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Postoperative pancreatic fistula after distal pancreatectomy for non-pancreas retroperitoneal tumor resection

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ABSTRACT

Introduction: Short-term outcomes after distal pancreatectomy (DP) for retroperitoneal (RP) tumors are unknown. We sought to identify rates of postoperative pancreatic fistula (POPF) and morbidity after en bloc DP with RP tumor resection.

Methods: A retrospective review of 43 patients who underwent DP with RP tumor resection (1/2011–12/2017) was performed.

Results: Seventeen patients had RP sarcoma, 12 renal cell carcinoma, 11 gastrointestinal stromal tumor, and 3 adrenocortical carcinoma. Grade III-IV complications occurred in 7 patients. Grade B POPF occurred in 14 patients, grade C POPF in none, and biochemical leak in 6. Of 22 patients who developed radiographically evident peri-pancreatic fluid collections, 7 required percutaneous drainage. The 90-day readmission rate was 33%.

Conclusions: DP with RP tumor resection is associated with high rates of clinically relevant POPF compared to historical results for DP for primary pancreatic tumors. Multi-center studies to identify targetable predictors and risk mitigation strategies for POPF in this rare high-risk population are needed.

Introduction

Distal pancreatectomy is associated with significant postoperative morbidity, with reported rates in the literature up to 64%.[1] The high incidence of postoperative pancreatic fistula (POPF) is the key driver of postoperative complications, which include infection, dehydration, malabsorption, hemorrhage, prolonged hospital stay and readmission.[1–3] For patients with retroperitoneal tumors who undergo multivisceral resection that include a distal pancreatectomy, major postoperative morbidities can also delay or prevent receipt of adjuvant therapies. Decreasing the incidence of postoperative complications following distal pancreatectomy will reduce healthcare costs and improve quality of life for these patients.

While some of the generally agreed upon risk factors for POPF include obesity and hypoalbuminemia,[4,5] a variety of single and multi-institutional studies have provided conflicting results on perioperative risk factors for POPF.[1–6] The method of parenchymal transection and duct closure has been an area of controversy for many years. Some studies have reported decreased POPF rates with suture ligation of the duct while others have found no significant difference in outcomes between stapling or suture ligation of the duct.[1,4,6] While the use of preoperative octreotide has not been demonstrated to decrease POPF rate,[5] in a randomized controlled trial of pasireotide vs. placebo, the POPF rate was 7% vs. 23% (RR 0.32; 95% CI 0.1–0.99).[7]

Additionally, most prior studies examining outcomes following distal pancreatectomy have focused on patients who had primary pancreas pathology. However, patients with non-pancreatic retroperitoneal tumors that involve the pancreas may also require distal pancreatectomy as part of a multivisceral resection. No study to date has specifically reported on the short-term postoperative outcomes for this cohort. Although patients with retroperitoneal tumors frequently undergo multivisceral resections, we

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hypothesize that in cases involving distal pancreatectomy, leak from the pancreas remnant is the major determinant of postoperative outcomes. Thus, it is important to assess the morbidity of distal pancreatectomy in this unique, albeit heterogeneous, group of patients, in order to better counsel patients in the preoperative setting and to identify unique risk factors and potential strategies to decrease risk of postoperative complications.

Within this context, the primary aim of this study was to describe the characteristics of this unique cohort of patients undergoing distal pancreatectomy at a single, high-volume, tertiary care cancer center, determine the incidence of POPF based on International Study Group for Pancreatic Fistulas (ISGPF) grade,[8] and evaluate for factors associated with increased risk of POPF.

Patients and methods

Study design

We performed a retrospective review of the medical records of all patients with retroperitoneal sarcoma (RPS), gastrointestinal stromal tumor (GIST), adrenocortical carcinoma (ACC), and renal cell carcinoma (RCC), who underwent distal pancreatectomy as part of a multivisceral resection at The University of Texas MD Anderson Cancer Center (MDACC) from January 2011 to December 2017. This study was approved by the Institutional Review Board (IRB) of the MDACC (Protocol PA17-0721).

