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#### NATURAL HISTORY OF DISEASE PROGRESSION AND INTERVENTIONS AFTER ABORTED PANCREATODUODENECTOMY FOR PANCREATIC ADENOCARCINOMA

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**Background:** Planned pancreaticoduodenectomy (PD) for pancreatic adenocarcinoma (PDAC) is sometimes aborted due to intraoperative finding of locally unresectable (UR) or metastatic disease (mets). Some patients subsequently develop biliary or gastric outlet obstruction (GOO), but there is little guidance regarding the need for prophylactic palliative bypasses when a resection is aborted. The aims of this study were to characterize the overall survival and interventional needs of these patients. **Methods:** Patients treated with neoadjuvant therapy (NT) before planned PD (2010-2015) were reviewed to identify those with aborted resection. Data were gathered on OS and symptoms of biliary obstruction or GOO requiring medical or procedural intervention. **Results:** Of 213 intended PDs, 37 (17.4%) were aborted (20 mets, 13 UR, 4 medically inoperable). Median overall survival for aborted PD patients was 11.4mo (IQR 7.5-18.8), with lower overall survival in patients aborted for mets than for other reasons (9.6 vs 14.3mo,  $p=0.04$ ). Patients with >2mo follow-up ( $n=28$ ) were analyzed for symptoms. Median follow-up for this group was 11mo (range 2.1-40.9). Five patients (18%) had a biliary bypass (BB) (2 prior to, 3 at time of aborted PD) and 5 (18%) had gastro-jejunostomy (GJ) (all at time of aborted PD). One patient had delayed gastric emptying requiring gastrostomy tube after prophylactic GJ bypass; there were no other complications after palliative bypass. Prior to intended PD, 21/28 had a metal biliary stent, with no duodenal stents. In all, 15/22 (68%) patients with no operative bypass required an intervention at a median of 10.2 mo (range 0.5-27.3 mo), but none required palliative surgery. Of 23 without GJ, 9 (39%) had GOO (3 managed medically, 6 endoscopically). Of 23 without BB, 15 (65%) developed obstruction (3 treated medically, 10 endoscopically, 2 percutaneously). All 5 patients with plastic stents required metal stent replacement. **Conclusions:** When intended PD is aborted, patients frequently develop obstructive symptoms. A metal endobiliary stent is recommended for all of these patients. Preemptive surgical bypass may be avoided as these symptoms can usually be managed with endoscopic/percutaneous interventions, especially given the unfortunately short OS.

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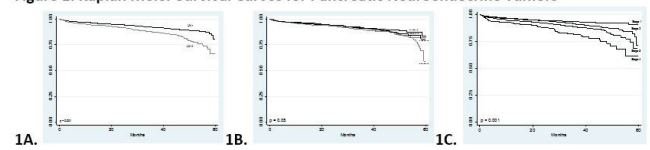
#### LYMPH NODE ASSESSMENT INFORMS PROGNOSIS BUT EXTENT OF LYMPHADENECTOMY IS NOT ASSOCIATED WITH SURVIVAL IN PATIENTS UNDERGOING RESECTION FOR PANCREATIC NEUROENDOCRINE TUMORS

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**BACKGROUND** Most resected pancreatic neuroendocrine tumors (PNETs) are moderate or well-differentiated tumors with relatively indolent biology. The optimal management of regional lymph nodes in the resection of PNETs has not been definitively determined. **METHODS** We queried the National Cancer Database (NCDB) to identify patients undergoing resection for PNET between 2010 and 2014. Patients with poorly differentiated tumors, metastatic disease and those having no nodal assessment were excluded. Parsimonious multivariable (MVR) regression was used to identify factors associated with lymph node involvement (LN+). Cox proportional hazard modeling was used to identify factors associated with overall survival (OS). Candidate variables were chosen a priori and included: age, gender, race, Charlson Comorbidity Index (CCI), insurance status, facility type, procedure, tumor size, histologic grade, margin status, LN+ and number of nodes examined broken by quartiles (1:1-5; 2:6-10; 3:11-16; 4:≥17). **RESULTS** 3709 patients met inclusion criteria. 2094 (57%) had tumors <3 cm in size. 3154 (85%) were well differentiated. 2665 (71%) had no LN+. Factors independently associated with LN+ included: male gender, undergoing pancreaticoduodenectomy (PD), moderately differentiated histology, positive margins, African American race ( $p<0.01$ ) and the number of nodes examined (6-10 nodes: OR 1.72; 11-16: OR 2.21; >16: OR 2.96;  $p<0.01$ ). In multivariable cox modeling of overall survival, age > 70 (HR 2.82;  $p<0.001$ ), male gender (HR 1.32;  $p<0.01$ ), CCI (HR 1.33;  $p<0.001$ ), having a total pancreatectomy (HR 1.76;  $p<0.01$ ), positive margins (HR 1.98;  $p<0.001$ ), undergoing treatment in a community cancer program (HR 1.58;  $p<0.001$ ) and LN+ (HR 1.32;  $p=0.023$ ) were all associated with an risk of death whereas the number of lymph nodes examined was not (5-10 LN: HR 1.15; 11-16 LN: HR 1.39; >16 LN: HR 1.03;  $p>0.05$ ). **CONCLUSION** In patients undergoing resection for PNET, lymph node involvement is associated with poor prognosis. The number of nodes examined is itself an independent

determinate of identifying nodal metastases, but the extent of regional lymphadenectomy does not impact overall survival.

