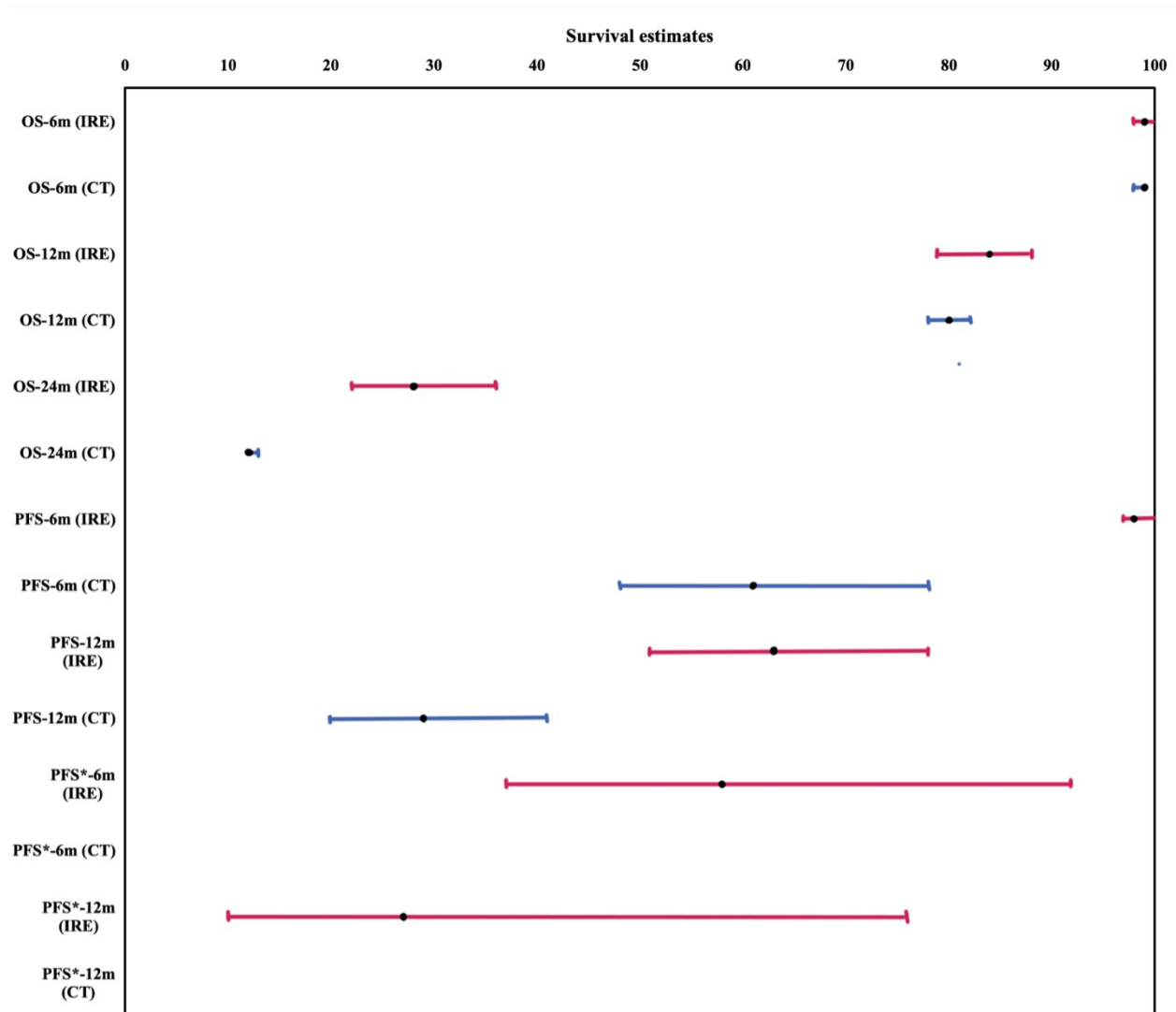
Presenter: Kavin Sugumar MD | Case Western Reserve University School of Medicine, United States

Background: Multi-agent chemotherapy (CT) +/- radiotherapy (RT) is the standard treatment for patients with non-metastatic, locoregionally unresectable pancreatic adenocarcinoma. Irreversible electroporation (IRE) has been described as a locoregional treatment modality for LAPC patients, but postoperative morbidity and mortality rates are high for an invasive, non-curative intervention. Few studies compare IRE with chemotherapy +/- RT. We performed a comprehensive meta-analysis of the available literature comparing overall survival, progression-free survival, and treatment-related complications between these groups.

Methods: A systematic literature search was performed in Medline and Embase in January 2020. Due to the paucity of studies (n=3) that compare IRE to chemotherapy +/- RT, two separate literature searches were performed. Studies evaluating the outcomes of IRE combined with or without CT were included and grouped into the IRE cohort. Studies in which CT +/- RT only were utilized were grouped as the chemotherapy (CT) cohort. The primary outcomes evaluated were overall survival (OS; at 6/12/24 months) and progression free survival (PFS; at 6/12 months) defined from the time of diagnosis. Additional OS/PFS analyses in the IRE group were performed starting from the time of procedure. Forest plot analyses were used to calculate the weighted average survival estimates (OS and PFS) at the specified time points. Secondary outcomes included treatment related morbidity and mortality.

Results: Of 585 published articles, 27 and 21 studies met inclusion criteria for the IRE and CT groups, respectively. All studies were observational cohort studies except for 4 phase I-II trials (8%). Combined, these studies included clinical data on 1420 (IRE) and 1348 (CT) patients. The pooled 6-, 12-, and 24-month OS estimates for the IRE group were 99%, 84%, and 28%. The pooled 6-, 12-, and 24-month OS estimates for the CT group were 99%, 80%, and 12% (Figure). There was overlap in the 95% confidence intervals of OS among the treatment groups. The pooled 6- and 12-month PFS estimates for IRE were 98% and 63%, and for CT were 61% and 29% (Figure-1). From the IRE procedure, 6-, 12-, and 24-month OS was 89%, 55%, and 12%, and 6-/12-month PFS was 58% and 27%. From the CT procedure, 6- and 12-month PFS was 58% and 27%. The median major complication (Clavien-Dindo ≥ 3) and 90-day mortality rates reported in the IRE group were 12% (range: 0-53%) and 2% (range: 0-17%), respectively. The median grade 3-4 adverse effect score in the CT group was 24% (range: 14-52%), and there were no associated treatment-related deaths.

Conclusion: There is a striking paucity of studies comparing IRE with the standard of care treatment approaches for LAPC. From time of diagnosis, it appears that IRE has similar OS compared to multiagent CT +/- RT and may have better PFS at 6- and 12-months. However, the majority of patients progress and nearly half die within 1 year of the IRE procedure. Reported non-curative IRE-related morbidity and mortality rates approach those associated curative-intent pancreatectomy. Until high quality, prospective studies with standardized indications are conducted, IRE should be used with caution and remains experimental in the treatment of pancreatic adenocarcinoma.



Time point	IRE	Chemotherapy
OS		
6-month	0.99 (0.98-1)	0.99 (0.98-0.99)
12-month	0.84 (0.79-0.88)	0.80 (0.78-0.82)
24-month	0.28 (0.22-0.36)	0.12 (0.12-0.13)
PFS		
6-month	0.98 (0.97-1)	0.61 (0.48-0.78)
12-month	0.63 (0.51-0.78)	0.29 (0.20-0.41)
PFS (from IRE procedure)		
6-month	0.58 (0.37-0.92)	N/A
12-month	0.27 (0.1-0.76)	N/A

*PFS from IRE procedure

P 49. MORBIDITY AND MORTALITY FOLLOWING PANCREAS SBRT

SG Ellsworth, A Desilva, SA Burton, AC Olson, KKW Lee, A Paniccia, N Bahary, AH Zureikat

Presenter: Susannah Ellsworth MD | University of Pittsburgh Medical Center, United States

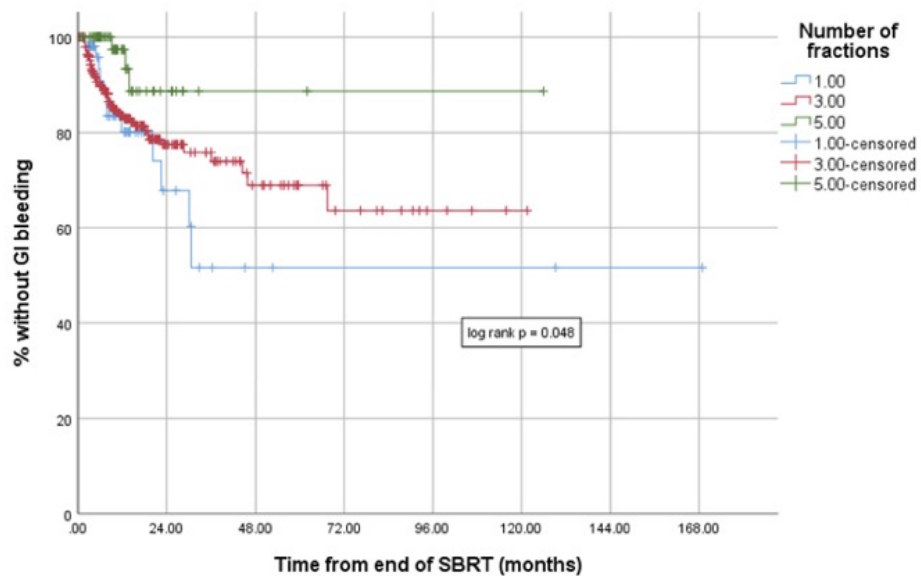
Background: Stereotactic body radiotherapy (SBRT) is frequently utilized to optimize local control in both resected and inoperable pancreatic cancer (PC). Short- and medium-term morbidity and mortality rates following SBRT for PC have not been previously reported. We analyzed acute morbidity and mortality rates and incidence of late vascular toxicity (GI bleeding and visceral pseudoaneurysm) following SBRT for PC.

Methods: Outcomes were abstracted from a single-institution registry-based series of 464 patients, representing 474 SBRT courses. Hospital and clinic records were reviewed to identify death date/cause of death, any hospital admission within 90 days of the last RT fraction, and instances of upper GI bleeding at any time following SBRT. Survival was calculated from the last day of radiation.

Results: Median age was 69 years (range 32-91); 49.8% of patients were women, and the majority (93%) had adenocarcinoma. SBRT was performed perioperatively in 184 patients (59/12.4% neoadjuvant and 125/26.4% adjuvant); the remainder had definitive (202/42.7%) or salvage (44/9.3%) treatment. Most patients received 3 fractions (n = 301, 63.5%); 91 (19.2%) received single-fraction SBRT, and 72 patients (15.2%) received 5 fractions. Nine patients (1.9%) died within 30 days of SBRT. Cause of death was unknown in 3 patients, with 3 dying of progressive disease, 2 of infection, and 1 of pulmonary embolism. Twenty-six patients (5.1%) died between 31 and 90 days after SBRT. Cause of death was unknown in 9; 12 died of disease progression, 4 of infection, and 1 of GI bleed. SBRT type (perioperative vs. definitive), patient age, and prior radiation to the pancreas were not correlated with early mortality risk. Thirty-eight patients (8.2%) were admitted within 30 days of SBRT, and 63 (13.6%) were admitted between 31 and 90 days. The most common admission diagnosis during both the first 30 and 90 days after RT was infection, followed by GI bleeding and bowel obstruction. For the whole cohort, crude GI bleed risk following SBRT was 13.3% (62/464) and was significantly correlated with fractionation scheme (Figure 1). After excluding patients who were lost to follow-up, crude rates of GI bleeding were 22.6% (12/53), 18.8% (47/250), and 4.5% (3/66) in patients treated with 1, 3, and 5 fractions, respectively.; compared with patients undergoing 1- and 3-fraction regimens, respectively, HR for GI bleeding in patients treated with 5 fractions was 0.172 (95% CI 0.046-0.645) and 0.205 (95% CI 0.062-0.681). Six patients (1.3%) developed visceral pseudoaneurysm.

Conclusion: SBRT for pancreatic cancer is associated with relatively low rates of acute morbidity and mortality, although infection and early disease progression are important causes of hospitalization and death in this medically fragile population. GI bleeding risk is highly sensitive to RT fractionation regimen, which may help inform future studies of SBRT dose escalation in PC.

Figure 1. Kaplan-Meier curve illustrating GI bleeding risk for differing SBRT fractionation regimens. Blue – 1 fraction; Pink – 3 fractions; Green – 5 fractions.



P 50. NATIONWIDE EXPERIENCE OF TOTAL PANCREATECTOMY WITH ISLET CELL AUTOTRANSPLANT FOR CHRONIC PANCREATITIS: BENCHMARK METRICS AND TRENDS IN OUTCOMES

TK Maatman, SP McGuire, KA McGreevy, EL Fogel, MG House, NJ Zyromski

Presenter: Thomas Maatman MD | Indiana University School of Medicine, United States

Background: Total pancreatectomy with islet cell autotransplant (TP-IAT) is increasingly performed for patients with small duct or genetic chronic pancreatitis (CP). This complex procedure is performed at a small number of highly experienced pancreatic centers; postoperative outcomes after TP-IAT have not been systematically evaluated at a national level. The aim of this study was to evaluate frequency and risk factors for major morbidity and mortality after TP-IAT. We hypothesized that postoperative outcomes have improved over time with increasing utilization of TP-IAT for chronic pancreatitis.

Methods: The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) Participant Use Files (PUF) were queried to identify patients undergoing TP-IAT for CP between 2006 and 2018. Major morbidity was defined as Clavien-Dindo grade III or higher level complications. Incidence and risk factors for major morbidity and mortality were evaluated with the chi-squared test, Student's t-test, and multivariable binary logistic regression. P values < 0.05 were accepted as statistically significant.

Results: A total of 453 patients underwent TP-IAT. The mean age was 42±12 years and 68% of patients were female. Major postoperative morbidity developed in 88 (19%) patients and most commonly included unplanned repeat operation (n = 56, 12%), organ space surgical site infection (n = 39, 9%), and failure to wean from mechanical ventilation (n = 19, 4%). Multivariable analysis identified increasing age (OR, 1.024; 95% CI, 1.003-1.046; p = 0.027) and operative time (OR, 1.12; 95% CI, 1.0003-1.236; p = 0.049) as independent risk factors for postoperative major morbidity. No differences in postoperative outcomes were observed between patients with and without pancreatic endocrine insufficiency. After TP-IAT, significant improvements in major morbidity (p = 0.030) and length of stay (p < 0.0001) were observed over the duration of the study (Figure 1). Thirty-day mortality was 0.2% (one patient).

Conclusion: In this large, national cohort of patients, total pancreatectomy with islet cell autotransplantation was performed safely and with acceptable rates of major morbidity. Major morbidity and postoperative length of stay have improved significantly over time.

Figure 1A.

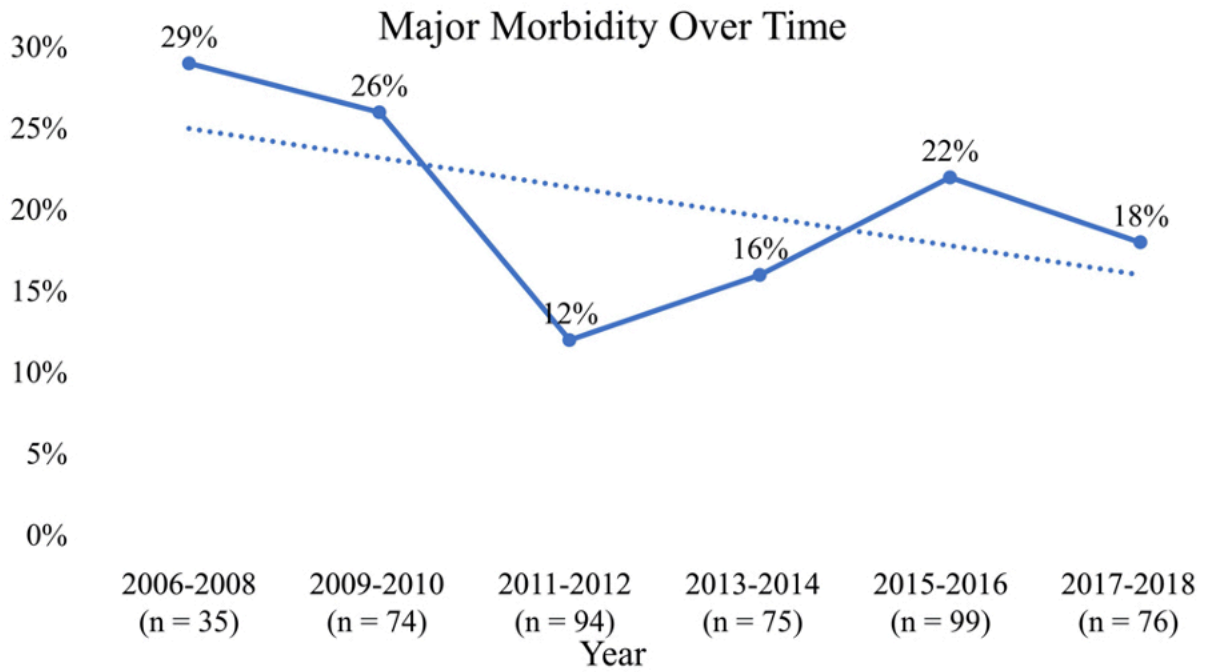
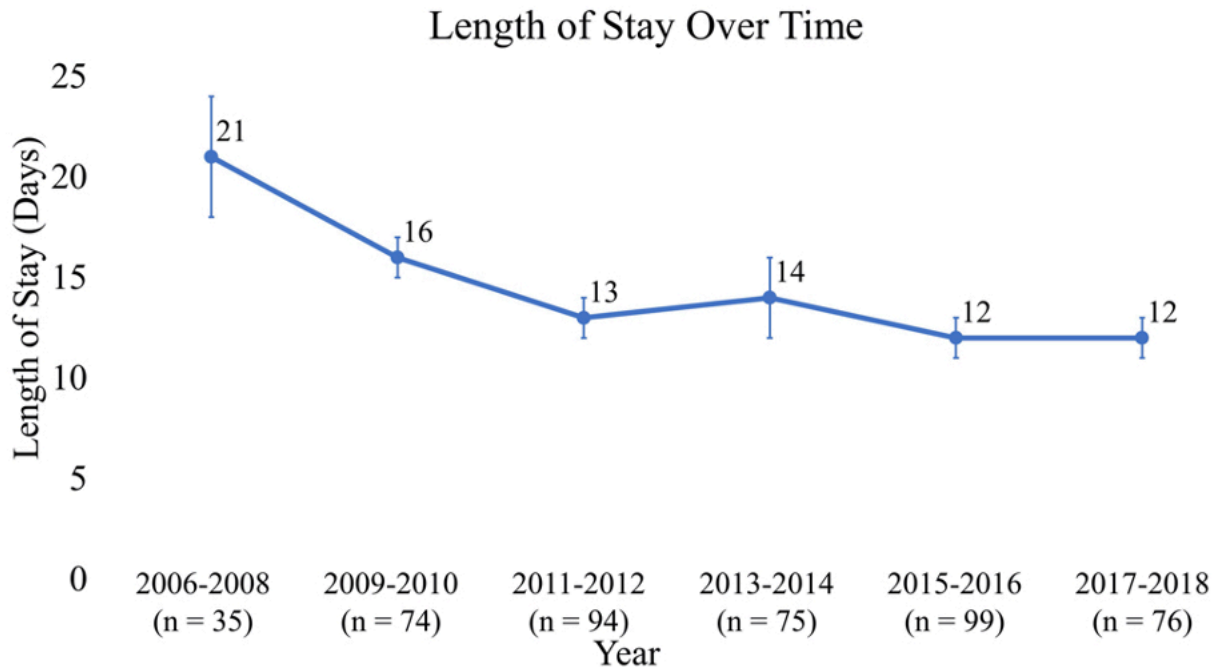


Figure 1B.



P 51. NOVEL CALCULATOR TO ESTIMATE THE RISK OF CLINICALLY RELEVANT POSTOPERATIVE PANCREATIC FISTULA FOLLOWING DISTAL PANCREATECTOMY

I Nassour, JC Hodges, SJ Hughes, S Al Masri, A Zureikat, A Paniccia

Presenter: Ibrahim Nassour MD | University of Pittsburgh Medical Center, United States

Background: Drain management algorithms are based on studies that predict CR-POPF using drain fluid amylase level on POD1 (DFA1). These studies are focused on pancreaticoduodenectomy which is inherently different than distal pancreatectomy. In addition, the change of DFA between POD1 and POD3 (Δ DFA) is underutilized despite its importance in predicting CR-POPF. The aim of this study is to create a calculator that estimates the risk of clinically relevant postoperative pancreatic fistula (CR-POPF) following distal pancreatectomy.

Methods: The 2014-2018 pancreas-targeted ACS-NSQIP database was used to identify patients who underwent elective distal pancreatectomies. Models to predict CR-POPF were constructed using DFA1 with and without change in Δ DFA. The fittest model was used to create a calculator.

Results: 692 out of 12,042 distal pancreatectomies met the inclusion criteria of the study. The risk of CR-POPF was 15.9% in the included cohort versus 14.8% in the excluded one ($P=0.421$). The predictors of the CR-POPF were age, operative time, DFA1 and Δ DFA. Adding Δ DFA decreased the Akaike's information criterion of the model (507.7 vs 544.7) indicating a significantly better model fit and improved the cross validated area under the curve from 0.731 to 0.791. An easy-to-use calculator was created for surgeons to estimate the risk of CR-POPF based on the above-mentioned variables. A sensitivity/specificity table was created at various cutoffs to direct clinical decision with respect to early drain removal.

Conclusion: This study highlights the importance of Δ DFA in addition to DFA1 in predicting CR-POPF. The provided calculator will facilitate predicting CR-POPF and postoperative drain management following distal pancreatectomy.

		Drain Amylase on POD 1							
		15	50	300	1,000	3,000	5,000	7,500	10,000
Change in Drain Amylase from POD 1 to POD 3	- 95%	0.2%	0.5%	2.1%	5.1%	11.1%	15.6%	20.0%	23.6%
	- 90%	0.4%	0.9%	3.1%	7.0%	13.9%	18.8%	23.4%	27.2%
	- 75%	0.8%	1.7%	5.0%	10.2%	18.5%	23.7%	28.5%	32.3%
	- 50%	1.3%	2.7%	7.3%	13.6%	22.6%	28.0%	32.8%	36.4%
	- 25%	1.9%	3.6%	9.0%	15.9%	25.3%	30.7%	35.4%	39.0%
	± 0%	2.4%	4.3%	10.4%	17.7%	27.3%	32.7%	37.4%	40.8%
	+ 50%	3.2%	5.7%	12.7%	20.5%	30.3%	35.6%	40.1%	43.4%
	+ 100%	4.1%	6.9%	14.5%	22.7%	32.6%	37.8%	42.1%	45.3%

Marginal Predicted Probabilities of CR-POPF Based on Reduced Model 2

P 52. OUTCOMES OF 8,985 PATIENTS UNDERGOING TOTAL PANCREATECTOMY: A RETROSPECTIVE POPULATION BASED STUDY (NIS 1998-2014)

SS Nagarkatti, JB Seok, S Patil, MJ Jacobs

Presenter: David Seok MD | Academic Medical Center, United States

Background: Total pancreatectomy (TP) is performed for certain select indications in patients with benign and malignant disease. The procedure, has however, received criticism due to its associated morbidity. Our aim was to perform a population based study to determine the peri-operative outcomes in TP patients

Methods: National Inpatient Database (NIS 1998 - 2014) was used to identify patients who underwent total pancreatectomy (ICD-9 52.6). Discharge weights were applied to get national estimates. Demographic, clinical and outcomes data was compared using standard statistical methodology.

Results: 8,985 patients underwent TP during the study period, with a mean age of 56.7 years (± 16.6). TP was performed more commonly for benign pancreatic disease (54.7%) than pancreatic cancer (45.3%). All-cause peri-operative mortality was 5.4% with overall morbidity of 33.5%. Respiratory (7.5%), GI (6.9%), Post-op infection (6.8%) and Post-op hemorrhage (4.3%) were most common complications. Majority of TP patients had Charlson's score >6 (42.3%). Males suffered from higher co morbidities than females (CCI >6 ; 54.7% vs 45.3%). TP patients were discharged home 56% of the time, with mean length of stay of 14.6 days. 28.1% required home health services and 10% were discharged to nursing home. The total overall cost of TP was \$129,959.

Conclusion: Total pancreatectomy was performed more commonly for benign pancreatic disease with low mortality rates. Male patients receiving TP were older, suffered from higher Charlson's score and higher mortality compared to females. Further studies are warranted to validate findings of this study.

Table 1 Demographic, Clinical Characteristic and Outcomes of Patients Undergoing Total Pancreatectomy, NIS (1998-2014)

	Total	Male	Female	p-value
N	8,985	4,349 (48.4%)	4,636 (51.6%)	
Demographics				
Age in years (Mean±SD)	56.7 (±16.6)	57.8 (±16.2)	55.7 (±16.9)	
Race N (%)				0.008
Caucasians	5,567 (62.0)	2747 (63.2)	2,820 (60.8)	
African Americans	641 (7.1)	301 (6.9)	340 (7.3)	
Hispanics	479 (5.3)	245 (5.6)	234 (5.0)	
Asian Pacific Islanders	172 (1.9)	66 (1.5)	106 (2.3)	
Others	2,127 (23.7)	990 (22.8)	1,137 (24.5)	
Charlson's Score, N (%)				<0.001
Charlson's Score 0	768 (8.5)	344 (44.8)	424 (55.2)	
Charlson's Score 1-3	2,533 (28.2)	977 (38.6)	1,556 (61.4)	
Charlson's Score 4-5	1,885 (21.0)	950 (50.4)	935 (49.6)	
Charlson's Score >6	3,798 (42.3)	2,078 (54.7)	1,720 (45.3)	
Primary Diagnosis, N (%)				<0.001
Benign	4916 (54.7)	2224 (51.1)	2692 (58.1)	
Malignant	4069 (45.3)	2125 (48.9)	1944 (41.9)	
Complications, N (%)	3012 (33.5)			
Mortality	482 (5.4)	280	202	
Respiratory	678 (7.5)	337 (49.7)	341 (50.3)	0.497
Cardiac	283 (3.1)	157 (55.5)	126 (44.5)	0.016
Sepsis	198 (2.2)	89 (44.9)	109 (55.1)	0.350
Gastrointestinal	619 (6.9)	349 (59.3)	252 (40.7)	<0.001
Post-op Infection	612 (6.8)	337 (55.1)	275 (44.9)	0.001
Post-op hemorrhage	383 (4.3)	162 (42.3)	221 (57.7%)	0.016
Disposition (% of total)				<0.001
Home	5,035 (56.0%)	2519 (57.9)	2,516 (54.3)	
Skilled nursing facility	873 (9.7%)	360 (8.3)	513 (11.1)	
Home with Home health	2,525 (28.1%)	1160 (26.7)	1,365 (29.4)	

P 53. PREOPERATIVE SARCOPENIA IS A NEGATIVE PREDICTOR FOR ENHANCED POSTOPERATIVE RECOVERY AFTER PANCREATICODUODENECTOMY

DO Nauheim, E Papai, HH, CJ Yeo, H Lavu, A Nevler

Presenter: David Nauheim | Thomas Jefferson University, United States

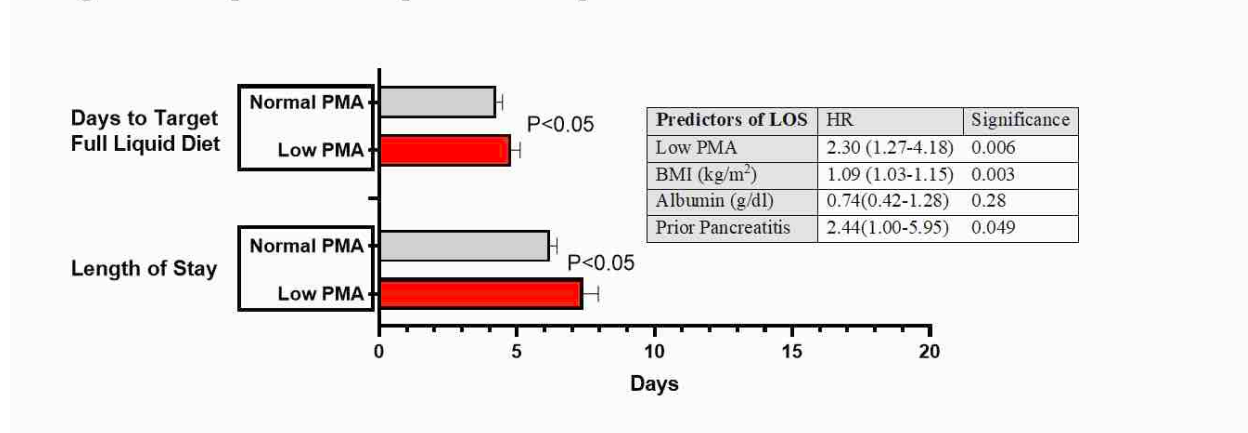
Background: Sarcopenia is common in pancreatic cancer patients. In light of the growing adoption of standardized protocols for enhanced recovery after surgery (ERAS), we examined the clinical impact of sarcopenia in pancreaticoduodenectomy (PD) patients in a 5-day accelerated ERAS program.

