

Blame it on the injury: Trauma is a risk factor for pancreatic fistula following distal pancreatectomy compared with elective resection

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BACKGROUND:	Postoperative pancreatic fistula (POPF) remains a significant source of morbidity following distal pancreatectomy (DP). There is a lack of information regarding the impact of trauma on POPF rates when compared with elective resection. We hypothesize that trauma will be a significant risk factor for the development of POPF following DP.
METHODS:	A retrospective, single-institution review of all patients undergoing DP from 1999 to 2017 was performed. Outcomes were compared between patients undergoing DP for traumatic injury to those undergoing elective resection. Univariate and multivariable analyses were performed using SAS (version 9.4).
RESULTS:	Of the 372 patients who underwent DP during the study period, 298 met inclusion criteria: 38 DPs for trauma (TDP), 260 elective DPs (EDP). Clinically significant grade B or C POPFs occurred in 17 (44.7%) of 38 TDPs compared with 41 (15.8%) of 260 EDPs ($p < 0.0001$). On multivariable analysis, traumatic injury was found to be independently predictive of developing a grade B or C POPF (odds ratio, 4.3; 95% confidence interval, 2.10–8.89). Age, sex, and wound infection were highly correlated with traumatic etiology and therefore were not retained in the multivariable model. When analyzing risk factors for each group (trauma vs. elective) separately, we found that TDP patients who developed POPFs had less sutured closure of their duct, higher infectious complications, and longer hospital stays, while EDP patients that suffered POPFs were more likely to be male, younger in age, and at a greater risk for infectious complications. Lastly, in a subgroup analysis involving only patients with drains left postoperatively, trauma was an independent predictor of any grade of fistula (A, B, or C) compared with elective DP (odds ratio, 8.6; 95% confidence interval, 3.09–24.15), suggesting that traumatic injury is risk factor for pancreatic stump closure disruption following DP.
CONCLUSION:	To our knowledge, this study represents the largest cohort of patients comparing pancreatic leak rates in traumatic versus elective DP, and demonstrates that traumatic injury is an independent risk factor for developing an ISGPF grade B or C pancreatic fistula following DP. (<i>J Trauma Acute Care Surg.</i> 2019;87: 1289–1300. Copyright © 2019 American Association for the Surgery of Trauma.)
LEVEL OF EVIDENCE:	Prognostic study, Therapeutic, level III.
KEY WORDS:	Distal pancreatectomy; trauma; fistula.

Pancreatic trauma is relatively rare, occurring in less than 5% of abdominal traumas. However, it is associated with significant morbidity, with rates ranging as high as 30% to 63% and mortality ranging from 15% to 33%.^{1–3} The proximity of the pancreas to adjacent organs and major vascular structures increases the likelihood of multiple injuries, severe complications, and death. Postoperative pancreatic fistula (POPF) remains the most common complication following surgical treatment of pancreatic trauma. Specifically, distal pancreatectomy (DP) for trauma is associated with a risk of fistula ranging from 14% to 60%.^{2,4–6} POPFs predispose patients to a wide variety of subsequent complications, ranging from intra-abdominal sepsis to postoperative hemorrhage and death. Therefore, understanding risk factors that influence the fistula rate in patients undergoing DP is important for improving outcomes.

Multiple factors have been associated with POPF rates following DP. Patient specific factors include body mass index (BMI), age and sex, nutritional status, and pancreatic parenchymal texture. Operative factors include closure method, laparoscopic versus open approach, simultaneous resection of adjacent organs, transfusion of blood products, and the presence of shock.^{1,4,7–9} The majority of available studies focus on patients undergoing elective resections, with fewer studies focusing on emergent operations for trauma. Our understanding of how pancreatic leak rates following DP for trauma compared with those performed electively remains unclear. In general,

there is concern that traumatic etiology may increase the risk of developing a fistula following DP; however, there is insufficient evidence to support this notion. In fact, few studies exist comparing fistula rates following elective DP (EDP) to those performed for trauma (TDP).

Understanding how trauma affects the risk of developing a POPF following DP can have a range of clinical implications, from counseling patients on the potential for POPF to operative decision making as well as increasing diagnostic awareness of potential fistulae in the postoperative period. We hypothesized that trauma patients would have a higher risk of POPF compared with elective patients following DP. We further sought to describe and compare POPF risk factors between trauma patients and elective patients undergoing DP.

