

Review Article

Tumors of the body and tail of the pancreas

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Abstract

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Introduction

Previously published comparisons of laparoscopic distal pancreatectomy (LDP) to open distal pancreatectomy (ODP) have consistently demonstrated a statistically shorter post operative length of stay (LOS) for patients undergoing LDP. None of these published comparisons have included data on readmissions occurring after initial hospital discharge and, consequently, may overstate the benefit of LDP relative to ODP. It was maintained a prospectively accruing database tracking 600 perioperative characteristics for patients presenting to our facility for treatment of pancreatic disease. This database includes initial LOS and data on type of post operative complication and the nature of postoperative interventions but does not track the length of time spent in the hospital for post operative readmissions. It was therefore queried this database to identify all patients undergoing either LDP or ODP between 2007 and 2009. Preoperative, operative and postoperative characteristics were culled from the database and compared using standard methods. The electronic medical records for these patients were then reviewed retrospectively to identify readmissions and to determine the cause, treatment required and LOS for each readmission. Initial LOS was then added to readmission LOS to determine the total hospital stay for each patient and that value was compared by standard methods. Fifty patients underwent ODP during the years studied. Twenty LDP were attempted. There were no conversions. Patients undergoing LDP were statistically identical to those undergoing ODP in regard to age, mode of presentation, clinical comorbidities, demographic characteristics, operative times, tumor size, overall morbidity rate, 30-day mortality rate and rate and grade of post-operative

pancreatic fistula. Patients undergoing LDP were statistically more likely to be female (80 % vs. 50 %), had a higher mean preoperative serum albumin level, had a lower estimated operative blood loss, were less likely to have ductal adenocarcinoma (0 % vs. 24 %), had a lesser average lymphadenectomy and a significantly shorter initial postoperative LOS (5 days vs. 9 days, $P<0.001$) than those undergoing ODP. There were a total of nine readmissions. The causes for readmission were similar in both groups including pneumonia, wound infection, pancreatic fistula and intra-abdominal abscess. Five of the readmissions were in patients that had had LDP, 4 were in patients that underwent ODP. The readmission rate for LDP was statistically higher than for ODP (25 % vs. 8 %). Adding the length of readmissions to the initial LOS statistically eliminated the perceived effect of LDP to shorten post operative LOS. The average overall length of stay for LDP was 7 days. That for ODP was 9 days, which was not a significant difference. It was concluded that LP is a safe, effective modality for managing premalignant pancreatic neoplasm providing morbidity comparable to that for SDP and an apparent benefit in initial postoperative LOS. Adding readmission data to the initial LOS, however, eliminates the perceived effect of laparoscopic resection to accelerate in-hospital recovery [1].

Distal pancreatectomy with splenectomy (DPS) has been the standard treatment for pancreatic body/tail tumors, but spleen-preserving distal pancreatectomy (SPDP) is increasingly used. Two methods exist – splenic vessel preservation (SPDP-VP) and excision (SPDP-VE). It is unknown how the method of SPDP impacts postoperative pancreatic fistula (POPF) rates. Records from patients

undergoing distal pancreatectomy at 9 academic medical centers were analyzed. 675 patients were included. Pancreatic pathology included: cysts (34 %), adenocarcinoma (19 %), neuroendocrine tumors (16 %), pancreatitis (15 %), metastases (5 %), and other (11 %). When POPF rates between DPS and SPDP were compared, there was no significant difference. When POPF rates were examined by method of splenic preservation, those undergoing SPDP-VP had significantly higher POPF rates than those with SPDP-VE for both total (36 % vs. 15 %) and clinically significant (grade B/C) POPF (23% vs. 7%, $P=0.02$). When multivariate analysis was performed to control for other contributing factors, SPDP-VP remained an important risk factor for POPF. In this multicenter data set, the approach to splenic vessels during SPDP had a significant independent impact on POPF rates. These results suggest that preservation of the splenic vessels during SPDP may be associated with higher rates of POPF when compared to vessel excision. This observation should be confirmed by prospective analyses because it has the potential to alter the risk/benefit ratio for splenic preservation [2].