Methods: A retrospective review was conducted of patients undergoing PD from 2017 through 2020 on the ERAS pathway. Pre-operative computerized tomographic scans taken within 45 days before surgery were analyzed to determine psoas muscle cross-sectional area (PMA) at the third lumbar vertebral body. Sarcopenia was defined as the lowest-quartile of PMA respective to sex. Outcome measures were compared between patients with or without sarcopenia.

Results: In this 333-patient cohort, 227 (68.1%) patients had final pathology revealing carcinoma. The median age was 66.7 years (16.4-88.4 years) with a 161:172 male to female ratio. Sarcopenia correlated with delayed tolerance of oral intake (4.2 ± 3.4 vs. 4.8 ± 2.9 days, $P < 0.05$), increased complication rates (OR 4.3; 95%CI 2.2-8.5, $P < 0.01$), and more extended hospital stays (LOS) (median [Inter-Quartile range], 5.0[5.0-6.0] vs. 6.0[5.0-8.0] days, $P < 0.05$). Pre-operative albumin levels, BMI, and past history of pancreatitis were found to correlate with LOS ($P < 0.05$). Multivariate regression analysis found PMA, BMI, familial history of breast cancer, and history of pancreatitis to be independent predictors of increased LOS ($P < 0.05$).

Conclusion: Sarcopenia correlated with increased length of stay and postoperative complications in ERAS patients after PD. Sarcopenia can be used to predict poor candidates for ERAS protocols who may require an alternative recovery protocol, promoting a clinical tier-based approach to ERAS for pancreatic surgery.

Figure 1: Preoperative Sarcopenia PMA Impact on ERAS



P 54. RACIAL DISPARITIES IN OPERATIVE MANAGEMENT OF LOCALIZED, NON-FUNCTIONAL PANCREATIC NEUROENDOCRINE TUMORS IN SURGICALLY FIT PATIENTS

K Bingmer, JJ Hue, K Sugumar, JB Ammori, LD Rothermel, JM Winter, JM Hardacre, LM Ocuin

Presenter: Katherine Bingmer MD | University Hospitals Cleveland Medical Center, United States

Background: Guidelines recommend resection of non-functional neuroendocrine tumors of the pancreas (NF-pNETs) that are ≥ 2 cm in size. We compared utilization of surgery based on race.

Methods: We identified non-Hispanic White and Black patients with localized NF-pNETs ≥ 2 cm and Charlson-Deyo score 0-1 in the NCDB (2004-2016). We compared utilization of surgery by race, adjusting for clinicodemographic variables. Overall survival was compared based on management.

Results: A total of 3459 patients were included (White=3005;Black=454). Black patients were younger (58vs63 years) and more often treated at academic facilities (65.3%vs60.3%). Overall, Black and White patients underwent surgery at similar rates (77.3%vs79.6%). When stratified by primary site, Black patients with body/tail tumors were less likely to undergo surgery (78.5%vs84.7%). On multivariable analysis, Black race was associated with a lower likelihood of surgery overall (OR 0.74,p=0.034) and in patients with body/tail tumors (OR 0.56,p=0.001). Non-operative management was associated with a higher risk of death (HR 3.19,p<0.001).

Conclusion: In a national cohort of patients with NF-pNETs meeting criteria for resection, Black race is associated with lower frequency of surgery. Operative intervention is associated with prolonged survival. Persistent racial disparities in management of a surgically curable disease should be targeted for improvement.

P 55. REASONS FOR CONVERSION BY EXPERIENCED SURGEONS DIFFER FOR LAPAROSCOPIC AND ROBOTIC DISTAL PANCREATECTOMY; A MULTI-INSTITUTIONAL ANALYSIS

S AlMasri, W Kwon, K Lee, A Thomas, A Paniccia, B Schrope, H Zeh III, J Chabot, M Hogg, A Zureikat, M Kluger

Presenter: Samer AlMasri MD | University of Pittsburgh Medical Center, United States

Background: Minimally invasive distal pancreatectomy (MIDP) is a popular technique for the management of pancreatic body and tail tumors. Despite accumulating experience with laparoscopic distal pancreatectomy (LDP) and robotic distal pancreatectomy (RDP), open conversion (OC) remains inevitable in up to 25% of cases. We aimed to identify preoperative predictors of OC and hypothesized that anthropometric factors would weigh heavily on this risk.

Methods: Between 2002 and 2019, patients treated by a group of surgeons performing LDP and RDP beyond the learning curve were identified from two high-volume pancreas-specialized programs. Univariate logistic regression modeling was used to identify individual predictors of OC. Covariates with a p-value < 0.20 were entered into multivariate logistic regression ($p < 0.05$). LDP and RDP models were generated separately owing to the statistically significant difference in OC rates between the two groups.

Results: Eight hundred twenty-five patients were identified (median age 63 years, 44.2% male, mean body mass index (BMI) 27.8 kg/m²). RDP was performed in 439 (53.2%) while LDP in 386 (46.8%). The indications for surgery were malignancy or neuroendocrine tumors in 66.5%, cystic neoplasm in 29.3%, and pancreatitis in 4.2%. Splenic preservation was performed in 10.8%. Multiorgan resection and vein resection were needed in 17.1% and 1.7% of the cases, respectively. OC was necessary in 13.9% (n=115) of the overall cohort. The conversion rates for RDP and LDP were 3.5% and 10.4%, respectively. The reason for conversions were failure to progress (36.5%), bleeding (33.9%), vascular involvement (13.9%), concern for safety margin (12.2%), and equipment limitations (3.5%). For LDP, age ($p=0.02$), removed pancreas length ($p < 0.01$), depth to the pancreas from the skin surface ($p=0.05$), malignancy ($p=0.02$), American Society of Anesthesiologists (ASA) class III/IV ($p < 0.01$), higher Charlson comorbidity index (CCI) ($p < 0.01$), splenic preservation ($p < 0.01$), and multiorgan resection ($p < 0.01$) were associated with OC on univariate analysis. On adjusted analysis, greater CCI [odds ratio (OR), 1.18; 95% confidence interval (CI), 1.02-1.35; $p=0.02$], splenic preservation (OR, 4.20; 95% CI, 1.16-12.08; $p < 0.01$), and multiorgan resection (OR 1.92; 95% CI, 1.02-3.60; $p=0.04$) were independently predictive of OC (Table 1). For RDP, weight ($p < 0.01$), BMI ($p=0.05$), and total pancreas length ($p=0.03$) were associated with OC while assistance by a fellow ($p < 0.01$) was inversely associated with OC on univariate analysis. On multivariate analysis, portal vein resection (OR, 9.17; 95% CI, 1.43-58.8; $p=0.02$) was predictive of OC while assistance by a fellow was protective (OR, 0.19; 95% CI, 0.06-0.62; $p < 0.01$).

Conclusion: Though some anthropometric data were associated with OC, they were not independent predictors for experienced minimally-invasive pancreatic surgeon's contrary to our hypothesis. Nor was OC affected by pathology. These factors should not preclude patients from MIDP. RDP can be performed safely for distal lesions without clear vascular involvement at the splenoportal confluence. When performing LDP, surgeons should be aware of a higher OC risk with an attempt at splenic preservation, multiorgan resection, and in comorbid patients. Based on these factors, surgeons may formulate an informed decision on the best approach for distal pancreatectomy.

Table 1. Univariate and multivariate regression analysis of predictors of conversion in the laparoscopic and robotic groups

Variables	Laparoscopic DP						Robotic DP					
	Univariate			Multivariate			Univariate			Multivariate		
	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value	OR	95% CI	P-value
Age	1.02	1.00-1.04	0.02				0.99	0.96-1.01	0.25			
Gender, male	1.43	0.89-2.32	0.14				1.53	0.72-3.26	0.27			
Anthropometrics												
Height, cm	0.99	0.96-1.01	0.22				1.03	0.99-1.07	0.12			
Weight, kg	0.99	0.95-1.01	0.42				1.02	1.01-1.04	<0.01			
BMI, kg/m ²	1.02	0.99-1.05	0.28				1.05	1.00-1.10	0.05			
Pancreas length, cm*	0.97	0.85-1.12	0.69				0.82	0.69-0.98	0.03			
Pancreas length removed, cm	3.61	1.68-7.72	<0.01				0.64	0.20-2.07	0.46			
Anterior-posterior depth, cm*	1.14	1.00-1.31	0.05				1.10	0.90-1.34	0.36			
Indication												
Cystic neoplasm & others		<i>Ref.</i>						<i>Ref.</i>				
Malignant neoplasm	1.86	1.10-3.15	0.02				0.92	0.36-2.34	0.86			
Pancreatitis	2.25	0.79-6.40	0.13				0.94	0.11-8.42	0.96			
Comorbidities												
ASA class III/IV	1.87	1.14-3.08	<0.01				0.67	0.31-1.46	0.31			
CCI	1.92	1.16-3.19	<0.01	1.18	1.02-1.35	0.02	1.71	0.77-3.80	0.19			
Chronic pancreatitis	1.57	0.62-3.94	0.34				1.30	0.43-4.00	0.64			
Previous abdominal operation	1.18	0.73-1.92	0.50				0.86	0.40-1.86	0.70			
Neoadjuvant therapy	0.80	0.16-3.96	0.78				0.77	0.22-2.68	0.68			
Splenic preservation	5.13	1.81-14.54	<0.01	4.20	1.16-12.08	<0.01	1.74	0.23-13.35	0.59			
Multiorgan resection	2.15	1.17-3.95	<0.01	1.92	1.02-3.60	0.04	1.11	0.44-2.82	0.82			
Portal vein resection							2.96	0.62-14.20	0.17	9.17	1.43-58.80	0.02
Staffing												
Primary attending, years practicing	1.00	0.44-2.29	0.99				1.37	0.63-2.98	0.42			
Second attending assisted	1.08	0.96-1.21	0.22				1.07	0.97-1.17	0.17			
Fellow assisted	1.00	0.64-1.58	0.99				0.44	0.27-0.71	<0.01	0.19	0.06-0.62	<0.01

*Based on preoperative cross-sectional imaging. DP, distal pancreatectomy; OR, odds ratio; CI, confidence interval; BMI, body mass index; ASA, American Society of Anesthesiologists; CCI, Charlson comorbidity index.

P 56. RECURRENCE, SURVIVAL, AND THE ROLE OF ADJUVANT THERAPY AFTER IRREVERSIBLE ELECTROPORATION FOR LOCALLY ADVANCED PANCREATIC ADENOCARCINOMA

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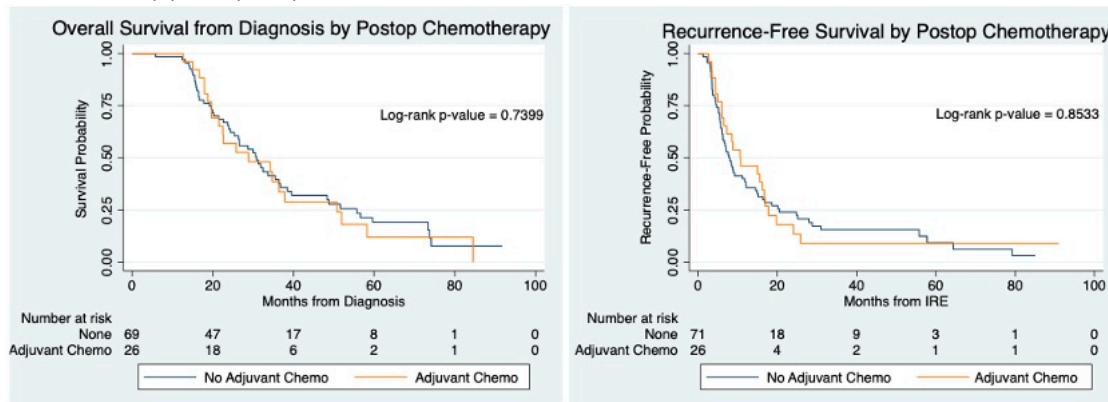
Presenter: Alexander Thomas MD | Columbia University, United States

Background: Irreversible electroporation (IRE) represents one of the few advancements in the treatment of locally advanced pancreatic cancer (LAPC) in recent years. As an ablation technique, IRE expands the surgical options for patients who do not meet criteria for standard resection because of involvement of vascular structures. Without IRE, these patients would receive palliative chemotherapy. Prior studies have shown that IRE is most effective when combined with chemotherapy, but the role of adjuvant therapy is rarely delineated. This study investigated the hypothesis that adjuvant chemotherapy does not improve overall survival in patients who have undergone extensive neoadjuvant therapy, and that IRE affords patients extended time off systemic therapy. This latter point may be an especially important and underrecognized advantage of IRE.

Methods: We performed a retrospective cohort study of patients who underwent IRE for LAPC at a single institution from 2012-2020. Included patients had T4M0 disease on preoperative imaging. We compared overall survival (OS) and recurrence free survival (RFS) by type of IRE (IRE in situ for local tumor control or IRE of potentially positive margins in concert with resection) and by receipt of adjuvant chemotherapy. Time off therapy was defined as the total number of months off chemotherapy after completing neoadjuvant treatment, factoring in time on adjuvant therapy and time on palliative chemotherapy if given for later recurrence.

Results: Of 108 patients treated with IRE, 44 were in situ and 64 were for margin extension. Most (95.37%) underwent neoadjuvant chemotherapy. Excluding 90-day mortalities, 36.08% experienced local recurrence and 58.76% had distant recurrence. Overall RFS was 8.58 months (IQR 5.15–19.77) with no difference for type of IRE ($p=0.9933$). OS was 30.86 (19.60–51.91) months from time of diagnosis and 18.65 (10.20–47.13) months from IRE, with no difference by IRE indication (Figure 1). Regarding postoperative chemotherapy, 26.8% received adjuvant chemotherapy and 73.2% did not. There were no differences in OS or RFS by type of postoperative chemotherapy, and patients treated with IRE benefited from median 12.08 (8.35-26.67) months off systemic treatment.

Conclusion: Our findings suggest that IRE improves OS compared to historical controls for patients with LAPC. Importantly, IRE also yielded more than 12 months off toxic systemic therapies for those who would otherwise be reliant on chemotherapy. We found no survival advantage for routine adjuvant chemotherapy after recovery from IRE. Further study of the effect of IRE and its associated time off chemotherapy on quality of life is warranted.



P 57. WNT DEPENDENCY IN PATIENT-DERIVED PANCREATIC ORGANOID MODELS FOR PRECISION MEDICINE APPROACHES

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Presenter: Haley Zlomke MD | Johns Hopkins University School of Medicine, United States

Background: Disease heterogeneity can drive the variable responses seen in pancreatic ductal adenocarcinoma (PDAC) to systemic therapies. Organoid models of disease have been shown to accurately recapitulate heterogeneity in early cultures and may be used to guide patient specific, personalized therapy. Historically WNT stimulation has been required to initiate cultures from fresh patient-derived specimens. Here, we evaluate the effect of exogenous WNT stimulation on PDAC organoid phenotype, tumorigenicity and chemotherapeutic sensitivity.

Methods: Patient derived organoids (PDOs) were established after digestion of fresh tissues obtained by biopsy or surgical specimens from eleven patients on an IRB-approved protocol. Seven were established using historical protocols reliant upon exogenous WNT supplementation. Four were established under two different protocols with and without WNT supplementation in the media. Growth characteristics, immunohistochemical analysis, and chemotherapeutic sensitivity analysis were performed under conditions of WNT supplementation and WNT restriction. Pharmacotyping was performed over clinically relevant dose ranges of five standard of care chemotherapeutics and a putative clinical response was determined by modeling based upon population distribution.

Results: WNT supplementation is not obligatory for the establishment, expansion and characterization of tissues derived for PDAC. In de-novo PDO establishment, WNT can be associated with an increased rate of success in establishment and an increased pace of biomass accumulation in the expansion phase. In lines previously established and expanded with WNT supplementation, the removal of WNT ligand did not significantly alter rates of cell proliferation and growth. No established cultures were lost after withdrawal of our exogenous WNT stimulation. The withdrawal of exogenous WNT can result in phenotypic changes to the culture that are evident under bright-light microscopy and immunohistochemical staining. Chemosensitivity determination can be performed by pharmacotyping in the presence, or absence, of exogenous WNT stimulation. Ex-vivo drug sensitivity, particularly to gemcitabine and irinotecan, can vary with WNT stimulation. Despite this heterogeneity, the putative clinical response of each individual tumor is not altered with WNT manipulation.

Conclusion: Intratumoral heterogeneity is a challenge to capture in real-time from patient-derived models of disease. When using these models to inform clinical care, the role of exogenous WNT stimulation and heterogeneity in culture conditions remains uncertain. Here we show that exogenous WNT can alter phenotype and growth rate. Despite this, pharmacotype was minimally altered with heterogeneous WNT conditioning, suggesting that patient derived organoid technology may be a robust predictor of clinical chemotherapeutic response. Exogenous WNT does not appear to alter the capacity of PDOs to serve as predictive biomarkers of clinical chemotherapeutic response.

P 58. ONCOLOGIC OUTCOMES AFTER NEOADJUVANT SYSTEMIC THERAPIES IN PANCREATIC NEUROENDOCRINE TUMORS

O Yoshino, M Aldakkak, M Josephson, KK Christians, S Tsai, B George, YL Wong, J Thomas, BA Erickson, WA Hall, A Khan, N Kulkarni, J Evans, DB Evans, CN Clarke

Presenter: Osamu Yoshino MD | Medical College of Wisconsin, United States

Background: Pancreatic neuroendocrine tumors (PNETs) are less common pancreatic neoplasms with a diverse clinical course and therefore, optimal treatment sequencing in advanced disease is not well defined. Recent advancements in non-surgical treatments has stimulated interest in neoadjuvant therapy for patients with more advanced disease. The aim of this study was to describe our experience with neoadjuvant therapy and surgery in patients with PNET.

Methods: We performed a retrospective analysis of patients with PNET obtained from our prospective Pancreas Cancer database who received neoadjuvant therapy followed by surgical resection between January 2009 and December 2015. Clinically relevant variables, including staging, operative data, and postoperative follow-up were extracted from the database. Radiologic response was reported using RECIST criteria.

Results: Neoadjuvant therapy was initiated in 19 patients (median age 57.0y [IQR 49.5-62.5]); G1 in 6, G2 in 12 and G3 in 1. Initial primary tumor size was 3.9cm (2.45-6.75cm), and 63.1% (12/19) patients had metastatic disease at diagnosis. Eleven patients received neoadjuvant chemotherapy (8, capecitabine+temozolimide; 1, streptozocin+leucovorin+5FU; 1, 5FU+adriamycin; 1, cisplatin+etoposide); all but 4 patients also received concomitant somatostatin analogue. 8 patients received neoadjuvant somatostatin analogue only. Indications for neoadjuvant therapy varied; in 8 patients with large volume distant metastasis at diagnosis it was used as a test of tumor biology prior to major pancreatectomy, 7 patients had locally advanced primary tumors with or without vascular encroachment, 1 patient had resectable PNEC, 1 patient was temporarily medically unfit for surgery at diagnosis, 2 patients chose to delay surgery. 17 patients imaging available for comparisons of treatment response to neoadjuvant therapy. 10 patients had partial radiographic, 1 patient had a complete radiographic response, 3 had stable disease and 3 progressed on therapy. Median radiographic tumor size after neoadjuvant therapy was 3.35cm (IQR 2.7-5.3cm) when compared to median radiographic size at presentation of 3.9 cm (IQR 2.45-6.75) (p=0.57). Surgery was successfully performed in 18 of the 19 patients to include Whipple procedure in 11 and distal pancreatectomy 6; 10 patients required concomitant liver resection/ablation. the largest tumor diameter on final pathology was 3.5cm (IQR 2.55-5.75). Fifteen patients had regional lymph node dissection at the time of pancreatectomy, 11 (73%) patients were node positive. On the final pathology, median primary tumor Ki67 was 4% (IQR 2.0-10.7%), the median number of positive lymph nodes was 3 (1-6) and the median lymph node yield was 29 (23-36), with an R0 resection rate of 83% (15/18). Progression-free survival was 7.3 months (IQR 3.8-17.0), and overall survival was 90.9 months (IQR 49.7-125.9).

Conclusion: Treatment sequencing to include neoadjuvant therapy and surgery may provide a benefit to select patients with PNET – especially those with locally advanced primaries or moderate/large volume distant metastatic disease. Neoadjuvant therapy is particularly attractive in those with liver metastases and a primary tumor in the pancreatic head where surgery warrants a biliary enteric anastomosis. This small experience provides a signal for improved overall survival after neoadjuvant therapy followed by surgery, despite a significant tumor burden at diagnosis.

P 60. VALIDATION OF THE EIGHTH EDITION OF THE AMERICAN JOINT COMMITTEE ON CANCER (AJCC) TNM STAGING SYSTEM IN PATIENTS WITH RESECTED AMPULLARY ADENOCARCINOMA

DHL Lemmers, G Nappo, S Robinson, M Bonds, M Mortimer, V Mavroeidis, F Burdio, L Bolm, P Pessaux, U Wellner, B Ielpo, Z Soonawalla, B Al-Sarireh, T Armstrong, A Alseidi, S White, A Zerbi, MG Besselink, M Abu Hilal
Presenter: Daniel Lemmers MD | Fondazione Poliambulanza, Italy

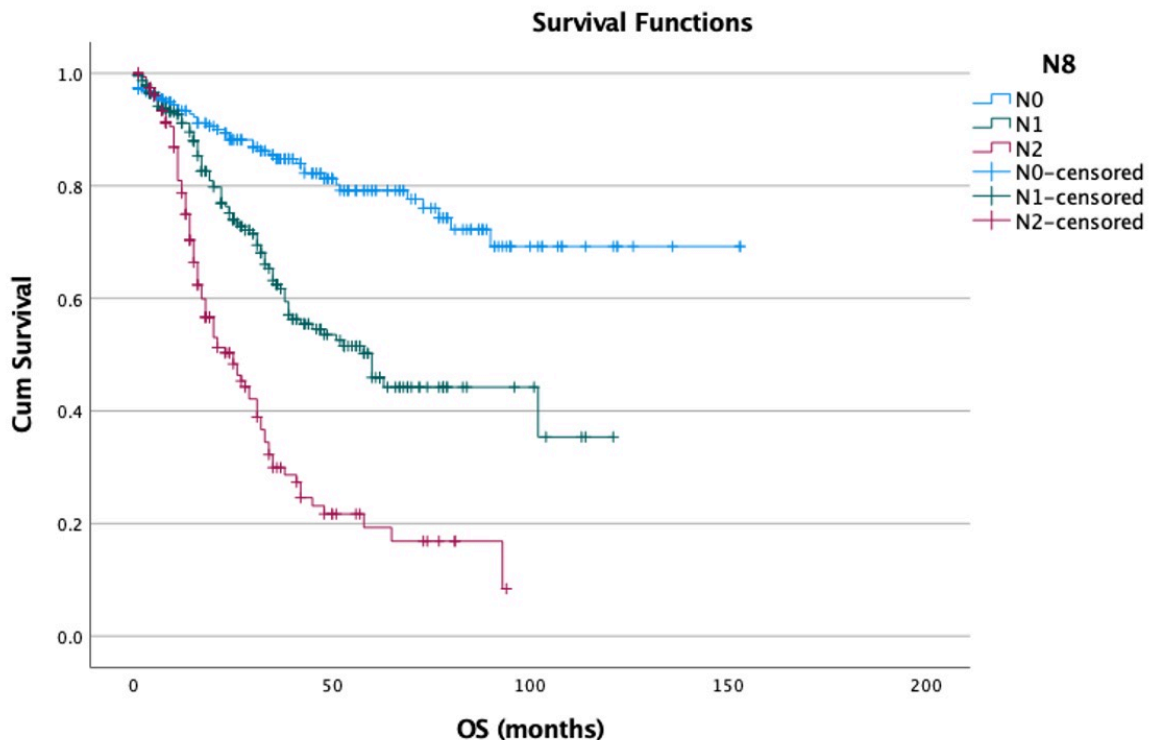
Background: The purpose of this study is to assess the prognostic accuracy of the 7th and 8th AJCC staging system for AAC and to externally validate the 8th edition of the AJCC for resected ampullary cancer in an international cohort.

Methods: This retrospective international multicenter cohort study included all patients who underwent pancreatoduodenectomy for AAC (2006-2020). Patients were retrospectively staged according to the AJCC TNM 8th edition. Prognostic accuracy on overall survival was compared between both TNM editions by Kaplan-Meier estimates and concordance statistics.

Results: In total, 640 patients were included for analysis. Stage IA, IB, IIA, IIB, III, and IV were 6.6%, 17.2%, 8.8%, 33.8%, 29.4%, and 2.6% in the 7th edition and Stage IA, IB, IIA, IIB, IIIA, IIIB and IV 13.7%, 15.1%, 2.6%, 2.3%, 40.2% 21.4%, and 2.3% in the 8th edition, respectively. Median overall survival for the entire cohort was 73 months. Five-year cumulative survival rates changed from 86%, 65%, 46%, 38%, 28%, 12% (log-rank $p < 0.0001$) in the 7th edition, to 58%, 70%, 81%, 84% and 38%, 9%, 14% (log-rank $p < 0.0001$) in the 8th edition. The 5-year survival rates for N0, N1, N2 (8th edition) were 67%, 37% and 12%, respectively (log-rank $p < .0001$) (Figure 1). The C-statistic improved from 0.677 (95% CI: 1.509-2.050) in the 7th to 0.695 (95% 1.345-1.671) in the 8th edition.

Conclusion: In this international cohort, the AJCC 8th edition of the TNM staging system for AAC demonstrated a better distribution and an increased prognostic accuracy compared to the 7th edition. The new N stage is highly prognostic for survival.