METHODS

Study Design and Population

Approval from the University of Oklahoma Health Sciences Center Institutional Review Board with a waiver of informed consent was obtained. This was a retrospective review of all patients undergoing DP at the University of Oklahoma Health Sciences Center between January 1, 1999, and October 1, 2017. All mechanisms of injury and pancreatic pathology were included. Patients who died within 72 hours of initial pancreatectomy were excluded. Patients were divided into groups and compared based on pathology, with traumatic injury compared to elective resections. This study was designed in accordance with the STROBE guidelines.¹⁰

Patient History and Preoperative Data

All patient information was extracted from our electronic medical records systems. Pertinent patient history was gathered from clinical documents and dictated operative reports. Information included: age at diagnosis or injury, sex, BMI, American Society of Anesthesiology score, tobacco smoking status and history at the time of diagnosis or injury quantified by pack-years,

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current and previous alcohol use, major comorbid conditions, history of previous major or abdominal surgical procedures, and mechanism of injury. Laboratory data were recorded from the preoperative work-up period for all elective cases and upon initial presentation for all trauma patients. Preoperative or initial presentation albumin levels were used as surrogates for preoperative nutritional status. Base excess and lactic acid values were obtained for all trauma patients directly prior to or during definitive resection. Presence of shock was defined as a systolic blood pressure less than 90 mm Hg at the time of initial presentation. The Abbreviated Injury Scale was used to determine anatomic injury patterns for body regions including head, chest, abdomen, and extremity, and was used to calculate the trauma Injury Severity Score for all trauma patients.

Operative Data and Techniques

Operative data were obtained from dictated operative reports, nursing logs, anesthesia records, blood bank records, and billing reports. Information collected included pancreatic transection method, pancreatic stump closure method, use of adjunct hemostatic agents, additional procedures performed, use of surgical drains, estimated blood loss (EBL), and the volume of intravenous fluids and blood products given during the operation. Grade of pancreatic injury was assessed intraoperatively using the American Association for the Surgery of Trauma's (AAST) injury grading scale.¹¹ Distal pancreatectomies were performed both open and laparoscopically. All operative decision making was left to the discretion of the operating surgeon. Pancreatic duct size, gross description, and pancreatic texture were not regularly documented in dictated operative reports but were included when available and supplemented by data from computed tomography scans, endoscopic retrograde cholangiopancreatography and endoscopic ultrasound reports, and official pathology reports.

For trauma patients, the Advanced Trauma Life Support guidelines were used to guide initial resuscitation upon presentation. Patients with various combinations of hemodynamic instability, positive Focused Assessment with Sonography for Trauma examination, abdominal examination indicative of peritonitis, or computed tomography scan significant for intra-abdominal hemorrhage or organ injury were taken emergently to the operating room for further treatment. All operations for trauma were performed open. All operative decision making was left to the discretion of the operating surgeon.

Postoperative Data

Postoperative data were gathered from clinical documentation, laboratory values, imaging and pathology reports, blood bank records, and microbiology reports. Pancreatic fistula was defined according to the International Study Group for Pancreatic Fistula (ISGPF) updated criteria, which classifies previous grade A fistulas as "biochemical leaks" and maintains grade B and C fistulas as clinically relevant.¹² For our study, ISGPF grade A "biochemical leaks" were counted as no fistula present. The management of POPF varied based on the discretion of the operating surgeon, but in general consisted initially of utilizing intraoperatively placed drains, followed by either percutaneous drainage by interventional radiology or endoscopic retrograde

cholangiopancreatography with ductal stenting for persistent fistulas. Reoperation for POPF was reserved for hemodynamically unstable patients, those with overt peritonitis on physical examination, or those recalcitrant to drainage and conservative therapy. In general, changes to or restriction of diet accompanied fistula management only when symptoms of feeding intolerance were present. Where drainage by an interventional radiologist is reported, it was performed specifically for treatment of a fluid collection directly related to a POPF. Length of hospital stay (LOS) was defined as time from the date of the initial pancreatectomy or initial pancreatic injury until hospital discharge. Re-admission was defined as admission to the hospital within 30 days of initial discharge for reasons related to the primary operation or injury. Death data was gathered from the United States Social Security Death Index as well as death certificates from clinic records and inpatient death notes.

