PancreasFest 2017

Abstracts

Posters Displayed: Art Deco Ballroom, Floor 1
from lunch on July 27 through lunch on July 28

National Pancreas Foundation Poster Reception:
Thursday, July 27 from 4:40 to 6:00 pm

PancreasFest 2017

Abstracts

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 # 1

Pancreatic Sufficiency Affects Changes in Weight, Pulmonary Function, and Fat Absorption in Patients with Cystic Fibrosis Treated with Ivacaftor

Naylor Brownell, MD
CAPER Scholarship Recipient – *Children's Hospital of Philadelphia*

Background: Treatment of CFTR mutations with Ivacaftor resulted in improved weight, pulmonary function, growth status, and other outcomes. The response to Ivacaftor for those with pancreatic insufficiency (PI) compared to pancreatic sufficiency (PS) was previously unknown, particularly with regard to fat absorption.

Methods: To determine if response to 3-month Ivacaftor treatment in subjects with CFTR gating mutations differed by pancreatic status, subjects (≥5 yrs old) with one or more CFTR mutations were recruited from the USA, Canada and Italy. Pancreatic status was determined by history and fecal elastase (µg/g stool). Anthropometrics were measured and Z scores calculated for those <20 yrs of age. Fat free mass (FFM), fat mass (FM), and % body fat (%Fat) were determined by whole body dual x-ray absorptiometry (DXA). Forced expiratory volume at one second percent predicted (FEV1%) was assessed by spirometry. Total energy expenditure (TEE) in kcal/d was assessed by doubly labeled water method. Resting energy expenditure (REE%, Schofield) was assessed after overnight fast by indirect calorimetry. Fat malabsorption was measured via coefficient of fat absorption (CFA), as well as a malabsorption blood test (MBT) using the ratio of the absorption of heptadecanoic acid (HA), a triglyceride, to pentadecanoic acid (PA), a free fatty acid.

Results: A total of 23 participants, n=17 with PI (5-42 yrs, mean±SD 15.0±9.9, 53% female, 94% Caucasian) and n=6 with PS (9-61 yrs, 23.8±18.8, 83% female, 83% Caucasian) completed the study. Compared to PI, those with PS had significantly greater weight, BMI, FFM and FM and lower REE% at baseline. Weight and BMI growth status (<20 yrs) was suboptimal for PI (-0.24 and -0.44 Z scores, respectively, n=13) and not for PS (0.01 and 0.18, respectively, n=5). After Ivacaftor, increases in pulmonary function, weight (both FFM and FM), and BMI were significant for PI, and of greater magnitude than for PS. Weight and BMI Z scores improved (+0.25 and +0.38, respectively, $p<0.01$) in PI with no change in PS. REE% decline tended to be greater in PI. TEE remained stable in both groups. Fecal elastase, higher at baseline in PS, increased by 52 to 390 µg/g stool in four out of six subjects. There was an overall insignificant increase in the coefficient of fat absorption (CFA) of 1.5±4.3%. CFA improved significantly (+3.1±3.0%) in subjects with PI only after treatment, as a result of a significant increase in dietary fat intake (13±21 g/day) and decrease in stool fat loss (-1.3±1.7g fat, $p<0.01$). There was no change in the HA:PA ratio, regardless of pancreatic sufficiency. PS subjects had higher HA:PA ratios than PI at both measurements, suggesting better triglyceride absorption at baseline (5.3±0.5 vs. 4.0±1.6, $p=0.057$) and after Ivacaftor (6.0±0.7 vs. 3.7±1.1, $p=0.0001$).

Conclusion: Treatment with Ivacaftor resulted in improved weight, FFM, FM, pulmonary function and reduced REE as well as total fat absorption via CFA in subjects with CF; the magnitude of improvement was greater in subjects with PI. The MBT did not demonstrate increased fat absorption with Ivacaftor; however, it confirmed greater relative absorption of triglycerides in PS subjects.

 # 2

Increased Fat Absorption from Enteral Formula Through a Novel In-line Enzyme Cartridge (RELiZORB®) in Patients with Cystic Fibrosis

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Objectives: Pancreatic Insufficiency and malabsorption of fats lead to reduced caloric intake, inability to maintain or gain weight, and increased gastrointestinal symptoms. As a result, Enteral Tube Feeding (ETF) is used in patients with CF with poor nutritional status. In addition to total fat malabsorption, low levels of long chain polyunsaturated fatty acids, such as DHA and EPA (omega-3 FAs), have been shown to be decreased in patients with CF and may play a role in the pathogenesis of inflammation in CF. RELiZORB® (Alcresta Therapeutics) is an in-line digestive cartridge that was developed to hydrolyze fat in ETF prior to ingestion. The current study evaluated the safety, tolerability, and effect on fat absorption of RELiZORB during administration of enteral formula to patients with CF.

Methods: Patients with CF and pancreatic insufficiency receiving ETF participated in a multicenter, randomized, double-blind, crossover trial with an open-label safety evaluation period. Safety and tolerability endpoints included adverse device effects and GI symptoms of fat malabsorption. Fat absorption was assessed by measuring plasma concentrations of long chain polyunsaturated fatty acids (LCPUFAs) such as docosahexaenoic acid (DHA) and eicosapentaenoic acid (EPA) which are important for growth and development.

Results: Thirty-three participants were recruited from 11 CF centers; mean (SD) age was 14.5 (6.2) years, and 20 (60.6%) were male. Mean duration of EN use was 6.6 years. Mean body mass index (BMI) for subjects age 18 years and older was 19.5+1.1, and mean BMI percentile for subjects less than 18 years of age was 33.6%. At baseline, the mean plasma concentrations of LCPUFAs were approximately 60% of those found in normal healthy people. There were no unanticipated adverse device effects. RELiZORB use was associated with a decrease in the occurrence and severity of reported GI symptoms and an increase in reported preservation of appetite and ability to consume breakfast relative to baseline. Compared with placebo, RELiZORB use resulted in a 3.5-fold increase in plasma $AUC_{0\text{-}24}$ for LCPUFAs ($P < 0.05$) and a 2.8-fold increase in plasma $AUC_{0\text{-}24}$ for Total DHA+EPA($P < 0.001$). Increased plasma concentrations of Total DHA+EPA were seen in the RELiZORB group in as little as 7 hours and remained elevated up to 24 hours and were consistent with plasma concentrations found in healthy humans. These findings of increased DHA and EPA absorption were consistent across age groups studied.

Conclusions: In patients with CF and pancreatic insufficiency receiving ETF, use of RELiZORB (immobilized lipase) digestive cartridge was safe and well tolerated, and when compared with placebo resulted in increased fat absorption as demonstrated by significantly higher plasma levels of LCPUFAs.

 # 3

Periprocedural Fluid Type and Volume Reduce the Risk of Post-ERCP Pancreatitis in High Risk Patients: A Secondary Analysis of a Randomized Controlled Trial

Venkata Sandeep Akshintala, MD
CAPER Scholarship Recipient – *Johns Hopkins University*

Background: Aggressive hydration with lactated Ringer's was recently shown to be efficacious in reducing the incidence of post-ERCP pancreatitis (PEP) in a randomized controlled trial (RCT) of average risk patients undergoing ERCP. The impact of fluid on the incidence of PEP has not been evaluated in high risk patients.

Methods: We conducted a secondary analysis of the effect of volume and type of intravenous fluid administered on the incidence of PEP in high risk patients who underwent ERCP as a part of a double blinded RCT comparing the efficacy of rectal indomethacin versus a combination of papillary spray of epinephrine and rectal indomethacin for the prevention of PEP. High risk patients were defined on the basis of prospectively validated patient and procedure-related risk factors. Patients who underwent planned therapeutic pancreatic stenting and those with suspected sphincter of Oddi dysfunction (SOD) type 3 were excluded from the study. PEP was defined as per the consensus criteria. The volume and type of fluid(s) infused during and after ERCP (periprocedural) were evaluated for their impact on the incidence of PEP using univariable logistic regression analysis.

Results: A total 959 patients (mean age of 52.33±14.96 years; 551 (57.4%) females) were randomized during the trial, of whom 476 (49.6%) received periprocedural fluids (mean fluid administered 1245±629mL). The incidence of PEP was reduced in patients who received periprocedural fluid vs those who did not receive periprocedural fluid (5.2% vs 8.0%, p=0.079; OR, 0.65; 95% CI 0.38-1.09). Patients who developed PEP received a lower mean volume of fluid compared to those who did not develop PEP (752±783mL vs. 1012±725mL, p=0.036). There were 174 patients (37%) who received lactated Ringer's (LR). Patients who developed PEP received a lower mean volume of LR compared to those who did not develop PEP (329±356 vs. 570±559mL, p=0.006). The use of LR was associated with a lower risk of PEP compared to those who received all other types of fluid (5.8% vs 9.8%, p=0.047; OR, 0.56; 95% CI 0.31-0.99, p=0.047).

Conclusion: Higher mean volume of periprocedural fluids and use of lactated Ringer's solution further reduces the incidence of post-ERCP pancreatitis beyond rectal indomethacin based on this subgroup analysis of a pharmacological prophylaxis PEP trial conducted in high risk patients. (Funded by 2014 ASGE Endoscopic Research Award)

 # 4

A Randomized Trial of Rectal Indomethacin and Papillary Spray of Epinephrine Versus Rectal Indomethacin Alone for the Prevention of Post-ERCP Pancreatitis in High Risk Patients

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Background: Rectal indomethacin and papillary spray of epinephrine have been separately shown tobe efficacious for the prevention of post-ERCP pancreatitis (PEP) in randomized controlled trials. Topical epinephrine induces arteriolar vasoconstriction in the papillary mucosa reducing edema and subsequent pancreatic ductal outflow obstruction. We hypothesized that the synergistic use of papillary spray of epinephrine and indomethacin may further reduce PEP over indomethacin alone.

Methods: We conducted a comparative effectiveness, multicenter, double-blind, randomized trial comparing the efficacy of indomethacin alone vs a combination of papillary spray of epinephrine and indomethacin for the prevention of PEP in high risk patients based on prospectively validated patient and procedure-related risk factors. Patients who underwent therapeutic pancreatic stenting and those with suspected sphincter of Oddi dysfunction (SOD) type 3 were excluded. Patients were randomized to receive either a combination of 100 mg of indomethacin and papillary spray of 20 mL of normal saline (indomethacin alone group) or a combination of 100 mg of indomethacin and papillary spray of 20 mL of 0.02% epinephrine (combination group) at the end of ERCP. A Data and Safety Monitoring Board monitored the study. The primary outcome was the incidence of PEP and the secondary outcome was the severity of PEP, both defined by the consensus criteria. A total of 948 patients (474 in each group) would provide a power of 80% at a 2-sided significance level of 5% to detect a 50% difference in the rates of PEP, assuming rates of PEP of 10% and 5%, respectively, for rectal indomethacin and the combination. A two-tailed Fisher's exact test was used to analyze the difference in the proportion of patients with PEP in the indomethacin alone vs. the combination groups.

Results: A total 959 of patients (mean age 52.33±14.96 years; 551 (57.4%) females) were randomized for this trial. All patients completed the follow up and were analyzed in the group to which they were randomized per the intention to treat principle. The baseline characteristics were similar between the two groups (Table1). Females <50 years of age(25.4%) and difficult cannulation (84.9%) were the most common patient and procedural risk factors, respectively. Trainees were involved in 24% of the cases. The incidence of PEP in indomethacin alone group (n=482) was 6.4% as compared to 6.7% in the combination group (n=477) (p=0.87). Severe PEP was found in 5 (12%) versus 7 (16%) of patients in the indomethacin alone and combination groups, respectively (p=0.87). The overall mortality was 0.6% which was unrelated to the primary outcome.

Conclusion: The combination of papillary spray of epinephrine and rectal indomethacin does not reduce the incidence of PEP compared to rectal indomethacin alone in high risk patients.

 # 5

Annular Pancreas: Endoscopic and Pancreatographic Findings From a Tertiary Referral ERCP Center

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Keywords: annular pancreas, ERCP, pancreas divisum

Introduction: Annular pancreas is a congenital anomaly where pancreatic tissue at least partially encircles the duodenum. Current knowledge of endoscopic findings of annular pancreas has been limited to small case series. The aim of this study is to describe the endoscopic and pancreatographic findings of patients with annular pancreas at a large tertiary care ERCP center.

Methods: This is a retrospective observational study. Our institutional prospective ERCP database was queried for cases of annular pancreas. The electronic medical record was searched for patient and procedure-related data. Technical success was defined as completion of intended imaging and therapy.

Results: From 1/1/94 - 12/31/16, there were 46 patients identified with annular pancreas who underwent ERCP at our center. The indication for ERCP was chronic abdominal pain (suspicion of sphincter of Oddi dysfunction, n=20, 42.6%), history of acute pancreatitis or recurrent acute pancreatitis (n=16, 34.8%), elevated liver tests (n=10, 21.7%) or other (n=11, 23.9%). Pancreatobiliary neoplasia was identified in 7 patients (17.9%). The mean age at index ERCP was 46.3 ± 17.2 years. The majority of patients were female (n=33, 71.7%) and Caucasian (n=40, 87.0%). Index ERCP was technically successful in 40 patients (87.0%) and in 45 patients after two attempts (97.8%). A duodenal narrowing or ring was found in the majority of patients (n=39, 84.8%), yet only two (4.3%) had retained gastric contents. Pancreas divisum was found in 21 patients (45.7%), 18 of which were complete divisum. The annular branch was visualized on pancreatogram in 34 patients (73.9%), arising from the ventral pancreatic duct in 30 patients (88.2%). Furthermore, there were findings of chronic pancreatitis in 15 patients (32.6%) noted at the index ERCP.

Conclusions: This is the largest series to date describing the endoscopic and pancreatographic findings of patients with annular pancreas. It demonstrates that patients with annular pancreas who receive ERCPs are mostly adults. While children with annular pancreas may undergo surgery for upper GI obstructive symptoms, adults appear to present with pancreatobiliary pathology. We found that 45.7% of patients had concurrent pancreas divisum, consistent with prior literature. Nearly one-third of patients had findings of chronic pancreatitis at the time of index ERCP. It is unclear whether this may be a feature of the natural history of annular pancreas.

Continued

Figure 1. Endoscopic image of circumferential narrowing of duodenum in a patient with annular pancreas, with minor papilla noted (yellow arrow) on rim of annulus.