Preservation of the spleen during distal pancreatectomy has been associated with fewer postoperative complications. Splenic preserving distal pancreatectomy (SPDP) can be accomplished with splenic artery and vein preservation or ligation. However, no data are available on the relative merits of these two techniques. The aim of one analysis, therefore, was to compare the outcomes of splenic preserving distal pancreatectomy with and without splenic vessel preservation. From 2002 through 2009, 434 patients underwent distal pancreatectomy, and 86 (20 %) had splenic preservation. Vessel preservation was accomplished in 45, and ligation was performed in 41. These patients were similar with respect to age, ASA class, pathology, surgeons, and minimally invasive approach (79 %). For further comparison, a matched group of 86 patients undergoing distal pancreatectomy with splenectomy was analyzed. The most common pathologies were cystic tumors (54 %) pancreatitis (24 %) and neuroendocrine tumors (12 %). Analysis of variance and appropriate two-way statistical comparisons were performed. The analysis suggests that outcomes are best for splenic preserving distal pancreatectomy (SPDP) with vessel preservation and that SPDP with vessel ligation provides no short term advantage over distal pancreatectomy with splenectomy. It was concluded that splenic vessel preservation is preferred when performing splenic preserving distal pancreatectomy [3].

Laparoscopic Technique

Multicenter data indicate that laparoscopic distal pancreatectomy (LDP) can be performed with safety equivalent to open DP (ODP) for benign pancreatic lesions. It was conducted a retrospective analysis of distal pancreatectomy (DP) for pancreatic adenocarcinoma (PAC) performed either open or laparoscopically to determine the relative safety and oncologic efficacy of LDP compared to ODP. It was analyzed perioperative outcomes and

cancer-specific survival in a consecutive series of 57 DP for PAC between 2002 and 2009. Perioperative, clinicopathologic, and oncologic outcomes data were evaluated by intention-to-treat. Thirty-two LDP (56 %) and 25 ODP (44 %) were identified with 45 month median observation time. Based on intent-to-treat, the LDP and ODP groups were identical in preoperative factors such as age, BMI, ASA score and CA 19-9 as well as tumor characteristics like size by CT scan and EUS. Perioperative outcomes like estimated blood loss (EBL), blood transfusion, ICU admission and length of stay were equivalent. Despite a 36 percent conversion rate to open, the LDP group demonstrated significantly shorter operating times. EBL was reduced following completed LDP, with a trend to reduced LOS (8 vs. 6 days). There were no severe complications, reoperations, or perioperative deaths. The frequency and clinical significance of postoperative complications (Clavien scale) as well as the frequency (15/57, 26 %) and severity (grade A, 73 %; grade B, 27 %) of pancreatic fistulae by ISGPF were similar. The rates of R0 resection (ODP 88 %; LDP 81 %), median lymph node harvest (ODP 11; LDP 10), and distribution of AJCC pathologic stages were equivalent regardless of technique. Eighty-one of patients received adjuvant treatment (ODP 79 %; LDP 83 %). No differences in median progression-free (ODP 5 months; LDP 6 months) or overall survival (ODP 15 months; LDP 19 months) were observed. Similarly, no differences in the rates of local (8 % ODP; 6 % LDP), or local and systemic (16 % ODP; 19 % LDP) recurrences were identified. In a multivariate Cox-regression model non-R0 resection, LN involvement ≥ 2 , tumor size > 4 cm, elevated preoperative CA 19-9 and blood transfusion requirement were associated with significantly shortened survival, but not surgical technique. It was concluded that no selection bias between the LDP and ODP groups was identified based on preoperative patient factors or CT/EUS findings. A high rate of margin-negative resection was maintained regardless of technique. It was observed no evidence for inferiority of LDP compared to ODP for pancreatic cancer on the basis of either postoperative outcomes or long-term cancer-specific survival data, with a trend to improved perioperative outcomes for completed LDP. The feasibility of a randomized clinical trial of LDP for distal pancreatic cancer is questionable [4].