Statistical Analyses

Means and proportions were used to summarize the data by etiology. Unadjusted comparisons between the different etiologies (trauma vs. elective) for patients undergoing DP were performed using the independent Student's *t* test or Mann-Whitney Wilcoxon test for continuous variables, and for categorical variables, the χ^2 or Fisher's exact tests were used. A univariate logistic regression model was used to compare the odds of POPF in trauma patients to that of the elective group. Logistic regression was used to determine independent risk factors of POPF. For multivariable modeling, key predictors/confounders were included *a priori*, regardless of statistical significance. Variables that were significant on univariate analysis were also considered as potential confounders or effect modifiers. Covariates considered included age, sex, BMI, albumin, transection method, postoperative transfusion, and other procedure. Since the study was conducted over a 17-year period, time was also considered as a covariate in all the models. We evaluated correlation between coefficients of variables to assess for potential multicollinearity of variables. When variables were found to be highly correlated ($r > 0.5$), only one of the variables was included in a model. The small sample size for the trauma group limited our ability to perform stratified multivariable analysis to identify independent risk factors for POPF. Owing to the heterogeneity of the two patient groups, stratified descriptive analyses were performed to identify risk factors for POPF within each patient population. All analyses were performed using SAS software version 9.4 (SAS 9.4, SAS Institute, Cary, NC).

RESULTS

A total of 372 patients underwent DP at the University of Oklahoma Health Sciences Center during the period from 1999 to 2017. After excluding 67 patients for incomplete or missing data, improper diagnoses, and alternate procedures, 305 patients met initial inclusion criteria. This included 43 TDPs and 262 EDPs. Of the 262 EDPs, 65 had benign pathology and 197 had malignant masses. We excluded seven patients who died within 72 hours of their surgery: five TDPs and two EDPs. Our results are based on a final sample size of 298: 38 TDP and 260 EDP. Table 1 summarizes selected demographic and clinical characteristics by etiology. There were more men than women among the

TABLE 1. Demographic and Clinical Characteristics by DP Etiology

Variables	Trauma	Elective	<i>p</i>
	n = 38	n = 260	
Age: mean (±SD), y	29.8 (11.7)	56.7 (15.0)	<0.0001*
Sex, n (%)			
Male	27 (71.1)	102 (39.2)	0.0002
Female	11 (29.0)	158 (60.8)	
BMI: Mean (±SD), kg/m ²	26.0 (5.17)	29.6 (6.85)	0.0006
BMI: n (%), kg/m ²			
Low or normal	20 (55.6)	72 (30.4)	0.0039
Overweight	9 (25.0)	56 (23.6)	
Obese	7 (19.4)	109 (46.0)	
DM, n (%)	1 (2.8)	73 (28.1)	0.0010**
Albumin at admission: mean (±SD), g/dL	3.3 (0.9)	3.7 (0.7)	0.0178*
Transection (dichotomous), n (%)			0.0008
Stapler	23 (62.2)	86 (33.6)	
Nonstapler	14 (37.8)	170 (66.4)	
Pancreatic closure method, n (%)			<0.0001**
Suture	9 (23.7)	200 (77.2)	
Stapled	23 (60.5)	45 (17.4)	
None	5 (13.2)	14 (5.4)	
Pancreatojejunostomy	1 (2.6)	0 (0.0)	
Over sew	12 (31.6)	85 (32.8)	0.8791
Bio glue	12 (31.6)	117 (45.2)	0.1144
Other procedure, n (%)	30 (78.9)	72 (27.7)	<0.0001
Splenectomy, n (%)	30 (78.9)	214 (82.3)	0.6154
Drains left, n (%)	38 (100.0)	90 (35.3)	<0.0001
EBL: mean (±SD), mL	979.4 (1163.7)	697.5 (873.1)	0.1856*
Blood product transfusion, n (%)			
PRBCs	19 (50.0)	70 (26.9)	0.0037
Platelets	6 (15.8)	9 (3.5)	0.0061**
FFP	15 (39.5)	19 (7.3)	<0.0001**
Operative time: mean (±SD), min	156.1 (67.4)	150.2 (54.0)	0.5378*
Wound infection, n (%)	17 (44.7)	5 (1.9)	<0.0001**
Gross description, duct, n (%)			0.0008
Dilated	0 (0.0)	54 (20.8)	
Not dilated	38 (100)	186 (71.5)	
Small	0 (0.0)	20 (7.7)	
Pancreas texture, n (%)			<0.0001
Soft	36 (94.7)	147 (56.5)	
Fibrotic/firm	2 (5.3)	50 (19.2)	
Not mentioned	0 (0.0)	63 (24.2)	
Duct size, mean (±SD)		3.5 (1.96)	
Laparoscopy vs open, n (%)			0.7415**
Open	38 (100)	248 (95.4)	
Lap	0 (0.0)	9 (3.5)	
Converted	0 (0.0)	3 (1.2)	

* *p* Value for Student's *t* test.** *p* Value for Fisher's exact test.