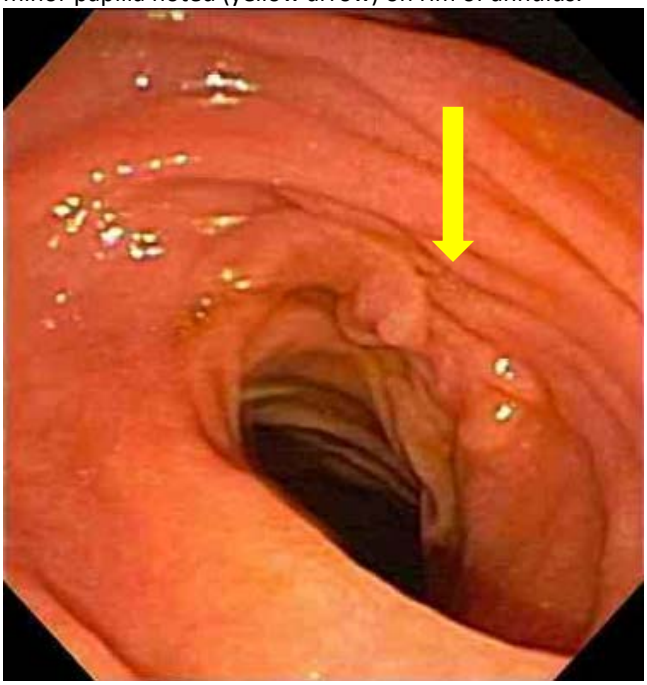
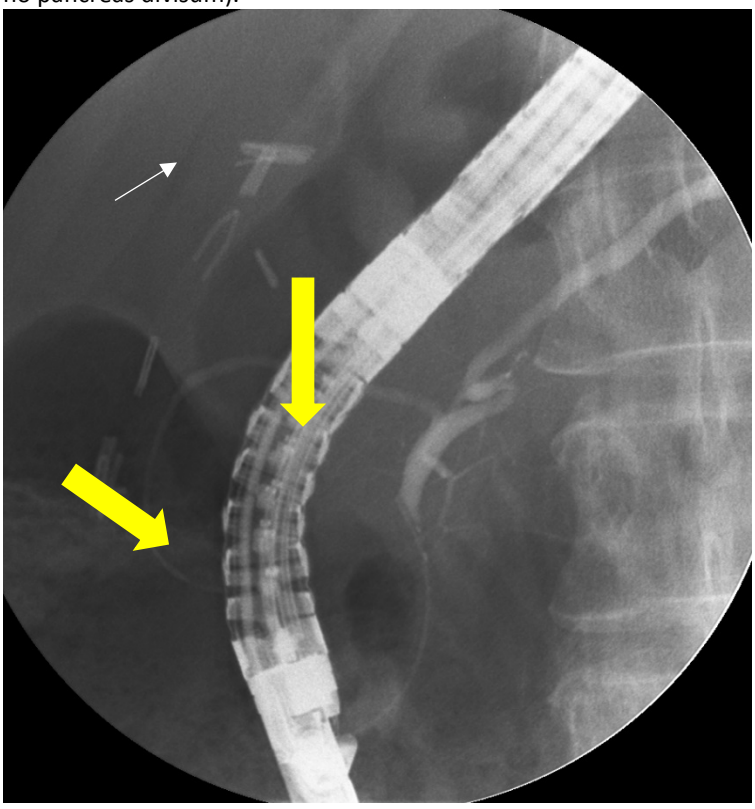


Figure 2. Pancreatogram demonstrating annular ring (yellow arrows), with otherwise normal ductal anatomy (i.e. no pancreas divisum).



 # 6

Scoring System to Predict Failure to Pure Endoscopic Therapy for Patients with Symptomatic Necrotizing Pancreatitis Treated with Endoscopic Step-up Approach

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Background and Aims: While endoscopic step-up approach for symptomatic necrotizing pancreatitis is widely used, little is known regarding factors associated with outcomes using this approach. We aimed to develop a model to predict endoscopic failure, defined as non-resolved necrosis at 1 year and/or requirement of percutaneous drainage and/or surgery.

Methods: We performed a retrospective study of 316 patients with necrotizing pancreatitis, of which 160 patients underwent endoscopic drainage, between 1/2009 and 5/2016 with the median follow-up of 19.2 months. All patients were managed using a consistent endoscopic step-up approach throughout. We selected variables to predict endoscopic failure. We created a multivariate model that was based on a 70% randomly selected cohort (n=111) and validated the model on the other 30% (n=49). Logistic regression was used for univariate and multivariate analyses.

Results: There were 72 patients (45%) who met the criteria for endoscopic failure. Factors that predicted endoscopic failure included the requirement of intensive care and/or vasopressor at any point prior to index endoscopic drainage, serum white cell count and serum albumin at the time of index endoscopic drainage, and bilateral extrapancreatic necrosis (Table 1). Mesenteric involvement, and the American Society of Anesthesiologists class improved the performance of the model, with receiver operating characteristic curve value of 0.889 in the training cohort. In the validation cohort, the model predicted endoscopic failure with receiver operating characteristic curve value of 0.772 (Figure 1). We proceeded with the optimal cutoff analysis, endoscopic failure score of more than 37.7% indicates that the symptomatic necrotizing pancreatitis would not resolve at 1 year after index endoscopic drainage, and/or require percutaneous drainage and/or surgery to achieve a complete resolution with sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 68.4%, 80.0%, 68.4%, 80.0%, and 75.5%, respectively.

Conclusion: We identified factors that can identify patients at risk of endoscopic failure. Cystenteric stent type did not affect this ultimate outcome. These patients should be closely monitored and endoscopists should have a low threshold to proceed with next algorithm on the endoscopic step-up approach.

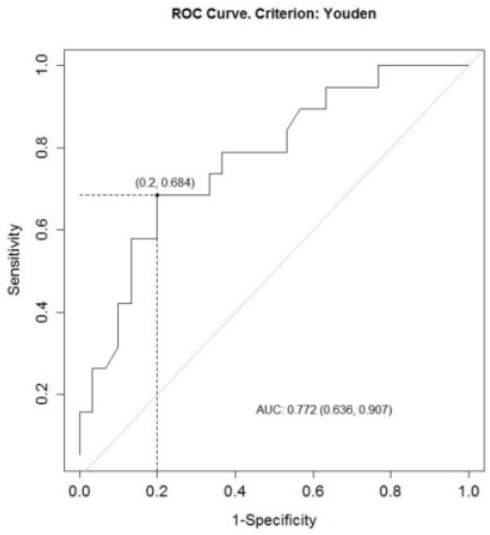
Continued

Table 1: univariate and multivariate analyses of factors associated with endoscopic failure (n=53) in the training set

Variables	Non-resolved necrosis at 1 year and/or percutaneous drainage and/or surgery (n=53)			
	Univariate		Multivariate	
	Odds ratio (95% CI)	*P* value	Odds ratio (95% CI)	*P* value
Biliary pancreatitis	1.25 (0.58-2.70)	0.57		
Intensive care requirement at any point prior to index endoscopic drainage [a]	7.26 (3.21-17.31)	<0.0001	8.16 (2.85-26.53)	0.00005
Serum white cell count at the time of endoscopic drainage ($x10^9$/L)		0.08		0.04
9.9 or less	1.00 (reference)	-	1.00 (reference)	-
10-14.9	0.84 (0.34-2.07)	0.71	0.37 (0.09-1.31)	0.12
15-19.9	0.68 (0.16-2.52)	0.57	0.20 (0.02-1.35)	0.10
20 or more	4.37 (1.21-20.87)	0.02	3.29 (0.55-26.14)	0.20
Serum albumin at the time of endoscopic drainage (g/dL)		0.0002		0.03
3 or more	1.00 (reference)	-	1.00 (reference)	-
2-2.9	2.44 (1.02-6.14)	0.046	1.59 (0.47-5.55)	0.45
1.9 or less	11.45 (3.42-47.04)	<0.0001	8.71 (1.67-56.03)	0.01
Size of necrosis (cm)		0.28		
14.9 or less	1.00 (reference)	-		
15-19.9	1.50 (0.61-3.72)	0.38		
20 or more	2.32 (0.77-7.53)	0.14		
Mesenteric involvement	5.41 (2.10-15.93)	0.0003	2.02 (0.54-8.17)	0.30
Bilateral extrapancreatic necrosis	4.46 (2.04-10.19)	0.0002	4.29 (1.37-14.82)	0.01
Type of cystenterostomy stent		0.46		
Lumen-apposing metal	1.11 (0.52-2.34)	0.79		
Fully covered metal	0.59 (0.21-1.44)	0.23		
Double-pigtailed plastic	1.35 (0.61-3.01)	0.46		

(n = 111)

Figure 1: Area under the receiver operating characteristic curve in the validation cohort (n=49)



 # 7

Pancreatic Cyst Fluid Carcinoembryonic Antigen: Same Mary, Different Hats

Adrianne Tsen, DO, David Henkes, MD, Sandeep Patel, DO, Sreedevi Atluri, MD, and Laura Rosenkranz, MD

Background: Carcinoembryonic antigen (CEA) is a monomeric glycoprotein widely used as a serum tumor marker in following gastrointestinal malignancies, as well as in the analysis of pancreatic cystic fluid, differentiating mucinous from nonmucinous lesions. Quantitative measurement of CEA is performed using an electrochemiluminescence immunoassay, with its concentration assessed by intensity of light emitted. CEA levels obtained from same specimens, yet, analyzed by separate laboratories should be consistent with each other, however this is not always the case. Lag periods may occur between cystic fluid sample analysis in various settings, thus affecting consistency of CEA measurements due to sample degradation. Non-serum CEA measurements are not routinely performed in community hospitals. Unlike serum CEA tests, which have been extensively studied by the analyzing manufacturers, most of the tests used for pancreas cystic fluid analysis, have not been validated. The aim of our study was to compare CEA levels measured in a community hospital setting with those analyzed by Interpace Diagnostic (RedPath) using the same sample, obtained via endoscopic ultrasound fine-needle aspiration (EUS guided FNA) from pancreatic cysts.

Methods: A retrospective chart review was conducted on adult subjects who underwent endoscopic ultrasound fine-needle aspiration (EUS guided FNA) from January 2013 to December 2015 for evaluation of pancreatic cystic lesions. All subjects who had pancreatic cystic fluid analysis performed both at our community hospital and at Interpace Diagnostics (RedPath) met inclusion criteria for the study.

Results: 125 cases underwent EUS guided FNA of pancreatic cystic lesions in this time period. 23 cases had fluid analysis performed at both places. The absolute difference in CEA measurements with values less than 100 mg/mL was 34.78% [N=8], whereas differences between 100 to 500 mg/mL, and greater than 500 mg/mL were: 21.74% [N=5], and 43.38% [N=10], respectively. Onsite CEA levels were greater than those performed at Interpace Diagnostics in 73.91% [N=17] of cases with a difference of less than 100mg/ml (29.41%, N=5), 100 to 500 mg/mL (23.52%, N=4), and greater than 500 mg/mL (47.06%, N=8). Interpace Diagnostics reported CEA levels greater than onsite in (26.08%, N= 6) of cases with values less than 100 mg/mL (50%, N=3), 100 -500 mg/mL (16.67%, N=2), and greater than 500 mg/mL (33.33%, N=1).

Conclusion: This study suggests that differences in fluid CEA measurements between different laboratories should be considered when evaluating pancreatic cystic lesions. Once identified, this difference may alter further workup. Community based gastroenterologists and primary care physicians need to be aware of this possibility.

	Differences in carcinoembryonic antigen levels (mg/mL)		
	<100	100-500	>500
Onsite carcinoembryonic antigen > Interpace Diagnostic carcinoembryonic antigen	5 (29.41%)	4 (23.52%)	8 (47.06%)
Interpace Diagnostic carcinoembryonic antigen >Onsite carcinoembryonic antigen	3 (50.00%)	1 (16.67%)	2 (33.33%)
Absolute Differences	8 (34.78%)	5 (21.74%)	10 (43.48%)

 # 8

An International Multicenter Study of Mortality in Infected Pancreatic Necrosis

Robert Moran, MD
CAPER Scholarship Recipient – *Johns Hopkins University*

Background: The incidence and determinants of mortality in a large cohort of consecutive patients with infected pancreatic necrosis (IPN) are not known.

Aims: To evaluate the incidence and key determinants of mortality of IPN.

Methods: A retrospective cohort study of consecutive patients with IPN was carried out across 17 centers from 2000 to 2016. Inclusion criteria included necrotizing pancreatitis on contrast enhanced CT or MRI. Definite IPN was defined as a positive culture from the (peri) pancreatic bed. Probable IPN was defined as a clinical suspicion of infection but in the absence of a positive culture from the (peri) pancreatic bed. Survival analysis was used to compare factors associated with inpatient mortality. Censoring was performed at the time of the last day of inpatient admission or at 365 days.

Results: A total of 787 patients were diagnosed IPN, of whom 743 had definite IPN. Of the 169 (21.4%) inpatient deaths over 1 year, 153 occurred during the index and 16 occurred during subsequent hospitalizations. There was no difference in mortality in patients with definitive vs probable IPN (155/743 vs 14/44, p = 0.09). On multivariable Cox proportional hazard analysis, organ failure (OF) (4.53 95%CI: 2.79-7.36, p < 0.001), advanced age (age < 60: HR = 1.00; age 60 to < 70: HR=1.49, 95%CI:1.01-2.22, p = 0.047; age ≥ 70: HR = 1.95, 95%CI: 1.30-2.93, p = 0.001), higher Charlson comorbidity index (CCI) scores (CCI 0-1: HR = 1.00; CCI = 2-3: HR = 1.74, 95%CI: 1.18-2.56, p = 0.006; CCI ≥ 4: HR = 2.73. 95%CI: 1.81-4.11, p = < 0.001) and open necrosectomy within 30 days from initial presentation (1.95 95%CI: 1.41-2.70, p < 0.001) were associated with mortality. Of the 169 patients who died, only 12% (20/169) did not have a history of preceding OF. Patients who died without a history of preceding OF had a higher mean age (69.8±1.6 vs 59.8±1.2, p = 0.03) and CCI (3.1±0.5 vs 1.9±0.2, p < 0.01) than patients who died with a history of preceding OF. Patients with transient OF, ≥ 60 years of age with a CCI score ≥ 1 had significantly higher inpatient mortality (n = 61/132, 59.8%) than patients with persistent OF, < 60 years of age with a CCI score < 1 (n = 41/138, 40.2%) (HR: 1.68, 95%CI 1.13-2.49, p = 0.01).

Conclusion: Advanced age and comorbidity are associated with increased mortality in IPN, particularly in those patients with transient OF or without OF. Our results have implications for future AP severity classification.

 # 9

Hospital Admission for Acute Pancreatitis in a Chinese Population, 2011-2014: Big Data Analytics of Incidence and Hospital Expenses

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Background: Acute pancreatitis (AP) is one of the most common diseases of the gastrointestinal tract. We performed database study to robust estimate the incidence of hospital admission for AP and hospital expenses in a megalopolis of southwestern China.

Methods: We searched the biomedical database of West China, which comprises anonymized hospital statistical records data from 2011 to 2014. We selected all admissions for AP as the principal diagnosis recorded in the database. We used admissions for AP as the numerator and the total resident population in the area covered by the data as the denominator to calculate the incidence of hospital admission. The costs of the average costs per years, per admission and per day were investigated.