Data source and study population

The study population included all patients who underwent a distal pancreatectomy from January 2011 to December 2017 at MDACC. Since 2011, these data has been entered into a prospectively maintained pancreatic surgery database.[9] Other patients whose billing codes were consistent with distal pancreatectomy were also screened. The electronic medical records of all distal pancreatectomy patients were reviewed. Of the records reviewed, only patients with the pathology diagnoses of RPS, GIST, ACC, or RCC were included in this study. Patients who received cytoreductive surgery with hyperthermic intraperitoneal chemotherapy were excluded. Operative notes were reviewed to ascertain whether the pancreatic duct was stapled or sutured. Other variables of interest were age at time of surgery, sex, receipt of preoperative or postoperative somatostatin analogue, POPF, peripancreatic fluid collection, 30-day postoperative complication, length of stay (LOS) and 90-day readmission.

Since 2011, we have used a prospective surveillance program to document adverse events (AEs). This system, which has been described previously in detail,[10] was used to detect and grade all perioperative AEs within 90 days of pancreatectomy. All postoperative AEs are reviewed and classified according to the Accordion grading system prospectively, but converted retrospectively in this study to the Clavien-Dindo system.[11] Pancreas-specific complications of delayed gastric emptying (DGE),[12] postpancreatectomy hemorrhage,[13] and POPF[8] were classified by the ISGPF system. Patients were not treated with our published risk-stratified pancreatectomy care pathways (RSPCP),[14] which was implemented in October 2016 on the pancreas surgery service but not on the other surgical services in our institution.[14]

Statistical analysis

The median and range were summarized for continuous variables. Incidence rates were calculated as a percentage. LOS was defined as the number of days between date of discharge and date of admission/surgery. The primary outcome of interest was the incidence of ISGPF grade B and C POPF. Secondary outcomes of interest were LOS, incidence of POPF stratified by technique of parenchymal transection, predictors of POPF, and major (Clavien-Dindo grade III-V) complications. Patients were grouped by pancreatic transection technique (stapled versus sutured), and groups were compared using Mann-Whitney test. All tests were two-sided with p-values <0.05 considered statistically significant. Univariate analyses to assess for factors associated with the following short-term outcomes were performed: POPF, need for percutaneous interventional radiology (IR) drain placement, readmission, major complications, wound infection and LOS. Due to the small sample size, all analyses were univariate. Data analysis was done using SPSS 23 (SPSS, Chicago, IL, USA).

Results

The final cohort included 43 patients. Table 1 summarizes the clinical characteristics of the patients, including age at the time of surgery, primary tumor histology, concomitant resection of additional organs, pancreatic transection technique and, if applicable, ISGPF POPF grade, and grade of Clavien-Dindo complication at 30-days. The median age was 60 years (range: 22–81 years) (Table 2). Patients who underwent stapled pancreatic transection were older than those who underwent suture technique (median 62 vs 55 years, $p = 0.049$). Of the 43 patients, 25 (58.7%) were male. Thirty-six patients (83.7%) had at least one concomitant organ resected in addition to the distal pancreas (Table 2). Seventeen patients (39.5%) underwent multivisceral resection with distal pancreatectomy for RPS, 12 (27.9%) for RCC, 11 (25.6%) for GIST and 3 (7.0%) for ACC. Only 2 patients had spleen preservation. Seventeen (39.5%) patients had suture ligation of the pancreatic transection edge while 26 (60.5%) patients underwent stapled transection. Somatostatin analogue was administered preoperatively in 2 (4.7%) patients, postoperatively in 8 (18.6%) patients, and both preoperatively and postoperatively in 1 (2.3%) patient.

There was a single postoperative death. This occurred in a patient with recurrent RCC who underwent distal pancreatectomy, splenectomy and left adrenalectomy. He developed postoperative bowel obstruction and subsequent multisystem organ failure without POPF or peri-pancreatic fluid collection. POPF (grade B) occurred in 14 (32.6%) patients, with biochemical leak detected in 6 (14.0%) patients (Table 2). There were no cases of grade C POPF. Among the patients who underwent stapled transection, 10 (38.4%) developed grade B POPF compared to 4 (23.5%) patients in the suture ligation group, ($p = 0.245$). The incidence of peri-pancreatic fluid collection was not significant between patients who underwent stapled parenchymal transection compared to patients in the suture ligation group (57.7% vs 41.2%, $p = 0.301$); however, all 7 patients who required percutaneous drain placement were in the stapled transection group (26.9% vs 0%, $p = 0.019$). Patients who underwent stapled pancreatic transection had lower incidence of wound infection (0% vs 17.6%, $p = 0.026$). Median LOS was 9 days (range 3–38 days, stapled, 8 days vs sutured, 12 days, $p = 0.245$) (Table 2). The longest LOS was 38 days, and occurred in a patient who had a gastric staple line leak that required re-operation. Another patient with no POPF but prolonged delayed gastric emptying (DGE) had a LOS of 28 days.