Robotic Surgery

Multicenter data indicate that laparoscopic distal pancreatectomy (LDP) has safety equivalent to open distal pancreatectomy (ODP). It was hypothesized that improved dexterity and visualization during robotic assisted distal pancreatectomy (RADP) would create improved outcomes compared to LDP. Outcomes of RADP for 12 benign lesions and 8 pancreatic ductal adenocarcinomas (PDA) were matched to a contemporaneous laparoscopic DP group with 28 PDA and 28 benign lesions, between 2004 and 2010. Perioperative outcomes and 30 days mortality were compared. The age, gender, and racial demographics of the cases/lap controls were statistically equivalent, and the groups were matched in terms of American Society of

Anesthesiologists Score and tumor size. RADP and LDP demonstrated similar operative times, estimated blood loss, rates and severity of pancreatic fistula, and lengths of hospital stay. However, RADP demonstrated a significantly reduced rate of conversion to open as well as a reduced frequency of blood transfusion with a trend toward improved lymph node harvest. RADP is equivalent to LDP in all important measures of outcome and safety without an increased OR time. However, RADP significantly reduced the risk of conversion to open as well as a trend toward a reduced risk of blood transfusion. These benefits were independent of the learning curve for RADP. It was speculate that improved dexterity and stereoscopic visualization enable superior control of bleeding and completion of intended minimally-invasive resections [5].

The daVinci surgical system (dVss) is a computer-assisted electromechanical device acting as a remote telepresence manipulator controlled by a surgeon. As compared to laparoscopy the dVss restores hand-eye coordination, thanks to real 3D high-definition view including 10x to 15x magnification, employs wristed instruments, avoiding the fulcrum effect seen in laparoscopy, and provides tremor filtration and scaled motion. These improvements are expected to result into significant operative advantage especially when the operative field is deep and narrow, and when fine dissection and microsuturing are required. As such the dVss could improve the rate of spleen preservation during laparoscopic distal pancreatectomy (DP). The medical records of 53 consecutive patients undergoing laparoscopic DP were reviewed. Standard laparoscopy was used in the first 30 consecutive patients (2000-2008) and dVss-AL in the following 23 operations (2008-2010). Based on preoperative diagnosis and imaging studies, spleen preservation was thought possible in 23 SL patients (77 %) and in 17 dVss-AL patients (74 %). No standard laparoscopy patient was converted to open surgery. Similarly, no dVss-AL was converted to either open surgery or standard laparoscopy. Spleen preserving DP was carried out in 18/23 standard laparoscopy patients (78 %) and in 15/17 dVss-AL patients (88 %). More specifically preservation of splenic vessels was possible in 16/23 standard laparoscopy patients (70 %) (2 Warshaw procedures) and in 15/17 dVss-AL patients (88 %). In one patient undergoing dVss-AL DP a segment of splenic vein was resected en-bloc with the specimen and reconstructed using a jump graft of greater saphenous vein. Seven standard laparoscopy patients (30%) had simultaneous cholecystectomy (n=4), resection of splenic aneurysm with end-to-end reconstruction of splenic artery (n=1), and resection of gastric GIST (n=1). Eight dVss-AL patients (47 %) had simultaneous adrenalectomy (n=2), subtotal parathyroidectomy (n=1), removal of liver segment III (n=1), abdominal wall repair (n=1), removal of ovarian cyst (n=1), bilateral adnexectomy (n=1). Although comparison of operative times is biased by associated procedures, average operative time was 294 minutes in standard laparoscopy and 364 minutes in dVss-AL.

Pancreatic stump was stapled in most standard laparoscopy patients (15/23; 65 %), and it always managed by selective duct ligation plus fish-mouth suture in dVss-AL. The rate of "clinically relevant" pancreatic fistula, corresponding to grade B pancreatic fistula according to ISGPF classification, was 7/23 (30 %) in SL DP and 4/17 (24 %) in dVss-AL DP. No grade C pancreatic fistula was observed, no patient required repeat surgery and none was readmitted after the initial hospital discharge. The mean length of hospital stay was 12 days after standard laparoscopy and 11 days after dVss-AL. In appropriately selected patients, spleen preservation is usually possible during laparoscopic DP, using either SL or dVss-AL. Although the study is biased by its retrospective nature and the fact that standard laparoscopy DP and dVss-AL DP are not used contemporarily, the enhanced operative abilities of the dVss do not seem to be conclusive to spare the spleen, but could possibly result in higher rates of preservation of splenic vessels [6].