Figure 1 cumulative survival N stage per 8th AJCC classification



P 61. A PERCEIVED PREPAREDNESS FOR SURGERY QUALITY IMPROVEMENT PROJECT IN A POPULATION OF PATIENTS WITH PANCREAS CANCER AND RELATED CONDITIONS

K O'Connor, D LaBruno, JRudderow, S Cannaday, C J Yeo, TP Yeo

Presenter: Shawwna Cannaday MSN, FNP-BC, AGCNP | Thomas Jefferson University, United States

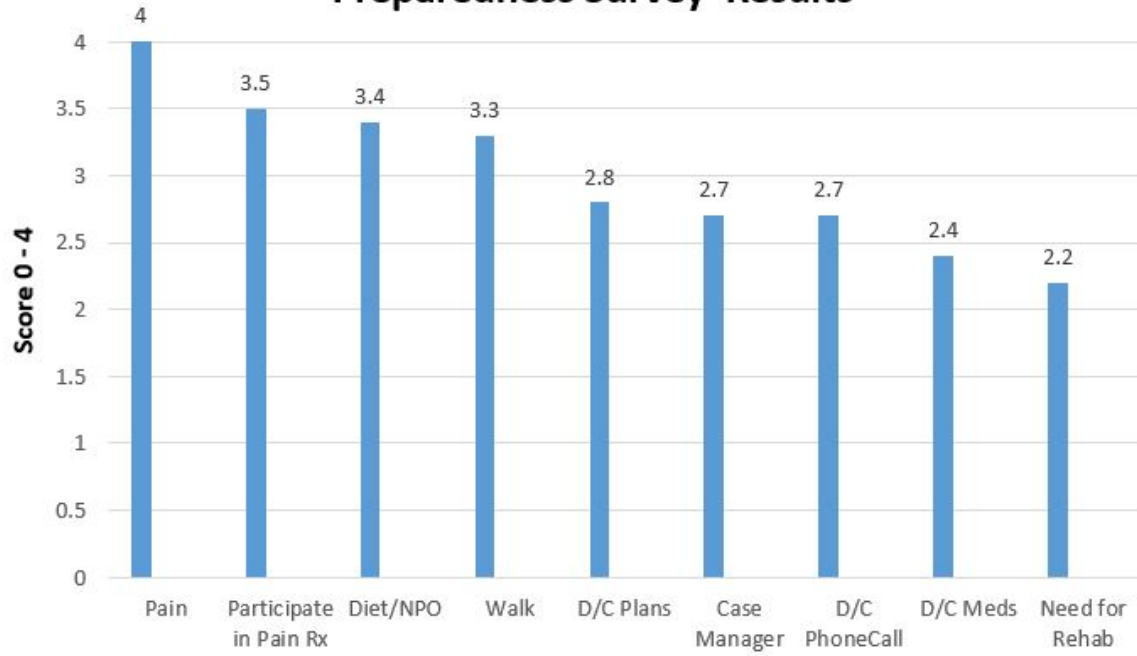
Background: According to the American Cancer Society 60,430 individuals will be diagnosed with pancreas cancer in 2021. Those with pre-malignant pancreas lesions and serious benign conditions are also eligible for resectional hepato-pancreatico-biliary (HPB) surgery. The purpose of this study was to determine the perceived level of surgery preparedness of patients at a high-volume NCI-designated cancer center specializing in surgery for HPB cancers and conditions, in order to improve the quality of the patient experience and clinical outcomes and to evaluate the pre-operative educational materials.

Methods: This observational study utilized convenience sampling to collect information via questionnaire and electronic medical record from post-operative HPB patients regarding their perceived level of surgery preparedness on 11 areas of post-operative importance. These areas broadly included: ambulation, pain management, diet restrictions, discharge planning, involvement of a case manager, and specific discharge medications. The questionnaires were administered to post-operative HPB patients on a single, high-volume inpatient unit over 6 months in 2019.

Results: Fifty individuals with HPB conditions were surveyed. There were 28 women; 22 men between the ages of 39 and 82 years. Cancer was the primary indication for surgery with pancreas cancer accounting for 56%, followed by 14% with pre-malignant intraductal papillary mucinous neoplasms and 12% with peri-ampullary cancers. The pylorus preserving pancreaticoduodenectomy was performed in 60% of patients; distal pancreatectomy was the second most common operations. The average post-op length of stay (LOS) was 5.5 days. Eighty percent of the respondents felt either well or moderately well-prepared for the planned procedure. Overall, more men (26%) felt well-prepared than did women (18%). The oldest patients (>80 yrs) felt only somewhat prepared. Of the 11 areas queried, patients seemed least aware of the discharge plan, the need for long term acid blockers, and the involvement of a case manager postoperatively. Individual comments indicate that there is room for improvement in the level of detail in the pre-op information.

Conclusion: As a result of this study we are developing targeted educational tools to integrate into the different stages of preoperative visits. Special focus on discharge planning and needs of the elderly is paramount. Improving preparedness for HPB surgery has the potential to improve clinical outcomes, increase quality and patient satisfaction, decrease LOS and reduce time to adjuvant therapy.

Preparedness Survey Results



Knowledge Variables

Average Total Score = 33.7 (range 14 - 44)

P 62. ACCURATE NODAL STAGING IN PANCREATIC CANCER IN THE ERA OF NEOADJUVANT THERAPY

AA Javed, D Ding, E Baig, MJ Wright, JA Teinor, D Mansoor, E Thompson, RH Hruban, A Narang, WR Burns, RA Burkhart, K Lafaro, MJ Weiss, JL Cameron, CL Wolfgang, J He

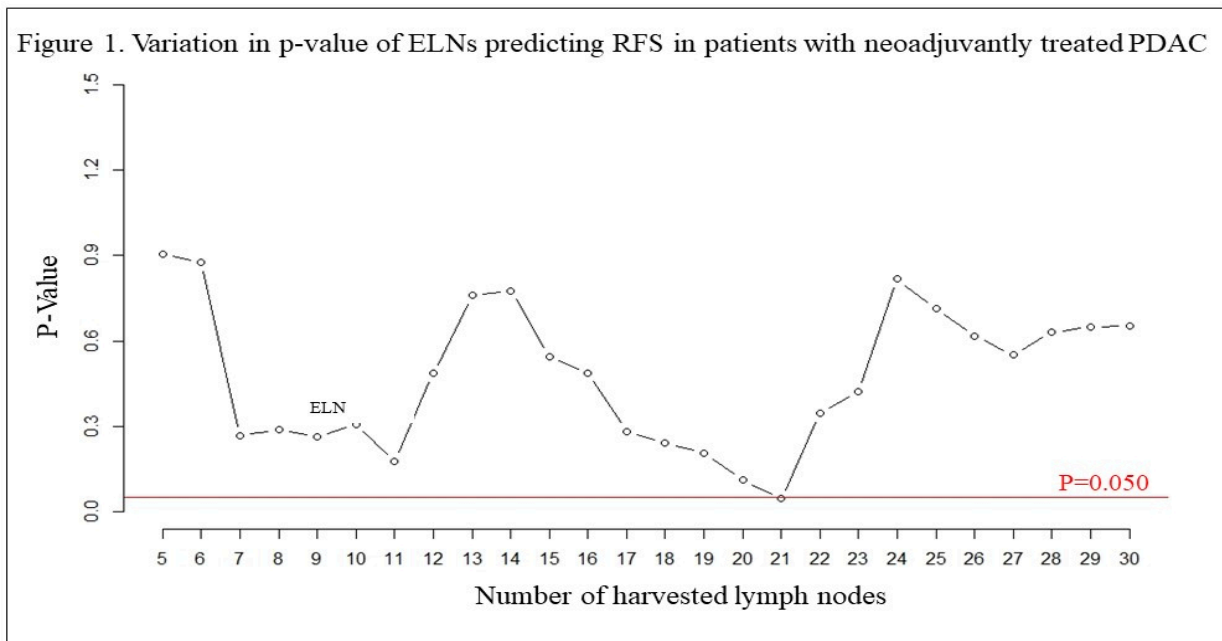
Presenter: Ammar Javed MD | Johns Hopkins University School of Medicine, United States

Background: Nodal disease is prognostic in pancreatic ductal adenocarcinoma (PDAC), however optimal number of examined lymph nodes (ELNs) required to accurately stage nodal disease in the current era of neoadjuvant therapy remains unknown. The aim of the study was to evaluate the optimal number of ELNs in patients with neoadjuvantly treated PDAC.

Methods: A prospectively maintained institutional registry was used to identify patients undergoing resection for PDAC following neoadjuvant treatment between 2011 and 2018. Clinicopathological data were extracted and analyzed.

Results: Of 546 patients included, 232 (42.5%) had lymph node metastases. The median recurrence free survival (RFS) was 10.6 months (95% confidence interval: 9.7-11.7) and nodal disease was independently associated with shorter RFS (9.1 vs 11.9 months; $p < 0.001$). A cutoff of 22 for ELNs was identified that stratified patients by RFS. Patients with N1 and N2 disease had similar median RFS (9.1 vs 8.9 months; $p = 0.410$). On multivariable analysis ELN of ≥ 22 was found to be significantly associated with longer RFS among patients with N0 disease (14.2 vs. 10.9 months, $P = 0.046$). However ELN has no impact on RFS for patients with N1/N2 disease (9.5 vs. 8.4 months, $p = 0.190$).

Conclusion: Lymph node metastases remains prognostic in PDAC patients after neoadjuvant treatment. Among N0 patients, a cutoff of 22 ELN was associated with improved RFS and resulted in optimal nodal staging.



P 63. ADJUSTING DRAIN FLUID AMYLASE FOR DRAIN VOLUME DOES NOT IMPROVE PANCREATIC FISTULA PREDICTION

C Blunck, S Vickers, T Wang, V Dudeja, S Reddy, JB Rose

Presenter: Conrad Blunck BS, MS | University of Alabama at Birmingham, United States

Background: Drain fluid amylase (DFA) levels have been used to predict clinically relevant postoperative pancreatic fistula (CR-POPF) and guide postoperative drain management. Optimal DFA cutoff thresholds vary between studies, prompting investigation of an alternative assessment technique. We hypothesized that adjusting DFA for daily collected volumes (vDFA), would improve CR-POPF prediction.

Methods: A single-institution retrospective cohort study of patients who underwent pancreatoduodenectomies (PD) and distal pancreatectomies (DP) between 2013 and 2019 was performed. All DFAs were measured on post-operative day 3. To calculate vDFA, the DFA (U/L) was multiplied by the average hourly volume over 24hrs (L/hr). A CR-POPF was defined as a composite of grades B/C POPF according to the 2016 ISGPF consensus guidelines. Clinicopathologic variables were compared between cohorts by univariable, multivariable, and ROC curves with Youden Index analyses.

Results: Of the 176 patients included in the study, 33 (19%) developed CR-POPF. Patients developing a CR-POPF were more likely to be male (61 vs. 41%) and have elevated median DFA (527 vs. 61 U/L), vDFA (662 vs. 173 U/hr), or BMIs (31 vs. 28) than those that did not. ROC analysis did not find a vDFA cutoff of 260 U/hr to be a better predictor of CR-POPF than a DFA cutoff of 337 U/L for all patients (AUC 0.715 vs. 0.761; $p=0.25$). This finding was consistent on sub-analysis of surgery type PD vs DP. When included into a model containing DFA, BMI, and male sex, only a DFA less than 337.5 U/L (OR 0.11 [0.05-0.27]; $p < 0.01$) and male sex (OR 2.49 [1.03-6.04]; $p=0.04$) were predictive of CR-POPF. When looking at surgery subtypes of PD vs DP, only a low DFA remained predictive for both, while male sex was not predictive in PD.

Conclusion: Postoperative DFA remains a preferred method of predicting CR-POPF as the proposed vDFA assessment technique only adds complexity without increased discriminability.

P 65. ARTIFICIAL INTELLIGENCE-BASED SEGMENTATION OF RESIDUAL TUMOR IN PANCREATIC CANCER AFTER NEOADJUVANT TREATMENT

BV Janssen, R Theijse, S van Roessel, R de Ruiter, A Berkel, J Huiskens, OR Busch, JW Wilmink, G Kazemier, P Valkema, A Farina, J Verheij, OJ de Boer, MG Besselink

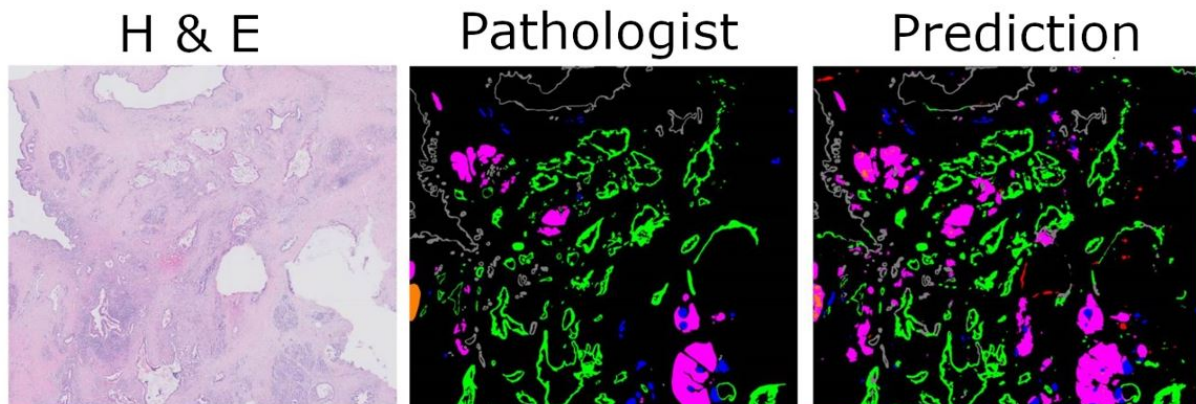
Presenter: Boris Janssen BSc | Amsterdam UMC, Netherlands

Background: Histologic examination of resected pancreatic cancer after neoadjuvant therapy (NAT) is essential to assess the effect of neoadjuvant treatment and guide the choice for adjuvant treatment. However, assessment of residual tumor burden in pancreatic cancer is challenging given high interobserver variability and the abundance of stroma. Artificial intelligence techniques may offer a more reproducible approach. This study aims to create an artificial intelligence algorithm that automatically segments histological residual tumor in resected pancreatic cancer after NAT.

Methods: Specimens of resected pancreatic cancer after NAT of 55 patients (FOLFIRINOX, n=33, chemoradiotherapy, n=22) were digitized. Tumor and pre-existent tissue types were annotated and labeled. Images and binary masks were generated (20x magnification, 0.5 μ m/px), and randomly distributed over a training (n=49) and validation set (n=6). Patches were generated (512*512px for training [n= 7.350] and validation [n=550]) and used to train and validate a U-net with a DenseNet161 encoder to recognize tumor. Accuracy of the validation set was expressed as Dice (F1) score (range 0.0-1.0).

Results: For tumor segmentation, we obtained an F1 score of 0.78 after 4 epochs of training. Figure 1 shows the patches of representative examples, of respectively the hematoxylin-eosin staining, annotations by the pathologists, and prediction by the algorithm.

Conclusion: Better techniques are urgently needed to evaluate residual tumor burden after NAT. This study shows that artificial intelligence techniques may be suited for this task given the promising Dice (F1) score. This algorithm could be developed into a tool to assess NAT response and guide the choice for adjuvant treatment.



Legend: H&E = hematoxylin and eosin, Pathologist = annotations by the pathologist, Prediction = prediction by the artificial intelligence algorithm, green segmentation = cancer tissue, magenta segmentation = atrophic metaplastic parenchyma, blue segmentation = islets of Langerhans, grey segmentation = normal ductal tissue, red segmentation = fat, orange segmentation = acinic tissue.

P 66. CA19-9 RESPONSE TO 1ST-LINE NEOADJUVANT FOLFIRINOX AND 2ND-LINE GEMCITABINE-BASED CHEMOTHERAPY IN PATIENTS WITH OPERABLE PANCREATIC CANCER

SZ Thalji, M Kamgar, B George, M Aldakkak, KK Christians, CN Clarke, BA Erickson, WA Hall, P Tolat, A Khan, DB Evans, S Tsai

Presenter: Sam Thalji MD | Medical College of Wisconsin, United States

Background: A benefit of neoadjuvant therapy for operable pancreatic cancer (PC) is the ability to assess treatment response. We examined carbohydrate antigen 19-9 (CA19-9) response to 1st and 2nd line chemotherapy.

Methods: We identified patients with operable PC and elevated CA19-9 (>35 U/mL with total bilirubin 50% decline in CA19-9 from previous peak value).

Results: Among 202 patients, 1st-line neoadjuvant FFX (2 mo) was associated with a CA19-9 response in 74 (37%) of 199 patients with evaluable CA19-9 levels. Following 2 mo of FFX, 85 (43%) of 199 patients were transitioned to radiotherapy, 15 (7%) had surgery, 4 (2%) stopped treatment, and 95 (48%) received an additional 2 mo of chemotherapy. Of these 95 patients, FFX was continued in 66 (69%) and switched to GnP in 29 (31%). Patients who remained on FFX were more likely to have had a significant CA19-9 response to the initial FFX ($p=0.001$). Of the 66 patients who stayed on FFX, 34 had a CA19-9 response to the initial 2 mo of chemo and 32 did not. Of these 32 patients, 19 additional patients (59%) had a response during the next 2 mo of FFX. Of the 29 patients who were switched to GnP, 4 had a CA19-9 response to the initial 2 mo of FFX (switched due to toxicity) and 25 did not. Of these 25 patients, 23 patients (92%) demonstrated a response when switched to GnP. Among patients that did not respond to the initial 2 mo of FFX, those that were switched to GnP had a significantly higher proportion of response (92%) compared to those that continued FFX (59%; $p=0.006$). In total, after 4 mo of chemotherapy, 51 (77%) of the 66 patients who stayed on FFX had a CA19-9 response compared to 27 (93%) of the 29 patients who switched to GnP ($p=0.06$).

Conclusion: Patients with operable PC who lack a CA19-9 response to initial neoadjuvant FFX have very high rates of biochemical response when switched to GnP. Longitudinal monitoring of CA19-9 during neoadjuvant therapy may help maximize treatment response prior to surgery. Differences in chemotherapeutic susceptibility may be related to cancer subtype and are being investigated in our clinical trials of adaptive neoadjuvant therapy.

P 67. EARLY POSTOPERATIVE SERUM HYPERAMYLASEMIA: HARBINGER OF MORBIDITY HIDING IN PLAIN SIGHT?

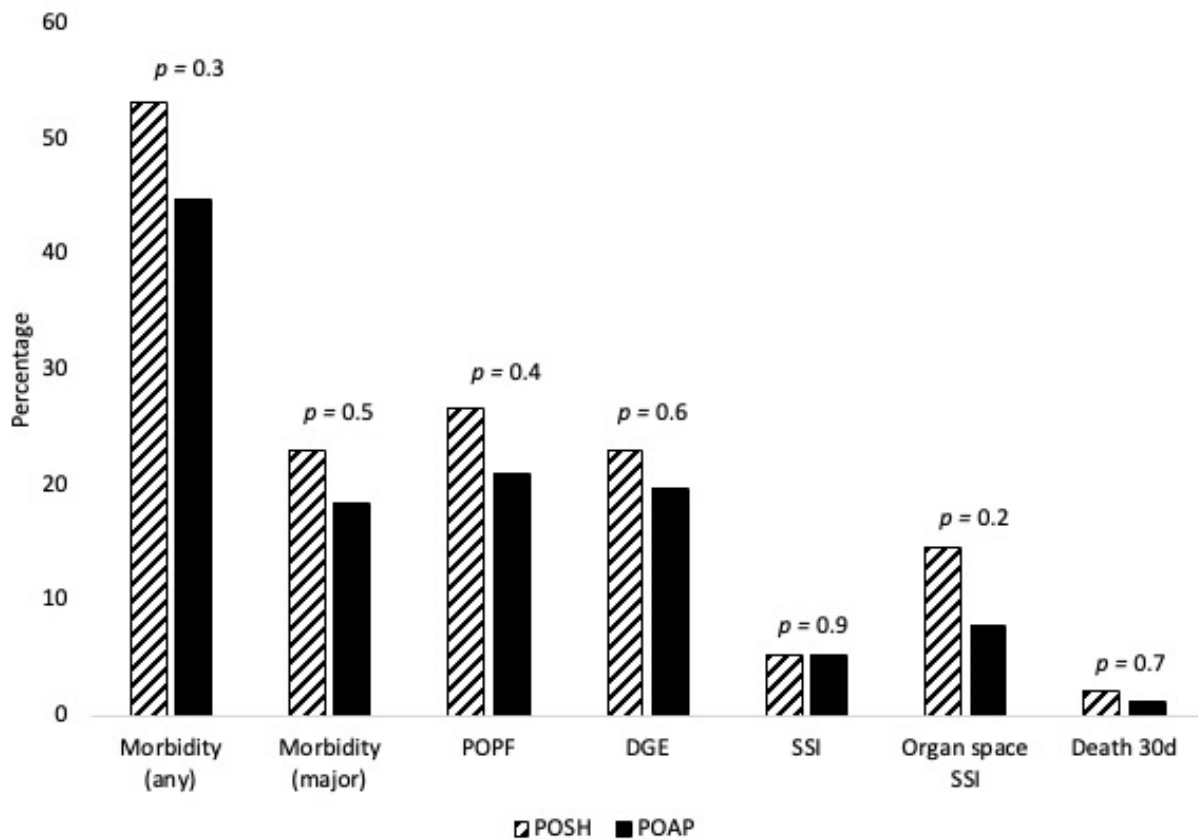
SP McGuire, TK Maatman, SL Keller, EP Ceppa, MG House, A Nakeeb, TK Nguyen, CM Schmidt, NJ Zyromski
Presenter: Sean McGuire MD | Indiana University School of Medicine, United States

Background: The clinical significance of postoperative serum pancreatic enzyme elevation following pancreatoduodenectomy (PD) is understudied. We hypothesized that elevation in serum enzymes predicts morbidity and mortality following PD.

Methods: Retrospective review of 677 patients who underwent pancreatoduodenectomy at a single institution from 2013-2019. Patients were categorized based on serum enzyme concentrations. Patient characteristics, drain amylase, and outcomes among groups were compared.

Results: 415 of 677 patients had postoperative serum amylase concentrations measured. Of these, 243 (59%) were normal, 96 (23%) were classified as postoperative serum hyperamylasemia (POSH), and 76 (18%) were classified as postoperative acute pancreatitis (POAP). Major morbidity was lower among patients with normal enzyme concentration (10%) and higher in patients with POSH (23%) and POAP (18%) ($p = 0.008$). Patients with normal enzymes were less likely to develop postoperative pancreatic fistula (5%) compared with patients with POSH (26%) and POAP (21%) ($p < 0.001$) and less likely to develop delayed gastric emptying (9% versus 23% and 20%, respectively); $p = 0.002$. No difference in mortality was seen among groups.

Conclusion: Elevated serum pancreatic enzyme concentration occurs frequently after pancreatoduodenectomy and is associated with increased postoperative morbidity. Serum enzyme concentration should be considered in management after pancreatoduodenectomy.



P 68. EFFECT OF BMI ON OUTCOMES FOR MINIMALLY INVASIVE APPROACHES FOR DISTAL PANCREATECTOMY

S Ross, C Syblis, V Przetocki, K Crespo, P Vasanthakumar, I Sucandy, A Rosemurgy

Presenter: Sharona Ross MD | AdventHealth Tampa, United States

Background: This study was undertaken to determine the impact of BMI on intraoperative and postoperative outcomes after minimally invasive distal pancreatectomy and splenectomy.

Methods: We prospectively followed 146 patients who underwent minimally invasive, either robotic or Laparo-Endoscopic Single Site (LESS), distal pancreatectomy and splenectomy. Regression analyses were utilized to determine the relationships between BMI and outcomes; then these analyses were stratified by approach (i.e., LESS vs. robotic). For illustrative purposes only, patients were categorized using CDC guidelines into 'underweight', 'normal weight', 'overweight', or 'obese', and data are presented as median (mean±SD).

Results: 122 vs. 24 patients underwent robotic vs. LESS distal pancreatectomy and splenectomy, respectively. BMI correlated with age for patients undergoing robotic pancreatectomy and splenectomy. Patients undergoing robotic vs. LESS pancreatectomy and splenectomy had greater BMI and more advanced CDC BMI Class (Table); similarly, they had longer operations but with less blood loss and fewer conversions to 'open', with similar tumor size, nodal harvests, and lengths of stay (Table). In overweight and obese patients (i.e., BMI ≥ 25 kg/m²), the robotic approach led to longer operations [243 (269±112.8) vs. 186 (186±53.7) minutes, $p < 0.01$], with less blood loss [100 (193±220.5) vs. 200 (311±377.6) mL, $p = 0.04$], and shorter lengths of stay [4 (5±3.0) vs. 4 (7±5.4) days, $p = 0.01$].

Conclusion: BMI of patients undergoing robotic distal pancreatectomy and splenectomy strongly correlated with age and was greater than BMI of patients undergoing LESS approach with a more advanced CDC BMI Class. Increasing BMI did not prolong hospitalization, frequency of complications, nor 30-day mortality. Patients with increased BMI (≥ 25 kg/m²) had less intraoperative blood loss with a shorter postoperative course when the robotic platform was used. We believe both approaches should be adopted and utilized situationally given the advantages of each; overweight / obese patients may best be served using the robotic platform.

Preoperative	Robotic	Robot vs. BMI	LESS	LESS vs. BMI	Robot vs. LESS
	Total (n=122)	p-value slope (m)	Total (n=24)	p-value slope (m)	p-value
Age (years)	68 (64±13.3)	p=0.05* m=-0.40	65 (61±13.8)	p=NS m=0.55	p=NS
Sex (M/W)	59M/63W	p=NS	12M/12W	p=NS	p=NS
BMI (kg/m ²)	28 (29±6.1)	N/A	25 (25±4.4)	N/A	p<0.01*
CDC Class (%)	1% Underweight 25% Normal 35% Overweight 39% Obese	N/A	4% Underweight 54% Normal 29% Overweight 13% Obese	N/A	p<0.01*
Intraoperative					
Operative Duration (min)	243 (269±112.8)	p=NS	186 (186±53.7)	p=NS	p<0.01*
Estimated Blood Loss (mL)	100 (193±220.5)	p=NS	200 (311±377.6)	p=NS	p=0.04*
Intraoperative Complications (N,%)	2(2%)	p=NS	2(8%)	p=NS	p=NS
Conversions to 'Open' (N,%)	12(10%)	p=NS	8(33%)	p=NS	p<0.01*
Nodes Examined	10 (10±5.6)	p=NS	9 (9±6.5)	p=NS	p=NS
Tumor Size (cm)	3 (4±2.8)	p=NS	3 (4±2.5)	p=NS	p=NS
Postoperative					
Complications (N,%)	13(11%)	p=NS	4(17%)	p=NS	p=NS
Clavien-Dindo Score ≥III (N,%)	7(6%)	p=NS	2(8%)	p=NS	p=NS
Length of Stay (days)	4 (5±3.0)	p=NS	4 (7±5.4)	p=NS	p=0.01*
30-Day Mortality (N,%)	3(2%)	p=NS	0(0%)	p=NS	p=NS

Note: "Robotic vs. BMI" / "LESS vs. BMI" p-value denotes regression analysis of variables against BMI for the given approach.

* represents significance with a p-value ≤ 0.05

P 69. ETHNIC REPRESENTATION IN GENOMIC STUDIES OF GASTROENTEROPANCREATIC NEUROENDOCRINE NEOPLASMS

B Herring, H Chen, JB Rose

Presenter: Brendon Herring MS | University of Alabama at Birmingham, United States

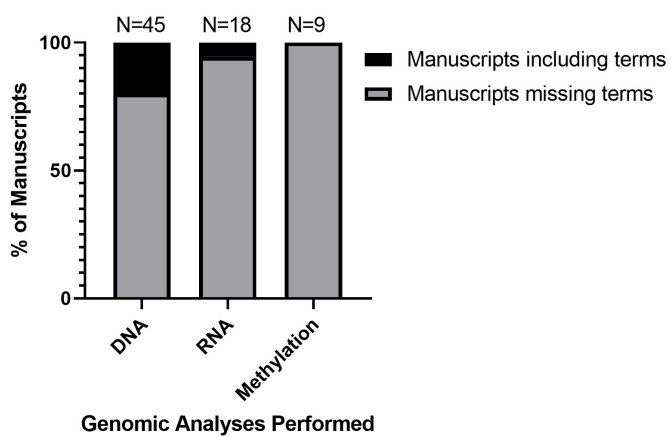
Background: The field of translational cancer genomics is growing at an exponential rate, bringing invaluable findings from the bench to clinical practice. Integrated genomics will be key to discovering areas of therapeutic susceptibility in gastroenteropancreatic neuroendocrine neoplasms (GEP-NENs), for which few effective therapies are available. However, not all populations are poised to benefit from these studies, as large-scale genomic analyses have consisted of mostly Caucasians. The goal of this study was to evaluate ethnic populations represented in genomic studies of GEP-NENs.

