

# Proceedings of the 48th Annual Pancreas Club Meeting

Marshall S. Baker · Nicholas J. Zyromski

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**Abstract** The 48th annual Pancreas Club meeting was held on May 2 and 3, 2014, at the Westin Lombard in Lombard, IL. Two hundred sixty attendees included pancreatologists from 17 countries. Two hundred eleven abstracts were submitted; from these, a record number (64) oral presentations and 136 posters were selected. Table 1 documents oral abstract titles with institutional affiliation. Full abstracts for all oral presentations and posters are available at the Pancreas Club website, <http://pancreasclub.com>. Representative abstracts from each of the eight sessions are summarized below.

**Keywords** Pancreas Club · Pancreatitis · Pancreatic cancer

more vascular resection) in the neoadjuvant treatment group, no increased morbidity or mortality was observed.

## Scientific Session I: Included Two Topics, Borderline Resectable Pancreatic Cancer and Neoadjuvant Chemotherapy/Radiation Therapy

Topics discussed in this session included cost of diagnostic laparoscopy, incidence of venous thromboembolism during neoadjuvant chemotherapy, effect of neoadjuvant treatment on body composition (sarcopenia), role of extended lymph node dissection, and effect of microscopic positive resection margins on survival. The MD Anderson group presented National Surgical Quality Improvement Project (NSQIP) Pancreatectomy Demonstration Project data comparing outcomes from patients with and without neoadjuvant treatment. Only 13 % of the 1,567 patients captured in NSQIP between November 2011 and December 2012 received neoadjuvant treatment. The major finding from this analysis was that despite requiring more lengthy and complex operations (including

## Scientific Session II: Minimally Invasive Techniques/Screening for Cancer

Data from the NSQIP Pancreatectomy Demonstration Project were used to evaluate outcomes of minimally invasive pancreatoduodenectomy (PD) compared to open PD. These data documented significantly increased morbidity and mortality in the minimally invasive group. Vigorous discussion centered on appropriate application of the technique and training paradigms. Data from the Mayo Clinic demonstrated oncologic equivalence of laparoscopic and open PD. Two papers addressed screening techniques: magnetic resonance imaging in a cohort of patients at high risk for developing pancreatic ductal adenocarcinoma (PDAC) and an exciting proof of principle study showing feasibility of functional imaging of proteolytic activity.

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M. S. Baker · N. J. Zyromski (✉)  
Department of Surgery, Indiana University School of Medicine, 545  
Barnhill Dr. EH 519, Indianapolis, IN 46202, USA  
e-mail: nzyromsk@iupui.edu

M. S. Baker  
NorthShore University Health Systems, Chicago, IL, USA

M. S. Baker  
University of Chicago, Chicago, IL, USA

## The How I Do It Session titled Borderline resectable adenocarcinoma of the pancreas: definitions and management

Utilized a point/counterpoint format contrasting initial resection versus neoadjuvant therapy in two scenarios—a patient with vascular (SMV) involvement and a frail patient with a