Radio-frequency Transaction

The pancreatic remnant is a significant source of morbidity after distal pancreatectomy. Oversewing the transected pancreas has been shown to decrease leaks but can be challenging laparoscopically. It was hypothesized that radiofrequency energy (RF) would seal the pancreatic cut-edge after laparoscopic distal pancreatectomy without the need to oversew. It was a retrospective review of prospectively collected data. Demographic, perioperative, and pathologic variables were compared. Pancreatic leaks were rated according to the International Study Group definitions. Between 2007 and 2010, 55 patients underwent laparoscopic distal pancreatectomy. Thirty patients (55 %) were transected with RF. Both groups were equivalent in terms of demographic and pre-operative variables. In the RF group, only 15 percent were oversewn and 5 patients (17 %) developed pancreatic leaks; in the non-RF group, 100 percent were oversewn and 6 patients (20 %) developed pancreatic leaks. The fistula rates were equivalent. Blood loss (RF 195 ± 192 vs. non-RF 210 ± 157 mL), operative time length of stay, and hospital charges (non-RF USD 50513 ± 15928 vs. RF USD 55357 ± 15507) were equivalent between groups [7].

Duct-stenting For Prevention Of Postoperative Complications

Pancreatic leak represents a significant cause of morbidity and mortality after distal pancreatectomies. In the literature, the role of preoperative pancreatic duct stent placement remains undefined. The objective of the study was to assess whether stenting of the ventral pancreatic duct prior to distal pancreatectomy reduces the rate of pancreatic leak. Between 2005 and 2008 a total of 61 patients underwent distal pancreatectomy. Nineteen patients had a distal pancreatectomy following ERCP and pancreatic duct stent placement and 42 patients had a distal pancreatectomy without preoperative stent placement. Clinical, perioperative and outcome data were

retrospectively analyzed and compared. No statistically significant difference was present in the pancreatic leak rate between the stented (S) and non-stented (NS) group. The stented group had a pancreatic leak rate of 36 percent compared with 45 percent for the not stented group. The most common complications in both groups were manifestations of pancreatic leak (fistula, abscess, pseudocyst) with abscess rate being similar in the stented group (26 %) versus the non-stented group (26 %). The wound infection rate was also similar in the two groups (S group 11 % vs. NS group 10 %). Morbidity and mortality rates were equivalent in both groups. The stented group had a median length of stay of 6 days compared to 7 days for the not stented group. It was concluded that pancreatic duct stent placement offers no therapeutic benefit compared to no intervention in prevention of pancreatic leaks prior to distal pancreatectomies. It also does not affect the severity of complications, length of stay, overall morbidity and mortality [8].

Routine Peritoneal Drainage Following Elective Distal Pancreatectomy

Peritoneal drainage (PD) of the operative bed following elective pancreatectomy has traditionally been utilized to hypothetically allow early recognition and potential therapeutic treatment of a pancreatic leak following reconstruction or ligation of the remnant gland. Recent literature suggests drainage is not helpful in those following pancreatectomy and in fact may be detrimental. Data specific to those having elective distal pancreatectomy (DP) has not received prior evaluation. It was hypothesized that PD does not mitigate the morbidity or the need for post-operative therapeutic intervention in those having DP and further may not be an effective means toward preventing or recognizing intra-abdominal complications when they do occur. It was retrospectively reviewed 69 patients having elective DP at a university hospital from 1997 to 2010. Factors examined included the development of post-operative intra-abdominal complications (fistula, pseudocyst, bleeding, abscess) particularly those that required therapeutic intervention (radiologic drainage or re-operative surgery). PD was utilized at the discretion of the attending physician. Criteria for drain removal include output <50 mL/day and/or amylase value < 3X serum level. Sixty-nine patients had DP during the study period, whereas 30 of who did not have PD. Sixty percent were female, 75 percent had surgery for malignancy and 23 percent had concurrent extra-pancreatic organ removal with no difference between groups. Thirty-four patients (49 %) suffered 45 complications post-operatively. The majority of the morbidity was intraabdominal in nature including 15 with abscess, 6 with pancreatic fistulae and 11 with pseudocysts. Twelve and 19 patients respectively required radiologic drainage, reoperation or both post-operatively. There was no difference between those with drains and those without with respect to overall or intra-abdominal

complications, the need for radiologic drainage or re-operation. Of the 39 patients having PD, 19 had post-operative abdominal morbidity. The drain was useful in preventing, identifying, and/or treating the complication in only 3. It was concluded that peritoneal drainage following elective major pancreatic resection does not confer a reduction in overall morbidity, post-operative intra-abdominal complications or the need for therapeutic intervention versus those with no drains. The presence of a drain, in general, was not helpful in preventing, detecting or treating a post-operative intra-abdominal complication [9].