Figure 1. Kaplan Meier Survival Curves for Pancreatic Neuroendocrine Tumors



1A. Kaplan-Meier curves showing overall survival by LN+ (Fig. 1A), quartiles (Fig. 1B), and stage (Fig. 1C).

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#### LOCAL AND SYSTEMIC EFFECTS OF AGING ON ACUTE PANCREATITIS

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**Background:** Acute pancreatitis (AP) in elderly patients in spite of similar occurrence of local complications is followed by a substantial increase in morbidity and mortality rates. Aging process has been found to influence the course and outcome of AP. The mechanisms underlying this age related vulnerability remain unknown. The aim of this study was to evaluate the local and systemic effects of aging on severity of AP in an experimental rat model in elderly animals. **Methods:** AP was induced in Wistar rats by intraductal 2.5% taurocholate injection and divided into 2 experimental groups: Young (3 month old) and Aged (18 month old). Two and 24 hours after AP induction blood samples were collected for determinations of amylase, AST, ALT, urea, creatinine, glucose, and of plasma ileal fatty acid binding protein (I-FABP). TNF- $\alpha$ , IL-6 and IL-10 levels were determined in serum and ascitic fluid. Liver mitochondrial function and malondialdehyde (MDA) contents, pancreas histological analysis, and pulmonary myeloperoxidase (MPO) activity were performed. Bacterial translocation was evaluated by bacterial cultures of pancreas expressed in colony-forming units (CFU) per gram. **Results:** A significant increase in serum amylase, AST, ALT, urea, creatinine, glucose, I-FABP, and IL-6 levels, and a reduction in serum and ascitic fluid TNF- $\alpha$  levels were observed in the aged group compared to the young group ( $p<0.05$ ). Serum IL-10 levels were similar in both groups. However, a marked increase in the ratio of IL-10/I-FABP levels was observed in animals of AP young group when compared with animals of AP aged group ( $p<0.05$ ). Liver mitochondrial dysfunction, MDA contents, and pulmonary MPO activity were increased in the aged AP group compared to the young AP group ( $p<0.05$ ). A significant increase in positive bacterial cultures and histological analysis obtained from pancreas tissue in aged group was significantly increased compared to the young group ( $p<0.05$ ). **Conclusions:** This study demonstrated that aging influences the course of acute pancreatitis evidenced by increased local and systemic lesions and the increased in bacterial translocation. These findings may have significant therapeutic implication in the clinical setting.

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#### EVALUATION OF PROCALCITONIN AS A PREDICTOR OF POST-OPERATIVE PANCREATIC FISTULA AFTER PANCREATODUODENECTOMY ( AN OBSERVATIONAL STUDY)

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**Introduction:** Postoperative pancreatic fistula (POPF) is a major complication after Pancreaticoduodenectomy (PD). In this study, we assess the values of preoperative and postoperative procalcitonin as early predictors of POPF. **Method:** 98 patients undergoing PD for various hepatobiliary and pancreatic diseases from November 2016 to November 2018 were included. Clinical, pathological, biochemical and intraoperative data were recorded along with preoperative, postoperative day 1 (POD1), postoperative day 3 (POD3) procalcitonin values and were analyzed. Patients were randomly divided into 2 groups- Training cohort ( $n=50$ ) and Validation cohort ( $n=48$ ). In each, they were classified into clinically relevant (Grade B+C) and clinically non relevant POPF ( No POPF + Grade A) according to the International Study Group on Pancreatic Surgery 2016 classification. High POD3 procalcitonin values in the training cohort were classified using cut off values based on ROC curve analysis and was applied to the validation cohort to re-define POPF. **Result:** In the Training cohort, 12 patients developed clinically relevant POPF. Both the groups- with and without POPF were comparable in terms of demographic data, presence of jaundice and comorbidities. The incidence of clinically relevant POPF was higher amongst the patients having POD3 procalcitonin value more than 1.18 ( AUC=0.71, sensitivity=66%, Specificity=76%,  $p=0.028$ ). In the Validation cohort, 16 developed clinically relevant POPF. When re-defined according to the new cut off value of POD3 procalcitonin 1.18 ( from training cohort), 20 were predicted to have clinically relevant POPF ( New test: sensitivity= 50%, specificity=62.5%, PPV=40%, NPV=71.4%) **Conclusion:** Patients having POD3 procalcitonin value less than 1.18 have a high probability of NOT developing POPF. Hence, procalcitonin can be used as an early predictor of POPF.