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Distal Pancreatectomy is Not Associated with Increased Perioperative Morbidity when Performed as Part of a Multivisceral Resection

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Abstract
Purpose To evaluate the indications for and the outcomes from distal pancreatectomy.
Methods Retrospective chart review of 171 patients who underwent distal pancreatectomy at Brigham and Women's Hospital between January 1996 and August 2005.
Results Nearly one-third of distal pancreatectomies were performed as part of an en bloc resection for a contiguous or metastatic tumor. Fifty-six percent of the patients underwent a standard distal pancreatectomy +/− splenectomy (group 1), whereas 44% of distal pancreatic resections included additional organs or contiguous intraperitoneal or retroperitoneal tumor (group 2). The overall post-operative complication rate was 37%; the most common complication was pancreatic duct leak (23%). When compared to patients undergoing standard distal pancreatectomy, those with a more extensive resection including multiple viscera and/or metastatic or contiguous tumor resection had no significant difference in overall complication rate (35% v. 39%, $p=0.75$), leak rate (25% v. 20%, $p=0.47$), new-onset insulin-dependent diabetes mellitus (3% v. 4%, $p=1.0$), and mortality (2% v. 4%, $p=0.656$).
Conclusion This series includes a large number of patients in whom distal pancreatectomy was performed as part of a multivisceral resection or with en bloc resection of contiguous tumor. Complications were no different in these patients when compared to patients undergoing straightforward distal pancreatectomy.

Keywords Distal pancreatectomy · Multivisceral resection · Pancreatic fistula

Introduction

Distal pancreatectomy is performed for a variety of indications ranging from trauma to malignant neoplasms. Several studies have demonstrated very low mortality rates after distal pancreatectomy, with some high-volume centers showing mortality rates of 0% to 4%.[1–3] Nevertheless, morbidity remains high, ranging from 10% to 47%.[4] Pancreatic leak or fistula is one of the most common complications following distal pancreatectomy.[1,3,5] Although several different definitions of pancreatic leak have been utilized amongst different studies, complicating comparisons across different series, pancreatic leak or fistula rates have been reported to range from 0% to 64% after this procedure.[4] In 2005, an international study group adopted a universal definition of pancreatic leak that should facilitate comparison across different studies.[6]

In addition to resection of isolated tumors of the pancreatic tail, distal pancreatectomy is performed for locally advanced primary and metastatic non-pancreatic neoplasms for potential cure as well as palliation.[7] Data

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suggest that distal pancreatectomy with en bloc resection of contiguous structures can be achieved with acceptable morbidity and mortality,[7] as can distal pancreatectomy for rare metastatic tumors to the pancreas.[8] Still, it is unclear whether these potentially more complex procedures share the favorable outcomes that have been demonstrated with straightforward distal pancreatectomy.

Given a broad experience with this procedure at our institution, we sought to evaluate our indications for and outcomes of distal pancreatectomy in the last decade. Our experience with distal pancreatectomy is somewhat unique due to the relatively high number of procedures performed for non-pancreatic tumors and a large number of pancreatectomies performed as part of a multivisceral resection for contiguous tumor. Given this experience, we wished to compare our experience with standard distal pancreatectomy to distal pancreatectomy associated with contiguous organ resection or metastatic non-pancreatic tumors.

Materials and Methods

Patients

We conducted a retrospective review of all patients who underwent distal pancreatectomy from January 1996 to August 2005 using the ICD-9 code (52.52) for distal pancreatectomy. Our database consisted of 171 consecutive patients who underwent distal pancreatectomy at Brigham and Women's Hospital. Approval was obtained from Brigham and Women's Hospital Institutional Review Board/Partners Human Research Committee. Demographic, clinical, operative, and pathologic details were collected. Pre-operative indications and post-operative complications were recorded.