**Table 1** Oral papers presented at the 48th Annual Pancreas Club meeting

Number	Title	Institution
Scientific session I		
Topic: Borderline resectable pancreatic cancer		
1	Diagnostic laparoscopy to detect occult metastatic disease prior to neoadjuvant chemoradiation in borderline resectable pancreatic ductal adenocarcinoma	Cleveland Clinic Foundation
2	Risk of venous thromboembolism during neoadjuvant therapy for resectable and borderline resectable (BLR) pancreatic adenocarcinoma (PC)	Medical College of Wisconsin
3	Impact of surgical resection after chemoradiotherapy for locally advanced unresectable pancreatic ductal adenocarcinoma	Mie University (Japan)
Topic: Neoadjuvant chemotherapy/radiation therapy		
4	A comprehensive assessment of neoadjuvant therapy for pancreatic adenocarcinoma: results from the National Cancer Database (NCDB)	University of Pennsylvania
5	Does the use of neoadjuvant therapy for pancreatic adenocarcinoma increase postoperative morbidity and mortality rates?	MD Anderson Cancer Center
6	Neoadjuvant chemoradiation versus neoadjuvant chemotherapy prior to pancreaticoduodenectomy for pancreatic cancer	Roswell Park Cancer Institute
7	Changes in body composition during preoperative therapy for resectable pancreatic cancer: do they matter?	MD Anderson Cancer Center
8	Prospective randomized controlled study comparing outcome between standard resection and an extended resection that included dissection of the nerve plexus and various lymph nodes in patients with pancreatic head cancer	Seoul National University
9	Microscopic residual tumor after pancreaticoduodenectomy for cancer. Preliminary results of a multicentric university of Rome prospective randomized trial	University of Rome
Scientific session II		
Topic: Minimally invasive techniques/screening for cancer		
10	Minimally invasive pancreatoduodenectomy: is the learning curve surmountable?	Indiana University
11	Total laparoscopic pancreatoduodenectomy for pancreatic ductal adenocarcinoma: oncologic advantages over open approaches?	Mayo Clinic
12	Preliminary results of a Swedish, MRI based, screening program for individuals at risk for pancreatic cancer	Karolinska Institute (Sweden)
13	Early detection of pancreatic intraepithelial neoplasia using non-invasive imaging to localize and grade protease activity	University of California San Francisco
Scientific session III: translational studies		
14	Role of CYB5A in pancreatic cancer: correlation with clinical outcome and functional characterization in the modulation of autophagy and oncogenic phenotypes	University of Pisa (Italy)
15	CA 19-9 response to neoadjuvant therapy predicts outcome in pancreatic adenocarcinoma	University of Pittsburgh
16	Detection of clinically relevant genetic alterations in fine needle aspirates of pancreatic cancer is possible using next-generation sequencing	Johns Hopkins University
17	New platforms for PDAC preclinical studies: 3D tissue-engineered models based on primary cancer cells and synthetic scaffolds	University of Pisa (Italy)
18	Bioluminescent orthotopic pancreatic-ductal-adenocarcinoma (PDAC) mouse models derived from primary PDAC cells as a platform for therapeutic discovery	University of Pisa (Italy)
19	Counteracting cancer cell survival strategy: sensitization of pancreatic cancer cells to trail induced cell death by jak2/stat3 pathway inhibition by preventing death receptor down regulation	University of Minnesota
Scientific session IV		
Topic: Pancreatitis		
20	Total pancreatectomy with islet autotransplantation for chronic pancreatitis: the price patients pay for improvements in quality of life	Medical University of South Carolina
21	Cost-effectiveness of total pancreatectomy with islet cell autotransplantation for the treatment of small duct chronic pancreatitis	University of Cincinnati
22	High readmission rates following surgery for chronic pancreatitis	University of Cincinnati
23	Pancreaticoduodenectomy for chronic pancreatitis: a long-term follow-up	Mayo Clinic
24	Risk of recurrent pancreatitis and progression to chronic pancreatitis after acute pancreatitis	Academic Medical Center, Amsterdam (Netherlands)
25	Severe acute pancreatitis: using a multidisciplinary percutaneous drainage protocol the main predictor of hospital length of stay is amylase or bacteria in the percutaneous aspirate	St. Luke's Health Care System Boise, ID
Topic: Neuroendocrine tumors		
26	Surgical resection provides a significant overall survival benefit for patients with small pancreatic neuroendocrine tumors	University of Chicago
27	Risk of malignancy in resected nonfunctioning pancreatic neuroendocrine tumors	Mayo Clinic Rochester, MN
28	An investigation of the utility of ki-67 expression in pancreatic neuroendocrine tumour fine needle aspiration samples	Glasgow Royal Infirmary (Scotland)
29	The gastrinoma triangle revisited: duodenal wall gastrinoma and pancreatic gastrinoma locations predict biological behavior and longevity	Loyola University Chicago, IL