Results: A total of 31894 people admitted to hospital with a principal diagnosis of AP were retrieved, of which 16934 (53.1%) were men. The mean age of the patients was 52.1 (SE 15.2) years overall. The incidences of hospitalization for AP were 56-63 /per 100 000 population from 2011-2014. Incidence rates for both men and women increased substantially during the study period. Average expenses per hospitalization and annual average expenses per patient exceeded the rising of Customer Price Index (CPI). Excluding the factor of CPI growth, the average cost per admission in 2014 escalated up to 1.13-folds of 2011, and the average cost per day was 1.22-folds. Hospital expenses due to AP occupies about 50% of Per-Capita Disposable Income (PCDI) for urban residents.

Conclusions: The incidence of hospitalization and hospital expenses for AP remarkably increased and caused a serious health economic burden.

 # 10

The Impact of Body Mass Index and Comorbidities on Outcomes in Acute Pancreatitis, Results from a Multicenter Registry of Acute Pancreatitis

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Background: The impact of comorbid disease has not been well defined in a large cohort of patient with acute pancreatitis (AP).

Aims: To evaluate the association between body mass index (BMI) and comorbidities on mortality and organ failure (OF) in AP.

Methods: A multicenter prospective study of consecutive patients admitted with AP was conducted from January 2014 to February 2015. BMI was defined as normal (19 to <25), overweight (25 to < 30) and obese (> 30). Comorbidities were defined per the Charlson comorbidity index (CCI) and were evaluated individually and in the following categories of CCI scores: CCI 0-1, CCI 2-3 and CCI ≥ 4. The occurrence of inpatient mortality and inpatient OF were the primary outcomes of interest. Cox model was used to compare factors associated with OF and inpatient mortality. Somers D was used to compare cox models for best fit. Censoring was performed at discharge from the index admission.

Results: During the study period 1660 patients were admitted with AP. Median (IQR) age was 66.2yrs (50.5-79.2), median (IQR) CCI was 0 (0-1) and 895 (53.92%) patients were male. There were 70 inpatient death, 120 patients developed persistent OF and 113 developed transient OF. BMI data was available on 1559 patients. Of these, 45.3% were overweight and 23.5% were obese. The individual components of the CCI that produced the cox model with the best fit for mortality were Ischemic heart disease (IHD), congestive heart failure (CHF), chronic lung disease, peripheral vascular disease and dementia. Two cox models were constructed to evaluate the impact of comorbid disease and BMI on Mortality. Model A (table 1) included Age, individual components of the CCI and BMI and model B (table 1) included Age, CCI scores and BMI. There was no difference in the model fit of the model that contained the individual components of the CCI compared to the model that contained the CCI scores (model A vs model B, p = 0.937). The individual components of the CCI that produced the cox model with the best fit for OF were IHD, CHF, Chronic liver disease and chronic kidney disease. Two cox models were constructed to evaluate the impact of comorbid disease and BMI on OF. Model C (table 2) included Age, individual components of the CCI and BMI and model D (table 2) included Age, CCI score and BMI. There was no difference in the model fit for the model that contained the individual components of the CCI compared to the model that contained the CCI scores (model C vs model D, p = 0.971).

Discussion: Age is an important determinant of mortality but not OF in AP. BMI and comorbidities are associated with mortality and organ failure, this has important implications for predictive scores and severity classifications in AP.

 # 11

Increased Opioid Analgesic Use Correlates with Morphologic Severe Acute Pancreatitis

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OBJECTIVE: To assess relationship between opioid use and morphologic severity in patients with acute pancreatitis (AP).

MATERIALS AND METHODS:
The records of all adult patients with a diagnosis of AP from 2006-2016 were reviewed. The revised Atlanta classification (RAC) was used to define AP. The CT severity index (CTSI) and modified CTSI (MCTSI) were used to grade the morphologic severity of AP. Exclusion criteria included outside hospital transfers, readmission for AP within 2 weeks of discharge, underlying chronic pancreatitis (CP) as defined by the presence of calcification(s) and/or a dilated main pancreatic duct (≥ 5 mm) on past or current imaging, psychiatric comorbidities, intubation with mechanical ventilation, chronic opioid use, illicit drug use and no contrast enhanced CT scan in first 72 hours of admission. Comorbidity was quantified using the Charlson index (CCI). All opioids administered in the first 7 days of hospitalization were recorded and converted to oral morphine equivalents (OME). The total OME per day of treatment for abdominal pain was used for the analysis. Data is adjusted for age, gender, race, etiology and CCI.

RESULTS:
There were 267 patients with AP, of whom 196 were underwent a contrast enhanced CT, with 58.2% male, the mean age of 46(± 14) years, alcoholic etiology in 55.6 % and 60% with the first episode of AP. The mean OME/day was 60±53 mg. Mild, moderate and severe AP was seen in 80.6%, 18.9% and 0.5% of patients according to CTSI and 50%, 45.9% and 4% of patients according to MCTSI, respectively.
Mean OME/day was higher in patients with moderate to severe AP compared to mild AP (69.5, 50 p=0.011) and this difference was also seen in the adjusted analysis.
Conclusion: Patients with morphologically moderate-severe AP required more opioids during the early phase of hospitalization.

KEYWORDS: Acute pancreatitis; Modified CT severity index; Opioid; Contrast-enhanced computed tomography

 # 12

Association of Dietary Habits with Severe Acute Pancreatitis

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Background: The revised Atlanta classification stratifies acute pancreatitis (AP) based on the development of local complications and/or organ failure into mild, moderate, and severe disease. The relation between diet and risk of AP has been suggested by prior studies, but the association of dietary habits with AP severity has not been previously evaluated.

Aim: Assess differences in severity of AP based on reported dietary habits.

Methods: A prospectively maintained cohort of patients with AP admitted to a tertiary medical center between 2008 and 2015 was utilized. A questionnaire with details on dietary habits was completed by interviewing enrolled subjects during their hospitalization. Patients were stratified into two groups: mild/moderate AP and severe AP. Dietary habits were categorized based on the overall type of diet, fruits/vegetables servings, fat content, dairy consumption, and fluid intake. Multivariate analysis was used to determine whether dietary habits have an independent association with severity of AP. P-value ≤ 0.05 was considered statistically significant.

Results: A total of 309 prospectively enrolled patients had available dietary habits questionnaires: 153 (49.5%) male, mean age was 51 years. Two hundred and forty (77.7%) patients developed mild/moderate AP and 69 (22.3%) developed severe AP. No differences in etiology of AP were present between both groups. Patients who developed severe AP were more likely to consume < 3 servings of fruits/vegetables per day (81% versus 60%, p=0.003), had a lower mean daily fluid intake (47.1 Oz versus 55.8 Oz, p=0.05), and a lower ratio of fluid intake to BMI (1.5 versus 1.9, p=0.03) prior to the onset of AP. No differences in the diet fat content (p=0.59), or dairy consumption (p=0.55) were present between both groups. Multivariate analysis controlling for gender, age, etiology of AP, smoking, and alcohol intake, showed an independent association between fruit/vegetables intake (odds ratio: 0.35) and ratio of fluid intake to BMI (odds ratio: 0.5) with the development of severe AP.

Conclusion: A diet poor in fruits and vegetables and decreased fluid intake are independently associated with severe disease in patients with AP. These important findings require further evaluation and may be useful in patient counseling and risk stratification.

Continued

Table 1: Dietary Habits Prior to Admission in Patients with Mild/Moderate AP and Severe AP			
	Mild/Moderate AP N=240	**Severe AP N=69**	**P-value**
Diet type			
Vegetarian	5/216 (2.3%)	0	0.48
Mainly vegetarian with occasional meat/poultry	66/216 (30.6%)	18/60 (30%)	
Daily meat/poultry	145/216 (67.1%)	42/60 (70%)	
Fat content			
Low fat	58/157 (36.9%)	12/42 (28.6%)	0.59
Average fat	81/157 (51.6%)	25/42 (59.5%)	
High fat	18/157 (11.5%)	5/42 (11.9%)	
Dairy consumption			
< 1 serving per day	54/216 (25%)	17/59 (28.8%)	0.55
≥ 1 serving per day	162/216 (75%)	42/59 (71.2%)	
Fruits and vegetable consumption			
< 3 servings per day	129/215 (60%)	47/58 (81%)	**0.003**
≥ 3 servings per day	86/215 (40%)	11/58 (19%)	
Mean fluid intake in Oz (SD)	55.8 (40)	47.1 (30)	**0.05**
Mean fluid intake / BMI (SD)	1.9 (1.3)	1.5 (1)	**0.03**

 # 13

12 Gene Pancreatitis Susceptibility Panel: Clinical Validation of a Targeted, High-Fidelity, Next Generation Sequencing Approach

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Background: Recurrent acute & chronic pancreatitis (CP) are inter-related complex disorders with features overlapping other known & idiopathic conditions of the pancreas & abdomen. At least 12 genes increase susceptibility and/or modify severity of pancreatic disorders: CaSR, CEL, CFTR, CTRC, CPA1, GGT1, PRSS1/2, SBDS, SPINK1, UBR1 & a CLDN2 risk haplotype (PDSG). Precision medicine for pancreatic disorders allows integration of demographics, other risk factors, biomarkers & clinical context. We hypothesize high-quality genetic data will improve patient classification & management. PancreasDx® is a new advanced next generation sequencing technology (NGS) evaluating 12 pancreatic disease susceptibility genes (PDSG).

Objective: Evaluate PancreasDx performance identifying PDSG DNA variants in deeply phenotyped patients with known PDSG variants.

Methods: PancreasDx was designed using Thunderstorm® (RainDance Technologies, Billerica, MA). The 1680 targets & sequencing method were technically validated as a laboratory-developed test under CLIA/CAP protocols at HudsonAlpha Institute of Biotechnology Clinical Services Laboratory (Huntsville, AL). De-identified genomic DNA acquired in IRB-approved protocols was obtained. Coded amplicons were sequenced with MiSeq (Illumina, San Diego, CA). NextGene (Softgenetics, State College, PA) aligned sequence files and determined genotypes. Variant calls required read depth >100, minor allele frequency 25-75% for heterozygotes, & high quality score. Mutation reports were compared.

Results: 36 subjects (34 pancreatitis, 2 control), mean age at sample collection of 40 yrs (range 6-81), were included. Most common TIGAR-O classification were genetic (>50%), alcohol and idiopathic. Mean DNA sequence depth was 1,404. PancreasDx correctly identified all known, clinically significant variants (CSV). Variants in all genes except PRSS2 were identified, most commonly in CFTR, PRSS1 & SPINK1. Previously unrecognized CSV were seen in 8 patients, including novel CFTR & CTRC variants. CSV occurred in all idiopathic CP patients & changed classification of 5 patients with alcohol and hyperlipidemic etiology to atypical cystic fibrosis. Variants with predicted functional effects were noted in all genes, including GGT1, CaSR & CEL. A significant enrichment of functional CaSR variants (> 50% of patients) were also identified and linked to a specific pathogenic pathway.

Conclusion: PancreasDx accurately identifies CSV in an established pancreatitis population. The broad coverage & deep sequencing method detected a likely etiologic mechanism in subjects classified as idiopathic pancreatitis. PancreasDx identified new mutations in patients with prior genetic testing. Clinical utility was demonstrated by identification of multiple clinically significant mechanistic variants, allowing for reclassifying patients by mechanistic etiology.

 # 14

Application of High-Content, High-Fidelity, Sequencing Technology to Genotyping Clinically Relevant Recurrent Acute- & Chronic Pancreatitis-associated Loci

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Background: The etiology of non-alcohol cases of recurrent acute and chronic pancreatitis (RAP/CP) is commonly noted as idiopathic. We hypothesize a combination of deep genetic sequencing of well-designed targets in an expanded number of susceptibility genes may identify additional etiologic mechanisms in RAP/CP patients. PancreasDx® is a new high-fidelity next generation sequencing (NGS) panel for patients with RAP/CP. Using the Thunderstorm® platform (Raindance Technologies, Billerica, MA), which uses parallel single-plex amplification for up to 200,000 targets, PancreasDx evaluates 12 pancreatic disease susceptibility genes (PDSG), 72 experimental genes and >100 SNPs.

Aims: 1) Demonstrate technical validation of PancreasDx in an end to end fashion in CLIA/CAP conditions 2) Evaluate PancreasDx ability to identify known variants in RAP/CP patients 3) Discover additional risk alleles to improve etiologic classification 4) Provide high quality sequence data for clinical use.

Methods: DNA specimens collected under IRB protocols were isolated from whole blood or saliva, normalized & sonicated to achieve a 3kb fragment size. Droplet generation on the Thunderstorm platform merged pico-droplets containing all 1,680 unique primer sets & PCR components with pico-droplets containing a single 3kb DNA fragment. 3 million nanodrops were created per sample. PCR amplification was completed & confirmed. Amplified samples were sequenced on an Illumina MiSeq 150 bp PE v2 Rapid Run (Illumina, San Diego, CA) in batches of 12, generating 72 fastq.gz files (forward & reverse reads). Fastq.gz files were downloaded using Basespace (Illumina) & unpacked with NextGene v. 1.2.2 (Softgenetics, State College, PA). Variant calls were acceptable with read depths of >30, minor allele frequencies 25-75% for heterozygous & quality score over 20. All samples and mutation reports were generated using CLIA/CAP protocols in triplicate at the HudsonAlpha Institute of Biotechnology Clinical Services Laboratory (Huntsville, AL).

Results: PancreasDx panel-based sequencing was successfully performed on DNA isolated from blood & saliva in 12 samples from RAP/CP patients and were consistent between all three runs. High quality sequence data reads (99.9% accuracy) were over 90% in each run. Average read depth over regions of interest was >1000. In the difficult to sequence, PRSS1 R112H a read depth over 8,000 on more than 46% of the runs was obtained. Turn-around time from genomic DNA to mutation report was 1 week for batches of 12 samples.

Conclusion: PancreasDx is a NGS technology that accurately & efficiently evaluates PDSG. Using advanced technologies additional research sequencing capabilities are possible. This study establishes technical validation of PancreasDx, laying the foundation for future prospective studies.

 # 15

A Trypsinogen Activation Peptide Mutation Worsens Cerulein-induced Pancreatitis in the Mouse

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Background: Mutations in the activation peptide of human cationic trypsinogen (PRSS1) have been found in association with hereditary pancreatitis. Biochemical experiments using recombinant proteins demonstrated that the activation peptide mutations strongly stimulate autoactivation of cationic trypsinogen. These observations supported the hypothesis that increased intra-pancreatic trypsinogen activation causes hereditary pancreatitis.

Aims: The aim of the present study was to generate a mouse model carrying a hereditary-pancreatitis associated activation peptide mutation and characterize the impact of the mutation on experimentally induced pancreatitis.