Statistical Analysis

Pancreatic leak was broadly defined according to the post-operative pancreatic fistula international study group definition as any measurable volume of drain fluid on or after post-operative day 3 with an amylase content greater than three times the upper normal serum value.[6]

Statistical analysis was performed using Fisher's exact test where appropriate. A p value <0.05 was considered statistically significant.

Patients who underwent straightforward distal pancreatectomy with or without splenectomy (group 1) were compared to patients with more extensive or multivisceral resections (group 2). The second group included patients who underwent distal pancreatectomy due to contiguous involvement of the pancreas from other primary tumors as well as patients who underwent distal pancreatectomy for resection of metastases to the pancreas.

Results

Patient Demographics

From January 1996 to August 2005, over the 10-year period of our evaluation, 171 patients underwent distal pancreatectomy. The mean age of the patients at time of operation was 54±14 years (median age 55 years; range 17–83 years) old (Table 1).

Indications

The indications for distal pancreatectomy included contiguous or metastatic tumor in 52 patients (30%), cystic neoplasm in 39 patients (23%), pancreatic mass in 36 patients (21%), chronic pancreatitis in 13 patients (7.6%), neuroendocrine tumor in 11 patients (6.4%), and miscellaneous reasons (e.g., trauma, pseudocyst, pancreatic necrosis, etc.) in 20 patients (12%). Indications for distal pancreatectomy are presented in Table 2.

Operative Details

The median post-operative length of stay was 7 days. Mean post-operative length of stay was 11 days. Median post-operative length of stay was 6 days for group 1 and 9 days for group 2. Mean post-operative length of stay was 9 days for group 1 and 13 days for group 2.

Distal pancreatectomy +/− splenectomy was performed in 96 patients (56%), whereas 75 patients (44%) underwent larger resections that included distal pancreatectomy plus resection of additional organs or contiguous intraperitoneal or retroperitoneal tumors. More extensive resections were performed for both pancreatic and non-pancreatic primaries. These procedures included a diverse combination of multivisceral resections. The most common extensive resections included partial or total gastrectomy in 29 patients (39%), partial colectomy in 25 patients (33%), nephrectomy in 17 patients (23%), resection of retroperitoneal tumor in 16 patients (21%), and small bowel resection in 14 patients (19%). Table 3 details the extent of multivisceral resections.

Table 1 Demographics

Demographics	Values
Age	
Mean	54±14 years
Median	55 years
Range	17–83 years
Gender	
Female	97 (57%)
Male	74 (43%)

Table 2 Pre-operative Indications for Distal Pancreatectomy in 171 Patients

Indication	Number	%
Cystic neoplasm	39	23
Pancreatic mass	36	21
Chronic pancreatitis	13	7.6
Neuroendocrine tumor	11	6.4
Contiguous/metastatic tumor	52	30
Other	20	12

Although 12 procedures were attempted laparoscopically, only six patients underwent a laparoscopic distal pancreas resection (two strictly laparoscopic and four hand-assisted/lap-assisted). The pancreatic stump was stapled in 76 patients (45%), oversewn in 38 patients (22%), and both stapled and oversewn in 55 patients (33%). All patients except for two had either a Jackson–Pratt or a Blake drain placed.

Final Pathology

The final pathology of the resected specimens is found in Table 4. Most commonly, in 49 patients (29%), the pathology revealed a non-pancreatic tumor such as contiguous spread from adjacent structures or metastasis from other sites. Table 3 summarizes the pathologic findings. Other common pathologic findings included mucinous cystadenoma in 20 patients (12%), chronic pancreatitis in 19 patients (11%), pancreatic adenocarcinoma in 19 patients (11%), neuroendocrine tumors in 17 patients (9.9%), and serous cystadenoma in eight patients (4.7%). Nineteen patients (11%) were categorized as having miscellaneous pathology, which included several patients with normal pancreatic tissue identified. The non-pancreatic contiguous and metastatic primary tumors necessitating distal pancreatectomy included liposarcoma (14 patients), gastrointestinal stromal tumor (11), leiomyosarcoma (6), gastric adenocarcinoma (4), ovarian cancer (3), and a variety of other primary tumors. Table 5 summarizes these results.