Fourteen (32.6%) patients were re-admitted after discharge. Three (21.4%) and 8 (57.1%) patients had a biochemical leak and grade B POPF, respectively, and 10 (71.4%) had peri-pancreatic fluid collections, of which 4 (40%) required percutaneous drainage. No factors were associated with increased risk of POPF or Clavien-Dindo grades III-V on univariate analysis (Tables 3 and 4 respectively). Preoperative somatostatin analogue was uncommonly used in the study period and was associated with an increased odds of

Table 1
Characteristics of cohort with non-pancreas primary retroperitoneal tumors who underwent distal pancreatectomy from 2011 to 2017.

Patient	Sex	Age (yrs)	Primary Tumor	Pancreatectomy	Pancreas Duct Closure	Other Resection	Postoperative-Pancreatic Fistula, grade[a]	30-day Complication, Clavien-Dindo Grade
1	F	59	RCC	DP + SP	Suture	Partial left ureterectomy, Left GV resection	–	–
2	F	56	Dendritic reticulum cell sarcoma	DP + SP	Staple	Left adrenalectomy	–	–
3	M	73	RCC	DP + SP	Suture	Left adrenalectomy	–	V
4	M	40	ACC	DP	Suture	Total gastrectomy, NAR of liver, wedge resection of jejunum	B	II
5	M	64	Gastric GIST	DP + SP	Suture	Partial gastrectomy	–	–
6	M	66	Leiomyosarcoma	DP + SP	Suture	PV resection with patch venoplasty	–	II
7	F	53	Gastric GIST	DP + SP	Suture	Esophagogastrectomy, partial left adrenalectomy	B	III
8	M	22	Ewing sarcoma	DP + SP	Staple	Left nephrectomy	B	II
9	F	29	ACC	DP + SP	Suture	Left nephrectomy, left adrenalectomy, NAR of liver	B	II
10	M	71	RCC	DP + SP	Staple	None	–	III
11	F	66	Liposarcoma	DP + SP	Staple	Partial gastrectomy, left nephrectomy, left adrenalectomy	–	II
12	M	69	RCC	DP + SP	Staple	Left nephrectomy, left adrenalectomy	–	III
13	F	67	Leiomyosarcoma	DP + SP	Suture	Left RV resection with primary anastomosis	–	II
14	M	48	ACC	DP + SP	Staple	Left nephrectomy, partial gastrectomy, left colectomy, left hemidiaphragm resection	–	I
15	F	76	RCC	DP + SP	Staple	Cholecystectomy	–	–
16	M	55	RCC	DP + SP	Suture	None	–	–
17	F	42	Liposarcoma	DP + SP	Staple	Transverse colectomy, partial left hemidiaphragm resection	–	–
18	F	42	RCC	DP + SP	Staple	Left nephrectomy, left adrenalectomy, sigmoid colectomy, left distal ureterectomy	–	I
19	M	62	Liposarcoma	DP + SP	Staple	Left nephroureterectomy, left orchiectomy, partial gastrectomy, left colectomy	–	III
20	M	71	Liposarcoma	DP + SP	Staple	Left nephrectomy	B	II
21	M	57	RCC	DP + SP	Staple	Left nephrectomy	–	I
22	F	28	Gastric GIST	DP + SP	Suture	Partial gastrectomy	–	–
23	M	63	RCC	DP + SP	Staple	Resection of left buttock metastasis	–	–
24	M	71	RCC	DP + SP	Suture	Cholecystectomy, bilateral components separation with mesh	B	II
25	M	36	Gastric GIST	DP + SP	Suture	Right hepatectomy, cholecystectomy	–	–
26	M	45	Gastric GIST	DP + SP	Suture	Partial gastrectomy, left colectomy, partial left hemidiaphragm resection, partial left hepatectomy	–	–
27	F	64	Leiomyosarcoma	DP + SP	Staple	RPM	–	–
28	F	60	Angiosarcoma	DP + SP	Suture	Left adrenalectomy, left nephrectomy	–	II
29	F	68	Jejunal GIST	DP + SP	Suture	Left colectomy, SBR	–	II
30	M	60	Gastric GIST	DP + SP	Staple	Partial gastrectomy, partial left hepatectomy, partial left hemidiaphragm resection	–	–
31	M	81	Gastric GIST	DP + SP	Staple	Partial gastrectomy	B	II
32	M	57	Liposarcoma	DP + SP	Staple	RPM, left colectomy, left nephrectomy, left adrenalectomy, partial left hemidiaphragm resection	B	I
33	F	62	Leiomyosarcoma	DP + SP	Staple	RPM, Left colectomy, left nephrectomy	B	I
34	F	26	Gastric GIST	DP + SP	Suture	Total gastrectomy, partial left hepatectomy	–	–
35	M	77	RCC	DP + SP	Staple	None	–	II
36	F	32	RCC	DP + SP	Suture	Partial (transverse) colectomy	–	II
37	F	69	Liposarcoma	DP + SP	Staple	Resection of intra-abdominal tumors	B	III
38	M	73	Gastric GIST	DP + SP	Staple	Partial distal gastrectomy	–	–
39	F	61	Leiomyosarcoma	DP + SP (Lap)	Staple	None	B	III
40	M	55	High grade pleomorphic spindle cell sarcoma	DP + SP	Staple	Small bowel resection, gastrostomy tube placement	B	III
41	M	73	Liposarcoma	DP + SP	Staple	RPM, left nephrectomy, left colectomy, partial left hemidiaphgram resection	B	III
42	M	45	Liposarcoma	DP + SP	Staple	RPM, left nephrectomy, resection of left hemidiaphragm	–	–
43	M	52	Gastric GIST	DP + SP	Staple	Partial gastrectomy	B	III