Methods: Our genetically modified mouse strain carries the p.K24R mutation in the activation peptide of the mouse cationic trypsinogen (isoform T7). This corresponds to the p.K23R mutation in PRSS1. Acute pancreatitis was induced by 12 hourly injections of cerulein. Pancreatitis severity was determined by histology scoring, measurement of edema, MPO and serum amylase. Pancreatic trypsin activity was measured at 30 min after a single dose of cerulein.

Results: Intra-pancreatic trypsin activity and all parameters of acute pancreatitis severity were markedly elevated in mice carrying the p.K24R mutation relative to the C57BL/6N controls.

Conclusions: A trypsinogen activation peptide mutation associated with hereditary pancreatitis in humans increases intra-pancreatic trypsin activity and worsens pancreatitis responses in this novel mouse model.

 # 16

Novel c.49C>A (p.P17T) Mutation in the Activation Peptide of Human Cationic Trypsinogen (*PRSS1*) in a Case of Chronic Pancreatitis

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Introduction: Mutations in the activation peptide of human cationic trypsinogen (*PRSS1*) cause chronic pancreatitis by promoting premature, intrapancreatic trypsinogen activation. Chymotrypsin C (CTRC) can process the activation peptide to a shorter form which results in accelerated autoactivation of trypsinogen. *PRSS1* mutation p.A16V stimulates autoactivation by increasing the rate of N-terminal processing by CTRC. The Hungarian Pancreatic Study Group (HPSG) performs genetic testing of young patients with idiopathic chronic pancreatitis. In this cohort we identified a novel *de novo* variant c.49C>A (p.P17T) in the activation peptide of human cationic trypsinogen.
Aims: Our aim was to investigate the biochemical characteristics and potential pathogenic effect of the novel p.P17T variant.

Patients and methods: The index patient and family members were recruited by HPSG. Sanger sequencing of all exons in *PRSS1, CTRC, SPINK1, CPA1* genes was performed in the index patient. Exon 2 of the *PRSS1* gene was sequenced in the index patient's parents. Trypsinogen was expressed recombinantly and its activation and N-terminal processing by CTRC were studied using enzymatic assays and SDS-PAGE.

Results: We identified a *de novo* c.49C>A (p.P17T) heterozygous mutation in exon 2 of the *PRSS1* gene in a patient with childhood-onset chronic pancreatitis. This patient also carried a heterozygous p.N34S mutation of the *SPINK1* gene. Compared to wild type trypsinogen, the p.P17T mutant showed accelerated N-terminal cleavage by CTRC and autoactivated markedly faster in the presence of CTRC. However, relative to the p.A16V mutation, these effects of the p.P17T mutation were slightly smaller.

Conclusion: The novel trypsinogen activation peptide mutation p.P17T showed similar biochemical characteristics as the pathogenic mutation p.A16V. Our results strengthen earlier findings that accelerated N-terminal processing of the trypsinogen activation peptide by CTRC is a relevant mechanism in the development of chronic pancreatitis.

 # 17

Pancreatitis Due to *De Novo PRSS1* Pathogenic Mutations: The Ambry Genetics Experience

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A combination of factors, including genetic and environmental, contribute to the development and recurrence of pancreatitis. The protease, serine 1 (*PRSS1*) gene encodes the cationic trypsinogen protein and is associated with hereditary pancreatitis (HP). Two common *PRSS1* pathogenic mutations, p.R122H and p.N29I, account for approximately 90% of pathogenic alterations observed in *PRSS1*-related HP. *PRSS1*-related HP is typically inherited in an autosomal dominant fashion with reduced penetrance; in cases without a family history of pancreatitis, the mutation is likely to be identified in one of the individual's parents. *De novo* pathogenic mutations in *PRSS1*-related HP have been previously reported; however, the proportion of cases is unknown. Here we report two unrelated individuals with acute pancreatitis and a *de novo PRSS1* mutation. Both individuals underwent gene sequencing analysis of the *CFTR*, *PRSS1*, *SPINK1*, and *CTRC* genes. The first individual was heterozygous for the *PRSS1* p.R122H pathogenic mutation. Targeted sequencing analysis of this individual's parents was negative for the familial alteration. The second individual was heterozygous for a *PRSS1* p.R122H pathogenic mutation and a *CFTR* p.G1069R likely pathogenic variant. This individual's parents underwent gene sequencing analysis of the same four genes as the proband; no pathogenic mutations or variants of unknown significance were detected in the mother. The unaffected father was positive for the familial *CFTR* alteration, but was negative for the familial *PRSS1* p.R122H mutation. Ambry Genetics has been offering pancreatitis genetic testing since 2003 and has tested approximately 9,000 individuals. The finding of two cases of *de novo PRSS1* mutations in over a decade's worth of genetic analysis of this gene suggests that *PRSS1*-related HP due to *de novo* alterations is rare, less than 0.05% of cases. Therefore, parental testing and genetic counseling should be considered for accurate risk assessment and appropriate clinical follow-up.

 # 18

Pancreatic Epithelial Cell Calcineurin, Rather than Immune Cell Calcineurin Mediates Acute Pancreatitis

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Calcineurin (Cn) is a central Ca2+ responsive signaling molecule in inflammation. Among Cn sources, immune cell Cn is thought to serve as a primary inflammatory mediator. However, emerging data suggest that epithelial sources of Cn that are intrinsic to an inflamed organ contribute to organ-specific diseases. Here we show that Cn within the epithelial cells of the exocrine pancreas mediates acute inflammation in pancreatitis. We used a mouse model of post-ERCP pancreatitis (PEP) as clinically representative model of acute pancreatitis. First, we selectively deleted pancreatic Cn sources using a novel intra-ductal delivery of adeno-associated virus (AAV) containing promoter-driven Cre recombinase into a Cn floxed mouse line. We found that the whole pancreatic ablation of Cn (using AAV6-CMV-iCre) resulted in a 73% reduction in PEP severity, and acinar-specific deletion of Cn (using AAV6-Ela-iCre) decreased the severity of PEP by 85%. However, ductal-specific Cn deletion (using AAV6-Sox9-iCre) did not affect the severity of PEP. Second, we deleted Cn in immune cell by making bone marrow chimeras and found that deletion of Cn solely in the hematopoietic system did not affect PEP outcomes. This study highlights a pivotal role for pancreatic epithelial Cn, rather than Cn in immune cell, during acute pancreatitis, and it provides the impetus to devise translationally relevant therapies for acute pancreatitis that target pancreatic Cn.

 # 19

Asparagine Synthetase is Highly Expressed in Pancreatic Acinar Cells and Upregulates with Asparaginase Exposure to Mitigate Cellular Injury

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Asparagine synthetase (ASNS) maintains cellular homeostasis by producing intracellular asparagine (Asn) from aspertate (Asp) and compared to other organs ASNS is highly expressed in the pancreas. Asparaginase, the primary chemotherapeutic drug for acute lymphoblastic leukemia (ALL) functions by depleting circulating Asn, is well documented for inducing pancreatitis in some ALL patients as a side effect. Asparaginase exposure is known to cause an upregulation in ASNS expression in mammalian cell lines and in mouse pancreas. However, little is known about the pathogenesis of asparaginase-associated pancreatitis (AAP) and the role of ASNS expression in AAP. In the present study our aim is to investigate the importance of ASNS expression in pancreatic acinar cells at baseline and with asparaginase exposure. We show, compared to other organs ASNS is predominantly expressed in the mouse pancreas. Asparaginase exposure in mouse (266-6) and rat (AR42J) pancreatic acinar cell lines leads to a time and dose dependent increase in ASNS expression. ASNS is also upregulated in mouse and human primary acinar cells in response to asparaginase exposure. However, treatment with other agents of pancreatitis does not induce ASNS expression. Moreover, knockdown of ASNS in 266-6 cells leads to pancreatic acinar cell injury and this injury is worsened by asparaginase exposure. Asparaginase exposure activates NF-kB signaling pathway in mouse 266-6 cells. These findings suggest that ASNS maintains acinar cell homeostasis at baseline and that its upregulation is required to mitigate asparaginase induced cellular injury.

 # 20

Prevalence and Risk Factors of Oral Feeding Intolerance (OFI) in Patients with Acute Pancreatitis - Perspective from Tertiary Care Referral Center in US

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Background and Aims: Oral feeding intolerance (OFI) complicates clinical recovery of 1 in 5 patients with acute pancreatitis. This is a syndrome characterized by recurrence of gastrointestinal symptoms upon refeeding such as abdominal pain, nausea and vomiting, often in association with biochemical abnormalities such as elevated serum lipase levels. This places significant burden on health care resources, secondary to prolonged hospitalization, poor quality of life during patient's hospital stay, and risk of readmission following hospital discharge. The aims of this study include determination of prevalence and risk factors of OFI in patients with acute pancreatitis.

Methods: The study population was derived from The Acute Pancreatitis Patient Registry to Examine Novel Therapies in Clinical Experiences (APPRENTICE). Only patients enrolled at Eastern Maine Medical Center were included in this study. This study includes detailed questionnaires to obtain information on demographics, etiology, pancreatitis history, co-existing comorbidities, risk factors, severity biomarkers, severity index, health-care utilization, management strategies, and outcomes of AP patients. Descriptive statistics were performed using STATA 12.

Results: A total of 72 patients with acute pancreatitis were enrolled in this study from September 2016 to June 2017. The demographics, clinical characteristics and prevalence of OFI has been shown in Table 1.

Discussion: The prevalence of OFI was 9% in our study. This is lower than what has been reported by previous investigators where the prevalence of OFI is in the 15-20% range. There are several possible explanations for these findings. Firstly a significant proportion of our patients (33, 47%) started refeeding more than 48 hours after hospital admission even though the vast majority of our patients only had mild AP (58, 83%). This is consistent with traditional management practices of AP where a period of NPO is recommended prior to institution of oral refeeding. Also 55 (81%) started feeds with clear liquid diet. This is in contrast to previous studies where patients were fed much earlier in the course of their hospitalization with AP and also resumed regular diet as the first oral refeeding strategy. The practice adopted in our institution has pros and cons. By delaying oral refeeding greater than 48 hours into hospital admission and starting with clear liquid diet a trend toward lower prevalence of OFI was observed. On the other hand this practice is not consistently supported by literature and has the potential of increasing health care costs due to prolonged hospitalization. It may also have an adverse impact on patient's quality of life during their hospitalization. Future prospective studies are needed to determine the optimal timing of oral refeeding in AP.

Continued

Table 1 - Demographics and Clinical Characteristics of Study Patients

	N=72
Median Age, years (IQR)	53 (40-67)
Male Sex, N(%)	42 (58)
BMI≥30, N(%)	33 (46)
Transfers, N(%)	28 (39)
Etiology, N(%)	
Biliary	26 (36)
Alcohol	20 (28)
Hypertriglyceridemic	7 (10)
Others	19 (26)
Recurrent AP, N(%)	25 (35)
	N=70
RAC of AP Severity, N(%)	
Mild	58 (83)
Moderate	11 (16)
Severe	1 (1)
Type of Initial Nutrition, N(%)	
Clear liquid	55 (81)
Full liquid	3 (4)
Soft Mechanical	2 (3)
Regular	8 (12)
Refeeding after 48h of admission, N(%)	33 (47)
Prevalence of OFI, N(%)	6 (9)

RAC - Revised Atlanta Classification

AP - Acute Pancreatitis, RAC - Revised Atlanta Classification 2012

OFI - Oral Feeding Intolerance

 # 21

Visceral Adiposity Predicts Severity Of Acute Pancreatitis

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Background: Recent evidence suggests an association between visceral adiposity, measured as visceral adipose tissue (VAT) area, and severity in acute pancreatitis (AP). However the reliability of VAT as a predictor of disease severity is not known. The aim was to determine the association of visceral adiposity with severe outcomes in AP and to compare it with validated predictors of severity.

Methods: This retrospective cohort study included consecutive patients admitted to a tertiary care hospital with AP between January 2010 and January 2015 who underwent a CT scan. Relevant laboratory, radiographic and other clinical data were collected. The VAT volume was estimated using the method of Linder and colleagues [Scientific Reports, 6, 2261, (2016)]. Severity was assigned based on the Revised Atlanta Classification (mild or moderate vs. severe AP). A univariable and multivariable logistic regression analysis was conducted to assess VAT as a predictor of severe AP compared with other validated predictors of severity.

Results: Five hundred and seventy four patients were admitted during the study period, of which 252 had a CT scan available. Patients with severe AP had a larger VAT area compared to those with mild or moderate AP (mean 184.9 cm2 vs 79.9cm2, p=0.006). Patients that developed MSOF had a larger VAT area than those that did not (150.6cm2 vs 91.0cm2, p=0.004). Patients with acute necrotic collections also had a significantly larger VAT area than those that did not (mean 174.0cm2 vs 91.9cm2, p=0.003). Visceral adipose tissue area demonstrated superior discrimination of severe AP compared with other predictors of severity. The combination of VAT area and BISAP score improved the prediction of severe AP compared with BISAP score alone (AUC, 0.83 vs 0.71 p= < 0.001).

Conclusion: Increased visceral adipose tissue is a strong predictor of severe pancreatitis, necrosis, and multi-system organ failure. Mechanistic studies are needed to explore and therapeutically target this association.

 # 22

Characterization of Long-term Prognosis in Acute Pancreatitis: Is Inpatient Severity Classification Enough?

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Background: Severity classification systems of acute pancreatitis (AP) such as the Revised Atlanta Classification (RAC) assess inpatient morbidity and mortality but may not be predictive of long-term prognosis. To provide effective outpatient care for these patients, determinants of long-term morbidity and mortality must also be identified. The aim of this study was to define clinical subgroups that indicate long-term prognostic significance in patients admitted with AP.

Methods: A retrospective cohort study was conducted that included patients admitted with AP to a tertiary care hospital between January 2010 and January 2015. Seven surrogates of morbidity occurring up to 1 year after discharge were collected. These were: emergency department visits and hospital admissions related/unrelated to AP, length of hospital stay from additional admissions, need for invasive intervention, and 30-day readmissions. Mortality data were also collected, as well as Charlson Comorbidity Index (CCI). To develop the first classification system that carry post-discharge prognostic significance, a clustering algorithm (k-medoids) was used to organize the heterogeneous dataset with many variables into a pre-determined number of homogenous groups. To mirror the 3 categories of severity proposed by RAC, the algorithm was set to produce three groups. Seven surrogates clinically judged to be candidates for determinants of long-term morbidity and mortality were imputed into the algorithm. Candidate variables included determinants of in-hospital severity as defined by RAC, as well as Determinant Based Classification, CCI, Modified CT Severity Index (MCTSI), etiology, and a list of all possible local complications (i.e. acute peripancreatic fluid collection, acute necrotic collection, pseudocyst, walled off pancreatic necrosis, infected local complications). Morbidity and mortality endpoints were also compared between the 3 severity categories of RAC to see if inpatient severity categories carry long-term prognostic significance.

