1. RADIOGRAPHIC, BIOCHEMICAL OR PATHOLOGIC RESPONSE TO NEOADJUVANT CHEMOTHERAPY IN RESECTED PANCREATIC CANCER: WHICH IS BEST?

C Javadi, JD Chang, E Forgo, MU Ahmad, GA Fisher, DT Chang, Dj Delitto, MM Dua, B Lee, BC Visser, JA Norton, GA Poultsides

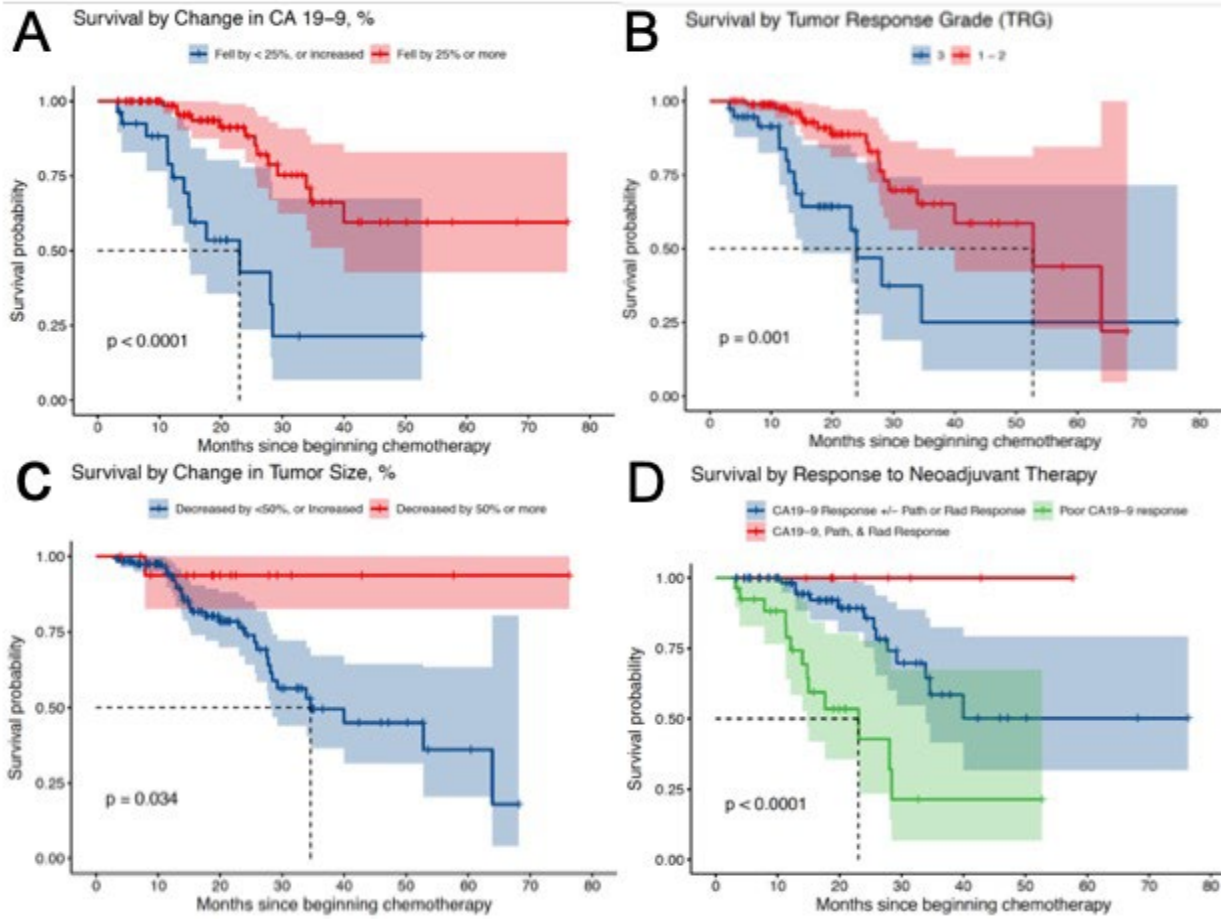
Presenter: Christopher Javadi MD, PhD | Academic Medical Center, United States

Background: Response to neoadjuvant therapy for pancreatic ductal adenocarcinoma (PDAC) can be assessed by radiographic (change in tumor size), biochemical (change in CA 19-9), and pathologic parameters (tumor regression grade, TRG). However, the relative prognostic significance of each type of response in comparison to the other two remains unclear. This study compared the individual and collective ability of these three types of response in predicting survival after neoadjuvant therapy and resection of PDAC.

Methods: Patients who underwent neoadjuvant chemotherapy and PDAC resection at a single institution were retrospectively analyzed. Several thresholds for radiographic, CA19-9 and pathologic response were assessed and compared to each other. Overall survival (OS) was calculated with the Kaplan–Meier method and compared with log rank and Cox proportional hazard methods.

Results: From 2011 to 2021,146 patients with PDAC received neoadjuvant chemotherapy (Folfirinox, n=101; Gem-Abraxane, n=30; other, n=15) followed by surgical resection. Thirty patients (21%) also received neoadjuvant radiation. Porto-mesenteric venous reconstruction was required in 75 (51%) patients. Median OS from initiation of chemotherapy was 53 months. Longer OS was observed in patients with CA19-9 decrease > 25% (NR vs 23 mos, p 50% (NR vs. 35 mos, p=0.034, Figure 1C). Interestingly, a RECIST radiographic response (decrease in tumor size > 30%) was not predictive of OS. In multivariate analysis, CA 19-9 decrease > 25% was independently associated with OS (HR=0.36, p=0.026), whereas pathologic (p=0.074) and radiographic response (p=0.16) were not. OS was optimal in the presence of all 3 types of response (Figure 1D) and intermediate in the presence of CA19-9 response with or without an additional type of response.

Conclusion: Pancreatic cancer patients with simultaneous radiographic, biochemical, and pathologic response to neoadjuvant chemotherapy have very favorable prognosis. In the absence of concordance between the three types of response, biochemical response (CA19-9 decrease by > 5%) best predicts long-term survival.


A
Survival by Change in CA 19–9, %
Fell by < 25%, or Increased
Fell by 25% or more
Survival probability
p < 0.0001
Months since beginning chemotherapy
B
Survival by Tumor Response Grade (TRG)
3
1 – 2
Survival probability
p = 0.001
Months since beginning chemotherapy
C
Survival by Change in Tumor Size, %
Decreased by <50%, or Increased
Decreased by 50% or more
Survival probability
p = 0.034
Months since beginning chemotherapy
D
Survival by Response to Neoadjuvant Therapy
CA19–9 Response +/– Path or Rad Response
Poor CA19–9 response
CA19–9, Path, & Rad Response
Survival probability
p < 0.0001
Months since beginning chemotherapy

2. OUTCOMES AND PREDICTORS OF PATHOLOGICAL COMPLETE RESPONSE AFTER PREOPERATIVE THERAPY IN RESECTED PANCREATIC ADENOCARCINOMA

A Oba, T Stoop, YHA Wu, S van Roessel, L Beaty, K Colborn, B Janssen, M Al-Musawi, A Jain, A Saiura, A Sauvanet, A Coppola, B Groot Koerkamp, B Miller, C Mack, D Hashimoto, D Caputo, D Kleive, E Sereni, G Belfiori, H Ichida, J van Dam, J Dembinski, K Akahoshi, K Roberts, K Tanaka, K Labori, M Falconi, M House, M Sugimoto, M Tanabe, N Gotohda, P Krohn, R Burkhart, R Thakkar, R Pande, S Dokmak, S Hirano, S Burgdorf, S Crippa, S Satoi, S White, T Hackert, T Nguyen, T Yamamoto, T Nakamura, W Burns, Y Inoue, Y Takahashi, Y Ushida, J Wilmink, W Messersmith, J Verheij, J Kaplan, R Schulick, M Besselink, M Del Chiaro

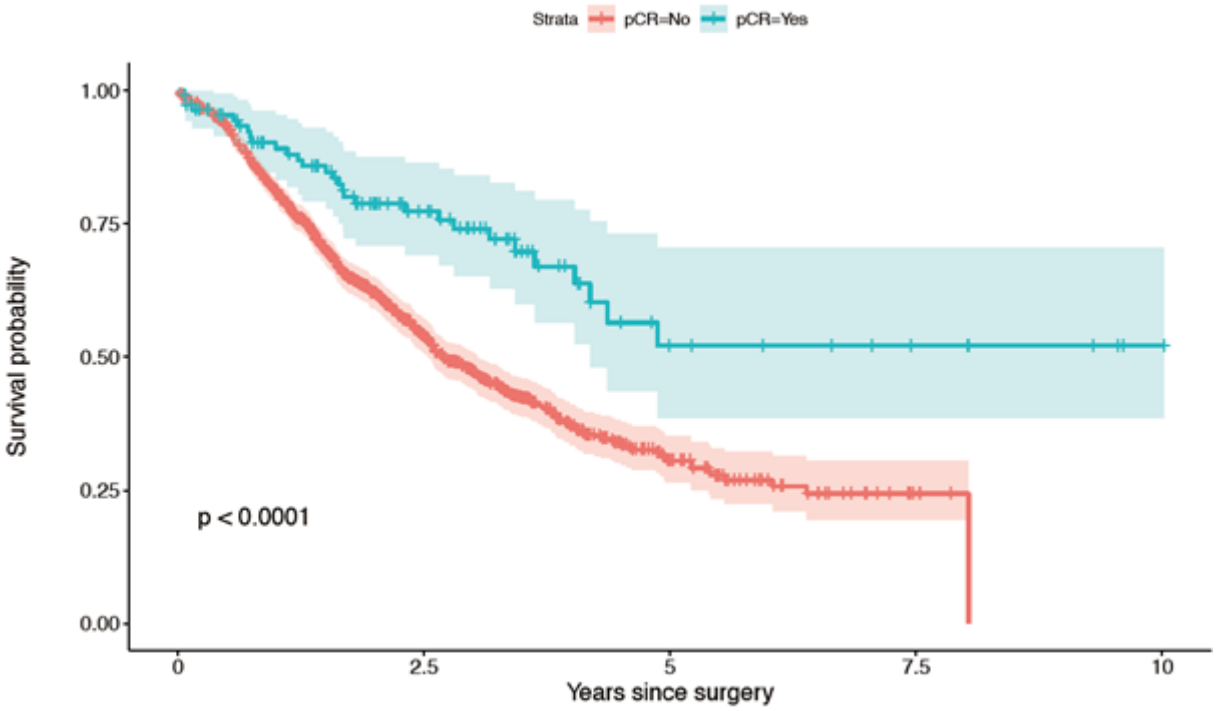
Presenter: Thomas Stoop MD, PhD | University of Colorado, United States

Background: Pathological complete response (pCR) is increasingly reported in patients with resected pancreatic cancer after chemo(radio)therapy. However, large, international multicenter studies on pCR following different preoperative regimens of chemo(radio)therapy in resected pancreatic cancer are lacking. This international multicenter study was designed to investigate the incidence, predictors, and outcomes of pCR.

Methods: This retrospective analysis included consecutive patients after resection of pancreatic cancer following at least two courses of preoperative chemo(radio)therapy from 20 centers, including those from Japan, the United States, and 7 European countries (2010-2018). Patients with pCR required preoperative pathology-confirmed pancreatic ductal adenocarcinoma. Two centers only provided pCR patients (n=66), and a sensitivity analysis was done to evaluate the impact by excluding their data. Factors associated with survival from time of surgery and predictors associated with pCR were investigated by Cox proportional hazards and logistic regression models, respectively.

Results: Among 1278 patients, 110 had pCR after resection of pancreatic cancer. The rate of pCR was 3.6% (44/1212 patients), after excluding the 66 pCR patients from the two sites with only pCR. Median survival in 110 patients with pCR was 27.5 months (interquartile range [IQR] 12.4-42.3) versus 20.6 (IQR 12.3-33.6) for patients without pCR (Wilcoxon rank sum p=0.02). pCR was associated with better overall survival (hazard ratio=0.48, 95% confidence interval [CI] 0.31-0.74). The use of preoperative FOLFIRINOX versus other multi-agent therapies was associated with a higher rate of pCR (odds ratio [OR]=3.03, 95%CI 1.69-5.56). Patients with radiotherapy (other than regular external beam radiotherapy; OR=9.91, 95%CI 4.90-20.61) and patients with preoperative chemotherapy duration ≥12 months (OR=4.26, 95%CI 1.75-10.93) had higher rates of pCR. Patients with stable/progressive disease after chemo(radio)therapy (OR=0.10, 95%CI 0.05-0.18) and patients with preoperative carbohydrate antigen 19.9 ≥37 U/ml (OR=0.22, 95%CI 0.10-0.42) had lower rates of pCR. The sensitivity analysis showed that predictors for pCR did not change after excluding the two above-mentioned centers.

Conclusion: This international study found pCR in 1 in every 28 patients with resected pancreatic cancer following chemo(radio)therapy. Although pCR does not reflect cure of pancreatic cancer, it is associated with more favorable survival. Predictors of pCR may have implications for pancreatic cancer treatment strategies and should be confirmed in prospective studies.


Strata
pCR=No
pCR=Yes
1.00
0.75
0.50
0.25
0.00
Survival probability
p < 0.0001
0
2.5
5
7.5
10
Years since surgery

3. BILIARY COMPLICATIONS DURING NEOADJUVANT THERAPY FOR PANCREATIC CANCER

SZ Thalji, D Fernando, KS Dua, AH Khan, S Madhavan, P Chisholm, M Aldakkak, KK Christians, CN Clarke, B George, M Kamgar, BA Erickson, WA Hall, DB Evans, S Tsai

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

Background: Neoadjuvant therapy (NeoTx) for pancreatic cancer (PC) requires durable biliary decompression. The impact of biliary complications (BC) during NeoTx are unknown.

Methods: BCs were identified in patients (pts) with operable PC of the pancreatic head/neck who had a biliary stent and received NeoTx prior to intended surgery. Association with early disease recurrence (< 1 year from surgery) and median overall survival (mOS) were assessed.

Results: Among 528 pts, 91 (17%) pts developed a BC during NeoTx at a median of 64 days (IQR 112) after initial stent placement. The cumulative incidence of BCs at 2 months (mo), 2-4 mo, >4 mo from diagnosis were 8%, 6%, and 20%. There were 113 BCs in the 91 pts: 41 (37%) stent occlusions without cholangitis, 34 (30%) stent occlusions with cholangitis, 26 (23%) cholecystitis, 1 (1%) hemobilia, 10 (9%) pancreatitis, and 1 (1%) hepatic abscess. Among 91 pts with BCs, 71 (78%) were hospitalized for a median of 4 days (IQR 4) and 25 (27%) had a delay in NeoTx (median of 7 days, IQR 8.5). Of the 528 pts, completion of NeoTx and surgery occurred in 59 (65%) of the 91 with BCs and 308 (71%) of the 437 without BCs (p=0.29). Among the 367 pts who completed NeoTx and surgery, 17 (29%) of the 59 pts with BCs had positive margins compared to 40 (13%) of the 308 pts without BCs (p=0.002). Early locoregional recurrence occurred in 47 (13%) of the 367 pts; 13 (22%) of the pts with BCs compared to 34 (11%) of 308 (p=0.02) pts without BCs. No differences were observed in rates of distant recurrence. The mOS for all 528 pts was 26 mo; 20 mo among 91 pts with a BC and 29 mo among 437 without a BC (p=0.006). For the 367 pts who completed NeoTx and surgery, mOS was 39 mo; 26 mo among 59 pts with a BC and 44 mo among 308 pts without a BC (p=0.02, Figure 1). BCs were associated with an increased risk of death (HR: 1.56; CI 1.10-2.23) in an adjusted hazards model.

Conclusion: The cumulative incidence of BCs during NeoTx was 17% and increased with duration of NeoTx but had no impact on the completion of all intended NeoTx and surgery. BCs were associated with worse outcome, possibly due to tumor-associated anatomy which predisposes to both recurrent disease and BCs.

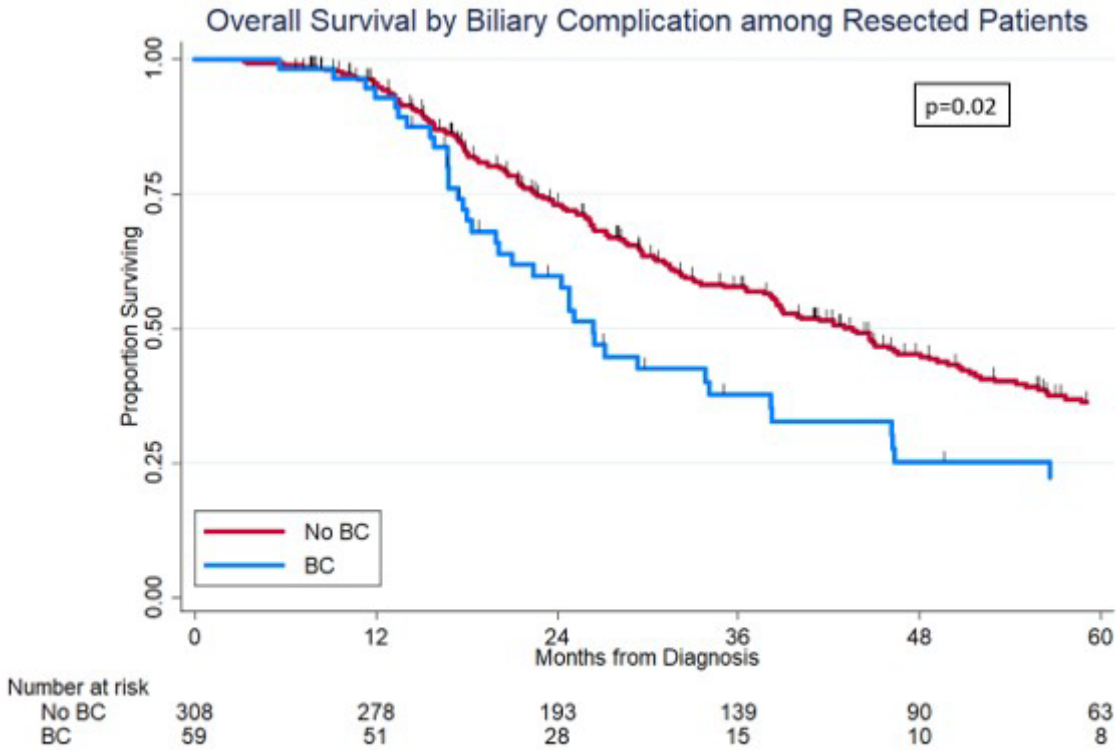


Figure 1: Overall survival from diagnosis by presence of biliary complication (BC) during neoadjuvant therapy for patients who underwent surgical resection (n=367). Among 59 patients with a prior BC, mOS was 26 months compared to 44 months among the 308 patients without a BC (p=0.02).

4. DEFINING EFFECTIVE NEOADJUVANT CHEMOTHERAPY (NAC) IN PDAC, IMPLICATIONS FROM SURVIVAL AND PATTERN OF FAILURE IN PATIENTS WHO RECEIVED NAC

H Liu, M D'Alesio, S AlMasri, A Hammad, A Desilva, S Lebowitz, C Rieser, E Ashwat, E Hampton, H Khachfe, M Laffey, A Singhi, N Bahary, K Lee, A Zureikat, A Paniccia

Presenter: Hao Liu MD, PhD | University of Pittsburgh Medical Center, United States

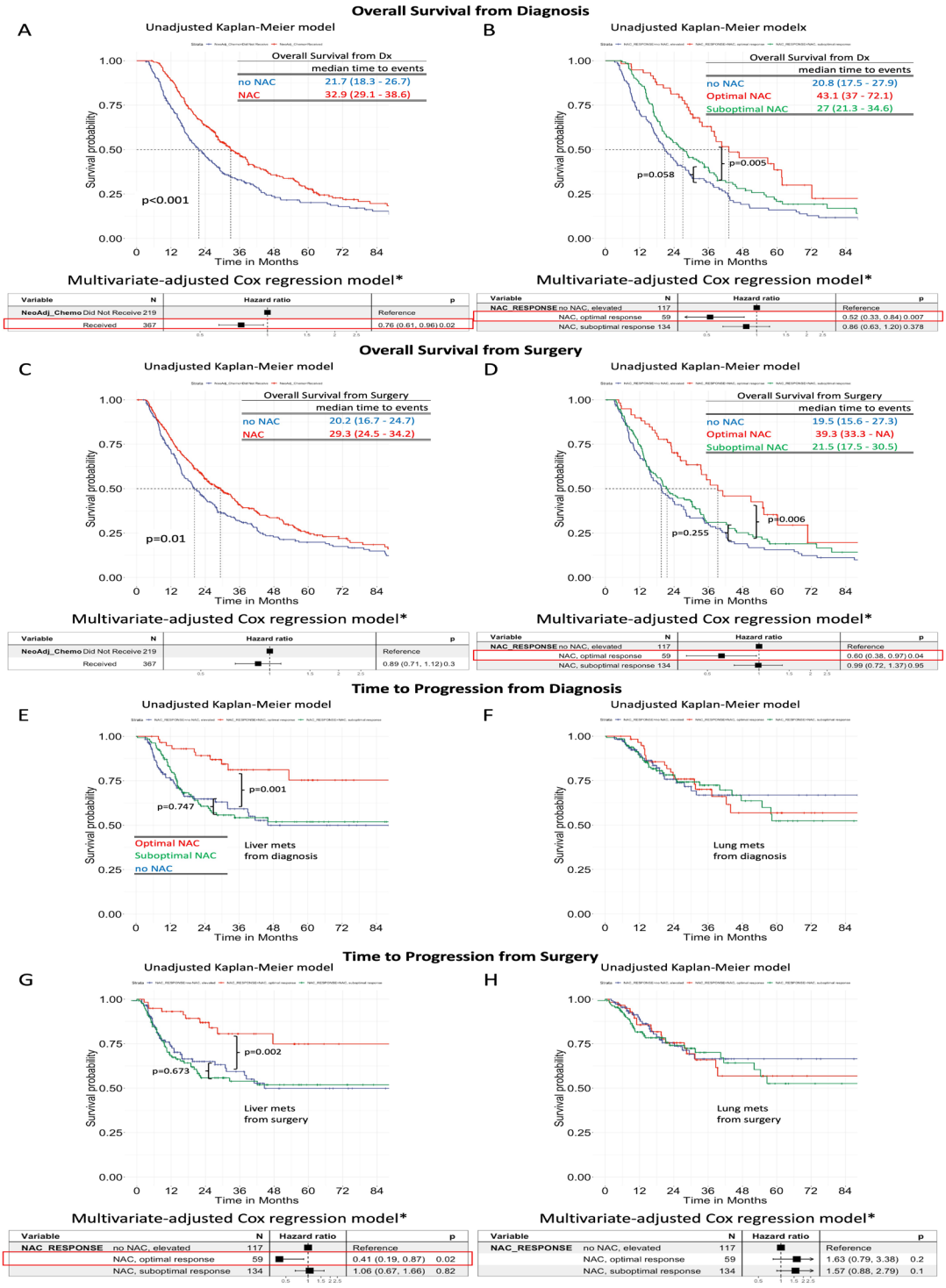
Background: Neoadjuvant chemotherapy (NAC) is gaining popularity over the surgery-first (SF) approach in treating resectable and borderline resectable pancreatic ductal adenocarcinoma (PDAC). Although CA19-9 change during NAC predicts oncological outcomes among NAC patients, what constitutes effective neoadjuvant chemotherapy in resectable or borderline resectable PDAC patients is unknown.

Methods: We retrospectively analyzed resectable and borderline resectable PDAC patients who underwent pancreaticoduodenectomy (2010-2019) at a single institution. Optimal CA19-9 response was defined as normalization AND >50% reduction. Radiological evidence of metastasis development in the liver, lung, peritoneal cavity, and local recurrence was defined as disease progression. We utilized Kaplan-Meier, multivariable-adjusted Cox models, and competing risk subdistribution methods for statistical analysis. The propensity score of receiving neoadjuvant chemotherapy was calculated by age, gender, age-adjusted CCI, pre-treatment CA19-9, and administration of neoadjuvant radiation therapy. Overall survival (OS) was calculated from both diagnosis and surgery to account for the immortal time bias of receiving NAC.

Results: 586 patients were included in this study. The multivariate-adjusted analysis demonstrated OS benefit in the NAC group only when OS was calculated from diagnosis (HR=0.77, p=0.021), but not from surgery (HR=0.89, p=0.312). However, in 59 patients who achieved optimal CA19-9 response, OS is significantly longer than the 134 patients with suboptimal CA19-9 response (39.3m vs. 21.5m, p=0.005) or the 117 SF patients (39.3m vs. 19.5m, p< 0.001). Notably, a suboptimal CA19-9 response conferred no OS advantage compared to SF patients in both unadjusted and multivariate-adjusted models, even when calculating OS from diagnosis (HR=0.86, p=0.378).

Liver metastasis was significantly reduced in patients with optimal CA19-9 response to NAC (HR 0.41, p=0.02). However, lung metastasis was not affected, even with optimal CA19-9 response (HR 1.63, p=0.2). There is also no significant reduction in peritoneal metastatic progression or local recurrence reduction, even with optimal CA19-9 response.

Conclusion: We identified a CA19-9 response to NAC of "normalization AND >50% reduction" as the marker for effective NAC. Suboptimal CA19-9 NAC responses did not correlate with a survival benefit compared to the SF approach, even when accounting for the NAC immortal-time bias. However, optimal CA19-9 is associated with longer survival with a significant reduction in metastatic progression in the liver, but not other sites. This result should be verified in a multi-institutional study.



Abstract Figure 1

Unadjusted Kaplan-Meier Survival Analysis (KM) and Multivariable-adjusted Cox Proportional Hazards Model (CPH) on patients with and without neoadjuvant chemotherapy (NAC) (A and C) and on patients who had optimal and suboptimal CA19-9 response to NAC (B and D), counting from the time of diagnosis (A and B) and surgery (C and D). Unadjusted Kaplan-Meier (KM) analysis on time to liver (E) and lung (F) metastatic progression from the time of diagnosis, as well as unadjusted KM and multivariate-adjusted Cox Proportional Hazards Ratio Model on time to liver (G) and lung (H) metastatic progression from the time of surgery.

*Covariates adjusted in multivariable CPH models include age, gender, Charlson Comorbidity Index (CCI), radiation therapy, vascular resection, tumor size, pre-treatment CA19-9, margin, lymph node ratio (LNR), lymphovascular invasion (LVI), perineural invasion (PNI), Grade, post-op complication, and adjuvant chemotherapy.

5. SHOULD NEOADJUVANT CHEMOTHERAPY BE CONSIDERED AS A STANDARD IN ELDERLY PATIENTS WITH RESECTABLE PANCREATIC ADENOCARCINOMA: A REVIEW OF NATIONAL CANCER DATABASE

NL Lad, O Standring, L Demyan, GB Deutsch, MJ Weiss, D DePeralta

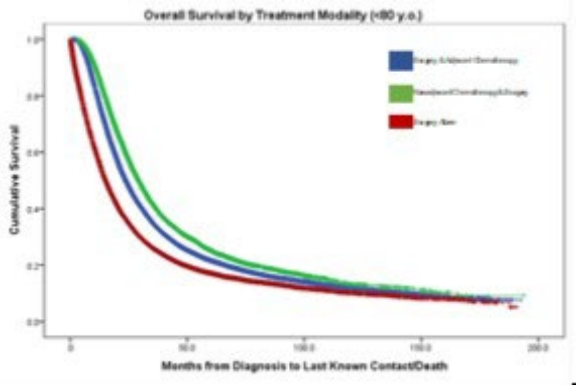
Presenter: Neha Lad MD | Northwell Health Cancer Institute, United States

Background: For resectable pancreatic ductal adenocarcinoma (PDAC) in elderly patients (>80y), timing of chemotherapy and surgery remains poorly defined. Clinical decision making is more challenging in elderly due to presence of comorbidities in addition to disease biology, which impacts treatment choice.

Methods: National Cancer Database (NCDB) was reviewed from 2007-2018 to identify elderly (>80y) vs non-elderly(< 80y) with PDAC. Statistical analyses were used to compare outcomes in elderly with upfront surgery (US) vs neoadjuvant+surgery (N+S). Subset analysis compared survival in upfront surgery alone (USa), surgery+adjuvant chemotherapy(S+A), and N+S groups.

Results: Total 75,806 with PDAC were identified, 568 were elderly N+S group. 6659 elderly patients underwent upfront surgery, of which 36.7% received adjuvant chemotherapy; as compared to non-elderly, where 63.4% received adjuvant chemotherapy. Elderly N+S vs US were comparable with age (82.2 vs82.9y), comorbidities (p=NS); however, N+S vs US, had slightly more males (51.2 vs 45.5%), presence of head tumor (74.1 vs 67%), larger tumor size (5.07 vs 2.78cm), higher presence of clinical stage2 (38.6 vs 25.5%), improved 30-day (3.1 vs 6.7%) and 90-day (8.5 vs 13.9%) mortality were statistically significant (all p< 0.05), respectively. On subset analysis, median OS in elderly undergoing USa compared to S+A, and N+S was significantly lower (11.7 vs 20.1 vs 22.6 months, p< 0.001).

Conclusion: Elderly with PDAC undergoing upfront surgery have significantly high mortality, fewer patients get adjuvant chemotherapy, and failure to receive chemotherapy either adjuvant or neoadjuvant setting leads to poor survival. Neoadjuvant chemotherapy should be strongly considered in all elderly patients for improved outcomes.



6. NUTRITIONAL IMPACT OF ACTIVE HEXOSE CORRELATED COMPOUND FOR PATIENTS WITH RESECTABLE/BORDERLINE RESECTABLE PANCREATIC CANCER TREATED WITH NEOADJUVANT THERAPY

S Satoi, T Yamamoto, S Yamaki, M Ishida, Y Matsui, S Hirooka, M Sekimoto

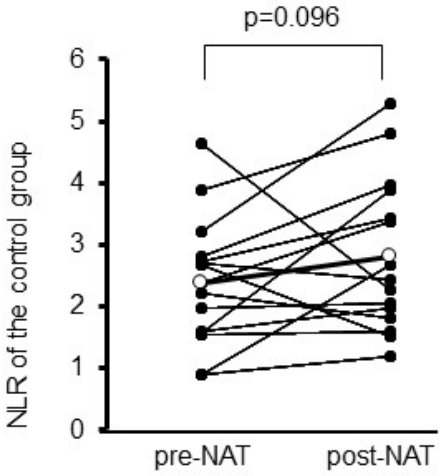
Presenter: Daisuke Hashimoto MD, PhD | Kansai Medical University, Japan

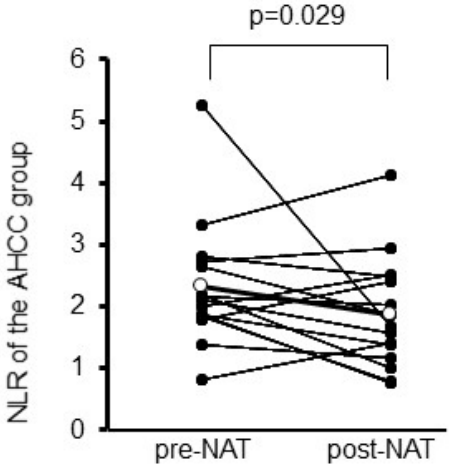
Background: One of the possible reasons for the worse prognosis of patients with pancreatic ductal adenocarcinoma (PDAC) is malnutrition. Malnutrition due to the cancer burden can exist at the initial diagnosis, and the entry and completion rate of neoadjuvant therapy (NAT) for PDAC can be decreased by malnutrition. NAT itself can lead malnutrition, hampering recovery after surgery. Thus, it is important to improve the nutritional status of patients with pancreatic ductal adenocarcinoma PDAC during NAT. Active hexose correlated compound (AHCC) is a standardized extract from cultured Lentinula edodes mycelia and is considered to be a potent biological response modifier in cancer treatment. The aim of this study was to evaluate the nutritional effect of AHCC during neoadjuvant therapy in patients with PDAC.

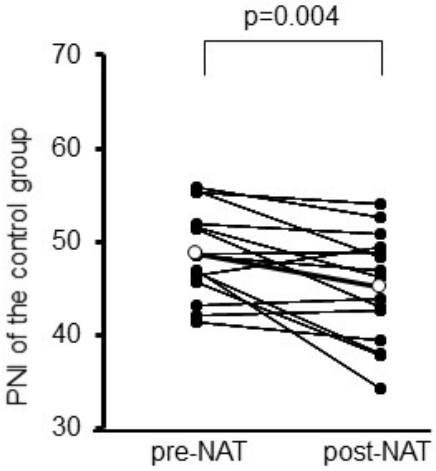
Methods: From June 2019 to May 2020, 30 consecutive patients with resectable/borderline resectable PDAC underwent planned neoadjuvant therapy with gemcitabine plus S-1 followed by surgery. The clinical course of patients who received AHCC combined with neoadjuvant therapy was evaluated retrospectively and compared with patients who did not receive AHCC. Patients of the AHCC group began taking AHCC at 3.0 g/day (1.0 g × 3 times/day) on the first day of NAT. AHCC intake was planned to be continued until the day before surgery. NAT was performed with GEM plus S-1 in this study.

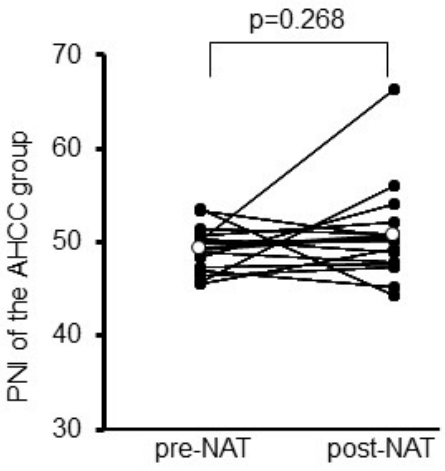
Results: Fifteen patients received AHCC with neoadjuvant therapy and 15 patients did not. Median (range) RDI was significantly higher (p=0.023) in the AHCC group (100 (77.1–100)%) than in the control group (81.4 (71.3–100)%). There were no significant differences in response rate (p=0.974), and carbohydrate antigen 19-9 (CA19-9) before NAT (p=0.266). However, median change (range) of CA19-9 after NAT was significantly lower (p=0.045) in the AHCC group (−83.6 (−99.7–115.0)%) than the control group (−58.8 (−99.9–871.4)%). Median (range) neutrophil-to-lymphocyte ratio (NLR) before NAT was similar (p=0.438) in both groups (2.67 (0.89–4.63) in the control group vs 2.10 (0.82–5.26) in the AHCC group). There was no significant change after NAT in the control group (2.44 (1.21–5.27), p= 0.096). However, NLR was significantly decreased after NAT in the AHCC group (1.68 (0.76–4.14), p=0.029). Median (range) prognostic nutrition index (PNI) before NAT was similar (p=0.344) in both groups (48.5 (41.3–55.8) in the control group vs 49.8 (45.5–53.6) in the AHCC group). PNI was significantly decreased after NAT in the control group (46.2 (34.3–54.1), p=0.004). However, there was no significant change after NAT in the AHCC group (50.2 (44.4–66.4), p=0.268). In this cohort, all patients who received NAT underwent pancreatectomy, and the resection rate was 100% in both groups. There were no significant differences in surgical time, surgical bleeding, and incidence of postoperative complications. There was no in-hospital mortality in both groups.

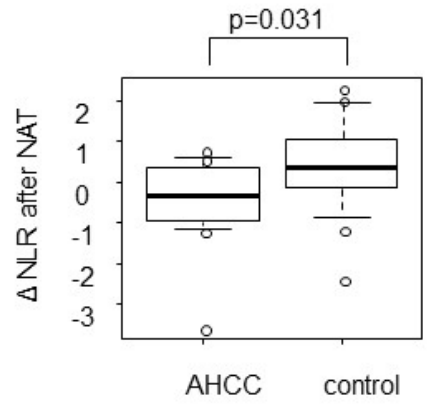
Conclusion: In conclusion, AHCC improved the nutritional status of patients with R/BR PDAC during NAT with GEM plus S-1. To validate this effect and to evaluate the long-term impact of AHCC, a double-blind randomized multicenter prospective phase II study of AHCC for patients with R/BR PDAC is ongoing.