PRBCs, packed red blood cells; lap, laparoscopic; converted, laparoscopic converted to open; other procedures, surgical repair, resection, or procedure other than DP and splenectomy performed during admission for the primary operation.

TDP population (71% vs. 29%), while there was a slight female predominance in our EDP patients (39% vs. 61%) [$p = 0.002$]. The median age of our trauma population was significantly younger than our elective population (29.8 years vs. 56.7 years,

$p < 0.0001$). While patients older than 65 years made up roughly a third (33.1%) of EDPs, there were no TDPs performed in this age group. Other significant differences ($p < 0.05$) between the two patient groups included TDP patients having lower average

BMI and lower incidence of preoperatively diagnosed diabetes mellitus (DM).

The majority of the EDPs were performed open, with only 9 (3.5%) performed laparoscopically and 3 (1.5%) converted from laparoscopic to open. Of note, a total of 16 different attending surgeons performed all TDPs, while four surgeons performed EDPs. There was a significant difference in pancreatic stump closure methods between groups, with 62% of TDPs closed with staplers, while 77% of EDPs were closed with sutures ($p < 0.0001$). There was no difference in the rate of splenectomy between groups (TDP, 78.9% vs. EDP, 82.3%). However, more TDPs had additional procedures other than splenectomy performed (79% vs. 28%, $p < 0.0001$). Patients undergoing TDPs all had drains left postoperatively, while in contrast only 90 (35.3%) EDPs had drains placed ($p < 0.0001$). As expected, there was a higher mean EBL in TDPs compared with EDPs; however, this did not reach statistical significance. This correlated with significantly more units of blood products transfused intraoperatively for TDPs. As expected, there was also a notable difference in parenchymal texture between the two groups, with trauma patients having softer gland texture.

Table 2 summarizes unadjusted patient outcomes by etiology. There were more overall complications and infectious complications in patients undergoing TDP compared with EDP. Importantly, clinically relevant ISGPF grade B and C

POPFs occurred in 17 (44.7%) of 38 TDPs compared with 41 (15.8%) of 260 EDPs ($p < 0.0001$). When comparing the association between etiology and fistula rate, the odds of developing a POPF in TDP patients were four times the odds of a POPF developing in the EDP group (odds ratio [OR], 4.3; 95% confidence interval, 2.1–8.9). Among patients with clinically significant fistulas, there was a higher rate of percutaneous postoperative pancreas related fluid collection drainage by interventional radiology in TDP patients; however, this trend did not reach statistical significance (76.5% vs. 53.7%, $p = 0.1060$). Hospital LOS was significantly longer for TDP patients, with a median stay of 16.5 days versus 6 days in EDP patients ($p < 0.0001$). Significantly more TDP patients were discharged to a rehabilitation facility compared with EDPs (13.2% vs. 0.8%), whereas over 95% of EDPs were discharged to home compared with 71% of TDPs ($p < 0.0001$). There were no significant differences between the two patient groups with regard to readmission, re-operation, 30-day or 90-day mortality.

We then analyzed different variables to assess their association with clinically relevant B and C fistulas. On univariate analysis, traumatic etiology, younger age, male sex, wound infection, and postoperative transfusion of blood products were all associated with an increased risk of developing clinically relevant POPF (Table 3). Importantly, stapled closure, BMI, preoperative albumin level, procedures performed other than splenectomy, and soft pancreatic texture did not have significant association with fistula development. Three multivariable analyses models were considered, one using the full sample size and two subgroup analyses determined *a priori* based on clinical relevance (Table 4). For all three models, in addition to the primary exposure variable of interest (trauma vs. elective), other variables including age, sex, BMI, albumin, transection method, wound infection, postoperative transfusion, and other procedure were initially considered for multivariable modeling. Age, sex, and wound infection were highly correlated with trauma etiology, and as such could not be retained in the multivariable models. Table 4 summarizes results from the multivariable analyses. On multivariable logistic regression analysis using the full sample size, trauma was found to be independently predictive of developing a grade B or C POPF compared with EDP (OR, 4.3; 95% CI, 2.10–8.89) and compared with benign EDP (OR, 2.70; 95% CI, 1.14–6.39). Body mass index, albumin, transection method, postoperative transfusion, texture, and other procedure did not independently predict POPFs ($p > 0.05$).