Results: 281 patients were included . The incidences of morbidity endpoints were comparable among the 3 RAC severity categories. Three clusters were identified that carried long-term prognostic significance. Each cluster was given a category name to reflect prognosis. The limited AP category had the best prognosis, and included patients without local complications with a low co-morbidity burden. The brittle AP group ran a very morbid course, but had excellent survival. This group had a low co-morbidity burden, but almost all had local complications (94%) and a high MCTSI. The high-risk AP group had the worst prognosis. Almost all death in the overall cohort occurred in this group, and the mortality rate was 28%. They had a high co-morbidity burden without local complications but 28% of them experienced at least moderately severe episode of AP.

Conclusion: Categories that carry long-term prognostic significance in patients with AP have been developed. The three severity categories by RAC does not accurately signify long-term prognosis of patients with AP. Prospective studies are needed to validate these findings. This study could help formulate appropriate follow-up care for the identified groups and ultimately improve AP outcomes.

Continued

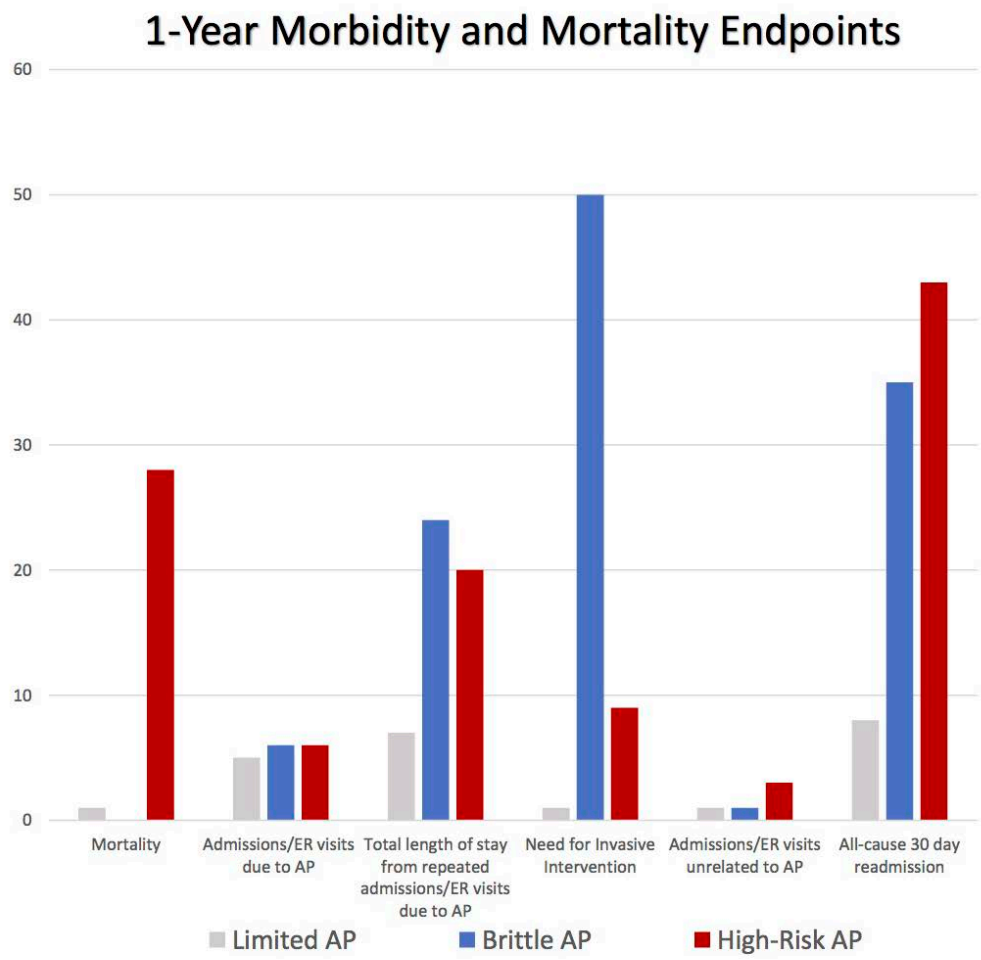

Figure 1. Admission/ER visit values given in mean per patient; Need for invasive intervention, 30-day readmission and mortality values are in %; Length of stay values given in average number of days per patient.

 # 23

Higher Fluid Volumes at 12 Hours May be Associated with Poorer Outcomes in Acute Pancreatitis: A Retrospective Analysis

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Introduction: Acute pancreatitis (AP) is a common gastrointestinal disorder associated with a high morbidity and mortality rate. Current guidelines advocate the need for aggressive fluid resuscitations within the initial 24 hours to prevent patient deterioration. This study aims to explore whether fluid volume by 12 hours post presentation is associated with poorer outcomes.

Methods: This retrospective cohort study was conducted at Long Island Jewish Medical Center (LIJ) and North Shore University Hospital (NSUH) between April and September 2015. 214 non-transferred, adult patients without organ failure were identified using the ICD-9 discharge code for AP (577.0). All patients met the criteria for AP on having two out of three criteria: (1) lipase or amylase > 3 times the upper limit of normal, (2) radiological findings of AP, (3) presence of epigastric pain. IV fluid volume at 12 hours was treated as a continuous variable. A univariate followed by a multivariate analysis was conducted to determine if there was an association between increasing fluid volumes and various outcome variables.

Results: Multivariate analysis revealed that fluid volume was independently associated with the development of necrosis ($p < 0.01$), length of stay ($p = 0.03$) and the development of pleural effusion ($p = 0.01$). Specifically, a 100 mL increase in volume was associated with a 10% increase in the odds developing necrosis and a 6% increase in the odds of developing pleural effusion. The multivariate analysis also revealed that hypertension was strongly associated with the risk of developing organ failure ($p < 0.001$).

Conclusions: These results further support the hypothesis that necrosis is an early phenomenon, and aggressive fluid resuscitation may not suppress it. The risk of pleural effusion development was higher with increasing fluid volumes. Current guidelines on fluid therapy in AP may not be appropriate for every patient.

 # 24

Drain Placement After Pancreatic Resections: A Retrospective Review

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Introduction: Post-operative intra-abdominal drains have historically been used for early detection of hemorrhages, anastomotic leaks and pancreatic fistulas. However, growing literature suggests drains may increase the risk of infection, causing mechanical damage to tissues, leading to major complications and longer hospital stays. This study examines the number of drains and its impact in postoperative outcomes post pancreatic resections.

Methods: A retrospective chart review of 132 adults who underwent pancreatic resections between July 2009 and September 2015 was performed. Fisher's exact test or chi-square test was used to compare categorical variables and Mann-Whitney for continuous variables.

Results: Of 132 patients, 6 (4.55%) did not receive a drain, 49 (37.12%) received one drain, and 77 (58.3%) two or more. Median drain duration was 27 days and 72 patients (57.14%) were discharged with the drains in place. Out of all patients, 7 (5.3%) developed a fistula, 12 (9.30%) developed a drain infection, 31 (24.6%) developed a new intra-abdominal fluid collection and 6 (4.55%) developed acute pancreatitis post operatively. Additionally, 40 patients (30.53%) were readmitted within a year of the resection. There was no association between number of drains and the development of acute pancreatitis, fluid collection, drain infection, fistula, readmission rate, need for reoperation or DVT incidence post operatively. There were significant associations between number of drains, ICU admission ($p = 0.0005$) and hospital length of stay ($p < 0.0001$).

Discussion: The number of drains placed after pancreatic resections is not significantly associated with the development of complications, including pancreatitis, intra-abdominal fluid collections, drain infections and pancreatic fistulas. Due to the small number of patients without drains, further studies are needed.

 # 25

Preoperative Biliary Drainage in Resectable Pancreatic Cancer: A Systematic Review and Network Meta-analysis

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Importance: There remains controversy about the best pre-operative management of jaundice in patients with resectable pancreatic head cancer (RPC) undergoing planned pancreaticoduodenectomy (PD).

Objective: The aim of this study was to systematically review the evidence to compare rates of post-operative complications in patients undergoing four pre-operative approaches (POA): preoperative biliary drainage with plastic stent (PBD-PS), metal stent (PBD-MS), and percutaneous transhepatic drain (PBD-PT), or no pre-operative biliary drainage (NPBD).

Data Sources: Literature search of English language studies regarding preoperative management of obstructive jaundice from MEDLINE, EMBASE and the Cochrane databases between 1945 and April 2016 was performed.
Study Selection: A study was included in the systematic review if it assessed the effects of PBD on post-operative outcomes in jaundiced patients with RPC. Data from a study was included in the network meta-analysis (NMA) if post-operative data for different PBD methods were reported separately, RPC patients accounted for 60% or more and the study reported a pre-specified endpoint of interest.

Data Extraction and Synthesis: PRISMA Extension guidelines were followed for abstracting data. ROBINS-I tool was used to assess study data quality and validity. Strength of evidence was assessed using GRADE.
Main Outcomes and Measures: Endpoints were the rate of any post-operative complication, wound infection, intra-abdominal infection and post-operative bleeding. Network meta-analysis was performed using direct and indirect evidence from pairwise comparisons. Odds ratios and probability scores (P-scores) were calculated to rank the POAs from the best to worst, for each outcome.

Results: The search identified 7232 studies, 32 of were included in the systematic review. All studies were observational in design except one randomized controlled trial. Ten out of 32 studies included in the systematic review reported at least one of the 4 outcomes of interest and thus were used for NMA. The calculated odds ratios and P-scores ranked NPBD as the best approach, followed by PBD-PS, PBD-MS and PBD-PT.

Conclusions: The available evidence indicates that not performing preoperative biliary drainage is the best management of preoperative jaundice in patients with RPC before PD. If patients are to undergo biliary drainage, then PBD-PS appears to be superior to PBD-MS and PBD-PT.

 # 26

Performance of a Multidisciplinary Team in Predicting and Managing Resectable Pancreatic Cancer

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Introduction: Complete surgical resection is the only potential curative treatment for pancreatic ductal adenocarcinoma (PDA). Successful resection rates are highly heterogeneous and rates of microscopic involvement (R1) vary markedly from 20% to over 75%. Furthermore, current guidelines recommend care of these patients to take place at large volume centers utilizing a multidisciplinary pancreatic cancer conference (MDPC) or clinic in order to appropriately manage patients. Initial studies have shown it is not uncommon for changes in staging and management plans after being referred to a MDPC at a large center. However, data is limited with respect to how MDPC perform in correctly predicting resectable PDA. The aims of this study are to report the performance of a MDPC in correctly predicting resectable PDA in addition to reporting the outcome of achieving negative surgical margins (R0).

Methods: The records of consecutive patients presented at a tertiary center's bi-monthly MDPC were prospectively collected from March 2013 to August 2016. A panel of gastroenterologists, medical, radiation and surgical oncologists, pathologists and body radiologists reviewed clinical history, endoscopic ultrasound results, cross-sectional imaging, and pathology to determine resectability. Patients were included if they were deemed to have resectable PDA by MDPC consensus and underwent upfront surgical exploration. Surgical outcomes were analyzed on an intention-to treat basis as all patients underwent surgery with curative intent.

Results: A total of 278 patients with PDA were presented at the MDPC. Ninety-one (32.7 %) were determined as resectable by MDPC team members. Twenty-one patients were excluded (11 patients lost to follow or declined surgery and 10 were medically unfit). Seventy patients underwent upfront surgical exploration with a curative intent and were included for final analysis. MDPC successfully predicted resection in 64 out of 70 patients (91.4%). Six patients were found to have metastatic disease on surgical exploration. 78.6% (55/70) patients had R0 resections and 12.8 % (9/70) patients had R1 margins. There were no grossly positive margins (R2 resection). Patients went to surgery at a median of 22 days from diagnosis and 15 days from the MDPC decision to resect.

Conclusion: A MDPC demonstrated a high rate of correctly predicting resectability along with achieving a high percentage of R0 resections at an experienced center. Data from other large centers may help validate the importance of utilizing a MDPC to predict resectability. Moreover, benchmark R0 resection rates are needed and can provide a quality metric for the treatment of resectable pancreatic cancer.

 # 27

Diagnosis of Early Stage Pancreatic Ductal Adenocarcinoma Using a Serum Biomarker Signature

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Background: Pancreatic ductal adenocarcinoma (PDAC) has a poor prognosis with a 5-year survival of less than 10% due to diffuse symptoms leading to late stage diagnosis. The survival could increase to over 50% if localized tumors can be detected earlier. Multiparametric analysis of blood samples was used to derive a novel biomarker signature of early stage PDAC. The signature was developed from a large cohort of well-defined early stage (I/II) PDAC patients and subsequently validated in an independent patient cohort.

Methods: A recombinant antibody microarray platform was utilized to decipher a biomarker serum signature associated with PDAC. The discovery study was a case/control study from Scandinavia, consisting of 16 stage I, 132 stage II, 65 stage III, 230 stage IV patients and 888 controls. The identified biomarker signature was subsequently validated in an independent US case/control study cohort with 15 stage I, 75 stage II, 15 stage III, 38 stage IV patients and 219 controls.

Results: Using the Scandinavian case/control study, signatures were created discriminating samples derived from stage I/II and stage III/IV patients vs. controls with ROC-AUC values of 0.96 and 0.98, respectively. Subsequently, a consensus signature consisting of 29 biomarkers was generated based on all PDAC stages and control samples. This signature was then validated in an independent US case/control study and produced a ROC-AUC value of 0.96 using samples collected from PDAC stage I/II patients.

Conclusion: The validated serum signature detected early stage localized PDAC with high sensitivity and specificity, thus paving the way for earlier diagnosis.

 # 28

Defining Pancreatitis as a Risk Factor for Pancreatic Cancer: The Role, Incidence, and Timeline of Development

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Introduction: Pancreatic cancer has a high mortality rate and is the fourth leading cause of cancer related deaths in the United States. Early detection may improve survival. Risk factors for developing pancreatic cancer have been recognized; these include age > 55, male gender, obesity, tobacco, and diagnoses of diabetes. Additionally, acute and/or chronic pancreatitis has been implicated as an important risk factor for pancreatic cancer, however, the incidence and temporal relationship of pancreatitis prior to the diagnosis of pancreas cancer is unclear.

Aim: To establish the role and incidence of pancreatitis temporally with the development of pancreatic cancer.

Methods: A retrospective population-based study, with a big-data IBM platform called Explorys was used to collect de-identified patient data. Over 50 million patients, spanning nationally in over 20 healthcare systems' electronic medical records is in this cloud-based, HIPPA-enabled platform. Data was obtained using ICD-9 code criteria with search terms "acute pancreatitis," "chronic pancreatitis," and "malignant tumor of the pancreas." A temporal relationship between pancreatitis diagnosis, followed by pancreatic cancer diagnosis was investigated. Intervals of 3, 6, 12, 24, and 36 months were developed. Demographical data, including age, gender, and race was also recorded and analyzed.