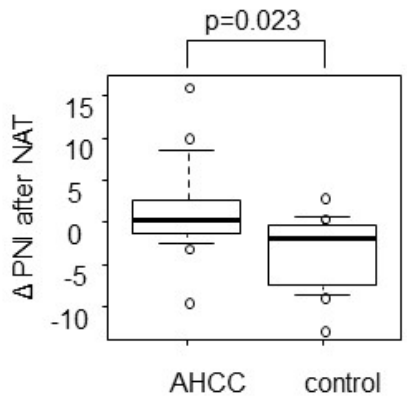

p=0.096
NLR of the control group
6
5
4
3
2
1
0
pre-NAT
post-NAT


p=0.029
NLR of the AHCC group
6
5
4
3
2
1
0
pre-NAT
post-NAT


p=0.004
PNI of the control group
70
60
50
40
30
pre-NAT
post-NAT


p=0.268
PNI of the AHCC group
70
60
50
40
30
pre-NAT
post-NAT


p=0.031
Δ NLR after NAT
2
1
0
-1
-2
-3
AHCC
control


p=0.023
Δ PNI after NAT
15
10
5
0
-5
-10
AHCC
control

7. EARLY RECURRENCE AFTER RESECTION OF LOCALLY ADVANCED PANCREATIC CANCER FOLLOWING INDUCTION THERAPY: A MULTICENTER STUDY

LWF Seelen, AF van Oosten, LJH Brada, VP Groot, LA Daamen, MS Walma, BF van der Lek, B Groot Koerkamp, OR Busch, IHJT de Hingh, CHJ van Eijck, MG Besselink RA Burkhart, IHM Borel Rinkes, CL Wolfgang, IQ Molenaar, J He, HC van Santvoort

Presenter: Leonard W.F. Seelen MD | UMC Utrecht, Netherlands

Background: Advancements in systemic treatment and surgery have increased the resection rate in locally advanced pancreatic cancer (LAPC). Nevertheless, a substantial part of patients will develop disease recurrence within a short time after resection. A universally accepted cut-off value to define early recurrence in LAPC is, however, not available. Moreover, it remains unclear which patients are at risk for early recurrence. This information may be useful to guide clinicians and patients in shared decision-making on treatment and postoperative follow-up regimes. Therefore, the aim of this study was to establish a cut-off value for early recurrence after resection for LAPC and to identify predictive factors for early recurrence.

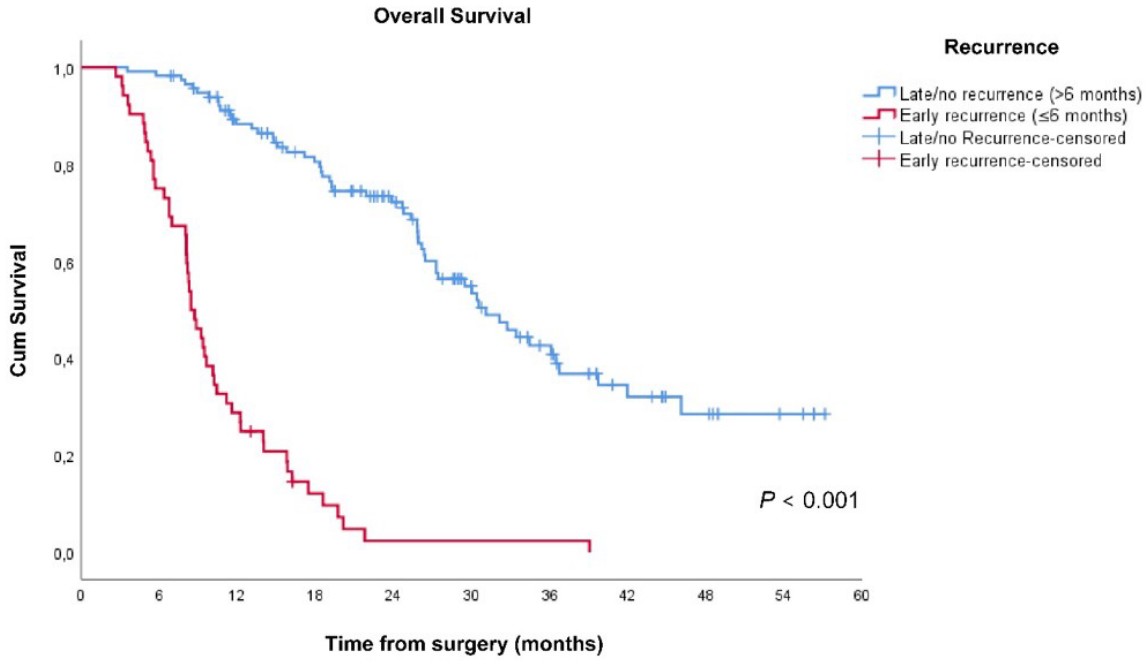
Methods: The present study is a post-hoc analysis of two prospective databases. All patients with histologically confirmed LAPC who underwent resection following induction therapy in eight tertiary pancreatic centers in the Netherlands (2015-2019) and one tertiary center in the United States of America (USA) (2016-2018) were included. LAPC was defined according to the National Comprehensive Cancer Network (NCCN) criteria. Using the log-rank test, post-recurrence survival (PRS) was compared between patients with early and late recurrence after LAPC resection, assessing different cut-off points for recurrence-free survival (RFS) to define "early recurrence". The cut-off point with the lowest P-value was chosen. Patients with early and late/no recurrence were compared with regard to overall survival (OS). Potential preoperative and postoperative predictors for early recurrence were evaluated using multivariable logistic regression analysis.

Results: A total of 170 consecutive patients were included. Median follow-up after resection was 25 months (interquartile range [IQR] 15-37). Disease recurrence occurred in 118 (69%) patients after a median RFS of 7 months. The optimal cut-off point for RFS to differentiate between early (n=52, 44%) and late recurrence (n=66, 56%) was 6 months (P< 0.001). OS was 8.4 months (95%-CI 7.3-9.6) in the early recurrence group (n=52, 31%) vs. 31.1 months (95%-CI 25.7-36.4) in the late/no recurrence group (n=118, 69%) (P< 0.001). The only independent preoperative predictor for early recurrence was post-induction therapy but preoperative CA 19-9 ≥100 U/ml (OR 5.09 [95%-CI 2.14-12.06]; P< 0.001). Postoperative predictive factors were poor tumor differentiation (OR 4.62 [95%-CI 1.51-14.08]; P=0.008) and not starting with adjuvant chemotherapy (OR 5.95 [95%-CI 2.45-14.49]; P< 0.001).

Conclusion: The optimal cut-off to define early recurrence after LAPC resection, based on subsequent prognosis, is a recurrence-free survival of six months. Early recurrence occurs in around 31% of patients and is associated with a very poor survival. Preoperative CA 19-9 ≥100 U/ml, poor tumor differentiation and no adjuvant therapy are predictors for early recurrence.

Knowledge of these predictors for early recurrence in LAPC can be used to inform patients on their prognosis and guide clinicians and patients in shared decision-making on perioperative counseling and postoperative treatments.

Figure 1. Overall Survival Kaplan-Meier Curve Comparing Early and Late/No Recurrence Cohorts



Number at risk (number censored):

Late/no recurrence	116 (0)	114 (10)	93 (5)	80 (10)	62 (11)	36 (5)	24 (6)	13 (4)	8 (4)	4 (4)
Early recurrence	52 (0)	39 (0)	15 (2)	5 (0)	1 (0)	1 (0)	1 (0)	-	-	-
Months	0	6	12	18	24	30	36	42	48	54

8. IMPACT OF ISOLATED POSITIVE VASCULAR GROOVE MARGIN ON RECURRENCE AND SURVIVAL FOLLOWING RESECTION FOR PANCREATIC DUCTAL ADENOCARCINOMA: A SINGLE CENTER EXPERIENCE

HH Khachfe, C Hlavin, A Chopra, A deSilva, A Y Hammad, S AlMasri, H Liu, J Kraftician, A Singhi, KK Lee, AH Zureikat, A Paniccia

Presenter: Hussein H. Khachfe MD | University of Pittsburgh Medical Center, United States

Background: Significant controversy exists regarding the definition of a positive vascular groove margin (VGm) and its prognostic value after pancreaticoduodenectomy for pancreatic ductal adenocarcinoma (PDAC). The updated version 4.2.0.0 of the College of American Pathologists no longer considers the VG a resection margin but rather a surface margin. Moreover, when all other surgical resection margins are negative, the impact of an isolated positive VGm remains poorly characterized. The aim of this study was to evaluate the impact of an isolated positive VGm on PDAC recurrence and survival.

Methods: We identified 195 patients who underwent a pancreaticodudenectomy for PDAC and met our inclusion criteria, between 2005-2019. Surgical margins were classified as R1 (with positive vascular groove being the only positive margin, with tumor within 1mm) or R0 (all margins negative). Recurrence free survival (RFS) and overall survival (OS) were evaluated using multivariate Cox-regression proportional hazard models. Estimates for RFS and OS were calculated using Kaplan-Meier analysis.

Results: An isolated positive vascular groove margin was identified in 90 (46.1%) patients and was associated with a significantly lower mOS (25 vs 42 months, p= 0.015) and mRFS (17 vs 27 months, p < 0.001) compared to patients with R0 resections. Patients with positive vacular groove margin were older (68.3 vs 67.5 years, p= 0.001), more likely to receive neoadjuvant chemotherapy (44.3 vs 55.7%, p = 0.013), and to have lymphovascular invasion (48.6 vs 51.4%, p = 0.012). Moreover, the use of neoadjuvant chemotherapy was not associated with improved OS in patient with positive VGm (HR= 0.84 [0.54-1.30], p=0.438). Local recurrence as first site of recurrence was more frequent in the positive VGm group (41.4 vs 58.5%) however this difference was not significant (p=0.097). Positive vascular groove margin proved to be an independent predictor of recurrence (HR: 2.83, p < 0.001) and decreased OS (HR: 1.48, p = 0.032) on multivariate analysis.

Conclusion: Positive vascular groove margins is significantly associated with OS and recurrence for patients with resected PDAC.

	Univariate Analysis		Multivariate Analysis	
	Hazard Ratio [95% CI]	Sig.	Hazard Ratio [95% CI]	Sig.
Age	1.00 [0.98-1.02]	0.830		
Sex	0.95 [0.69-1.30]	0.745		
BMI	0.97 [0.94-1.00]	0.140		
CCI Age Adjusted	1.10 [0.98-1.23]	0.106		
Tumor Site	1.01 [0.94-1.09]	0.716		
Neoadjuvant Chemotherapy	1.04 [0.75-1.45]	0.795		
# of Neoadjuvant Chemotherapy Cycles	1.02 [0.91-1.14]	0.716		
Vein Resection/Repair	1.36 [0.97-1.88]	0.061		
Gx	**REF**			
G1	1.29 [0.27-6.07]	0.748		
G2	1.15 [0.28-4.65]	0.847		
G3	1.57 [0.37-6.53]	0.537		
Lymph Node Positive	2.01 [1.40-2.88]	<0.001	1.40 [0.94-2.07]	0.096
Lymphovascular Invasion	1.97 [1.32-2.94]	0.001	1.45 [0.92-2.25]	0.105
Perineural Invasion	2.14 [1.20-3.80]	0.010	1.46 [0.80-2.65]	0.211
Positive Vascular Groove Margin	**1.51 [1.078-2.12]**	**0.017**	**1.48 [1.03-2.11]**	**0.032**
Adjuvant Chemotherapy	1.27 [1.06-1.51]	0.009	0.50 [0.34-0.73]	<0.001
# of Adjuvant Chemotherapy Cycles	0.94 [0.80-1.09]	0.433		
Recurrence	2.77 [1.88-4.07]	<0.001	2.84 [1.91-4.20]	<0.001
1st Site of Recurrence	1.26 [0.85-1.86]	0.254		

9. IMPORTANCE OF NODAL METASTASES LOCATION IN PANCREATODUODENECTOMY FOR PANCREATIC DUCTAL ADENOCARCINOMA: RESULTS FROM A PROSPECTIVE LYMPHADENECTOMY PROTOCOL

L Maggino, G Malleo, F Casciani, G Lionetto, S Nobile, G Lazzarin, S Paiella, A Esposito, P Capelli, C Luchini, A Scarpa, C Bassi, R Salvia

Presenter: Laura Maggino MD | University of Verona, Italy

Background: The issue of lymph node (LN) metastases location in upfront pancreatoduodenectomy (PD) for pancreatic ductal adenocarcinoma (PDAC) is unclear. Implementing a prospective lymphadenectomy protocol, we investigated the nodal yields and metastases per anatomical stations and nodal echelon. Next, the relationship between the extension of nodal dissection, the number of examined/positive nodes (ELN/PLN), disease staging and prognosis was assessed.

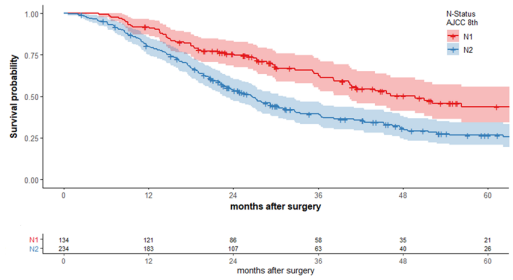
Methods: A protocol for LN dissection in upfront PD for presumed PDAC was established from January 2013 and one academic institution. Slightly modifying the standard ISGPS concept, the lymphadenectomy included stations 5, 6, 8a-p, 12a-b-c-p, 13, 14a-b, 17, and jejunal mesentery nodes per the Japanese Pancreas Society definition. Tumors were staged according to the 8th edition of the AJCC manual. Stations embedded in the specimen (13/14/17/jejunal mesentery) were defined as first-echelon, those sampled separately (5/6/8/12) as second-echelon. Recurrence and survival were analyzed. To avoid collinearity, nodal-related parameters were analyzed in separate multivariable models.

Results: Overall, 424 PDs (2013-2018) were enrolled. The median number of ELN and PLN was 42 (IQR 34-50) and 4 (IQR 2-8). A total of 11.8% of the patients were N0 (n=50), 31.8% were N1 (n=135) and 56.4% were N2 (n=239). The commonest metastatic sites were stations 13 (77.8%) and 14 (57.5%) while jejunal mesentery LNs were positive in 9.9% of the patients. Overall, 248 patients (58.5%) had metastases only in the first echelon, 4 (0.9%) only in the second, 122 (28.8%) in both. The median number of ELN and PLN in the first echelon was 28 (IQR 23-34) and 4 (IQR 1-7). Second-echelon nodes increased nodal counts by 10 ELN (IQR 6-14) and 0 PLN (IQR 0-1), translating in only minor changes in staging.

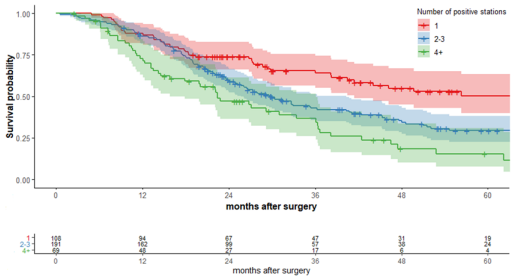
After multivariable adjustment, nodal-related factors independently associated with survival in the subset of node-positive patients were N-status (HR 1.958, 95%CI 1.368-2.803, p< 0.001), multiple metastatic stations (HR=1.225, 95%CI 0.862-1.742, p=0.258 for 2-3 versus 1 and HR=1.816, 95%CI 1.149-2.871, p=0.011 for ≥4 versus 1 metastatic stations), metastases to station 14 (HR=1.774, 95%CI 1.100-2.861, p=0.019) and jejunal mesentery nodes (HR=3.740, 95%CI 1.983-7.054, p< 0.001). Survival curves stratified by these nodal-related parameters are shown in the Figure. Notably, the highest concordance was reached in the model including metastases location (c-index=0.709). Similar results were obtained when analyzing recurrence.

Conclusion: First-echelon dissection provides an adequate number of ELN for optimal staging during PD for PDAC. Nodal metastases occur mostly at stations 13/14, although second-echelon involvement is frequent. Station 14 and jejunal mesentery nodes involvement is prognostically relevant. They should be included in the standard nodal map and analyzed pathologically.

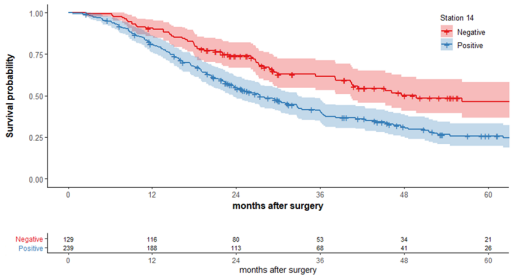
A


N-Status
AJCC 8th
N1
N2
Survival probability
1.00
0.75
0.50
0.25
0.00
0
12
24
36
48
60
months after surgery
N1 134 121 86 58 35 21
N2 234 183 107 63 40 26

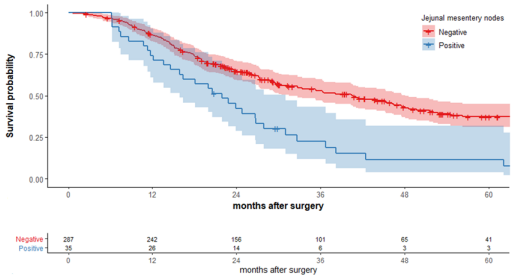
B


Number of positive stations
1
2-3
4+
Survival probability
1.00
0.75
0.50
0.25
0.00
0
12
24
36
48
60
months after surgery
1 108 94 67 47 31 19
2-3 101 93 59 37 30 24
4+ 69 46 27 17 6 4

C


Station 14
Negative
Positive
Survival probability
1.00
0.75
0.50
0.25
0.00
0
12
24
36
48
60
months after surgery
Negative 129 116 80 53 34 21
Positive 239 188 113 68 41 26

D


Jejunal mesentery nodes
Negative
Positive
Survival probability
1.00
0.75
0.50
0.25
0.00
0
12
24
36
48
60
months after surgery
Negative 287 242 156 101 65 41
Positive 35 26 14 6 3 3

10. A NOVEL SCORING SYSTEM FOR THE PREDICTION OF CLINICALLY RELEVANT POSTOPERATIVE PANCREATIC FISTULA IN PATIENTS UNDERGOING DISTAL PANCREATECTOMY

W Wong, C Vining, R Perez Holguin, C Stahl, V Chinchilli, C Pameijer, M Dixon, J Peng
Presenter: William Wong DO | Academic Medical Center, United States

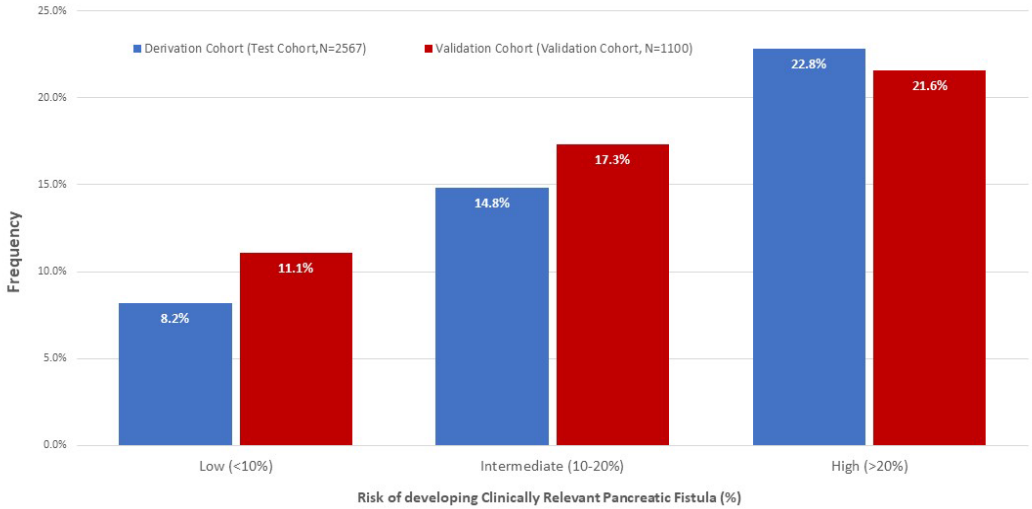
Background: Clinically relevant postoperative pancreatic fistula (CR-POPF) is a major source of morbidity and mortality after a pancreatectomy. While there is a Fistula Risk Score (FRS) to predict CR-POPF after a Whipple procedure, the FRS is not validated for distal pancreatectomy (DP). The goal of this study is to develop and validate a predictive fistula risk score for distal pancreatectomy (DP-FRS).

Methods: The 2014-2019 American College of Surgeons National Surgical Quality Improvement Project pancreatectomy Participant User Data File was queried for patients who underwent elective DP. A randomly generated 70% of the final cohort was used as the derivation cohort to identify independent predictors of CR-POPF based on multivariable logistic regression and backward selection. A value was assigned to each statistically significant variable (1 if odds ratio (OR) ≥1 and 2 if OR ≥2); a DP-FRS was developed and stratified into three risk categories. The remaining 30% of patients were used as the validation cohort to determine the receiver operator characteristic curve and area under the curve (AUC).

Results: The final cohort consisted of 3,667 patients who underwent DP. CR-POPF was identified in 13.2% (N=338/2567) and 15.0% (N=165/1100) of the derivation cohort and validation cohort, respectively. Predictors of CR-POPF utilized for the DP-FRS model included: body mass index ≥25kg/m2 (OR=1.5), male gender (OR=1.3), non-White race (OR=1.5), history of chronic obstructive pulmonary disease (OR=2.1), histologic subtype other than adenocarcinoma or chronic pancreatitis (OR=1.5), operation time >4 hours (OR=1.7), and blood transfusion (OR=1.6) (all $p< 0.05$). A value was assigned depending on the presence of the associated risk factor. An eight-point model was developed and patients were stratified into low (score ≤2; < 10% CR-POPF), intermediate (score 3; 10-20% CR-POPF), and high (score ≥4; >20% CR-POPF) risk. Under these categories, the associated CR-POPF rates were 8.2%, 14.8%, and 22.8% in the derivation cohort, respectively, and 11.1%, 17.3%, and 21.6% in the validation cohort, respectively. The AUCs for the derivation and validation cohorts were 0.63 and 0.60, respectively.

Conclusion: This is the largest study to date to establish and validate a DP-FRS in patients undergoing DP. This novel scoring system may aid surgeons in evaluating patients at risk for developing CR-POPF, in decision-making for drain placement, and in postoperative care management after DP. Additional studies are required to further improve the predictive ability of the DP-FRS for CR-POPF.

Figure 1. Percentage of Clinically Relevant Pancreatic Fistula after Distal Pancreatectomy by Risk Categories in the Derivation and Validation Cohorts.



11. A PERIOPERATIVE BUNDLE FOR REDUCTION OF INCISIONAL SURGICAL SITE INFECTIONS FOLLOWING PANCREATICODUODENECTOMY: A PRE-POST INTERVENTION STUDY

TL Sutton, K Potter, J O'Grady, J Chuong, SC Mayo, E Gilbert, BC Sheppard
Presenter: Thomas L. Sutton MD | Oregon Health & Science University, United States

Background: Patients undergoing pancreaticoduodenectomy are at high risk of incisional surgical site infections (iSSIs) due to violation of the biliary and upper gastrointestinal tracts. Multiple perioperative interventions have been proposed to reduce SSIs in patients undergoing pancreaticoduodenectomy, however high quality data following implementation of these interventions are lacking.

Methods: In July 2017 a multidisciplinary perioperative bundle was implemented at our center aimed at enhancing recovery and reducing iSSIs. Interventions included pre-habilitation, pre-operative nutritional supplementation, routine use of wound protectors and closure trays, ensuring appropriate intra-operative antibiotic redosing, and utilization of multimodal pain control.

Using prospective National Surgical Quality Improvement Project (NSQIP) data, patients undergoing pancreaticoduodenectomy from July 2013 to April 2020 were identified. Multivariable logistic and linear regression were utilized to generate odds ratios (OR) for experiencing the primary outcomes of interest, NSQIP-defined iSSIs and length of stay (LOS).

Results: Four-hundred-fifty-seven patients underwent pancreaticoduodenectomy during the study period, with 228 (49.9%) receiving the perioperative bundle. Groups were not significantly different in most clinicopathologic characteristics (Table). Following adoption of the bundle, the proportion of patients developing NSQIP-defined iSSIs declined from 23.1% (n=53) to 8.8% (n=20; P< 0.001).

On multivariable analysis controlling for age, comorbidities, blood loss, stent presence, and neoadjuvant therapy, bundle implementation was independently associated with reduced odds of iSSI (OR 0.31; 95% CI 0.18-0.54; P< 0.001). LOS was also significantly reduced following implementation (median 10 versus 11 days), with bundle implementation remaining independently associated with reduced LOS on multivariable regression (size of effect: -2.05 days; 95% CI -3.56, -0.55; P=0.008).

Conclusion: In a pre-post intervention analysis utilizing standardized NSQIP definitions, implementation of a comprehensive perioperative bundle reduced iSSIs and LOS in patients undergoing pancreaticoduodenectomy. We recommend protocolization of similar perioperative interventions to reduce iSSIs at centers where pancreaticoduodenectomy is performed.

Table: Clinicopathologic Characteristics of Patients Undergoing Pancreaticoduodenectomy

Characteristic	Pre- Bundle Implementation (n=229); No. (%)	Post- Bundle Implementation (n=228); No. (%)	*P*
Age, Years; median [IQR]	67 [60-73]	68 [59-73]	>0.99
Gender			0.93
Female	109 (47.6)	110 (48.2)	
Male	120 (52.4)	118 (51.8)	
Reason for Resection			0.08
Other Malignant	42 (18.3)	58 (25.4)	
Benign	27 (11.8)	37 (16.2)	
PDAC	143 (62.4)	120 (52.6)	
PNET	17 (7.4)	13 (5.7)	
NSQIP-defined Comorbidities			0.95
0	51 (22.3)	52 (22.8)	
1-2	127 (55.5)	123 (53.9)	
≥3	51 (22.3)	53 (23.2)	
Pre-operative Chemotherapy	32 (14.0)	72 (31.6)	<0.001
Biliary Stent	143 (62.4)	136 (59.6)	0.57
Minimally Invasive Approach	9 (3.9)	21 (9.2)	0.02
Vascular Reconstruction	53 (23.1)	53 (23.2)	>0.99
Surgical Duration, Hours; median [IQR]	8.2 [6.9-9.9]	8.2 [6.9-9.7]	0.97
Intraoperative Blood Loss, mL; median [IQR]	700 [400-1100]	600 [300-1025]	0.14
Wound Protector Use	98 (42.8)	207 (90.8)	<0.001
Intraoperative Antibiotics			<0.001
1st generation cephalosporin	25 (10.9)	44 (19.3)	
2nd/3rd generation cephalosporir	164 (71.6)	99 (43.4)	
Broad spectrum	33 (14.4)	85 (37.3)	
Other	7 (3.1)	0 (0)	
Soft Gland Texture	73 (31.9)	67 (29.4)	0.61
Pancreatic Duct Size			0.007
<3 mm	72 (31.4)	49 (21.5)	
3-6 mm	102 (44.5)	133 (58.3)	
>6 mm	38 (16.6)	24 (10.5)	
Not Specified	17 (7.4)	22 (9.6)	

Abbreviations: IQR=Interquartile Range; PDAC=Pancreatic Ductal Adenocarcinoma; PNET=Pancreatic Neuroendocrine Tumor; NSQIP=National Surgical Quality Improvement Project

12. GENDER AND YEARS IN PRACTICE CONTRIBUTE TO DISCREPANCY BETWEEN SURGEONS' PERSONAL PREFERENCES AND RECOMMENDATIONS FOR PALLIATIVE CARE REFERRAL. RESULTS FROM AN INTERNATIONAL SURVEY

L Demyan, G Wu, A Blumenthaler, C Nofi, N Kohn, GB Deutsch, JM Herman, W Nealon, MJ Weiss, DK DePeralta
Presenter: Lyudmyla Dmeyan MD, MS | Northwell Health Cancer Institute, United States

Background: Early palliative care (PC) consultation has been promoted for patients with gastrointestinal cancers. However, the timing of PC consultation for patients with resectable pancreatic cancer is often dictated by their surgeon. We hypothesized that pancreatic surgeons may want early PC for themselves, if they had a potentially resectable pancreatic cancer, but would not recommend early PC referral to their patients.

Methods: An anonymous international survey was distributed to Pancreas Club members in 2021. Chi-square test or Fisher's exact test were used for analyzing categorical variables and the Wilcox test was utilized for analyzing Likert scaled questions. Statistical significance was set at $p< 0.05$.

Results: 138 surveys were completed. 83% of surgeons were male, 85% completed a fellowship, 80% practiced in academia, 46% performed >30 annual curative-intent operations for PDAC and 90% have been in practice ≤30 years. 88% of surgeons were from the US. 94% of surgeons reported that they would pursue a standard of care treatment if they had a potentially curative pancreatic cancer. However, female surgeons (75%) were less likely to report that they would pursue a standard of care treatment if they had a potentially curative pancreatic cancer compared to male surgeons (98%) (p 30 years were more likely to report that they would not want PC referral prior to resection if diagnosed with resectable pancreatic cancer (p=0.043).

Conclusion: The overweighing majority of surgeons report that they would pursue a standard of care for resectable pancreatic cancer with the treatment in line that they recommend to their patients. However, surgeons are more inclined to pursue early palliative care for themselves during disease-modifying treatment compared to their patients. Gender, fellowship training, and years in practice influence surgeons' personal preference and their recommendations for their patients regarding PC referral. Further studies are needed to elucidate factors that influence physicians' recommendations for their patients and the impact of their own personal biases and preferences on their practice.

Potential benefits to pre-operative palliative care consultation	**n (%)**	**Surgeons Supporting Respective Statements p-value (OR)**
More support for patients	102 (74%)	
Access to additional support resources (nutrition, psychosocial support)	99 (72%)	US Surgeons (p=0.0028; OR 4.53[CI1.58-12.97])
More support for families	97 (70%)	US Surgeons (p=0.025; OR 3.12 [CI 1.11-8.80])
Symptom management	91 (66%)	Female (p=0.047; OR 3.02 [CI 1.97-9.45]) Fellowship training (p=0.0162; OR 4.16 [CI 1.30-13.32])
Improved prognostic awareness	66 (48%)	US Surgeons (p=0.0078; OR 5.06 [CI 1.38-18.5])
Less aggressive treatment once the patient reaches the end of life	57 (41%)	
No – I don't see any potential benefits	8 (6%)	

Table 1. Surgeons' perceptions regarding benefits of preoperative palliative care.

13. PANREATICOGASTROSTOMY AS A FISTULA MITIGATING STRATEGY FOR A HIGH-RISK PANCREATIC ANASTOMOSIS FOLLOWING PANCREATICODUODENECTOMY

G Kazantsev, A Spitzer, P Peng, R Ramirez, CK Chang, M Huyser, D Dominguez
Presenter: Dana Dominguez MD | Kaiser Permanente Oakland Medical Center, United States

Background: Clinically relevant postoperative pancreatic fistula (CR-POPF) heavily dominates the spectrum of morbidity following pancreaticoduodenectomy (PD). It leads to extended hospital stay and increased rates of readmission, reoperation, and mortality. Multiple studies have shown that CR-POPF is much more likely to occur in patients with so-called "high-risk" pancreatic remnant which is characterized by soft gland texture and small pancreatic duct size. We hypothesized that selective use of pancreaticogastrostomy (PG) in that group of patients should lead to a decrease in the rate of CR-POPF compared with a standard two-layer pancreaticojejunostomy (PJ).

Methods: An IRB-approved retrospective review of all PD's performed at a single institution between 2009 and 2019 was conducted focusing on the type of procedure, clinical and biochemical parameters, intraoperative surgeon's assessment of gland texture (soft versus hard) and pancreatic duct size (< 3 mm was classified as "small"). Primary endpoints included morbidity, mortality, and CR-POPF rates. The pancreatic remnant was labeled "high-risk" if at least one risk factor was present (soft gland or small duct). The use of PG during the study period was restricted to patients in the high-risk group, while PJ was performed in the settings of both high-risk and low-risk pancreatic remnant per surgeon's discretion.

Results: A total of 309 patients underwent PD for benign (19.7%) and malignant (80.3%) disease. Pancreatic ductal adenocarcinoma (PDAC) was the most common malignancy (58.9%). PJ was performed in 199 cases including 147 low-risk and 52 high-risk gland remnants; PG was done in 110 cases (all high risk). There was no difference in the length of the procedure, blood loss, transfusion requirements, rates of reoperation and readmission, overall morbidity (Clavien-Dindo Grade III and higher), and mortality. The rate of gastrointestinal (GI) bleeding was higher in the PG group:10% vs. none in PJ group (P=0.001); only 2 patients required intervention. Overall CR-POPF rate was 11.9% for the whole study population with no significant difference between PJ and PG groups. Risk-stratified analysis revealed that the use of PJ in low-risk group was associated with CR-POPF rate of 5.4%, however, there was a 6-fold increase in CR-POPF rate when PJ was used in patients with high-risk gland: 36.5.1%, (p=0.0001). The use of PG was associated with much lower rate of CR-POPF (9.1%) in the similar group of patients ($p < 0.0001$). Univariate analysis of 16 variables showed that soft gland texture, affiliation with "high risk" group, obesity, and unfavorable histology (any etiology other than PDAC or chronic pancreatitis) were associated with increased risk of CR-POPF amongst PJ patients; duct size and blood loss did not reach statistical significance. On multivariate analysis, soft gland texture remained the strongest independent predictor of CR-POPF (OR=11.25, 95% CI 3.035-41.7).

Conclusion: Our results demonstrate that PG after pancreaticoduodenectomy is associated with considerable reduction in the rate of CR-POPF in patients with high-risk pancreatic remnant. This technique can be regarded as a fistula-mitigating strategy in these challenging group of patients. Increased rate of GI bleeding calls for further refinement of the technique and postoperative management.

14. PREOPERATIVE CHEMORADIOTHERAPY IS ASSOCIATED WITH REDUCED RISK OF POSTOPERATIVE PANCREATIC FISTULA AFTER PANCREATODUODENECTOMY: A NATIONWIDE ANALYSIS

LV Wismans, JA Suurmeijer, JC van Dongen, BA Bonsing, HC van Santvoort, JW Wilmink, G van Tienhoven, IH de Hingh, DJ Lips, E van der Harst, VE de Meijer, GA Patijn, K Bosscha, MW Stommel, S Festen, M den Dulk, JJ Nuyttens, MP Intven, J de Vos-Geelen, IQ Molenaar, OR Busch, B Groot Koerkamp, MG Besselink, CH van Eijck for the Dutch Pancreatic Cancer Group

Presenter: JA Suurmeijer MD | Academic Medical Center, Netherlands

Background: Postoperative pancreatic fistula (POPF) remains the main cause of morbidity and mortality after pancreatoduodenectomy for pancreatic ductal adenocarcinoma (PDAC). This study aimed to investigate the effect of preoperative chemotherapy (PCT) and preoperative chemoradiotherapy (PCRT) on postoperative pancreatic fistula (POPF) and other pancreatic-specific surgery related complications.

Methods: All patients after pancreatoduodenectomy for PDAC were included from the mandatory nationwide prospective Dutch Pancreatic Cancer Audit (DPCA; 2014-2020). Baseline and treatment characteristics were compared between immediate surgery, preoperative chemotherapy (PCT) and preoperative chemoradiotherapy (PCRT). The relationship between preoperative chemo(radio)therapy and clinically relevant POPF (ISGPS grade B/C) was investigated using multivariable logistic regression analyses.

Results: Overall, 2019 patients after pancreatoduodenectomy for PDAC were included, of whom 1678 underwent immediate surgery (83.1%), 192 (9.5%) received PCT, and 149 (7.4%) received PCRT. POPF occurred in 8.3% of patients after immediate surgery, 4.2% after PCT, and 2.0% after PCRT (p=0.004). In multivariable analysis, the use of PCRT was associated with reduced risk of POPF (OR 0.21, 95%CI 0.03-0.69, p=0.033) compared to immediate surgery, whereas PCT was not (OR 0.59, 95%CI 0.25-1.25, p=0.199). During surgery, firm pancreas texture was most often observed after PCRT (53% immediate surgery, 62% PCT, 77% PCRT, p< 0.001).

Conclusion: In this nationwide analysis in patients with PDAC after pancreatoduodenectomy PCRT was associated with a reduced risk of POPF.

15. TREATMENT OF PANCREATIC CANCER AT HIGH-VOLUME CENTERS IS ASSOCIATED WITH IMPROVED OUTCOMES AND IS UNDERUTILIZED BY SOCIOECONOMICALLY AND GEOGRAPHICALLY DISADVANTAGED PATIENTS

TL Sutton, A Johnson, F Rocha, P Worth, BC Sheppard
Presenter: Thomas L. Sutton MD | Oregon Health & Science University, United States

Background: Patients with pancreatic adenocarcinoma (PDAC) treated at high-volume centers (HV) experience improved overall survival (OS) than at low-volume centers (LV) in population-level datasets. However, it is often difficult to account for selective referral of patients with better prognosis to HV centers in such datasets. Additionally, predictive factors for HV center treatment are poorly characterized.