Methods: Natural Language Processing (NLP) using the python package NLTK was used to determine the frequency of the words "Race," "Ethnicity," "African American," "Black" "Hispanic," "Latino," "Asian" "Native American," "Pacific Islander" "Caucasian," and "White," in 75 published original research manuscripts performing sequencing on GEP-NENs gathered by a systematic review of the literature. Subject numbers by ethnicity were then evaluated following NLP.

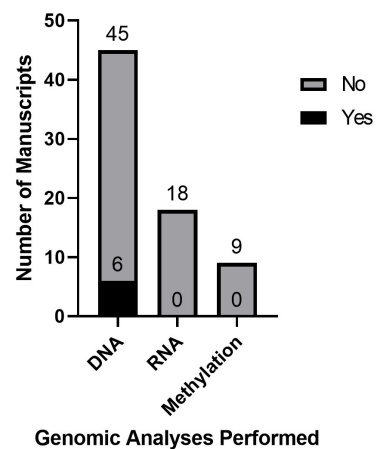
Results: 0/9 studies conducting epigenetic sequencing included any words evaluated, while 9/45 and 1/21 studies conducting whole genome/whole exome DNA or RNA sequencing studies did, respectively. DNA sequencing studies included 5.3% (12) African-American subjects (n=1, where n = # of studies including subject demographics), 0% Hispanic/Latino subjects, 27% Asian subjects (n=2), 0% Native American/Pacific Islander subjects, 8.3% "Other" (n=3), and 90.6% Caucasian subjects (n=5) ($p < .001$). The single RNA sequencing study included 5% "Other" and 95% Caucasian subjects.

Conclusion: There is little representation of ethnic minorities in genomic studies of GEP-NENs. Inclusion of data on these populations is integral for understanding GEP-NEN biology, generalizing findings, and improving therapy.

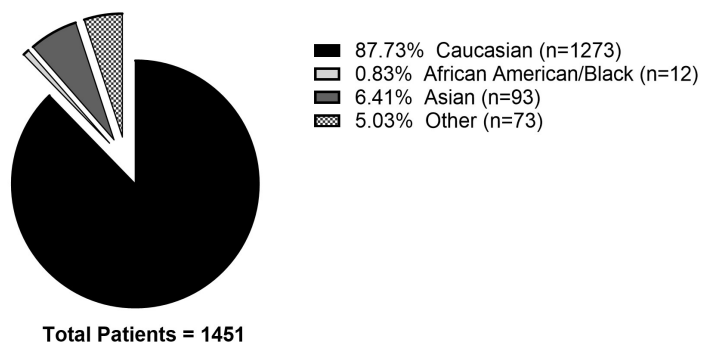
Presence of NIH Race Category Terms in Manuscripts



Manuscripts Reporting Patient Race



of Patients by Race in DNA Studies



P 70. HEMATOLOGICAL PREDICTORS OF LONG TERM OUTCOMES IN PANCREATIC DUCTAL ADENOCARCINOMA

J Gong, K Sugumar, LD Rothermel, JM Hardacre, JB Ammori, LM Ocuin, JM Winter

Presenter: Jenny Gong BS | Case Western Reserve University School of Medicine, United States

Background: Immune markers present a potential predictive factor for prognosis and treatment effectiveness across multiple cancer types. Prognostic markers can be used to identify individuals at higher risk for recurrence who may benefit from further treatment beyond resection. The prognostic role of systemic inflammatory markers in resectable pancreatic ductal adenocarcinoma (PDAC) has been studied, yet their role in the perioperative period is unclear. We conducted a comprehensive analysis of the prognostic capability of white blood cells (WBCs) and platelets in PDAC in both the preoperative and perioperative period.

Methods: We conducted a retrospective review of 282 PDAC patients who underwent resection for PDAC between 2004-19 at a tertiary referral hospital. WBC and platelet counts were recorded just prior to surgery or neoadjuvant therapy (preoperative), the median of their postoperative course, and 1 month prior to adjuvant therapy (preadjuvant) if applicable. Counts were stratified into low, normal, and high groups according to standardized laboratory ranges. Changes in count groups between these three time points were classified as increasing, decreasing, or stable. Analyses were stratified by pancreatectomies with splenectomies, since a surge of hematopoiesis occurs post-splenectomy. Multivariate Cox proportional hazards regression models were used for analysis with primary outcomes of overall survival (OS) and recurrence-free survival (RFS).

Results: In patients undergoing pancreaticoduodenectomies, high median post-operative platelets (HR 4.20, $p=0.021$) and high preadjuvant platelets (HR 12.61, $p<0.001$) were associated with decreased OS. Patients with high preoperative WBCs (HR 0.48, $p=0.03$) had an increase in RFS. In contrast, low preadjuvant WBCs (HR 3.10, $p=0.006$) were associated with decreased RFS. In patients undergoing distal pancreatectomies, a decreasing trend in WBCs between the preoperative and preadjuvant period (HR 7.49, $p=0.003$) led to decreased OS. These results persisted when 30 and 90-day mortalities were excluded.

Conclusion: Postoperative thrombocytosis was generally predictive of poor long-term outcomes in patients undergoing pancreaticoduodenectomies. Decreased WBCs following resection were also adverse predictors in patients undergoing pancreatectomies. These results suggest that perioperative WBC and platelet counts can be used as prognostic markers of survival in patients undergoing resection for PDAC. Further studies are required for validation and to delineate if these abnormalities are drivers or prognostic.

P 71. MANAGEMENT OF PANCREATIC FISTULA AND BILIARY LEAKAGE AFTER PANCREATODUODENECTOMY THROUGH PERCUTANEOUS TRANSHEPATIC BILIARY DRAINAGE

AC Henry, FJ Smits, K van Lienden, DAF vd Heuvel, OR Busch, OM van Delden, M van Leersum, MJL van Strijen, JA Vos, WW te Riele, IQ Molenaar, MG Besselink, HC van Santvoort

Presenter: Anne Claire Henry | Regional Academic Cancer Center Utrecht, Netherlands

Background: Biliary and biliopancreatic leakage through a hepaticojejunostomy or pancreaticojejunostomy after pancreatoduodenectomy are difficult to treat and associated with high morbidity and mortality. The aim of this study was to assess the technical and clinical success rates of percutaneous transhepatic biliary drainage (PTBD) in these patients.

Methods: A retrospective cohort study was performed in two high-volume centers including all patients undergoing PTBD for hepaticojejunostomy or pancreaticojejunostomy leakage after pancreatoduodenectomy (2014 – 2019). Technical success was defined as placement of an intrajejunal PTB drain. Clinical success was defined as hospital discharge with a resolved leak without the need for additional interventions other than intra-abdominal percutaneous catheter drainage.

Results: Out of 822 pancreatoduodenectomies, 67 patients (8%) underwent PTBD. Indications were leakage of the pancreaticojejunostomy (n=23; 34%), hepaticojejunostomy (n=15; 22%) and of both anastomoses (n=22; 33%). PTBD was performed on median postoperative day 12 (IQR 9–17) and technically successful in 91% (n=61). Revision of the PTB drain was performed in 41 patients (63%) due to obstruction (21 times) or dislodgement (29 times). The clinical success rate was 94% (n=62). Leakage was resolved on median day 33 (IQR 21 – 59) since PTBD. PTBD related complications (n=26; 34%) included cholangitis (n=12), hemobilia (n=8) and PTBD related bleeding (n=3; 2 requiring embolization). In hospital mortality was 6% (n=4). PTBD related mortality was 1% (n=1), due to respiratory failure after pleural perforation.

Conclusion: PTBD is effective in the treatment of biliopancreatic leakage after pancreatoduodenectomy. Revisions of the PTB drain are often needed and complications are not infrequent.

P 72. MORTALITY AND SURVIVAL AMONG OCTOGENARIANS WITH LOCALIZED PANCREATIC HEAD CANCER: A NATIONAL CANCER DATABASE ANALYSIS

JJ Hue, K Bingmer, K Sugumar, LM Ocuin, LD Rothermel, JM Winter, JB Ammori, JM Hardacre

Presenter: Jonathan Hue MD | University Hospitals Cleveland Medical Center, United States

Background: The average life expectancy in the United States has increased by four years since 1990 and is currently 79 years. People are living longer, therefore more patients are likely to be diagnosed with cancer later in life. Patients diagnosed with pancreatic ductal adenocarcinoma (PDAC) have historically poor outcomes. Difficult decisions must be made by patients and providers, especially in the elderly for whom treatment morbidities may not be tolerable. Herein we report treatment-dependent outcomes of octogenarians with localized PDAC of the pancreatic head.

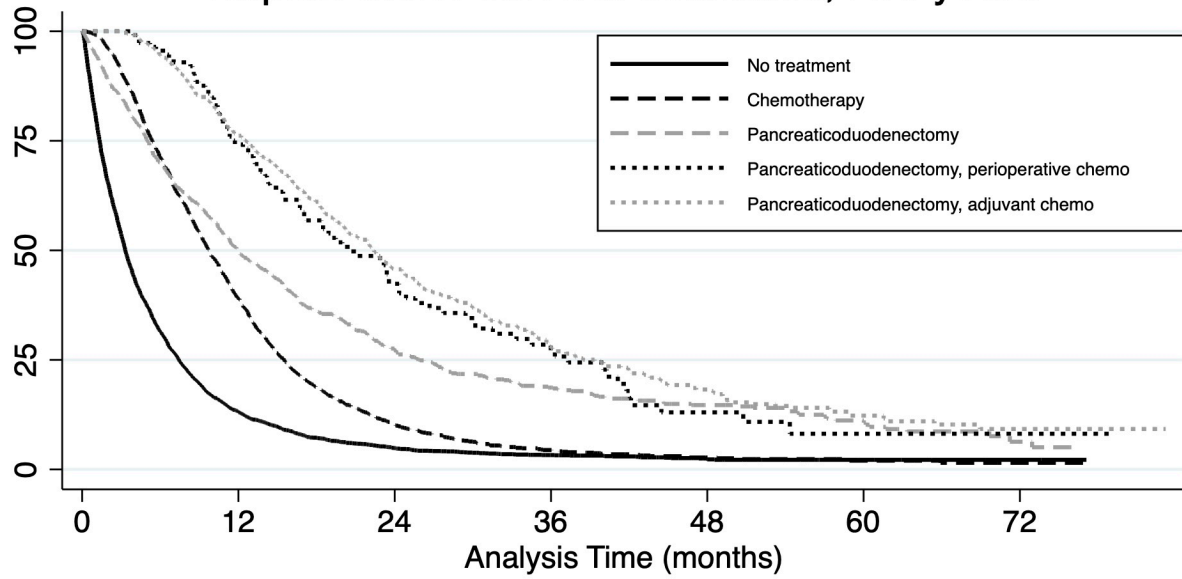
Methods: The National Cancer Database identified patients ≥ 60 years with localized PDAC of the pancreatic head (2011-2016). Patients were grouped by age (60-79 and ≥ 80 years) and categorized by treatment regimen: no treatment, chemotherapy alone, pancreaticoduodenectomy alone, pancreaticoduodenectomy with perioperative chemotherapy (neoadjuvant with or without adjuvant), or upfront pancreaticoduodenectomy with adjuvant chemotherapy. Postoperative outcomes and survival were analyzed. Multivariable models were used to account for confounding.

Results: A total of 35,409 patients were included, 8,745 (24.7%) of which were ≥ 80 years. Over 52% of octogenarians did not receive any treatment, compared to 19.1% of younger patients ($p < 0.001$). Patients ≥ 80 years who underwent a pancreaticoduodenectomy had a significantly greater 90-day mortality rate compared to patients 60-79 years (11.0% vs. 6.7%, $p < 0.001$). This association remained on multivariable logistic regression controlling for demographics, stage, facility type, and neoadjuvant therapies (odds ratio (OR)=1.66, 95% confidence interval (CI)=1.39-1.99). The 90-day mortality rate among patients ≥ 80 years was similar at both academic (10.4%) and non-academic medical centers (11.6%, $p = 0.269$). Only 42.2% of octogenarians who underwent upfront pancreatectomy received adjuvant chemotherapy, of which only 18% received multi-agent chemotherapy, while the remaining 82% received single-agent therapy. However, among patients ≥ 80 years who received neoadjuvant chemotherapy, over 67% received multi-agent chemotherapy. Neoadjuvant chemotherapy was also associated with a reduced likelihood of 90-day mortality (OR=0.58, 95% CI=0.44-0.78). Age ≥ 80 was associated with poor survival relative to ages 60-79 when adjusting for treatment regimen (hazard ratio (HR)=1.19, 95% CI=1.15-1.23). Median survival for octogenarians was 3.3 months without any treatment, 9.7 months with chemotherapy alone, 12.0 months with pancreaticoduodenectomy alone, and greater than 20 months with either perioperative or adjuvant chemotherapy in addition to pancreaticoduodenectomy. Multimodal therapy (pancreaticoduodenectomy with perioperative or adjuvant chemotherapy) was associated with a survival benefit relative to pancreaticoduodenectomy alone on multivariable Cox regression. Chemotherapy alone was associated with worsened survival compared to pancreatectomy without systemic therapy (HR=1.68, 95% CI 1.59-1.77).

Conclusion: Increasing age is associated with worse overall survival in PDAC, but select octogenarians can achieve reasonable survival with multimodal therapy. Given the poor survival and increased perioperative mortality of octogenarians, patient selection for surgery and consideration of neoadjuvant therapy may be increasingly important. Shared, patient-centered decision-making is critical in this patient cohort.

1b

Kaplan-Meier survival estimates, ≥ 80 years



P 73. ORGANOTYPIC SLICE CULTURES OF PANCREATIC DUCTAL ADENOCARCINOMA AS PRECLINICAL MODEL FOR DEVELOPMENT OF PERSONALIZED TREATMENT STRATEGIES

R Braun, O Lapshyna, B Heckelmann I, S Eckelmann, L Bolm, K Honselmann, O Schilling, T Keck, P Bronsert, M Brandenburger, U Wellner

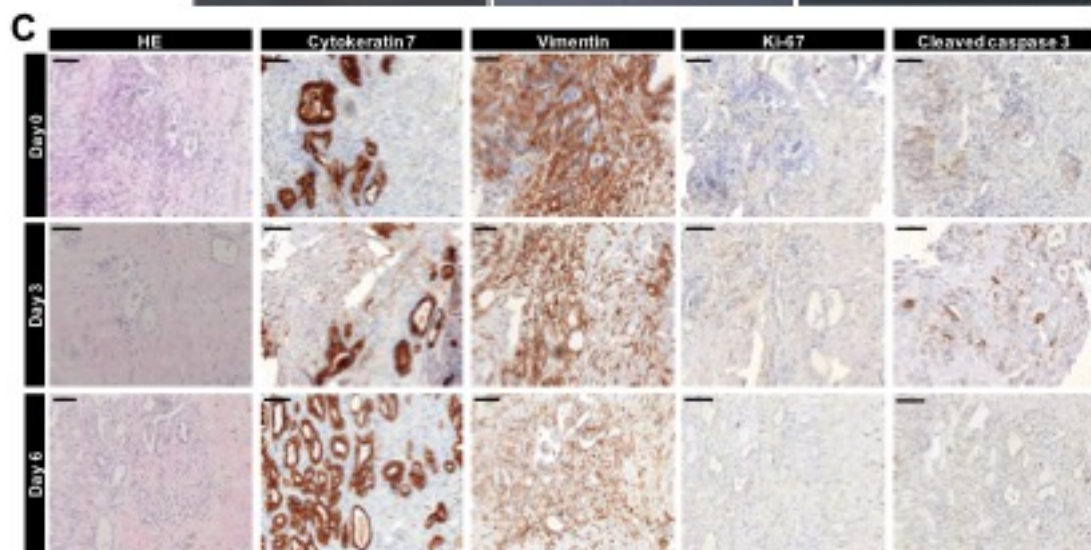
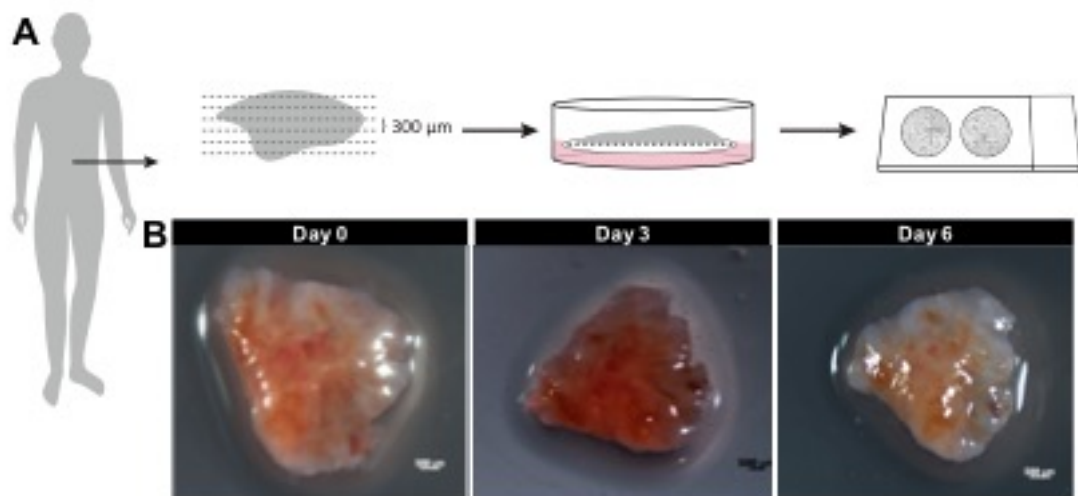
Presenter: Rüdiger Braun MD | University Medical Center Schleswig-Holstein, Campus Luebeck, Germany

Background: The prognosis of ductal adenocarcinomas of the pancreas (PDAC) is exceedingly poor and these tumors are notably resistant to conventional (radio)chemotherapy. Realistic preclinical models of PDAC reflecting the individual intratumor heterogeneity are urgently needed to test therapy response ex vivo and facilitate personalized patient treatment. However, currently used models such as patient-derived cell lines and xenografts lack the specific tumor microenvironment and therefore allow only limited response prediction. Ex vivo cultures of fresh tumor specimens as organotypic slice cultures (OTSCs) are a close approximation of the tumor in situ. OTSCs comprise an intact multicellular tissue composition. We aimed to refine the technique of OTSCs for PDAC to test the respective response to drugs ex vivo in a multicellular environment.

Methods: Tissue slices of 300µm thickness were generated using a vibratome. Slices were cultured at an air-liquid interface on PTFE membranes and treated with gemcitabine. Changes in cell differentiation and viability were monitored by resazurin reduction and histopathology.

Results: Macroscopic morphology of OTSCs was not altered substantially during cultivation, but the size of the surface area decreased over time. At defined periods of cultivation, OTSCs were fixed for histopathological characterization. H&E stain showed that the overall structure of the tissue was preserved during cultivation. No substantial changes in the tumor-to-stroma ratios were detected during cultivation. We did not detect increased apoptosis for about 9 days, but during extended cultivation periods as measured by cleaved caspase 3 staining. OTSCs were treated with 100µM gemcitabine and overall viability was measured by resazurin viability assay every 24 hours. We observed substantial differences in response to treatment of distinct OTSCs.

Conclusion: OTSCs provide a unique opportunity to test individual treatment response to specific drugs ex vivo timely after surgical resection within 10-12 days. Perspective, OTSCs allow to identify individual transcriptomic and proteomic profiles associated with the respective response. We conclude that OTSCs are a precious ex vivo tool for personalized treatment of PDAC.



P 74. PORTAL-MESENERIC VEIN RESECTION FOR PANCREATIC ADENOCARCINOMA IN GREECE: AGAINST WIDESPREAD LOCAL PESSIMISM, ACTUAL RESULTS MAY EXCEED THE DEFINED BENCHMARK OUTCOMES

N Ballian, G Tsiotos

Presenter: Nikiforos Ballian MBBS | Mitera Hospital, Greece

Background: In Greece, pancreatectomy is rarely offered to patients with pancreatic adenocarcinoma cancer (PDAC) involving major peripancreatic vessels due to lack of local expertise and nihilistic misconceptions about expected outcomes. We report the largest Greek series of portomesenteric vein resection for PC.

Methods: Retrospective analysis of prospectively collected data on consecutive patients with PDAC undergoing pancreaticoduodenectomy or distal pancreatectomy with en-block portal/mesenteric vein resection in our tertiary referral center in Greece between 2014 and 2019.

Results: Thirty patients were included. Neoadjuvant therapy was administered to 47%, and was associated with smaller resected tumor size (median: 2.5cm vs 4.2cm, $p=0.001$) but not overall survival. Vascular invasion was present in 63% and was associated with increasing resected tumor size (median: 4cm vs 2.7cm, $p<0.05$) and worsening Eastern Cooperative Oncology Group (ECOG) status (ECOG-0: 50%, ECOG-1: 90%, $p<0.05$). A median of 24 lymph nodes were retrieved, R0 resection rate was 87%, and median length of resected vein was 3cm. Median ICU and hospital length of stay was 0 and 9 days respectively. Postoperative mortality was 3.3%. Median follow-up was 20 months and median overall survival was 24 months. Two-, 3- and 5-year overall survival was 53%, 28% and 17%, respectively. ECOG status was significantly associated with survival (ECOG-0: 31m, ECOG-1: 13m, $p=0.002$). All outcomes exceeded benchmark cutoffs.

Conclusion: This first series of portomesenteric vein resection for PDAC in Greece demonstrates that pancreatectomy has postoperative and oncologic outcomes exceeding defined benchmarks and should be offered to patients meeting criteria.

P 76. PROGRESSIVE TECHNIQUES FOR VASCULAR PANCREATIC SURGERY: SUPERIOR MESENTERIC VEIN RECONSTRUCTION AND PERIADVENTITIAL DISSECTION OF ARTERIES

B Kinny-Köster, JR Habib, AA Javed, EK Fishman, J He, CL Wolfgang

Presenter: Benedict Kinny-Köster MD | New York University Grossman School of Medicine and NYU-Langone Health, United States

Background: With improved response to multi-agent chemotherapies in pancreatic cancer, the demand for pancreatic surgery to deliver curative-intent treatment regimens is rising. However, local involvement of major veins and arteries often challenges technical resectability. Therefore, innovative operative techniques to safely perform oncologic resections and vascular reconstructions are required to increase surgical candidacy and offer patients a chance for favorable clinical outcomes.

Methods: We present advancing strategies and principles of vascular pancreatic surgery. Major vessels that limit resectability comprise the superior mesenteric vein (SMV), superior mesenteric artery (SMA) and common hepatic artery (CHA). The technical maneuvers were developed in patients after the administration of preoperative chemotherapy. Furthermore, the impact and opportunities of high-resolution imaging with its critical value and novel hints on preoperative surgical planning are emphasized.

Results: SMV involvement substantially contests reconstruction from a technical stance, particularly for pancreatic head and uncinate lesions affecting the distal SMV at the jejunal and ileal tributaries. Furthermore, cavernous collateralization may complicate the intraoperative control of hemorrhage. Complimentary strategies for oncologic resections that we deliberate on include collateral preservation, mesoportal bypass (pre-resection), mesoportal interposition graft (post-resection) and mesocaval shunt (temporary or permanent). To bridge defects with often >5 cm distance, autologous left renal vein or greater saphenous vein are utilized as conduit material. Individual anatomic and physical characteristics of the mesoportal flow should be considered for reconstruction to prevent portal hypertension and postoperative thrombosis. For this purpose, preoperative three-dimensional and cinematic rendering of CT scans allows for precise evaluation and surgical planning.

For patients with involvement of the SMA or CHA, surgical exploration after preoperative (radio-)chemotherapy improved the understanding of arterial infiltration and revealed that tumors often did not invade the muscular layer of the arterial wall. In these patients, carefully entering the anatomic plane between the tunica media and tunica adventitia allows for periadventitial dissection of the artery while maintaining arterial continuity. Periadventitial dissection demonstrates an important alternative to segmental arterial resection, when feasible and performed safely. Thereby, the microscopic depth of tumor infiltration at the arterial vessel wall rather than the circumferential degree of attachment guides technical resectability. We identified and describe the radiologic "halo" and "string" signs as promising indicators of arterial tunica media non-involvement and invasion, respectively.

Conclusion: The presented techniques exemplify modern tools to surgically manage the considerable fraction of patients that present with localized pancreatic cancer involving surrounding veins and arteries. Understanding the current opportunities and outcomes of SMV reconstruction and periadventitial dissection of arteries is critical for patient selection in a precision medicine approach. Vascular pancreatic surgery is rapidly progressing as a discipline and will become paramount at high-volume centers given the contemporary scientific efforts and trends of improving systemic disease control.

P 78. RISK FACTORS OF DEVELOPING NONALCOHOLIC FATTY LIVER DISEASE FOLLOWING PANCREATIC RESECTION: A SYSTEMATIC REVIEW AND META-ANALYSIS

K Sugumar, L Naik, JJ Hue, LD Rothermel, LM Ocuin, JB Ammori, JM Hardacre, JM Winter

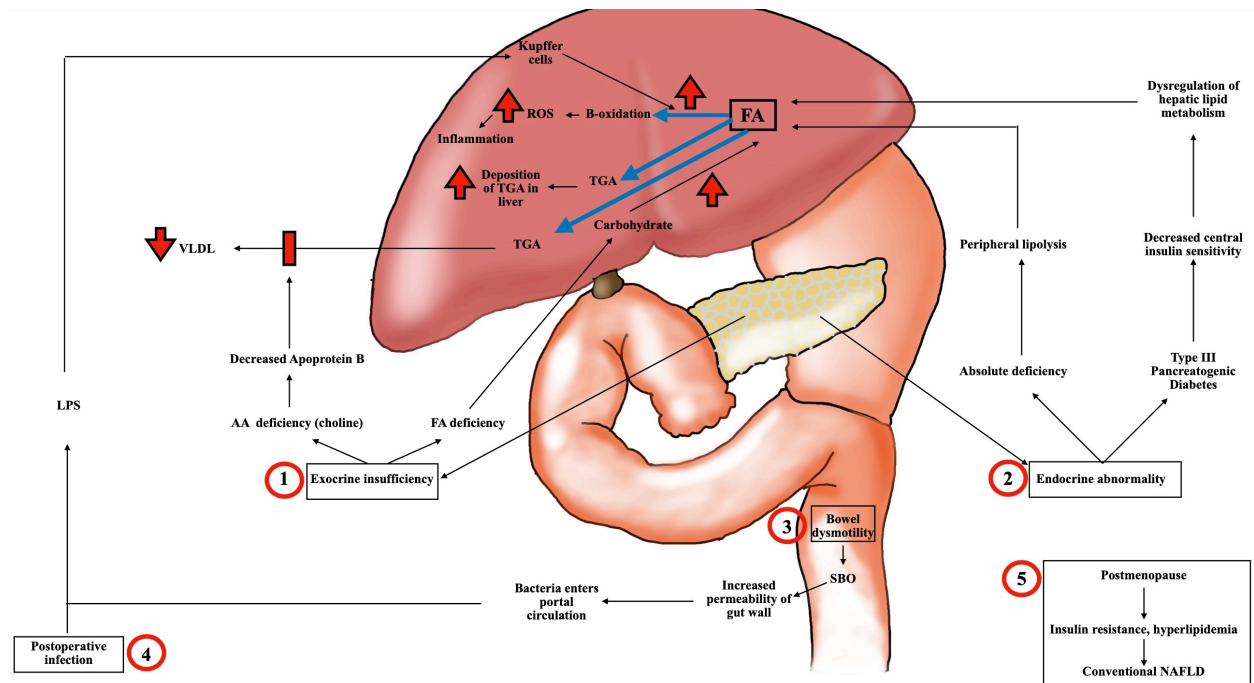
Presenter: Kavin Sugumar MD | Case Western Reserve University School of Medicine, United States

Background: Nonalcoholic fatty liver disease occurs in 10-40% of patients following pancreatic resection. We perform a comprehensive systematic review and meta-analysis to better understand the risk factors of hepatic steatosis and illustrate all the possible mechanisms of NAFLD.