Results: A total 50,080 patients were found to have a diagnosis of pancreatic cancer. 7,420 of these patients were found to have a diagnoses of pancreatitis prior to their cancer diagnoses (14.8%). Of those, 91.6% were between the ages of 45-89. Interestingly, there was a higher incidence of pancreatic cancer in the African-American population vs. the Caucasian population (21.2% vs 14.8%, $p<0.05$) group with prior pancreatitis diagnosis. Further analysis of pancreatic cancer diagnosis revealed that 6,030 of the 7,420 patients were diagnosed within 3 months of their acute and/or chronic pancreatitis (81.3%) diagnosis. Finally, 7,340 patients (98.9%) had established diagnoses of pancreatic cancer within 3 years of the pancreatitis diagnosis.

Conclusions: Treatment of pancreas cancer is often challenging because symptoms are not common or specific until advanced stage disease occurs. Early detection of pancreatic cancer may lead to improved survival. This study shows that almost 15% of patients with a diagnosis of pancreatic cancer have a prior diagnoses of pancreatitis, of which 90% of these cases occur over age 45. Additionally, nearly 99% of pancreas cancer diagnoses occur within 3 years of the pancreatitis diagnosis. Given our large sample size, early detection and screening in patients with pancreatitis over the age of 40 with unclear etiology of pancreatitis may be reasonable. Limitations include inability to track etiology of pancreatitis as well as unclear histologic types of pancreas cancer in this database.

Continued

Table 1. Demographics and Risk Factors of Pancreatitis prior to diagnosis of Pancreatic Cancer

Diagnosis Cancer (%)	Pancreatitis Prior to Cancer	Total Pancreatic Cancer	Pancreatitis Prior to
N	7,420	50,080	14.8
Males	4,030	25,540	15.8
Ethnicity			
Caucasian	5,470	37,030	14.8
African-American	1,360	6,410	21.2
Age- yr			
20-24	0	50	0.0
25-29	10	90	11.1
30-34	20	150	13.3
35-39	70	310	22.6
40-44	130	540	24.1
45-49	290	1,240	23.4
50-54	540	2,330	23.2
55-59	790	4,070	19.4
60-64	1030	5,740	17.9
65-69	1080	7,020	15.4
70-74	1050	7,540	13.9
75-79	880	6,900	12.7
80-84	650	5,770	11.3
85-89	490	4,480	10.9
90+	340	3,480	9.8

Table 2: Pancreatic Cancer Within Different Intervals After Diagnosis of – III – rmt:1

Time Interval	Pancreatic Cancer (N=7,420)
3 months	6,030 (81.3%)
6 months	6,480 (87.3%)
12 months	6870 (92.6%)
24 months	7,190 (96.9%)
36 months	7,340 (98.9%)

 # 29

Pancreatic Cancer Incidence Trends and Recent Patterns by Sex and Racial/Ethnic Group: Evidence from the Surveillance, Epidemiology and End Results (SEER) Population-based Data

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Introduction: Annual pancreatic cancer incidence rates have been increasing. We examine pancreatic cancer incidence trends by demographics and histologic type.

Methods: Data from the Surveillance, Epidemiology and End Results (SEER) registries were available to assess temporal trends and pancreatic cancer rates from 1974-2013.

Results: Pancreatic cancer incidence rates declined from 1974-1991 but increased significantly from 1992-2013 among non-Hispanic white males aged ≥55 years older. Among non-Hispanic and Hispanic males, the annual percent change (APC) in incidence was 0.84% and 0.73%, respectively). Rates also rose significantly among white non-Hispanic, Hispanic, and Asian females (APC=0.81%, 0.56% and 1.23%, respectively), and even more rapidly among females ages 25-34 years (APC≥2.5%). Rates among black males and females did not significantly change. By histologic type, the increases were greatest for non-secretory endocrine cancers (>6%), followed by ductal adenocarcinomas (~5%), and adenocarcinoma, NOS (~1.4%) – the largest histologic subgroup of pancreatic cancer. Rates for mucinous adenocarcinomas and poorly specified pancreatic cancer decreased.

Overall, incidence rates during 2000-2013 were significantly higher among males than females (MF incidence rate ratio, (IRR)=1.28). The IRR was >1.00 at all ages ≥35, but rates among females were higher at younger ages (IRRs 15-24: 0.66, 25-34: 0.81). The MF IRRs for most of the histologic types were significantly elevated among males apart from solid pseudopapillary adenocarcinoma and cystic carcinomas (IRR=0.22, CI: 0.14-0.34 and 0.52, 0.41-0.65, respectively).

Conclusion: Pancreatic cancer has been increasing overall, but patterns differ by demographic group and histologic type. Many of the trends parallel changing prevalence of lifestyle risk factors such as smoking, overweight and obesity, and diabetes in the US, particularly for pancreatic adenocarcinoma, and improved diagnosis methods during the past 40 years.

 # 30

Lung Metastasis in Pancreatic Cancer: Should Staging Chest CT be Routinely Performed?

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Introduction: National Comprehensive Cancer Network (NCCN) guidelines recommend chest x-ray or chest computed tomography (CT) for the staging of potential resectable pancreatic adenocarcinoma (PDA). However, there is limited data supporting these guidelines and the prevalence of lung metastasis is not well defined on staging CT scans. We report our findings of patients with lung metastasis during initial staging and follow-up of patients with PDA.

Methods: Data was prospectively collected from May 2013 to September 2016 for PDA patients who were presented at a multidisciplinary pancreas conference (MDPC) at a large tertiary care center. All patients were staged with CT pancreatic protocol, CT chest and Endoscopic Ultrasound. Patients with findings of lung lesions on initial staging chest CT were followed prospectively. Metastatic lung lesions were determined based on definite imaging characteristics with clinical consensus or lung biopsy results.

Results: A total 278 PDA patients referred to MDPC were staged with CT chest (Table 1). Out of these, 36 (12.6%) patients were found to have either malignant (N= 6) or indeterminate (N= 30) lung lesions on initial staging CT chest (Figure 1). Out of the 6 malignant lung lesions, 5 (1.8%) patients had metastatic PDA lesions and 1 (0.35%) patient had incidental primary lung cancer. On a follow up of 30 patients with indeterminate lung lesions, 8 patients (26.7 %) were later determined to be lung metastasis. Overall prevalence of definite lung metastasis was at least 4.8% (13/278). The prevalence of lung metastasis in pancreatic head cancer was 3.0 %, while body and tail masses was 10.5 %. Lung metastasis was almost 4 times more likely in body and tail masses (OR=3.83, CI 1.2-11.8, p=0.02) compared to head. Overall CT chest resulted in change in management plan in 9 (2.9%) patients due to change in stage to metastatic (8) and diagnosis primary lung cancer (1). Staging with CT chest changed otherwise resectable disease to unresectable/metastatic in 5 patients (1.8%) and borderline resectable to metastatic disease in 2 (0.7 %) patients. Prevalence of isolated PDA lung metastasis without any other metastasis was 2.8 % (8/278).

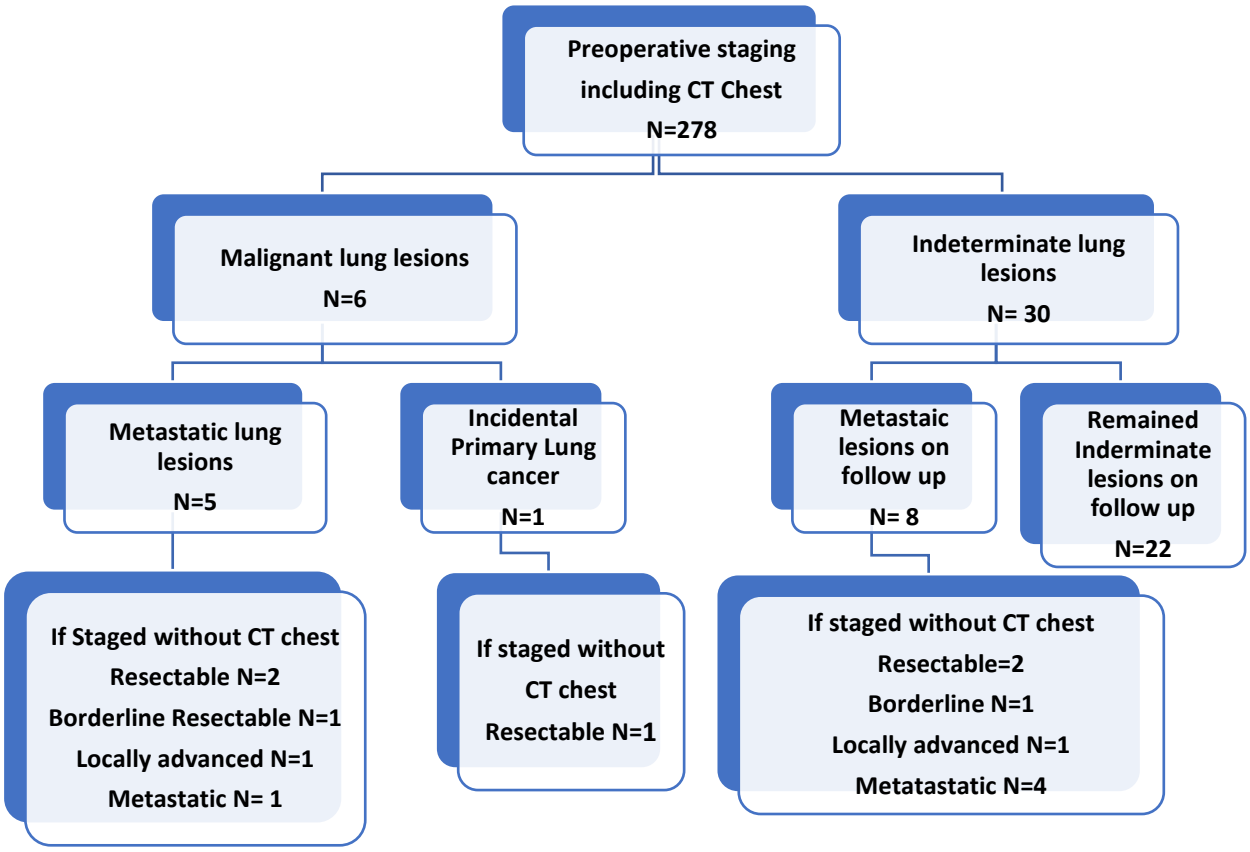
Conclusion: Our study showed that the prevalence of pulmonary metastasis in PDA was clinically relevant to mandate routine staging with CT chest. Prevalence was significantly higher for pancreatic body and tail cancer compared to head. Staging CT chest resulted in change in staging of PDA and management decisions.

Table 1: Comparison of patient and tumor characteristics.

Characteristics	Patients without Lung metastasis N=265	Patients with Lung Metastasis N=13	P value
Age (yrs), mean (S.D)	68.6	64.8	0.22
Male (%)	48.4	69.2	0.14
Race, Caucasian (%)	90.2	100	0.36
Mass size (mm), mean (S.D)	26.9	31.1	0.16
Mass Location Head (%) Body/Tail (%)	 76.7 23.3	 46.2 53.8	0.01
CA 19-9, mean (S.D)	899 (1528)	961 (482)	0.90

Continued

Figure 1 Flow diagram showing prevalence of lung metastasis in pancreatic cancer.



 # 31

Antibody Blockade of IL-6 Combined with Novel Targeted Therapeutics in Pancreatic Cancer

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Background: Pancreatic ductal adenocarcinoma (PDAC) is the fourth leading cause of cancer in America with few efficacious therapeutic options other than surgery. PDAC is characterized by dense and heterogeneous stroma that secretes elevated levels of the proinflammatory cytokine Interleukin-6 (IL-6). Our laboratory has previously reported that higher IL-6 in PDAC patients is strongly associated with poor overall survival. Additionally, patients with pancreatic and gastrointestinal cancers have the highest incidence of cachexia. This syndrome, characterized by the loss of skeletal muscle and adipose tissue, cannot be reversed by nutritional intervention and is mediated impart by IL-6 signaling. Further, work completed by our group and others have also shown that IL-6 and other factors can promote cross-talk between the STAT3 and MEK pathways. Thus, we hypothesized that IL-6 blockade can be utilized to enhance the efficacy of novel immune or targeted therapeutics (anti-PD-L1 and MEK inhibitor) in pancreatic cancer.

Methods: *In vivo* efficacy studies were conducted with antibodies (Ab) blocking IL-6, in combination with checkpoint immunotherapy (anti-PD-L1) or MEK inhibition (MEKi). Experiments were conducted in mice bearing subcutaneous KPC-derived MT5 tumors; orthotopically injected KPC-luciferase expressing tumor cells in the pancreas; and Colon26 tumor bearing CD2F1 mice to determine effects on cancer cachexia.

Results: IL-6 blockade combined with anti-PD-L1 ($p<0.02$) or MEKi ($p=0.007$) elicited anti-tumor efficacy in mice bearing subcutaneous KPC derived MT5 tumors, compared to vehicle controls. IL-6 blockade in combination with anti-PD-L1 antibodies limited tumor growth of orthotopic KPC-luciferase expressing tumor cells compared to isotype controls ($p=0.05$). As a pancreatic cachexia model is not currently available, we tested IL-6 blockade in combination with MEKi on a classically accepted tumor cachexia model (CD2F1 mice bearing Colon26 tumors). Only mice treated with MEKi or the combination of IL-6 plus MEKi resulted in significant tumor inhibition compared to IL-6 alone or vehicle controls ($p<0.0001$). Furthermore, mice administered IL-6 alone or in combination with MEKi prevented tumor-induced body weight loss ($p<0.005$) and protected lean mass and hindlimb muscles as compared to vehicle-treated mice ($p < 0.05$).

Conclusions: These pre-clinical results indicate that inhibition of IL-6 may affect the efficacy of novel targeted therapeutics on tumor progression, immunosuppression, and cachexia in pancreatic cancer.