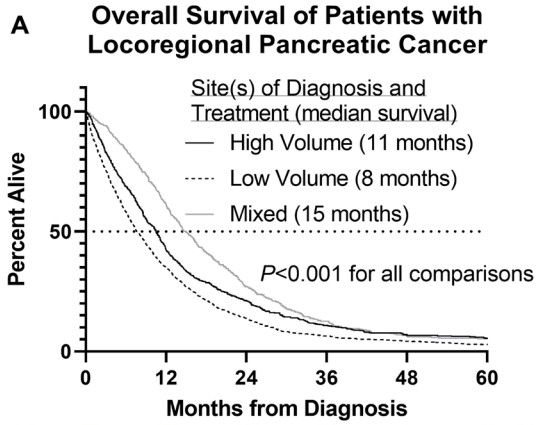
Methods: We queried a statewide cancer registry for patients with PDAC diagnosed from 1997-2018. All facilities reporting data for each patient record were classified as HV (≥50 pancreatectomies for PDAC/year) or LV (< 50/year). Patients were grouped by characteristics of reporting facilities: HV-only, LV-only, and mixed (containing all LV to HV referrals). Kaplan-Meier analysis was used to evaluate OS from diagnosis, and logistic regression was utilized to evaluate odds of HV treatment.

Results: We identified 8026 patients with complete clinical staging (n=3419 locoregional, n=4607 metastatic). Diagnosis and treatment were entirely at LV centers in 75% (n=5606), at HV in 16% (n=1563), and at mixed settings in 9% (n=857). Patients diagnosed and treated in mixed settings were younger (mean 66 years) than those in LV (mean 72 years) and HV settings (mean 68 years, both P< 0.001). Mixed settings had improved median OS for locoregional and metastatic disease (15 and 6 months, respectively) compared to patients in only HV (11 and 4 months, respectively) or LV (8 and 2 months, respectively, P< 0.001 for all comparisons, Figure).

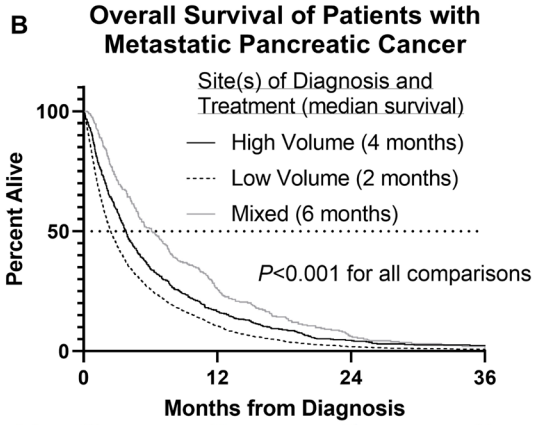
Patients with locoregional disease were more likely to undergo resection in HV (OR 2.80, P< 0.001) and mixed settings (OR 5.01, P< 0.001) compared to LV settings after adjusting for relevant clinicopathologic characteristics. Compared to LV settings, odds of receiving chemotherapy were not different in HV settings for either locoregional (OR 1.07, P=0.43) or distant disease (OR 1.15, P=0.11), but were higher in mixed settings (OR 3.30 and 2.66, respectively, P< 0.001).

On multivariable logistic regression, factors independently associated with lower odds of HV treatment included older age (OR 0.95/year, P< 0.001), farther distance to nearest HV center (OR 0.84/20km, P< 0.001), lower estimated income (OR 1.12, P< 0.001), and distantly metastatic disease (OR 0.37, P< 0.001).

Conclusion: The improved outcome of mixed setting compared to HV-only treatment may reflect improved prognostic or comorbid features of this cohort—prompting referral to HV centers—or previously unknown benefits of mixed setting treatment. Independent of this phenomenon, HV-only treatment is associated with improved OS versus LV-only treatment in all PDAC stages. Additionally, significant disparities in receipt of HV treatment exist, as patients with lower income, longer distance to nearest HV center, and older age are less likely to receive HV treatment. Efforts to promote referral of socioeconomically disadvantaged and geographically remote patients to HV centers may significantly improve outcomes in PDAC in rural states.



High Volume Only	900	331	147	68	39	28
Low Volume Only	1951	600	207	90	58	38
Mixed Setting	568	312	124	53	25	19



High Volume Only	663	96	21	10
Low Volume Only	3655	338	55	22
Mixed Setting	289	74	17	5

16. PRIMARY VS. SALVAGE OPERATIVE PANCREATIC DEBRIDEMENT: DISCRETE INTERVENTIONS FOR UNIQUE POPULATIONS

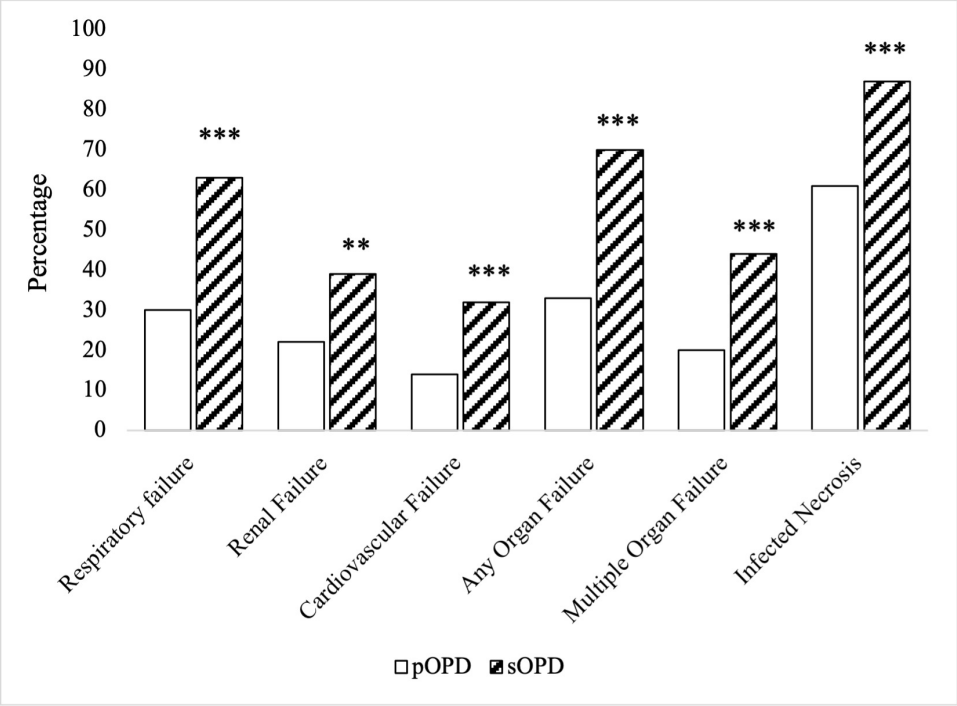
S McGuire, A Roper, T Maatman, E Ceppa, M House, A Nakeeb, T Nguyen, C Schmidt, N Zyromski
Presenter: Sean McGuire MD | Indiana University School of Medicine, United States

Background: A minimally invasive step-up approach is the initial treatment strategy for necrotizing pancreatitis (NP); however, operative pancreatic debridement (OPD) remains an important therapy. OPD is applied as a primary approach in biliary pancreatitis with concomitant cholecystectomy or when there is concern for ischemic/perforated viscus. Conversely, OPD is applied after failure to progress with percutaneous or endoscopic interventions. We hypothesized that primary OPD and salvage OPD represent discrete interventions for unique patient populations and may have different outcomes.

Methods: Single institution retrospective review of 468 NP patients treated between 2011-2019. Operative pancreatic debridement included video-assisted retroperitoneal debridement (VARD), open and minimally invasive transgastric debridement (TGD), and open debridement with external drainage. Primary OPD was defined as OPD performed prior to any other necrosis intervention; salvage OPD was defined as OPD performed following either percutaneous or endoscopic necrosis intervention. NP patients treated with primary OPD were compared with patients treated with salvage OPD.

Results: 273/468 (58%) of patients underwent OPD. 194 (71%) were primary OPD and 79 (29%) were salvage OPD. No difference was seen in etiology of NP or comorbidity profile between groups. Organ failure was present in 33% (64/194) of the primary OPD group and 77% (55/79) of the salvage OPD group, $p < 0.001$ (Figure). Infected necrosis was present in 60% (117/194) of the primary OPD group and 87% (69/79) of the salvage OPD group, $p< 0.001$. The percentage of pancreatic parenchymal necrosis was similar between groups. In the salvage group, the initial intervention included placement of a percutaneous drain in 87% (69/79) of patients and endoscopic debridement in 13% (10/79) of patients. The indication for primary OPD was most commonly biliary pancreatitis with need for concomitant cholecystectomy (53%, 103/194). In the primary OPD group, the initial intervention for pancreatic necrosis was performed later than in the salvage OPD group (76 ± 6 days versus 45 ± 6 days after NP diagnosis, $p = 0.006$). The primary group underwent fewer total procedures during NP disease course (3.5 ± 0.3 vs 6.7 ± 0.4, $p< 0.001$). Overall disease duration (190 ± 12 days (primary) versus 228 ± 21 days (salvage), $p=0.1$) and mortality (7% (primary) versus 13% (salvage), $p=0.2$) were similar between groups. Disease duration after first necrosis intervention was shorter in the primary OPD group than the salvage OPD group (121 ± 12 days versus 192 ± 21 days, $p=0.003$).

Conclusion: Primary and salvage operative pancreatic debridement are important therapies for patients with necrotizing pancreatitis. Salvage OPD is employed later in disease course in patients with high rates of organ failure and infected necrosis. Despite this challenging clinical context, salvage OPD achieves necrosis resolution with similar mortality rates to primary OPD.


100
90
80
70
60
50
40
30
20
10
0
Percentage
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Respiratory failure
Renal Failure
Cardiovascular Failure
Any Organ Failure
Multiple Organ Failure
Infected Necrosis
pOPD
sOPD

17. PERSPECTIVE OF POINT-OF-CARE SPECIALISTS ON THE INITIAL MANAGEMENT OF ACUTE PANCREATITIS: AN INTERNATIONAL MULTIDISCIPLINARY SURVEY FOCUSED ON DAILY PRACTICE

N Lluis, HJ Asbun, MG Besselink, G Capurso, PK Garg, A Gelrud, W Khannoussi, HS Lee, A Leppäniemi, M Löhr, SJ Mahapatra, C Mancilla, HC van Santvoort, SS Vege, P Zapater, F Lluís, E de-Madaria, JM Ramia
Presenter: Nuria Lluis MD | Miami Cancer Institute, United States

Background: In the past decade, various international scientific associations have endorsed clinical practice guidelines for the management of patients with acute pancreatitis. However, the implementation of expert recommendations in daily health care can be suboptimal. Point-of-care decisions have been reported to differ from clinical guideline recommendations. Identifying factors associated with these discrepancies could guide improvement strategies.

Methods: The questionnaire consisted of two parts. The first aimed at characterizing the professional profile of the participants, the second was designed to characterize the management strategies currently used by professionals in the management of patients with acute pancreatitis during the first 72 hours after admission. It focused on fluid resuscitation, prophylactic antibiotics, early oral, enteral, or parenteral feeding, and the timing of cholecystectomy. Potentially interested scientific societies were contacted. In parallel, the summary and the link were distributed via social media. This was a completely anonymous survey. Study data were collected and managed using REDCap tools. Multivariable logistic regression was used to identify the characteristics of participants associated with compliance with the recommendations provided by the clinical guidelines.

Results: A total of 1,054 participants from 94 countries completed the questionnaire; median age (IQR) was 39 (32-47) years; 30.7% were women. Thirty-seven % of the participants opted for non-moderate flow of i.v. fluid, 31% for fluid type other than Ringer's lactate; 73.4% were in favor of nil per os to patients who could eat, 75.5% for other than enteral feeding to patients with oral intolerance; 15.5% used prophylactic antibiotic in patients with severe acute pancreatitis, 34.1% in necrotizing acute pancreatitis, and 27.4% in patients with systemic inflammatory response syndrome; 27.8% delayed cholecystectomy after biliary acute pancreatitis (Fig 1-A). The degree of compliance was good / excellent (meaning 5 to 8 matching responses) in 62.2% of participants, and poor / moderate (0 to 4 matching responses) in the remaining 37.8% (Fig 1-B). In multivariable analysis, participants from Asia / Oceania (P=.01), surgeons (P=.046), other specialists (P<.001), and those participants unaware of the number of patients with AP admitted annually (P=.02) were more likely to poorly / moderately comply with the recommendations of the clinical practice guidelines. Participants with publications in PubMed on acute pancreatitis showed better compliance (0R, 1.62; 95% CI, 1.15 – 2.32; P=.007) with recommendations of the clinical guidelines (Fig 1-B).

Conclusion: Despite a significant effort in the development of evidence-based guidelines through complex scientific processes, the results of this study appear to emphasize that attention also needs to be placed on the implementation and adoption of these well-developed guidelines. Feeding and nutrition appear to require the greatest need for wider adoption. Awareness campaigns, medical society educational programs, and structural changes should be invested to increase the compliance of these guidelines in the initial management of patients with acute pancreatitis.

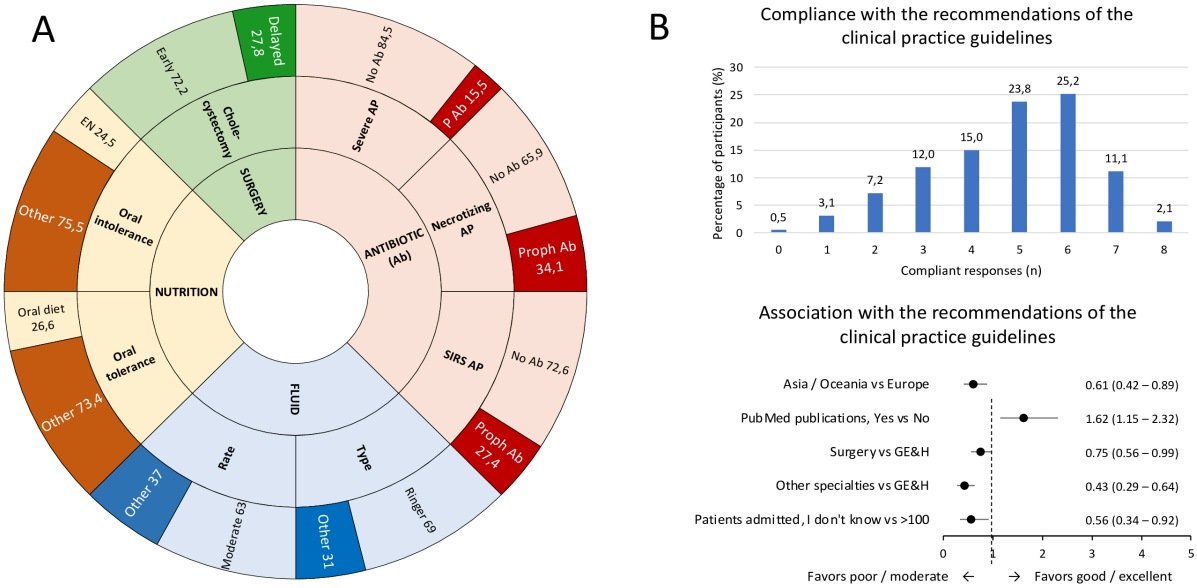


Figure 1. A) Sunburst chart: Case management. B) Bar graph and forest plot: Compliance and association with the recommendations of the clinical practice guidelines

18. OPERATIVE PANCREAS DEBRIDEMENT IN 2022: WHO AND WHEN

S McGuire, T Maatman, E Ceppa, M House, A Nakeeb, T Nguyen, C Schmidt, N Zyromski
Presenter: Sean McGuire MD | Indiana University School of Medicine, United States

Background: Treatment of necrotizing pancreatitis (NP) has shifted in favor of a minimally invasive step-up approach rather than primary operative pancreatic debridement (OPD). We evaluated the contemporary role of OPD in NP treatment.

Methods: Single institution retrospective review of 468 NP patients treated between 2011-2019. Operative pancreatic debridement included video-assisted retroperitoneal debridement (VARD), open and minimally invasive transgastric debridement, and open debridement with external drainage. NP patients whose treatment included OPD were compared with patients treated definitively without OPD.

Results: Since 2011, 256/468 (55%) of patients were treated with OPD. Gender and comorbidity profile were similar between groups. Necrotizing pancreatitis etiology was more likely biliary (52% vs 32%) and less likely secondary to alcohol (19% vs 35%) in patients treated with OPD ($p< 0.001$). Computed tomography severity index (CTSI) of pancreatic necrosis was similar between groups; however, infected necrosis was more common in patients who underwent OPD (68% versus 33%, $p < 0.001$). Patients treated with OPD were more likely to have disconnected pancreatic duct syndrome (DPDS) (53% vs 29%, $p < 0.001$). Among patients who underwent OPD during their treatment, 73% underwent OPD as their initial intervention at 73 ± 6 days after disease onset while 27% underwent OPD as salvage therapy at 95 ± 16 days after disease onset, $p=0.1$.

Conclusion: Operative pancreatic debridement remains an important treatment modality in patients with pancreatic necrosis. OPD is employed as either primary or salvage therapy most frequently in patients with NP of biliary etiology, infected necrosis, and patients with disconnected pancreatic duct.

19. INCIDENCE AND PREDICTORS OF EARLY AND LATE READMISSION AFTER ACUTE PANCREATITIS

B Richter, C Tarabanis, L Khanna, G Haber, P Sinha, C Wolfgang, T Gonda
Presenter: Benjamin Richter MD | Northwestern Medicine, United States

Background: Acute pancreatitis (AP) incidence is increasing globally. Despite advances in management of and diagnostic testing for AP, recurrence and readmission remain common. Identifying modifiable risk factors for readmission and useful interventions during hospitalization or in the early post-discharge period may have a significant impact on long term outcomes. Our goal was to identify predictors of readmission in patients admitted with AP at a tertiary medical center.

Methods: This is a retrospective cohort study of patients at a large urban academic medical center. Consecutive patients over the age of 18 with a discharge ICD-10-CM diagnosis of AP between 2/5/2013 and 1/28/2021 were included. Data was extracted from the Electronic Health Record via the Enterprise Data Warehouse. Separate multivariate regressions were performed to evaluate predictors of pancreatitis-related readmissions for all patients, for only non-biliary pancreatitis patients, and for early (0 to 30 days) vs. late (31 to 180 days) readmissions.

Results: Our study included 1079 patients. 129 (10.6%) patients were readmitted for all causes and 114 (8.5%) for pancreatitis-related complications (recurrence, infected pancreatic necrosis or fluid collections, and procedural complications). 43.5% of readmissions occurred 30 days post-discharge; 56.5% occurred from 31 to 180 days post-discharge. All the following regressions were performed using pancreatitis-related readmissions as the dependent variable: Biliary pancreatitis (OR 2.11, $p < 0.05$), male sex (OR 1.69, $p < 0.05$), and history of prior AP (OR 3.58, $p < 0.01$) were predictors of 180-day readmission. Gallbladder resection during hospital stay was associated with a significantly decreased risk of readmission (OR 0.156, $p < 0.01$). When gallbladder resection was removed from the regression, biliary pancreatitis was no longer associated with readmission (OR 1.19, P 0.58). When non-biliary pancreatitis was evaluated independently, history of alcohol abuse (OR 1.94, $p < 0.05$) and prior AP (OR 4.01, $p < 0.01$) were predictors of readmission. Predictors of early readmission included gallbladder resection (OR 0.69, $P < .05$), prior AP (OR 2.79, $p < .05$) and early outpatient follow up (OR 2.34, $P < .05$). Predictors of late readmission were male sex (OR 2.5, $p < .05$) and prior acute pancreatitis (OR 3.85, $P < .01$).

Conclusion: About one-tenth of patients discharged with AP will be readmitted, with the majority of the readmissions (56%) occurring after 30 days. We identified male sex and biliary pancreatitis as independent risk factors for late readmission, though gallbladder resection during hospitalization attenuates the risk of the latter. Recurrent AP was the only risk factor for both early and late readmission and was the strongest predictor of both. Unexpectedly, close outpatient follow up did not prevent readmission.

20. ROUTINE INTENSIVE CARE UNIT OBSERVATION AFTER PANCREATECTOMY: TREATING THE PATIENT OR THE SURGEON?

TL Sutton, KC Potter, J O'Grady, M Aziz, SC Mayo, R Pommier, EW Gilbert, F Rocha, BC Sheppard
Presenter: Thomas L. Sutton MD | Oregon Health & Science University, United States

Background: Routine intensive care unit admission (ICUA) is commonplace following pancreatectomy, particularly pancreaticoduodenectomy, and aims to allow early postoperative complications to occur in a high acuity setting. The value of this practice in avoiding failure-to-rescue or impacting perioperative mortality is poorly studied, however.

Methods: We queried our institutional National Surgical Quality Improvement Project (NSQIP) database for patients undergoing pancreatectomy from 2013-2020. Initial postoperative dispositions, ICU courses, subsequent ICU transfers, and hospital cost data in United States Dollars (USD) were reviewed. Patients were analyzed in three groups by postoperative disposition and level of care as defined by the Society of Critical Care Medicine: those with ICUA requiring ICU-level care (e.g., invasive ventilation, vasopressors, inotropes, intravenous antiarrhythmics), those with ICUA requiring ward-level care, and those admitted to the ward. Data were analyzed with multivariable logistic regression.

Results: Six-hundred-thirty-seven patients were identified; 404 (63%) underwent pancreaticoduodenectomy (Table 1). At postoperative admission, two-thirds (n=318, 63%) of patients were only receiving ward-level interventions. Of 318 patients with ICUA requiring ward-level care, 235 (74%) had no identified disturbances or complications, 66 (21%) had minor disturbances requiring ward-level care, and 17 (5%) required ICU-level interventions during initial ICUA, most commonly antiarrhythmic infusion (n=12). 30-day and 90-day mortality in patients requiring ICU-level interventions was 5% (n=10) and 8% (n=16) versus 0.3% (n=1) and 1.2% (n=4) in those without, respectively. Hospital length of stay was significantly longer with initial ICU-level interventions (median 11 versus 9 days, P< 0.001), as were total ICU costs (mean 8683 versus 14611 USD, P< 0.001).

On multivariable analysis, factors associated with higher odds of requiring ICU-level care at case closure were older age (OR 1.04/year, P< 0.001), additional NSQIP-defined comorbidities (OR 1.34/comorbidity, P=0.003), pancreaticoduodenectomy (OR 1.93, P=0.04), higher intraoperative blood loss (OR 3.88/liter, P< 0.001), longer surgical duration (OR 1.44/hour, P< 0.001), and higher intraoperative crystalloid volume (OR 1.11/liter, P=0.008. There were no identified factors associated with new ICU-level interventions in patients admitted to ICU for observation.

Conclusion: At high-volume pancreas centers, patients undergoing pancreatectomy who require only ward-level care at ICUA are at very low risk of requiring ICU-level care during observation, or of 30- and 90-day mortality. In patients with ward-level care needs postoperatively, ward admission with a low threshold for care escalation presents a significant opportunity for costs-savings and un-burdening ICUs.

Table 1: Clinicopathologic Characteristics of Patients Undergoing Pancreatectomy by Postoperative Disposition and Level of Care

Characteristic	ICU with ICU Interventions; N=190; No. (%)	ICU without ICU Interventions; N=318; No. (%)	Admitted to Ward; N=129; No. (%)	*P*
Age, Years; median [IQR]	67 [58-74]	66 [57-72]	58 [44-69]	<0.001
NSQIP-Defined Comorbidities				0.004
0	39 (20.5)	89 (28.0)	48 (37.2)	
1-2	112 (58.9)	187 (58.8)	68 (52.7)	
3+	39 (20.5)	42 (13.2)	13 (10.1)	
Operation				<0.001
DP/RAMPS	43 (22.6)	67 (21.1)	123 (95.3)	
Whipple/Total Pancreatectomy	147 (77.4)	251 (78.9)	6 (4.7)	
Vascular Reconstruction	76 (40.0)	30 (9.4)	0 (0)	<0.001
Surgical Duration, Hours; median [IQR]	9.4 [7.6-11.4]	7.3 [5.8-8.5]	3.9 [3.2-4.7]	<0.001
Intraoperative Blood Loss, mL; median [IQR]	1200 [700-2000]	500 [300-750]	150 [55-400]	<0.001
Intraoperative Crystalloid, L; median [IQR]	9.1 [6.0-12.5]	5.5 [4.2-7.4]	3.0 [2.3-3.9]	<0.001
Initial ICU LOS, days; median [IQR]	2 [2-3]	1 [1-2]	N/A	<0.001*
Hospital LOS, days; median [IQR]	11 [8-17]	10 [8-15]	6 [5-7]	<0.001
90-day Mortality, %	16 (8.4)	3 (0.9)	1 (0.8)	<0.001
Total ICU Costs, Thousand USD; median [IQR]	10.8 [6.4-14.8]	6.1 [4.0-8.8]	4.8 [4.7-5.6]	<0.001*
Total Ward Costs, Thousand USD; median [IQR]	9.9 [6.6-18.1]	9.4 [6.6-15.0]	7.5 [6.2-8.9]	<0.001
ICU Cost Share of Postoperative Costs, %; median [IQR]	48.3 [35.9-61.8]	38.0 [27.1-50.0]	0 [0-0]	<0.001*

*Comparison between groups with initial ICU admission

Abbreviations: IQR=Interquartile Range; ICU=Intensive Care Unit; NSQIP=National Surgical Quality Improvement Project; DP=Distal Pancreatectomy; RAMPS=Radical Antegrade Modular Pancreatosplenectomy; LOS=Length of Stay; USD=United States Dollars

21. CHRONIC PANCREATITIS PATIENTS: ENDOSCOPIC PROCEDURES AND QUALITY OF LIFE

M Parhiala, C Nøjgaard, A Bartholdy, A Waage, P Ignatavičius, E Trond, G Dimcevski, I Nordaas, E Kalaitzakis, AM Drewes, A Hadi, SS Olesen, JL Poulsen, J Laukkarinen

Presenter: Mikael Parhiala MD | Tampere University Hospital, Finland

Background: Chronic Pancreatitis (CP) may cause chronic or intermitting abdominal pain, as well as endocrine and exocrine pancreatic insufficiency. Morphological changes in the pancreatic tissue, leading to and complications such as biliary strictures and pseudocysts may need endoscopic interventions.

Our aim was to investigate the frequency of endoscopic procedures in the CP patients, and to study pain and quality of life in these patients after the procedures.

Methods: SBPC database is the largest prospectively multicentre CP database, containing over 2000 CP patients meeting M-ANNHEIM diagnostic criteria (1). In this study, 1176 CP patients from 4 countries and 8 centres were included. We analysed patients who underwent endoscopic procedures (endoscopic group; E-CP) and gathered all related information, such as types of endoscopic procedures, pancreatic function, pain, time after diagnosis and EORTC C-30 Quality of life (QOL) questionnaire. Patients who did not have any invasive interventions were used as a control group (C-CP;n=916)

Results: 260 patients (22%) of the CP patients underwent endoscopic procedures. Procedures were performed median one year (range 0-39 years) after the CP diagnosis. 68% of the patients were males. Age median was 59 years (range 20-90 years). Most common etiological factors were alcohol in 65% and smoking in 71%. Biliary duct stenting was performed in 37% of the patients. Pancreatic stenting was performed in 56% of the patients and out of these 72% had multiple pancreatic stents.

Exocrine pancreatic insufficiency was slightly more common in the endoscopic group compared to the control group, 62% vs 53% (p=0.020). Endocrine insufficiency was found similar between the groups (45% vs 40%, p=0.144).

Fewer patients were painless in the endoscopy group compared to the control group (42% vs 51%, p=0.020). The number of patients with constant pain was similar (16.5 v 14.7% p=0.516).

39% of the patients with one pancreatic stent and 45% the patients with multiple pancreatic stents were painless (p=0.523). 23% of the patients underwent pancreatic surgery later. EORTC QOL was similar in functioning and in symptom scores in the endoscopic and control population.

Conclusion: One out of five of the CP patients underwent endoscopic procedures in the SBCP database. 56% underwent pancreatic and 37% biliary stenting. Exocrine pancreatic insufficiency was slightly more common in the endoscopic group compared to the control group. Constant pain and Quality of life were similar between the groups.

1. SS Olesen, J L Poulsen, A M Drewes, J B Frøkjær, J Laukkarinen, M Parhiala et al. The Scandinavian baltic pancreatic club (SBPC) database: design, rationale and characterisation of the study cohort. Scand J Gastroenterol. 2017 Aug;52(8):909-915. doi: 10.1080/00365521.2017.1322138. Epub 2017 May 4.

22. CHANGES IN ACTIVITY OF HEAT SHOCK PROTEIN-70 FAMILY GENES IS ASSOCIATED WITH EARLY ACUTE PANCREATITIS SEVERITY

J Gaizevska, A Sestokaitė, R Sabaliauskaite, K Snipaitiene, S Jarmalaite, K Strupas, R Damaseviciute
Presenter: Aiste Kielaite-Gulla MD, PhD, MBA | Vilnius University Hospital Santaros Clinics (VULSK), Lithuania

Background: Acute pancreatitis is a severe inflammatory disease, which is able to affect multiple organ systems and impair patients' health, often requiring hospital admission. There has been advancements made in understanding the pathophysiology of the disease, however a method, which could accurately predict the severity and clinical outcome is still lacking. We hypothesized that Heat Shock Protein 70 (HSP70) single nucleotide polymorphisms (SNPs) may play a role in early detection of acute pancreatitis severity.

Methods: A total of 109 patients, of which 57 were diagnosed with AP and 52 did not have the disease, were tested prospectively. The patients were admitted to Vilnius University Hospital Santaros Klinikos from 2018 to 2021. Peripheral blood samples from pancreatitis patients were collected upon admission. The severity of AP was determined according to the revised Atlanta classification. Genomic DNA was extracted from the blood samples of patients and controls groups. Two SNPs of the HSP70-gene family were selected. The polymorphism frequencies were determined by performing quantitative polymerase chain reaction (qPCR) and using TaqMan allelic discrimination assays. Additionally, RNA was extracted parallel to genomic DNA from AP patients (N&#3f57) and healthy controls (N&#3f52). Gene expression of two HSP70 family members HSPA1A and HSPA1L was measured using TaqMan gene expression assays via reverse transcription quantitative polymerase chain reaction (RT-qPCR).

Results: Major allele frequency for HSPA1A frequency was 0.672 (A>C) for patients and 0.7 (A>C) for controls, while for HSP70-HOM and HSPA1A, the major allele frequencies were 0.638 (A>G) and 0.672 (G>C) for patients and 0.85 (A>G) and 0.65 (G>C) for controls, respectively. Patients with alcohol-induced AP and those with other causes of disease and mild or severe course had the allele frequencies of 0.638. Furthermore, after gene expression of HSPA1L and SNP relationship analysis we identified that AP patients with heterozygous genotype had higher expression levels as compared to non-AP patients (p=0.014).

Conclusion: Our data suggest that polymorphism of the HSP70 promoter region may be a risk factor for developing severe acute pancreatitis.

Further study to determine the serum and/or urine levels of HSP70 protein expression is needed to confirm the protective mechanism of HSP70.

23. WEIGHT TRACKING AS A NOVEL PROGNOSTIC MARKER AFTER PANCREATECTOMY

JJ Hue, LM Ocuin, RK Kyasaram, J Shanahan, G Rao, LD Rothermel, JB Ammori, JM Hardacre, JM Winter, SM Markt
Presenter: Jonathan J. Hue MD | University Hospitals Cleveland Medical Center, United States

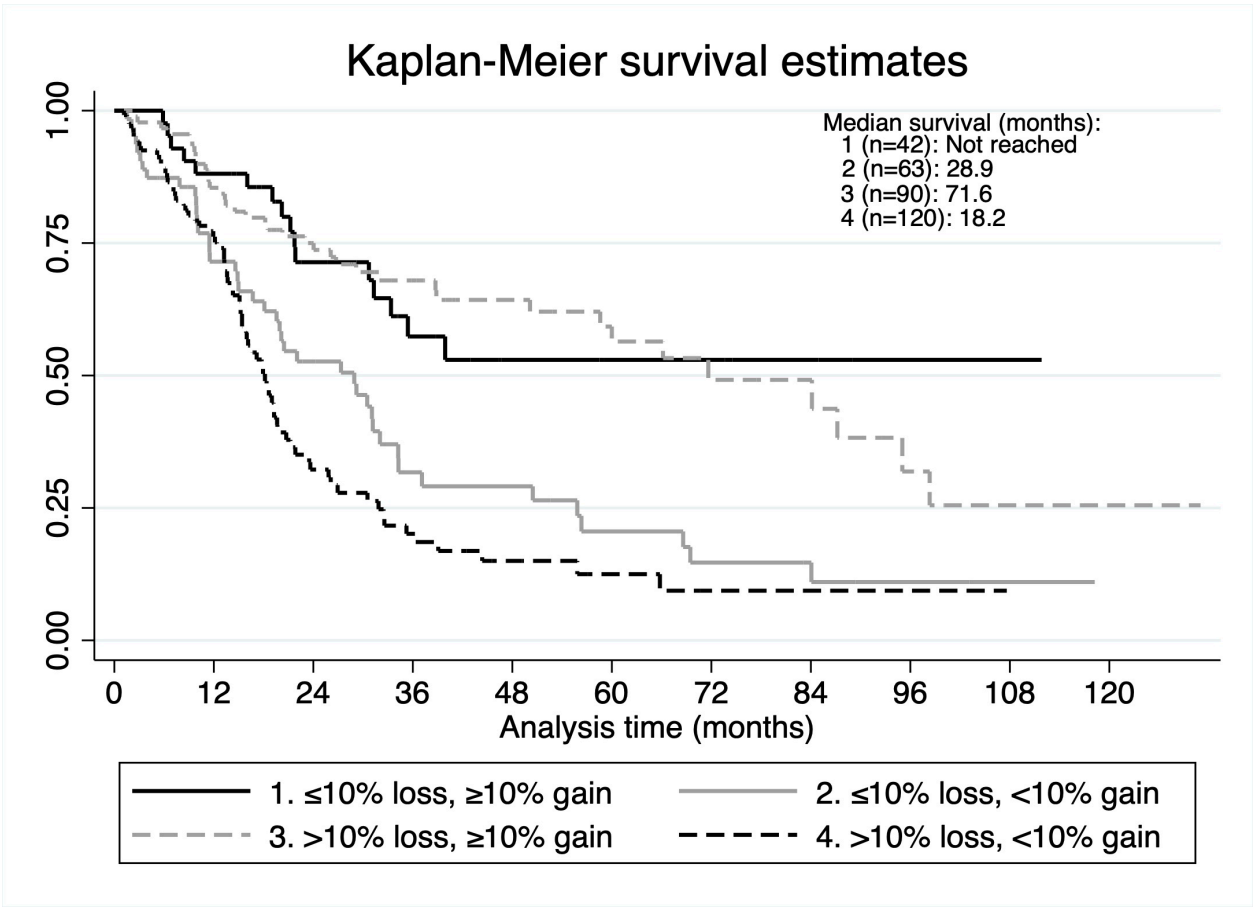
Background: Objective measures of post-pancreatectomy weight change for pancreatic ductal adenocarcinoma (PDAC) have not been extensively studied for long-term outcomes. We aimed to use weight measurements in our institutional medical record to analyze trends in post-pancreatectomy weight and determine the association with disease status and survival.

Methods: Pancreatectomies for PDAC (n=315) and benign indications (n=111) were identified. Preoperative baseline, minimum postoperative (Min #1), and subsequent postoperative maximum (Max) weights were abstracted. Multivariable logistic regression was used to assess if the time from surgery to Min #1 was predictive of PDAC recurrence, when controlling for age, sex, operation, margin positivity, lymph node positivity, and receipt of chemotherapy. Multivariable Cox proportional hazards regressions were conducted to analyze the association between weight change and survival.

Results: Preoperatively, patients with PDAC were 12 lbs lighter as compared to the benign group (166 vs. 178 lbs, p=0.01). Postoperatively, both groups lost greater than 20 lbs (22.7 lbs PDAC vs. 20.1 lbs benign, p=0.33) from their Baseline. Over 28% of PDAC patients lost >20%, which was a greater proportion as compared to the benign group (15.3%, p=0.02). PDAC patients gained 10 lbs after Min #1, compared to 15 lbs in the benign cohort (p< 0.001). Few patients returned to their Baseline weight (29.8% PDAC vs. 40.5% benign, p=0.04).

Patients with early PDAC recurrence (20% loss: HR 1.11, 95% CI 0.75-1.65). However, the ability to regain weight (Min #1 to Max) was associated with a significant survival advantage (5-10% vs. 10% vs. 10%).

Conclusion: Pancreatectomy is often followed by substantial postoperative weight loss without an associated survival impact based on these data. However, PDAC patients who are unable to eventually regain weight fare significantly worse. Weight loss persisting for ≥12 months is a strong predictor of PDAC recurrence, as is additional weight loss after weight recovery. Greater emphasis on accurate body weight tracking in the postoperative period may provide easily captured and useful information regarding disease status after pancreatectomy for PDAC.


