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Title

Total Pancreatectomy and Islet Autotransplantation: A Decade Long Nationwide Analysis

Permalink

<https://escholarship.org/uc/item/7cz9442t>

Journal

PANCREAS, 44(8)

ISSN

0885-3177

Authors

Alizadeh, R Fazl
Moghadamyeghaneh, Z
Demirjian, AN
et al.

Publication Date

2015

Peer reviewed

guided cystenterostomy in all: single cystgastrostomy (CG) in 15 pts, dual site CG in 3 pts, and CG plus cystduodenostomy (CD) in 4. 6 pts required percutaneous drainage in addition to LAMS placement, 2 pts eventually underwent surgery. LAMS placement was successful in 28/29 attempts. There were no immediate complications. Fever developed within 6 days of LAMS placement in 2/5 initial pts treated with LAMS; both pts had LAMS occlusion due to impacted necrotic tissue. When feasible, all subsequent pts were treated with one (12 pts) or more (1 pt) 10 F double pigtail plastic stents through the lumen of the LAMS to maintain patency, however fever occurred within first 2 weeks in 6/13 and stent occlusion in 7/13. To date, ETN has been done in 19/21 pts. ETN was done after LAMS removal in 7 pts and through the LAMS lumen in 9 pts. LAMSs were removed in 16 pts after a mean of 2.5 procedures (range 2-5) and remained in situ for a mean of 25 days (range 3 – 88 days).

Conclusions: Endoscopic drainage of WON using EUS-guided LAMS stents is a safe and effective for initial drainage; however, despite the large lumen, stent occlusion by solid necrosis occurs early and frequently, so that scheduled ETN is advisable. LAMS offer a convenient conduit for ETN.

The Effect of an Integrated Health System Algorithm Based on 2012 International Consensus Guideline on the Local Practice Pattern for the Management of Pancreatic Cystic Neoplasms

A. Eskandari,¹ E. Alonso,¹ A. Ko,^{1,3} B. Lim.^{1,2} ¹School of Medicine, University of California, Riverside, CA; ²Department of Gastroenterology, Kaiser Permanente Riverside Medical Center, Riverside, CA; ³Department of Surgery, Kaiser Permanente Riverside Medical Center, Riverside, CA.

Aim: To examine the local practice pattern, i.e. gastroenterology (GI)/surgery referrals and endoscopic ultrasound (EUS), for pancreatic cystic neoplasms (PCL) after a region-wide incorporation of an algorithm based on the 2012 international consensus guideline (ICG) in an integrated health system.

Background: PCLs have become an increasingly common challenging clinical entity for primary/acute care physicians, gastroenterologists, radiologists and surgeons. ICG has been developed to aid in the management of PCLs; revised version was published in 2012. Based on this, Kaiser Permanente Southern California (KPSC) published a regional algorithm in October 2013 with radiology reports including a brief summary of recommendations.

Method: Retrospective review was performed; patients with PCL diagnosis given between April 2012 and April 2015 (18 months before and after the publication of the algorithm) at a single medical center within KPSC were identified.

Results: 237 patients (142 pre and 95 post-algorithm) received a new diagnosis of PCLs in the study period. There was no difference in the mean cyst size for pre (19.6 mm) and post (17.3 mm), $p = 0.26$. The mean age of the post population was slightly greater (69 vs 66 years, $p = 0.05$). Compared to pre, post period had significantly less proportion of patients with EUS (40% vs 60%, $p = 0.0026$), GI consults (55.7% vs 85.4%, $p < 0.0001$), and surgery consults (23.7% vs 55.3%, $p < 0.0001$). Fewer patients underwent surgical resection for post (3.2%) vs pre (8.5%), $p = 0.1010$.

Discussion: In current healthcare climate, there is increased pressure to optimize resource utilization. Dissemination of an algorithm for PCL management an integrated health system resulted in fewer EUS and GI/surgery referrals, possibly due to increasing the confidence level of physicians ordering imaging studies, mostly primary and acute care physicians, in managing PCLs.

Conclusion: There was a drastic change in local practice pattern in the management of PCLs after a region-wide incorporation of an algorithm based on ICG-2012 in an integrated health system, namely significantly fewer EUS and GI/surgery referrals.

Open and Minimally Invasive Pancreaticoduodenectomy for Pancreatic Cancer: Perioperative, Oncologic, and Survival Outcomes

M.F. Eskander, S.W.L. de Geus, L.A. Bliss, S.C. Ng, A.J. Moser, J.F. Tseng. *Surgical Outcomes Analysis & Research, Beth Israel Deaconess Medical Center, Boston, MA.*

Background: Although minimally invasive pancreaticoduodenectomy (PD) has been described favorably in single-institution studies, national data is lacking.