The Appleby Operation

There are data to suggest that 30 percent of patients who present with locally advanced pancreatic cancer will not develop systemic metastases and succumb to local progression alone. Encasement of the celiac trunk by tumors of the pancreatic body frequently precludes surgical resection for adenocarcinomas of the pancreatic. It was hypothesized that selected patients may derive prolonged survival benefit from aggressive surgical resection following neoadjuvant treatment. It was analyzed the outcomes of modified Appleby procedures for pancreatic adenocarcinoma between 2002 and 2010. Eleven patients underwent a modified Appleby procedure for adenocarcinoma of the body of the pancreas. All patients received at least three months of gemcitabine-based neoadjuvant chemoradiation therapy. Median operative time was eight hours, fourteen minutes and median estimated blood loss was 700 ml. There was no clinically significant hepatic or gastric ischemia postoperatively. Median length of stay was nine days. Four patients (35 %) had pancreatic leaks; all but one were ISGPF grade A. There were no perioperative deaths in the first 30 days; one patient died on day 54. Ten patients achieved R0 status (91 %). Median pathologic tumor size was 4.0 cm, and the median lymph node harvest was 13. Six patients recurred; four systemic and two locoregional (median follow-up nine months). Three patients have died; two with no evidence of disease at the time of death. Two patients are alive for more than 36 months (18 %). It was concluded that resection of pancreatic body adenocarcinoma with en bloc celiac axis resection is technically feasible with acceptable perioperative morbidity and mortality. Aggressive surgical resection can provide long term survival in select patients [10].

Splenic Artery Invasion In Body And Tail Cancer

The value of splenic vessels invasion (which identified T3 tumors) in prognosis after resection for pancreatic ductal adenocarcinoma (PDA) of the body and tail has been scarcely investigated. Aim of one study was to evaluate prognostic factors in PDA of the body/tail, emphasizing the role of splenic vessels infiltration. Between 1990 and 2008, 87 patients who underwent distal pancreatectomy (DP) for histologically proven PDA of the body and tail

were analyzed. Clinico-pathological prognostic factors for survival were evaluated. Univariate and multivariable analyses were performed. Postoperative morbidity was 31 percent with no mortality. The 1-, 3- and 5-year overall survival rates were 77 percent, 48 percent and 25 percent, respectively. Invasion of the splenic artery (SA) was observed in 19 patients (22 %). All 19 patients with SA invasion had also SV involvement. The sensitivity and specificity of preoperative imaging in detecting SA infiltration resulted 37 percent and 96 percent, respectively. Patients with SA invasion had a significantly worse prognosis compared with those without SA invasion (median survival: 15 vs. 39 months). Of the 19 patients with SA infiltration, 17 had a recurrence. In all those 15 patients with SA involvement who died, 14 (93 %) died within 2 years from surgery. Also patients with SV invasion had a poorer survival respect of patients without SV invasion (24 vs. 44 months). On multivariable analysis, adjuvant therapy, poorly differentiation (G3/G4), R2 resection, the presence of lymph node metastases, and SA invasion were independent predictors of survival. It was concluded that invasion of SA is an independent predictor of poor survival in PDA of the body/tail. PDAs with SA invasion should be classified as T4 tumors rather than T3. The SA involvement implies a more aggressive tumor biology, although a radical resection can be achieved safely by a surgical standpoint. In the presence of SA infiltration, neoadjuvant treatment should be considered [11].

Number Of Lymph Nodes

While clinical benefits of laparoscopy for distal pancreatectomy have been described, the procedure has been used sparingly for cancer since it is unknown if the associated lymphadenectomy is equivalent to the open approach. To address this question, it was performed a case-control study to compare lymph node clearance rates for the two procedures. It was reviewed surgical pathology and lymph node removal rates for open and laparoscopic distal pancreatectomy and splenectomy procedures over a three-year period (2006-2009). Laparoscopic distal pancreatectomy patients were matched to open distal pancreatectomy patients by tumor size. Spleen-preserving distal pancreatectomies were excluded from this analysis. It was identified 31 patients who had a laparoscopic distal pancreatectomy and splenectomy (mean age 61 years, 52 % female) and 31 patients who had the equivalent open procedure (mean age 62 years, 55 % female). There was an equivalent lymphadenectomy count in the laparoscopic group (15 nodes, range 6-60) compared to the open group (16 nodes, range 8-38). There was no difference in postoperative pancreatic leak rates. There were no wound infections in the laparoscopic group and the laparoscopic group had a significant shorter LOS (6 days vs. 8 days). It was concluded that a laparoscopic resection of the distal pancreas can achieve an equivalent lymph node resection rate compared to the open operation and therefore should be considered as an option in patients with malignancy of the pancreas body and tail [12].