Complications

One hundred eight patients (63%) had no post-operative complications. The overall post-operative complication rate was 37%; 63 patients had one or more complications. The most common complications were pancreatic duct leak in 39 patients (23%), intraabdominal abscess in 13 patients (7.6%), new-onset insulin-dependent diabetes mellitus (IDDM) in six (3.5%), and portal vein thrombosis in three patients (1.8%). Ten patients (6%) required reoperation; the indications were small bowel obstruction (two patients), wound closure status post-trauma operation (2), small bowel perforation (1), gastroesophageal junction leak status post-subtotal gastrectomy (1), colon perforation (1), small bowel ischemia (1), necrotic stoma (1), and hemorrhage (1). Table 6 summarizes post-operative complications.

There were five deaths (2.9%) either in-hospital or within 30 days of operation. The causes of death included trauma from abdominal gun shot wound (1), intraabdominal hemorrhage (1), sepsis (1), and respiratory failure (2).

Table 3 Multivisceral Resections with Distal Pancreatectomy (n=75): 136 Organs/Tumors Resected (Exclusive of Spleen)

Organ/tissue	*N*	Additional organs/tumors resected
Stomach	29	Colon (10), adrenal (7), retroperitoneal tumor (7), kidney (6), small intestine (4), partial diaphragm (3), esophagus (2)
Colon	25	Retroperitoneal tumor (15), stomach (10), kidney (10), small intestine (10), adrenal (9), partial diaphragm (4)
Kidney	17	Retroperitoneal tumor (12), adrenal (11), colon (10), stomach (6), small intestine (6), partial diaphragm (4), lung wedge (1)
Adrenal	16	Kidney (11), retroperitoneal tumor (11), colon (9), stomach (7), small intestine (5), partial diaphragm (4), lung wedge (1)
Retroperitoneal tumor	16	Colon (15), kidney (12), small intestine (12), adrenal (11), stomach (7), partial diaphragm (5), lung (1)
Small intestine	14	Retroperitoneal tumor (12), colon (10), kidney (6), adrenal (5), stomach (4), partial diaphragm (3), lung wedge (1)
Liver (1 left hepatectomy, 8 non-anatomic wedge)	9	Partial diaphragm (1), lung wedge (1)
Diaphragm (partial)	6	Retroperitoneal tumor (5), colon (4), kidney (4), adrenal (4), stomach (3), small intestine (3), liver wedge (1), lunge wedge (1)
Esophagus	2	Liver wedge (1)
Lunge (wedge)	2	Liver wedge (1), retroperitoneal tumor (1), partial diaphragm (1), small intestine (1), kidney (1), adrenal (1)

Table 4 Final Pathology in 171 Patients Undergoing Distal Pancreatectomy

Pathology	Total number (%)	Group 1	Group 2
Contiguous/metastatic tumor from another organ	49 (29)	2	47
Mucinous cystadenoma	20 (12)	17	3
Chronic pancreatitis	19 (11)	14	5
Pancreatic adenocarcinoma	19 (11)	13	6
Neuroendocrine tumor	17 (9.9)	13	4
Serous cystadenoma	8 (4.7)	6	2
Intraductal papillary mucinous neoplasm	5 (2.9)	5	0
Solid pseudopapillary tumor	5 (2.9)	4	1
Pancreatic necrosis	5 (2.9)	3	2
Acinar cell carcinoma	3 (1.8)	2	1
Mucinous cystadenocarcinoma	2 (1.2)	2	0
Miscellaneous	19 (11)	15	4

Group 1=distal pancreatectomy +/− splenectomy; group 2=multivisceral resection

Fisher's exact test revealed that, when compared to patients undergoing standard distal pancreatectomy (group 1), those with a more extensive resection (group 2) including multiple viscera and/or metastatic or contiguous tumor resection had no significant difference in overall complication rate (35% v. 39%, $p=0.75$), leak rate (25% v. 20%, $p=0.47$), new-onset IDDM (3% v. 4%, $p=1.0$), and mortality (2% v. 4%, $p=0.656$) (see Table 7).