Methods: 2010-2011 National Cancer Data Base was queried for patients with pancreatic adenocarcinoma who had a PD, excluding those with metastatic disease. Open surgery was compared to robotic or laparoscopic minimally invasive surgery (MIS) based on intention to treat. Outcomes were overall survival from diagnosis, margin status, post-operative length of stay (LOS), and 30-day unplanned readmission rate. Patient characteristics compared by chi-square.

Kaplan-Meier analysis and Cox proportional hazards models used to evaluate overall survival.

Results: Of 5302 PDs, 725 (13.7%) were begun via MIS and of those, 232 (32.0%) were completed open. MIS group vs. open more likely to have comorbidities (38.8% vs. 34.4%, $p = 0.0226$), surgery at an academic center (72.8% vs. 64.1%, $p < 0.0001$), and poorly differentiated tumors (40.7% vs. 35.1%, $p = 0.0119$). There was a higher rate of R0 resection margins for MIS (79% vs. 75.3%, $p = 0.0317$) and a shorter median LOS (8 vs. 9 days, $p < 0.0001$); 30-day readmission rates did not significantly differ ($p = 0.5757$). Overall median survival was 20.2 months for MIS vs. 20.4 months for open (log-rank p value 0.6911). In patients who received neoadjuvant therapy, open surgery was associated with a significant survival benefit (25.8 vs. 21.7 months; HR 1.50, 95% CI 1.13-1.99) which lost significance when cohort was limited to high volume MIS centers.

Conclusions: In this national study, MIS demonstrated a superior R0 resection rate and shorter LOS but no difference in 30-day readmission rate or overall survival compared to open surgery. Particularly in the neoadjuvant setting, MIS PD should be limited to centers of excellence. Further investigation into oncologic outcomes after pancreatic surgery is warranted.

New Therapeutic Approach in the Successful Surgical Therapy of Pancreatic Cancer

G. Farkas, Jr, L. Leindler, G. Lazar. *Department of Surgery, University of Szeged, Szeged, Hungary.*

Introduction: Even nowadays the only successful therapy for pancreatic cancer treatment is surgery, but postoperative mortality still can be occur decreasing the number of survivals.

Aim: Postoperative grade Bassi C pancreatic fistula is still the main reason for postoperative death. Our aim was to decrease or stop pancreatic leakage with new conservative therapy.

Materials and methods: After operation catabolism is the main metabolic change in human therefore proper postoperative therapy has absolute necessity. We used 20% soil oil and 80% olive based 3 CBS (three chambers bag) central vein parenteral infusion in 2000 ml/day dosage. Between 01.2014-05.2015 16 patients received this therapy. The mean age was 62.3 and 65.2 years, male and female respectively. Operations were: 10 Whipple, 3 distal resections and 3 atypical pancreas resections. For pancreatic fistula detection we measured the amylase content of the drains. We checked the drain amount and content from the onset until healing.

Results: The amount of juice was 200-500 ml/day and the amylase content was higher than 50000U in all cases from the second or third postoperative days. Total amount of 2000 ml/day 3 CBS parenteral infusion was used from second postoperative day, with Saline and RL infusion in extra. Sandostatin was performed 3 times per day. The drain amount started to decrease 6-8 days after this treatment. Enteral feeding started 10-12 days after with overlap. No reoperation was necessary. All patients left the hospital 21-28 days after surgical intervention.

Conclusion: With this new therapy we could treat problematic cases successfully with whom in the past reoperations should have been done and death could have been detected. We hope due to this therapy the successful surgical therapy can be widened moreover new patients can be involved for surgical intervention, which in the past were excluded just because old age week physical status and soft pancreatic tissue to prevent fatal complications.

Total Pancreatectomy and Islet Autotransplantation: A Decade Long Nationwide Analysis

R. Fazl Alizadeh, Z. Moghadamyeghaneh, A.N. Demirjian, D.K. Imagawa, C.E. Foster, M.J. Stamos, H. Ichii. *Department of Surgery, University of California, Irvine, CA.*

Background: Total pancreatectomy (TP) is the last resort to control the severe pain in patients with chronic pancreatitis due to the morbidity of the operation and the frequent severe resultant diabetes. Islet autotransplantation (IAT) following TP is reported, by well experienced groups, to be an effective therapy to prevent post-surgical diabetes. However, there is limited nationwide data analysis during the last few decades. The aim of our study was to investigate outcomes, predictors of in-hospital morbidity, and mortality after TP+IAT.

Methods: The nationwide inpatient sample (NIS) database was used to identify patients who underwent TP+IAT during 2002-2012 in the US. Multivariate regression analysis was used to identify predictors of in-hospital morbidity.