**Table 1** (continued)

Number	Title	Institution
30	Patterns of practice and survival among patients with non-metastatic pancreatic neuroendocrine tumors under 2 cm	Mercy Medical Center Des Moines, IA
Scientific session V: IPMN		
31	Re-classification of combined-type IPMNS allows for a better definition of two disease entities	Massachusetts General Hospital
32	Clinical validation of new international consensus guidelines for the resection of branch duct type intraductal papillary mucinous neoplasms (BD-IPMN)	Seoul National Medical University
33	Intraductal papillary mucinous neoplasm of the pancreas, one manifestation of a more systemic disease?	Indiana University
34	The biology of small IPMN cancers (<20 mm invasive component): a multi-institutional analysis	Thomas Jefferson University
35	A national perspective of invasive intraductal papillary mucinous neoplasm (IPMN)	University of Pennsylvania
36	Characterization of pancreatic stromal cells isolated from pancreatitis and pancreatic adenocarcinoma surgical specimens	University of Florida
37	Current indications for surgery of IPMNs may overlook some patients with cancer: recommendations for change	University of California Los Angeles
38	Main pancreatic duct size and risk of malignancy in intraductal papillary mucinous neoplasm	Johns Hopkins University
39	Does EUS improve outcome in surveillance of non-resected presumed branch-duct intraductal papillary mucinous neoplasms?	Yale-New Haven Hospital
40	Resected pancreatic adenocarcinomas with recurrence limited in lung have a significantly better prognosis than those with other recurrence patterns	Johns Hopkins University
41	The indolent nature of pulmonary metastases from pancreatic cancer	University of Pittsburgh
Scientific session VI		
Topic: Cancer Basic		
42	Pancreatic stellate cell secreted IL-6 mediates stat3 dependent cancer cell invasion	Vanderbilt University
43	Neutrophil extracellular traps (NETS) are upregulated in pancreatic cancer as a result of autophagy and contribute to hypercoagulability	University of Pittsburgh
44	Isolation and characterization of DCLK1+ tumor cells of pancreatic adenocarcinoma patients	University of Oklahoma
45	Sequence alterations in the WEE1 non-coding region is a facilitator and marker for pancreatic tumorigenesis	Thomas Jefferson University
46	Chemotherapy resistant pancreatic cancer tumor-associated fibroblasts are protumorigenic	University of California
47	PTK6 increases apoptosis with gemcitabine treatment in pancreatic cancer cells by enhancing DNA damage	Michigan State University
Scientific session VII		
Topic: Early complications after pancreaticoduodenectomy/drains and fistulas		
48	The value of drains as a fistula mitigation strategy for pancreatoduodenectomy: something for everyone? results of a randomized prospective multi-institutional study	University of Pennsylvania
49	A randomized prospective multicenter trial of pancreaticoduodenectomy with and without routine intraperitoneal drainage	Baylor College of Medicine
50	Risk-adjusted outcomes of clinically-relevant postoperative fistula following pancreatoduodenectomy: a model for performance evaluation	University of Pennsylvania
51	High performing whipple patients: factors associated with short length of stay after open pancreatoduodenectomy	Massachusetts General Hospital
52	The association between pancreatic fistula grade C and survival after pancreatic resection for pancreatic cancer	Multicenter Group Study of Pancreatobiliary Surgery (Japan)
53	Does drain fluid amylase accurately predict pancreatic fistula?	University of Wisconsin
54	Early drain removal: the middle ground between the drain versus no drain debate in patients undergoing pancreatoduodenectomy: a prospective validation study	Massachusetts General Hospital
Topic: Quality/predictors/regionalization		
55	The HYSLAR Trial: a prospective randomized trial on the use of a restrictive fluid regimen with 3 % hypertonic saline (HS) versus lactated ringers (LR) in patients undergoing pancreatoduodenectomy (PD)	Thomas Jefferson University
56	Current management of delayed bleeding after pancreatoduodenectomy	Johns Hopkins University
57	Bile-culture based antimicrobial prophylaxis reduces surgical site infections (SSIs) in pancreatic surgery	University of Milan (Italy)
58	It is quality and quantity: a single institution's experience in quality measures of pancreatic cancer care	University of Pittsburgh
Scientific session VIII		
Topic: Quality/predictors/regionalization (continued)		
59	Mobile risk calculator app for operative and oncologic outcomes in patients considering pancreatoduodenectomy for pancreatic adenocarcinoma	Roswell Park Cancer Institute
60	Predictors of early readmission after pancreatectomy	Johns Hopkins University
61	High-volume surgeons versus high-volume hospitals: are best outcomes more due to who or where?	Florida Hospital
62	What are the financial implications of centers for regional healthcare	Florida Hospital

**Table 1** (continued)

Number	Title	Institution
Topic: Late postoperative issues		
63	The incidence of pancreatogenic diabetes after major partial pancreatic resection may be greater than you think	Thomas Jefferson University
64	Effect of high-dose pancreatic enzyme replacement therapy on the development of non-alcoholic fatty liver disease after pancreaticoduodenectomy, paying attention to etiology of diseases and the remnant pancreatic volume	Mie University (Japan)

resectable primary tumor. Four experts presented case arguments.