Methods: A systematic literature search was performed in MEDLINE, Scopus, and Cochrane Library in November 2020. Studies focused on the risk factors associated with NAFLD in post pancreatic resection patients were included. The Odds ratio (OR) denoting the association of the various risk factors with NAFLD post resection was curated from the included articles.

Results: Of the 563 published articles, 16 studies met inclusion criteria. All were retrospective observational cohort studies. Combined, these studies included clinical data on 2494 patients. The incidence of NAFLD in the studies ranged from 7% to 46%. Among the various risk factors analyzed, the following had a higher likelihood of NAFLD on forest plot analysis: female gender (OR: 2.36), pancreatic ductal adenocarcinoma (OR: 2.25), portal vein or superior mesenteric vein resection (OR: 2.53), dissection of nerve plexus around the superior mesenteric artery (OR: 1.93), postoperative pancreatic endocrine insufficiency (OR: 3.15), and adjuvant chemotherapy (OR: 1.59). Due to heterogeneity of included studies, the effect of exocrine insufficiency on NAFLD could not be studied. Based on our results and previously published studies, the possible mechanisms of NAFLD are shown in Figure 1.

Conclusion: Numerous factors are associated with the incidence of NAFLD. Further studies focusing on pancreatic enzyme supplementation and exocrine insufficiency are needed.



P 79. ROLE OF INFLAMMATORY AND NUTRITIONAL MARKERS IN PREDICTING COMPLICATIONS FOLLOWING PANCREATICODUODENECTOMY

J Rajeshwar, H Singh, SS Rana, J Kaur, R Nada, R Gupta

Presenter: Rajeshwar Jotheeswaran MD | Postgraduate Institute of Medical Education and Research, India

Background: Pancreaticoduodenectomy (PD) is attended with considerable morbidity and also mortality. Early recognition of patients likely to develop severe postoperative complications will allow timely institution of tailored approach. Present study was planned to predict post-operative complications using inflammatory and nutritional markers measured early in the post-operative period.

Methods: Patients undergoing PD between June 2019 and November 2020 were included. Postoperative pancreatic fistula (POPF), delayed gastric emptying (DGE), and post-operative pancreatic hemorrhage (POPH) were graded according to the International Study Group of Pancreatic Fistula and the International Study Group of Pancreatic Surgery. We also documented other complications like wound infection, intraabdominal collection and non-surgical complications. Inflammatory and nutritional markers were analysed on postoperative day (POD) 1 and 3 which included albumin and Prognostic Nutritional Index (PNI), procalcitonin, C-Reactive Protein (CRP), Systemic Immune Inflammation Index (SII), Neutrophil Lymphocyte Ratio (NLR), Platelet Lymphocyte Ratio (PLR), serum and drain fluid Interleukin- 6 (IL6), serum and drain fluid Tumour Necrosis Factor alpha (TNF α), drain fluid lactate, pyruvate, glucose, lactate/pyruvate, urine trypsinogen-2 and modified Glasgow Prognostic Score (mGPS). Patients were followed up for a period of 30 days or till discharge whichever was longer.

Results: Of the total 58 patients enrolled, 51 patients were included in this study. The incidence of POPF was 51% [Grade A - 12 (23.5%), Grade B - 12 (23.5%) and Grade C - 2 (3.9%)], DGE 80.4% [Grade A- 19 (37.3%), grade B - 17 (33.3%) and grade C - 5(9.8%)], POPH 3.9% [Grade A- 1 (2%), grade B - 0 and grade C - 1 (2%)], intraabdominal collection in 23.5% and wound infection in 29.4%. Mean CRP levels on POD1 and POD3 were significantly higher in patients developing CR-POPF than those who did not develop [217 (\pm 79) mg/dL vs 156 (\pm 49) mg/dL [p= 0.016]] on POD1 and 231 (\pm 29) mg/dL vs 161 (\pm 57) mg/dL (p= 0.032)] on POD3. Similarly, median drain fluid IL6 levels on POD1 and POD3 were significantly higher in patients developing CR-POPF than those who did not develop CR-POPF [211 (125, 425) fg/dl vs 99 (15, 170) fg/dl [p= 0.045] on POD1 and 110 (22,28) fg/dl vs 10 (1.8, 45) fg/dl (p= 0.002)] on POD3. Patients who tested negative for Urine trypsinogen-2 on POD 3 had significantly lesser probability for developing CR-POPF compared to those who tested positive [1 VS 24 (p<0.001)]. A model comprising both drain fluid IL6 and urine trypsinogen-2 on POD3 confidently rules out occurrence of CR-POPF.

Conclusion: Drain fluid IL6 and urine trypsinogen-2 on POD3 can rule out occurrence of CR-POPF in postoperative period.

P 80. SURGICAL APPROACH FOR PANCREATIC ADENOCARCINOMA: UNCOMPLICATED ENDS JUSTIFY THE MEANS (PART 1: PANCREATICODUODENECTOMY)

S Naffouje, D Pointer, M Satyadi, P Hodul, D Anaya, J Pimiento, M Malafa, D Kim, J Fleming, J Denbo

Presenter: Samer Naffouje MD | Moffitt Cancer Center, United States

Background: Surgical resection remains the cornerstone of the oncologic management of pancreatic ductal adenocarcinoma (PDAC). However, major pancreatic resections, such as pancreaticoduodenectomy (PD), are associated with high rates of complications with delayed gastric emptying (DGE) and postoperative pancreatic fistula (POPF) being the most common pancreatotomy-specific morbidities (PSM). Herein, we hypothesize that, in the absence of PSM, minimally-invasive surgery (MIS) may result in improved immediate postoperative outcomes compared to the open approach in PD.

Methods: NSQIP pancreatotomy-targeted database 2014-2019 was used for the analysis. We selected patients with adequate functional status (ECOG 0-1) who underwent elective oncologic PD for the diagnosis of stage T1-T3 non-metastatic PDAC with a reported surgical approach and without any additional visceral or vascular resection. Also, selection included only patients who have available report on PSM. We divided the patients into two groups based on their postoperative morbidity profiles: No-PSM and PSM groups. Then, each group was divided into subgroups based on the surgical approach: Open vs. MIS. The analysis was performed based on the intention-to-treat including conversions in the Open subgroup. We propensity-score matched patients between the subgroups of Open and MIS on a ratio of 3:1 and postoperative outcomes were compared in the matched datasets.

Results: NSQIP database included 39,779 patients. We selected 8,121 PD patients based on the above criteria. 6,267 (77.2%) patients fell in the No-PSM group, whereas 1,854 (22.8%) had PSM. In the No-PSM group, 5,707 (91.0%) had Open PD vs. 560 (9%) who had MIS. After calculating the propensity score, 1,656 patients from the Open subgroup were matched to 552 peers in the MIS subgroup. Upon outcomes analysis, MIS patients underwent significantly longer procedures (423 ± 113 vs. 359 ± 114 minutes; $p < 0.001$) but had lower rates of organ space infections (3.3% vs. 5.9%; $p = 0.015$), postoperative transfusions (8.9% vs. 13.4%; $p = 0.005$), sepsis (2.7% vs. 5.6%; $p = 0.006$), major morbidity (15.4% vs. 19.9%; $p = 0.001$) and general morbidity (22.1% vs. 29.1%; $p = 0.004$). Importantly, MIS patients had a one-day shorter median hospitalization (6 vs. 7 days; $p = 0.027$). There was no difference in mortality, reoperation, or 30-day readmission rates between these two subgroups. In the PSM group, 1,686 (90.9%) had Open PD vs. 168 (9.1%) who had MIS. 441 patients from the Open subgroup were matched to 147 in the MIS subgroup. Upon comparison of outcomes, MIS patients continued to have longer operative times (454 ± 133 vs. 366 ± 114 minutes; $p < 0.001$). However, there was no difference in postoperative morbidity, mortality, reoperation, length of hospitalization, discharge destination, or 30-day readmission rates.

Conclusion: PSM, including DGE and POPF, is common among patients who undergo PD for PDAC. In the absence of PSM, MIS provides lower rates of morbidity and results in shorter hospitalization. These benefits of MIS over Open PD cease in the occurrence of PSM.

P 81. THE USE OF VASOPRESSORS DURING DECEASED DONOR PANCREAS PROCUREMENT DECREASES THE RISK OF PANCREAS TRANSPLANT GRAFT FAILURE

E Siskind, R James, N Koizumi, A Christian, R Plews, S Patel, J Ortiz

Presenter: Eric Siskind MD | University Medical Center of Southern Nevada, United States

Background: Pancreas transplantation from deceased donors is a recognized cure for type 1 diabetes in appropriate patients. There is scant data on the management of deceased donors to ensure optimal quality pancreatic allografts for transplantation

Methods: A retrospective analysis of the UNOS database between 2000 and 2019 was performed to analyze the correlation between use of vasopressors during deceased donor pancreas procurement on pancreas transplant graft failure and patient survival. Patient and graft survival rates (at 3-, 6-month, and 1-, 3- and 5- year post-transplant) were analyzed. The analyzed data included 17,348 pancreas transplant recipients, including 12,857 (74%) simultaneous pancreas-kidney (SPK), 1,440 (8%) pancreas transplant alone (PTA), and 3,051 (18%) pancreas-after-kidney (PAK) transplant recipients

Results: Use of dopamine during deceased donor procurement was found to increase the risk of graft failure by 18% (HR=1.18, p0.10).

Conclusion: In conclusion, the absence of use of any vasopressors, or the use of dopamine is associated with a higher risk of both pancreas transplant graft failure and patient mortality, while the use of phenylephrine and norepinephrine reduce the risk of patient mortality. This information should guide deceased donor hemodynamic support management in anticipation of pancreas procurement for future transplantation.

P 82. TRENDS AND PROGNOSTIC SIGNIFICANCE OF TIME-TO-TREATMENT IN PANCREATIC CANCER: A POPULATION-BASED STUDY

K Sugumar, JJ Hue, S Gupta, S Markt, LM Ocuin, LD Rothermel, JB Ammori, JM Hardacre, JM Winter

Presenter: Kavin Sugumar MD | Case Western Reserve University School of Medicine, United States

Background: Time-to-treatment (TTT) is an important quality-of-care metric in the management of cancer patients. Previous studies show that a delay in TTT in esophageal, breast, and liver malignancies results in poor outcomes, however this remains unclear in pancreatic adenocarcinoma (PDAC). In this study, we evaluate the recent trends in TTT, causes for delay and its effect on long-term survival.

Methods: We included patients with PDAC of all stages from the National Cancer Data Base (NCDB, 2006-16), who either underwent surgical resection or chemotherapy/radiotherapy (CT/RT). We excluded treatment-naïve patients. For this study, the TTT was defined as the duration between the tissue diagnosis and the first treatment. For patients who did not receive a biopsy prior to surgery, treatment and biopsy are synonymous and TTT is recorded as 0 days in the NCDB. Linear regression coefficient (β) was used to study the trends in time delay (in days) between 2006-16.

Results: A total of 149,284 patients were included. The median TTT was 24 days. Patients that received neoadjuvant CT/RT with surgery had a longer TTT (27 days) compared to patients that received upfront surgery (15 days, $p=0.01$, Table 1). Using multivariable logistic regression, we found that increasing age (OR: 1.48, $p<0.0001$), Black race (OR: 1.3, $p<0.0001$), lower educational status (OR: 1.2, $p<0.0001$), Medicaid insurance (OR: 1.4, $p<0.0001$), treatment at academic centers (OR: 1.3, $p<0.0001$), higher Charlson-Deyo Comorbidity Index (OR: 1.2, $p<0.0001$), and CT/RT (OR: 1.5, $p<0.0001$) were associated with an increased TTT. There was a steady rise in median TTT from 22 to 26 days over the ten-year study period ($\beta=0.4$, $p<0.001$), suggestive of a worsening trend. On subgroup analysis, the increase was more evident for stage I ($\beta=1.4$, $p<0.0001$) and II ($\beta=0.74$, $p<0.0001$) disease. Concurrently, there was an increasing trend in utilization of neoadjuvant CT/RT between 2006-16 in early stage PDAC. On Cox regression, TTT delay was associated with poor overall survival in stage I (HR: 1.5, $p<0.0001$) & II (HR: 1.1, $p<0.0001$) patients, but better survival in stage III (HR: 0.93, $p<0.0001$) & IV (HR: 0.64, $p<0.0001$) patients.

Conclusion: While TTT is acceptable for the majority of patients, delayed treatment approaching 2 months was observed in 10% of the population. There is a dire need to address disparities in initiation of treatment in PDAC. The rising temporal trend in TTT may be attributed due to the increasing shift toward neoadjuvant CT/RT in early stage PDAC and/or the increasing use of tissue biopsy prior to surgery. We also underscore the detrimental effect on the survival with delay in treatment of early stage PDAC.

Table 1. Time-to-treatment (time duration from tissue diagnosis to initial treatment, days)

Parameter	Mean	10 th percentile	25 th percentile	50 th percentile	75 th percentile	90 th percentile
Overall time-to-treatment (days)	30.22	4	13	24	39	59
Time-to-treatment by stage						
Stage I	33.87	0	13	27	43	69
Stage II	27.35	0	9	22	36	56
Stage III	36.85	11	19	29	45	69
Stage IV	30.07	8	14	24	37	56
Time-to-treatment by type of initial treatment						
Surgery	20.57	0	0	15	29	46
Chemotherapy or radiotherapy	34.04	10	17	27	42	63

P 85. GUIDELINES ON PANCREATIC CYSTIC NEOPLASMS: MAJOR INCONSISTENCIES WITH AVAILABLE EVIDENCE AND CLINICAL PRACTICE

G Marchegiani, R Salvia on behalf of the "Verona EBM 2020 on IPMN"

Presenter: Alberto Balduzzi MD, PhD | University of Verona, Italy

Background: Most of available guidelines for the management of pancreatic cystic neoplasms (PCNs) have been developed starting from a low level of evidence, except for European evidence-based guidelines. The aim of this project is to assess their dissemination in Europe with particular attention to low human development index countries where the absence of experienced centers may produce disparities in the treatment offered.

Methods: An online survey was sponsored through UEG official channels and linked to a new application for smartphones specifically designed for guidelines dissemination. To catch the real-life scenario of guidelines application in Europe, no restrictions were imposed in terms of specialty or center caseload.

Results: Response rate was 52.4% (225/429). Surgery (59.5%) and gastroenterology (36.4%) were the most represented specialties. Participants coming from academic/teaching hospitals were 84.8% and 50% were from centers with a high caseload for PCN. About 77% were aware about European guidelines and 37.3% stated to follow them in the clinical practice. Case vignettes were then used to verify the actual application of European guidelines among their followers revealing that only 10.5% would follow their suggestions in case of main duct dilatation (5-9.9mm), 43.5% in case of an IPMN > 40mm and 74.1% in case of small multifocal branch duct IPMNs. Regarding low-evidence areas, 17.7% stated that there is enough evidence to suggest surgery in case of main duct dilatation (5-9.9mm) and 38% on the basis of cyst size. In absence of indication for surgery, most of participants would never recommend lifetime discontinuation (78.3%), but only 41.7% believe that there is enough evidence to recommend a lifetime surveillance.

Conclusion: European guidelines dissemination is still partial and requires implementation programs in all European countries. Only one out of three specialists prefer them, but the actual application in the clinical practice is even lower especially when dealing with recommendations that come from low-evidence areas.

P 86. SPECIALTY PALLIATIVE CARE PROVIDER PERSPECTIVES ON PREOPERATIVE CONSULTATION FOR PATIENTS WITH PANCREATIC DUCTAL ADENOCARCINOMA

G Wu, L Demyan, A Blumenthaler, E Burns, G Deutsch, JM Herman, W Nealon, MJ Weiss, D Deperalta

Presenter: Grace Wu MD | Zucker School of Medicine at Hofstra/Northwell, United States

Background: Currently two randomized trials are enrolling patients to determine whether there is benefit to early specialty palliative care evaluation in patients undergoing curative-intent cancer surgery. The aim of this study is to evaluate specialty palliative care (SPC) providers' insights, perceptions, and current experiences regarding preoperative SPC consultation in patients with pancreatic cancer. We hypothesize that while SPC providers may view preoperative palliative care favorably, barriers such as limited resources and the reluctance of other providers and patients, may prevent wide-spread adoption in practice.

Methods: A qualitative investigation using 1:1 interviews consisting of 40 open-ended questions was conducted from January 2021 to May 2021 using convenience sampling. Data accrual continued until theme saturation was achieved. Grounded theory approach was used for data coding and analysis.

Results: A total of 9 interviews were conducted with expert SPC providers from 3 academic medical centers—6 female and 3 male, 5 inpatient and 4 outpatient. The median number of years in practice was 10 (IQR 1.25-19). 78% of SPC providers reported being infrequently consulted during the perioperative period, with 89% reporting that medical oncology was the most likely team member to place a consultation. All providers believed there is a role for SPC in potentially curative malignancy, and 78% stated SPC can occur in parallel with curative intent treatment. Most consistently cited benefits include symptom management, third-party expert communication, and normalizing SPC. Similarly, 89% of providers said there is a role for end-of-life conversations in potentially curative malignancies, which gives patients the opportunity to consider the "what-ifs." While all SPC providers had a positive view of seeing pancreatic cancer patients at diagnosis, common concerns include staffing limitations, primary provider resistance to SPC, and perceived intangible benefits of SPC by asymptomatic patients (Table 1). A majority of SPC providers (67%) believed that the surgeon is best suited to lead preoperative advance care planning and end-of-life conversations. However, 78% of SPC providers felt that patients are not comfortable discussing long-term goals of care with their surgical oncologists.

Conclusion: Specialty palliative care providers view the introduction of SPC at or shortly after diagnosis of pancreatic cancer as beneficial for goal-concordant care and improved quality of life. A common theme, however, is that though SPC may be beneficial at many stages, it is most accepted when patients are actively symptomatic, or if combined with another provider's visit when something "tangible" is being offered. While there are many identifiable benefits to early introduction of SPC, there may be an opportunity to improve delivery of primary palliative care provided by surgical teams with more regular SPC involvement upon increased case complexity. Further research on how SPC providers introduce their role in the management of intention-to-cure cancer surgery is warranted.

Table 1: Perceived benefits and barriers to preoperative SPC consultation

Benefit (% of SPC providers)	Representative Quotes
Symptom management (89%)	<p>“When people walk into a doctor’s office, they probably have five problems connected to [their cancer]. The disease, the wanting to get better, the nausea, the pain, the constipation or the diarrhea. The oncologist is probably going to get to two of those. Having another [provider] available allows you to get to three four and five, which improves quality of life.”</p> <p>“Our goal is not only end of life... it’s following a patient throughout their journey—early, mid, and end stages of the disease. Treatment, and surgeries, can come with a lot of side effects, so palliative care especially at an earlier involvement has been shown to increase survival and better quality of life for patients.”</p>
Expert communication (78%)	<p>“We have the luxury of time... we can make sure that there’s better communication between the medical providers as a whole and the patient and their families.”</p> <p>“There is a sizable amount of data out there that says, a patient and physician pair are predisposed to try to please each other and that results in patients trying to do what doctors want, and doctors trying to do what they think patients want... having a third party... help[s] the two people realize that it’s okay to take a different path than what they’re expecting of each other.”</p> <p>“Experience has really helped me be able to be comfortable with those conversations... because we do it all the time in palliative medicine, it’s a lot different from someone who does it every once in awhile. I don’t want to say it’s more mundane, that’s not the word, but I think it’s not as emotional for us, too.”</p>
Navigation through disease process (67%)	<p>“I’m like their medical friend in the system... trying to patch the holes of understanding... trying to give them a more informed sense of what their diagnosis is, and helping them navigate through it.”</p> <p>“... helping prepare for those decision points if they come, celebrating and supporting patients if they don’t have to make those decisions, but if they do need to... being able to be alongside and helping them navigate.”</p>
Barrier (% of SPC providers)	
Resource limitations (67%)	<p>“The problem comes if there’s this gap where you might have to follow people for two or three years... and we just don’t have the ability to do that. There’s not enough of us.”</p> <p>“There’s always resources... do you have enough palliative care providers to actually see all those patients, that’s a big barrier.”</p>
Reluctance of patients, lack of “tangibles” early on (56%)	<p>“When you make an appointment for a palliative care doctor, especially first visit that’s not on the same day as one of the cancer doctors, they don’t happen, people don’t show up.”</p> <p>“Ideally coordinating it with lab work or something else they’re already coming in for... takes a little bit of that pressure of what that visit means down.”</p> <p>“The stigma of involving palliative care, and providing the education that it isn’t just end of life care, it’s not something to scare you... We’re not saying go to palliative care because you’re dying.”</p>
Reluctance of other providers (33%)	<p>“Sometimes [surgical oncologists] are not aware of what we do and how they can use us for their patients.”</p> <p>“I think it’s patient reluctance... patients and doctors and surgeons both, really didn’t want to concentrate on the negative.”</p>

P 87. THE USE OF A MOBILE APPLICATION TO DISSEMINATE GUIDELINES ON CYSTIC NEOPLASMS OF THE PANCREAS - A SNAPSHOT STUDY OF 1000 CASE-SIMULATIONS

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Presenter: Alberto Balduzzi MD, PhD | University of Verona, Italy

Background: The existence of pancreatic cystic neoplasm (PCN) management guidelines is acknowledged by the European scientific community. However, no data exist on their actual application in clinical practice, resulting in the risk of treatment disparities among different countries and hospitals. Our objective is to implement PCN guidelines dissemination through a mobile application named "iCyst" and to assess the guidelines chosen for specific case scenarios.

Methods: The iCyst app is a digital tool that provides access to the three main existing guidelines (European evidence-based, International Association of Pancreatology, and American Gastroenterological Association). Through a case simulation system, for one year, the app prospectively registered users' guideline choice.

Results: During the study period, 276 users downloaded iCyst and entered 1,020 completed simulations. Most users were European (88%) and were either surgeons (69%) or gastroenterologists (29%). Six different representative scenarios were identified among the simulated cases. Overall, the European guidelines were the most commonly preferred guidelines (52%). In 16% of cases, the users did not choose any of the available guidelines. The rate of users not following any of the guidelines markedly increased in scenarios pertaining to unfit for surgery or cyst growth rate ($p < 0.05$).

Conclusion: Digital apps can be used to disseminate guidelines in clinical practice. Guideline dissemination might serve as the basis for future research lines on specific clinical scenarios that iCyst identifies as critical among the digital community involved in pancreatic cystic neoplasm treatment.

P 88. ASSESSING THE UTILITY OF THE 2012 ATLANTA CONSENSUS TERMINOLOGY ON POST-INFLAMMATORY PERI-PANCREATIC COLLECTIONS: TOWARDS A MODERN CLASSIFICATION

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Presenter: Louise Finch MPhil, MBChB | Manchester Royal Infirmary, United Kingdom

Background: The 1992 Atlanta consensus conference was a pathfinding document which provided a framework for standardization of the terminology for description of acute pancreatitis and its complications. The 2012 update of the Atlanta consensus criteria incorporated new insights relating to the temporal course of the disease and the nature of fluid collections. This study assesses the use of the 2012 terminology in the current literature.

Methods: A systematic review of the literature was performed using Medline, Embase and Cochrane databases. Separate searches were performed for two time periods 1992 to 2012 and 2013 to 2020 in order to reflect the time when the new Atlanta classification was published. The keywords and MESH headings "acute peripancreatic fluid collection", "acute necrotic collection", "pseudocyst" and "walled-off pancreatic necrosis" were used. Searches were also conducted for use of terms not recommended in the 2012 update including "pancreatic phlegmon" (removed in 1992), "pancreatic abscess" and "infected pseudocyst".

Results: Searches identified 56,309 publications on pancreatitis between 1992 and 2012 and 46,874 on pancreatitis between 2013 and 2020. There was a significant increase in the use of current 2012 Atlanta consensus terminology (acute peri-pancreatic fluid collection, acute necrotic collection, walled-off necrosis and pseudocyst; $P < 0.0001$; $\times 2$ with Yates correction for each term) between 1992 and 2012. Since 2012, the term "phlegmon" was used in 4 publications, 348 publications used "pancreatic abscess" and 61 "infected pseudocyst".

Conclusion: There is general compliance with the current system of nomenclature for peri-pancreatic post-inflammatory fluid collections based on time course and fluid consistency. However, there is a case for future modifications to incorporate the presence of symptomatic infection.

P 89. OPPORTUNITY COSTS OF SURGICAL RESECTION AND PERIOPERATIVE CHEMOTHERAPY FOR PANCREATIC ADENOCARCINOMA

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Presenter: Breana Boyd BA | Brody School of Medicine, United States

Background: Due to the intensity of multimodality treatment and high perioperative morbidity rates, patients with resected pancreatic ductal adenocarcinoma (PDAC) spend a substantial amount of time in clinical care. However, time spent in receipt of care relative to overall survival time has not been previously described. The primary aim was to determine the total time spent in receipt of surgical care and perioperative chemotherapy in patients undergoing resection for PDAC.

Methods: A retrospective cohort study of all patients who underwent curative-intent resection for PDAC at a single-institution tertiary care center was performed (2015-2019). Patients who died within 30 days of resection were excluded. Exact times for all relevant clinician visits, laboratory, radiologic and procedural studies, and treatment visits were abstracted from the primary medical record, and estimated travel time was calculated based on patient address. Care time was divided into preoperative, surgical (including

Results: A total of 107 patients were included. Patients spent a median of 5.0% (IQR 2.4-10.1%) of survival time in receipt of clinical care for PDAC (Table). Preoperative, surgical, and systemic therapy phases of care required a median of 5 (IQR 3-9), 14 (IQR 11-24), and 53 (IQR 38-66) separate healthcare encounter dates. Median per-visit travel time was 30 minutes (IQR 18-54), and cumulative travel time for patients was 19.4 hours (IQR 11.8-46.0). A small cohort of patients (13.0%, n=14) spent more than 10% of total survival time in surgical care, and 7.7% (n=4) patients spent more than 10% of survival time in receipt of systemic therapy.

Conclusion: Time spent in receipt of surgical care does not appear to represent a substantial time burden relative to survival time for most patients with resected PDAC; however, for a subset of patients, the time burden is considerable. Further research to determine predictors of increased time spent in receipt of care is warranted to inform patient and surgeon communication and decision-making.