ACC: adrenocortical carcinoma; DP: distal pancreatectomy; GIST: gastrointestinal stromal tumor; GV: gonadal vein; NAR: non-anatomic resection; PV: portal vein resection; RCC: Renal cell carcinoma; RPM: Retroperitoneal mass; SBR: small bowel resection; SP: splenectomy.
[a] Defined per 2016 International Study Group in Pancreatic Surgery (ISGPS) definition and grading system.

postoperative fluid collection requiring percutaneous drain, OR 14.0 (95% CI; 1.0–184.2, p = 0.045, Table 5).

Discussion

Despite advances in surgical technique and perioperative care, the morbidity associated with distal pancreatectomy remains substantial. To our knowledge, this is the first study to specifically report on the short-term outcomes for patients who underwent distal pancreatectomy during multivisceral resection of non-pancreas retroperitoneal tumors. The results demonstrate that POPF is a key determinant of early postoperative complications and outcomes among patients undergoing multivisceral resection of non-pancreas retroperitoneal tumors with distal pancreatectomy.

Table 2
Clinicopathologic features of patients undergoing distal pancreatectomy during multi-visceral resection for non-pancreas primary retroperitoneal tumors (n = 43).

Variable	All patients (n=43)	Pancreatic Transection Technique		P value
		Stapled (n = 26)	Sutured (n = 17)	
	Number (%) or Median (range)	Number (%) or Median (range)	Number (%) or Median (range)	
Age, years	60 (22–81)	62 (22–81)	55 (26–73)	0.089
Gender				0.334
Female	18 (41.9)	9 (34.6)	9 (52.9)	
Male	25 (58.1)	17 (65.4)	8 (47.1)	
Primary tumor histology				0.055
Adrenocortical carcinoma	3 (7.0)	1 (3.8)	2 (11.8)	
Gastrointestinal stromal tumor	11 (25.6)	4 (15.4)	7 (41.2)	
Other retroperitoneal sarcoma	17 (39.5)	14 (53.8)	3 (17.7)	
Leiomyosarcoma	5 (11.6)	3 (11.5)	2 (11.8)	
Liposarcoma	8 (18.6)	8 (30.8)	0 (0)	
Sarcoma, other	4 (9.3)	3 (11.5)	1 (5.9)	
Renal cell carcinoma	12 (27.9)	7 (26.9)	5 (29.4)	
Type of distal pancreatectomy				0.999
Distal pancreatectomy and splenectomy	41 (95.3)	25 (96.2)	16 (94.1)	
Distal pancreatectomy, spleen preserving	2 (4.7)	1 (3.8)	1 (5.9)	