Kaplan-Meier survival estimates
Median survival (months):
1 (n=42): Not reached
2 (n=63): 28.9
3 (n=90): 71.6
4 (n=120): 18.2
1.00
0.75
0.50
0.25
0.00
0
12
24
36
48
60
72
84
96
108
120
Analysis time (months)
1. ≤10% loss, ≥10% gain
2. ≤10% loss, <10% gain
3. >10% loss, ≥10% gain
4. >10% loss, <10% gain

24. MACHINE LEARNING ALGORITHM IDENTIFIES PATIENTS AT RISK FOR PANCREATIC CANCER IN A 3-YEAR TIMEFRAME

W Zhu, MB Pochapin, Y Aphinyanaphongs, F Kastrinos, N Razavian, T Gonda
Presenter: Tamas Gonda MD | NYU Langone Health, United States

Background: Early detection of pancreatic cancer (PC) remains challenging largely due to the low population incidence and few known risk factors. However, screening in at-risk populations and detection of early cancer has the potential to significantly alter survival. We used an Electronic Health Records (EHR) based large-scale machine learning algorithm to identify disease codes that are associated with the development of PC at least 3 years before diagnosis and developed a predictive model to identify patients at risk for PC 27-33 months later.

Methods: EHR data was analyzed between 2000 and 2021 and individuals with at least 3 years of continuous presence in the database were included. A 1:4 case-control matching based on age, sex, length of medical history to all diagnosed with PC was performed. In one model, all patients meeting database presence were included, whereas in a second model only those without known prior pancreatic disease were evaluated. We introduced PheWas study to select the significant variables. Among demographic, 19,304 disease variables, and 10 lab values 27-33 months prior to PC diagnosis, we used the p-value of associations to select significant variables (cut-off p-value < 0.01), and trained a logistic regression model. Final predictive performance was tested on a held-out validation cohort.

Results: 537,410 patients were analyzed. 1923 patients with PC were matched to 7728 cancer-free patients. We identified 77 variables (73 diagnosis codes and 4 lab values) with significant association of development of PC, including pancreatic cysts, diabetes, family or personal history of breast cancer, and chronic pancreatitis (ranked results and statistical analysis are shown for top 10 variables in Table 1). These variables were selected for the regression model, which we trained in over 598,725 patients. In our second model, in patients without prior pancreatic diseases, 594,802 patients were included. The area under the receiver operating characteristic curve (AUROC) were 0.810 [0.792, 0.828] and 0.778 [0.759, 0.789] in the two models respectively.

Conclusion: In a robust EHR-based analysis, we identified a list of diagnostic variables associated with pancreatic cancer development in a 3-year time frame and developed a model to identify patients at risk. Although the inclusion of additional variables such as laboratory results and radiomics will likely improve the accuracy of the model, the current algorithm will allow us to develop an EHR-based identification of patients at risk for PC.

Codes	Description	P-value	Unadjusted Odds Ratio [95% Confidence Interval]	P-value (Model 1)	Adjusted odds Ratio (Model 1) [95% Confidence Interval]	P-value (Model 2)	Adjusted odds Ratio (Model 2) [95% Confidence Interval]
K86.89	Other specified diseases of pancreas	1.50E-06 **	5.49 [2.52, 11.96]	0.00E+00 ***	6.429 [4.734, 8.124]	NA	NA
D49.0	Neoplasm of unspecified behavior of digestive system	1.05E-08 **	8.05 [3.44, 18.84]	6.99E-08 ***	4.106 [2.243, 5.970]	6.35E-07***	4.581 [2.146, 7.016]
K85.90	Acute pancreatitis without necrosis or infection, unspecified	4.98E-03	4.01 [1.41, 11.45]	8.44E-14 ***	4.019 [1.568, 6.470]	NA	NA
C64.9	Malignant neoplasm of unspecified kidney, except renal pelvis	7.89E-03	2.87 [1.27, 6.46]	2.00E-15 ***	3.947 [2.634, 5.259]	1.42E-06 ***	4.377 [1.846, 6.908]
M19.049	Primary osteoarthritis, unspecified hand	9.46E-03	3.21 [1.26, 8.14]	1.39E-10 ***	2.868 [1.984, 3.752]	4.00E-05 **	2.681 [1.436, 3.926]
Z80.9	Family history of malignant neoplasm, unspecified	2.51E-04	3.35 [1.69, 6.66]	2.22E-16 ***	2.768 [2.136, 3.399]	1.11E-06 **	2.841 [1.587, 4.094]
Z15.09	Genetic susceptibility to other malignant neoplasm	1.17E-05 **	5.23 [2.29, 11.94]	0.00E+00 ***	2.159 [0.597, 3.720]	1.30E-13 ***	2.270 [1.103, 3.436]
K86.2	Cyst of pancreas	6.21E-29 **	14.45 [7.79, 26.80]	2.44E-15 ***	1.924 [1.127, 2.720]	NA	NA
Glucose	Glucose > 126.0	3.01E-06 **	2.06 [1.52 , 2.81]	1.45 E-04 *	1.910 [1.223, 2.596]	6.74E-04 *	1.153 [1.059, 1.247]
C50.919	Malignant neoplasm of unspecified site of unspecified female breast	2.89E-03	1.72 [1.20, 2.46]	0.00E+00 ***	1.880 [1.660, 2.100]	0.00E+00 ***	2.129 [1.844, 2.414]

25. POTENTIAL ROLE FOR OBSERVATION IN SMALL SOLID PSEUDOPAPILLARY ENDOCRINE NEOPLASIA (SPEN)

O Standring, S Benitez Sanchez, S Patel, L Demyan, N Lad, S Ruff, S Anantha, E Newman, G Deutsch, W Nealon, M Weiss, D DePeralta

Presenter: Oliver Standring MD | Northwell Health Cancer Institute, United States

Background: Solid Pseudopapillary Epithelial Neoplasms (SPEN) are rare tumors of the pancreas which predominantly affect young women. Surgical resection is the mainstay of treatment and offers definitive management, but is associated with significant morbidity and potential mortality. With increased utilization of high-resolution abdominal imaging, small SPEN may be increasingly identified incidentally. We aim to test the hypothesis that there may be a subset of small SPEN that could be safely observed.

Methods: A retrospective review of the Pancreas National Cancer Database from 2004-2018 was performed using histology code 8452 to identify invasive SPEN. Type of surgical resection was noted. Accuracy of clinical staging was performed exclusively in patients with full clinical and pathologic staging profiles.

Results: A total of 994 SPENs were identified, with a 7-fold increase from 19 (2004) to 144 (2018), making up 0.1-0.4% of pancreatic tumors within the NCDB. Mean age was 36.8 ± 0.5 years, 84.9% (n=844) were female, and most had a Charlson-Deyo Comorbidity Coefficient (CDCC) of 0-1 (96.6%, n = 960). Patients were most likely staged as clinically cT2 (69.5%, n = 457) followed by cT3 (17.6%, n = 116), cT1 (11.2%, n = 74), and cT4 (1.7%, n = 11). Overall lymph node and distant metastasis rates on clinical assessment were 3.0% and 4.0% respectively. Surgical resection was performed in 96.6% of patients (n=960), most commonly partial pancreatectomy (i.e. distal, 44.3%, n=440) followed by pancreatoduodenectomy with or without gastrectomy (31.3%, n=311), and total pancreatectomy (8.1%, n=81).

Staging accuracy was evaluated by comparing clinical staging to pathologic assessment post-resection. In patients clinically staged as node (N0) and distant metastasis (M0) negative, occult lymph node involvement was found in 0% (0/28) of stage cT1 and 0.5% (1/185) of cT2 patients (Table 1). The risk of incorrect nodal staging significantly increased to 8.9% (5/61) for cT3 patients compared to cT2 patients ($p < 0.001$). This risk further increased to 50% (1/2) in cT4 patients. No patients harbored occult metastatic disease at the time of resection. Survival was similarly excellent for localized cT1, cT2, and cT3 disease, but was notably worse for those with lymph node or distant metastasis. There was one case of a healthy 22-year-old woman who died within 90 days of an extended pancreatectomy for T3N0M0 disease.

Conclusion: Due to the rarity of SPEN, the literature lacks granularity regarding stage specific treatment, particularly for patients with clinical T1 tumors. In this study, the specificity of excluding nodal involvement clinically is 99.5% in tumors ≤ 4cm (cT1-2) and 100% in tumors ≤ 2cm (cT1). There may be a role for close observation in patients with cT1N0 lesions in order to mitigate morbidity from major pancreatic resection. Further prospective investigation is warranted, and given the rarity of small SPEN, will require multicenter collaboration.

Risk of Occult Lymph Node Involvement and Distant Metastasis in SPEN

AJCC $cT_xN_0M_0$

cT_1	**pT**	1	71.4% (20)	**N**	0	100% (28)	**M**	0	100% (28)
(n=28)		2	14.3% (4)		**1**	**0% (0)**		1	0% (0)
		3	14.3% (4)						
		4	0% (0)						
cT_2	**pT**	1	1.6% (3)	**N**	0	99.5% (184)	**M**	0	100% (185)
(n=185)		2	78.9% (146)		**1**	**0.5% (1)**		1	0% (0)
		3	18.4% (34)						
		4	1.1% (2)						
cT_3	**pT**	1	0% (0)	**N**	0	91.8% (56)	**M**	0	100% (61)
(n=61)		2	11.5% (7)		**1**	**8.9% (5)**		1	0% (0)
		3	86.9% (53)						
		4	1.6% (1)						
cT_4	**pT**	1	0% (0)	**N**	0	50% (1)	**M**	0	100% (2)
(n=2)		2	0% (0)		**1**	**50% (1)**		1	0% (0)
		3	0% (0)						
		4	100% (2)						

Nodal and distant metastasis negative patients with full clinical *and* pathologic assessment were included in this analysis. Data presented as % (n)

26. NON-INVASIVE GRADING OF NONFUNCTIONAL PANCREATIC NEUROENDOCRINE TUMORS WITH A CT-DERIVED RADIOMICS-SIGNATURE

AA Javed, Z Zhu, BKinny-Köster, JR Habib, S Kawamoto, EK Fishman, CL Wolfgang, J He, L Chu
Presenter: Ammar A. Javed MD | NYU Langone Health, United States

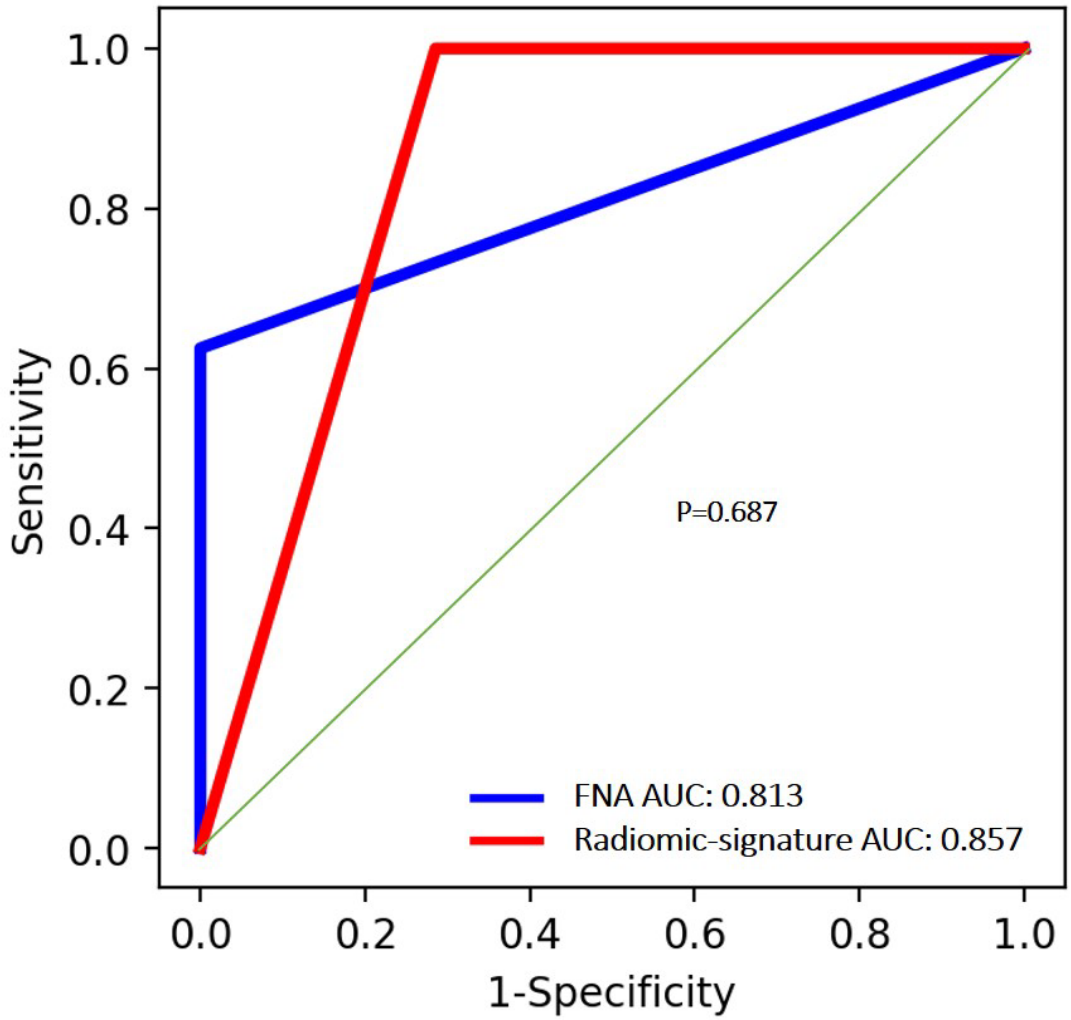
Background: Nonfunctional pancreatic neuroendocrine tumors (NF-PanNETS) exhibit a wide range of biologic behaviors. Tumor grade is indicative of disease biology and the WHO grading system has been established to guide patient management. However its preoperative assessment through endoscopic ultrasound-fine needle aspiration (EUS-FNA) remains challenging. The aim of this study was to develop a radiomics-signature for preoperative prediction of tumor grade in patients with NF-PanNETs.

Methods: A retrospective study was performed on patients undergoing resection for NF-PanNETs at Johns Hopkins between 2010 and 2019. A total of 2436 radiomic features were extracted from the arterial and venous phases of pancreas-protocol CT scans. Radiomic features that were associated with the pathologic grade observed in the surgical specimens were then subjected to Joint Mutual Information Maximization for hierarchical feature selection and the development of the radiomic-signature. Youden-index was used to identify optimal cutoff for determining tumor grade. A random forest prediction model was trained and validated internally. The performance of this tool in predicting tumor grade was then compared to that of EUS-FNA.

Results: A total of 111 patients were included and a fusion radiomic-signature based on 10 selected features was developed. Upon internal validation a strong discrimination was observed with an area under the curve (AUC) of 0.858 (95%CI: 0.856-0.860). The corresponding sensitivity and specificity were 94.4% and 76.0% respectively. Of the study population, 50 patients underwent EUS-FNA. Intriguingly, in the 28 patients where biopsies could not be graded due to insufficient sample the radiomic signature was able to accurately grade tumors in 27 patients (accuracy: 96.4%). For those in whom biopsies were graded (N&#3f22), the radiomic-signature demonstrated a similar performance as compared to EUS-FNA (AUC: 0.857 vs. 0.813, p=0.687), however a higher sensitivity i.e. ability to accurately identify G2/3 lesion was observed (62.5% vs. 100%) (Figure 1).

Conclusion: Non-invasive assessment of tumor grade in patients with PanNETs using the proposed radiomic-signature demonstrated high accuracy. Prospective validation and optimization could overcome the commonly experienced diagnostic uncertainty in the assessment of tumor grade in patients with PanNETs and could facilitate clinical decision-making.

Figure 1. Comparison between the performance of EUS-FNA and Radiomics-signature in predicting tumor grade in patients with NF-PanNETs



27. PREDICTION OF R STATUS IN RESECTIONS FOR PANCREATIC CANCER USING SIMPLIFIED RADIOLOGICAL CRITERIA

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

Background: Negative surgical margins (R0) are a key predictor of local recurrence and overall survival in pancreatic ductal adenocarcinoma (PDAC). Anticipating R status prior to surgery is warranted.

Methods: Patients undergoing pancreatic resection with curative intent for PDAC were identified from two high-volume centers. Using the CT scans from the time of diagnosis, the 2019 NCCN borderline resectability criteria were compared to novel criteria: Presence of any alteration of the superior mesenteric-portal vein (SMPV) and perivascular stranding of the superior mesenteric artery (SMA). Accuracy of predicting R status was evaluated for both criteria. Patient baseline characteristics, surgical, histopathological parameters and long-term overall survival (OS) after resection were evaluated.

Results: A total of 593 patients undergoing pancreatic resections for PDAC between 2010 and 2018 were identified. Three-hundred and twenty-five (54.8%) patients underwent upfront surgery while 268 (45.2%) received neoadjuvant therapy. In upfront resected patients, positive SMA stranding was associated with 56% margin positive resection rates while positive SMA stranding and SMPV alterations together showed a margin positive resection rate of 75%. In contrast to these criteria, the 2019 NCCN borderline criteria failed to predict margin status. In patients undergoing neoadjuvant therapy, only perivascular SMA stranding remained a predictor of margin positive resection, leading to a rate of 33% R+ resections. Perivascular SMA stranding was related to higher clinical T stage (p=0.003) and clinical N stage (p=0.043) as well as perineural invasion (p=0.022). SMA stranding was associated with worse survival in both patients undergoing upfront surgery (36 vs. 22 months, p=0.002) and neoadjuvant therapy (47 vs. 34 months, p=0.050).

Conclusion: The novel criteria were accurate predictors of R status in PDAC patients undergoing upfront resection. After neoadjuvant treatment, likelihood of positive resection margins is approximately halved, and only perivascular SMA stranding remained a predictive factor.

28. PANCREATIC CANCER PATIENT-DERIVED ORGANOIDS ACCURATELY PREDICT RESPONSE TO NEOADJUVANT CHEMOTHERAPY

L Demyan, DA King, A Habowski, A Deschênes, D Plenker, H Patel, L St. Surin, O Standring, S Pasha, R Parakrama, A Rishi, JM Crawford, J Boyd, C Metz, PK Gregersen, C Valente, S Abadali, S Matadial-Ragoo, DK DePeralta, GB Deutsch, J Herman, WH Nealon, M Talamini, D Tuveson, MJ Weiss

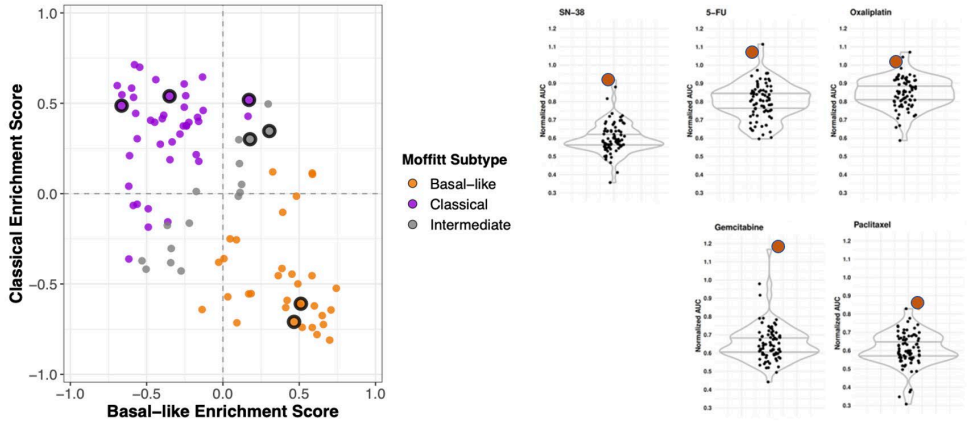
Presenter: Lyudmyla Dmeyan MD, MS | Northwell Health Cancer Institute, United States

Background: Patient-derived organoids (PDOs) have been explored as a biomarker of therapy response and personalized therapeutics for patients with pancreatic cancer. We hypothesized that PDOs may predict response to neoadjuvant (NAT) chemotherapy in patients with pancreatic adenocarcinoma (PDAC).

Methods: During 2017-2021, PDO cultures were established from surgical specimens and fine needle aspiration or biopsies (FNA/FNB) obtained from consented patients with pancreatic cancer. Patient recruitment for the generation of PDOs was accomplished under IRB-approved protocols. Organoids of interest were analyzed through a translational pipeline incorporating DNA sequencing, RNA sequencing, and high-throughput drug sensitivity testing utilizing 123 compounds. A retrospective chart review was performed to obtain clinicopathological information, pathological chemotherapy response, somatic and germline DNA analysis, surgical, and oncological outcomes.

Results: 136 samples from 117 patients with pancreatic cancer were collected. Among these, 80 samples were from surgical resections and 56 samples were from FNBs/FNAs. 51 % of patients were male. 37 (32%) of PDOs were derived from minority populations, consisting of 16% Black, 9% Asian, 7% Hispanic/Latino. 94 PDAC samples were subjected to molecular profiling and drug screening. 56% (n=53) of patients were clinical AJCC stage I and II, and 43% (n=41) AJCC stage III and IV. Organoids were established in an average 3-8 weeks. Among surgical specimens, PDO generation was successful in 71% (15 out of 21) of patients who had received NAT prior to sample collection and in 76% (39 out of 51) in patients who were chemotherapy and radiation naïve at the time of collection. 54% of PDO were successfully established from FNBs/FNAs pre-treatment. PDO transcriptomic subtypes were classified by the Moffitt system (Figure 1A) and correlated with clinical patients' outcome. Pathological response to NAT correlated with PDO chemotherapy response; a representative example of poor NAT response (grade 3) based on pathology correlated with PDO pan-resistance to standard of care chemotherapy agents (Figure 1B).

Conclusion: Herein we report the largest single-institution pancreatic cancer PDO library, including its recruitment of ethnic minorities. PDOs were successfully established from surgical specimens and FNBs, irrespective of tumor stage. The ability to establish PDOs from chemotherapy-naïve and post-NAT tissue enables longitudinal PDO generation to maintain dynamic chemotherapy sensitivity profiling. The proposed pipeline for PDO generation and drug testing is feasible to predict chemotherapy sensitivity and potentially enable patient-specific therapy, inclusive of patients with diverse backgrounds.



A B

Figure 1. A) Classical and Basal-like subtypes of PDOs based on Moffitt classification. B) PDO drug screening utilizing the standard of care chemotherapy agents. The orange dot represents the case of interest; black dots represent the other sampled PDOs.

29. VAGUS NERVE CHOLINERGIC NEURONS ORIGINATING IN THE DORSAL MOTOR NUCLEUS MITIGATE THE SEVERITY OF MURINE ACUTE PANCREATITIS

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Presenter: Dane Thompson MD | Feinstein Institutes for Medical Research, United States

Background: The efferent component of the inflammatory reflex, the cholinergic anti-inflammatory pathway, originates in the dorsal motor nucleus (DMN) and travels through the vagus nerve to the organs of the body, including the pancreas. Stimulation of this pathway can dampen maladaptive immune responses and cytokine production by nicotinic acetylcholine receptor-positive macrophages. Acute pancreatitis is a common disease, affecting hundreds of thousands of people, with few therapeutic options. We reasoned that stimulation of this pathway will mitigate the severity of pancreatitis in a preclinical model.

Methods: Pancreatitis was induced with two intraperitoneal injection of caerulein (50 mcg/kg), one hour apart. To target the DMN cholinergic neurons, an optogenetic probe was surgically placed in the brainstem of ChAT-ChR2 mice, which express channel rhodopsin (ChR2), on choline acetyltransferase-positive (ChAT) cholinergic neurons. These neurons were activated by 473 nm wavelength light (5 minutes, 20 Hz, 25% duty cycle, 8-12 mW total power). For vagotomy experiments, mice underwent bilateral subdiaphragmatic vagotomy and pyloric dilation, or sham surgery, 1 week prior to pancreatitis. The nicotinic acetylcholine receptor antagonist mecamylamine (1 mg/kg) was administered prior to optogenetic stimulation. Mice were euthanized 4 hours after final caerulein injection.

Results: Stimulation of cholinergic neurons in the DMN significantly attenuates levels of serum amylase (light vs. sham stimulation: 2940 ± 512.8 vs. 4043 ± 877 mU/mL, p = 0.0164; n = 9-11 mice/group), pancreatic IL-6 (1046 ± 288.1 vs. 1907 ± 879.3 pg/mg, p = 0.033), and pancreatic Monocyte chemoattractant protein-1 (MCP-1) (471.2 ± 241.7 vs. 953.1 ± 461.8 pg/mg, p = 0.0123), indicating a lower level of pancreatic inflammation. In addition, DMN stimulation also decreases the histological severity of pancreatitis, including reduced inflammatory cell infiltration and edema (histological score: light vs sham stimulation 5.352 ± 1.435 vs. 6.863 ± 1.67, p = 0.462; n = 9-11 mice/group). Ablation of vagus nerve-mediated signals by subdiaphragmatic vagotomy abolished the protective effects of DMN cholinergic stimulation (light vs sham: 2517 ± 746.7 vs. 2761 ± 787.3 mU/mL, p = 0.30; n = 3). Mice pre-treated with mecamylamine had significantly higher amylase compared to mice that did not receive the antagonist (Sham stimulation vs. DMN vs. DMN + Mecamylamine: 5047 ± 315.4 vs. 3769 ± 241.5 vs. 5620 ± 385.9, p = 0037; n = 10 mice/group).

Conclusion: Our studies demonstrate that activation of DMN cholinergic neurons reduces the severity of acute pancreatitis in a vagus-nerve mediated and nicotinic acetylcholine receptor-dependent manner. Together these studies provide new insights into the identity and central origin of the efferent vagus nerve fibers regulating acute pancreatitis.

30. PATENCY FOR AUTOLOGOUS VEIN IS SUPERIOR TO CADAVERIC VEIN IN PORTAL-MESENTERIC VENOUS RECONSTRUCTION

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Presenter: Thomas L. Sutton MD | Oregon Health & Science University, United States

Background: Portal vein reconstruction is often needed during resection of hepato-pancreato-biliary malignancies. Primary repair or interposition grafting with either autologous vein or cryopreserved cadaveric vein may be required; however, relative patency and oncologic outcomes between techniques are largely unknown.

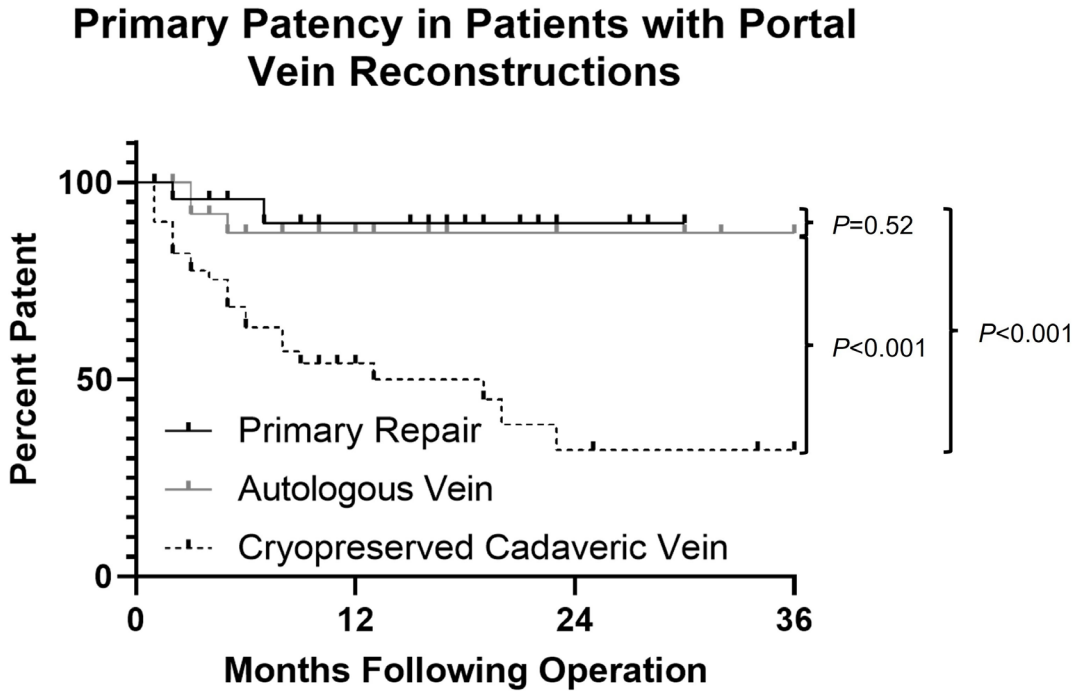
Methods: A single center review was performed for all patients undergoing portal vein reconstruction between 2007-2019. Primary patency was defined as time to first occlusion or intervention for patency-threatening stenosis, while survival-adjusted patency was defined as time to either first occlusion or death. Primary patency, overall survival, and survival-adjusted patency at 3 years were evaluated with Kaplan-Meier and Cox proportional hazards modeling. Operative time, costs, and clinical presentation of patency loss were assessed.

Results: One-hundred-twenty patients were identified with a median follow-up of 12 months (range 3-112 months). Most underwent pancreaticoduodenectomy (n=102, 85%) or distal pancreatectomy (n=16, 13%). The method of reconstruction was primary repair in 28 (23%), autologous vein graft in 35 (29%), and cryopreserved vein graft in 57 (48%). Operative time and costs were lower for primary repair but did not significantly differ between reconstructions with autologous and cryopreserved cadaveric vein.

For primary repair, autologous vein, and cryopreserved cadaveric vein reconstructions there were two (7%), four (11%), and 29 (51%) thromboses, respectively. Most (n=20, 57%) thromboses were symptomatic with either new-onset ascites (n=13), abdominal pain (n=2), or gastrointestinal hemorrhage requiring intervention or admission (n=5).

On Kaplan-Meier analysis, 3-year primary patency was greater for both primary repair (90%) and autologous vein (83%) reconstruction compared to cryopreserved cadaveric vein reconstruction (33%, log-rank P0.4 for all comparisons). On multivariable analysis, reconstruction with cryopreserved cadaveric vein had independently worse 3-year primary patency (HR 7.89, 95% CI 1.87-33.2, P=0.005) and survival-adjusted patency (HR 2.09, 95% CI 1.13-3.86, P=0.02) compared to primary repair, while autologous vein reconstructions were equivalent to primary repair (P>0.4 for both primary patency and survival adjusted patency).

Conclusion: For portal vein reconstructions, primary repair and reconstruction with autologous vein demonstrate superior patency to reconstructions utilizing cryopreserved cadaveric vein. Reconstruction with autologous vein is recommended when primary repair is not technically achievable, as cryopreserved cadaveric vein is associated with high rates of symptomatic patency loss without benefits to operative time or costs. Frequent surveillance of patency in patients with cryopreserved vein grafts is recommended.



Primary Repair	28	12	3	0
Autologous Vein	34	13	6	4
Cadaveric Vein	56	15	5	3

31. ORGANOTYPIC SLICE CULTURES: EX VIVO THERAPY PREDICTION IN PANCREATIC CANCER

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

Presenter: Benjamin Heckelmann | University Medical Center Schleswig-Holstein, Germany

Background: Despite the increase in the incidence of pancreatic ductal adenocarcinoma (PDAC) since the 1970s, therapeutic options that sufficiently reduce mortality are still very limited. We have been studying ex vivo Organotypic Slice Cultures (OTSCs) as a solution to the lack of realistic preclinical models of PDAC for therapy prediction. OTSCs differ from other culture models such as xenografts, primary cell cultures, and organoids. They are both time and cost efficient and realistically preserve the specific tumor microenvironment in situ. OTSCs retain the specific tissue architecture of solid tumors and therefore allow to provide insights into structural changes that occur under treatment ex vivo. By refining the OTSC model for PDAC, we aimed to collect information on individual intra- and intertumoral changes for response to therapy.

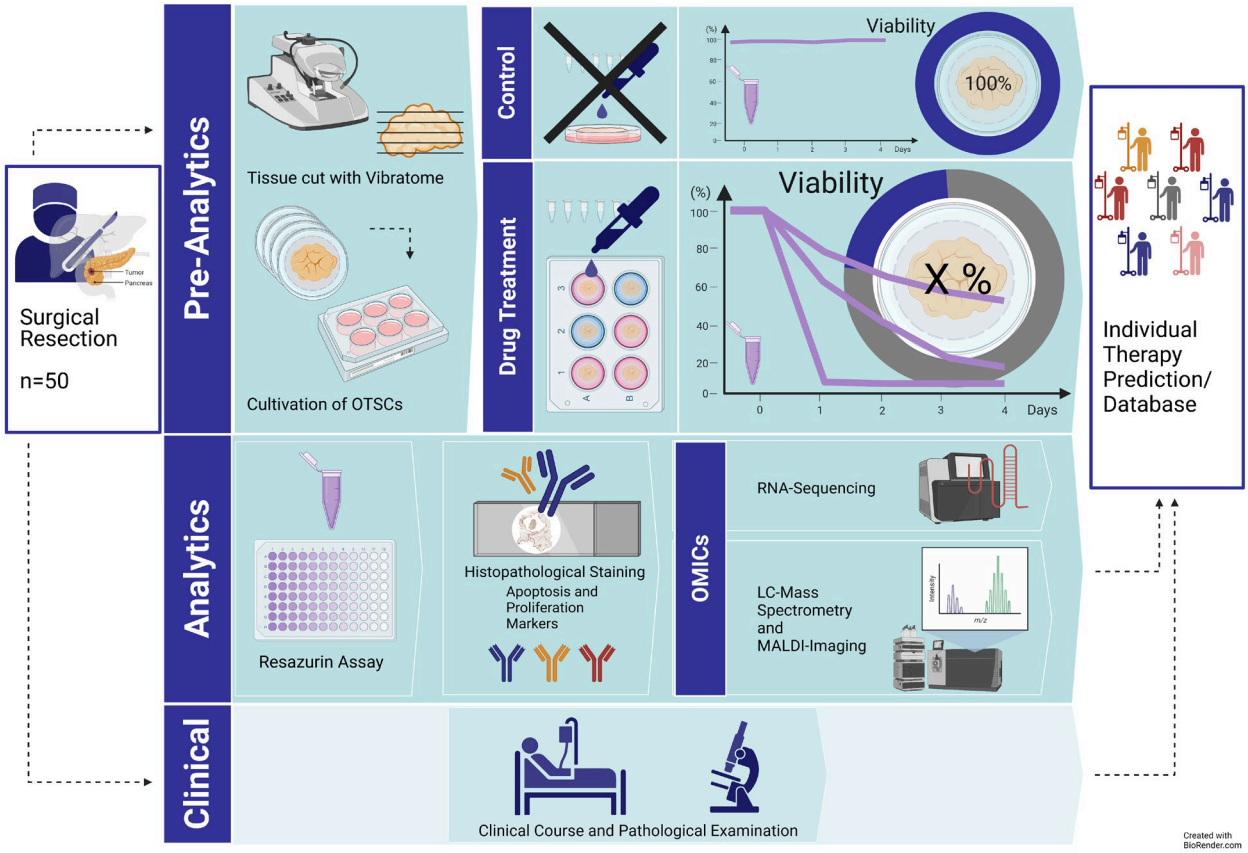
Methods: PDAC-tissue slices of 300µm thickness were generated using a vibratome. Sections were paired according to their location in the original tumor biopsy and cultured for up to 9 days at the air-liquid interface on PTFE membranes in modified DMEM/F12 medium in 6-well plates for ideal O2 supply. OTSCs were treated with gemcitabine (-paclitaxel), mFOLFORINOX, and puromycin as positive control for treatment response. Viability was determined by resazurin reduction, histopathological (HE), immunohistochemical staining (vimentin and cytokeratin 7 for tumor stromal differentiation, cleaved caspase 3 for apoptosis), and TUNEL apoptosis assay. MALDI imaging was used for spatially resolved proteomic analysis.

Results: Untreated OTSCs can be cultivated up to 9 days, with viability rates increasing, remaining constant, or decreasing only slightly. Histopathological evaluation revealed a decrease in tissue diameter, but the histological structure maintained intact. The staining of cleaved caspase 3 showed no difference from day 0 in most cases and agreed well with the results of the viability assay. However, the staining of cleaved caspase 3 increased remarkably after 15 days in culture. After treatment with gemcitabine and mFOLFORINOX, a decrease in viability was observed compared with untreated controls, although the individual response varied greatly depending on the sample and specific tissue conformation. In contrast, positive control samples treated with puromycin showed a consistent and strong decrease in viability.

Compared to other ex vivo culture models, OTSCs facilitate spatially resolved molecular analyses. In initial experiments, we generated spatially resolved proteomic profiles of PDAC-OTSCs using MALDI imaging. Simultaneous HE staining enabled analysis of mass spectrometric profiles and morphology. In this way, we were able to identify tissue-specific mass signatures.

Conclusion: OTSCs provide a unique, short-term and adequate opportunity for personalized and individualized therapy prediction. Viability testing and staining methods can be used to evaluate multiple therapeutic options within 10-12 days of surgical resection of the tumor. The interplay of classical viability assessment, OMICs approaches, and clinical data collection will benefit basic research in understanding intra- and inter-tumoral differences and has the potential to improve clinical outcomes by adding to the field of personalized medicine in the area of precision medicine.