The incidence of pancreatic duct leak in relation to technique of pancreatic stump closure was 18% after suture closure, 18% after staple closure, and 33% after combined staples and suture closure.

Table 5 Non-pancreatic Contiguous and Metastatic Tumors Resected With Distal Pancreas

Primary tumor	Patients (%)
Liposarcoma	14 (29)
GIST	11 (22)
Leiomyosarcoma	6 (12)
Gastric adenocarcinoma	4 (8)
Ovarian cancer	3 (6)
Endometrial adenocarcinoma	2 (4)
Adrenal cortical adenoma	1 (2)
Esophageal adenocarcinoma	1 (2)
Mantle cell lymphoma	1 (2)
Colon adenocarcinoma	1 (2)
Malignant melanoma	1 (2)
Meningeal hemangiopericytoma	1 (2)
Renal cell cancer	1 (2)
Desmoid/spindle cell neoplasm	1 (2)
Total	49 (100)

Table 6 Post-operative Complications in 171 Distal Pancreatectomies

Complication	Number	%
Leak	39	23
Intraabdominal abscess	13	7.6
IDDM (new onset)	6	3.5
Portal vein thrombosis	3	1.8
Re-bleed	1	0.6
Cardiac arrest	1	0.6
DVT	1	0.6
Pulmonary embolus	1	0.6
Abdominal compartment syndrome	1	0.6
Reoperation	10	5.8
Death	5	2.9
LOS		
Mean	11±11 days	
Median	7 days	

Discussion

Our series of 171 patients who underwent distal pancreatectomy describes a high-volume single institution's experience with this procedure. This series is unique in the high number of patients (30%) who underwent distal pancreatectomy as part of an en bloc resection of contiguous tumor or for metastatic disease. Though infrequently an indication for distal pancreatectomy in other series, contiguous or metastatic disease was surprisingly the most common surgical indication in this cohort. Of these, liposarcoma and gastrointestinal stromal tumor (GIST) were the most common primary tumors. Other series have documented the most common indication for surgery as solid pancreatic neoplasm,[5,9] mucinous cystic neoplasm,[10] and chronic pancreatitis.[4] The overall complication rate was 37%, with pancreatic leak the most common complication. Compared with standard distal pancreatectomy, a more extensive resection had no greater complication rate.

Favorable morbidity and mortality has been cited in limited small series of patients with metastatic disease to the pancreas and with multivisceral resections involving pancreatectomy. In one series involving eight patients with

Table 7 Complication Rates: Standard Distal Pancreatectomy v. Extensive Resection

Complication	Standard distal pancreatectomy	Extensive resection	*p* value
Complication rate	35%	39%	0.75
Leak rate	25%	20%	0.47
New-onset IDDM	3%	4%	1.0
Mortality	2%	4%	0.656

pancreatectomy for metastatic tumors to the pancreas, primary tumors included colon carcinoma, renal cell carcinoma, duodenal leiomyosarcoma, and malignant fibrous histiocytoma.[8] In this group, average survival was 23 months although precise data on complications are not available for comparative purposes with the current study. Similarly, Pingpank et al.[7] detailed their experience with pancreatic resection for locally advanced primary and metastatic non-pancreatic neoplasms and found that median survival was 56 and 46 months, respectively. They advocate an aggressive surgical approach for the management of advanced intraabdominal malignancies, frequently requiring the resection of additional abdominal viscera, while stressing the importance of a margin-negative resection. Yao et al.[11] reviewed the records of 55 patients who were treated for primary gastrointestinal sarcomas and found that adjacent organ resection including distal pancreatectomy was required in 15 patients (27%) and that this did not adversely effect survival. It is agreed that negative margins remain the most important determinant of survival. In a recent large series, Kleeff et al.[12] suggested that multivisceral resections were associated with increased morbidity, particularly pancreatic fistula. The explanation for this observation is speculative, and was suggested to possibly relate to ischemia at the pancreatic stump margin.