In a subgroup analysis, we analyzed all EDPs with drains placed prophylactically in the surgical bed and compared them to TDPs, all of which received prophylactic drain placement. To assess the rate of pancreatic stump closure breakdown in these populations, we analyzed the rate of any grade pancreatic fistula, including biochemical leaks, or grade A fistulas, between the two groups. On multivariable analysis, trauma was an independent risk factor for developing a biochemical leak compared with EDP with prophylactic postoperative drainage (OR, 6.5; 95% CI, 2.15–19.86; Table 4). In addition, trauma was independently associated with the development of any ISGPF grade POPF (OR, 8.6; 95% CI, 3.09–24.15) when all patients with intraoperatively placed drains were considered.

TABLE 2. Postoperative Outcomes by DP Etiology

Variables	Trauma n = 38	Elective n = 260	p
Overall complications, n (%)	36 (94.7)	66 (25.4)	<0.0001*
Infectious complications any, n (%)	24 (63.2)	41 (15.8)	<0.0001
Noninfectious complications any, n (%)	12 (31.6)	27 (10.4)	0.0011*
VTE n (%)	5 (13.2)	6 (2.3)	0.0011*
Respiratory failure n (%)	9 (23.7)	11 (4.2)	0.0002*
**Interventional radiology, n (%)	13 (76.5)	22 (53.7)	0.1060
Reoperation, n (%)	2 (5.3)	7 (2.7)	0.3218*
Postoperative transfusion, n (%)	16 (42.1)	35 (13.6)	<0.0001
Readmission, n (%)	9 (23.7)	76 (29.5)	0.4627
Hospital LOS, median (IQR)	16.5 (24.0)	6.0 (3.0)	<0.0001†
Disposition, n (%)			<0.0001*
Home	27 (71.1)	248 (95.4)	
Facility	6 (15.8)	6 (2.3)	
Other	5 (13.2)	6 (2.3)	
30-d Mortality, n (%)	0 (0)	3 (1.2)	1.0000*
90-d Mortality, n (%)	0 (0)	5 (1.9)	1.0000*
Pancreatic fistula grade, n (%)			
A	16 (42.1)	28 (10.8)	<0.0001*
B	15 (39.5)	38 (14.6)	
C	2 (5.3)	3 (1.2)	
None	5 (13.2)	191 (73.5)	

*p Value for Fisher's Exact test.

**Out of the patients with B and C fistulas.

†p Value for Wilcoxon two-sample test.

PE, pulmonary embolism; VTE, venous thromboembolism; AKI, acute kidney injury; UTI, urinary tract infection; PNA, pneumonia; Cdiff, *Clostridium difficile* colitis; ARDS, acute respiratory distress syndrome; HLOS, hospital length of stay; Facility, skilled nursing facility, long-term acute care hospital, physical rehabilitation center; Other, department of corrections medical examiner; left against medical advice.

TABLE 3. Univariate Analysis of the Association Between Selected Demographic and Clinical Characteristics With POPF

Effects	OR (95% CI)	P
Trauma vs. benign	2.70 (1.14–6.39)	0.0239
Age, y	0.97 (0.95–0.997)	0.0313
Sex		
Female	Reference	
Male	3.30 (1.34–8.13)	0.0095
BMI, kg/m ²	0.94 (0.87–1.01)	0.0724
Albumin, g/dL	0.77 (0.45–1.33)	0.3505
Wound infection	22.0 (5.95, 81.31)	<0.0001
Transection		
Nonstapler	Reference	
Stapler	1.10 (0.48, 2.55)	0.8167
No postoperative transfusion	Reference	
Postop transfusion	2.95 (1.14, 7.61)	0.0252
Other procedure		
No	Reference	
Yes	1.68 (0.72, 3.92)	0.2277
Texture		
Fibrotic/firm	Reference	
Soft	1.39 (0.48, 3.99)	0.5442

Other procedures, surgical repair, resection, or procedure other than DP and splenectomy performed during admission for the primary operation.

Within each patient population, we compared demographic and clinical variables to identify risk factors for POPF. Table 5 summarizes unadjusted comparisons between patients with grades B and C POPFs to those with no POPF or grade A in trauma patients. The pancreatic duct was unable to be found and/or closure technique was not documented in 5 (29.4%) patients with POPF compared with none (0%) in those without fistula, and patients without fistulas had more sutured duct closure than those who developed fistulas (33% vs. 11.8%, $p = 0.0213$). As expected, TDPs that developed fistulas had a significantly higher wound infection rate than those without POPFs (64.7% vs. 28.6%, $p = 0.0259$). There was also a higher incidence of infectious complications (88.2% vs. 42.9%, $p = 0.0039$) and a longer median hospital LOS (29 days vs. 10 days, $p = 0.0109$) in patients that developed POPFs. Table 6 summarizes unadjusted comparisons in the elective patient group based on the presence of a clinically significant POPF. In the EDP group, POPF were more likely to be in younger, predominantly male patients and were associated with a higher incidence of wound infection. While there was only a trend toward higher EBL in EDP patients who developed POPF, they were more likely ($p < 0.05$) to be transfused platelets and fresh frozen plasma (FFP). In terms of other outcomes in the elective patient group, patients with POPF were significantly more likely to have a higher incidence of overall complications, infectious and noninfectious complications, as well as a longer hospital LOS.