In the first debate, Dr. Charles Vollmer argued for a surgery-first approach, giving a brief review of the literature on neoadjuvant treatment for resectable and borderline resectable cancers. In summary, no compelling data definitively show that neoadjuvant treatment impacts survival. Dr. Syed Ahmed followed and argued in favor of the use of neoadjuvant chemoradiotherapy, presenting data from MD Anderson Cancer Center demonstrating improved overall survival in borderline resectable patients treated with neoadjuvant chemoradiotherapy.

In the second debate, Dr. Charles Yeo argued that chemotherapy does not work and is expensive. Surgery is the only therapy that has ever resulted in cure in any patient with pancreatic cancer. He cited hospital-based receipts for the typical (uncomplicated) neoadjuvant chemotherapy course, which average more than \$140,000 per patient. This price was compared to that for the cost of the average uncomplicated pancreatoduodenectomy, \$40,000/patient. Dr. Matthew Katz provided the counterpoint by summarizing multiple retrospective and national database studies. These data show that patients over age 80 are more likely to be hospitalized long term or die in the hospital than younger counterparts. Dr. Katz also reviewed the MD Anderson experience with neoadjuvant chemoradiotherapy, which may provide a survival advantage over upfront operation.

### Scientific Session III: Translational Studies

Among several interesting papers in this session, the Pittsburgh group presented data on the prognostic implications for response of CA19-9 to neoadjuvant chemoradiotherapy. In 78 appropriately selected patients, they noted a trend toward improved R0 resection among patients who had a decrease in CA19-9 with neoadjuvant treatment. CA19-9 decrease of more than 50 % was also associated with improved overall and disease-specific survival. This paper generated substantial discussion regarding the relevance of the rate of change in CA19-9 and the utility of a target level of CA19-9. The authors examined fast and slow responders and found no difference in survival outcomes. There were no data to answer

the question regarding the target of CA19-9 as this group typically used a short course of neoadjuvant chemotherapy.

The group from Johns Hopkins presented work directed at developing Next-Generation sequencing technology to evaluate pancreatic cancers preoperatively. The group first simulated preoperative FNA by aspirating tumors in the operating room and then performing Next-Generation sequencing on those aspirates and excisional biopsies of the tumor. Very good correlation was seen between the pseudo FNA and the tumor in terms of genetic variability, suggesting that EUS-guided FNA samples would be adequate samples for sequencing. This paper generated significant interest with questions from the audience centered on the possible use of core needle biopsy to enhance the efficacy of preoperative gene sequencing and others on the possible use of this method to better identify the biologic potential of ambiguous cystic tumors or neuroendocrine tumors.

### Scientific Session IV also Included Two Topics, Pancreatitis and Neuroendocrine Tumors

In the first half of session IV, the group from Charleston, SC, presented their series of total pancreatectomy with auto islet transplantation (TP-IAT) collected over 4 years. Forty-two percent of these operations were done for sphincter of Oddi dysfunction, median OR time was 237 min, and median islet yield was 200,000. The overall mortality rate was 1.6 %, and 24 % of the total number was insulin-independent at the end of the series. The Cincinnati group presented a study comparing costs of medical management or TP-IAT for patients with minimal-change chronic pancreatitis. Medical management was associated with increased cost of care (\$196,000/11.5 QALY) compared to TP-IAT (\$150,569/15 QALY).

The second half of session IV was dedicated to pancreatic neuroendocrine tumors. The group from Evanston, IL, presented an evaluation of small (<2 cm) neuroendocrine tumors from the National Cancer Database. Among 309 patients that underwent resection and 71 that underwent observation, a marked improvement in overall 5-year survival was seen in the resection group (82 vs. 34 %).

The Mayo group also presented a retrospective review of 169 patients with neuroendocrine tumors resected at their

center between 2004 and 2012. Overall, 69 % of these patients were managed with distal pancreatectomy and 25 % with pancreaticoduodenectomy. Median tumor size was 2.7 (6 mm to 16.5 cm). Malignant histologic features were identified in 22 % of tumors between 1 and 1.9 cm. Lymph node metastasis was identified in 12 % of patients with tumors <2 cm. This paper also generated significant discussion with members of the audience questioning the wisdom of resecting all small tumors and identifying an alternative strategy of short-interval surveillance imaging looking for size change that would potentially identify small tumors with more high-grade histology and potential for aggressive behavior.

### Scientific Session V: IPMN

The group from Massachusetts General Hospital evaluated over 400 intraductal papillary mucinous neoplasm (IPMN) patients treated there between 1990 and 2013. They reclassified the mixed type into two categories: those that had extensive (predominantly) main duct involvement vs. those with predominantly side branch IPMN. Nearly 40 % of predominantly main duct IPMN patients had adenocarcinoma, whereas those with predominantly side branch IPMN had a much lower risk (6 %) of developing adenocarcinoma.