The current study demonstrates a perioperative mortality rate of 2.9% and an overall post-operative complication rate of 37%, which is comparable to other series. Mortality rates from distal pancreatectomy have variously been reported as 0%,[5] 0%,[10] 0.9%,[1] 3.2%,[9] and 4%.[3] Recently, Rodriguez et al.[10] published a series of 66 patients who underwent distal pancreatectomy; overall post-operative morbidity was 52%, and 33% had complications directly related to pancreatic leak. Lillemoe et al.[1] analyzed 235 patients who underwent distal pancreatectomy and reported an overall post-operative complication rate of 31%; the most common complication was new-onset insulin-dependent diabetes (8%), and pancreatic fistula occurred in 5%.

Pancreatic stump leak, the most common complication in this series, occurred in 23% of patients who underwent a distal pancreatectomy. Of note, a meta-analysis including two randomized clinical trials and eight observational studies reported pancreatic fistula rates after distal pancreatectomy ranging from 0% to 61%.[4] Comparison of pancreatic leak or fistula rates between different series is difficult due to the lack of uniformity in defining this complication. The current study utilizes an internationally accepted definition of pancreatic leak that is relatively broad, including any patient with amylase-rich drain fluid that was 3× above normal serum levels at our institution. Fahy et al.[3] define leak as persistent drain output longer than 7 days or drain fluid amylase greater than 5,000 IU/l. Lillemoe et al.[1] did not precisely define pancreatic fistula. Sheehan et al.[5] defined pancreatic fistula as amylase-rich fluid in the drain after patients began a general diet. Knaebel et al.[4] notes that available studies use different concentrations of amylase in the fistula fluid, fluid amounts, methods of detection, and time points for description; some even omitted a definition. Going forward, the international study group definition and grading system should help standardize comparisons.[6]

Several groups have tried to ascertain the optimal method of pancreatic stump closure in order to reduce the frequency of pancreatic duct leak/fistula. In the current study, we found the incidence of pancreatic duct leak in relation to technique of pancreatic stump closure to be 18% after suture closure, 18% after staple closure, and 33% after combined staples and suture closure. Fisher's exact test revealed no significance difference in leak rate based on closure technique. Given this finding, and also because this study was not designed to compare closure techniques, we cannot recommend the optimal closure method.

One group found that the incidence of pancreatic fistula formation was not related to the method of closure of the pancreatic remnant (sewn v. stapled v. sewn and stapled) nor to the underlying pathologic process.[5] However, another group found that, although the method of closure of the pancreatic parenchyma had no effect on pancreatic leak rate, patients who had identification and direct ligation of the pancreatic duct had a significantly lower incidence of leak when compared to those who did not undergo pancreatic duct ligation (9.6% v. 34%, respectively, $p=0.001$). In addition, they did not find a significant association between pancreatic leak and pancreatic (versus non-pancreatic) pathology or contiguous organ resection.[9] Likewise, Fahy et al.[3] did not find a significant association between leak rate and method of pancreatic stump closure, presence of malignancy, or concomitant splenectomy. Meta-analysis of six studies failed to show a significant difference in leak rate when comparing stapled versus hand-sewn closure.[4]

Conclusion

In conclusion, this series demonstrates a wide variety of indications for distal pancreatectomy, with a unique experience in pancreatectomy for contiguous or metastatic tumor. Morbidity and mortality are comparable to that previously reported, even for more extensive or multivisceral resections. Patients with locally invasive or

metastatic disease to the pancreas may safely undergo distal pancreatectomy in an attempt to offer a palliative or survival benefit.

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