Time	Median	IQR
Overall Survival (months)	17.5	9.3-24.4
Median Overall % Survival Time	5.0%	2.4-10.1%
Preoperative Care		
Median # Healthcare Encounter Dates	5	3-9
Median Care Time (hours)	22.8	10.1-114.7
Median % Survival Time	0.3%	0.1-0.9%
Surgical Care		
Median # Healthcare Encounter Dates	14	11-24
Median Care Time (hours)	223.3	164.8-391.4
Median % Survival Time	2.1%	1.2-5.1%
Systemic Therapy Care		
Median # Healthcare Encounter Dates	53	38-66
Median Care Time (hours)	481.0	266.9-696.4
Median % Survival Time	3.6%	1.7-6.0%

P 90. PREDICTORS OF RELATIVELY FAVORABLE SURVIVAL AMONG PATIENTS WITH UNTREATED STAGE IV PANCREATIC CANCER

P Ahorukomeye, J Hue, K Sugumar, J Winter

Presenter: Peter Ahorukomeye | Case Western Reserve University School of Medicine, United States

Background: Past clinical trials demonstrated that patients with stage IV pancreatic cancer (PC) receiving single-agent chemotherapy have an overall survival of 5 months. Multi-agent chemotherapy extended survival to 9-12 months. Many patients diagnosed with advanced disease never receive chemotherapy for numerous reasons, yet little is known about the natural history of these patients. We aimed to identify predictors of favorable survival among patients with untreated stage IV PC using real-world institutional data as well as the National Cancer Database (NCDB).

Methods: Patients with untreated stage IV PC were identified using the institutional electronic medical record (2011-2019) and the NCDB (2011-2017). Patients were categorized based on survival: ≥ 4 months (top quartile) or < 4 months (bottom three quartiles). Multivariable models were used to account for confounding.

Results: Within our institution, 178 patients were included. Median age was 72 years (range: 19-93). Most patients presented with hepatic metastases (60.5%), while 24.6% presented with multi-organ metastatic disease. Median survival of the full cohort was 1.8 months (interquartile range (IQR): 0.9-4.0 months). 40 patients (22.5%) survived ≥ 4 months, of whom 50% survived ≥ 8 months, 37.5% survived ≥ 12 months, and 10% survived ≥ 24 months. There were no differences in demographics or the proportion of patients with diabetes based on survival. Performance status and Charlson comorbidity index were similar between groups. Patients who survived ≥ 4 months more frequently presented with pulmonary, peritoneal, or other metastatic sites (27.8% vs 11.4%) as compared to patients who survived < 4 months, and less frequently with hepatic metastases (52.8% vs 62.6%) or multiple metastatic sites (19.4% vs 26.0%) ($p=0.05$). Median CA19-9 was lower among patients who survived ≥ 4 months (261.0 U/mL, IQR: 123.32, 6791.12 U/mL) relative to those who survived < 4 months (2173.51 U/mL, IQR: 214.52, 26738.46 U/mL) but this was not statistically significant ($p=0.29$). Within the NCDB, 25,854 patients met inclusion criteria. The median overall survival was 1.4 months (IQR: 0.7, 3.0 months): 82% survived < 4 months and 18% survived ≥ 4 months from diagnosis. Of patients who survived ≥ 4 months, 48.6% survived ≥ 8 months, 32.7% survived ≥ 12 months, and 14.6% survived ≥ 24 months. Patients who survived ≥ 4 months were younger (70 vs 73 years, $p<0.001$) and less comorbid (Charlson-Deyo score 0: 66.6% vs 57.9%, $p<0.001$). Patients who survived ≥ 4 months were less likely to present with multiple metastatic sites (19.6% vs 29.8%, $p<0.001$). A greater proportion of patients who survived ≥ 4 months had a CA19-9 < 980 U/mL compared to those who survived < 4 months (66.7% vs 76.8%, $p<0.001$). On multivariable logistic regression, multiple metastatic sites was associated with a reduced likelihood of surviving ≥ 4 months (odds ratio (OR)=0.66, 95% confidence interval (CI)=0.51-0.85) relative to isolated hepatic metastases. Additionally, CA19-9 ≥ 980 U/mL was associated with a reduced likelihood of surviving ≥ 4 months, relative to CA19-9 values between 5-37 U/mL (OR=0.61, 95% CI=0.39-0.94).

Conclusion: There is a small cohort of patients with stage IV PC who survive ≥ 4 months without any treatment. Interestingly, almost half of patients who survive ≥ 4 months will survive ≥ 8 months. This patient population may gain significant benefit from administration of systemic therapies.

P 91. SINGLE-STAGE ROBOTIC-ASSISTED MANAGEMENT OF NECROTIZING GALLSTONE PANCREATITIS WITH WALLED-OFF PANCREATIC NECROSIS

Z Senders, K El-Hayek

Presenter: Zachary Senders MD | MetroHealth Medical Center, United States

Background: Necrotizing gallstone pancreatitis with walled-off pancreatic necrosis (WOPN) is a complex disease for which endoscopic, percutaneous image guided, and surgical approaches have been described to treat the pancreatic necrosus. Regardless of approach to the pancreas, patients ultimately require cholecystectomy to prevent recurrent gallstone pancreatitis. A single-stage approach, as described here, may avoid multiple interventions and their associated morbidity.

Methods: This is an institutional review board approved case series of patients undergoing planned robotic-assisted transgastric cystogastrostomy, pancreatic necrosectomy, and cholecystectomy (RTGC/PN/C) for necrotizing gallstone pancreatitis with WOPN. Patient demographics, history, and peri-operative data and outcomes were collected.

Results: A total of 5 patients with necrotizing gallstone pancreatitis with WOPN underwent planned RTGC/PN/C between 2019-2020. Patient characteristics and outcomes are shown in Table 1. Time interval from onset of symptoms to operation ranged from 30 to 103 days. Maximum diameter of pancreatic necrosus on cross-sectional imaging was between 6.5 and 17 cm. Operative indications included intractable pain, failure to thrive, and early satiety. No patient had a history of alcohol abuse. Of the 5 patients taken to surgery, one patient underwent robotic-assisted cholecystectomy alone as intraoperative ultrasound noted significant regression of the necrosus. One patient with a complicated cysto-duodenal fistula and extensive retrogastric saponification underwent a retrocolic approach to necrosectomy, and ultimately died on post-operative day 18 due to progressive necrotizing pancreatitis. RTGC/PN/C was successfully completed in 3 patients. Among these patients, length of stay ranged from 1-3 days and there were no intra-operative or post-operative complications. None of these patients developed recurrent WOPN or required additional procedures, and their symptoms were completely resolved at last follow-up.

Conclusion: In select patients, robotic transgastric cystogastrostomy, pancreatic necrosectomy, and cholecystectomy is safe and feasible.. The described approach treats both the etiology and sequelae of this complex disease in a single stage.

Table 1. Patient characteristics, peri-operative data, and outcomes of patients undergoing planned robotic transgastric cystogastrostomy, pancreatic necrosectomy, and cholecystectomy for necrotizing gallstone pancreatitis.

	Patient 1	Patient 2	Patient 3	Patient 4	Patient 5
Age	58	46	84	67	50
Gender	Male	Male	Female	Female	Male
BMI	26.7	30.6	23.6	30.7	29.8
Co-morbidities	DM, HTN, HLD	None	HTN, HLD	HTN, HLD, COPD	DM, HTN
Time from symptoms to OR (Days)	64	103	100	30	57
WOPN diameter (cm)	17	6.5	8.6	14	16
WOPN location	Head	Body	Body	Body	Head/Body
Inpatient at time of OR	Yes	No	No	No	Yes
Indication for OR	FTT	ES	P	P	P, FTT
Operation	RTGC/PN/C	RTGC/PN/C	Chole	RTGC/PN/C	Retrocolic PN/TGC/C
OR time (min)	226	227	207	277	331
LOS (days)	3	1	1	2	18
Positive pancreatic culture	Yes	No	No	No	Yes
Complication	No	No	No	No	Death
Recurrent WOPN	No	No	No	No	N/A
Repeat OR or intervention	No	No	No	No	Yes
Time to symptom resolution (days)	20	13	13	88	N/A

BMI body mass index, *WOPN* walled-off pancreatic necrosis, *LOS* length of stay, *DM* diabetes mellitus type 2, *HTN* hypertension, *HLD* hyperlipidemia, *FTT* failure to thrive, *ES* early satiety, *P* pain, *RTGC* robotic transgastric cystogastrostomy, *PN* pancreatic necrosectomy, *C* cholecystectomy, *TGC* transgastric cystogastrostomy

P 92. SURGICAL APPROACH FOR PANCREATIC ADENOCARCINOMA: UNCOMPLICATED ENDS JUSTIFY THE MEANS (PART 2: DISTAL PANCREATECTOMY)

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Presenter: Samer Naffouje MD | Moffitt Cancer Center, United States

Background: Pancreatic resection remains the cornerstone of the oncologic management of pancreatic ductal adenocarcinoma (PDAC) albeit associated with high rates of complications. Delayed gastric emptying (DGE) and postoperative pancreatic fistula (POPF) remain the most common pancreatectomy-specific morbidities (PSM). In a previous work, we demonstrated that in the absence of PSM, minimally-invasive surgery (MIS) provided improved short-term outcomes compared to Open pancreaticoduodenectomy, whereas in the occurrence of PSM these benefits resolve. We aim to analyze distal pancreatectomy (DP) as a separate procedure to conclude whether MIS provides short-term advantage in the absence and occurrence of PSM.

Methods: NSQIP pancreatectomy-targeted database 2014-2019 was used for the analysis. We selected patients with adequate functional status (ECOG 0-1) who underwent elective oncologic DP for the diagnosis of stage T1-T3 non-metastatic PDAC with a reported surgical approach and without any additional visceral or vascular resection. We divided the patients into two groups based on their postoperative morbidity: No-PSM and PSM groups. Each group was then divided into subgroups of Open vs. MIS. The analysis was performed based on the intention-to-treat including conversions in the Open subgroup. We propensity-score matched patients between the subgroups of Open and MIS on a ratio of 1:1 and postoperative outcomes were compared in the matched datasets.

Results: NSQIP database included 39,779 patients. 2,312 DP patients met the selection criteria. 1,878 (81.2%) had No-PSM, whereas 434 (19.8%) had PSM. In the No-PSM group, 1,057 (56.3%) had Open DP vs. 821 (43.7%) who had MIS. 708 patients from the Open subgroup were propensity-score matched to 708 peers in the MIS subgroup. Upon outcomes analysis, MIS patients had significantly longer operations (240 ± 91 vs. 222 ± 103 minutes; $p < 0.001$) but had lower rates of postoperative transfusions (6.1% vs. 10.9%; $p = 0.001$), major morbidity (12.6% vs. 18.9%; $p = 0.001$) and general morbidity (15.1% vs. 20.9%; $p = 0.005$). Moreover, MIS patients had a one-day shorter median hospitalization (5 vs. 6 days; $p = 0.001$). There was no difference in mortality, reoperation, discharge destination, or 30-day readmission rates between these two subgroups. In the PSM group, 226 (52.1%) had Open PD vs. 208 (47.9%) who had MIS. 145 pairs of patients were matched between the subgroups. Upon comparison of outcomes, MIS patients continued to have a trend toward longer operative times (265 ± 100 vs. 242 ± 105 minutes; $p = 0.053$). No difference was noted in postoperative morbidity, mortality, reoperation, length of hospitalization, discharge destination, or 30-day readmission rates.

Conclusion: PSM, including DGE and POPF, influence the postoperative course in patients who undergo DP for the diagnosis of PDAC. In the absence of PSM, MIS provides lower rates of morbidity and results in a one-day median shorter hospitalization. These benefits of MIS over Open PD disappear if PSM occur.

P 93. THE IMPACT OF COVID-19 ON TIME-TO-TREATMENT IN PANCREATIC ADENOCARCINOMA: A SINGLE INSTITUTIONAL EXPERIENCE

K Sugumar, L Cao, JJ Hue, LD Rothermel, LM Ocuin, JB Ammori, JM Hardacre, JM Winter

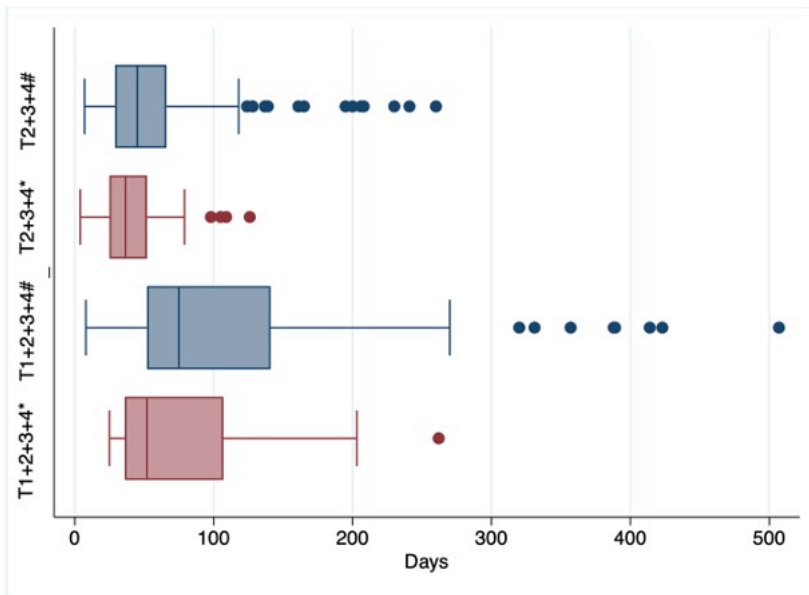
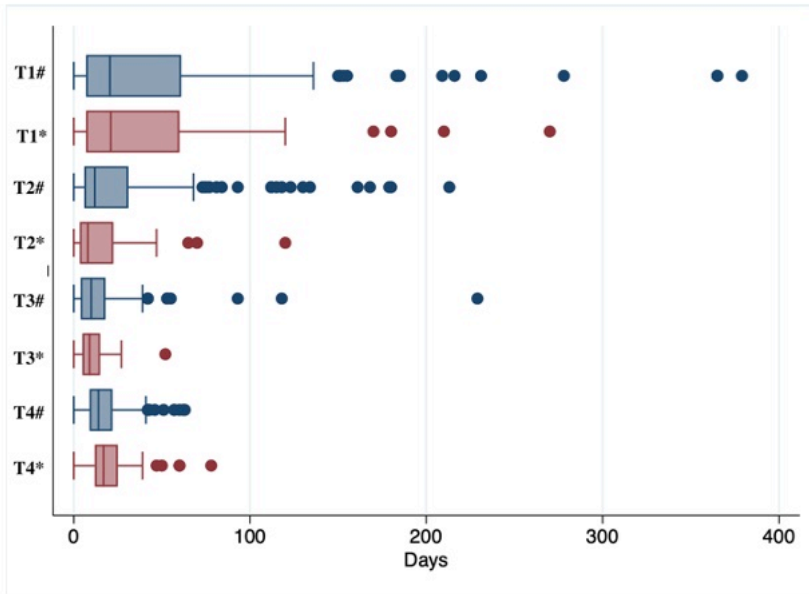
Presenter: Kavin Sugumar MD | Case Western Reserve University School of Medicine, United States

Background: The COVID-19 pandemic has resulted in a major shift in healthcare delivery among cancer patients. Herein, we evaluate the time-to-treatment (TTT) in patients with pancreatic adenocarcinoma (PDAC) during the pandemic.

Methods: A retrospective study of PDAC stage I-IV patients was conducted at a single institution after the onset of the COVID-19 outbreak (March 2020-February 2021). TTT (in days) was divided into four categories: T1: symptom onset to initial provider evaluation, T2: initial provider evaluation to tissue diagnosis, T3: diagnosis to treating specialist consultation, T4: specialist visit to treatment. The post-COVID-19 TTT data was compared with PDAC patients managed before the pandemic (2017-19).

Results: 217 and 81 patients met inclusion criteria in pre-COVID and COVID periods. At presentation, 107 (49%) and 51 (62%) patients had advanced disease (stage III-IV) in these groups respectively. Though this change was not statistically significant, there was a trend towards an increased proportion of stage III-IV patients in the COVID cohort ($p=0.056$). The median T1, T2, T3, T4, and T1+2+3+4 was 30, 7, 4, 14, and 75 days in the pre-COVID cohort compared to 21, 8, 9, 17, and 52 days in the COVID cohort respectively (Figure 1). The TTT intervals were similar in both cohorts ($p>0.05$) except T1+2+3+4 ($p<0.05$), with a faster TTT in the COVID period.

Conclusion: The time-to-treatment in PDAC patients remains unchanged even amidst the COVID-19 pandemic. However, a greater proportion have advanced disease. These data suggest maintenance of patient flow-through the system, but perhaps a delay in clinical presentation by patients at symptom onset.



- pre-COVID patient cohort
 *- COVID patient cohort

P 94. THE IMPACT OF MULTI-AGENT CHEMOTHERAPY IN PANCREATIC ADENOCARCINOMA: A POPULATION-BASED STUDY UTILIZING THE SEER DATABASE

K Sugumar, S Gupta, LM Ocuin, LD Rothermel, JM Hardarce, JB Ammori, JM Winter

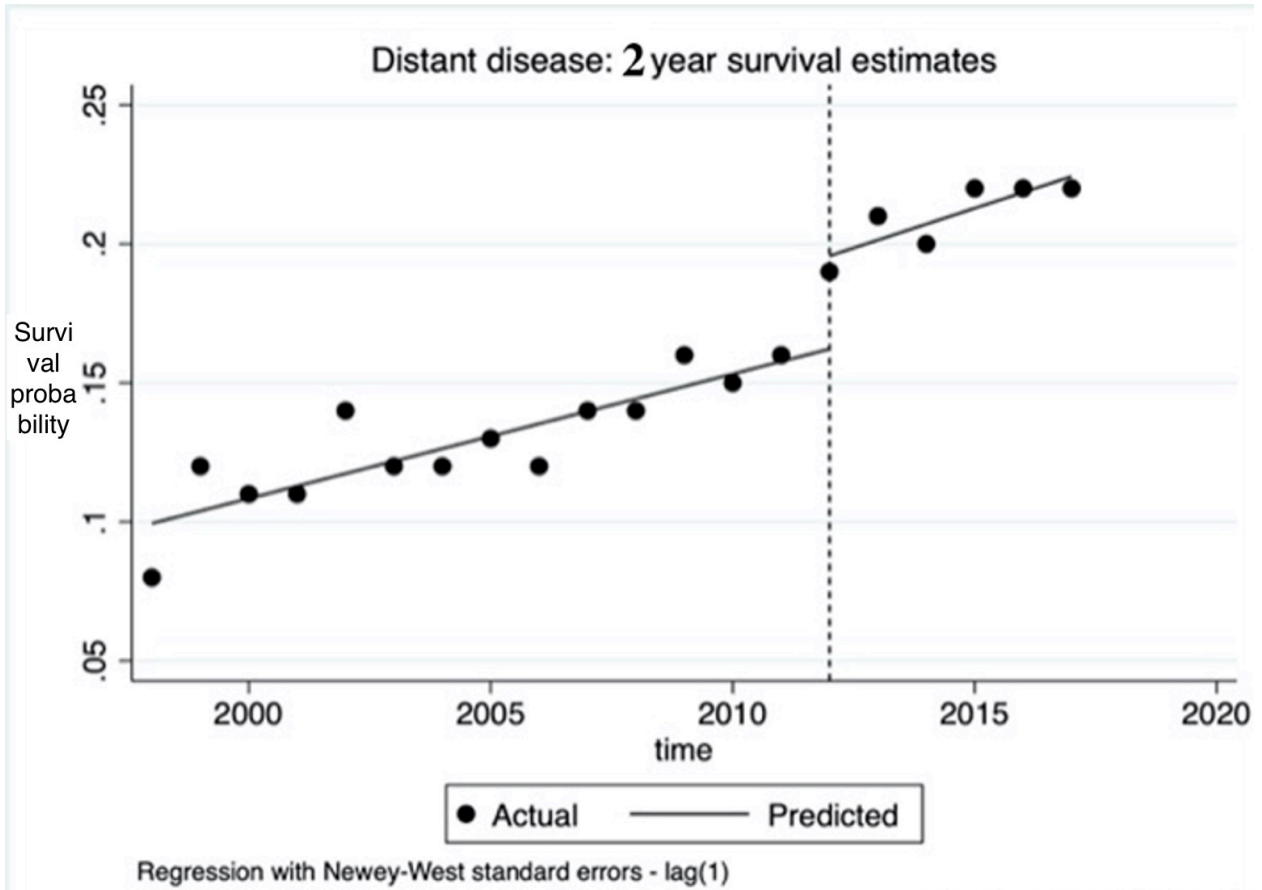
Presenter: Kavin Sugumar MD | Case Western Reserve University School of Medicine, United States

Background: Chemotherapy is the mainstay of controlling systemic disease in pancreatic adenocarcinoma (PDAC). Over the last decade, various landmark trials have demonstrated the usefulness of multi-agent chemotherapy in the treatment of PDAC. The ACCORD trial (2011) represented the first phase III trial comparing combination chemotherapy (FOLFIRINOX) and single agent (gemcitabine) for advanced disease. Following this trial, there has been an increasing trend towards using multi-agent chemotherapy for all stages of PDAC. Our goal was to study the population trends in overall survival of PDAC before and after the results of the ACCORD trial.

Methods: We used the Surveillance, Epidemiology, and End Results (SEER) database to identify the patients diagnosed with PDAC between 1998 and 2017. The cohort was divided into two groups; 1998-2011 and 2012-2017. We analyzed the overall survival between these two groups using Kaplan Meier analysis and multivariate Cox proportional hazards models. An interrupted time series analysis was also used to compare the temporal trends in 2-year survival between 1998 and 2017.

Results: A total of 47,134 patients were diagnosed with PDAC between 1998 and 2017. Eight percent of patients had localized disease, 35% had regional disease and 57% had distant disease. On univariate survival analysis, there was a significant increased survival probability in the 2012-17 group compared to the 1998-2011 group ($p < 0.05$). This difference remained significant on multivariate analysis while adjusting for covariates (HR=0.08, 0.78-0.92, $p = 0.05$). Subgroup analysis of individual stages of cancer also revealed significant results ($p < 0.05$). On interrupted time series analysis, we observed a steady rise in 2-year survival between 1998 and 2017 (Figure 1). However, the most significant jump in survival after 2011 was seen in distant disease ($\beta = 0.02$, 0.004-0.03, $p < 0.0001$).

Conclusion: There has been a steady rise in the overall survival of PDAC patients over the last two decades including after the ACCORD trial. This increase can be attributed due to advancements in improved chemotherapeutic agents including a global shift towards multi-agent chemotherapy. This occurs despite any paradigm shifting experimental improvements in cancer care in recent years.



P 95. THE INCIDENCE AND ETIOLOGY OF ACUTE PANCREATITIS IN FINLAND TODAY – A POPULATION-BASED STUDY

A Nikkola, J Nikkola, E Kari, A Roponen, A Tapaninaho, J Sand, J Laukkarinen

Presenter: Anssi Nikkola MD | Tampere University hospital, Finland

Background: The incidence of acute pancreatitis (AP) in Finland is reported as 70-100 per 100 000 inhabitants, the etiology being alcohol in 70% of the cases. These figures have not been updated since the 1990s. In other countries, biliary etiology is the most common. The diagnostics of different etiologies has improved during the past years. Our aim was to determine the current incidence and etiology of AP in Finland in a population-based study.

Methods: All patients treated for AP in Tampere area hospitals (Pirkanmaa Hospital District; second largest hospital district in Finland) during 2014-2015 were identified from the hospital register. Patient demographics and information about AP, including all etiology related factors, were collected.

Results: Pirkanmaa Hospital district population was 525 926 inhabitants in average during years 2014-2015. Out of these, 563 patients were treated for AP during 2014-2015. The incidence of AP was 53.5 per 100 000 inhabitants. 458 (81.4%) of the patients had their first AP episode. In 11.1% of the patients the etiology was not reliably studied or determined during the hospitalization. The etiology was determined during hospitalization in 88.9% of the patients: the etiology was biliary in 179 (31.8%) and alcoholic in 182 (32.3%) of the patients. Other etiologies included post-ERCP in 3.0%, tumor in 3.2%, drug-induced in 2.7%, autoimmune in 1.6%, post-operative in 1.1%, hypertriglyceridemia in 0.7%, hypercalcemia in 0.2%, miscellaneous in 1.6% and idiopathic in 10.5%.

Conclusion: The incidence of AP in Finland is 53.5/100.000, which is lower than reported in the 90s. Biliary and alcohol etiologies are equally common, in contrast to reported earlier. Thus, today alcohol is no more a dominating etiology in Finland.

P 96. THE PANCREATIC INFLAMMATORY MILIEU INFLUENCES THE DEVELOPMENT OF POSTOPERATIVE PANCREATIC FISTULA

K Herremans, A Riner, P Underwood, J Trevino, S Hughes

Presenter: Kelly Herremans MD | University of Florida College of Medicine, United States

Background: The development of postoperative pancreatic fistula (POPF) is a dreaded complication following pancreatic resection and has the potential to lead to intra-abdominal abscesses, hemorrhage and in severe cases, multisystem organ failure and death. Efforts have been focused on improving surgical techniques and optimizing prediction models in order to mitigate the risk of POPF. Recently the inflammatory milieu of the pancreatic tumor microenvironment has been shown to impact clinicopathologic variables, chemoresistance and survival. We hypothesized that the local pancreatic inflammatory milieu of the may also play a role in the development of POPF.

Methods: Surgical specimens obtained directly from patients undergoing pancreatic ductal adenocarcinoma resection were homogenized and analyzed for soluble proteins. Tissue homogenates were probed for 41 unique inflammatory proteins using a commercially available multiplex assay. Data were acquired using the MAGPIX system and analyzed using MILLIPEX Analyst 5.1. Descriptive statistics and postoperative clinical outcomes were obtained through a retrospective review. Statistical analysis was performed using the Wilcoxon rank sum test.

Results: 51 patients with pancreatic ductal adenocarcinoma underwent pancreatic surgical resection with a POPF rate of 17.6%. Three patients had drainage fluid rich in amylase but an uneventful postoperative course (biochemical leak), 3 patients required long term pancreatic drainage or percutaneous drain placement (grade B) and the remaining third required reoperation or their postoperative course lead to organ failure or death. In patients that developed POPF, the tumor microenvironment exhibited markedly reduced levels of macrophage-derived chemokine ($p=0.012$) and IL-17A ($p=0.045$).

Conclusion: POPF remains a devastating complication following the surgical resection of pancreatic cancer. These findings indicate that the development of POPF may be influenced by the local pancreatic inflammatory milieu at the time of resection. In addition to improving surgical technique and patient stratification using prediction models, the local inflammatory response should be considered in the development of POPF following pancreatic resections. Further research on the modification of the pancreatic inflammatory milieu would be beneficial to reducing POPF and improving patient outcomes.

P 97. THE TIMING AND THE DOSE OF ADVANCED CARE PLANNING IN PATIENTS WITH RESECTABLE PANCREATIC CANCER: WHO MAKES THE CALL?

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Presenter: Lyudmyla Demyan MD | Academic Medical Center, United States

Background: The timing and extent of Advance Care Planning (ACP) in patients with pancreatic ductal adenocarcinoma (PDAC) undergoing curative-intent resection are generally dictated by the operative surgeon. The aim of this study is to evaluate surgeons' insights, perceptions, and biases regarding preoperative ACP. We hypothesize that many surgeons harbor significant reservations about extensive preoperative ACP.

Methods: Pancreatic surgeons participated in a nationwide internet-based anonymous multiple choice question survey regarding preoperative ACP, between February 2021 and May 2021. Chi-square test or Fisher's exact test were used for categorical questions and the Mann-Whitney and Kruskal-Wallis tests were utilized for Likert scale. Statistical significance was set at $p < 0.05$.