DISCUSSION

The purpose of this study was to compare POPF rates in patients undergoing TDP to those undergoing EDP and determine the impact that traumatic injury has on pancreatic leak rates

following DP. In addition, we performed a stratified descriptive analysis of each population separately (trauma and elective) to further establish the risk factors for POPF in each separate patient population. After controlling for various other risk factors, we determined that traumatic etiology is an independent risk factor for the development of clinically significant POPFs following DP compared with elective resections. Importantly, we found no evidence that this difference in leak rates was attributable to differences in pancreatic parenchymal texture, pancreatic remnant closure method, preoperative nutritional status, BMI, or higher numbers of simultaneous additional procedures performed. When analyzing risk factors in TDPs and EDPs separately, we found that TDP patients who developed POPFs had less sutured closure of their pancreatic duct, higher incidence of infectious complications, and longer hospital LOS. In EDP patients, we found male sex, younger age, and a higher incidence of infectious complications were associated with an increased rate of POPF development. In addition, EDP patients, who developed clinically significant fistulas trended toward higher EBL, were more likely to receive platelets and FFP, had an increased incidence of overall complications, and a longer hospital LOS compared with those without POPF. Lastly, when analyzing only patients with intraoperative drains placed, trauma remained a significant risk factor for the development of any postoperative pancreatic leak, including clinically significant grade B and C POPFs.

Previous studies have identified several different risk factors for the development of pancreatic fistulae following DP, including higher BMI, male sex, younger age, DM, extended lymphadenectomy, soft parenchymal texture, concomitant splenectomy, larger pancreatic remnant, and increased operating time.^{13–18} There is still debate about which pancreatic closure method is superior for reducing POPFs. Makni et al.¹⁹ demonstrated sutured closure was associated with fewer fistulae. Similarly, Kleef et al. showed stapled closure was an independent risk factor for development of POPF compared with sutured closure.¹⁷ However, several studies have found stapled closure to decrease POPF,^{4,18,20,21} while others have found equivocal results.^{13–16,22–24} Only two randomized trials are included in these studies, one finding stapled closure superior²⁰ and one finding no difference between methods.²³ In our study population, significantly more patients undergoing elective resection had sutured closure compared with those resected for trauma;

TABLE 4. Multivariable Analyses of Risk Factors for POPF

Models	n	OR (95% CI)	AUC (95% CI)
*Trauma vs Elective	298	4.3 (2.10–8.89)	0.60 (0.54–0.66)
**Trauma vs. Benign	103	2.70 (1.14–6.39)	0.62 (0.52–0.72)
†Trauma vs Elective (Only Drains)	128	8.6 (3.09–24.15)	0.68 (0.62–0.75)
‡Trauma vs Elective (Only Drains)	97	6.5 (2.15–19.86)	0.65 (0.57–0.73)

* Trauma vs. benign; trauma vs. elective (benign + malignant) with drains and outcome of any fistula grade (A, B or C).

** Trauma vs elective (benign + malignant).

† All models initially included age, sex, BMI, albumin, transection method, postoperative transfusion, and other procedure; high correlation was observed for etiology and age, therefore age was dropped from all reduced models. Correlation coefficient for age and etiology ($r = -0.52439$); age and sex ($r = 0.21422$).

‡ Trauma vs. elective (benign + malignant) with drains and outcome of fistula grade A.