Pancreatic transection technique				–
Stapled	26 (60.5)	–	–	
Suture	17 (39.5)	–	–	
Additional organs resected en bloc				0.215
No additional organ resected	7 (16.3)	6 (23.1)	1 (5.9)	
Additional organ(s) resection	36 (83.7)	20 (76.9)	16 (94.1)	
1	18 (41.9)	9 (34.6)	9 (52.9)	
2	8 (18.6)	4 (15.4)	4 (23.5)	
3	5 (11.6)	3 (11.5)	2 (11.8)	
4	5 (11.6)	4 (15.4)	1 (5.9)	
Estimated Blood Loss, intraoperative	700 (30–12000)	662.5 (30–12000)	800 (250–2500)	0.667
EBL				0.685
<300	7 (16.3)	5 (19.2)	2 (11.8)	
≥300	36 (83.6)	21 (80.8)	15 (88.2)	
EBL				0.663
<500	16 (37.2)	9 (34.6)	7 (41.2)	
≥500	27 (62.8)	17 (65.4)	10 (58.8)	
EBL				0.850
<700	21 (48.8)	13 (50)	8 (47.1)	
≥700	22 (51.2)	13 (50)	9 (52.9)	
Received somatostatin or analogue				0.454
Preoperative only	2 (4.7)	2 (7.7)	0 (0)	
Postoperative only	8 (18.6)	6 (23.1)	2 (11.8)	
Both preoperative and postoperative	1 (2.3)	1 (3.8)	0 (0)	
Received preoperative somatostatin				0.266
Yes	3 (7.0)	3 (11.5)	0 ()	
No	40 (93.0)	23 (88.5)	17 (100)	
Received postoperative somatostatin				0.281
Yes	9 (20.9)	7 (26.9)	2 (11.8)	
No	34 (79.1)	19 (73.1)	15 (88.2)	
Length of stay, days	9 (3–38)	8 (3–38)	12 (5–28)	0.281
POPF, grade				0.520
None	23 (53.5)	12 (46.2)	11 (64.7)	
Biochemical leak	6 (14.0)	4 (15.4)	2 (11.8)	
B	14 (32.6)	10 (38.4)	4 (23.5)	
POPF, grade				0.343
No (None + biochemical leak)	29 (67.5)	16 (61.6)	13 (76.5)	
Yes (B, no grade C POPF)	14 (32.6)	10 (38.4)	4 (23.5)	
Postoperative fluid collection				0.358
No	21 (48.8)	11 (42.3)	10 (58.8)	
Yes	22 (51.2)	15 (57.7)	7 (41.2)	
Not requiring percutaneous drainage	15 (34.9)	8 (30.8)	7 (41.2)	
Requiring percutaneous drainage	7 (16.3)	7 (26.9)	0 (0)	
Postoperative fluid collection requiring percutaneous drainage				**0.031**
No	36 (83.7)	19 (63.1)	17 (100)	
Yes	7 (16.3)	7 (26.9)	0 (0)	
Wound infection				0.055
No	40 (93.0)	26 (100)	14 (82.4)	
Yes	3 (7.0)	0 (0)	3 (17.6)	
Postoperative complication at 30-days, Clavien-Dindo classification				**0.020**
None	12 (27.9)	8 (30.8)	7 (41.2)	
I	5 (11.6)	5 (11.6)	0 (0)	
II	12 (27.9)	5 (11.6)	8 (47.1)	
III	6 (14.0)	8 (30.8)	1 (5.9)	

(*continued on next page*)

Table 2 (*continued*)