 # 32

Potential Bi-directional Effects of Nerve Growth Factor Sequestration on Pancreatic Cancer Progression

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Analysis of both human specimens and genetically engineered mouse models (GEMM) of pancreatic ductal adenocarcinoma (PDAC) reveals that inflammation is a key component of the tumor microenvironment. Starting early in disease progression there is an up regulation of nerve-derived pro-inflammatory peptides, growth factors/receptors, and neuronal hypertrophy that indicate the presence of neurogenic inflammation (NI). Our previous studies in a PDAC GEMM demonstrate that significant NI is already present early in the disease process, at the time pancreatic intraepithelial neoplasias (PanINs) are present. This study also revealed that neonatal sensory nerve ablation slowed and in some cases prevented tumor development. In patients with pancreatic ductal adenocarcinoma (PDAC), up regulation of growth factors is correlated with a poorer prognosis, greatest neural invasion, and in the case of NGF, the most severe pain. Based on these observations, we hypothesized that NGF sequestration reduces neural inflammation and impedes PDAC development in a physiologically relevant GEMM. We preformed our studies on the commonly utilized PKC GEMM in which p48-cre is used to drive expression of the KrasG12D gain of function mutation and a single allele deletion of the tumor suppressor gene p53. We administered systemic anti-NGF antibody at a dose (200µg/kg) shown to be efficacious in human clinical trials for other conditions (e.g. osteoarthritis pain). Mice were enrolled in the study beginning at 4wks of age (healthy) or 8 wks of age (PanIN stage) and received bi-weekly injections of anti-NGF or vehicle until they were euthanized for analysis (~16wks of age). Interestingly, mice that began treatment at 8 wks of age exhibited reduced spinal inflammation as measured by a marker of astrocyte activation, GFAP, whereas the 4 wk mice showed no effect on GFAP, but exhibited increased levels of spinal p-ERK (marker of inflammation and cell activation). Furthermore, 30% of the 8 wk anti-NGF group exhibited no disease in the pancreas at the time of euthanasia whereas some level of disease was present in all mice from the other treatment groups. In a subset of PKC mice, we also expressed tdtomato fluorescent reporter under p48-cre (PKCT mice), allowing us to follow cells that disseminate from the pancreas. 100% of PKCT mice in the 4wk group, regardless of treatment, exhibited invasion of individual pancreas-lineage cells into the spinal cord while only 60% of the 8 wk anti-NGF group showed similar invasion. Interestingly, the 8 wk anti-NGF group also exhibited no grossly detectable metastases whereas the 4 wk anti-NGF group exhibited metastases involving a greater number of organs as compared to the vehicle treated group. In summary, early intervention with anti-NGF could be driving neural invasion and metastases, which are correlated with an increase in the activation marker, p-ERK. However, later intervention (presumably after the onset of pancreatic disease), anti-NGF treatment reduces spinal glial activation, neural invasion, and the severity of disease. These data suggest that NGF may play bi-directional time-dependent roles in the progression of PDAC.

 # 33

How Are We Doing? A Survey of 125 Physicians on Inpatient Management of Chronic Pancreatitis Pain

Adrianne Tsen, DO
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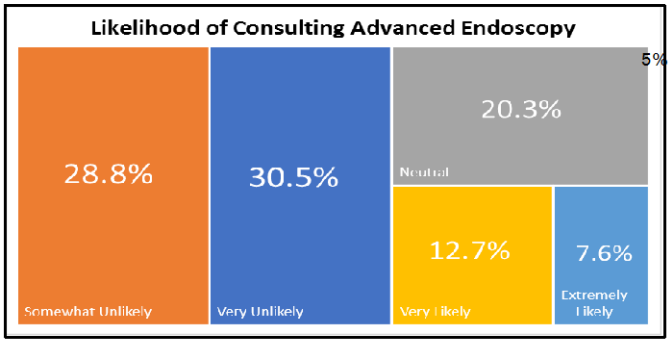
Background: Ninety percent of patients with chronic pancreatitis (CP) suffer from pain. Pain in relation to CP is the primary reason for hospital admissions in 93% of cases and results in annual healthcare costs of $638 million in the United States. Due to the progressive nature of CP, optimization of analgesia for each patient is challenging. Although guidelines regarding the proper management of patients with chronic pancreatitis pain have been established by various organizations including the Italian Association for the Study of the Pancreas and the PancreasFest 2012 consensus meeting, admission and cost statistics remain relatively unchanged. The goal of this study was to evaluate physician approaches in managing patients hospitalized for pain due to chronic pancreatitis within a single institution.

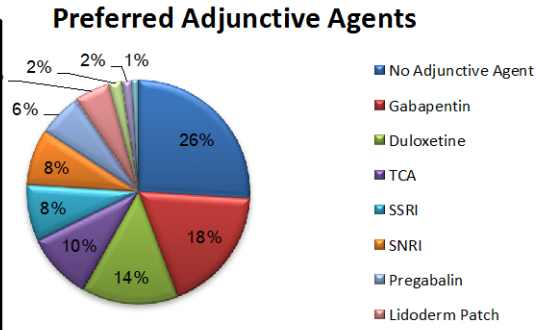
Methods: Physicians at our institution were administered a survey regarding management in treating CP patients hospitalized due to acute flares of pain. The surveys were provided in hard-copy format and were structured to collect both nominal and ordinal data types based on the variable of interest. All surveys were distributed at the same time to participants and each physician was given ten minutes to complete the questionnaire. Variables measured included first line and adjunctive agent preferences, likelihood of utilizing pancreatic enzymes, and likelihood of consultation with Advanced Endoscopy. Physicians were provided 14 specific selection options for first line agents and 10 specific selection options for adjunctive agents, including an option of "none." The scale used for likelihood data collection ranged from 1 to 5 with 1=least likely and 5=extremely likely. The study was reviewed and approved by the institutional review board of the University of Texas Health Science Center at San Antonio.

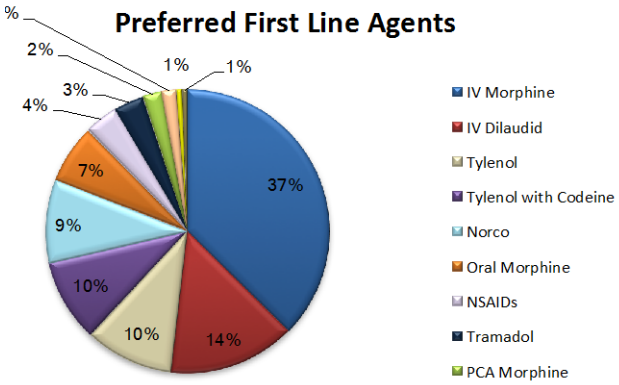
Results: Of 125 subjects asked to participate in the survey, 124 of the participants completed it. The majority of physicians (59.3%) reported that they were unlikely to consult Advanced Endoscopy compared to other services. A plurality of physicians (37.4%) preferred using intravenous morphine as the first line agent. The category of adjunctive agents most popular with physicians (26%) was "None." Most physicians were neutral (32.8%) or unlikely (27.2%) to use pancreatic enzymes to assist in pain management.

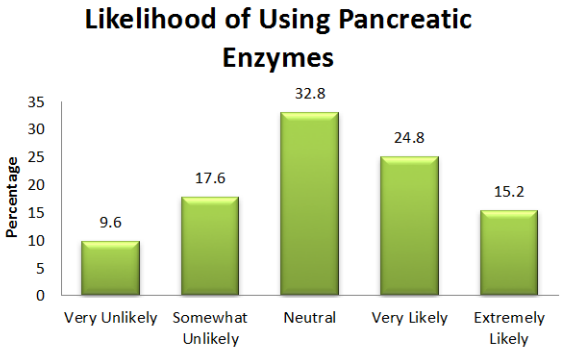
Conclusion: When managing patients hospitalized for pain due to chronic pancreatitis, the majority of physicians do not adhere to the guidelines established by various professional organizations. Recommendations such as initial assessment with endoscopic evaluation necessitating Advanced Endoscopy consultation, use of tramadol as a first line agent, and use of neuromodulating agents as adjunctive agents were not preferred by the surveyed physicians. Effectiveness of pancreatic enzymes remains under investigation which was reflected in the likelihood responses collected in the survey. Based on the results of our study, increased education regarding CP pain management therapies is needed among physicians at our institution and providing standardized treatment algorithms may assist physicians in providing optimal analgesia to CP patients hospitalized for pain.

Continued


Likelihood of Consulting Advanced Endoscopy
28.8%
Somewhat Unlikely
30.5%
Very Unlikely
20.3%
Neutral
12.7%
Very Likely
7.6%
Extremely Likely


Preferred Adjunctive Agents
26%
18%
14%
10%
8%
8%
6%
5%
2%
2%
1%
No Adjunctive Agent
Gabapentin
Duloxetine
TCA
SSRI
SNRI
Pregabalin
Lidoderm Patch


Preferred First Line Agents
37%
14%
10%
10%
9%
7%
4%
3%
2%
1%
1%
%
IV Morphine
IV Dilaudid
Tylenol
Tylenol with Codeine
Norco
Oral Morphine
NSAIDs
Tramadol
PCA Morphine


Likelihood of Using Pancreatic Enzymes
Percentage
35
30
25
20
15
10
5
0
9.6
17.6
32.8
24.8
15.2
Very Unlikely
Somewhat Unlikely
Neutral
Very Likely
Extremely Likely

 # 34

Internal Medicine Versus Family Medicine: Approaches to Inpatient Management of Chronic Pancreatitis Pain

Adrianne Tsen DO, Christopher Moreau BSBME, Archish Kataria MD, Sreedevi Atluri MD, Sandeep Patel DO, Laura Rosenkranz MD

Background: The Incidence and Prevalence of Chronic pancreatitis (CP) are estimated to be 5-12 per 100,000 and 50 per 100,000 persons respectively. CP-related pain is the reason for hospital admissions in 93% of cases, and results in annual healthcare costs of $638 million in the United States. Although guidelines regarding proper management of patients with CP pain have been established by various organizations, differences in training and education among residency programs may result in variable compliance with these guidelines. Of the 41 Family Medicine (FM) and 103 Internal Medicine (IM) residents enrolled at our Institution, 90% treat less than 3 CP patients per month. The goal of this study was to compare IM and FM resident approaches in management of patients admitted for chronic pancreatitis pain at a single institution.

Methods: IM and FM residents at our Institution were administered a survey regarding practices in managing therapy of patients with CP hospitalized due to acute flares of pain after all other causes have been ruled out. All surveys were distributed at the same time to participants, and each physician was given ten minutes to complete the questionnaire. Variables measured included: likelihood of obtaining abdominal imaging (in addition to imaging performed in the Emergency Department or outside hospital) and likelihood of consulting specialty inpatient services (General Gastroenterology, Advanced Endoscopy, and General Surgery). The scale used for likelihood data collection ranged from 1 to 5 with 1=least likely and 5=extremely likely. The study was reviewed and approved by the Institutional Review Board of the University of Texas Health - San Antonio.

Results: 74 IM residents and 22 FM residents completed the survey. Likelihood data was split into two groups for odds ratio comparison: Group 1 – Unlikely (Rating = 1 or 2) and Group 2 – Likely (Rating = 4 or 5**).** Rating of 3, neutral, was excluded. The likelihood of obtaining additional abdominal imaging was greater among Family Medicine residents (OR=5.28, p=0.04). FM residents were more likely to consult both General Gastroenterology (OR=5.62, p=0.008) and General Surgery (OR=22.28, p<0.0001) compared to IM residents. In a comparison of post-graduate year 1 (PGY1) with PGY2 IM residents, the likelihood of obtaining abdominal imaging (OR=3.43, p=0.06), consulting General Gastroenterology (OR=7.00, p=0.08), Advanced Endoscopy (OR=15.06, p=0.07), and General Surgery (OR=4.50, p=0.18) decreased with advancing PGY levels. Between PGY2 and PGY3 IM residents, the likelihood of obtaining abdominal imaging (OR=0.68, p=0.64), General Gastroenterology (OR=2.45, p=0.59), Advanced Endoscopy (OR=1.26, p=0.90), and General Surgery (OR=2.52, p=0.58) consults remained relatively unchanged.

Conclusion: When managing patients hospitalized for pain due to chronic pancreatitis, IM residents were less likely to adhere to guidelines established by various professional organizations compared to FM residents. Furthermore, the likelihood of obtaining abdominal imaging and consulting services decreased with advancing PGY level among IM residents. Based on the results of our study, increased education regarding CP pain management therapies is needed among physicians at our Institution and providing standardized treatment algorithms may assist physicians in delivering optimal management of patients with CP hospitalized for related pain.

Continued

Family Medicine vs Internal Medicine – All Post-Graduate Year Levels		
	Odds Ratio	**p value**
Obtain Abdominal Imaging	5.2800	0.0425
Consult General Gastroenterology	5.6250	0.0087
Consult Advanced Endoscopy	0.8889	0.8900
Consult General Surgery	22.2857	<0.0001

Internal Medicine – Post Graduate Year (PGY) Comparisons				
	PGY1 vs PGY2		**PGY2 vs PGY3**	
	Odds ratio	**p value**	**Odds ratio**	**p value**
Obtain Abdominal Imaging	3.4375	0.0654	0.6818	0.6489
Consult General Gastroenterology	7.000	0.0840	2.4545	0.5916
Consult Advanced Endoscopy	15.0690	0.0712	1.2609	0.9095
Consult General Surgery	4.5000	0.1892	2.5200	0.5835

 # 35

Predictors of Mortality in Emphysematous Pancreatitis: A Systematic Analysis and Review of the Literature

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Background: Emphysematous pancreatitis (EP) is a subtype of acute necrotizing pancreatitis (ANP) characterized by the presence of gas in and around the pancreas. While investigators have studied prognostic factors in ANP, less is known about EP. We aimed to determine predictors of mortality and identify changes in management strategies for emphysematous pancreatitis.

Methods: A PubMed search was performed to identify cases of EP. Data was gathered about patient demographics, clinical findings, laboratory results, radiological studies, procedures, outcomes and mortality. Chi-Square or Fisher exact tests were used for categorical data. T-test was used for parametric and Mann-Whitney U test was used for non-parametric testing when appropriate. Statistical testing including univariate and multivariate analyses were completed using SPSS v. 22.0.

Results: Including a case from our institution, the study cohort included 64 subjects. The mean age of study population was 60.3 +/− 15.7 years. The average duration of symptoms prior to presentation was 5.6 +/− 11.5 days. Figure 1 shows comparison of baseline demographics between patients who died during hospitalization versus survived. The overall mortality rate was 32.8% (21/64). On univariate analysis, age (p=.019), hypotension (p=.007), gas outside of the pancreas on CT imaging (p=.003), initial surgical evacuation (p=.007) and the development of multi-organ failure (p=.008) were associated with mortality (Figure 2). On multivariate analysis, only the development of multi-organ failure was found to be an independent predictor of mortality (p=.039). The overall mortality rate of 32.8% for EP is similar to the mortality rates published for ANP.

Conclusion: EP has been associated with high rates of morbidity and mortality in the past but this has been decreasing. The development of multi-organ failure in EP is strongly associated with increased mortality. Percutaneous and endoscopic approaches have been replacing surgical interventions.

Summary: Emphysematous pancreatitis (EP) is a subtype of acute necrotizing pancreatitis (ANP) characterized by the presence of gas in and around the pancreas. We performed a systemic analysis of published cases to determine the predictors of mortality in EP. Our study included 64 subjects and the overall mortality rate was 32.8%. On multivariate analysis, only the development of multi-organ failure was found to be an independent predictor of mortality (p=.039). Percutaneous and endoscopic approaches have been replacing surgery and mortality rate of EP has been decreasing.