We intend to integrate novel therapeutic strategies and further expand the data already collected through transcriptomics and proteomics approaches, in particular using MALDI imaging.


Surgical Resection
n=50
Pre-Analytics
Tissue cut with Vibratome
Cultivation of OTSCs
Control
Drug Treatment
Viability
100%
X %
Days
Analytics
Resazurin Assay
Histopathological Staining
Apoptosis and Proliferation Markers
OMICs
RNA-Sequencing
LC-Mass Spectrometry and MALDI-Imaging
Clinical
Clinical Course and Pathological Examination
Individual Therapy Prediction/ Database
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32. HARNESSING THE POWER OF FLUORESCENT NANOBODIES FOR BRIGHT AND SPECIFIC LABELING OF HUMAN PANCREATIC CANCER IN MOUSE MODELS

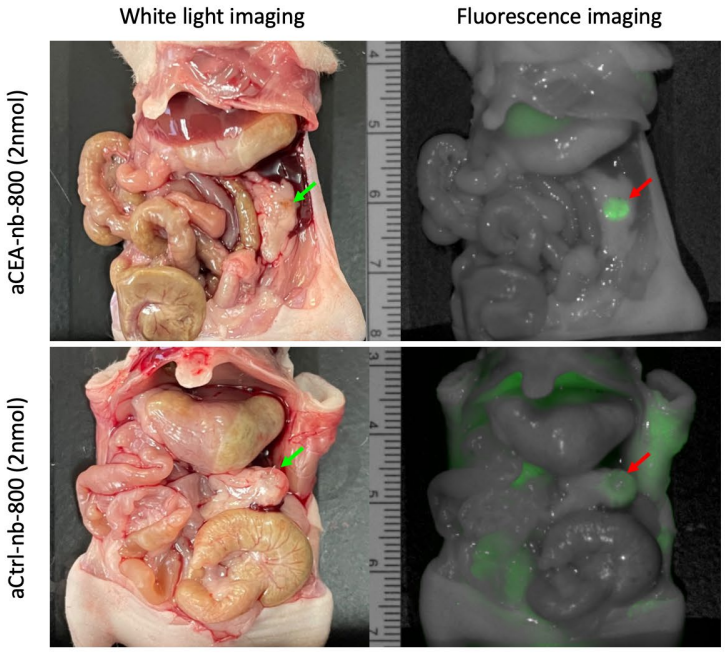
MA Turner, H Nishino, S Amirfakhri, S Hernot, RM Hoffman
Presenter: Thinzar M. Lwin MD, MS | University of California, San Diego, United States

Background: Pancreatic cancer is an aggressive malignancy and surgery can offer a cure when the disease is localized. Traditional approaches to determining resectability and determining extent of resections are subjective. Neoadjuvant treatment effect can further confound intraoperative visualization of the tumor. Local recurrence at the surgical bed occurs in 50-65% of patients after curative-intent pancreatic surgeries despite adjuvant therapies, indicating the challenge in obtaining truly negative oncologic margins. Real-time intra-operative tumor-specific labeling using nanobodies tagged with a fluorescent near-infrared dye can enhance visualization of viable tumor, determine and secure resection margins, and confirm completeness of resection within the surgical bed.

Methods: Anti-CEA nanobodies were conjugated with the NIR dye IRDye800CW to establish an aCEA-nb-800 probe. Control scrambled nanobodies were conjugated with IRDye800CW to establish aCtrl-nb-800. Human pancreatic cancer from surgical specimen obtained with an IRB approval protocol were implanted into either subcutaneous pockets or the pancreatic tail of nude mice to establish mouse models of localized pancreatic cancer. BxPC3-GFP human pancreatic cancer cells (5x106 cells suspended in 500 uL of PBS) were injected intraperitoneally into the abdomen of nude mice to establish peritoneal carcinomatosis models. After tumors and cancer cells were allowed to engraft for 3-4 weeks, 2 nmol of aCEA-nb-800 or aCtrl-nb-800 was injected intravenously. Mice were subsequently serially imaged over time under NIR fluorescence.

Results: Pancreatic tumors were rapidly labeled with anti-CEA fluorescent nanobodies. Tumors as small as ~2-3mm demonstrated a fluorescence signal within 3 hours of intravenous probe administration. Mean fluorescence intensity (MFI) at the tumor using aCEA-nb-800 was 1.65 a.u. with a background MFI of 0.61 and a tumor-to-background ratio (TBR) of 2.7 (top panel). The control probe aCtrl-nb-800 showed a faint signal at the tumor but this was not above background. MFI at the tumor using aCtrl-nb-800 was 0.60 a.u. with a background MFI of 0.35 and a TBR of 1.7 (Bottom panel). A representative pancreatic orthotopic patient-derived orthotopic xenograft tumor was bivalved and a tissue section was further imaged under NIR fluorescence ex-vivo using the LICOR-Odyssey. Images of the tumors injected with aCEA-nb-800 and aCtrl-nb-800 were also obtained under white light, fluorescence, and a pseudo-color intensity map. The fluorescence signal was clearly localized at the tumor and did not show a signal in the surrounding pancreatic parenchyma. Under magnification, the tumor showed a TBR of 11.97 in the tumor using aCEA-nb-800 and a TBR of 2.97 using the aCtrl-nb-800.

Conclusion: Fluorescent anti-CEA nanobodies were able to clearly and specifically label orthotopic pancreatic xenografts. There was stability of the tumor-specific signal that persisted over time while background signals in the liver and other soft tissue decreased. Even small lesions that were millimeters were detectable using this probe. Compared to traditional antibodies, nanobody labeling kinetics permit same day administration and imaging. Fluorescent nanobody probes are promising molecules for to enhance accurate localization of pancreatic cancer.


White light imaging
Fluorescence imaging
aCEA-nb-800 (2nmol)
aCtrl-nb-800 (2nmol)

33. TARGETING CELLULAR METABOLISM IN CHOLANGIOCARCINOMA USING REPURPOSED NOVEL MITOCHONDRIAL INHIBITORS

S Khalilieh, A Jain, WB Bowne, CJ Yeo, H Lavu, A Nevler
Presenter: Saed Khalilieh MD | Thomas Jefferson University Hospital, United States

Background: Cholangiocarcinoma is a rare, aggressive cancer of the biliary tree which accounts for 10-20% of periampullary cancers. Its annual incidence has slowly increased to approximately 2-cases per 100,000 people. The prognosis is grim and the 5-year overall survival rate is 9-10%. Therapy for cholangiocarcinoma is challenging, as this cancer is extremely resistant to standard chemotherapy regimens which act through the induction of DNA damage. The cholangiocarcinoma microenvironment is relatively hypovascular and as such, is characterized by relative hypoxia and nutrient depletion. We therefore hypothesized that metabolic inhibitors, targeting mitochondrial function might be a useful adjunct for cholangiocarcinoma treatment. We have shown that the previously FDA-approved anti-parasitic compound, Dithiazanine Iodide (CDI), is a strong, targeted mitochondrial inhibitor. We assessed the potential of this compound as an anti-cancer drug in in-vitro cell cultures of patient-derived cholangiocarcinoma cell lines.

Methods: Two human cholangiocarcinoma cell lines, EGI-1 and CCC-5 were cultured in normal conditions (37°C, 5% CO2). Five-day cell viability assays were performed using Picogreen® dsDNA measurement. Cellular ATP measurements were performed by initial incubation of the cells in glucose-free media for 24 hours and then dosing of the drug compounds and collection of samples after an 8-huors incubation period. Cell viability and ATP quantification were preformed using the GloMax® Explorer Multimode Microplate Reader (Promega, Madison, WI). Mitochondrial RNA expression was quantified by qRT-PCR after 24 hours of drug treatment utilizing RPS as references (Rneasy Mini Kit, Qiagen was used for RNA extraction). Expression of mitochondrial electron transport chain (ETC) proteins was assessed by western blot of OxPhos staining (#ab110411, 1:1000, Abcam, Boston, MA) after 48 hours of exposure to CDI and the control compounds (DMSO and Oxaliplatin). Data were plotted and IC50s were calculated utilizing non-linear dose-response curve fitting in GraphPad Prism 8.0.1. (GraphPad Software, San Diego, CA).

Results: EGI-1 and CCC-5 cells displayed a marked sensitivity to CDI compared to 5-Flourouracil and Irinotecan. Mitochondrial RNA expression of CCC-5 cells was significantly decreased with CDI treatment compared to controls (DMSO and Oxaliplatin) as shown in Figure 1A ($P < 0.05$). A 48-hour dosing study assessing mitochondrial ETC protein expression in CDI treated cholangiocarcinoma cells further revealed a marked decrease in expression of complexes I-IV (Figure 1A), suggesting the cause of the mitochondrial inhibition to be through a decrease in mitochondrial gene expression or increased ETC degradation. ATP Quantification of CCC-5 cells grown in a-glycemic conditions showed normal ATP levels with control (DMSO) and chemotherapeutic drugs (5-Fluorouracil, Gemcitabine and Oxaliplatin) and decreased ATP levels with CDI and with known mitochondrial inhibitors (Rotenone, FCCP and Pyrvinium Pamoate), as shown in Figure 1B.

Conclusion: Cholangiocarcinoma is an aggressive cancer, highly resistant to standard chemotherapeutic agents. Metabolic targeting through mitochondrial inhibition can potentially overcome the resistance. The previously FDA-approved anti-parasitic drug, CDI, shows anti-cancer properties in-vitro and is associated with decreased ETC protein expression, decreased mitochondrial RNA expression and cellular ATP depletion in cholangiocarcinoma cells. A phase-1 study is currently underway to assess the ability of similar mitochondrial inhibitors to target pancreatic and periampullary adenocarcinomas.

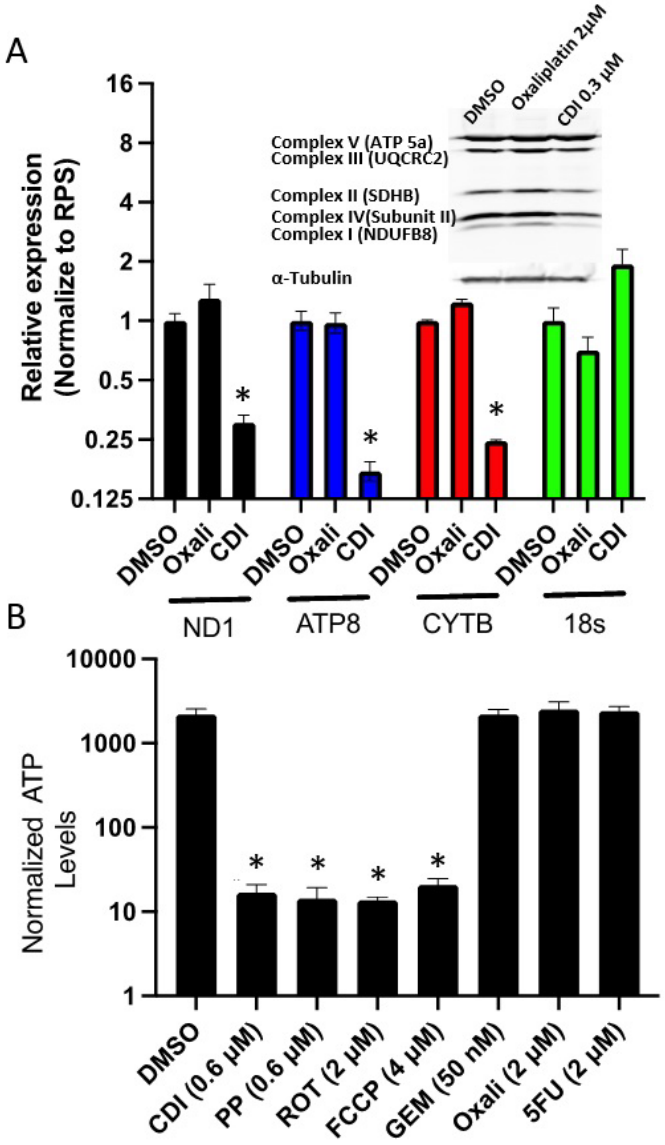


Figure 1. qRT-PCR showing mitochondrial RNA expression in CCC-5 cells treated with CDI utilizing RPS as reference (**A)** and sub-panel of Western-Blot of ETC Chain proteins in EGI-1 cells showing decreased levels of complexes I-IV in cells treated with CDI (0.3 μM) compared to DMSO control and Oxaliplatin.**(B**) ATP quantification study of CCC-5 cells grown in glucose-deficient media, 8-hours incubation with drugs, values normalized to control (DMSO). PP – Pyrvinium Pamoate; ROT–Rotenone; GEM – Gemcitabine; Oxali – Oxaliplatin; 5-FU – 5-Flourouracil. * P<0.05.

34. DISTRESS SCREENING AND CANCER: AN ASSESSMENT IN PANCREATICOBILIARY CANCER PATIENTS AND THEIR SIGNIFICANT OTHERS

TP Yeo, S Cannaday, R Thompson, R Fogg, H Lavu, CJ Yeo
Presenter: Theresa P. Yeo PhD, MPH, ACNP-BC | Thomas Jefferson University Hospital, United States

Background: The diagnosis of cancer provokes sadness, fear and turmoil in affected individuals and in family members and significant others. The American Cancer Society and other investigators estimate that 24% to 52% of cancer patients suffer from uncontrolled and undiagnosed distressing symptoms, and that their cancer care suffers as a result. Distress screening has been mandated for NCI-designated facilities since 2015 and is an important component of oncological care. Clinical implementation remains limited for individuals with pancreaticobiliary cancers in outpatient settings. The purpose of this observational study was to identify differences in mean distress scores based on the National Comprehensive Cancer Network's Distress Thermometer/Problem List® in pancreatic cancer patients as compared to those with periampullary cancer and benign pancreatic conditions. Distress scores in spouses and significant others (SOs) of the pancreatic cancer patients were also assessed. The goal were to quantify the level of distress and to identify specific problem areas in this patient population.

Methods: The Distress Thermometer/Problem List® was offered to patients and SOs at a pancreaticobiliary surgical oncology clinic between March 2018 - July 2019. Patients and SOs were asked to independently complete the paper and pencil survey about their own level of distress over the past seven days including on the day of the visit. The DT/Problem List was reviewed by a health care provider in real time. Summary statistics for cancer type and SOs were calculated for sex, age and race. Distress scores (0 to 10) were dichotomized at a cut-off point of ≤5 vs >5 (moderate-severe distress). The U.S. Zip Code database was used to identify income range, percent poverty, racial composition and educational level in the patient's self-identified zip code. Regression models were fitted using these data to identify independent predictors of distress.

Results: Of 603 screenings completed, 547 individuals had evaluable data: 404 pancreatic cancers; 52 periampullary cancers; 91 benign conditions; and 184 SOs. The mean score for the patient cohort was 3.9 and 4.5 for SOs. 30% of the patients had a score >5. There was a strong association between the number of preexisting medical conditions and distress scores, such that having ≥ 3 medical problems correlated with a score > 5 (p=0.02). Distress scores were highest for those with treatment decision concerns, insurance coverage worries, and preexisting emotional problems. Amongst all patients, pancreatic cancer reported the highest levels of distress. Higher distress scores correlated with fatigue, pain, indigestion, depression, and transportation to treatment. Spouses of pancreatic cancer patients reported greater distress than did the patients. Higher income level independently predicted higher distress; higher percent of poverty in zip code of residence predicted lower distress. Zip code correlated with distress based on income and percentage of poverty, but not on race.

Conclusion: Significant distress is found in pancreatic cancer patients and family members and has implications for screening, underscoring the need for focused interventions and supportive care referrals. This is the first DT/Problem List survey specifically in pancreaticobiliary cancer patients reported in the literature.

Table: Distress Thermometer Scores, Problem List Items, & Zip Code Findings, By Group

Characteristics:	Pancreatic Cancer Group (N=403)	Periampullary Cancer Group (N=52)	Benign PB Disease Group (N=92)	Significant Other Group (N=184)
Mean DT Score (SD)	3.9 (3.2)	3.3 (3.2)	3.5 (3.0)	4.5 (3.0)
Number of items reported on Problem List when DT score ≥5	13 items*	1 item*	13 items*	12 items*
DT score for patients who live in zip code with highest income level	4.3	3.4	2.8	N/A
DT score for patients who live in zip code with highest percent poverty	3.7	2.7	2.9	N/A

DT = distress thermometer score, DT scores range from 0 (lowest) - 10 (highest), SD = standard deviation,*(p-values = 0 .001 to 0.03).

35. FAILED RECOVERY OCCURS WITHOUT SURGICAL COMPLICATIONS FOR A SIGNIFICANT NUMBER OF PATIENTS AFTER PANCREAS SURGERY

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Presenter: Guido Fiorentini MD | Mayo Clinic, United States

Background: The absence of surgical complications has traditionally been used to define successful recovery after pancreas surgery. However, patient-reported outcomes (PRO) measures may better able to identify patients at risk of failed recovery than surgical complications alone.

Methods: Patients scheduled for pancreaticoduodenectomy were prospectively enrolled. PROs were collected using the LASA questionnaire which covers on several factors impacting on quality of life preoperatively and on post-operative days 2, 7, 14, 30 and monthly until 6 months. Thirty-day surgical complications were prospectively assessed; clinically significant pancreatic fistulas and delayed gastric emptying (DGE) within 30 days postoperatively were recorded. Patients were asked if they felt fully recovered at 30 days and 6 months. The comprehensive complication index (CCI) was utilized to group patients by 30-day complications, where patients with CCI ≥ 26.2 were grouped as major complication (major complication or multiple minor complications) and patients with CCI < 26.2 were grouped as uncomplicated. Chi-square and Kruskal-Wallis tests were used to assess associations with recovery by 6 months.

Results: Of 116 patients that met inclusion criteria, 32 (28%) were grouped as having a major complication. However, fewer than 1 in 10 patients (7%) reported feeling fully recovered at 30 days postoperatively and only half (55%) reported feeling fully recovered at 6 months. Of patients within the major complication group, over half (62%) did not recover by 6 months, while 38% of those in the uncomplicated group reported not being recovered at 6 months (p=0.03). Patients who experienced DGE were less likely to report full recovery at 6 months (36%) compared to those with no DGE (60%, p=0.048). Further, full recovery at 6 months did not significantly differ by pancreatic fistula (p=0.51), age, gender, ASA classification, receipt of neoadjuvant therapy, or cancer status (all p>0.05). Lastly, higher preoperative pain severity was higher in patients with failed recovery at 6 months (preoperative pain mean 2.3 [SD 2.4] among 6-month failed recovery vs 1.6 [2.2] among 6-month successful recovery, p=0.04), while preoperative PRO measures of quality of life, social activity, and fatigue were not associated with failed recovery at 6 months. Patients who underwent MIS surgery reported a clinically, but not statistically significant, higher rate of full recovery at 6 months (48.5% of MIS vs 67.6% of open, p=0.07). Individual patient level recovery trajectory as defined by PROs over the full 6-month postoperative course suggested a failed recovery was not observed only in patients with complications by all 4 LASA domains investigated (Fig. 1). Among patients in the uncomplicated group, poor 30-day postoperative pain severity, quality of life, and social activity were associated with failed recovery at 6 months.

Conclusion: A significant number of patients without a 30-day complication failed to recover from pancreas surgery at 6 months. In patients with a complication, DGE appeared to be a more significant driver of failed recovery than pancreatic fistula. However, in patients without a complication, short-term post-operative deficits in pain severity, quality of life, and social activity may be able to identify patients at risk of failed long-term recovery.

36. TOTAL PANCREATECTOMY AND ISLET CELL AUTOTRANSPLANTATION: A 10-YEAR UPDATE ON OUTCOMES AND ASSESSMENT OF LONG-TERM DURABILITY

KM Turner, E Donovan, AM Delman, J Brunner, S Wahab, K Choe, M Smith, SH Patel, SA Ahmad, GC Wilson

Presenter: Eileen Donovan MD | University of Cincinnati, United States

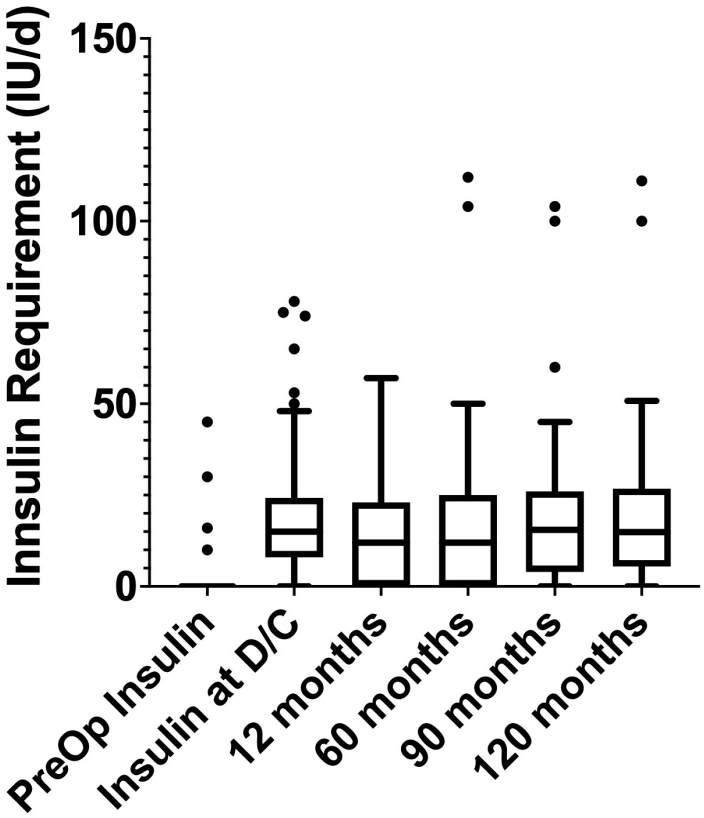
Background: Total pancreatectomy and islet cell autotransplantation (TPIAT) offers an effective, durable solution for

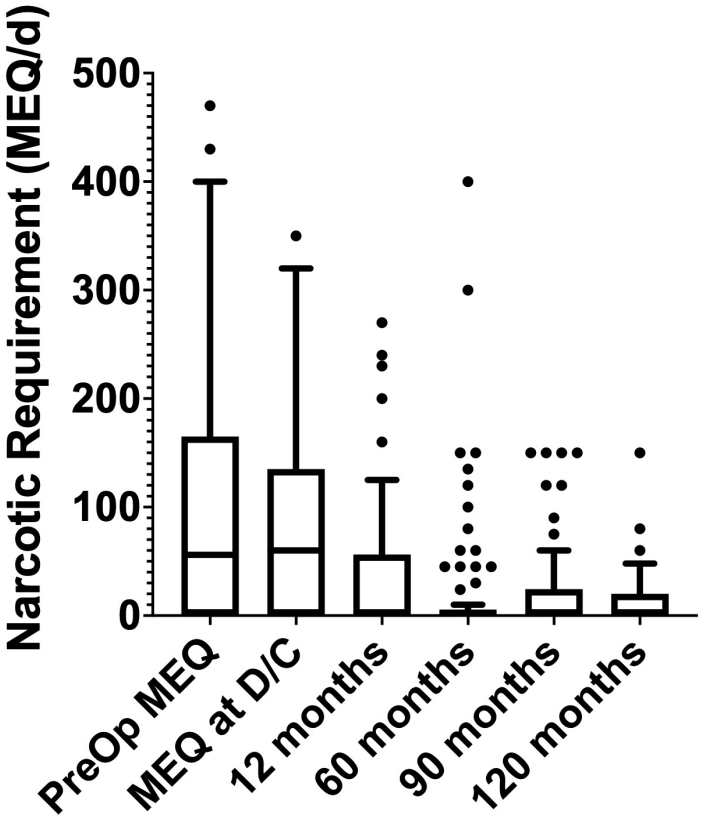
the management of chronic pancreatitis, as previously reported by our group. The aim of this study was to assess the durability of TPIAT at 10-years post-operatively.

Methods: Patients undergoing TPIAT for chronic pancreatitis eligible for 10-year follow-up were included. Primary outcomes, including insulin requirement, glycemic control, and narcotic requirement, were reported at 5-, 7.5-, and 10-years post-operatively.

Results: Of the 223 patients who underwent TPIAT at our institution, 142 patients were eligible for inclusion. All patients underwent successful TPIAT with a median of 4,928 islet equivalents per body weight isolated, with no perioperative mortality. Overall 5-, 7.5-, and 10-year survival was: 87.9%, 78.4%, and 68.5%, respectively. Median insulin requirement remained similar over time (Figure 1); however, there was a trend toward lower rates of insulin independence (25.3% vs. 16.7% vs. 11.8%, p=0.21). Glycemic control, measured by median HbA1C, declined from 5- to 7.5-years and then plateaued (7.1 vs. 8.4 vs. 8.5, p=0.03). The majority of patients remained opioid independent throughout the study period (74.0% vs. 70.5% vs. 68.6%, p=0.82). (Figure 1) Furthermore, these trends continued beyond 10-years, with 20 of 26 patients remaining opioid independent and 2 patients remaining insulin independent at a median follow-up of 14.6-years.

Conclusion: This study represents one of the largest series reporting on long-term outcomes after TPIAT, demonstrating excellent long-term pain control. While islet function demonstrated some decline, glycemic control remained stable with some patients insulin independent greater than 10-years post-operatively.


Innsulin Requirement (IU/d)
150
100
50
0
PreOp Insulin
Insulin at D/C
12 months
60 months
90 months
120 months


Narcotic Requirement (MEQ/d)
500
400
300
200
100
0
PreOp MEQ
MEQ at D/C
12 months
60 months
90 months
120 months

37. SHORT- AND LONG-TERM OUTCOMES OF PANCREATIC CANCER RESECTION IN ELDERLY PATIENTS: A NATIONWIDE ANALYSIS

AC Henry, TJ Schouten, LA Daamen, MS Walma, P Noordzij, GA Cirkel, M Los, 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, MWJ Stommel, IQ Molenaar and HC van Santvoort for the Dutch Pancreatic Cancer Group

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

Background: The number of elderly patients with pancreatic cancer is growing. Clinical data on the short-term outcomes, rate of adjuvant chemotherapy and survival in these patients are, however, limited. We therefore performed a nationwide analysis.

Methods: Data from the prospective Dutch Pancreatic Cancer Audit were analyzed, including all patients undergoing pancreatic cancer resection between January 2014 to December 2016. Patients were classified into two age groups: < 75 and ≥75 years. Major complications (Clavien-Dindo grade≥3), 90-day mortality, rates of adjuvant chemotherapy and survival were compared between age groups. Factors associated with start of adjuvant chemotherapy and survival were evaluated with multivariable Cox regression and logistic regression analysis.

Results: Out of 836 patients, 198 patients were aged ≥75 years (24%) and 638 patients were aged < 75 years (76%). Median follow-up was 38 (interquartile range [IQR] 31-47) months. Major complications (31% versus 28%; P=0.43) and 90-day mortality (8% versus 5%; P=0.18) did not differ. Adjuvant chemotherapy was started in 37% versus 69% of patients (P< 0.001). Median overall survival was 15 (95% confidence interval [CI] 14-18) months versus 21 (95% CI 19-24; P< 0.001) months. Age ≥75 years was not independently associated with OS (HR 0.96 [95% CI 0.79-1.17]; P=0.71). Age ≥75 years was, however, associated with a lower rate of adjuvant chemotherapy (OR 0.27 [95% CI 0.18-0.40]; P< 0.001).

Conclusion: The rate of major complications and 90-day mortality after pancreatic resection did not differ between elderly and younger patients. Elderly patients were, however, less often treated with adjuvant chemotherapy and their overall survival was shorter.

38. THE INCIDENCE OF DEPRESSION AND ANXIETY PRECEDING A DIAGNOSIS OF PANCREATIC CANCER

NE Davis, JJ Hue, HJ Graor, M Zarei, K Ji, ES Katayama, O Hajihassani, AW Loftus, RK Kyasaram, J Shanahan, A Vaziri-Gohar, JM Winter

Presenter: Nathaniel Davis BS | University Hospitals Cleveland Medical Center, United States

Background: Patients with pancreatic cancer frequently develop depression and anxiety after they learn of their cancer diagnosis. This is likely multifactorial, but may be due to physical and psychiatric stressors that impact mental health, including historically poor survival, chemotherapy toxicities, weight loss, and pain, among others. However, prodromal psychiatric symptoms have been reported as an early warning sign of pancreatic cancer. Relatively few studies have examined this relationship. We aimed to determine the incidence of depression/anxiety preceding a diagnosis of pancreatic neoplasm and compare to the general population. Further, we aimed to determine if prediagnosis depression/anxiety was associated with treatment compliance or survival.

Methods: 1,000 patients with a pancreatic neoplasm from a single institution were identified using International Classification of Diseases (ICD) codes. For each case, two non-cancer age- and sex-matched controls were included. Dates of depression/anxiety diagnosis, identified using ICD codes, were compared to the date of pancreatic neoplasm diagnosis. The medical record was queried to further explore psychiatric symptoms. Multivariable models were performed to determine if prediagnosis depression/anxiety was associated with receipt of treatment or survival.

Results: A greater proportion of patients diagnosed with a pancreatic neoplasm experienced depression/anxiety preceding diagnosis relative to controls (4.5% vs 2.6%, p=0.006) based on ICD codes. However, upon review of the medical record 20.2% of patients with a pancreatic neoplasm exhibited signs of prodromal depression/anxiety, which was greater relative to controls (6.7%, p< 0.001). Females were nearly twice as likely to exhibit prodromal psychiatric symptoms. Prediagnosis depression/anxiety was associated with a reduced likelihood of receiving chemotherapy (OR=0.61, p=0.04), but was not associated with pancreatectomy rates among those with localized disease. There was an association between prediagnosis depression/anxiety and poor overall survival among patients with metastatic disease (HR=1.32, p=0.04). A similar association was not identified among those with localized disease.

Conclusion: The incidence of depression/anxiety among patients with a pancreatic neoplasm is higher than the general population, but may be underestimated by ICD codes. Patients with prediagnosis psychiatric conditions were less likely to receive chemotherapy. The presence of prodromal psychiatric symptoms was also associated with poor survival among patients with metastatic disease. Thus, timely identification and treatment of mental health changes may improve survival outcomes and quality of life.

Table: Summary of depression and anxiety diagnoses among patients with a pancreas neoplasm and non-cancer controls.

	Pancreas Neoplasm	Control	p
N	920	1,994	---
Depression, by ICD code	123 (13.4%)	29 (1.4%)	0.160*
Remote	9 (1.0%)		
Prediagnosis	20 (2.2%)		
Post-diagnosis	94 (10.2%)		
Anxiety, by ICD code	174 (18.9%)	32 (1.6%)	0.018*
Remote	14 (1.5%)		
Prediagnosis	27 (2.9%)		
Post-diagnosis	133 (14.5%)		
Either, by ICD code	240 (26.1%)	51 (2.6%)	0.006*
Remote	20 (2.2%)		
Prediagnosis	41 (4.5%)		
Post-diagnosis	179 (19.5%)		
Either, by documentation Prediagnosis	140 (15.9%)	71 (3.6%)	<0.001
Either, by medications Prediagnosis	140 (15.9%)	76 (3.8%)	<0.001
Either, combined Prediagnosis	186 (20.2%)	134 (6.7%)	<0.001

*Statistical comparisons are between control patients and prediagnosis values among patients with a pancreas neoplasm.

39. VALIDATION OF THE ISGPS RISK CLASSIFICATION SYSTEM FOR POSTOPERATIVE PANCREATIC FISTULA AFTER PANCREATODUODENECTOMY IN A NATIONWIDE COHORT

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Presenter: Anouk Emmen MD | Academic Medical Center, Netherlands

Background: Predicting the risk of postoperative pancreatic fistula (POPF) after pancreatoduodenectomy may be useful for tailored patient management, benchmarking, and clinical studies. Recently, the International Study Group of Pancreatic Surgery (ISGPS) presented a four-tier risk classification based on pancreatic duct size (PD) and pancreatic texture, consisting of categories: A (not-soft texture and PD > 3mm), B (not-soft texture and PD ≤ 3mm), C (soft texture and PD > 3mm), and D (soft texture and PD ≤ 3mm). The aim of this study was to validate the ISGPS classification system for POPF in a nationwide audit.

Methods: All patients after pancreatoduodenectomy were included from the mandatory nationwide Dutch Pancreatic Cancer Audit (2014-2020). Rates of clinically relevant POPF grade B/C according to the ISGPS 2016 definition were calculated in the current cohort for the four ISGPS risk categories (A, B, C, D) and compared to the original ISGPS cohort. In addition, the median updated-alternative Fistula Risk Score (ua-FRS) was calculated for the patients in each risk category. The association between the ISGPS risk categories and POPF were assessed in multivariable regression analysis.

Results: Overall, 3300 patients after pancreatoduodenectomy for all indications were included and categorized in the ISGPS risk categories: A (N = 919), B (N = 420), C (N = 831), and D (N = 1130). The POPF rates in the risk categories (A-D) were 3.5%, 13.6%, 14.4%, and 28.8%, respectively, which differed from the original ISGPS rates (3.5%, 6.2%, 16.6%, 23.3%, see Table 1). Median (IQR) ua-FRS scores for the risk categories (A-D) were 11 (7–14), 24 (18–31), 24 (17–29), and 47 (38–55), respectively. After adjustment for sex, BMI, ASA score and diagnosis, the ISGPS risk categories were independent predictors for pancreatic fistula (OR 1.87 95%CI 1.68-2.08, P < 0.001). However, the risk prediction of pancreatic fistula for category B and type C did not differ significantly (OR: 0.88, 95%CI 0.61-1.26, P value = 0.50).

Conclusion: This nationwide validation of the ISGPS classification for POPF after pancreatoduodenectomy confirmed the risk prediction for the lowest and highest risk category (A and D) but found no clinically relevant difference between the two middle risk categories (B and C). We propose to simplify the ISGPS risk categories from a four- to a three-tier system (e.g., Type A, B, C based on 0, 1, or 2 risk factors) which would require further validation studies.

Table 1. Postoperative pancreatic fistula grade B/C per ISGPS risk category in the current cohort (N = 3300) versus the ISGPS cohort (N = 5533)

	Current validation cohort				ISGPS cohort		
	POPF	No POPF	Rate	ua-FRS score	POPF	No POPF	Rate
Type A	32	887	3.5%	11 (7 - 14)	56	1533	3.5%
Type B	57	363	13.6%	24 (18 - 31)	56	854	6.2%
Type C	120	711	14.4%	24 (17 - 29)	169	847	16.6%
Type D	326	804	28.8%	47 (38 - 55)	471	1547	23.3%

40. INCIDENCE AND RISK FACTORS OF CHYLE LEAK AFTER PANCREATECTOMY: A SINGLE HIGH-VOLUME INSTITUTION EXPERIENCE.

J Ishida, S Rodriguez Franco, T Sugawara, S Grandi, MH Al-Musawi, KL Colborn, A Gleisner, RD Schulick, M Del Chiaro
Presenter: Jun Ishida MD, PhD | University of Colorado, United States

Background: Chyle leak is not a rare complication after pancreatectomy. Limited evidence exists on the chyle leak after pancreatectomy based on the 2017 International Study Group on Pancreatic Surgery (ISGPS) definition.

Methods: A total of 1086 of patients who underwent pancreatectomy for any diseases at the University of Colorado Cancer Center between June 2012 and May 2021 were reviewed. Risk factors for chyle leak were investigated using univariate and multiple regression analyses. Outcomes were assessed based on the grade of the ISGPS definition. Correlation models between volume of drainage fluid and time to drain removal and hospital stay after surgery were conducted.

Results: Chyle leak occurred in 100 patients (9.2%). In the multiple regression, body mass index < 25 kg/m2 (OR 1.66 [95% CI 1.07-2.56]), number of examined lymph node ≥16 (OR 2.47 [95% CI 1.35-4.50]), and time to start diet ≤ 4 days (OR 2.08 [95% CI 1.32-3.27]) were identified as independent risk factors for chyle leak.

Based on the ISGPS classification, there were 5, 93, and 2 patients with grade A, B, and C, respectively. All patients with grade A received only low-fat diet as conservative treatment. In 93 patients with grade B, 28 (30.1%) and 36 (38.7%) patients received total parenteral nutrition and octreotide, respectively. One (1.1%) patient with grade B received percutaneous drainage. All patients with grade C received lymphangiography. Median time to drain removal after surgery was 9 days, 27 days, and 57.5 days in patients with grade A, B, and C, respectively. Median hospital stay after surgery was 10 days, 11 days, and 30.5 days in patients with grade A, B, and C, respectively. Seventy-nine (88.8%) patients with grade B and two (100%) patients with grade C were discharged with drain in place. There was no mortality related to chyle leak (Table).