Variable	All patients (n=43)	Pancreatic Transection Technique		P value
		Stapled (n = 26)	Sutured (n = 17)	
	Number (%) or Median (range)	Number (%) or Median (range)	Number (%) or Median (range)	
IV	0 (0)	0 (0)	0 (0)	
V	1 (2.3)	0 (0)	1 (5.9)	
Postoperative complication at 30-days, Clavien-Dindo classification				0.269
None, I, or II	33 (76.7)	15 (88.2)	18 (69.2)	
III, IV, or V	10 (23.3)	2 (11.8)	8 (30.8)	
Readmission				0.343
No	29 (67.4)	16 (61.5)	3 (17.6)	
Yes	14 (32.6)	10 (38.5)	14 (82.4)	

EBL: estimated blood loss.
POPF: postoperative pancreatic fistula.
*Defined per 2016 International Study Group in Pancreatic Surgery (ISGPS) definition and grading system.

Possibly because of the limited sample size, there was no statistically significant difference in the rate of POPF based on the technique of pancreas parenchymal transection, but our observations highlight this technical issue as an important clinical question that remains unresolved.

Previous single and multi-institutional studies of patients undergoing distal pancreatectomy have reported clinically significant (grade B) POPF rates (12–15%). In a prospective randomized multi-institutional trial of 344 patients undergoing distal pancreatectomy, Van Buren et al. reported a POPF rate of 15%.[2] A retrospective review of 2026 patients who underwent distal pancreatectomy in a multi-institutional, international collaborative investigation found the rate of clinically significant POPF to be 15.1% while a single institution retrospective review of 462 patients by Ferrone et al. also reported a clinically significant POPF rate of 14.9%.[4,5] We found the rate of clinically significant (grade B) POPF in our cohort to be 32.5%. Unlike other studies where the majority of the tumors were of primary pancreas origin,[3-5] all patients in this cohort underwent distal pancreatectomy for primary retroperitoneal non-pancreas tumors and were therefore likely to have normal, soft-textured glands more prone to leak. The POPF risk in these operations has likely little to do with the underlying pathology (e.g. sarcoma, RCC, ACC) and more to do with the quality of the normal pancreas. The increased odds of peripancreatic fluid collection in patients who received preoperative somatostatin analogues may be an indication that these patients were selected by the surgeon to be extremely high risk for pancreas leak which was not mitigated with pharmacologic prophylaxis in this limited sample size.

Multiple recent studies evaluating pancreatic transection technique have failed to find any significant difference in the rate of POPF between stapled and suture ligation of the duct.[4,6] While clinically significant (grade B) POPF occurred in 38.4% of patients who underwent a stapled transection, compared to 23.5% in those who underwent sutured pancreatic transection, this difference was not statistically significant (p = 0.245). We support continued investigation into this technically important issue. None of the

Table 3
Univariate analysis of factors associated with grade B/C POPF[a].

Univariate Analysis	OR	95% CI	p value
Age (ref <60)			
≥60	1.59	0.48–5.31	0.452
Gender (ref Male)			
Female	0.63	0.19–2.13	0.456
Histology (ref Adrenocortical carcinoma)			
Gastrointestinal stromal tumor	X		
Retroperitoneal sarcoma	X		
Renal cell carcinoma	X		
Type of distal pancreatectomy (ref spleen preserving)			
Distal pancreatectomy + splenectomy	X		
Preoperative somatostatin analogue (ref No)			
Yes	X		
Additional organ resection (ref No)			
Yes	3.13	0.53–18.29	0.206
Number of additional organs resected	1.45	0.86–2.44	0.164
Transection technique (ref Stapled)			
Sutured	0.51	0.15–1.77	0.292
EBL (ref < 300)			0.206
≥300	3.13	0.53–18.29	
EBL (ref < 500)			0.172
≥500	2.42	0.68–8.64	
EBL (ref < 700)			0.098
≥700	2.84	0.83–9.80	

EBL: estimated blood loss.
POPF: postoperative pancreatic fistula.
[a] Defined per 2016 International Study Group in Pancreatic Surgery (ISGPS) definition and grading system.

Table 4
Univariate analysis of factors associated with Clavien-Dindo grade III-V complication.