Results: A total of 923 patients underwent IAT after pancreatectomy during 2002-2012. There were 754 patients who had TP+IAT. The most common indication of surgery was chronic pancreatitis (86%) followed by acute pancreatitis (12%). The number of patients undergoing TP+IAT annually significantly increased during the 11 years of study from 53 cases in 2002 to 155 cases in 2012. Overall mortality and morbidity of patients were 0% and 57.8%, respectively. Post-surgical hypoinsulinemia was reported in 42.3% of patients, indicating 57.7% of patients were insulin independent during hospitalization. Predictors of in-hospital morbidity were obesity (AOR: 3.024, $P < 0.05$), fluid and electrolyte disorders (AOR: 2.71, $P < 0.01$), alcohol abuse (AOR: 2.63, $P < 0.01$), and weight loss (AOR: 2.43; $P < 0.01$).

Conclusion: During 2002-2012, the overall number of patients who underwent TP+IAT has been increasing. Our study showed TP+IAT is a safe and feasible procedure with no mortality, acceptable morbidity rates and achieved high rate of early insulin independence. Obesity, fluid and electrolyte disorders, and alcohol abuse are the most significant predictors of in-hospital morbidity.

Pancreas-Specific Secretory Pathway Ca^{2+} -ATPase 2 Affects GPCR-mediated Ca^{2+} Signalling

M. Fenech,^{1,2} C. Pin^{1,2,3} *Departments of ¹Pediatrics, ²Physiology & Pharmacology, ³Oncology, Western University, Children's Health Research Institute, London, Ontario, Canada.*

Background: Enzymes are released from acinar cells through regulated exocytosis, which involves a signalling network that regulates spatial and temporal accumulation of Ca^{2+} . Cytosolic Ca^{2+} levels are lowered, in part, by Ca^{2+} -ATPase pumps. Our laboratory has previously identified a novel isoform of secretory pathway Ca^{2+} -ATPase 2 (SPCA2) that appears to be pancreas specific. However, this isoform, designated SPCA2c (c for carboxy) contains only the last 136 amino acids of SPCA2, making it unlikely that SPCA2c functions as a Ca^{2+} -ATPase. Other studies report that SPCA2 can increase cytosolic Ca^{2+} concentrations via interaction with the plasma membrane Ca^{2+} channel, Orai1. The goals of this study were to determine if SPCA2c could affect cytosolic Ca^{2+} levels and Ca^{2+} movement in response to GPCR-mediated signalling.

Methods and Results: SPCA2c tagged with FLAG (SPCA2c-FLAG) was transiently transfected into HEK293 with and without the stable expression of Orai1 or AR42J cells in combination with GFP. Co-immunofluorescence analysis (IF) for FLAG and cell organelle markers was performed to localize SPCA2c within the cell. Also, transfected cells were identified by GFP expression, and then assessed for cytosolic Ca^{2+} levels using Fura2 ratiometric analysis before and after stimulation with carbachol. IF analysis revealed SPCA2c localization to both the endoplasmic reticulum and golgi apparatus in AR42J and HEK 293 cells. Transient expression of SPCA2c in HEK293 cells, both with and without the stable expression of Orai1, resulted in elevations in resting cytosolic Ca^{2+} levels, and altered responses to carbachol stimulation, indicating a functional role for SPCA2c in Ca^{2+} homeostasis.

Conclusions: Our findings suggest SPCA2c plays a unique role in maintaining cytosolic Ca^{2+} that involves interacting with Orai1. Further work is aimed at determining SPCA2c's role in affecting the acinar cell response to injury.

Evaluation of Proposed Biomarkers in Early Stage Pancreatic Ductal Adenocarcinoma

M.A. Firpo,¹ A. Rosati,² G.D. Khanderao,¹ D.G. Adler,¹ C.S. Scaife,¹ K.M. Boucher,¹ M.C. Turco,² S.J. Mulvihill.¹ *Huntsman Cancer Institute, University of Utah, Salt Lake City, UT; University of Salerno, Fisciano, Italy.*

Development and deployment of an accurate, blood-based assay that could be used to screen asymptomatic patients for pancreatic ductal adenocarcinoma (PDAC) risk would likely improve outcomes by identifying treatable disease. We evaluated serum levels of 30 analytes previously identified as potential circulating biomarkers in at least two prior studies involving pre-malignant rodent models, gene expression studies of PanIN lesions in clinical samples, or specifically evaluated in serum from early stage PDAC cases. Analytes were measured in each of 180 serum samples from healthy control subjects, chronic pancreatitis cases, and stage IA, IB, or IIA PDAC cases. Nineteen analytes (ALCAM, AXL, CA 19-9, CEACAM1, COL18A1, EPCAM, HA, HP, ICAM1, IGFBP2, IGFBP4, MMP2, MMP7, PRG4, SPP1, TGFB1, THBS1, TIMP1, TNFRSF1A) had significant differences between the three classes, while and additional four analytes (BAG3, BSG, LCN2, PARK7) trended towards significance. We evaluated the 30-analyte panel using a technique that maximizes area under