Results: 131 surveys were completed (50% response rate). Surgeons demographics are presented in table 1. Surgeons reported that they discuss ACP preoperatively always (24%), often (26%), sometimes (26%), rarely (21%) or never (3%). 98% of surgeons identified benefits of preoperative ACP citing that it promotes delivery of goal-concordant care (83%), prognostic awareness and sets realistic expectations (82%) and provides patients with an opportunity for life planning (74%). 63% cited fear of causing confusion and sending mixed messages as one of the barriers to preoperative ACP. Surgeons also reported lack of time (56%), fear of taking away hope and motivation (54%), the emotional burden for the patient (46%), and language and cultural differences (21%) as additional barriers. 62% reported that preoperative ACP should be led by someone who understands the nuances of pancreatic cancer management and 56% of participants believed that the surgeon is best suited for this discussion; others reported that the medical oncologist (45%) or palliative care provider (43%) should lead preoperative ACP discussions. 62% of surgeons reported that ACP should occur before surgery and 22% reported that it should be deferred until recurrence. On bivariate analysis there were no significant differences in ACP discussion practices by region, number of operations performed per year or surgeon's estimate of percentage of patients cured. However, academic surgeons ($n=105$) more frequently reported lack of time as a barrier to preoperative ACP, compared to surgeons practicing in non-academic settings (hybrid and community, $n=26$) ($p=0.0384$). Surgeons who completed Complex Surgical Oncology Fellowship ($n=80$) more often reported that preoperative ACP promotes the delivery of goal-concordant care ($p=0.03$) and minimizes unnecessary aggressive treatments ($p=0.048$) compared to surgeons with other fellowship training or no training ($n=51$). Surgeons with >30 years of practice ($n=15$) were less likely to report that preoperative ACP ensures goal-concordant care ($p=0.0327$) compared to surgeons with < 30 years of experience ($n=116$). Female surgeons ($n=24$) were more likely to report that a Palliative Care Provider is best suited for preoperative ACP discussion ($p=0.0088$).

Conclusion: While almost all surgeons identified benefits of preoperative ACP, only half of the respondents typically discuss ACP with their patients preoperatively. Surgeons' gender, practice type, years in practice, and fellowship training may influence preoperative ACP discussion practices. Further studies are warranted to evaluate reasons underlying lack of concordance of surgeon's perceptions and to explore perceptions of patients with PDAC regarding timing and dose of preoperative ACP.

Table 1: Surgeons demographics.

Demographics	n (%)
Gender	
Female	24 (18%)
Male	107 (82%)
Type of practice	
Academic	105 (80%)
Hybrid	22 (17%)
Community	4 (3%)
Geographic location of practice	
Northeast	41 (31%)
Southeast	24 (18%)
Midwest	31 (24%)
Southwest	9 (7%)
West	13 (10%)
International	13 (10%)
Years in Practice	
< 5	29 (22%)
5-15	52 (40%)
16-30	35 (27%)
>30	15 (11%)
Fellowship	
Complex Surgical Oncology	80 (61%)
Hepatobiliary	23 (17%)
No fellowship	12 (9%)
Other	17 (13%)
Curative intent operations for PDAC per year	
< 10	12 (9%)
10-30	57 (44%)
31-50	34 (26%)
>50	28 (21%)
Estimated Percentage of patients cured	
<5 %	21 (16%)
5-15%	53 (41%)
16-30%	41 (31%)
31-50%	13 (10%)
>50%	3 (2%)
Typically discuss ACP preoperatively	
Always	31 (24%)
Often	34 (26%)
Sometimes	34 (26%)
Rarely	27 (21%)
Never	4 (3%)

P 98. UNEXPECTED OVER-EXPRESSION OF ALPHA-SYNUCLEIN IN PANCREATIC ADENOCARCINOMA DISCLOSES A NOVEL BIOLOGICAL MARKER OF THE DISEASE

MA Giambelluca, M Bianchini, MC Scavuzzo, G Di Franco, M Palmeri, N Furbetta, S Guadagni, D Gianardi, LE Pollina, N Funel, G Di Candio, L Morelli, F Fornai

Presenter: Luca Morelli MD | University of Pisa, Italy

Background: Alpha Synuclein (α -Syn) is a protein involved neuronal degeneration. However, it has been hypothesized that neurodegeneration may share common mechanisms with oncogenesis and certain forms of α -Syn may selectively accelerate cellular processes leading to cancer. Indeed, its expression has been found in various tumors including ovarian, colorectal and melanoma tumors. Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal human cancers, with a specifically high neurotropism. The molecular bases of this biological behavior are currently poorly understood and we aimed to investigate if α -Syn could be involved in this process, since it shares with PDAC a marked neurotropism and given its possible association with cancerogenity.

Methods: Samples from tumors of 20 patients undergone pancreatic resections from January 2019 to December 2020 at our institution were collected. Western blotting was used to detect, quantify and compare the expression of PrPc in PDAC and control tissues, such as those of non-affected neighboring pancreatic tissue of the same patient. Furthermore, immune-gold electron microscopy was used in order to reveal the localization of α -Syn.

Results: All patients were affected by moderately differentiated PDAC. According to the western-blot analysis, α -Syn was markedly expressed in PDAC tissues (215.22 ± 44.65 OD) respect to controls (100 ± 29.19 OD, $p < 0.001$). Electron microscopy confirmed these findings, with a higher count of α -Syn immune-gold particles in PDAC cells (107 ± 6.1 vs 18 ± 4 , $p < 0.0001$), revealing also the presence of α -Syn in the intracellular compartment of PDAC cells and particularly around the cellular nuclei.

Conclusion: As far as we know, our work provides evidence for increased levels of α -Syn in PDAC for the first time in literature. This might contribute to PDAC carcinogenesis and neurotropism, thus providing a potential new biomarker. Work is in progress to decipher its clinical implications.

P 100. THE CURRENT MANAGEMENT OF AMPULLARY CANCER: A SURVEY AMONG HEALTHCARE WORKERS WORLDWIDE

EJM de Jong, DHL Lemmers, A Benedetti Cacciaguerra, SME Geurts, Valkenburg-van Iersel, JW Wilmink, VCG Tjan-Heijnen, M Besselink M Abu Hilal, J de Vos-Geelen

Presenter: Evelien de Jong MD | Maastricht UMC+, Netherlands

Background: Ampullary adenocarcinoma is a rare disease accounting for less than 1% of all gastrointestinal malignancies. As a result, research is limited and guidelines for the management of patients diagnosed with ampullary adenocarcinoma are not available. To gain insight in the current daily practice and treatment of ampullary adenocarcinoma worldwide, this international survey study was performed.

Methods: Surgeons and medical oncologists, whom were members of the Dutch Pancreatic Cancer Group (DPCG) or the International Study Group on Ampullary Cancer (ISGACA), or contributed to (peri)ampullary cancer research, were invited through email. Participants were also approached through their colleagues and online media platforms.

Results: Overall, 57 (72%) surgeons and 22 (28%) medical oncologists completed the survey, 5% of the respondents were in training. Most respondents work in Europe (81%; 28 in the Netherlands and 36 in other European countries), followed by Asia (9%), North-America (8%) and South-America (3%), 90% of the respondents work in a pancreas expertise center. In general, the majority (94%) of the respondents take the patients performance status and the presence of metastatic disease into consideration when choosing treatment for patients with ampullary adenocarcinoma. Tumor classification (70%), lymph node involvement (70%), histological subtype (64%), expected toxicity of systemic treatment (51%), and patient preference (64%) are also found to be important factors. Neoadjuvant treatment is considered by 20% of respondents, with the majority (33%) opting for neoadjuvant treatment with (modified) fluorouracil, leucovorin, irinotecan, and oxaliplatin (FOLFIRINOX). Adjuvant therapy after resection of ampullary adenocarcinoma is considered by 75% of the respondents, with 71% choosing for adjuvant chemotherapeutic treatment alone (mFOLFIRINOX) and 4% choosing for combined chemoradiation therapy. The formation of multidisciplinary teams, improvement in (minimally invasive) surgical procedures, possibilities of local resection, increased availability of chemotherapy, and increased knowledge on tumor biology are interpreted as major improvements in the last five years. However, the necessity for international registries and randomized controlled trials on neoadjuvant and adjuvant chemo(radio)therapy was mentioned frequently.

Conclusion: This international survey study highlights the worldwide variation in the management of patients diagnosed with ampullary cancer, especially regarding neoadjuvant and/or adjuvant therapy. Consensus is reached that more data, including international registries and randomized controlled trials are needed to develop evidence-based guidelines for a more standardized surgical, and oncological management.

P 101. SYSTEMATIC REVIEW AND META-ANALYSIS OF OBSERVATIONAL STUDIES ON BD-IPMNS PROGRESSION TO MALIGNANCY

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Presenter: Alberto Balduzzi MD, PhD | University of Verona, Italy

Background: The vast majority of presumed branch-duct intraductal papillary mucinous neoplasms (BD-IPMNs) of the pancreas are referred to a surveillance program due to the relatively low risk of malignancy. We aim to evaluate all available data from observational studies focused on the risks of BD-IPMN progression and malignancy to provide vital insights into its management in clinical practice.

Methods: A comprehensive search was conducted at PubMed, Cochrane, Web of Science and Embase for observational studies published before January 1st, 2020. The progression of BD-IPMN was defined as the development of worrisome features (WFs) or high-risk stigmata (HRS) during surveillance. Overall malignancy was defined as all malignancies, such as malignant IPMN, concomitant pancreatic ductal adenocarcinoma (PDAC) and other malignancies, including BD-IPMN with high-grade sec. Baltimore consensus 2015 or BD-IPMN with high-grade dysplasia (carcinoma in situ) sec. WHO 2010. A meta-analysis was performed to investigate the presence of a mural nodule as a possible predictor of malignancy.

Results: Twenty-four studies were included, with a total of 8941 patients with a presumed BD-IPMN. The progression rate was 20.2%, and 11.8% underwent surgery, 29.5% of whom showed malignancy at the final pathology. Of those, 78% had malignant IPMNs, and 22% had concomitant pancreatic cancer. Overall, 0.5% had distant metastasis. The meta-analysis showed that the risk of malignancy in the presence of a mural nodule >5 mm had a RR of 5.457 (95% CI 1.404–21.353), while a nonenhancing mural nodule or an enhancing mural nodule < 5 mm had a RR of 5.286 (95% CI 1.805–15.481) of harboring malignancy.

Conclusion: Most presumed BD-IPMNs entering surveillance do not become malignant. Of those submitted to surgery, concomitant PDAC adds to the overall risk of detecting malignancy.

P 102. ACCURACY OF VALIDATED FISTULA RISK SCORES MAY BE INFLUENCED BY PATIENT DEMOGRAPHICS

C Blunck, S Vickers, T Wang, V Dudeja, S Reddy, JB Rose

Presenter: Conrad Blunck BS, MS | University of Alabama at Birmingham, United States

Background: Clinically relevant post-operative pancreatic fistula (CR-POPF) is among the most morbid complications following pancreatic surgery. Multiple fistula risk score (FRS) models have been proposed to identify patients at high-risk for developing a CR-POPF. Studies validating these models did not include centers with high Black patient populations. This study aims to: 1) Identify factors associated with CR-POPF development in patients in the Deep South, and 2) Assess the validated FRS models discriminatory capacity when applied patients in the Deep South.

Methods: A single-institution retrospective cohort study of patients who underwent elective pancreatoduodenectomy between 2013 and 2019 at the only comprehensive cancer center in the Deep South was performed. CR-POPF was defined by the 2016 ISGPF consensus guidelines. The original FRS (O-FRS), the alternative FRS (A-FRS), the updated alternative FRS (UA-FRS), and the Sun FRS were tested. The discriminatory ability of these models in patients from the Deep South were assessed using ROC curves.

Results: Of the 197 patients included in this study, 35 (18%) developed CR-POPF. This dataset included 35 (18%) Black patients. Of the seven risk factors used by the four FRS models, only soft pancreatic gland texture and pancreatic duct size were significantly associated with CR-POPF. When analyzed together in a multivariate analysis, only pancreatic duct size significantly improved the predictive capacity of the model. Of the four FRS analyzed in this study, the O-FRS, A-FRS, and UA-FRS maintained adequate discriminatory ability (AUC>0.7) and performed significantly better the Sun FRS (p<0.05)

Conclusion: The A-FRS can adequately discriminate between patients at varying risk of developing CR-POPF in the Deep South. Future validation studies should include more diverse patient populations before generalizability can be inferred.

P 103. CHRONIC JETLAG ACCELERATES FIBROSIS TO PROMOTE THE DEVELOPMENT OF PANCREAS CANCER

P Schwartz, M Walcheck, K Matkowskyj, S Ronnekleiv-Kelly

Presenter: Patrick Schwartz MD | University of Wisconsin, United States

Background: Pancreatic ductal adenocarcinoma (PDAC) is one of the deadliest malignancies, with a 5-year mortality of 90%. A better understanding of PDAC development is required to develop novel treatments. One factor that may contribute to PDAC development is circadian disruption. We sought to determine whether a chronic jetlag (CJ) model of circadian disruption contributed to PDAC development.

Methods: Mice predisposed to pancreatic cancer development (Kras^{LSL-G12D/+}; Pdx-1 Cre) were bred and subjected to either normal circadian (NC) conditions or CJ conditions whereby the 12-hour LD cycle is advanced 4 hours every 2-3 days. Pancreatic pathology was compared at 5 and 9 months of age. To better evaluate the progression between pathology observed at 5 and 9 months, additional mice were subjected to scRNAseq at 7 months of age, and data was then analyzed with the Seurat pipeline. Differential gene expression (DGE) analysis was performed with MAST and pathway testing with gene set enrichment analysis (GSEA).

Results: By 9 months of age, 100% of CJ (n=32) and NC (n=22) mice developed chronic pancreatitis and pancreatic intraepithelial neoplasia 1 (PanIN-1). Interestingly, we observed a statistically significant increase PanIN-2 (21.9% vs 0%; p=0.03) and non-significant increases in both PanIN-3 (12.5% vs 4.5%) and PDAC (12.5% vs 9.1%). At 5 months of age, there were no differences in the incidence of pancreatic pathology between CJ (n=26) and NC (n=36), however, the percent involvement of chronic pancreatitis associated fibrosis and PanIN-1 was significantly higher (p=0.027). On scRNAseq analysis, proportionality testing revealed a significant expansion of the stromal compartment (fibroblasts, endothelial cells, and pancreatic stellate cells) with CJ (log₂FC>0.58; q < 0.05). Following CJ, in fibroblasts, the circadian gene Nr1d1 (log₂FC=1.12; p=8.17E-37) and protooncogene Jun (log₂FC=1.35; p=7.37E-19) were significantly upregulated on DGE, and subsequent pathway testing revealed a corresponding enrichment of both the circadian and AP1 pathways (q < 0.05).

Conclusion: Chronic jetlag led to an early increase in chronic pancreatitis-associated fibrosis and later increase in preneoplastic lesions on histopathologic analysis. Follow-up scRNAseq revealed an expansion of stroma cells following CJ, with an associated activation of the AP1 and circadian pathways in fibroblasts. Thus, activation of the circadian transcription factor Nr1d1 by CJ may lead to enhanced Jun expression - a known central regulator of fibrosis. Further, drugs targeting Nr1d1 have been used to reverse fibrosis in other conditions. Given that increased fibrosis in pancreas cancer is associated with worse survival and chemotherapeutic resistance, future studies are needed to determine the mechanistic link between circadian dysregulation and fibrosis to potentially identify novel treatment strategies.

P 104. COMBINED THERAPY AND ISCHEMIA PRECONDITIONING TO ACHIEVE SAFE AND ONCOLOGICALLY COMPLETE RESECTION FOR LOCALLY ADVANCED PANCREATIC CANCER

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Presenter: Scott Kizy MD | Moffitt Cancer Center, United States

Background: Tumor vessel encasement of hepatic arterial anatomy often prevents safe surgical resection of locally advanced pancreatic cancer (LAPC). Loss of hepatic arterial inflow via the common and right hepatic arterial system is associated with liver ischemia, abscess and stricture of the common bile duct. To achieve resection and minimize risk, we have developed an approach that employs ischemia preconditioning of hepatic arterial segments encased by tumor prior to planned resection of LAPC after preoperative chemotherapy and radiation. Our hypothesis is that this approach will meet known benchmarks of safety while providing the highest potential for complete local control of the tumor.

Methods: Patients with LAPC deemed unresectable by Intergroup criteria were reviewed prospectively at a multidisciplinary tumor board to identify hepatic arterial involvement favorable for pre-operative ischemia preconditioning. Prior to planned resection, the involved segment of hepatic arterial branches were coil-embolized using interventional radiology techniques. Subsequently, surgical resection included en-bloc arterial resection of the involved segment during pancreatectomy. Clinical data was extracted for review. We evaluated patient demographics, preoperative treatment, tumor markers, surgical outcomes, pathologic characteristics, liver function tests, adjuvant treatment, recurrence, and survival.

Results: Six patients with LAPC with involved hepatic arterial anatomy were identified and received our planned approach from January of 2018 to May of 2021. The median age was 63. Four patients were female. Five patients had adenocarcinoma with the other patient having adenosquamous pathology. Median pre-treatment tumor size was 3.05 cm. Half of the patients had suspicious lymph nodes on pre-operative imaging. Median pretreatment Ca 19-9 was 177 U/ml. Five patients underwent pre-operative FOLFIRINOX as 1st line therapy. The other patient underwent Gemcitabine/abraxane. Five patients underwent pre-operative stereotactic body radiation therapy. Four patients underwent pre-operative embolization of an involved replaced right hepatic artery. The remaining two patients underwent embolization of an involved common hepatic artery after identification of a replaced left hepatic artery. The patient with adenosquamous pathology was found to have a liver metastasis at the time of surgery and resection was aborted. All patients who proceeded had resection of the involved embolized arterial anatomy, and three of the five patients underwent combined venous resection and reconstruction. The estimated blood loss for all patients was < 500cc and one patient received 1 unit PBRC on post-operative day 2. The median length of stay was 7 days; three patients experienced grade 1 complications and one patient experienced a grade A pancreatic fistula. The median peak total bilirubin was 1.6 mg/dl and alkaline phosphatase was 176 U/L with no clinical evidence of postoperative biliary stricture. The margins of resection and harvested lymph nodes were negative for all patients, with a partial response of the primary tumor identified in four patients and a complete response in one. Although follow up is short, no patient has suffered a recurrence.

Conclusion: Based on this early experience, we find that pre-operative ischemia preconditioning is feasible and allows for safe, margin negative resection of select patients with LAPC and suitable anatomy. Larger analyses are necessary to confirm the findings of this study.

Sex	Pre treatment Tumor size (cm)	Pre treatment N stage	Pre treatment CA 19-9	Histology	Involved anatomy	Underwent Resection	Pathologic Stage	Margin	Total bilirubin peak	Alkaline phosphatase peak	LOS	POPF
Male	4	N1	545	Adenocarcinoma	Replaced RHA	Yes	yp T0 N0	Negative	1.2	176	7	No
Female	3.1	N1	24	Adenocarcinoma	CHA, with LHA	Yes	yp T1a N0	Negative	1.6	186	6	No
Female	2.3	N1	138	Adenocarcinoma	Replaced RHA	Yes	yp T1c N0	Negative	1.2	128	8	Yes
Female	3	N0	216	Adenocarcinoma	Replaced RHA	Yes	yp T1a N0	Negative	1	160	10	No
Female	2.6	N0	253	Adenocarcinoma	Replaced RHA	Yes	yp T1b N0	Negative	0.5	177	7	No
Male	3.2	N0	491	Adenosquamous	CHA, with LHA	No (liver metastases)						

P 105. EFFECT OF THE SARS-COV-2 PANDEMIC ON THE EXPERIENCE AND OUTCOMES OF PATIENTS WHO UNDERWENT RESECTION FOR PANCREATIC CANCER AT A HIGH-VOLUME TERTIARY CARE CENTER

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Presenter: Rachel Kim MD | Indiana University School of Medicine, United States

Background: During the COVID-19 pandemic, many institutions restricted non-emergent surgeries in order to appropriately allocate limited hospital resources including ICU capacity in the setting of increasing demand. In this study, we aim to determine the outcomes of patients who underwent resection for pancreatic cancer before and during the COVID-19 pandemic.

Methods: All patients who completed neoadjuvant therapy for pancreatic adenocarcinoma and subsequently underwent oncologic resection between March 2018 and February 2020 at a single comprehensive care center were compared to those between March 2020 (when institutional COVID-19 policies were implemented) and December 2020.

Results: 114 patients who underwent surgery in the pre-COVID-19 period (93 pancreatoduodenectomies, 20 distal pancreatectomies, 1 total pancreatectomy) and 66 patients who had surgery during the pandemic restrictions (49 pancreatoduodenectomies, 15 distal pancreatectomies, 2 total pancreatectomies) were included in this study. Demographics such as age, gender, race, and BMI did not differ between groups. More patients received chemotherapy outside of our comprehensive cancer center during the pandemic (86.4% vs. 59.6%, $p < 0.01$). Average time from completion of neoadjuvant therapy to surgery was comparable between groups (41.6 vs 38.2 days, $p = 0.46$). Only one patient's surgery was rescheduled due to COVID-19 positivity. Length of stay, mortality and readmission rate within 30 days, and pathologic T and N staging did not differ between groups.

Conclusion: The COVID-19 pandemic necessitated provider adaptations in the effort to not compromise patient care and outcomes. No changes in quality of care were observed for pancreatic cancer patients, including no difference in time to surgery. The change in chemotherapy treatment location may reflect more patients electing to minimize travel during the pandemic. Further studies investigating the effect of the pandemic on long term outcomes are needed.

Table 1. Comparison of patients who underwent surgery prior to and after the implementation of COVID-19 surgery scheduling restrictions^a

	Before Pandemic Restrictions (n=114)	After Pandemic Restrictions (n=66)	p-value
Chemotherapy treatment at outside location	68 (59.6%)	57 (86.4%)	<0.01
Referred from outside institution	82 (71.9%)	54 (81.8%)	0.15
Received radiation therapy	28 (24.6%)	15 (22.7%)	0.86
Time to surgery ^b (days)	38.2 ± 20.0	41.6 ± 23.5	0.46
Length of stay (days)	7.7 ± 5.5	8.2 ± 4.0	0.11
Readmission within 30 days	10 (8.8%)	7 (10.6%)	0.79
Mortality within 30 days	3 (2.6%)	2 (3.0%)	1.00

^aData presented as either mean ± SD or frequency (percentage)

^bAfter completion of neoadjuvant therapy

P 106. HEADS OR TAILS – ANATOMIC LOCATION OF PANCREATIC DUCTAL ADENOCARCINOMA INFLUENCES CACHEXIA AND NUTRITIONAL STATUS

A Riner, K Herremans, D McClish, S Raman, K Tossas, S Shah, T George, S Judge, A Judge, S Hughes, J Trevino

Presenter: Andrea Riner MD | Virginia Commonwealth University, United States

Background: Pancreatic ductal adenocarcinoma (PDAC) is a lethal malignancy with high incidence of cachexia, a syndrome of unintentional weight loss and reduction in skeletal muscle mass that limits patients' ability to tolerate chemotherapy and renders them less fit for surgical resection, culminating in reduced survival. PDAC may arise throughout the pancreas, with distal tumors historically being considered more aggressive. While cancer-associated cachexia is driven by the tumor's effect on the body, data is lacking on how the tumor's anatomic location may affect cachexia. We hypothesize that anatomic location of the primary tumor influences incidence and severity of PDAC-associated cachexia.

Methods: Treatment naïve patients with PDAC who underwent pancreatectomy at a tertiary care hospital from August 2012 – December 2020 were identified retrospectively. Exact and caliper matching were used to pair patients in each cohort (head or body/tail) based on sex, age +/- 5 years, N and T stage (n=21 per group). The primary outcome was presence of cachexia (> 5% body weight (BW) loss in the 6 months prior to diagnosis). Clinical, serologic and anthropometric variables were obtained at the time of diagnosis. Vital status was determined as of the last date of data collection. Skeletal muscle index (SMI), muscle radiation attenuation (MRA), and adiposity were calculated from computed tomography images at the L3 vertebrae using Tomovision SliceOmatic software. Descriptive statistics, signed rank (continuous variables) and Cochran Mantel Haenszel tests (binary and ordinal variables) are presented.

Results: Numerically, cachexia appeared more prevalent in patients with pancreatic head tumors compared to body/tail tumors, although the comparison did not reach statistical significance (71.4% vs 42.9%, p=0.0833). The percentage BW loss was higher with head compared to body/tail tumors (7.4% vs 2.6%, p=0.0246). Despite differences in percentage BW loss, patients in the two groups had similar body mass indices (26.6 vs 28.0, p=0.6141), SMI (39.4 vs 41.6 cm²/m², p=0.2538), MRA (29.9 vs 30.2 HU, p=0.9066), and adiposity (383.4 vs 332.7 HU, p=0.9066). When BW loss, SMI and MRA were combined into a score based on a more robust definition of cachexia, patients with pancreatic head tumors were more likely to be cachectic compared to patients with body/tail tumors (p=0.0196). Serum albumin (3.8 vs 4.4 g/dL, p=0.0009) and bilirubin (4.45 vs 0.4 mg/dL, p<0.0001) differed between groups. More patients in the body/tail group tended to be alive at endpoint (36.1% vs 14.3%, p=0.0588), although median survival did not differ statistically (16.0 vs 22.3 months, p=0.3085).

Conclusion: In this matched study, PDAC located within the pancreatic head was associated with higher prevalence and greater degree of cachexia, although cachexia was present in a large proportion of patients at the time of diagnosis, regardless of tumor location. Biliary obstruction and lower albumin in patients with pancreatic head tumors suggest compounding effects of malnutrition on cachexia, as well as shorter survival. These findings suggest that PDAC-associated cachexia is rather heterogenous and may be influenced by primary tumor location. Select patients with PDAC located in the pancreatic head may benefit from nutritional prehabilitation as a means to improve outcomes.

P 107. THE FATE OF RESECTABLE PANCREATIC ADENOCARCINOMA FOLLOWING NEOADJUVANT CHEMOTHERAPY

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Presenter: Ahmer Irfan MBChB, MRCS | University of Alabama at Birmingham, United States

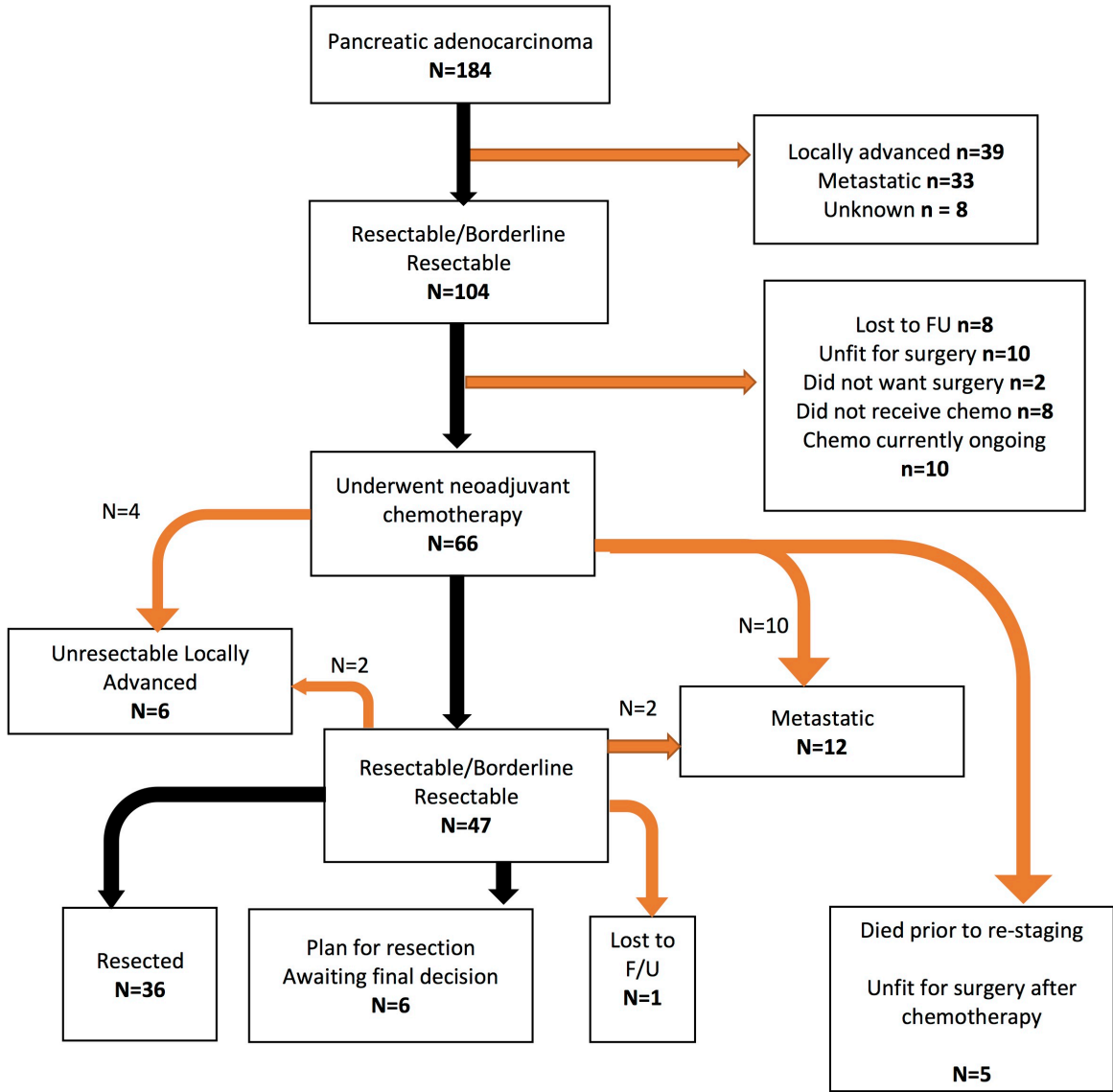
Background: Pancreatic cancer continues to be a major cause of cancer-related mortality. There has been a greater implementation of upfront chemotherapy for pancreatic adenocarcinoma patients. Although there are many theoretical benefits to neoadjuvant chemotherapy, its clinical impact is uncertain. We sought to understand the outcomes of patients with resectable and borderline-resectable pancreatic adenocarcinoma who undergo neoadjuvant chemotherapy.