Peak drain triglyceride concentration was not correlated with time to drain removal after surgery (rho = -0.09, p = 0.39), while it had a weak negative correlation with hospital stay after surgery (rho = -0.23, p = 0.024). However, peak drain output volume had a slight positive correlation with both time to drain removal after surgery (rho = 0.17, p = 0.019) and hospital stay after surgery (rho = 0.27, p = 0.008).

Conclusion: Lower body mass index, number of examined lymph node, and early initiation of diet are independent risk factors for chyle leak after pancreatectomy. The ISGPS definition is useful for detecting the clinically relevant chyle leak and its grading system stratifies the outcomes in patients with chyle leak well.

42. PANCREATIC STELLATE CELLS REGULATE ACINAR CELL ORGANIZATION IN A THREE-DIMENSIONAL CO-CULTURE MODEL

M Bläuer, J Sand, J Laukkarinen
Presenter: Merja Bläuer PhD | Tampere University Hospital, Finland

Background: Culturing cells in three-dimensional (3D) in vitro environments allows them to replicate some of the structures and functions present in normal tissues and tumors in vivo. Various 3D culture models supporting the 3D organization of tumor cells, including pancreatic carcinoma cells, have been described. Given the importance of stromal-epithelial interactions in both normal and cancerous tissues, 3D culture models enabling such interactions provide valuable tools for a variety of biomedical studies. Pancreatic acinar cells and stellate cells and their intercellular communication are central players in exocrine pancreatic pathobiology. The aim of this study was to establish a 3D environment for co-culturing normal pancreatic acinar and stellate cells and to study the effects of stellate cells on the 3D organization of acinar cells in vitro.

Methods: Pancreatic acinar and stellate cells were obtained from mouse pancreatic tissue using the explant outgrowth technique with cell-type-specific culture media and cryopreserved for on-demand use. Sandwich cultures were built in Matrigel matrix in cell culture inserts (24-well format) with a total cell number of 20, 000 per insert. Both acinar and stellate cell monocultures and co-cultures (1:1 cell ratio) were maintained for 4 days and their morphological development was monitored under a phase-contrast microscope.

Results: Within the first day of culture, acinar cell monocultures showed organization into hollow spheroids. As a result of apparent fusion of individual spheroids, continuous expansion in spheroid diameter (>300 µm) was observed. Stellate cells in 3D monocultures showed long membrane protrusions and gradual gathering together to form dense cell masses. In acinar-stellate co-cultures small groups consisting of both cell types were formed. Their organization at day 4 was that of several small (~50 µm) acinar buds emerging from a central core of stellate cells.

Conclusion: A 3D culture environment was established and optimized to support acinar-stellar interactions in vitro. The data demonstrate that the presence of stellate cells is needed to control epithelial organization in 3D culture. Heterotypic cellular interactions prevent uncontrolled growth and fusion of acinar cell spheroids typical of homotypic 3D cultures.

43. TREATMENT WITHIN A MULTIDISCIPLINARY CLINIC INCREASES TREATMENT AND ELIMINATE SOCIOECONOMIC SURVIVAL DISPARITIES FOR PANCREATIC CANCER: A REGIONAL HOSPITAL SYSTEM ANALYSIS

C Rieser, R Hoehn, M Zenati, A Paniccia, A Zureikat
Presenter: Caroline Rieser MD | University of Pittsburgh Medical Center, United States

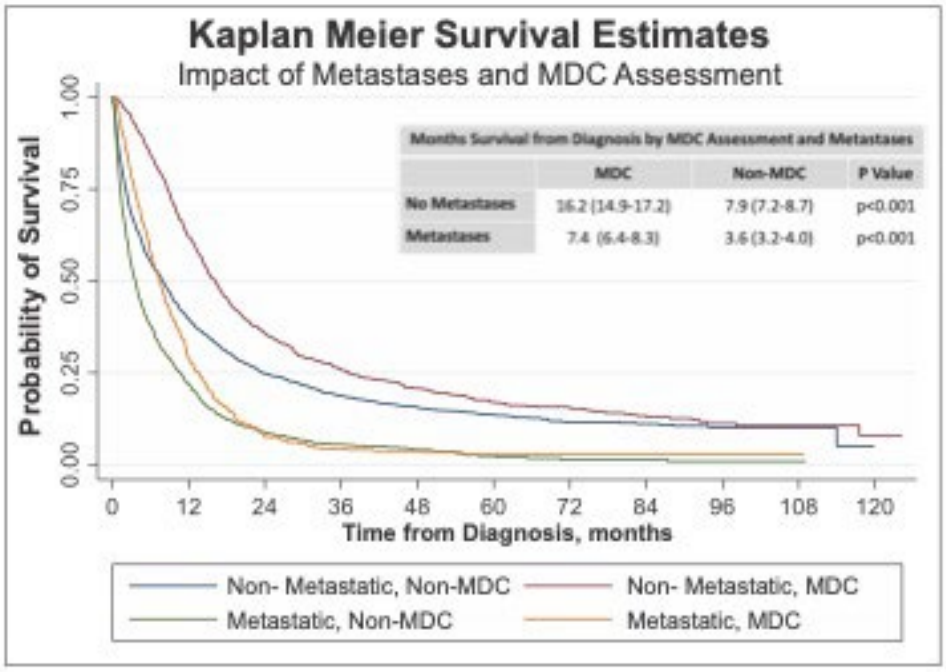
Background: National studies suggest pancreatic cancer patients receive surgery and indicated therapies at surprisingly low rates. Social determinants of health such as socioeconomic status (SES) have been shown to impact treatment and survival. We have previously shown that management by a pancreatic cancer multidisciplinary clinic (MDC) improves outcomes and eliminates socioeconomic disparities in survival for patients undergoing surgery. The aim of this analysis was to examine patient factors that predict referral to MDC and subsequent outcomes for all pancreatic cancer patients treated within a large regional health network.

Methods: We conducted a retrospective cohort study examining all patients diagnosed with pancreatic cancer from 2010-2018 at any of 15 hospitals in our network, including a high-volume pancreatic cancer. Low SES as assessed by the national area deprivation index (ADI) was our primary independent variable of interest. Baseline patient characteristics, oncologic features, treatment, and survival were also evaluated. Predictors of MDC referral were assessed by logistic regression.

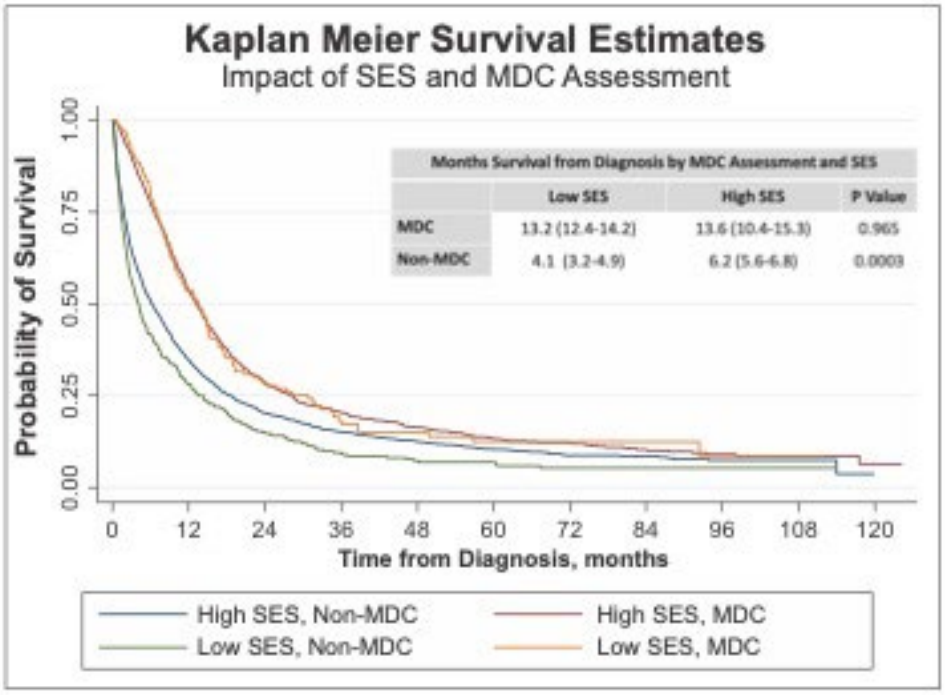
Results: During the study period, 4,539 patients were identified with pancreatic cancer. Among these, 1,516 (33.4%) were evaluated in the MDC. Patients seen outside of the MDC were older (70 vs 69 years), less married (34% vs 45%), and had lower rates of private insurance (34% vs 43%; all $p< 0.001$). On adjusted analysis, older age (OR 0.87 per decade), low SES (OR 0.78), travel distance (OR 0.54), and metastatic disease on diagnosis (OR 0.39) were all significant negative predictors of MDC assessment (all $p< 0.05$). Marriage (OR 1.42) and private insurance (OR 1.23) were associated with MDC assessment (both $p< 0.001$). On adjusted analyses, MDC was associated with higher odds of chemotherapy (OR 2.8), surgery (OR 1.75), and radiation treatment (1.89; all $p< 0.001$). Additionally, there were higher odds of clinical trial participation (OR 3.92) and palliative care referral (1.22; both $p< 0.001$). Median survival was longer in the MDC group compared to the non-MDC cohort (13.2 vs 5.9 mos, $p< 0.001$) in when examined by both early stage and metastatic disease (Figure 1A). Examining survival by SES, outside of the MDC, high SES patients had improved survival (6.2 vs 4.1 mos, $p< 0.001$). However, among patients treated within the MDC, there was no survival difference between high and low SES patients (13.6 vs 13.2 mos, $p=0.97$) (Figure 1B).

Conclusion: This analysis is the first to evaluate barriers to MDC referral for patients with pancreatic cancer. We find that an interplay of patient and oncologic factors were associated with MDC assessment. MDC was also associated with higher rates of treatment and improved survival. Addressing barriers to MDC referral could improve care for patients with pancreatic cancer of all stages and help ensure more equitable outcomes.

A)


Kaplan Meier Survival Estimates
Impact of Metastases and MDC Assessment
Months Survival from Diagnosis by MDC Assessment and Metastases
MDC
Non-MDC
P Value
No Metastases
16.2 (14.9-17.2)
7.9 (7.2-8.7)
p<0.001
Metastases
7.4 (6.4-8.3)
3.6 (3.2-4.0)
p<0.001
Probability of Survival
0.00
0.25
0.50
0.75
1.00
0
12
24
36
48
60
72
84
96
108
120
Time from Diagnosis, months
Non- Metastatic, Non-MDC
Non- Metastatic, MDC
Metastatic, Non-MDC
Metastatic, MDC

B)


Kaplan Meier Survival Estimates
Impact of SES and MDC Assessment
Months Survival from Diagnosis by MDC Assessment and SES
Low SES
High SES
P Value
MDC
13.2 (12.4-14.2)
13.6 (10.4-15.3)
0.965
Non-MDC
4.1 (3.2-4.9)
6.2 (5.6-6.8)
0.0003
Probability of Survival
0.00
0.25
0.50
0.75
1.00
0
12
24
36
48
60
72
84
96
108
120
Time from Diagnosis, months
High SES, Non-MDC
High SES, MDC
Low SES, Non-MDC
Low SES, MDC

44. SURVIVAL BENEFIT OF STEREOTACTIC BODY RADIATION THERAPY VERSUS CONVENTIONAL RADIATION THERAPY IN PATIENTS WITH PANCREATIC CANCER

H Patel, M Baker, B Azab

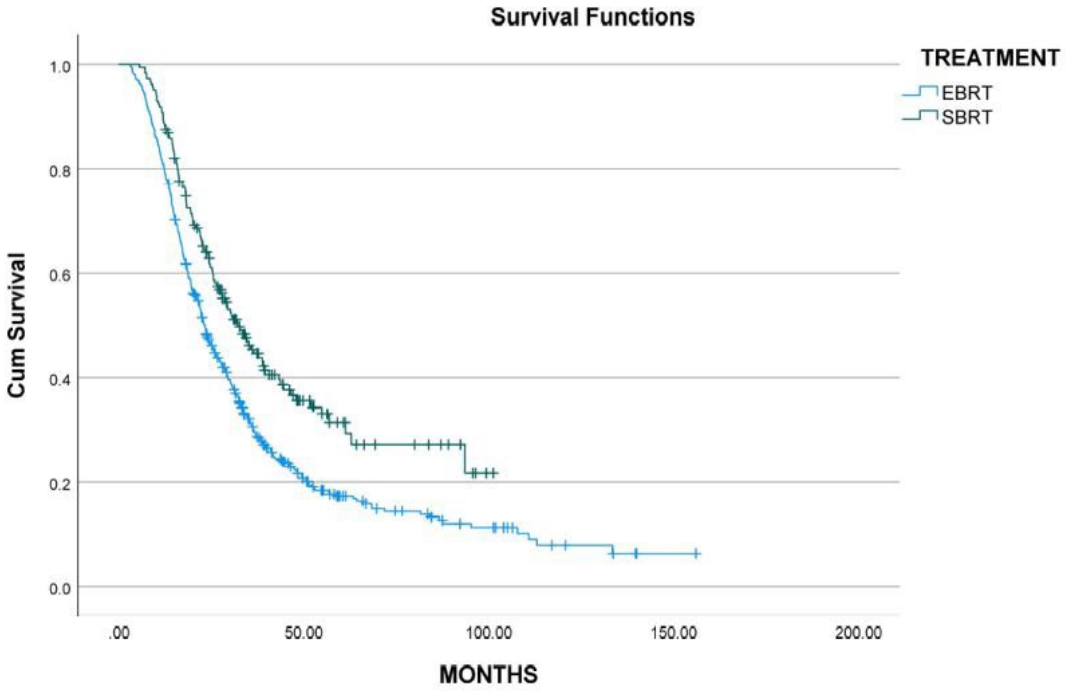
Presenter: Hardik Patel DO | Northwell Health - Staten Island University Hospital, United States

Background: Pancreatic cancer is the seventh leading cause of cancer-related death worldwide, with a higher incidence in developed countries. Despite emerging therapeutic options, mortality remains abysmally high. Neoadjuvant concepts are increasingly being used due to the complication rate of pancreatic surgery and the high rate of primary irresectability. Recent literature suggests utilizing neoadjuvant chemoradiotherapy can increase R0 resection. Neoadjuvant Stereotactic Body Radiation Therapy (SBRT) is gaining increasing interest as it reduces radiation associated toxicity and minimized delay to conventional neoadjuvant chemotherapy as compared to conventional therapy.

Methods: NCDB data were obtained for all patient diagnosed with Pancreatic cancer from 2004 – 2018. Patients included in this study include those who underwent neoadjuvant radiation therapy, neoadjuvant chemotherapy, and had available overall survival metrics recorded. Additionally, patients who had unknown doses of radiation therapy or unknown modality of radiation therapy were also excluded. Overall survival was compared using Kaplan-Meier (log-rank) analysis.

Results: 184 patients were identified who received neoadjuvant SBRT and 467 patients were identified who received neoadjuvant EBRT in the form of Conformal/3-D Conformal therapy or Intensity Modulated Radiation Therapy (IMRT). The median age at the time of diagnosis was slightly higher for SBRT group compared to EBRT (66 vs 64). Patients receiving SBRT received 5 fractions for an average total of 3400cGy. Patients receiving conventional EBRT received 25 fractions for an average total of 4730cGy. Median survival for patients undergoing EBRT compared to SBRT was 23.2 months versus 32.1 months respectively, $p < 0.001$.

Conclusion: Patients who underwent neoadjuvant SBRT compared with conventional EBRT had higher overall median survival. Further clinical study in the form of multi-institutional trials is warranted to establish the role of neoadjuvant SBRT in the treatment of pancreatic cancer.


Survival Functions
TREATMENT
EBRT
SBRT
Cum Survival
1.0
0.8
0.6
0.4
0.2
0.0
.00
50.00
100.00
150.00
200.00
MONTHS

45. IS SURVIVAL ENHANCED WITH THE ROBOTIC APPROACH FOR PANCREATICODUODENECTOMY: A PROPENSITY SCORE-MATCH STUDY

S Ross, I Sucandy, A Espeut, D Nguyen, K Crespo, C Syblis, P Vasanthakumar, A Rosemurgy
Presenter: Harel Jacoby MD | Digestive Health Institute Tampa, United States

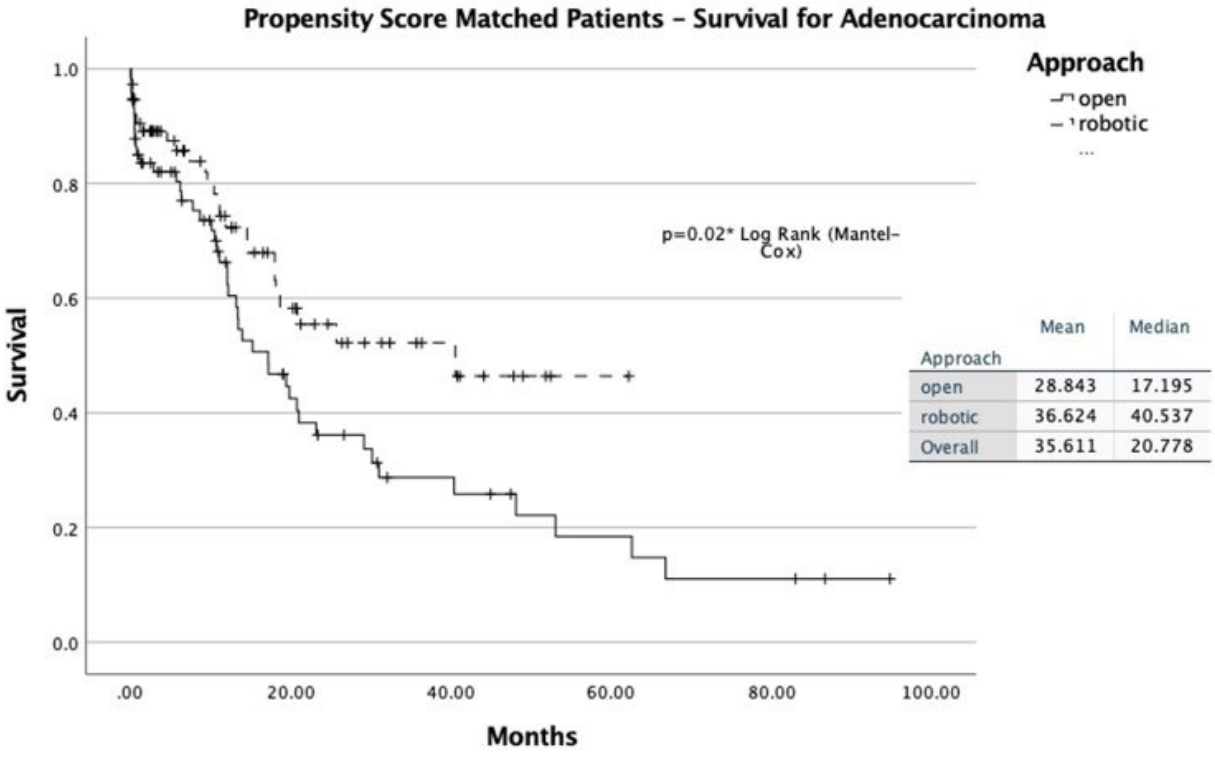
Background: Robotic surgery is a burgeoning minimally invasive approach to pancreaticoduodenectomy. This study was undertaken to compare survival after robotic vs. 'open' pancreaticoduodenectomy for ductal adenocarcinoma utilizing 'all comers' and propensity score-matched patients.

Methods: With IRB approval, we prospectively followed 521 patients who underwent robotic (N=311) or 'open' (N=210) pancreaticoduodenectomy. Patients who underwent robotic (N=75) or 'open' (N=75) pancreaticoduodenectomy were propensity score-matched by age, sex, and AJCC stage. Neoadjuvant therapy was very uncommonly administered, and adjuvant therapy was stressed (FOLFIRINOX for patients < 70 years and gemcitabine + abraxane for patients >70 years). Data are presented as median(mean±SD).

Results: Operative duration was longer and estimated blood loss (EBL) and length of stay (LOS) were less with robotic pancreaticoduodenectomy [421(409±94.0) vs. 267(254±81.2) minutes; 307(150±605.3) vs. 444(255±353.1)mL; 7(5±5.1) vs. 11(8±9.5) days; pIII, p=0.30), in-hospital mortality (p=0.61), or 30-day readmission rate (p=0.19). Median survival after robotic vs. 'open' pancreaticoduodenectomy was 37 vs. 24 months (p=0.02).

For propensity score-matched patients, operative duration for robotic pancreaticoduodenectomy was longer [442(438±117.7) vs. 261(249±67.1) minutes] and EBL was less [269(200±296.1) vs. 468(300±394.9)mL], as was LOS [7(5±5.1) vs. 10(7±8.6) days, (pIII, p=0.31) or in-hospital mortality (p=0.40); 30-day readmissions were fewer after robotic pancreaticoduodenectomy [7% vs. 20%, p=0.03]. Median survival for the robotic vs. 'open' approach was 41 vs. 17 months (p=0.02).

Conclusion: Patients that underwent robotic pancreaticoduodenectomy had longer operations, less EBL, shorter LOS, and fewer 30-day readmissions; they lived much longer than patients who underwent 'open' pancreaticoduodenectomy. We believe robotic pancreaticoduodenectomy provides salutary and survival benefits for reasons yet unknown.



Approach	Mean	Median
open	28.843	17.195
robotic	36.624	40.537
Overall	35.611	20.778

46. PROGNOSTIC VALUE OF CARCINOEMBRYONIC ANTIGEN (CEA) FOR PATIENTS WITH LOCALIZED PANCREATIC CANCER

EP Ward, AN Krepline, KK Christians, CN Clarke, B George, PS Ritch, M Kamgar, P Chisholm, S Doucette, SD O'Connor, WA Hall, BA Erickson, DB Evans, S Tsai

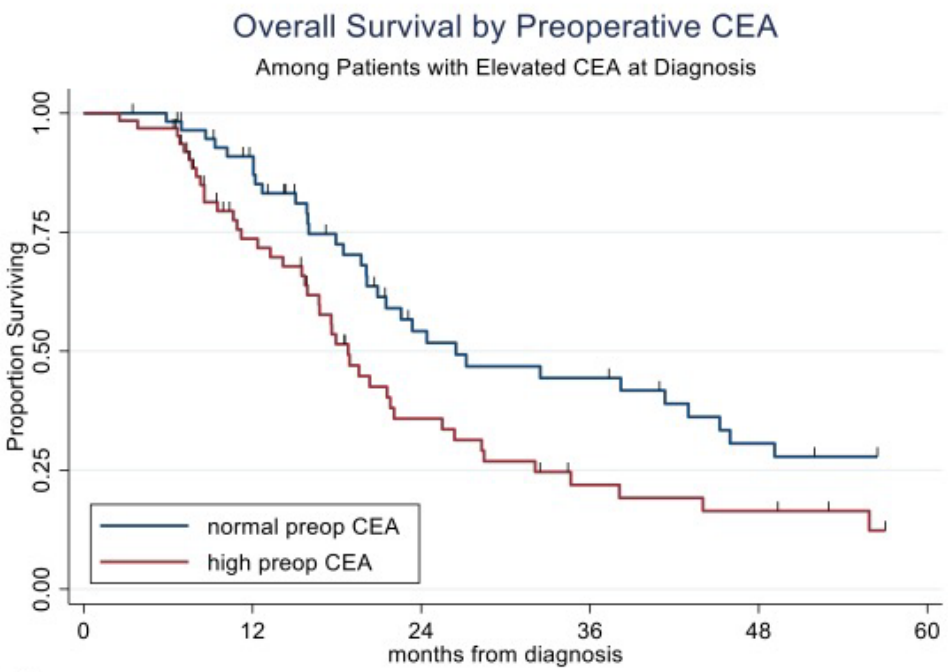
Presenter: Erin P. Ward MD | Medical College of Wisconsin, United States

Background: Carbohydrate antigen 19-9 (CA19-9) is the most common biomarker utilized in pancreatic cancer (PC). However, 20-30% of patients will have a non-informative CA19-9. Carcinoembryonic antigen (CEA) is an alternative biomarker whose utility in PC is not well described.

Methods: Patients with operable PC treated with neoadjuvant therapy from 2009-2019 were identified. CEA and CA19-9 values were abstracted at diagnosis and after neoadjuvant therapy (preop) and classified as high or normal (normal: CEA</= 4.7 ng/mL; CA19-9 </= 35 U/mL).

Results: Of the 415 patients, CEA at diagnosis was high in 123 (30%) and normal in 292 (70%). CA19-9 was non-informative in 113 (27%) patients, of theses, CEA was elevated in 27 (22%). Of the 123 patients with a high CEA at diagnosis, following neoadjuvant therapy, CEA levels normalized in 59 (48%) patients. The median overall survival (mOS) for all 415 patients was 27 months (mo); 31 mo for the 292 patients with a normal CEA at diagnosis and 22 mo for the 113 patients with a high CEA (p=0.004). Of the 123 patients with a high CEA at diagnosis, the mOS was 26 mo for the 59 patients with normal preop CEA and 19 mo for the 64 patients with high preop CEA (p=0.02). On multivariable analysis, elevated preop CEA was associated with a 1.80-fold (95% CI: 1.13-2.89) increased risk of death.

Conclusion: CEA is an important prognostic biomarker in patients with PC and is elevated in 22% of patients with a normal CA19-9. CEA response to neoadjuvant treatment is prognostic of survival.



Number at risk						
normal preop CEA	58	47	22	18	11	8
high preop CEA	63	38	16	8	6	2

47. BIOTISSUE TRAINING CURRICULUM CORRELATES WITH INTRAOPERATIVE PERFORMANCE FOR ROBOTIC PANCREATICODUODENECTOMY

JD Kraftician, K Kuchta, MS Zenati, S AlMasri, HH Khachfe, M Maalouf, A Desilva, AY Hammad, A Paniccia, KK Lee, HJ Zeh, AH Zureikat, ME Hogg

Presenter: Jasmine D. Kraftician BS | University of Pittsburgh Medical Center, United States

Background: There has been a rise in the use of the robotic platform for minimally invasive pancreatic surgery. Robotic training curricula aim to aid surgeons in attaining robotic proficiency, but their success remains to be examined. We hypothesized that performance on inanimate drills correlates with intraoperative (intra-op) performance during a robotic pancreaticoduodenectomy (RPD).

Methods: Thirty-one surgical oncology fellows participated in a 5-step proficiency-based robotic training curriculum from 2014-2018. The curriculum included inanimate drills of a continuous hepaticojejunostomy (HJ) and gastrojejunostomy (GJ) and operative experience. Video review of biotissue and intra-op performance during these anastomoses was performed. Performance was evaluated by time, errors, and Objective Structured Assessment of Technical Skills (OSATS). Spearman's correlations were calculated for prior experience, biotissue performance, and intra-op performance.

Results: Fellows completed an average of 14.1±10.5 biotissue drills including 5.1±3.7 HJ and 4.3±3.3 GJ. Biotissue GJ and HJ showed a decrease in time and errors, and an increase in OSATS. Longer total time on biotissue GJ and HJ correlated with improvement in time (ρ=-.51) and errors (ρ=-.45). Average errors on biotissue GJ and longer time on the last attempt correlated with lower average intra-operative GJ OSATS (ρ=-.64; ρ=-.66). More errors on the last biotissue GJ correlated with longer average intra-op GJ time (ρ=.58). Errors on the first and average biotissue HJ correlated with lower OSATS for the first intra-op HJ (ρ=-.737; ρ=-.80). The more days separating biotissue and the second intra-op HJ correlated with more time to complete the intra-op HJ (ρ=.92).

Conclusion: The results support correlation between inanimate and intra-op performance which may expedite surgeon proficiency. Further research is warranted to examine whether benefits translate to fewer surgical complications and improved patient outcomes.

	Hepaticojejunostomy				Gastrojejunostomy			
	Time		OSATS[a]		Time		OSATS[a]	
Biotissue	First	Average	First	Average	First	Average	First	Average
First Errors	.64*	.49	-.74*	-.42	.01	-.15	-.32	-.49
Last Errors	.28	.24	-.46	-.08	.28	.58*	-.16	-.19
Average Errors	.57	.03	-.80*	-.43	.11	.18	-.50	-.64*

*$p < .05$

[a]Objective Structured Assessment of Technical Skills

48. SERUM B7-H3 LEVELS AS A NOVEL PROGNOSTIC BIOMARKER TO PREDICT RESECTABILITY IN PDAC PATIENTS TREATED WITH NEOADJUVANT FOLFIRINOX

M Nebbia, S Arya, G Lionetto, M Ventin, V Deshpande, S Ferrone, CR Ferrone
Presenter: Martina Nebbia MD | Massachusetts General Hospital, United States

Background: B7-H3 is a member of the B7 family of immune-regulatory ligands and is a costimulatory molecule promoting the T cell response in vitro. B7-H3 suppresses the tumor antigen-specific immune response, leading to aggressive cancer biology and increased metastatic potential. Specifically, high expression of membranous B7-H3 is an independent predictor of poor survival in PDAC patients. In addition to the membranous form of B7-H3, serum B7-H3 (sB7-H3) has been identified as a potential tumor marker in different cancer types. Several studies have demonstrated an association between increased serum B7-H3 (sB7-H3) levels and poor prognosis in patients with malignancies. The aim of this study was to investigate the ability of sB7-H3 to predict the burden of disease in patients with pancreatic ductal adenocarcinoma (PDAC).

Methods: The B7-H3 sera levels were tested at the time of the operation for PDAC in patients receiving neoadjuvant FOLFIRINOX or no neoadjuvant therapy between April 2016 and April 2019 at our Institution. Serum B7-H3 was measured using an enzyme-linked immunosorbent assay (ELISA). Healthy donors (HD) were used as a negative control. Cox proportional hazards regression model was used to assess disease-free survival (DFS).

Results: In our pilot experiment, we analyzed the sera of patients of 21 patients of whom 1) were treated with neoadjuvant FOLFIRINOX and underwent pancreatic resection (n= 15); 2) were treated with neoadjuvant FOLFIRINOX and deemed inoperable in the operating room due to locally advanced disease (n= 4) or microscopic metastatic disease (n=2); 3) healthy donors (HD) with no history of malignancy as control group. Our preliminary data demonstrate that serum B7-H3 levels are significantly higher in PDAC patients who received neoadjuvant FOLFIRINOX and were unresectable compared to those who were resected (mean 20 ng/mL; range: 0–60.5 ng/mL vs 1.3 ng/mL; range: 0–4 ng/mL; $p < 0.05$). Moreover, higher sB7-H3 was associated with shorter survival in PDAC patients who received neoadjuvant treatment with FOLFIRINOX followed by surgical resection. Serum B7-H3 was not detectable in the control group.

Conclusion: Our preliminary data suggest that serum B7-H3 may be a useful biomarker to assess the burden of disease in PDAC patients. Patients treated with neoadjuvant FOLFIRINOX, but continue to have high levels of sB7-H3, may benefit from additional systemic therapy as this may be a marker of locally advanced or metastatic disease.

49. DOES MINIMALLY INVASIVE SURGERY HAVE DIFFERENT IMPACT ON RECURRENCE AND OVERALL SURVIVAL IN PATIENTS WITH PANCREATIC HEAD VERSUS BODY/TAIL CANCER?

SH Choi, K Kuchta, AE Rojas, D Sood, P Paterakos, MS Talamonti, ME Hogg
Presenter: Sung Hoon Choi MD | Academic Medical Center, United States

Background: The technical difficulty and perioperative outcomes of minimally invasive surgery (MIS) are quite different between pancreatic head cancers and body/tail cancers. Therefore, we aimed to investigate the impact of MIS and tumor location on recurrence and overall survival between patients with pancreatic head versus body/tail cancers.

Methods: This study is a retrospective analysis of patients who underwent curative-intent surgical resection for pancreatic ductal adenocarcinoma between March 2007 to December 2020 at a single institution. The clinical characteristics of the patients and perioperative outcomes, as well as risk factors associated with recurrence and long-term outcomes were compared according to tumor location and operative modality using Kaplan-Meier curves and multivariate analysis.

Results: During the study period, 288 patients underwent surgical resection for pancreatic head cancer and 87 patients for body/tail cancer. More patients were treated by an MIS approach in the body/tail group (33.3% vs. 10.1% $p< 0.0001$) than the head group. The baseline characteristics were comparable between both groups including the initial resectability categorization and rate of neoadjuvant therapy; however, the body/tail group was older (71 ± 10 vs. 68 ± 10, $p=0.0209$). The rates of clinically relevant postoperative pancreatic fistula and major postoperative complication were similar between groups. Despite a larger mean tumor size and higher T-stage in the body/tail group, the pathologic AJCC stage was higher in head group with increased N-stage (69.5% vs. 50.0% of ≥N1, $p=0.0030$). R0 resection rates were comparable with 81.3% [head] versus 83.9% [boday/tail] ($p=0.5728$). The receipt of adjuvant chemotherapy was also similar between groups 68.4% [head] vs. 71.3% [body/tail] ($p=0.6128$). There was no difference in local or systemic recurrence patterns according to the primary tumor location and surgical modality. There was no significant difference in disease-free and overall survival between head versus body/tail groups and open versus MIS groups. On sub-group analysis by-stage, the MIS group had a significantly worse disease-free survival in patients with Stage III pancreatic head cancer ($p=0.0203$). On multivariate analysis, vascular resection, adjacent organ resection, lymph node metastasis, and poor differentiation were risk factors of any recurrence, while vascular resection, lymph node metastasis, and R1 resection were for local recurrence.

Conclusion: Recurrence patterns and overall-survival rates of patients were not different in tumor location and surgical approaches. However, care must be taken in the application of MIS in stage III pancreatic head cancer, which showed inferior disease-free survival, but similar overall survival than patients who underwent open surgery.

50. DEFINING THE OPERATIVE TIME THRESHOLD FOR SAFETY IN PATIENTS UNDERGOING ROBOTIC PANCREATICODUODENECTOMY

AM Delman, EC Donovan, KM Turner, J Whitrock, RC Quillin III, SA Shah, SH Patel, SA Ahmad, GC Wilson
Presenter: Eileen Donovan MD | University of Cincinnati, United States

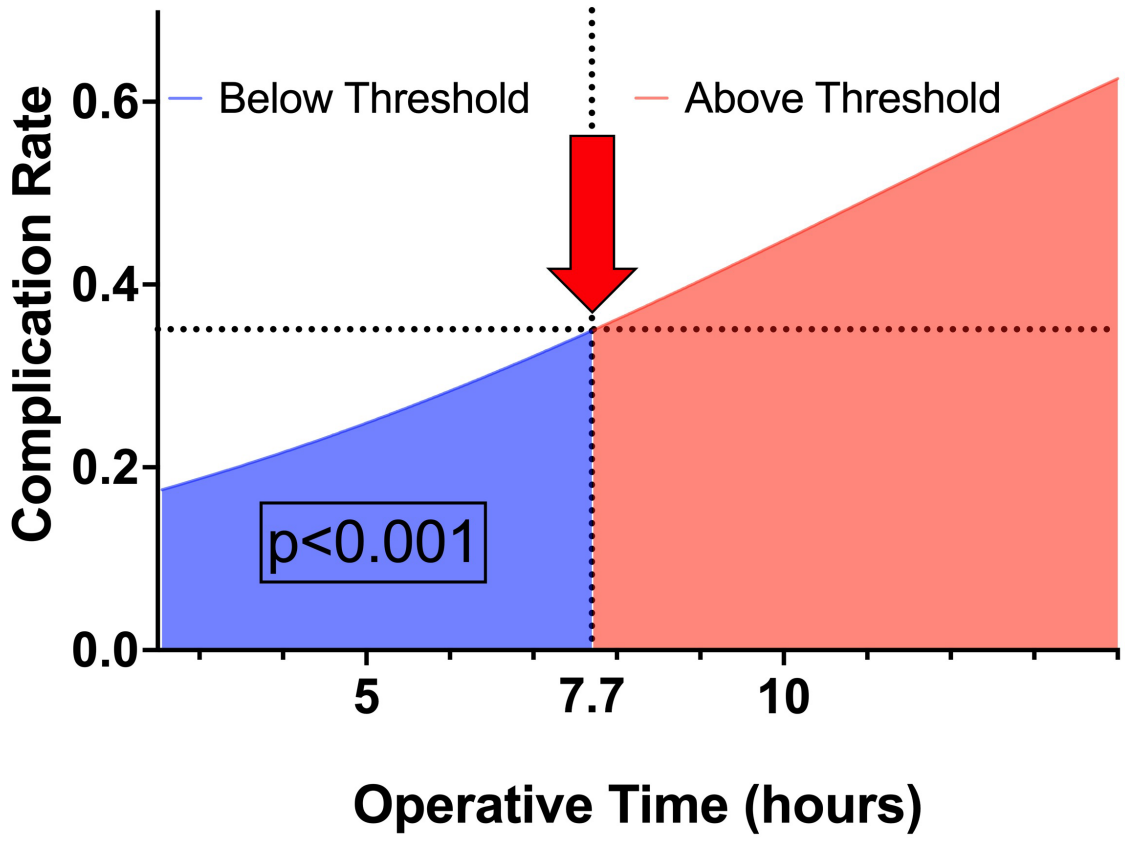
Background: Robotic pancreaticoduodenectomy (RPD) is a safe and efficacious operation in appropriately selected patients. However, the increased complexity of a robotic approach results in longer operative times. It is unknown at what operative time the risks of a longer RPD exceed those of a shorter open pancreaticoduodenectomy (OPD).