TABLE 5. Trauma Patients: Demographic, Clinical Characteristics and Outcomes by Presence of POPF

Variables	Pancreatic Fistula None (A or None)	Pancreatic Fistula Present (B or C)	<i>P</i>
	<i>n</i> = 21	<i>n</i> = 17	
Age: mean ($\pm$ SD), y	31.5 (11.5)	27.8 (12.4)	0.7609*
Sex, n (%)			
Male	14 (66.7)	13 (76.5)	0.7210**
Female	7 (33.3)	4 (23.5)	
BMI: mean ($\pm$ SD), kg/m ²	27.3 (6.2)	24.6 (3.3)	0.1203*
MOI, n (%)			
Blunt	12 (57.1)	11 (64.7)	0.6353
Penetrating	9 (42.9)	6 (35.3)	
Shock (SBP < 90 mm Hg), n (%)	2 (9.5)	3 (17.7)	0.6396**
Wound Infection, n (%)	6 (28.6)	11 (64.7)	0.0259
Pancreatic injury grade, n (%)			
2	6 (28.6)	2 (11.8)	0.4834**
3	14 (66.7)	13 (76.5)	
4	1 (4.8)	2 (11.8)	
Hollow viscus injury, n (%)	8 (38.1)	7 (46.7)	0.6071
ISS, mean ($\pm$ SD)	25.1 (13.2)	27.2 (17.4)	0.6775*
ISS > 16, n (%)	16 (76.2)	12 (70.6)	0.7268**
Severe injury by body region (AIS $\geq$ 3), n (%)			
AIS all	18 (85.7)	16 (94.1)	0.6131**
Head	1 (4.8)	2 (11.8)	0.5768**
Thorax	11 (52.4)	8 (47.1)	0.7442
Abdomen	16 (76.2)	15 (88.2)	0.4267**
Extremities	2 (9.5)	2 (11.8)	1.0000**
External	1 (4.8)	0 (0.0)	1.0000**
Albumin at admission: mean ($\pm$ SD), g/dL	3.3 (0.75)	3.3 (1.05)*	0.8564
Base excess: mean ($\pm$ SD), mmol/L	-9.5 (6.6)	-6.3 (6.3)	0.1707*
Lactic acid: mean ($\pm$ SD), mmol/L	3.6 (1.8)	3.5 (2.8)	0.9475*
Transection (dichotomous), n (%)			
Stapler	13 (65.0)	10 (58.8)	0.6995
Nonstapler	7 (35.0)	7 (41.2)	
Pancreatic closure method, n (%)			
Suture	7 (33.3)	2 (11.8)	0.0213**
Stapled	13 (61.9)	10 (58.8)	
None	0 (0.0)	5 (29.4)	
Pancreatojejunostomy	1 (4.8)	0 (0.0)	
Bio glue	6 (28.6)	6 (35.3)	0.6576
Over sew	7 (33.3)	5 (29.4)	0.7960
Other procedure, n (%)	17 (81.0)	13 (76.5)	1.0000**
Splenectomy, n (%)	15 (71.4)	15 (88.2)	0.2575**
EBL: mean ($\pm$ SD), mL	1068.4 (1185.5)	866.7 (1166.6)	0.6232*
Blood product transfusion, n (%)			
PRBCs	9 (42.9)	10 (58.8)	0.3277
Platelets	3 (14.3)	3 (17.7)	1.0000**
FFP	9 (42.9)	6 (35.3)	0.6353
Operative time: mean ($\pm$ SD), min	162.7 (54.4)	148.0 (81.6)	0.5106*
Outcomes			
Overall complications, n (%)	19 (90.5)	17 (100.0)	0.4922**
Infectious complications any, n (%)	9 (42.9)	15 (88.2)	0.0039
Noninfectious complications any, n (%)	4 (19.1)	8 (47.1)	0.0647
VTE n (%)	2 (9.5)	3 (17.7)	0.6396**
Respiratory failure n (%)	3 (14.3)	6 (35.3)	0.2493**

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TABLE 5. (Continued)

Variables	Pancreatic Fistula None (A or None)	Pancreatic Fistula Present (B or C)	<i>p</i>
	<i>n</i> = 21	<i>n</i> = 17	
Reoperation, <i>n</i> (%)	0 (0.0)	2 (11.8)	0.1935**
Postoperative transfusion, <i>n</i> (%)	6 (28.6)	10 (58.8)	0.0604
Readmission, <i>n</i> (%)	2 (9.5)	7 (41.2)	0.0514**
Median hospital LOS: (IQR), d	10 (10.0)	29 (31.0)	0.0109†
Disposition, <i>n</i> (%)			
Home	15 (71.4)	12 (70.6)	0.4035**
Facility	2 (9.5)	4 (23.5)	
Other	4 (19.1)	1 (5.9)	

p* Value for Student's *t* test.*p* Value for Fisher's exact test.†*p* Value for Wilcoxon two-sample test.

MOI, mechanism of injury; SBP, systolic blood pressure; ISS, Injury Severity Score; AIS, Abbreviated Injury Scale; HLOS, hospital length of stay.

however, closure method was not found to predict the development of POPF.