Methods: Patients were collected in a secure database from September 2018 to May 2020. Patients were excluded if they presented with locally advanced or metastatic disease, inability to complete chemotherapy or if they were not a surgical candidate. Anatomic resectability was determined by the 2017 International Consensus Definition.

Results: 66 patients with resectable disease underwent chemotherapy. FOLFIRINOX was used in 41 (62%) patients, gemcitabine-based regimens in 28 (42%) patients (total greater than 100% as some patients underwent both regimens). Following re-staging, 47 patients (71.2%) were thought to have resectable disease. Of these patients, 36 have been successfully resected to date. Metastatic disease was found in 12 patients (18.2%) and 6 patients (9.1%) had locally advanced disease.

Conclusion: Most patients with resectable pancreatic cancer are resected after neoadjuvant chemotherapy, but a subset will develop local or distant progression. Further studies will be needed to determine which patients will progress locally and may benefit from an upfront surgical approach.

Figure 1: Flowchart showing patient selection



P 108. TREATING LOCALLY ADVANCED PANCREATIC CANCER WITH A NOVEL, DUAL-OCCLUSION BALLOON CATHETER

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Presenter: Hui Li | RenovoRx, United States

Background: Patients with pancreatic cancer tend to exhibit few signs of the disease. As such, diagnosis of the disease tend to be in later stages when it has become locally advanced or metastatic, where resection, the primary curative treatment, is no longer an option. In patients with locally advanced disease, who are not a surgical candidate, systemic chemotherapy is the mainstay of treatment. However, the avascular nature of pancreatic tumor has been a major limitation for efficacy of systemic chemotherapy. To address this issue, a novel dual-occlusion balloon catheter (RenovoCath) has been developed which seeks to isolate an arterial segment nearest the pancreatic tumor and infuse chemotherapeutic agents locally though forced infusion of drug across the arterial wall- independent of the presence of tumor feeders. After a Phase I maximum tolerated dose escalation study of 1000mg/m² was performed to assess safety and tolerability of intra-arterial (IA) delivery of gemcitabine in patients with LAPC, a registry study was launched to assess the efficacy of IA therapy.

Methods: Twenty-five patients (10 Male, 15 Female; mean age = 72.4 years) were enrolled across seven US sites and a total of 109 treatments were administered. Two of the patients were rollovers from the previous safety study and received more than 8 total treatments. Each patient on-study otherwise could receive up to 8 intra-arterial treatments with an average of 4.4 treatments Per patient. Each treatment was two weeks apart, and survival (overall and from time of first treatment) was assessed. Further analyses were performed to assess the effect of prior treatment, and arterial treatment location on survival.

Results: In terms of patient cohorts, average age was 72.4 and 40% were male. Ten patients were treatment naïve, six had prior chemotherapy, eight had prior chemoradiation, and one patient had surgery (Whipple procedure). Across the entire cohort, median overall survival (OS) was 13.0 months and median survival from time of first treatment was 5.4 months. Patients having prior chemoradiation showing the best survival results (median OS: 23.1 months) compared to patients with prior chemotherapy (median OS: 16.6 months) or no prior treatments (median OS: 5.7 months). Furthermore, treatment via superior mesenteric artery (SMA; n=6) showed the best survival benefits (median OS: 31.7 months) compared to mixed treatments between SMA and other arteries (common hepatic artery, splenic artery, or celiac axis; n=8) (median OS: 13.4 months) or treatment via any of the aforementioned other arteries (n=11; median OS: 10.4 months).

Conclusion: Taken together, IA delivery of gemcitabine via the RenovoCath device is a viable treatment option for locally advanced pancreatic cancer. Radiation treatment prior to IA therapy showed increased survival benefit. Prior animal study suggests the mechanism of benefit with radiation is reduction of arterial microvasculature, allowing enhanced drug penetration at the treatment location. Furthermore, treatment via the SMA showed the greatest survival benefit; as SMA has the highest contact area with the tissue/tumor, we postulate that this allows highest concentration of drug into the tumor/tissue.

P 109. CHRONIC JETLAG ALTERS THE PANCREATIC LIPID PHENOTYPE TO PROMOTE DIACYLGLYCEROL FORMATION

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Presenter: Patrick Schwartz MD | University of Wisconsin, United States

Background: The circadian clock controls a myriad of homeostatic processes in the body. Disruption of these processes leads to human disease. Pancreatic circadian disruption (CD) leads to obesity and diabetes and may promote the development of pancreas cancer; however, the mechanisms are poorly understood. One mechanism for pathogenesis involves CD-mediated alterations in lipid metabolism, but circadian control over the pancreatic lipidome has not been investigated. Therefore, we sought to first demonstrate circadian control over the lipidome, then determine the effects of a chronic jetlag protocol (CJ) known to induce CD on the lipid phenotype.

Methods: To evaluate CD-induced impact on the pancreatic lipidome, four-week-old C57BL/6J mice (n=72) were subjected to normal circadian (NC) or CJ conditions (12-hour light-dark cycle phase-shifted 4 hours every 2-3 days) for 9 months. Mice were sacrificed (n=3 male/female per condition) every 4 hours for 24 hours and the pancreas extracted followed by LC-MS. Comparisons were made with LipidR and rhythmicity tested with RAIN. Lipid rhythm characteristics (i.e. phase, amplitude, mesor) were determined with Metacycle.

Results: Seventeen lipid subclasses were collectively detected. On rhythmicity analysis, there was a statistically significant increase in rhythmic lipids detected on Chi-Squared analysis ($p=0.001$). In total, 4.7% (12/256) of NC and 12.9% (33/256) of CJ pancreatic lipids were considered rhythmic ($q0.05$), indicating circadian control over the pancreatic lipidome. These changes in rhythmicity with CJ were associated with a significant ($p=0.003$) shift in the phase of lipid expression. CJ conditions also led to a significant enrichment of triglycerides and diacylglycerols ($p<0.05$), while NC conditions were associated with enrichment of phosphatidylethanolamines.

Conclusion: CJ led to an induction of rhythmic lipid expression and enrichment of diacylglycerols, which are known mediators of hepatic insulin resistance. Future studies will focus on how CJ drives diacylglycerol formation, and whether alterations in diacylglycerol signaling promote pancreatic carcinogenesis.

P 110. RESECTION OF THE UNCINATE PROCESS AS AN ALTERNATIVE TO PANCREATODUODENECTOMY FOR LOW-GRADE PANCREATIC NEOPLASMS: A PANCREAS-SPARING OPERATION

M Machado, M Aufran

Presenter: Marcel Machado MD | University of São Paulo-Brazil, Brazil

Background: Abstract
Objective: To present the techniques and the results of the largest series of isolate resection of the uncinata process of the pancreas in the literature and to describe three different approaches.
Background: Pancreatoduodenectomy is the treatment of choice for tumors in the head of the pancreas and in the periampullary area. However, some low-grade or benign lesions may benefit from pancreatic-sparing techniques such as enucleation and isolate resection of the uncinata process. This latter technique, although described in 1996, has been rarely performed and reported. The main reason is that it is a complex operation that needs a careful patient selection and accurate knowledge of the pancreatic anatomy. The study was performed to examine 12 years of experience in a single center and its evolution towards minimally invasive technique.
Methods: This observational study comprehends patients at a referral center for pancreas tumors in São Paulo, Brazil. Preoperative variables included age, sex, and indication for surgery. Intraoperative variables encompassed operative time, bleeding, and blood transfusion. Diagnosis, tumor size and margin status were determined from final pathology reports. Pancreatic fistula was assessed and graded according to the International Study Group on Pancreatic Fistula recommendations. Pancreatic endocrine and exocrine functions in the post-operative period were assessed through clinical data.
Results. Twenty-nine patients underwent isolate resection of the uncinata process of the pancreas. The median age was 57 years old (range 26-77 years). Twenty-one patients were male and eight females. Nine patients underwent open operations, 14 were operated by laparoscopic and six patients underwent robotic resection of the uncinata process of the pancreas. Clinically relevant postoperative pancreatic fistula was observed in one patient (3.4%). Biochemical leakage was present in 44.8% of our patients.
Conclusion: Isolate resection of the uncinata process of the pancreas is a complex but a feasible procedure for benign or low-grade malignancy that allows the preservation not only of pancreatic endocrine and exocrine function but also of the upper digestive tract.

P 111. CASE REPORT: A RARE CASE OF SYNCHRONOUS BREAST AND PANCREATIC ADENOCARCINOMA

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Presenter: Daniel Matienzo MD | Westside Regional Medical Center, United States

Background: The presence of two primary malignancies in a patient is extremely rare, warranting a unique diagnostic, surgical and medical approach to treatment. This is a case of an 83-year old female with a past medical history of breast cancer status post right modified radical mastectomy who presented with painless jaundice and weight loss. Subsequent workup revealed an obstructing, however resectable, mass of the pancreatic head. Additionally, she was found to have a right axillary mass, which was biopsy-proven recurrent breast adenocarcinoma. Of note, the patient had a significant family history of malignancy, which included a sister who died of pancreatic cancer, 2 other sisters who had breast cancer, and a brother with an unknown malignancy. Additional work-up determined that there were no other sites of malignancy. It was uncertain if the pancreatic mass was from metastatic disease or a primary tumor. Attempts at tissue diagnosis were not successful by EUS or percutaneous route. After multidisciplinary discussion, it was decided to proceed with resection of both sites. Pathology confirmed the axillary mass was recurrent metastatic ER+/PR-, HER2-NEU(-) invasive ductal carcinoma pT3, N1a, M0. Pathology of the pancreatic mass demonstrated primary pancreatic ductal adenocarcinoma pT3, pN1, pM0. The patient tolerated both surgeries and recovered well after. She was started on adjuvant chemotherapy with gemcitabine and radiation to the axilla. This is a presentation of a rare case of two different malignancies presenting at the same time in a patient with a significant family history of cancer.

P 112. HYPONATREMIA FOLLOWING COVID-19 INFECTION IS ASSOCIATED WITH HIGHER MORTALITY FOLLOWING PANCREATIC SURGERY

MV Bhargava, D Kumar, S Singh Rana, R Gupta

Presenter: M Venu Bhargava MD | Postgraduate Institute of Medical Education and Research, India

Background: The covid-19 pandemic has changed the behavioral pattern and lifestyles of people across the globe. The most common presentations of this disease include fever, upper respiratory and lower respiratory symptoms. It was found that patients infected with covid-19 had hyponatremia and is one of the risk factors for mortality. Neurological symptoms like encephalopathy, encephalitis are not unusual in patients infected with Covid-19. Surgical outcomes were poor in infected patients in comparison to non-infected patients, the most common cause of morbidity and mortality is due to pulmonary complications. In order to reduce morbidity and mortality we at our center follow testing with RT-PCR one week before surgery and RT-PCR was repeated within 48 hrs of surgery, patients were operated on only if the test results were negative. We present a case series of three patients who had hyponatremia post-surgery, all these patients acquired covid-19 infection post-surgery leading to mortality of all three patients.

P 113. TWO CANCERS, ONE TUMOR: ROBOTIC DISTAL PANCREATECTOMY AND SPLENECTOMY OF CARCINOMASARCOMA WITH INTRAOPERATIVE ULTRASOUND

B El-Attrache, CW Clark

Presenter: BenFauzi El-Attrache DO | AdventHealth Tampa, United States

Background: A 66-year-old male was found to have an incidental pancreatic mass while undergoing workup for a cholecystectomy in 2018. He had an EUS which did not show any abnormality. He was monitored with an MRI and CT in 2019 which showed a 2-3cm mass at the junction of the pancreatic body and tail with close proximity to the splenic vessels. This was confirmed on EUS with biopsy showing fibrotic stroma with a concern for a possible neuroendocrine tumor. Even though endoscopic surveillance is an option, with the ambiguity of the pathology, we recommended surgery for a definitive diagnosis.

Five laparoscopic ports were placed in the periumbilical and subcostal areas. We entered into the lesser sac and took down the greater curve and short gastric vessels of the stomach. We used intraoperative ultrasound to confirm the location of the tumor and determine our transection point. After dissecting around the pancreas, we identified the splenic vessels and clipped the splenic artery. The distal pancreas and splenic vessels were transected. Lastly, we took down the remaining attachments for us to complete the distal pancreatectomy and splenectomy. Pathology had shown poorly differentiated carcinoma with sarcomatoid features (carcinosarcoma) with negative margins and 0/11 lymph nodes. He did not have any postoperative complications and was started on adjuvant chemotherapy.

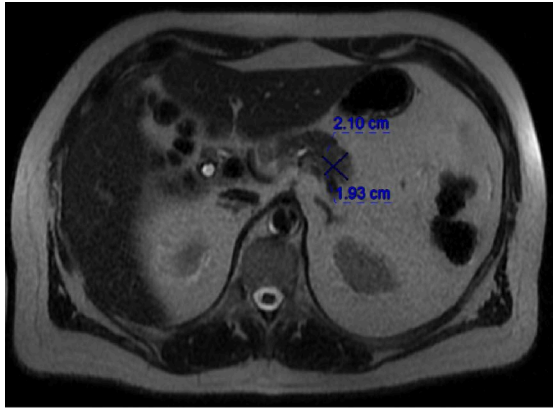
To our knowledge, there have been 25-30 other cases of carcinosarcoma of the pancreas reported in the literature. Mostly this presents in the elderly population but age of presentation can range from 24-90 years with a slightly higher female predominance. These pancreatic tumors are identified more so in the head than in the body/tail. Lesions in the head tend to be more solid, while in the body/tail they tend to be more cystic. The origin of this rare type of tumor has not been well established. Three suggested mechanisms include: single stem cell differentiation, early carcinoma with partial sarcoma transformation, and tumors of different origin growing together without incorporation.

Treatment consists of radical surgery with systemic chemotherapy. Chemotherapeutic options consist of gemcitabine alone or gemcitabine combined with other drugs such as raltitrexed, doxorubicin, and cisplatin. Prognosis is poor given the high rate of metastasis. Although a wide range of survival rates have been reported from 2 weeks to 2 years, the median survival time postoperatively is 6 months.

1. Zhou, X., Li, M., Wang, P., Teng, X., Sun, L., Chen, J., & Jia, Z. (2018). Carcinosarcoma colliding osteosarcoma of the pancreas: a rare case report of multiple clonal originated pancreatic tumors. *International Journal of Clinical and Experimental Pathology*, 11(3), 1746–1753. Retrieved from <http://www.ijcep.com/files/ijcep0071842.pdf>

2. Jia, Z., Zhang, K., Huang, R., Zhou, X., & Jiang, L. (2017). Pancreatic carcinosarcoma with rare long-term survival: Case report and review of the literature. *Medicine*, 96(4), e5966. doi: 10.1097/MD.0000000000005966

Conclusion:



MRI (Fig. 1 - upper left) and CT (Fig. 2 - upper right) showing a 2-3cm mass at the junction of the pancreatic body/tail with close proximity to splenic vessels

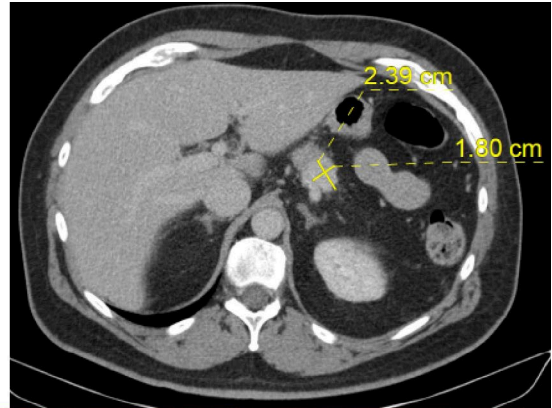
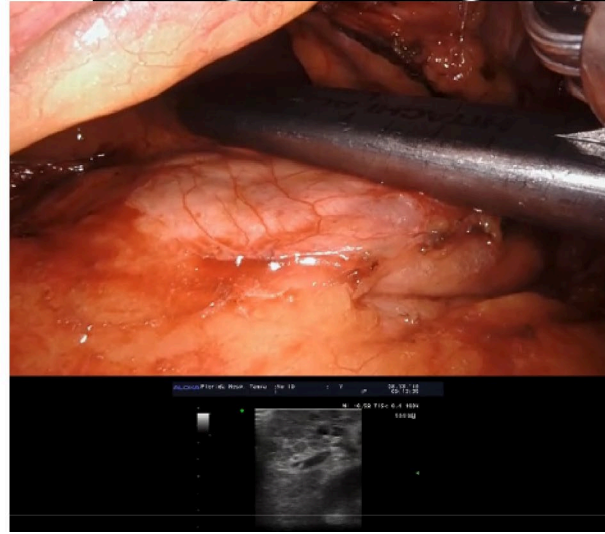


Fig. 3 - Pancreatic mass on Intraoperative ultrasound (bottom right)

Fig. 4 - Distal pancreas and spleen specimen being placed in a retrieval bag (bottom left)



P 114. CRUCIAL ASPECTS OF SURGICAL TREATMENT OF PANCREATIC CANCER

I Zhvitiashvili, R Alibegov, O Sergeev

Presenter: Igor Zhvitiashvili MD | Academic Medical Center, Russian Federation

Background: Background. Surgical treatment of pancreatic cancer (PC) is one of the most difficult problem of surgery. Currently, there is a large range of surgical procedures on the pancreas and methods of combined treatment, but the problem remains relevant to this day.
Methods. We analyzed the results of surgical treatment of 187 patients with PC. St.I-16 (8.6%), St.II – 104 (55.6%), and St.III – 62 (33.1%), St.IV-5 (2.7%). Men-128 (68.5%), women – 59 (31.5%), age - 61.1±6.7 years. Localization of tumor: head of pancreas – 166, distal tumors - 19, total lesion - 2. Pancreatoduodenectomy (PD) was performed in 167 patients, 18 patients undergone distal pancreatic resection: RAMPS – 13, Kimura's procedure – 1, Warshaw – 1, Applbey – 3; total pancreatectomy - 2. In cases of vascular invasions was performed: portal vein (PV) resection – 2, resection superior mesenteric vein (SMV) – 6, resection of the porto-mesenteric junction - 6, resection of the side wall of PV/SMV – 4, graft implantation – 3, plastic of the SMA – 1, celiac trunk resection – 3. Patients are divided into 2 groups: 1st - standard PD - 162, 2nd - operations with blood vessels resection - 25.
Results. Morbidity and mortality rate were evaluated within 30 days after surgery. Pancreatic fistula (PF) - 14.9% (28): gr. A-14, gr. B-10, gr. C-4. Bile leakage - 7.2% (12), pancreatitis – 2.7% (5), delayed gastric emptying – 4.3% (8), bleeding – 8.6% (gr. A-6, gr. B-6, gr. C-4), abscess - 3.7% (7), wound infection – 3.7% (7), others – 8.0% (15). Morbidity -59.1% (98), and mortality - 4.8% (9). In 1st gr. Morbidity and mortality rate is 51,5% (83) and 4,3% (7), in 2nd gr. - 60% (15) and 8% (2) respectively. PF in 1st gr. – 14.5% (24), 2nd gr. - 16% (4). R1 resections in the 1st group - 4 (2.5%), 2nd gr. – 2 (8%). Long-term results: overall survival – 23.5 months, relapse-free survival – 17.1 months. In the 1st gr. - 26.8 and 18.9 months accordingly, in the 2nd – 20.2 and 16.4 months. One year survival – 54.3%, 3-years-17.1%, 5-years - 11.4%.
Conclusions. Surgical treatment patients with borderline resectable PC is more difficult and is accompanied by slightly worse immediate results. Performing vascular resection during tumor invasion with the achievement of marginR0 allows for comparable rates of overall and relapse-free survival.
Comments. Patients from the 2nd group had at least the 3 stage of the tumor at the time of surgery, that's why the morbidity and mortality rate was higher. But all these patients undergone radical surgical treatment, which allowed almost equalize the long-term survival in both groups.

P 115. CECAL VOLVULUS PRESENTING AS A LONG-TERM COMPLICATION AFTER PANCREATODUODENECTOMY

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Presenter: Colleen Nofi DO | Academic Medical Center, United States

Background: Complications after pancreatoduodenectomy (PD) are common and range widely in timing of presentation, relation to pancreatobiliary pathology, and necessity of operative intervention. We present a case of a 74-year-old male with history of PD for pancreatic adenocarcinoma who presented to the emergency department eleven months after index operation with abdominal pain, distension, and obstipation. Cross-sectional imaging revealed a coffee bean shaped cecum in the left upper quadrant with dilated colon and evidence of mesenteric swirling in the right lower quadrant, consistent with cecal volvulus. The patient was taken urgently for exploration. Laparotomy revealed a massively dilated cecum and right colon with complete 360-degree clockwise rotation along the ileocolic pedicle. Extensive adhesions involving the afferent biliopancreatic limb and the gastrojejunal anastomosis to the transverse mesocolon were encountered. Once mobilized, the transverse colon was divided to the right of the middle colic vessels and right colon resection was performed. Four small (< 2cm) uninvolved peritoneal implants were additionally identified, removed, and sent for permanent pathology.
 In considering the etiology of our patient's disease process, it is likely that history of PD played a role. Prior operations whereby the right colon is mobilized through release of lateral retroperitoneal attachments may predispose patients to cecal volvulus by increasing mobility of the right colon. This is frequently performed through Cattell-Braasch maneuver during initial PD, commonly done in patients with borderline resectable or locally advanced tumors. Overall, late complications can occur in as high as one-third of post-PD patients and often require operative re-intervention. In planning re-interventions in the post-PD patient, understanding altered anatomy from index operation is crucial. In PD reconstruction, the afferent limb may be brought through either the ligament of Trietz defect or transverse mesocolon. Understanding the location of the afferent biliopancreatic limb is of particular importance as it is encountered when mobilizing the transverse colon in performing a right colectomy, and post-operative adhesions may complicate the necessary dissection, as in this case.
 Moreover, at time of re-operation our patient was found to have peritoneal implants that were consistent with metastatic pancreatic adenocarcinoma. Late complications often occur in the setting of disease recurrence. In these cases, it is important to employ a multidisciplinary treatment approach that balances disease control, quality of life, and patient preference when deciding whether to pursue additional therapy for asymptomatic, radiographically occult recurrent disease.
 The high incidence of complications after PD and rates of recurrence for malignancies treated with PD highlight the importance of frequent and long-term follow up after index operation. Specifically, cecal volvulus may present as a long-term sequela after PD and should be included in the differential for obstruction in the post-PD patient.

P 117. TOTAL PANCREATECTOMY, SPLENECTOMY, AND REMNANT GASTRECTOMY FOR INVASIVE IPMN AFTER PRIOR ROUX-EN-Y GASTRIC BYPASS

JT Swinarska, ME Dixon, JS Peng

Presenter: Joanna Swinarska MD | Penn State College of Medicine, United States

Background: Background: The prevalence of obesity and utilization of bariatric surgery continues to increase world-wide. As a result, all surgical subspecialties are encountering an increasing number of post-operative bariatric patients and need to be familiar with the anatomic variations and implications for surgical care. Patients with pancreatic head pathology and pancreatic cancer after Roux-en-Y gastric bypass (RYGB) are particularly challenging due to lack of access to the remnant stomach and duodenum for endoscopic ultrasound (EUS) and endoscopic retrograde cholangiopancreatography (ERCP).
Case Description: We present the case of a 56-year-old female who had undergone RYGB for obesity 12 years prior to presentation. The patient presented with nausea, right upper quadrant pain, and obstructive jaundice. Serum total bilirubin was 14.3 mg/dL, CA 19-9 was 38.3 unit/mL, and INR was 1.4. CT and MRI of the abdomen showed a 3.2 x 1.8 cm hypodense pancreatic head mass without arterial or venous abutment, intrahepatic and extrahepatic biliary dilation, a dilated pancreatic duct to 16 mm, and numerous cysts in the remaining pancreas (Fig. 1A/B). The patient's medical history was significant for a body mass index (BMI) of 52.5 kg/m² and family history was significant for pancreatic adenocarcinoma in her mother.
Treatment: The approaches for diagnosis and treatment were discussed in a multidisciplinary fashion. The options for preoperative tissue diagnosis and biliary decompression included a percutaneous approach with transhepatic drainage and brushings or percutaneous biopsy, or an endoscopic approach with stenting and biopsy via laparoscopic transgastric endoscopy or an EUS-directed transgastric ERCP (EDGE) procedure. After discussion with the involved teams and patient, upfront surgery was recommended since the primary lesion was resectable and without vascular involvement. Due to diffuse involvement of the pancreas by IPMN, the plan was to perform a total pancreatectomy and splenectomy. The patient's coagulopathy was corrected preoperatively with vitamin K.
Diagnostic laparoscopy was performed and was negative for metastatic disease. Open total pancreatectomy and splenectomy was performed in standard fashion. En bloc remnant gastrectomy was performed based on literature suggesting this approach to be associated with lower complication rates in patients undergoing Whipple after RYGB (Fig. 1C). Reconstruction was performed with a hepaticojejunostomy using the remaining biliopancreatic limb, without need to revise the existing jejunojunctionostomy.
Outcome: Pathology demonstrated a T2N1 pancreatic head adenocarcinoma with 1/29 positive lymph nodes, and negative margins. The entire pancreas was replaced by IPMN with low and high-grade dysplasia (Fig. 1D). The patient tolerated surgery well and was admitted to the intensive care unit for glycemic control. Her postoperative course was complicated by an episode of coagulopathic bleeding and an intra-abdominal hematoma, managed with transfusion and correction of coagulopathy. The patient began adjuvant FOLFIRINOX two months following the initial operation.
Discussion: For patients with history of RYGB who present with a resectable pancreatic head mass, consideration should be given to upfront surgical resection. Resection of the gastric remnant is preferable with RYGB anatomy due to avoidance of the enteric anastomosis. Due to biliary obstruction, coagulopathy is common and should be corrected preoperatively, with continued postoperative monitoring and correction.