Univariate Analysis	OR	95% CI	p value
Age (ref <60)			
≥60	2.48	0.55–11.28	0.24
Gender (ref Male)			
Female	0.51	0.11–2.34	0.39
Histology (ref Adrenocortical carcinoma)			0.931
Gastrointestinal stromal tumor	X		
Retroperitoneal sarcoma	X		
Renal cell carcinoma	X		
Type of distal pancreatectomy (ref spleen preserving)			
Distal pancreatectomy + splenectomy	0.28	0.02–4.95	0.386
Preoperative somatostatin analogue (ref No)			
Yes	8.00	0.64–99.67	0.106
Additional organ resection (ref No)			
Yes	0.32	0.06–1.78	0.194
Number of additional organs resected	0.83	0.45–1.53	0.548
Transection technique (ref Stapled)			
Sutured	0.30	0.06–1.63	0.164
EBL (ref < 300)			0.717
≥300	0.71	0.12–4.40	
EBL (ref < 500)			0.835
≥500	0.86	0.20–3.66	
EBL (ref < 700)			0.933
≥700	0.94	0.23–3.88	

EBL: estimated blood loss.

variables assessed herein was associated with increased odds of a clinically significant POPF.

Our wound infection rate of 7% is similar to rates reported in previously published studies (4–6%).[2,6,15] In a retrospective review of 159 patients who had available postoperative CT or MRI scans after distal pancreatectomy, Tjaden et al. observed fluid collections in 43% of patients in the first few weeks following surgery although only 9% of patients required an intervention.[15] We report a peripancreatic fluid collection rate of 51.2% and a clinically significant POPF rate of 32.6%. Large-volume multivisceral resection may be contributory to the higher rate of postoperative fluid collection in this cohort.

Van Buren et al. observed a hospital readmission rate of 23% within 60 days of discharge.[2] The overall rate of readmission within 90 days of discharge in our cohort was 14 (32.6%), of which 8 (57.1%) had clinically significant POPF. Other reasons for readmission in our study cohort included myocardial infarction, acute urinary retention, dehydration and poor oral intake.

Our median LOS of 9 days falls within the range of 5–10.5 days in the literature from single and multi-institutional studies of patients who underwent distal pancreatectomy,[2–5,15] although the median LOS for these multivisceral operations is much longer than the median 5-day LOS we see with RSPCP patients with primary pancreatic tumors.[14] Clinically significant POPF accounted for 2/3 of patients with LOS >14 days in our cohort, while non-pancreas related complications including gastric leak and DGE accounted for LOS>14 days in the remaining 2 patients.

This study has important limitations related to its retrospective cohort design and the rarity of the combination procedure itself. The small sample size limits the power to detect significant statistical differences, should they exist. However, trends in observations (such as the possible difference in POPF between stapled and suture ligation of the pancreatic duct) can generate useful hypotheses for future multicenter studies. In addition, the single-institution design and highly selective nature of the cohort potentially limits the generalizability of our findings. However, despite these limitations, this is the largest cohort to date on this rare combination operation which is relevant to surgical oncologists worldwide.

Conclusion

This study highlights the clinically relevant short-term outcomes among patients who undergo distal pancreatectomy during multivisceral resection of non-pancreas retroperitoneal tumors. While the rate of clinically significant POPF in patients with non-pancreas tumors who undergo distal pancreatectomy as part of multivisceral resection appears to be higher than that for patients who undergo distal pancreatectomy for primary pancreatic lesions, downstream morbidity and mortality related to POPF could

Table 5
Univariate analysis of factors associated with postoperative fluid collection requiring percutaneous IR drain procedure.

Univariate Analysis		OR	95% CI	p value
Age (ref <60)				
≥60		2.50	0.43–14.61	0.309
Gender (ref Male)				
Female		0.50	0.09–2.93	0.442
Histology (ref Adrenocortical carcinoma)				0.453
Gastrointestinal stromal tumor		X		
Retroperitoneal sarcoma		X		
Renal cell carcinoma		X		
Type of distal pancreatectomy (ref spleen preserving)				
Distal pancreatectomy + splenectomy		0.71	0.01–3.13	0.234
Preoperative somatostatin analogue (ref No)				
Yes	13.99		1.06–184.16	**0.045**
Additional organ resection (ref No)				
Yes	0.40		0.06–2.68	0.347
Number of additional organs resected	0.97		0.50–1.90	0.937
Transection technique (ref Stapled)				
Sutured	X		X	X
EBL (ref < 300)				0.876
≥300	1.20		0.12–11.87	
EBL (ref < 500)				0.607
≥500	1.59		0.27–9.35	
EBL (ref < 700)				0.730
≥700	1.33		0.26–6.83	