Long-Term Outcome

The outcome of resected pancreatic adenocarcinoma of the body/tail of the pancreas requiring distal pancreatectomy (DP) is less well studied than head/uncinate tumors resected by pancreaticoduodenectomy (PD). Between 1990 and 2010, patients who underwent DP (n=215) or PD (n=1703) for adenocarcinoma were identified. Information on demographics, operative characteristics, pathology and survival were compared between DP and PD. The DP and PD patients were comparable in age, gender and Charlson score at presentation. PD patients had a longer hospital length of stay than DP patients (10 vs. 7 days). When comparing DP to PD, there was a higher proportion of T1, T2, and T4 lesions with less T3 lesions. The median total lymph nodes harvested were comparable across the groups, however, DP was associated with a significantly lower rate of lymph node positivity. DP also had a lower risk of vascular invasion and margin positivity. DP was associated with a significantly better unadjusted overall long-term survival than PD. However, there were no significant differences in the perioperative mortality and long-term survival between PD and DP after adjusting for multiple clinico-pathological factors. It was concluded that patients who are found to be resectable at the time of presentation and undergo DP have better pathological tumor characteristics in contrast to PD. Despite differences at the time of initial presentation, DP for adenocarcinoma has similar perioperative outcomes with no significant differences in adjusted long-term survival compared to PD [13].

Postresectional Diabetes

Diabetes is a known, but poorly understood sequela of pancreatic resection in a subset of patients. Our aim was to define the incidence and risk factors of postresection diabetes (PRD) after distal pancreatectomy (DP). A retrospective review of all consecutive patients undergoing DP from 2004 through 2010 was performed. Data was obtained from medical records, pathology reports, and postoperative imaging. Postoperative CT scans were evaluated to determine extent of resection, defined by site of transection as limited (adrenal or left), standard (superior mesenteric artery or left to adrenal), extended (neck), subtotal (into head). Of 583 patients undergoing DP, 90 patients with pre-existing type I (n=24) or type II (n=66) diabetes were excluded. The remaining 493 patients represent the study population with a mean age of 57 years and BMI (kg/m^2) of 27.4. Operative indications included benign lesions in 253 patients (51 %) and malignancy in 240 (49 %). Extent of pancreatic resection was limited in 141 patients (37 %), standard in 87 (23 %), extended in 128 (33 %), and subtotal in 30 (8 %). Postoperatively, 179 patients (36 %) required no postoperative treatment, 269 (55 %) required perioperative hyperglycemic control, and 45 (9 %) developed diabetes including 34 requiring insulin, and 11 oral hypoglycemic medication. Patients developing PRD had higher mean preoperative glucose levels (98 vs. 112), BMI (27 vs. 29), estimated blood loss (594 vs. 845 mL), longer operative

time (238 vs. 269 min), and greater pancreatic specimen length (9.3 vs. 10.9 cm). Incidence of PRD correlated with CT extent of pancreatic resection, occurring after limited resection in 4 percent, standard in 5 percent, extended in 13 percent, and subtotal in 30 percent. On multivariate analysis, factors associated with increased risk of PRD included preoperative glucose >126 (OR 10.06), BMI 5 unit increase (OR 1.6), extended (OR 3.37) or subtotal resection (OR 9.86), and blood transfusion (OR 2.38). It was concluded that postresection diabetes occurs in approximately 9 percent of patients after DP. Factors associated with increased risk include elevated preoperative glucose, BMI, extent of resection, and need for blood transfusion. Three of these factors are easily attained preoperatively by clinical evaluation and expected pancreatic remnant based on CT imaging. These findings will help counsel patients pre- and postoperatively about the risks of postresection diabetes after DP [14].

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