Continued

Figure 1

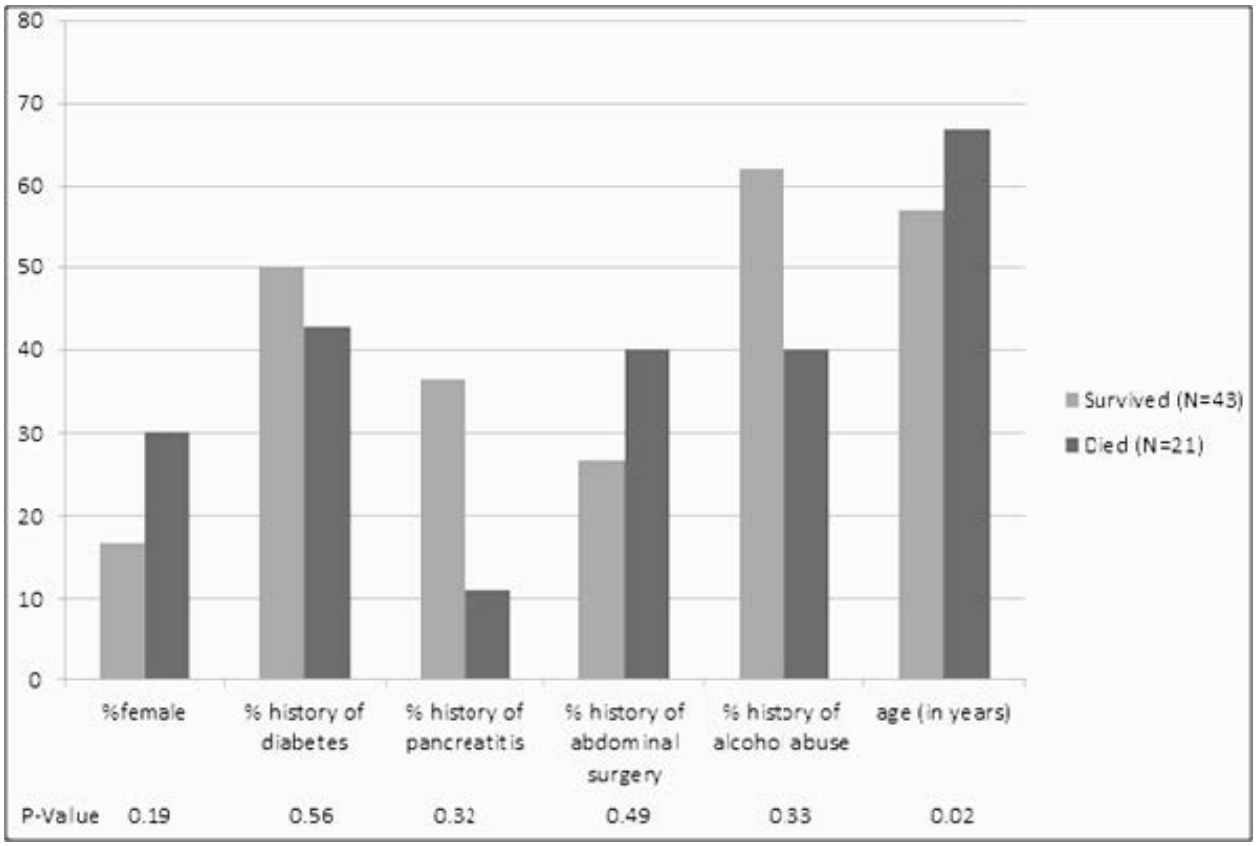

Figure 2

	Survived, n (%)	Died, n (%)	*P*
Age, mean (SD), y	57.1 (16.9)	66.9 (13.7)	.019
Hypotension	2 (10.5)	7 (58.3)	.007
Gas outside of pancreas on CT	13 (40.6)	13 (86.7)	.003
Lack of initial percutaneous drainage	19 (50)	17 (85)	.008
Initial surgery	14 (35)	15 (71.4)	.007
Development of multi-organ failure	7 (43.8)	12 (92.3)	.008

 # 36

Early Predictors of Severe Acute Pancreatitis in a Prospective Pediatric Cohort Abstract

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CAPER Scholarship Recipient
with Lindsey N. Hornung[2], Tom K. Lin[1], Tyler Thompson[1], Jaimie D. Nathan[1], Maisam Abu- El-Haija[1]
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Introduction: Acute pancreatitis (AP) is increasing in incidence in the pediatric population, but nonetheless is poorly studied. The natural course of patients who develop AP can range from a mild presentation to severe acute pancreatitis (SAP), associated with morbidity and mortality. A new pediatric classification of AP was recently published by the North American Society for Pediatric Gastroenterology, Hepatology and Nutrition (NASPGHAN) Pancreas Committee, which defines mild AP, moderately SAP and SAP. Early identification of pediatric patients at higher risk for developing SAP is crucial, as it is associated with increased health system cost and mortality. Szabo et al recently utilized retrospective data to develop a prognostic tool to predict SAP. There are no studies, however, evaluating predictors of SAP using the newly defined pediatric AP classifications and prospectively collected data. The aim of this study was to evaluate for early predictors of developing SAP during first episode of AP in a prospective pediatric cohort.

Methods: Pediatric patients presenting with first episode of AP between May 2013 and January 2017 to the Cincinnati Children's Hospital Medical Center (CCHMC) were prospectively recorded in a local database. Clinical data collected during admissions were analyzed, including laboratory values within 24 hours of AP attack, any manifestations of SAP, fluid resuscitation rates and feeds on admission. Differences in groups of mild AP and SAP were analyzed using Wilcoxon-Mann-Whitney tests and a multivariable logistic regression model was derived based on significant p-values, AIC and ROC curve using stepwise selection.

Results: There were 118 patients included in analysis, of which 22 (18.6%) developed SAP. Patients who developed SAP had significantly higher BUN (20.0 vs 10.0, p = .007), magnesium (2.1 vs 1.8, p = .04), glucose (121.5 vs 98.5, p = .03), sodium (141.0 vs 139.0, p = .03), and CRP (5.5 vs 1.0, p = .02) [Table 1]. Patients who developed SAP had less aggressive hydration (32% vs 44%, p = .15), and were less likely to have feeds started within 24 hours (18% vs 27%, p = .52), however these findings did not achieve statistical significance. A significant multivariable model with white blood cell count, sodium and calcium (AUROC 0.79, 95% CI: 0.67 – 0.91, Sn 72.2%, Sp 76.5%, PPV 44.8%, NPV 91.2%) was generated during stepwise selection. However, when BUN was added to the model, BUN by itself as a predictor was superior to any other combination of variables (AUROC 0.75, 95% CI 0.61 – 0.89, Sn 63.2%, Sp 81.2%, PPV 42.9%, NPV 90.8%).

Conclusion: This study is the first to evaluate a prospective pediatric cohort of patients presenting with first episode of AP using the newly published pediatric SAP classification. Within 24 hours of presenting with AP, patients who developed SAP had higher BUN, magnesium, glucose, sodium and CRP than those who developed mild AP. A logistic regression model with BUN as a significant predictor of SAP was derived from our variables. These findings are useful for early identification of pediatric patients at higher risk for progression to SAP.

Continued

Table 1

SAP vs mild AP: First AP Attack Characteristics

	SAP (n=22)	Mild AP (n=96)	P-value
Age (years)	13.8 (7.9, 15.9) *n=22*	13.5 (10.2, 15.9) *n=96*	0.96
Sex (male)	14 (64%)	48 (50%)	0.25
Weight percentile	59.1 (9.1, 88.9) *n=22*	48.3 (23.1, 86.9) *n=92*	0.45
Height percentile	56.5 (3.1, 83.3) *n=22*	49.3 (21.9, 76.2) *n=90*	0.83
BMI percentile	63.1 (20.1, 89.2) *n=22*	58.4 (23.6, 92.6) *n=87*	0.96
Lipase x ULN	8.6 (4.8, 17.8) *n=21*	8.4 (3.8, 25.3) *n=90*	0.90
Amylase	386.0 (131.5, 521.0) *n=12*	194.0 (104.0, 507.0) *n=75*	0.35
Albumin	3.3 (2.5, 3.8) *n=19*	3.7 (3.1, 4.1) *n=86*	0.08
WBC	13.2 (8.9, 17.9) *n=18*	9.9 (7.3, 14.8) *n=75*	0.18
Creatinine	0.6 (0.5, 0.7) *n=20*	0.6 (0.4, 0.6) *n=85*	0.43
GFR	114.6 (93.1, 129.7) *n=19*	111.6 (98.7, 138.0) *n=73*	0.77
Calcium	8.6 (8.2, 9.2) *n=20*	9.0 (8.5, 9.4) *n=83*	0.10
AST	35.0 (24.0, 130.0) *n=15*	40.5 (21.0, 114.5) *n=80*	0.54
ALT	37.0 (13.0, 266.0) *n=15*	29.0 (21.0, 177.0) *n=79*	0.85
Hematocrit	38.8 (31.8, 46.2) *n=14*	38.1 (33.3, 41.6) *n=67*	0.64
Hemoglobin	13.8 (10.8, 15.9) *n=16*	12.8 (11.5, 14.0) *n=66*	0.44
BUN	20.0 (10.0, 23.0) *n=19*	10.0 (8.0, 13.0) *n=85*	0.0007
Mg	2.1 (1.8, 2.1) *n=12*	1.8 (1.7, 2.0) *n=31*	0.04
Phosphorus	3.4 (2.6, 4.0) *n=18*	3.8 (3.2, 4.4) *n=62*	0.21
Glucose	121.5 (95.5, 148.5) *n=20*	98.5 (88.0, 117.0) *n=86*	0.03
Sodium	141.0 (138.0, 143.0) *n=20*	139.0 (137.0, 141.0) *n=84*	0.03
Total Bilirubin	0.6 (0.3, 1.6) *n=15*	0.5 (0.3, 1.2) *n=75*	0.98
CRP	5.5 (1.8, 18.1) *n=5*	1.0 (0.4, 2.6) *n=28*	0.02
Procalcitonin	0.1 *n=1*	0.1 (0.1, 0.1) *n=2*	-
ICU admission (yes)	10/21 (48%)	7/95 (7%)	<0.0001

Data presented as median (25^{th}, 75^{th} percentile) or frequency (%)

 # 37

Peritoneal Cavity is a Secondary Extrahepatic Site for Islet Autotransplantation in Children with Larger Tissue Mass

Marie Cook MPH, Sarah Jane Schwarzenberg MD, Martin Freeman MD , Gregory Beilman MD, Ty Dunn MD, Varvara Kirchner MD, Timothy Pruett MD, Louise Berry RN, Joshua J. Wilhelm MS, David E.R. Sutherland MD PhD, Srinath Chinnakotla MD, MBA, Melena D. Bellin MD MS.
University of Minnesota Medical School and University of Minnesota Masonic Children's Hospital, Minneapolis MN, 55455

Purpose: Total pancreatectomy and islet auto transplantation (TP-IAT) is increasingly used for treatment of childhood pancreatitis that fails medical, endoscopic, and surgical drainage/resection procedures. An important observation from our pediatric series is that the addition of islet autotransplantation to TP did not increase morbidity compared to TP alone. Islets are infused into the portal vein, and the portal pressure routinely measured at 3 minute intervals during islet cell infusion, because of concern about the possibility of portal vein thrombosis. We did not continue infusion if portal pressure reached 25cm of saline. Beyond this threshold there is an increased risk of bleeding and portal vein thrombosis. The maximum amount of islet cell infused intraportal in our series is 0.25cc/Kg. If infusion was stopped because of elevated portal pressure, the remainder of the islets were placed in the peritoneal cavity. The aim of this study is to assess the safety and document the degree of engraftment at this intraperitoneal site compared to the traditional intrahepatic site of islet cell implantation.

Methods: Seventy six patients that underwent TPIAT between May 2011 and October 2016 were evaluated. Of these, 21 patients had part of the islets transplanted in the intraperitoneal site and 1 had islets transplanted exclusively in the peritoneal cavity. This group was compared to 54 patients that received only intrahepatic site implantation. Statistical significance was assessed by student t-test for continuous variables and chi-square for categorical variables.

Results: The indication for TPIAT in all children was painful recurrent or chronic pancreatitis that failed medical/endoscopic and/or surgical therapy. The median age was 11.8 ± 4.1 years and duration of pancreatitis 4.9 ± 3.9 years. Etiology was genetic in 85% of patients. Surgical characteristics are listed in Table I. The patients that had some of the islets transplanted in the extrahepatic site had a shorter duration of disease, greater IEQ transplanted, higher tissue volumes and higher peak portal pressures. This group also has a trend toward higher incidence of fever, prolonged ileus and more abdominal pain requiring higher dose of narcotics in the immediate (7 days) post-operative period. There was no difference in the incidence of intra-abdominal bleeding, or incidence of insulin independence between the groups. The hemoglobin A1C level was lower at 6 months and 1 year and fasting glucose lower at 1 year in the group that has islets transplanted extrahepatically (Table I). The single patient that had islets transplanted exclusively intraperitoneal had a detectable c-peptide >.05 and was on insulin pump therapy.

Conclusions: Peritoneum is a good secondary extrahepatic site for implantation of islets when the infusion peak portal pressure is >25 mm Hg or the islet mass is > 0.25 cc/Kg in children. The lower hemoglobin A1c level at 6 mos and 1 year is likely reflecting the higher islet mass transplanted in this group.

Continued

Table I

Variable	All Intraportal		+ extrahepatic (peritoneal)		p-value
continuous	**Mean**	**SD**	**Mean**	**SD**	
Age	11.56	4.22	12.45	3.85	0.3912
Duration Pancreatitis	5.42	3.84	3.48	2.79	0.0353
IEQ	183461	118875	291266	113503	0.0005
IEQ/kg	4524.5	2820.4	6975.3	3212.3	0.0015
Tissue volume (cc)	6.32	4.36	13.39	5.06	<.0001
Peak portal pressure	15.20	9.43	28.76	5.92	<.0001
categorical	**n**	**%**	**n**	**%**	
Sex (F)	29	53.7	16	72.7	0.1259
Etiology Hereditary	51	94.4	14	63.4	0.002

Variable	All Intraportal		+ extrahepatic (peritoneal)		p-value
continuous	**Mean**	**SD**	**Mean**	**SD**	
Total Daily Insulin (u/day, n=6)1	10.40	14.13	8.77	15.79	0.6925
HbA1c (%, n=70)	6.66	1.46	6.01	0.66	0.0123
Fasting Glucose (mg/dL, n=64)	113.4	45.5	96.2	16.0	0.0292
Fasting C-peptide (ng/mL, n=63)	1.00	0.55	1.07	0.50	0.6167
categorical	**n**	**%**	**n**	**%**	
Off Insulin	18	34.6	9	40.9	0.6072