Methods: The NSQIP database was queried for patients who underwent RPD and OPD between 2014-2019. Emergent operations and vascular resections were excluded. The benchmark OPD control was defined as the fastest tertile with regards to operative time. Multivariable and sensitivity analysis were employed to identify the operative time threshold (OTT).

Results: 6,270 patients were included in the study with 939 (15.0%) undergoing RPD and 5,331 (85.0%) as a benchmark OPD control. Incidence of major morbidity or mortality was similar in the RPD and OPD cohorts (32.8% vs. 35.1%, p=0.17). The median operative time for RPD was longer than OPD (6.7 vs. 4.1 hours, p< 0.01). Stepwise logistic regression analysis identified operative time as the only variable associated with increased complications in RPD patients (OR: 1.20, 95% CI: 1.12-1.29, p< 0.01). The OTT – the time above which RP patients experience greater than the 35.1% OP benchmark complication rate - was identified as 7.7 hours (FIGURE 1). Furthermore, on subgroup analysis of RPD patients, the slowest tertile had more complications than the middle and fastest tertiles (41.5% vs. 32.2% vs. 24.5%, p< 0.01).

Conclusion: RPD is associated with similar or improved outcomes when the operative time threshold of 7.7 hours is met when compared to OPD.

Operative Time Threshold for Robotic Pancreaticoduodenectomy



51. VIDEO ANALYSIS OF GASTRO-JEJUNOSTOMY TO PREDICT DELAYED GASTRIC EMPTYING AFTER ROBOTIC PANCREATODUODENECTOMY; PRELIMINARY ANALYSIS OF TWO CENTERS

MJW Zwart, B van den Broek, DSJ Paijens, SLM Zwetsloot, A Comandatore, T Geraedts, RJ Schipper, OR Busch, TCK Tran, MD Luyer, J Schreinemakers, JH Wijsman, GP van der Schelling, IHJT de Hingh, JSD Mieog, BA Bonsing, K Takagi, RF de Wilde, L Morelli, HJ Zeh III, AH Zureikat, ME Hogg, B Groot Koerkamp, MG Besselink

Presenter: Diederik Paijens | Academic Medical Center, Netherlands

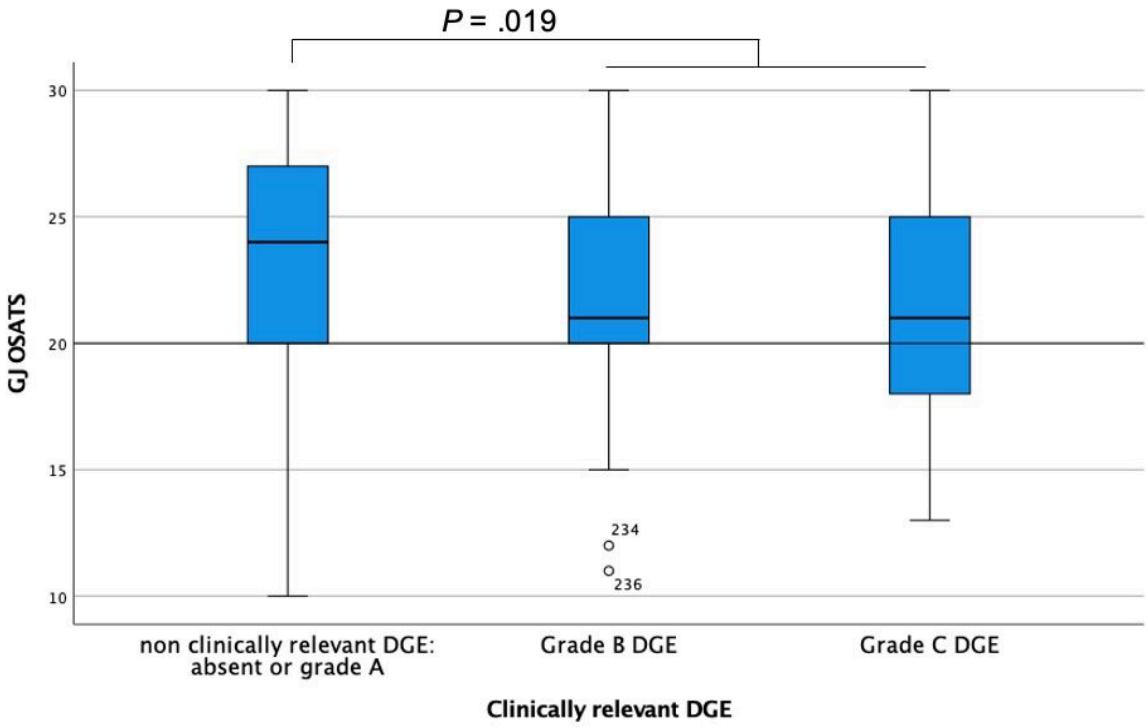
Background: Robotic pancreatoduodenectomy (RPD) has proven to be as safe as open pancreatoduodenectomy (OPD), sometimes even more favorable in terms of overall length of hospital stay and complication rates. However, postoperative incidence of morbidity is still substantial. To this day, improved surgical performance has not yet been linked to a decrease in gastric complications in RPD.

The aim of this study is to identify learning curves for robotic gastrojejunostomy during RPD and the predictive value of the OSATS score for gastrojejunostomy (GJ) complications according to the Birkmeyer and UPMC method.

Methods: Videos of GJ during RPD were analyzed in a retrospective multicenter (LAELAPS-3) cohort by a grader blinded for surgeon and surgical experience. Surgical performance was scored with OSATS. The main outcome measures are the combined OSATS scores over time (learning curve). Secondary outcome is the correlation between OSATS scores and delayed gastric emptying (DGE, ISGPS grade A/B/C).

Results: Between 2017 and 2021, 324 patients underwent RPD with videos of the GJ available in 97 patients. DGE occurred in 42.6% of patients. Mean GJ-OSATS was 22.4 (SD = 5.0). CUSUM analysis of GJ-OSATS identified an inflection point at 47 RPD procedures. The rate of DGE B/C was 41% before and 20% after this inflection point (P=0.005). Overall, patients without DGE had higher OSATS scores (23.4, 95%CI 22.1-24.6) vs patients with DGE (21.1 95%CI 19.6-22.7), this remained consistent for DGE Grade B/C (P=0.019), see Figure 1. When surgical performance was scored > 21, DGE rates were significantly lower (57% vs 25%, P=.006).

Conclusion: Using OSATS to score GJ in RPD is a useful tool for identifying learning curves. Higher OSATS scores correlate with a decreased risk of DGE. OSATS could serve as a tool for assessment of robotic GJ in training programs and during implementation.


P = .019
30
25
20
15
10
GJ OSATS
234
236
non clinically relevant DGE: absent or grade A
Grade B DGE
Grade C DGE
Clinically relevant DGE

52. HYPERGLYCEMIA SENSITIZES PANCREATIC CANCER TO MACROPHAGE-SPECIFIC IMMUNOTHERAPIES: AN UPDATE

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

Background: Pancreatic cancer (PC) is resistant to immunotherapies. This may be due to the harsh, hypoglycemic tumor microenvironment which is not conducive to anti-tumor immune cell function. To this point, anti-tumor M1 macrophages are glycolytic and require high concentrations of glucose. Conversely, tumor-associated M2 macrophages rely on mitochondria, which utilize glucose more efficiently. Herein, we attempt to sensitize PC to macrophage-specific immunotherapies by augmenting glucose levels.

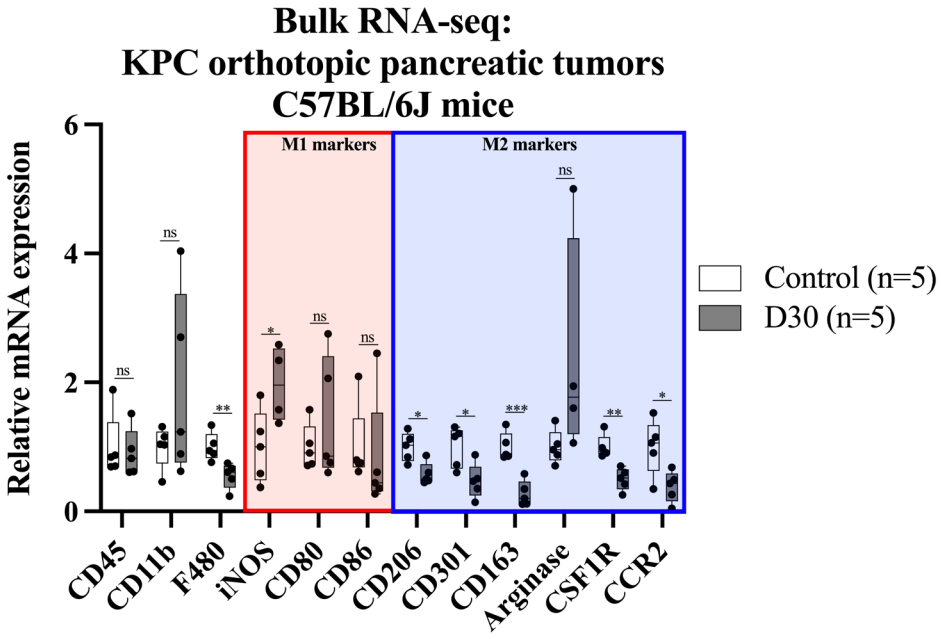
Methods: Murine PC cells (KPC) and macrophages were cultured in hypoglycemic (≤2.5mM) or hyperglycemic (25mM) conditions. Phenotypic (western blot, flow cytometry) and metabolic (seahorse, LC-MS metabolomics) assays were performed in vitro. KPC cells were orthotopically injected into the pancreas of mice for in vivo studies. Bulk RNA-sequencing was performed on tumor-bearing mice provided with regular drinking water or 30% dextrose water (D30). Additionally, tumor-bearing mice were randomized to pexidartinib (a CSF1R inhibitor) or vehicle and received either normal water or D30.

Results: The bidirectional role of macrophages was demonstrated using an in vitro co-culture experiment: M2 macrophages increased KPC cell growth by 30%, whereas M1 macrophages decreased growth by 95%. Further, immunocompromised mice bearing KPC tumors survived a median of 19 days and developed hepatic metastases. However, immunocompetent mice bearing identical tumors survived a median of 45 days ($p< 0.001$) and did not develop metastases.

As glucose concentrations decreased in culture media over time, protein levels of an M1 marker (inducible nitric oxide, iNOS) decreased and an M2 marker (arginase) appeared, suggesting a phenotypic switch. Similarly, M1 macrophages underwent a metabolic shift in hypoglycemic conditions and adopted an M2-like profile (i.e., greater mitochondrial energy production and decreased glycolysis) assessed using both seahorse and LC-MS metabolomics assays. Using bulk RNA-sequencing, tumors of mice provided with regular water or D30 had similar mRNA expression of CD45 (a pan-immune cell marker), but decreased expression of F4/80 (a pan-macrophage marker). In line with our in vitro data, mice treated with D30 had higher expression of iNOS (a M1 macrophage marker) and decreased expression of CD206, CD301, CSF1R, and CCR2 (all tumor-associated M2 markers) (Figure).

Pexidartinib augmented M1 iNOS protein levels and simultaneously decreased M2 arginase levels. On an in vitro flow cytometric analysis, the percentage of M2 macrophages decreased as glucose concentrations were increased (33.7% vs 38.0%), and decreased further when pexidartinib was combined with hyperglycemia (20.5%). Mice treated with pexidartinib and D30 had improved median survival relative to mice receiving pexidartinib alone (median survival: 42 (IQR: 38, 52) vs 34 (IQR: 32, 38) days, $p< 0.05$). Of note, pexidartinib alone did not improve survival as compared to vehicle or D30.

Conclusion: Hyperglycemic conditions promote M1 survival and function, while preventing a switch to an M2 phenotype in both in vitro and in vivo assays. Hyperglycemia appears to sensitize PC to an otherwise ineffective CSF1R inhibitor. We are currently testing the efficacy of D30 and pexidartinib in a model of hepatic metastases and studying effectiveness of D30 combined with PF-4136309, a CCR2 inhibitor. We hope these data further support the concept of increasing peripheral glucose levels to sensitive PC to immunotherapies.


Bulk RNA-seq:
KPC orthotopic pancreatic tumors
C57BL/6J mice
Relative mRNA expression
6
4
2
0
M1 markers
M2 markers
ns
ns
**
*
ns
ns
*
*
***
ns
**
*
CD45
CD11b
F480
iNOS
CD80
CD86
CD206
CD301
CD163
Arginase
CSF1R
CCR2
Control (n=5)
D30 (n=5)

53. THE EFFECT OF NEOADJUVANT THERAPY ON IMMUNE PROFILING OF PANCREATIC DUCTAL ADENOCARCINOMA: A PROSPECTIVE STUDY OF THE PREOPANC-1 RANDOMIZED CONTROLLED TRIAL.

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Presenter: Dana A. Mustafa PhD | Academic Medical Center, Netherlands

Background: The randomized phase III trial (PREOPANC-1) that was performed in 16 centers in the Netherlands compared the effects of preoperative chemoradiotherapy (Gemcitabine and 2.4 Gy radiation) versus immediate surgery for resectable and borderline resectable pancreatic cancer. The outcomes of the secondary endpoints and predefined subgroup analyses suggest an advantage of the neoadjuvant approach. The aim of the present study was to investigate the changes in the immune microenvironment and infiltration caused by the neoadjuvant treatment.

Methods: To that aim, we collected formalin-fixed, paraffin-embedded pancreatic cancer samples from all centers that participated in the PREOPANC -1 trial. We performed targeted gene expression using the PanCancer Immune Profiling panel of NanoString.

Results: Comparing 50 samples of the patient who were subjected to neoadjuvant treatment to 46 treatment-naïve samples showed a distinct genetic profile induced by the neoadjuvant therapy. More than 250 immune-related genes were significantly differentially expressed between the two groups of samples.

The results indicate that neoadjuvant therapy resets the innate immune activation in the tissue samples. A significantly higher infiltration of CD14+, CD33+, CSF1R+, and CD163+, MRC1+ cells were found in samples of the neoadjuvant arm. In contrast, B cells and various subtypes of T cells like CD8+ and FOXP3+ showed a significant decrease in the same samples. Pathway analysis revealed that the neoadjuvant treatment stimulated the expression of genes related to the complement activation, chemotaxis, and wound repair, while genes related to lymphocyte activation and adaptive immune responses were dominant in the treatment-naïve arm.

Conclusion: In conclusion, this is the first comprehensive study to describe the immune-molecular changes as a result of neoadjuvant therapy in a randomized clinical trial. The results reveal the enrichment of the myeloid compartment following neoadjuvant therapy which was significantly associated with a survival benefit for the patients. Studying the personalized effect of neoadjuvant therapy will guide choosing the appropriate combined therapy for pancreatic cancer.

54. DOES ONE CYCLE OF FFX TREATMENT CHANGE THE BLOOD IMMUNE PROFILE IN PDAC PATIENTS?

CWF van Eijck, F van der Sijde, W de Koning, B Groot Koerkamp, CHJ van Eijck, DAM Mustafa
Presenter: Casper W. van Eijck BSc | Erasmus University Medical Center, Netherlands

Background: FOLFIRINOX (FFX) chemotherapy has emerged to become one of the most favorable treatments for pancreatic ductal adenocarcinoma (PDAC). The aim of this study was to investigate the earliest possible effect of FFX in the blood of PDAC patients to create a gene signature capable of predicting the response outcome.

Methods: PDAC patients of different disease stages who received FFX treatment were included in this study. Clinical information including age, gender, the systematic immune inflammation index (SIII), the neutrophil-to-lymphocyte ratio (NLR) and CA19-9 was collected for all patients. The treatment response was repeatedly evaluated following the Response Evaluation Criteria in Solid Tumors (RECIST) criteria 1.1 after every 4 cycles of FFX treatment. Tempus blood samples of PDAC patients were collected before and after the first cycle of FFX treatment. RNA was isolated and profiled using the PanCancer Immune profile panel of NanoString Technology that includes 730 immune-related genes and 40 housekeeping genes. Expression data were analyzed by using the nSolver Advanced Analysis 4.0 software. Paired analysis was conducted, and the adjusted p-value was calculated using the Benjamini-Hochberg method.

Results: In total, 68 patients were included in this study (136 blood samples). FFX treatment induced a significant change in the immune profile of the blood sample: more than 395 genes were differentially expressed when comparing before and after one cycle of FFX samples (p-value 2). Conversely, FFX treatment suppressed the overall cell, NK cell and T cell functions pathway (p-value 2). Moreover, FFX treatment increased the relative abundance of conventional dendritic 2 and monocyte cells ($p < 0.01$). In-depth analysis based on the clinical information and the response to therapy is being performed and the results will be presented at the conference.

Conclusion: This is the first study that describes the earliest effect of FFX chemotherapy on the immune-related genes and cells in blood samples of PDAC patients. The data helps in predicting the response to FFX treatment which avoids giving ineffective but toxic treatment to PDAC patients.

55. VENOUS THROMBOSIS FOLLOWING VASCULAR RESECTION DURING PANCREATICODUODENECTOMY: INCIDENCE AND RISK FACTORS

HH Khachfe, M Maalouf, AY Hammad, S lMasri, A deSilva, I Nassour, H Liu, J Kraftician, KK Lee, AH Zureikat, A Paniccia

Presenter: Hussein H. Khachfe MD | University of Pittsburgh Medical Center, United States

Background: Various techniques have been described for venous resection and reconstruction during pancreaticoduodenectomy (PD), but the incidence of thrombosis associated with each method remains undefined. Our aim is to explore the risks factors and the outcomes associated with different techniques of vein resections employed at our institution during PD and their effect on venous thrombosis.

Methods: Patients who underwent venous resection during PD from 2010 to 2020 were identified. Medical records and imaging were retrospectively reviewed for perioperative outcomes, with particular emphasis on vein patency and thrombosis. Patients who had at least 6 months follow-up were considered.

Results: Two hundred three patients met inclusion criteria and vein thrombosis was identified in 25 (12.3%) patients. The portal vein was the most commonly resected vein (PV; n=109, 53.6%).Tangential resection (n=78, 38.4%) was the most commonly used approach and had the lowest rate of thrombosis (7/78; 8.9%) regardless of if performed along the PV (4/48; 8.3%) or the superior mesenteric vein [(SMV) 2/23; 8.6%]. Vascular conduit (vein graft) reconstructions had the highest rate of thrombosis (n=11/27, 40%), and shortest time to thrombus formation (median: 59 days [49-149], p-value < 0.001). Other median days to thrombosis according to the various resection techniques were 139 [22-288], 119 [66-168]) and 185 [147-222] for tangential, end-to-end, and venorrhaphy respectively. The rate of thrombosis did not vary according to type of operative approach (robotic vs. open; p=0.456), vein resected (PV vs. SMV vs. PV/SMV confluence; p=0.558), or tangential resection technique [hand sewn vs. stapled (p=0.779)]. The use of a vascular conduit was associated with a statistically significant higher rate of thrombosis compared to all other approaches (p value < 0.001). Postoperative administration of antiplatelet/anticoagulant was not associated with thrombosis prevention.

Conclusion: Vascular conduit reconstructions were associated with the highest rate of thrombosis. No difference in thrombosis rate exists between operative approach, type of antiplatelet/anticoagulant given on discharge, and type of vein resection performed.

		Vein Status		
		Patent (n=176) Count (%)	Thrombosed (n=27) Count (%)	p-value
Sex				0.020
	Male	101 (91.8)	9 (8.2)	
	Female	75 (80.6)	18 (19.4)	
Neoadjuvant Chemotherapy		147 (85.4)	25 (14.6)	0.222
Neoadjuvant Radiotherapy		30 (73.2)	11 (26.8)	0.004
Vein Resected	Portal Vein	92 (84.4)	17 (15.6)	0.565
	Superior Mesenteric Vein	55 (91.7)	5 (8.3)	
	PV/SMV Confluence	28 (84.8)	5 (15.2)	
	Jejunal Vein	1 (100)	0 (0)	<0.001
Type of Vascular Resection/Repair	Tangential	71 (91)	7 (9)	
	End-to-End	57 (89.1)	7 (10.9)	
	Vein Conduit	16 (59.3)	11 (40.7)	
	Venorrhaphy	30	2 (6.3)	
	Patch	2 (100)	0 (0)	
Tangential Resection Type	Staple	47 (90.4)	5 (9.6)	0.779
	Handsewn	24 (92.3)	2 (7.7)	
Vein Thrombosed	Portal Vein	0 (0)	10 (100)	0.558
	Superior Mesenteric Vein	0 (0)	8 (100)	
	PV/SMV Confluence	0 (0)	7 (100)	
Antiplatelet/Anticoagulation Given on Discharge				0.450
	None	38 (92.7)	3 (7.3)	
	Antiplatelet Alone	73 (82)	16 (18)	
	Anticoagulation Alone	12 (85.7)	2 (14.3)	
	Both	14 (87.5)	2 (12.5)	
Margin				0.217
	R0	113 (89)	14 (11)	
	R1	63 (82.9)	13 (17.1)	
Surgical Approach				0.456
	Open	109 (84.5)	20 (15.5)	
	Robotic	66 (90.4)	7 (9.6)	
	Laparoscopic	1 (100)	0 (0)	

56. COMPARISON OF SHORT-TERM RESULTS BETWEEN SUPERIOR MESENTERIC ARTERY RESECTION AND SUPERIOR MESENTERIC/PORTAL VEIN RESECTION DURING PANCREATECTOMY: A PROPENSITY SCORE MATCHING ANALYSIS

M Ginesini, N Napoli, EF Kauffmann, C Gianfaldoni, A Salomone, C Cappelli, D Campani, F Vistoli, U Boggi
Presenter: Michael Ginesini MD | University of Pisa, Italy

Background: The efficacy of neoadjuvant therapies renews the possibility of resection of peripancreatic arteries during pancreatectomy for cancer. If the vein resection is worldwide accepted, the resection of superior mesenteric artery remains debated because of the high morbidity and mortality. In this analysis we compared pancreatectomies with superior mesenteric vein/portal vein resection (VR-p) and superior mesenteric artery resection (SMA-p) using a propensity score (PS) matching.

Methods: Data were prospectively entered into a database and retrospectively analyzed. Incidence of severe post-operative complications (Clavien-Dindo≥3b) and 90-day mortality were considered the main outcome measures. The PS matching (1-to-1) was performed by using genetic method (R package MatchIt) to balance possible confounders (age, gender, BMI, ASA score, diabetes, heart disease, pulmonary disease, neoadjuvant chemotherapy, preoperative abdominal surgery) between the two groups.

Results: Between 1994 and 2021, 327 patients underwent VR-p and 69 underwent SMA-p at our institution. A summary of baseline characteristics, operative and post-operative results is provided in table 1.

Severe post-operative complications occurred in 48 (14.7%) and 14 (20.3%) patients after VR-p and SMA-p (p=0.24), respectively. The crude odd ratio (OR) was 1.47 (0.76-2.87). Equivalent figures for 90-day mortality were 23 (7%) and 8 (11.6%) (p=0.20). The crude OR was 1.73 (0.74-4.06).

According to PS, 69 Vr-p were matched to 69 SMA-p (table 1). A summary of baseline characteristics, operative and post-operative results is provided in table 1. Severe post-operative complications occurred in 12(17.4%) and 14 (20.3%) patients after VR-p and SMA-p (p=0.66), respectively. The adjusted odd ratio (OR) was 1.21 (0.51-2.84). Equivalent figures for 90-day mortality were 3 (4.4%) and 8 (11.6%) (p=0.13). The adjusted OR was 2.88 (0.73-4.37).

Conclusion: The resection of the superior mesenteric artery for pancreatic cancer remains a challenging operation with a high morbidity and mortality. However, this analysis demonstrates that there are no statistically significant differences with VR-pr. Nevertheless, this procedure is recommendable only in high volume centers for vascular resections during pancreatectomy.

Table 1 - Baseline characteristics, operative and post-operative results

	Before PS				After PS			
	Overall population	**VR-p**	**SMA-p**	**p**	**Overall population**	**VR-p**	**SMA-p**	**p**
Baseline characteristics								
Number (%)	396 (100%)	327 (82.6%)	69 (17.4%)		138 (100%)	69 (50%)	69 (50%)	
Age; median (IQR); year	66.4 (60-73.9)	67.8 (60.8-74.8)	63 (54.4-69.1)	<0.0001	61.2 (54-68.3)	60.9 (53.9-68)	63 (54.4-69.1)	0.82
Gender male; n (%)	220 (55.6%)	185 (56.6%)	35 (50.7%)	0.37	71 (51.4%)	36 (52.2%)	35 (50.7%)	0.86
BMI; median (IQR); Kg/m2	23.7 (21.6-25.6)	23.8 (21.8-25.7)	23.1 (21.3-25)	0.21	23.1 (21.5-24.9)	23 (21.8-24.9)	23.1 (21.3-25)	1.00
ASA; median (IQR)	2 (2-3)	2 (2-3)	2 (2-3)	0.14	2 (2-3)	2 (2-3)	2 (2-3)	0.90
Diabetes; n (%)	106 (26.8%)	82 (25.1%)	24 (34.8%)	0.09	46 (33.3%)	22 (31.9%)	24 (34.8%)	0.72
Heart disease; n (%)	61 (15.4%)	58 (17.7%)	3 (4.4%)	0.003	7 (5.1%)	4 (5.8%)	3 (4.4%)	1.00
Pulmonary disease; n (%)	26 (6.6%)	26 (8%)	0 (0%)	0.01	2 (1.4%)	2 (2.9%)	0 (0%)	0.50
Preoperative abdominal surgery; n (%)	150 (37.9%)	148 (45.3%)	2 (2.9%)	<0.0001	21 (15.2%)	19 (27.5%)	2 (2.9%)	<0.0001
Neoadjuvant chemotherapy; n (%)	87 (22%)	31 (9.5%)	56 (81.2%)	<0.0001	87 (63%)	31 (44.9%)	56 (81.2%)	<0.0001
Surgical procedure								
Pancreaticoduodenectomy; n (%)	231 (58.3%)	224 (68.5%)	7 (10.1%)	<0.0001	52 (37.7%)	45 (65.2%)	7 (10.1%)	<0.0001
Total pancreatectomy; n (%)	144 (36.4%)	82 (25.1%)	62 (89.9%)	<0.0001	82 (59.4%)	20 (29%)	62 (90%)	< 0.0001
Distal pancreatectomy; n (%)	21 (5.3%)	21 (6.4%)	0 (0%)	0.03	4 (2.9%)	4 (5.8%)	0 (0%)	0.12
Post-operative								
Clavien 0; n (%)	126 (31.8%)	109 (33.3%)	17 (24.6%)	0.16	37 (26.8%)	20 (29%)	17 (24.6%)	0.56
Clavien 5; n (0%)	31 (7.8%)	23 (7%)	8 (11.6%)	0.20	11 (8%)	3 (4.4%)	8 (11.6%)	0.21
Clavien >2; n (%)	86 (21.7%)	69 (21.1%)	17 (24.6%)	0.52	32 (23.2%)	15 (21.7%)	17 (24.6%)	0.69
Clavien >3a; n(%)	62 (15.7%)	48 (14.7%)	14 (20.3%)	0.24	26 (18.8%)	12 (17.4%)	14 (20.3%)	0.66
Comprehensive Complication Index; median (IQR)	22.6 (0-33.5)	22.6 (0-33.5)	24.2 (4.4-33.5)	0.23	21.8 (0-33.5)	20.9 (0-33.5)	24.2 (4.4-33.5)	0.29

57. PROSPECTIVE, MULTI-INSTITUTIONAL, REAL-TIME NEXT-GENERATION SEQUENCING OF PANCREATIC CYST FLUID REVEALS DIVERSE GENOMIC ALTERATIONS THAT IMPROVE THE ASSESSMENT OF PANCREATIC CYSTS

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Presenter: Alessandro Paniccia MD | University of Pittsburgh Medical Center, United States

Background: Next-generation sequencing (NGS) of pancreatic cyst fluid is a useful adjunct in the assessment of pancreatic cyst (PC) patients. However, previous studies have been retrospective or single institutional experiences. The aim of this study was to prospectively evaluate NGS on a multi-institutional cohort of PC patients in real-time.

Methods: Within a two-year timeframe, a 22-gene NGS panel (PancreaSeq) was used to evaluate endoscopic ultrasound (EUS)-guided fine-needle aspiration PC fluid from 31 institutions. PancreaSeq results were correlated with EUS findings, ancillary studies, follow-up, and expanded molecular testing of postoperative specimens.

Results: Among 1933 PCs, 1887 (98%) specimens from 1832 patients were satisfactory for PancreaSeq testing. Follow-up was available for 1216 (66%) patients (median, 23 months). Based on 251 (21%) patients with surgical pathology, MAPK/GNAS mutations had 90% sensitivity and 100% specificity for a mucinous cyst. The combination of MAPK/GNAS mutations and TP53/SMAD4/CTNNB1/mTOR gene alterations had 88% sensitivity and 95% specificity for advanced neoplasia. Exclusion of low-level variants and inclusion of cytology improved the sensitivity to 93%. The sensitivities and specificities of VHL and MEN1/LOH alterations were 71% and 100% for serous cystadenomas (SCAs), and 68% and 98% for pancreatic neuroendocrine tumors (PanNETs), respectively. Upon follow-up, SCAs with TP53/TERT mutations often exhibited interval growth, while PanNETs with LOH of ≥3 genes had distant metastasis. None of the remaining 965 patients reported a malignancy. Postoperative testing identified mucinous cysts with BRAF fusions and ERBB2 amplification, and advanced neoplasia with CDKN2A alterations.

Conclusion: Prospective PancreaSeq testing was not only sensitive and specific for mucinous cysts and advanced neoplasia arising from mucinous cysts, but also reveals the diversity of genomic alterations seen in PCs and their clinical significance.

Sensitivities and specificities of PancreaSeq testing and other diagnostic modalities based on 246 diagnostically confirmed pancreatic cysts.

Parameter	Sensitivity (95% CI)	Specificity (95% CI)
IPMN		
MAPK/*GNAS* mutations	95% (0.91 - 0.98)	89% (0.78 - 0.94)
Presence of multiple cysts (n=245)*	54% (0.46 - 0.62)	80% (0.69 - 0.88)
Increased fluid viscosity (n=238)*	79% (0.72 - 0.85)	81% (0.70 - 0.89)
Elevated CEA (n=173)*	74% (0.65 - 0.81)	73% (0.59 - 0.84)
IPMN with advanced neoplasia		
TP53, *SMAD4* and/or mTOR gene alterations	87% (0.78 - 0.93)	76% (0.69 - 0.83)
TP53, *SMAD4, CTNNB1* and/or mTOR gene alterations	89% (0.80 - 0.94)	74% (0.67 - 0.81)
MAPK/*GNAS* mutations with *TP53*, *SMAD4* and/or mTOR gene alterations	84% (0.75 - 0.91)	92% (0.87 - 0.96)
MAPK/*GNAS* mutations with *TP53*, *SMAD4, CTNNB1* and/or mTOR gene alterations	87% (0.78 - 0.93)	91% (0.85 - 0.95)
MAPK/*GNAS* LOH or *TP53*, *SMAD4* and/or mTOR gene AFs = MAPK/*GNAS* AFs	86% (0.76 - 0.92)	95% (0.90 - 0.98)
MAPK/*GNAS* LOH or *TP53*, *SMAD4, CTNNB1* and/or mTOR gene AFs = MAPK/*GNAS* AFs	88% (0.79 - 0.94)	94% (0.89 - 0.97)
Associated clinical symptoms (n=244)*	38% (0.28 - 0.49)	71% (0.64 - 0.78)
Jaundice (n=131)**	31% (0.20 - 0.44)	89% (0.78 - 0.95)
Index cyst size >3.0 cm (n=242)*	56% (0.45 - 0.66)	55% (0.46 - 0.63)
Main pancreatic duct dilatation (n=244)*	71% (0.60 - 0.80)	65% (0.57 - 0.73)
Presence of a mural nodule (n=245)*	44% (0.34 - 0.55)	80% (0.72 - 0.85)
Increasing index cyst size (n=125)*	50% (0.34 - 0.66)	54% (0.43 - 0.65)
Malignant cytopathology***	46% (0.35 - 0.56)	95% (0.90 - 0.98)
IPMN and MCN		
MAPK/*GNAS* mutations	90% (0.85 - 0.94)	100% (0.93 - 1.00)
Increased fluid viscosity (n=238)*	77% (0.70 - 0.83)	92% (0.81 - 0.97)
Elevated CEA (n=173)*	73% (0.64 - 0.80)	94% (0.79 - 0.99)
IPMN and MCN with advanced neoplasia		
TP53, *SMAD4* and/or mTOR gene alterations	88% (0.79 - 0.93)	79% (0.72 - 0.85)
TP53, *SMAD4, CTNNB1* and/or mTOR gene alterations	90% (0.81 - 0.95)	77% (0.70 - 0.84)
MAPK/*GNAS* mutations with *TP53*, *SMAD4* and/or mTOR gene alterations	85% (0.76 - 0.92)	96% (0.91 - 0.98)
MAPK/*GNAS* mutations with *TP53*, *SMAD4, CTNNB1* and/or mTOR gene alterations	88% (0.79 - 0.93)	95% (0.89 - 0.98)
MAPK/*GNAS* LOH or *TP53*, *SMAD4* and/or mTOR gene AFs = MAPK/*GNAS* AFs	87% (0.78 - 0.92)	99% (0.95 - 1.00)
MAPK/*GNAS* LOH or *TP53*, *SMAD4, CTNNB1* and/or mTOR gene AFs = MAPK/*GNAS* AFs	89% (0.80 - 0.94)	98% (0.94 - 1.00)
Associated clinical symptoms (n=244)*	38% (0.28 - 0.48)	72% (0.64 - 0.79)
Jaundice (n=131)**	31% (0.20 - 0.44)	89% (0.78 - 0.95)
Index cyst size >3.0 cm (n=242)*	59% (0.48 - 0.68)	57% (0.48 - 0.65)
Main pancreatic duct dilatation (n=244)*	68% (0.58 - 0.77)	65% (0.57 – 0.73)
Presence of a mural nodule (n=245)*	45% (0.35 - 0.56)	81% (0.74 - 0.87)
Increasing index cyst size (n=125)*	52% (0.37 - 0.67)	56% (0.44 - 0.67)
Malignant cytopathology***	46% (0.36 - 0.56)	97% (0.92 - 0.99)

Abbreviations: AF, allele frequency; CEA, carcinoembryonic antigen; IPMN, intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm

*n designates the number of patients with data available for analysis.