EBL: estimated blood loss.
IR: interventional radiology.

potentially be minimized with RSPCP[14] tailored to multivisceral resections, standardized drain management,[16] standardized surgical technique for pancreatic transection, and/or pharmacologic prophylaxis.[17] Our findings on postoperative morbidity in this unique cohort will be informative to patients and clinicians during the consent process. Future studies should explore multi-institutional collaborations to increase sample size as well as examine the role of specific aforementioned clinical and technical interventions to mitigate the rate of POPF in this high-risk population.

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References

1. Knaebel HP, Diener MK, Wente MN, Büchler MW, Seiler CM. Systematic review and meta-analysis of technique for closure of the pancreatic remnant after distal pancreatectomy. *Br J Surg*. 2005;92(5):539–546.
2. Van Buren G, Bloomston M, Schmidt CR, et al. A prospective randomized multicenter trial of distal pancreatectomy with and without routine intraperitoneal drainage. *Ann Surg*. 2017;266(3):421–431.
3. Nathan H, Cameron JL, Goodwin CR, et al. Risk factors for pancreatic leak after distal pancreatectomy. *Ann Surg*. 2009;250(2):277–281.
4. Ferrone CR, Warshaw AL, Rattner DW, et al. Pancreatic fistula rates after 462 distal pancreatectomies: staplers do not decrease fistula rates. *J Gastrointest Surg*. 2008;12(10):1691–1697.
5. Ecker BL, McMillan MT, Allegrini V, et al. Risk factors and mitigation strategies for pancreatic fistula after distal pancreatectomy: analysis of 2026 resections from the international, multi-institutional distal pancreatectomy study group. *Ann Surg*. 2019;269(1):143–149.
6. Diener MK, Seiler CM, Rossion I, et al. Efficacy of stapler versus hand-sewn closure after distal pancreatectomy (DISPACT): a randomised, controlled multicentre trial. *Lancet*. 2011;377(9776):1514–1522.
7. Allen PJ, Gönen M, Brennan MF, et al. Pasireotide for postoperative pancreatic fistula. *N Engl J Med*. 2014;370(21):2014–2022.
8. Bassi C, Marchegiani G, Dervenis C, et al. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. *Surgery*. 2017;161(3):584–591.
9. Hwang RF, Wang H, Lara A, et al. Development of an integrated biospecimen bank and multidisciplinary clinical database for pancreatic cancer. *Ann Surg Oncol*. 2008;15(5):1356–1366.
10. Schwarz L, Bruno M, Parker NH, et al. Active surveillance for adverse events within 90 days: the standard for reporting surgical outcomes after pancreatectomy. *Ann Surg Oncol*. 2015;22(11):3522–3529.
11. Dindo D, Demartines N, Clavien P-A. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg*. 2004;240(2):205–213.
12. Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery*. 2007;142(5):761–768.
13. Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage (PPH): an international study group of pancreatic surgery (ISGPS) definition. *Surgery*. 2007;142(1):20–25.
14. Denbo JW, Bruno M, Dewhurst W, et al. Risk-stratified clinical pathways decrease the duration of hospitalization and costs of perioperative care after pancreatectomy. *Surgery*. 2018;164(3):424–431.
15. Tjaden C, Hinz U, Hassenpflug M, et al. Fluid collection after distal pancreatectomy: a frequent finding. *HPB*. 2016;18(1):35–40.
16. Seykora TF, Liu JB, Maggino L, Pitt HA, Vollmer CM. Drain management following distal pancreatectomy: characterization of contemporary practice and impact of early removal. *Ann Surg*. 2019. https://doi.org/10.1097/SLA.0000000000003205.
17. Denbo JW, Slack RS, Bruno M, et al. Selective perioperative administration of pasireotide is more cost-effective than routine administration for pancreatic fistula prophylaxis. *J Gastrointest Surg*. 2017;21(4):636–646.