the receiver operating characteristic curve and identifies analytes that most contribute to class discrimination using the lasso procedure. For the comparison of healthy controls from early stage PDAC, an optimal panel included analytes BAG3, CA 19-9, CEACAM1, HA, IGFBP2, PARK7, and SPP1 yielding an area under the ROC curve (AUC) of 0.92. For the comparison of healthy controls and chronic pancreatitis from early stage PDAC, an optimal panel included analytes BAG3, CA 19-9, CEACAM1, EPCAM, LCN2, MSLN, PARK7, PRG4, SPP1, and TNFRSF1A, yielding an AUC of 0.88. These data suggest that suitably accurate algorithms (>90% accuracy) can be devised using subsets of the 30 analyte panel. It is expected that increased accuracy can be realized by incorporating additional analytes into the resulting algorithms.

The Effect of Cystathionine-Gamma-Lyase Gene Deletion on the Renin-Angiotensin System in Cerulein-Induced Acute Pancreatitis in Mice

R.R. Gaddam,¹ A. Badii,¹ S.T. Chambers,¹ I. Ishii,² M. Bhatia.¹ *¹Department of Pathology, University of Otago, Christchurch, New Zealand; ²Department of Biochemistry, Graduate School of Pharmaceutical Sciences, Keio University, Tokyo, Japan.*

Background: Cystathionine- γ -lyase (CSE) is an endogenous hydrogen sulfide (H_2S)-producing enzyme involved in inflammation. We previously demonstrated that, H_2S synthesized by CSE has a pro-inflammatory role in cerulein-induced acute pancreatitis and associated lung injury. The renin-angiotensin system (RAS) components (ACE, ACE2, Ang II, and Ang-(1-7)) play an important role in the regulation of inflammation. The present study investigated the effect of CSE gene deletion on RAS metalloproteases and their bioactive peptides in caerulein-induced acute pancreatitis and associated lung injury in mice.

Methods: Wild-type and CSE-deficient (CSE-KO) C57BL6 mice (male, 25-30 g) were each assigned into control (saline) or interventional (cerulein) groups. Acute pancreatitis was induced by hourly cerulein injections (50 μ g/kg) for 10 hours. Mice were sacrificed 1 h after the last saline/cerulein injection. Pancreas and lung tissues were collected and processed to measure ACE, ACE2, Ang II and Ang-(1-7) activity/levels.

Results: The RAS components in pancreas (ACE2 activity and levels, Ang-(1-7)) and lung (ACE and ACE2 activity and levels, Ang II and Ang-(1-7)) were significantly lower in CSE-KO mice. The cerulein treatment resulted in significant decreases in ACE2 activity (pancreas and lung) and Ang II levels (lung) in wild-type mice but not in CSE-KO mice.

Conclusion: These findings suggest that acute inflammation inhibits activation of the RAS system. However, in the absence of baseline H_2S production (CSE deletion) both ACE and ACE2 and their bioactive peptides were reduced suggesting H_2S has a role in the maintenance of normal homeostasis of the RAS system. This requires further study.

Laparoscopic Pancreaticoduodenectomy (LPD) With Uncinate Process First Approach

W. Gao, K. Jiang, J. Wu, Q. Li, F. Guo, J. Chen, J. Wei, Z. Lu, M. Tu, X. Dai, C. Dai, Y. Miao. *Pancreas Center, The First Affiliated Hospital of Nanjing Medical University, Nanjing, China.*

Background: Complete resection for pancreatic head cancer is of prognostic relevance; however, most patients will develop recurrence around superior mesenteric artery (SMA) and celiac trunk (CT). PD with uncinate process first approach dissect the pancreatic head in a caudal-cranial direction, aiming to improve exposure and complete dissection of SMA. LPD has flexible and unique view advantage from caudal, posterior and lateral side, which is ideal for uncinate process first approach.

Technique: After initial exploration, pancreas is tunneled above the portal vein; laparoscope was transferred to left lateral trocar, which provides a left lateral and posterior view. Then SMA trunk below pancreas was reached by incise Treitz ligament, the dissection followed SMA cranially, it is possible to follow SMA at this stage all the way downward towards its origin. The proximal jejunum is then transected and pulled to right. Laparoscope was transferred to right lateral trocar, which provides a right lateral and posterior view. Kocher's maneuver is well facilitated by this view, pancreas head was complete mobilized, SMA root were dissected and looped above left renal vein. The uncinate was then completely dissected in a caudocranial direction along SMA axis, tissue between SMA and CT was resected. Finally laparoscope was transferred to