The group from Seoul National University in Korea presented their effort to validate the Fukuoka Consensus guidelines on IPMN in 350 patients who underwent surgery for branch duct IPMN. They demonstrated an overall malignancy rate of 27.7 %, with a malignancy rate of 26 % in cysts <3 cm and 29 % in cysts >3 cm. No consistent relationship between cyst size and cancer risk was observed. Multivariate analysis identified main pancreatic duct dilation, mural nodule presence, and elevated cyst fluid CA19-9 as predictors of malignant change. The Fukuoka criteria, which have de-emphasized size as a predictor of malignancy, seem to be more accurate for predicting malignancy in branch-type IPMN.

### Scientific Session VI: Cancer Basic

Three long and three short papers in this session covered a broad spectrum of high-quality, cutting-edge basic science. Topics included the role of stellate cells and tumor-associated fibroblast-mediating tumorigenesis and invasion, pancreatic cancer stem cells (DCLK1+ cells), mechanisms of chemoresistance, and the role of non-coding DNA modulating the RNA-stabilizing protein HUR.

The University of Pittsburgh group presented data relating autophagy to establishment of neutrophil extracellular traps (NETS). These investigators have taken bench observations to

clinical trials using chloroquine (downregulating autophagy) as a therapeutic agent for pancreatic cancer patients.

### Scientific Session VII: Included Two Topics, Early Complications After Pancreaticoduodenectomy/Drains and Fistulas and Quality/Predictors/Regionalization

Two abstracts in this session were presented from the US Pancreaticoduodenectomy Drain Study Group. The first summarized a randomized trial of drain vs. no drain placement following pancreaticoduodenectomy. Improved 90-day mortality rates were observed in the drain group (3 vs. 12 %,  $p < 0.05$ ), causing early termination of the study by the data safety monitoring board. The second paper examined the risk of pancreatic fistula in the same patient cohort. This analysis showed that the overall rate of pancreatic fistula was higher when no drain was placed, particularly in patients thought to have high risk of postoperative pancreatic fistula (i.e., patients with soft glands and small ducts). Patients thought to be at high risk of fistula formation had a fivefold increased incidence of fistula when they were randomly assigned to the no drain cohort. Discussion of these studies included the value of drain amylase measurement, the importance of adequately grading the fistula complications, technical approach to pancreaticojejunostomy, and octreotide use. The vast majority of members of the Pancreas Club attendants reported using drains routinely after pancreaticoduodenectomy.

In the second half of session VII, the Thomas Jefferson group presented a randomized evaluation of 264 patients undergoing a restrictive intraoperative fluid resuscitation protocol with hypertonic saline. The primary endpoint of this study was postoperative complication rate. The hypertonic saline group demonstrated a 26 % relative risk reduction in overall complication rate. Perioperative mortality was similar between groups. This study generated significant discussion including questions about the use of epidural catheters, use of pressors and central venous catheters, and grading of complications. Treating staff was not blinded to the treatment randomization.

### Scientific Session VIII: Also Included Two Topics, a Continuation of Quality/Predictors/Regionalization and Late Postoperative Issues

The Thomas Jefferson group reported results of over 1,000 pancreatectomy patients followed long term for glucose control. They documented 22 % new-onset diabetes and 40 % worsening of glucose control. This study represents the largest study to date with long-term follow-up specifically focusing on glucose control. Importantly, many of these patients developed diabetes more than 2 years postoperatively.

## Awards

Three awards were presented: The PanCAN Award sponsored by the Pancreatic Cancer Action Network was given to Dr. Brian A. Boone of the University of Pittsburgh for their paper (43) “Neutrophil extracellular traps (NETS) are upregulated in pancreatic cancer as a result of autophagy and contribute to hypercoagulability.” The Kenneth K. Warren Award was presented to Dr. Giovanni Marchegiani of the Massachusetts

General Hospital for their paper (31) “Re-classification of combined-type IPMNs allows for a better definition of two disease entities.” The John M. Howard Award was presented to Dr. Jordan Winter of Thomas Jefferson University for their paper (34) “The biology of small IPMN cancers (<20 mm invasive component): a multi-institutional analysis.”

The meeting concluded with an invitation to attend the 49th Pancreas Club meeting on May 15–16, 2015, in Washington, DC.