**Jaundice was evaluated for patients with a cyst in the pancreatic head, uncinate and/or neck

***Malignant cytopathology was defined as at least suspicious for adenocarcinoma.

58. DISTAL PANCREATECTOMY FISTULA RISK SCORE (D-FRS): DEVELOPMENT AND INTERNATIONAL VALIDATION

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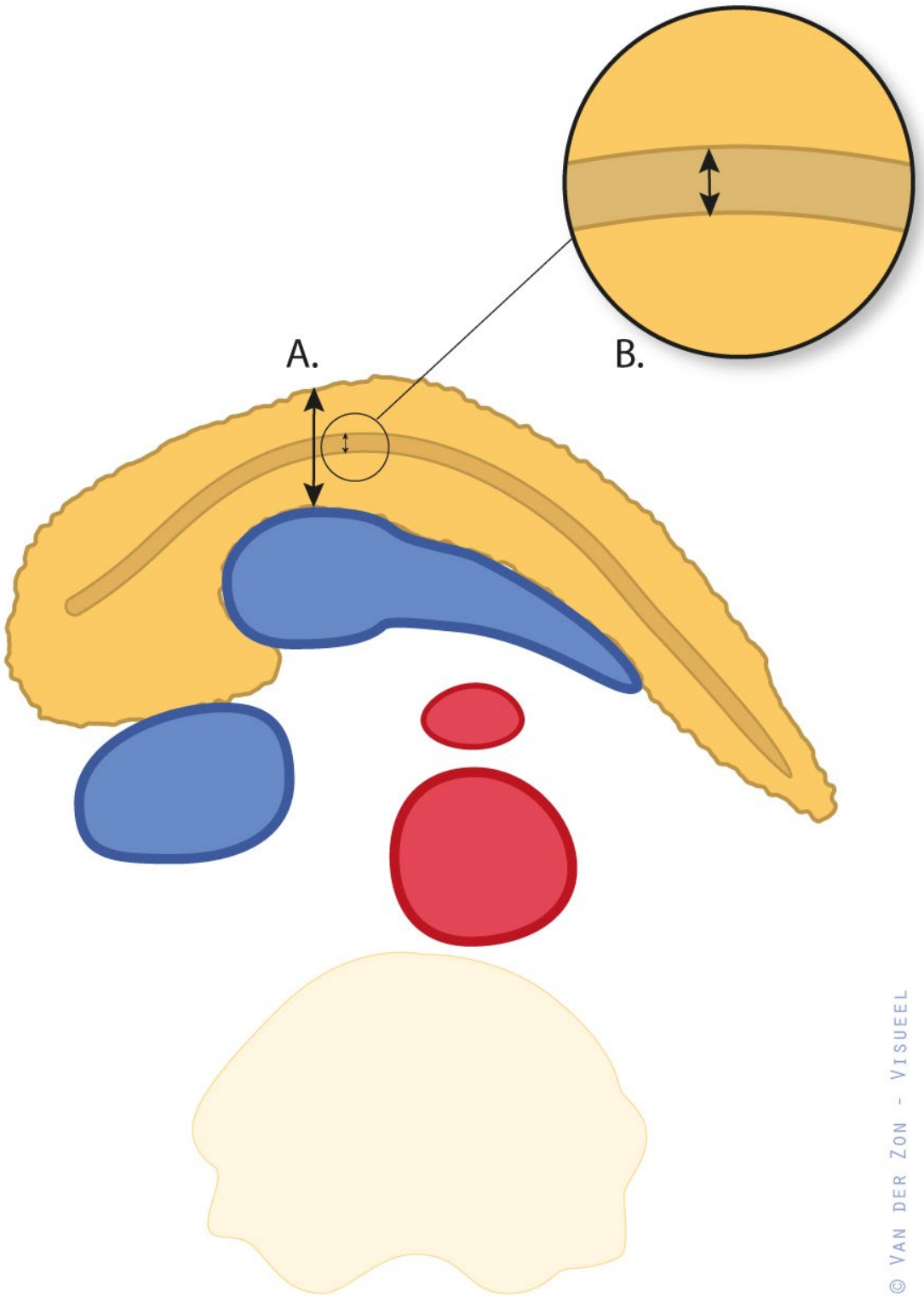
Presenter: Eduard A. van Bodegraven MD | Academic Medical Center, Netherlands

Background: Preoperative estimation of the risk of postoperative pancreatic fistula (POPF) after distal pancreatectomy (DP) can be used for the selection of preventive strategies, for benchmarking across centers, and stratifying patients by baseline risk in clinical studies. The aim was to develop and externally validate the first clinical risk score for POPF after DP.

Methods: Predictive variables for POPF were found using data of patients undergoing DP in two Italian centers (2014-2016) utilizing multivariable logistic regression. A prediction model was designed based on the significant variables. These data were pooled with the data of three Dutch centers and in two US centers (2007-2016). Discrimination and calibration were assessed in an internal-external validation procedure.

Results: Overall, 1336 patients were included, of whom 291 (22%) developed a POPF grade B/C. A preoperative risk score was developed, including two variables: pancreatic neck thickness (OR: 1.14 [95% CI:1.11-1.17] per mm increase) and pancreatic duct diameter (OR: 1.46; [95%CI: 1.32-1.65] per mm increase). The model performed well in the design cohort (AUC: 0.80 (95% CI: 0.76-0.84)) and after internal-external validation (AUC: 0.73 (95% CI: 0.70-0.76)). Three risk groups were identified: low-risk (0-10%), intermediate-risk (10-25%), and high-risk (>25%).

Conclusion: The Distal Fistula Risk Score (D-FRS) is the first externally validated risk score that successfully predicts the risk of POPF after distal pancreatectomy. It can be easily calculated preoperatively using www.pancreascalculator.com. The three distinct risk groups may facilitate personalized treatment.



59. PREDICTING POST-RECURRENCE SURVIVAL FOR PATIENTS WITH PANCREATIC CANCER RECURRENCE AFTER PRIMARY RESECTION: A BI-INSTITUTIONAL VALIDATED RISK CLASSIFICATION

AF van Oosten, LA Daamen, VP Groot, NC Biesma, JR Habib, IWJM van Goor, B Kinny-Koster, RA Burkhart, CL Wolfgang, HC van Santvoort, J He, IQ Molenaar

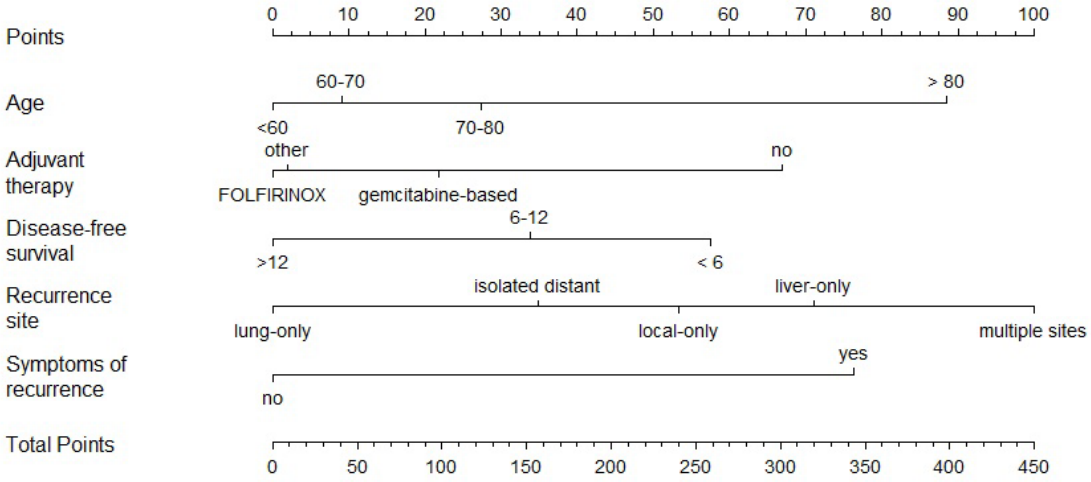
Presenter: Lois A. Daamen MD, PhD | UMC Utrecht, Netherlands

Background: Over 80% of patients will develop disease recurrence after radical resection of pancreatic ductal adenocarcinoma (PDAC). It remains unclear which factors carry prognostic significance at time of recurrence. This study aims to develop and validate a clinical risk score to predict post-recurrence survival (PRS) at time of recurrence in patients with resected PDAC.

Methods: All patients who had recurrence after undergoing pancreatectomy for PDAC at the Johns Hopkins Hospital, between 2016 and 2018, or at the Regional Academic Cancer Center Utrecht between 2014 and 2019 were included. Kaplan-Meier curves were used to estimate PRS. A Cox proportional hazard model was used to develop the risk model in a training set. Based on Akaike's information criterion, predictive variables were selected. Performance of the final model was assessed in a test set after internal validation in 1000 bootstrap samples.

Results: Of 718 resected PDAC patients, 514 (72%) had recurrence after a median follow-up of 32 months. The median overall survival calculated from surgery was 21 months and the median PRS was 9 months. Prognostic factors associated with a shorter PRS were age (hazard ratio [HR] 1.02; 95% confidence interval [95% CI] 1.00 – 1.04; P = 0.02), multiple-site recurrence (HR 1.57; 95% CI 1.08 – 2.28; P = 0.02), and symptoms at time of recurrence (HR 2.33; 95% CI 1.59 – 3.41; P < 0.001). Recurrence-free survival (RFS) longer than 12 months (HR 0.55; 95% CI 0.36 – 0.83; P = 0.004), FOLFIRINOX adjuvant chemotherapy (HR 0.45; 95% CI 0.25 – 0.81; P = 0.01) and gemcitabine-based adjuvant chemotherapy (HR 0.58; 95% CI 0.26 – 0.93; P = 0.02) were associated with a longer PRS. The risk score designed with these variables had a good predictive accuracy (C-index: 0.73).

Conclusion: This study developed and validated a clinical risk score based on an international cohort that can predict PRS in patients who underwent surgical resection for PDAC. This risk score will become available on www.evidencio.com and can help clinicians with patient counseling on prognosis and shared decision-making regarding treatment.


Points
0
10
20
30
40
50
60
70
80
90
100
Age
60-70
> 80
<60
70-80
Adjuvant therapy
other
no
FOLFIRINOX
gemcitabine-based
Disease-free survival
6-12
>12
< 6
Recurrence site
isolated distant
liver-only
lung-only
local-only
multiple sites
Symptoms of recurrence
yes
no
Total Points
0
50
100
150
200
250
300
350
400
450

60. SUCCESSFUL IMPLEMENTATION OF AN OPIOID REDUCTION TOOLKIT IN PANCREATECTOMY PATIENTS SIGNIFICANTLY DECREASES NUMBER OF OPIOIDS PRESCRIBED AND CONSUMED

S Cannaday, F Ponzini, D Moskal, JE Williamson III, B Wummer, R Huang, G Sun, SG Song, B Im, LL Kowal, WB Bowne, A Nevler, T Yeo, CJ Yeo, H Lavu

Presenter: Ryan Lamm MD | Thomas Jefferson University Hospital, United States

Background: Post-operative opioid prescriptions contribute to the community diversion pool of narcotics at-risk for abuse. Previous efforts have been directed towards opioid reduction in minimally invasive procedures, but few have targeted open surgery, such as pancreatectomy. This study sought to create an opioid reduction toolkit to be used to inform patients and providers on safe opioid practices. The goal was to reduce the number of opioids prescribed and consumed, as well as to inform patients about appropriate disposal techniques.

Methods: A single academic surgical department reviewed opioid treatment patterns for patients undergoing common procedures, including open pancreatectomy, and an opioid reduction toolkit using the data collected was created. Providers were educated on the use of the toolkit and it was implemented as a standard of practice. Data were collected on pancreatectomy patients via telephone interview (performed at 2 weeks post-op) and by reviewing the state prescription drug monitoring program. Outcome variables included morphine milliequivalents (MME) of pills prescribed, MME of pills consumed, number of patients aware of proper unused pill disposal, number of patients requesting refills, and pain scores. As an example of MME, a 5-milligram tablet of oxycodone (Roxicodone) converts to 7.5 MME. Categorical and continuous outcomes were compared within and between groups.

Results: Eighty-one (81) patients were included in the analysis: 24 in the pre-intervention group and 57 in the post-intervention group. There were no significant demographic or clinical differences between the groups. In the pre-intervention group, there was a significant difference in the MME prescribed compared to those that were consumed (225 (225 - 281.3) v 75 (75 - 112.5), p< 0.0001). Based upon this information and following implementation of the toolkit, the number of MME prescribed was significantly reduced from 225 (225 - 281.3) in the pre-intervention group to 108.8 (37.5 - 187.5) in the post-intervention group (p< 0.0001). The post-intervention group was observed to have a significant reduction in the MME consumed compared to the pre-intervention group (7.5 (0 - 112.5) v 75 (75 - 112.5), p=0.0004), while the mean pain score in the post-intervention group, on a scale of 1-10, was 3.3 + 0.5. The number of patients who were aware of how to properly dispose of unused pills significantly increased after toolkit implementation (Pre: 25% v Post: 65%, p=0.001) while those requesting refills did not significantly change (Pre: 17% v Post: 19% v, p=0.781) (Table 1).

Conclusion: Implementing an opioid reduction toolkit successfully reduced the number of postoperative opioids prescribed by the provider and consumed by the patient following discharge after pancreatectomy. Pain scores after surgery remained at an acceptable level, suggesting pain management was not compromised. Patient awareness of the proper way to dispose of unused opioid pills more than doubled. Continued efforts to reduce the opioid discharge prescriptions with education on how to dispose of unused pills can reduce the number of pills available for abuse in the community.

Table 1. Opioid-related outcomes for pre- and post- opioid reduction toolkit implementation

	PRE-INTERVENTION GROUP (N = 24)	POST-INTERVENTION GROUP (N = 57)	*P-VALUE*
MME PRESCRIBED, MEDIAN (IQR)	225 (225 - 281.3)	108.8 (37.5 - 187.5)	*<0.0001*
MME CONSUMED, MEDIAN (IQR)	75 (75 - 112.5)	7.5 (0 - 112.5)	*0.0004*
PATIENTS AWARE OF PROPER DISPOSAL, N (%)	6/24 (25.0)	37/57 (64.9)	*0.001*
NUMBER OF PATIENTS REQUESTING REFILLS, N (%)	4/24 (16.7)	11/57 (19.3)	*0.781*

Abbreviations: MME=Morphine Milliequivalents; IQR=Interquartile Range

61. POSTOPERATIVE PANCREATIC FISTULA TENDS TO BE OF A HIGHER GRADE IN MINIMALLY INVASIVE VS. OPEN PANCREATICODUODENECTOMY: TRUTH OR MYTH?

F Dahdaleh, J Denbo, M Malafa, J Pimiento, D Anaya, P Hodul, J Fleming
Presenter: Samer Naffouje MD | Moffitt Cancer Center, United States

Background: Pancreaticoduodenectomy (PD) remains a complex and highly morbid procedure even in high-volume centers. Several studies have studied the outcomes of open PD (OPD) to minimally-invasive PD (MIPD) and demonstrated comparable short-term outcomes including the rates of postoperative pancreatic fistula (POPF). However, it has been proposed that POPFs following MIPD tend to be of a higher grade and are associated with higher morbidity compared to OPD. The aim of the study is to test this hypothesis.

Methods: NSQIP pancreatectomy 2014-2020 was used for the analysis. Patients who underwent elective PD without concomitant vascular or visceral resection, who had available report on the reconstruction technique, gland texture, duct size and POPF grade were selected. To test the proposed hypothesis, we only included patients who were reported to have POPF following their PD. Clinically-relevant POPF (CR-POPF) was defined as grade B & C.

We matched patients who had OPD to those who had MIPD based on a propensity score model that adjusts for all clinical and demographic variables. Postoperative outcomes were compared between the matched groups using conditional logistic regression and mixed effect modeling.

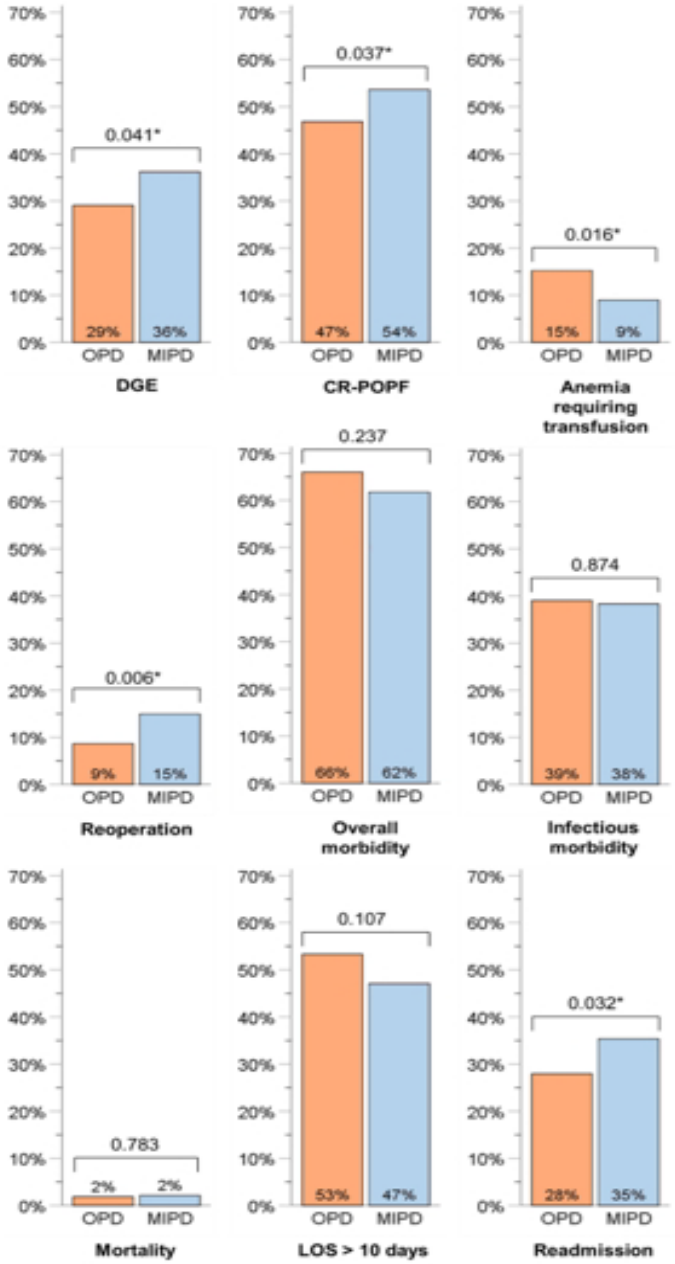
Results: The initial database contained 47,275 pancreatectomy cases. 3,083 elective PD cases complicated by POPF were selected. 1,498 (48.6%) of POPFs were grade A, 1,400 (45.4%) were grade B, and 185 (6.0%) were grade C. 2,843 patients (92.2%) underwent OPD vs. 240 (7.8%) who underwent MIPD. We performed a multivariable logistic regression for predictors of CR-POPF which concluded male sex, benign indications, neoadjuvant chemotherapy, MIPD, operative time, and pancreaticojejunostomy (PJ) invagination (vs. the standard PJ duct-to-mucosa) as unfavorable predictors of CR-POPF. Additionally, drain placement was significantly associated with lower rates of CR-POPF (HR 0.14 [0.08-0.23]).

We matched 705 OPD patients to 235 MIPD peers (ratio 3:1) based on a propensity score model. In the matched dataset, MIPD patients had higher rates of CR-POPF (54% vs. 47%; p=0.037), with the main difference being attributed to grade C (grades A, B, C were 53%, 44%, 3% in OPD vs. 46%, 45%, 9% in MIPD; p=0.002). MIPD patients also had higher rates of delayed gastric emptying (36% vs. 29%; p=0.041), and reoperation (15% vs. 9%; p=0.006), whereas they had lower rates of postoperative transfusions (9% vs. 15%; p=0.016). No difference was detected in median hospitalization (10 days vs. 11 days; p=0.143) with higher rates of 30-day readmission in the MIPD group (35% VS. 28%; P=0.032). There was no difference in non-POPF overall morbidity (62% vs. 66%; p=0.237), infectious morbidity (38% vs. 39%; p=0.874), or mortality (2% vs. 2%; p=0.783) between the matched groups.

Conclusion: In the occurrence of POPF, rates of CR-POPF are higher in males, MIPD (vs. OPD), and PJ invagination (vs. PJ duct-to-mucosa). Drain placement mitigates the occurrence of CR-POPF by 6.5-fold.

When POPF occurs following MIPD, it tends to be of a slightly higher grade (mostly due to grade C). The postoperative course of OPD and MIPD complicated by POPF is generally comparable with higher tendency for transfusions in OPD and higher rates of readmission in MIPD.

Figure: Comparison of key postoperative outcomes of OPD vs. MIPD in the matched dataset of patients who underwent PD complicated by a POPF. **CR-POPF**: Clinically-Relevant Postoperative Pancreatic Fistula (B&C); **DGE**: Delayed Gastric Emptying; **LOS**: Length of Stay; **MIPD**: Minimally-Invasive Pancreaticoduodenectomy; **OPD**: Open Pancreaticoduodenectomy, **PD**: Pancreaticoduodenectomy. ***** Statistically significant.



62. EVALUATING THE IMPACT OF PRE-OPERATIVE GERIATRIC-SPECIFIC VARIABLES AND MODIFIED FRAILTY INDEX ON POST-OPERATIVE OUTCOMES AFTER ELECTIVE PANCREATIC SURGERY

WJ Kane, CM Lattimore, FE Turrentine, VM Zaydfudim
Presenter: Christopher Cramer MD | University of Virginia, United States

Background: Geriatric patients represent a growing proportion of the surgical population. Previous studies investigating post-operative outcomes after a broad range of major abdominal operations have demonstrated the utility of geriatric-specific variables (GSVs) and the 5-factor modified frailty index (mFI-5). The goal of this study was to examine the association of pre-operative GSVs and the mFI-5 with post-operative outcomes in patients selected for elective pancreatic surgery.

Methods: Patients in the ACS NSQIP Geriatric Surgery Research File pilot program who underwent elective pancreatic operations between 2014 and 2018 were included. Patients were stratified into three age groups: 65-74, 75-80, and 81 years or older. GSVs were categorized as: whether the patient lives at home or at a facility, use of a mobility aid, history of falls within the past year, and whether a patient can sign their own consent. Three clinically meaningful comorbid conditions scores were calculated for each patient: presence or absence of at least one GSV, a mFI-5 score, and a composite score of the GSV and mFI-5 scores (GSV+mFI-5). Multivariable logistic regression with adjustment for ACS NSQIP calculated risk or morbidity and mortality was performed to evaluate the associations between these geriatric and frailty variables and the post-operative outcomes: morbidity, mortality, need for re-operation, readmission, and discharge destination.

Results: A total of 1266 patients were included in the study: 808 (64%) age 65-74, 302 (24%) age 75-80, 156 (12%) age ≥ 81. A total of 843 (67%) patients underwent pancreatoduodenectomy. The operations were performed for pancreatic adenocarcinoma in 628 (50%) of patients. Patients ≥ 81 years were more likely to have at least one GSV present prior to resection ($p < 0.001$) while the median mFI-5 score was not different between age groups ($p = 0.82$). Patients ≥ 81 years had a greater likelihood of post-operative morbidity (35% vs 31% vs 47%, by age group, $p = 0.004$) and discharge to a facility (12% vs 23% vs 48%, by age group, $p < 0.001$). After adjusting for ACS NSQIP predicted probabilities of morbidity and mortality, patients with the pre-operative presence of at least one GSV were more likely to require a re-operation or to be discharged to a facility (OR 1.81 [95% CI 1.03-3.16] and 3.95 [95% CI 2.91-5.38], respectively). Similarly, the composite GSV+mFI-5 score was also associated with a greater likelihood of re-operation or discharge to a facility (OR 1.87 [95% CI 1.10-3.18] and 3.60 [95% CI 2.68-4.82], respectively).

Conclusion: Pre-operative presence of at least one geriatric-specific variable is significantly associated with the need for re-operation and discharge to a skilled facility following elective pancreatic surgery. Geriatric-specific variables should be considered in joint pre-operative decision making to help address specific needs of the elderly patient surgical population.

63. A COMPARISON OF THE USE OF EXTENDED VENOUS THROMBOEMBOLISM PROPHYLAXIS ON THE RATES OF VENOUS THROMBOEMBOLISM AND POST-PANCREATECTOMY HEMORRHAGE FOLLOWING PANCREATECTOMY FOR MALIGNANCY

JJ Hue, M Elshami, RS Hoehn, LD Rothermel, JB Ammori, JM Hardacre, JM Winter, LM Ocuin
Presenter: Henry J. Stitzel BS | Case Western Reserve University School of Medicine, United States

Background: Venous thromboembolism (VTE) is a major cause of postoperative morbidity and mortality. Guidelines recommend up to 28 days (d) of VTE prophylaxis with enoxaparin after discharge following major abdominal cancer surgery. We compared VTE and post-pancreatectomy hemorrhage (PPH) rates among patients with pancreatic and periampullary cancers treated at our institution prior to and following implementation of routine extended postoperative VTE prophylaxis.

Methods: We identified patients who underwent pancreatectomy for a pancreatic or periampullary malignancy (2004-2021). Common post-pancreatectomy outcomes (length of stay [LOS], clinically relevant postoperative pancreatic fistula [CR-POPF], delayed gastric emptying [DGE], 30/90d mortality rate) were abstracted from patient charts. VTE and PPH rates within 90d of discharge were compared based on the receipt of extended VTE prophylaxis with enoxaparin. Additional subset analyses were performed in patients who received antiplatelet medication at discharge.

Results: A total of 478 patients underwent pancreatectomy for a pancreatic or periampullary malignancy during the study period. Pancreatoduodenectomy was performed in 339 patients (70.9%), distal pancreatectomy was performed in 104 patients (21.8%), and total pancreatectomy was performed in 35 patients (7.3%). Overall, the length of stay was 7d and the unplanned readmission rate was 21.7%. In patients who underwent PD or DP, the CR-POPF rate was 7.4%. For all patients, DGE occurred in 7.0%. The 30/90d mortality rate was 0.8% and 3.1%, respectively.

A total of 22 patients (4.6%) developed a postoperative VTE, 12 (2.5%) of which occurred post-discharge. A total of 25 patients (5.2%) experienced a PPH, 13 (2.7%) of which occurred post-discharge. There was no difference in the development of post-discharge VTE between patients who received extended VTE prophylaxis and those who did not (2.3% vs. 2.6%, p=1.00). There was no difference in post-discharge PPH between patients who received extended VTE prophylaxis as compared to those who did not (3.4% vs. 1.9%, p=0.425). Antiplatelet agents with or without enoxaparin did not appear to be associated with higher VTE (0.0% vs 3.9%, p=0.313) or PPH (4.5% vs. 3.0%, p=0.643) rates.

Conclusion: Extended VTE prophylaxis following pancreatectomy for malignancy does not appear to be associated with differences in post-discharge VTE and PPH rates. These data suggest the use of extended VTE prophylaxis is safe but may not be necessary following pancreatectomy.

64. THE ORGANOTYPIC-LIVER SLIDE CULTURE SYSTEM FOR THE INVESTIGATION OF THE ROLE OF EXOSOMES IN PANCREATIC CANCER

A Comandatore, D Arguedas, C Carpenito, G Di Franco, M Palmeri, N Furbetta, S R Baglio, G Kazemier, M Besselink, E Giovannetti, L Morelli

Presenter: Annalisa Comandatore MD | University of Pisa, Italy

Background: Despite the morphological proximity and common vascular infiltration, the very high frequency of liver metastasis in pancreatic ductal adenocarcinoma (PDAC) is still not fully understood. Recent findings show how cell-to-cell communication through extracellular vesicles (EVs) might explain the formation of metastatic niches in target organs. Metastastic processes are the main responsible for the grim outcome of PDAC and new models are needed to evaluate the role of EVs in such processes. Organotypic models overcome the limitations and costs of in vitro and in vivo models. Moreover, these systems include both tumour cells and the metastatic site/tumour microenvironment (TME) reflecting the physiological and pathological consequences of their interaction with EVs.

The aims of our study were to: 1) evaluate whether EVs are transferred to tumour cells and change their invasive phenotype; 2) establish new models of organotypic liver slice cultures to study the role of EVs in PDAC.

Methods: After characterizing PDAC primary cells according to their metastatic potential, EVs were isolated from the supernatant of the most aggressive primary cell culture (PDAC3). EVs were then isolated using Size Exclusion Chromatography.

Liver tissues from immunocompetent and immunocompromised mice were cut with a vibratome to obtain slices with a thickness of 300 µm. These slices were subsequently incubated with EVs derived from PDAC3. After 24 hours, PDAC cells (previously transduced with Firefly-luciferase) were added to the liver slices, and the adhesion and invasion of these cells was quantified and compared to the control group (slices with cells, EVs, or cells and EVs). through bioluminescence (BLI)after 24-48h Tissues were included in paraffin to perform histopathological studies.

Results: EVs increase the ability of the PDAC cells to migrate as assessed through the wound healing assay (Fig.1). Furthermore, we established an innovative organotypic liver slide model which allows to study EV-educated PDAC cells in the liver metastatic TME. Our studies showed that pre-treatment with EVs increases the invasiveness of PDAC cells (as measured by BLI - Fig.2).

Conclusion: The described method turns out to be a valid and versatile system for the study of liver metastases. The major limitation of the study is represented by the use of liver slices obtained from athymic mice that have an altered immune response and contain cells that may react differently to human EVs when compared to human hepatic TME cells. However, our results may open the way for future studies with human liver metastatic tissues, decreasing the use of expensive organic or animal models. These samples may be obtained during palliative surgery or for occasional intraoperative findings in patients considered resectable prior to surgery. The use of these organotypic tools offers the great opportunity to evaluate the role of EVs in the metastatic context of PDAC.

Fig.1. Wound-healing assay

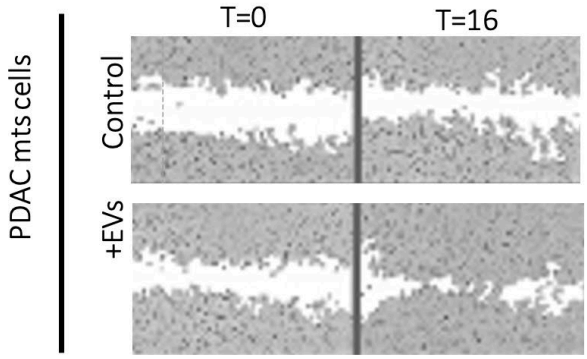
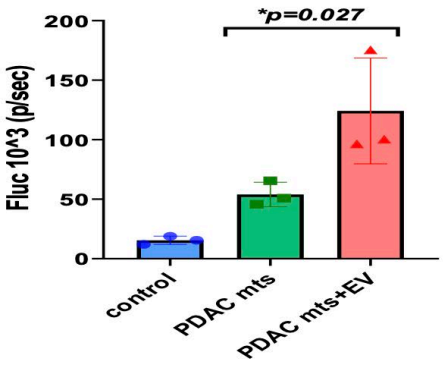


Fig.2. BLI



65. INTRAOPERATIVE BLOOD LOSS ESTIMATION IN HEPATO-PANCREATO-BILIARY SURGERY: AS RELEVANT AS NON-STANDARDIZED. RESULTS FROM A SYSTEMATIC REVIEW AND A WORLDWIDE SNAPSHOT SURVEY

G Perri, G Marchegiani, F Reich, C Bassi, R Salvia
Presenter: Giampaolo Perri MD | University of Verona, Italy

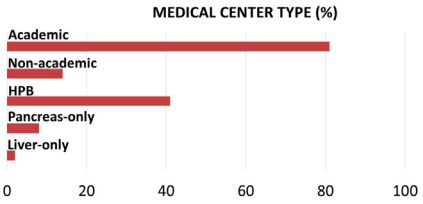
Background: Intraoperative blood loss (BL) is a major quality marker in hepato-pancreato-biliary (HPB) surgery, predictor of perioperative outcomes. However, the method for BL estimation is not standardized. The aim of this study is to picture the current practice of BL estimation in HPB surgery.

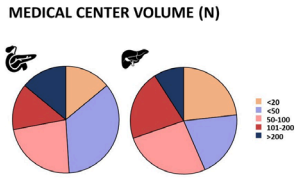
Methods: A systematic review was performed including original studies published between 2006 and 2021, reporting intraoperative BL of patients undergoing pancreatic or hepatic resections. A web-based snapshot survey was distributed globally to all members of the International Hepato-Pancreato-Biliary Association (IHPBA) and its regional chapters.

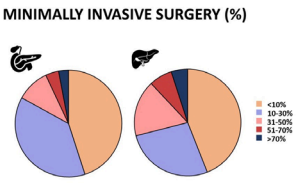
Results: A total of 806 studies were included, 480 (60%) had BL as their primary outcome and 105 (13%) as their secondary. However, 669 (83%) did not specify how BL estimation was performed, and 9 different methods were found among the remaining 136 (17%) studies.

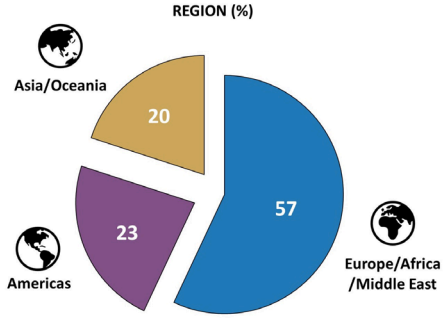
The survey was completed by 252 surgeons. Most of the responders (94%) declared to systematically perform BL estimation and considered BL highly predictive of postoperative complications after pancreatic (73%) and liver (74%) resection. All the 9 methods previously identified in literature were used by responders, with different frequency. A calculation based on suction fluid amounts, operative gauze weight, and irrigation was the most used method both in literature (7%) and among responders (49%). Most responders (83%) felt that BL estimation in HPB surgery needs better standardization.

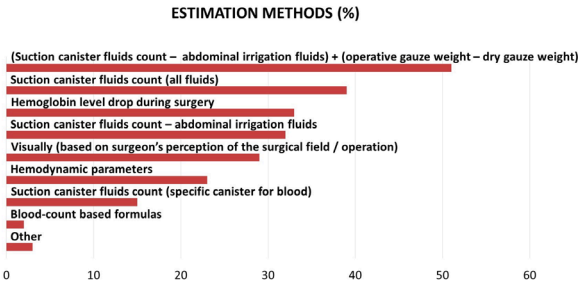
Conclusion: Standardization of intraoperative BL estimation is urgently needed in HPB surgery, to ensure consistency of reporting and reproducibility.


MEDICAL CENTER TYPE (%)
Academic
Non-academic
HPB
Pancreas-only
Liver-only
0
20
40
60
80
100


MEDICAL CENTER VOLUME (N)
<20
<50
50-100
101-200
>200


MINIMALLY INVASIVE SURGERY (%)
<10%
10-30%
31-50%
51-70%
>70%


REGION (%)
Asia/Oceania
20
57
23
Americas
Europe/Africa
/Middle East


ESTIMATION METHODS (%)
(Suction canister fluids count – abdominal irrigation fluids) + (operative gauze weight – dry gauze weight)
Suction canister fluids count (all fluids)
Hemoglobin level drop during surgery
Suction canister fluids count – abdominal irrigation fluids
Visually (based on surgeon's perception of the surgical field / operation)
Hemodynamic parameters
Suction canister fluids count (specific canister for blood)
Blood-count based formulas
Other
0
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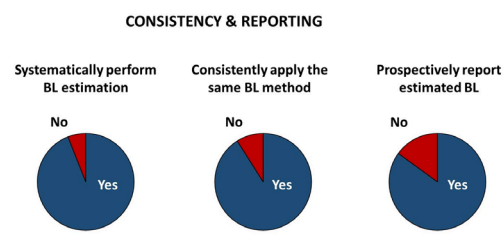
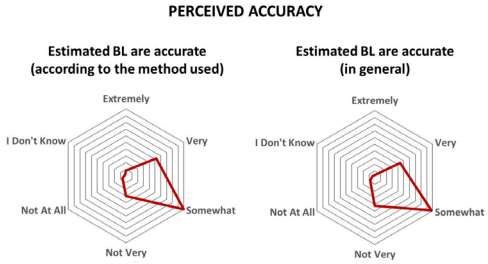
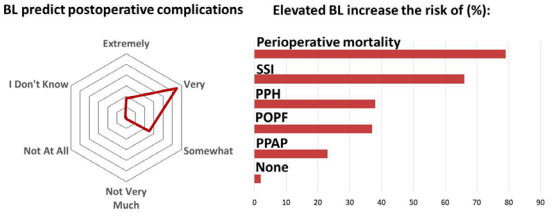
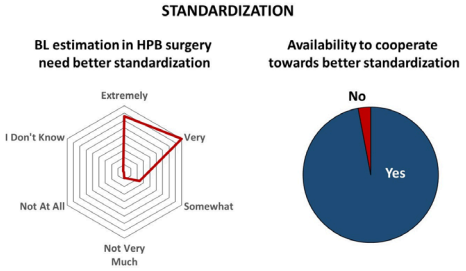
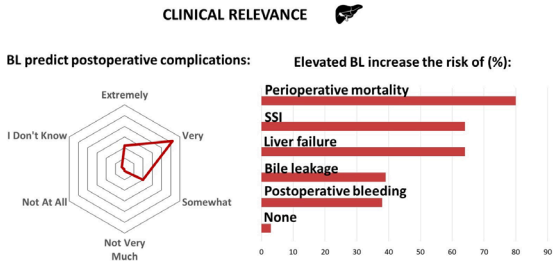
20
30
40
50
60


CONSISTENCY & REPORTING
Systematically perform BL estimation
Consistently apply the same BL method
Prospectively report estimated BL
No
Yes
No
Yes
No
Yes


PERCEIVED ACCURACY
Estimated BL are accurate (according to the method used)
Estimated BL are accurate (in general)
Extremely
Very
Somewhat
Not Very
Not At All
I Don't Know
Extremely
Very
Somewhat
Not Very
Not At All
I Don't Know


CLINICAL RELEVANCE
BL predict postoperative complications
Elevated BL increase the risk of (%):
Extremely
Very
Somewhat
Not Very Much
Not At All
I Don't Know
Perioperative mortality
SSI
PPH
POPF
PPAP
None
0
10
20
30
40
50
60
70
80
90


STANDARDIZATION
BL estimation in HPB surgery need better standardization
Availability to cooperate towards better standardization
Extremely
Very
Somewhat
Not Very Much
Not At All
I Don't Know
No
Yes


CLINICAL RELEVANCE
BL predict postoperative complications:
Elevated BL increase the risk of (%):
Extremely
Very
Somewhat
Not Very Much
Not At All
I Don't Know
Perioperative mortality
SSI
Liver failure
Bile leakage
Postoperative bleeding
None
0
10
20
30
40
50
60
70
80
90