Pancreatic duct size and soft parenchymal texture are known risk factors for POPF following pancreaticoduodenectomy,²⁵ yet studies have mixed findings regarding the effect of these variables following DP.^{15,16,25} To control for these potential risk factors, we performed an analysis comparing TDP to benign etiology EDP, assuming that gland texture and duct size would be more similar when excluding malignant disease from EDPs. On multivariable analysis, traumatic etiology was still shown to be a risk factor for POPF. These findings strengthen the notion that gland texture and duct size are not prominent risk factors for POPF following DP while further highlighting the significance of trauma as a risk factor for developing a fistula.

It is worthwhile to note that TDPs were performed by 16 different surgeons while the vast majority of EDP were performed by only four surgeons. Studies have shown that variability of surgeon training and experience, even at the same high-volume institution, can affect outcomes following pancreatic resection, including POPF rate.^{26,27} However, the effect of surgeon training and experience for pancreatic resections in the setting of trauma has not been extensively studied. Nevertheless, available data suggest that outcomes following hepatopancreaticobiliary trauma specifically are not significantly different between general surgeons and fellowship trained trauma surgeons.²⁸ Future studies are needed that more thoroughly evaluate how training and experience affect outcomes in pancreatic trauma requiring resection.

Wound infection rate was significantly higher in TDP at 44.7% compared with EDP with 1.9%. When analyzing each population individually, wound infection was significantly associated with the development of POPF in each population. The high incidence of infectious complications is well documented with both pancreatic injury and elective pancreatic surgery, typically ranging from 12% to 18%.^{3,29,30} While POPF has been cited as risk factor for surgical site and organ space infections,³¹ less is understood about the relationship between wound infections and POPFs. In our study, wound infection was found to be associated with POPF on univariate analysis, yet, similar to age and sex, was significantly correlated with traumatic etiology

and therefore not retained in the multivariable model. It is reasonable to infer that hollow viscus injuries may predispose patients to infectious complications. However, our data, as well as those of several other studies, do not support the notion that hollow viscus injuries or resultant multi-visceral resections increase the risk for developing a POPF.^{13–18} Likely, the etiology of high wound infection rates in trauma patients is multifactorial.

Several studies have examined risk factors for the development of a pancreatic leak following surgery for trauma. Bradley et al.³² found that injury to the main pancreatic duct was predictive of pancreatic fistula, and Kao et al.³³ found that AAST Organ Specific Injury score for the pancreas was associated with pancreas specific postoperative complications. Similar to EDPs, the debate over stapled versus sutured pancreatic remnant closure for TDPs is unsettled. While fewer studies are available, the existing evidence shows no significant difference in POPF rate between techniques.^{2,6,22,24} Yet, there is a trend favoring stapler use for TDPs, given that they are relatively easy to use, quick, and provide secure closure with equal or improved POPF rates compared with sutured closure.^{5,34} Our data reflect this trend in the trauma population, favoring stapled closure over sutured closure. Interestingly, however, our data did show that fewer TDPs with sutured closure developed POPFs, while there was no significant difference in fistula development in those with stapled closure.

There were several patients who underwent damage-control surgery (DCS), undergoing definitive distal pancreatic resection after initial operative intervention to control hemorrhage and clinically stabilize the patient. Hwang et al.³⁵ demonstrated that a base deficit ≤ -5.8 mm/L, as a surrogate for hypovolemia or hemorrhagic shock, in patients with pancreatic trauma was an independent predictor of morbidity. Therefore, minimizing hemodynamic instability at the time of resection may potentially decrease the rate of POPF development. Additionally, studies have shown that delayed resection does not increase the fistula rate following TDP.^{2,36} Our study corroborated these findings, demonstrating no significant difference in mean days delayed for surgery between patients who developed fistulas and those who did not (0.71 days vs. 0.86 days, respectively, *p* = 0.7867). Furthermore, undergoing

TABLE 6. Elective patients: Demographic, Clinical Characteristics and Outcomes by Presence of POPF

Variables	Pancreatic Fistula None (A or None)	Pancreatic Fistula Present (B or C)	<i>p</i>
	n = 219	n = 41	
Age: mean ($\pm$ SD), y	57.9 (14.7)	50.1 (14.9)	0.0020*
Sex, n (%)			
Male	81 (37.0)	21 (51.2)	0.0867
Female	138 (63.0)	20 (48.8)	
BMI: mean ($\pm$ SD), kg/m ²	29.5 (7.0)	30.0 (5.9)	0.6688*
BMI: n (%), kg/m ²			
Low or normal	63 (32.1)	9 (22.0)	0.3847
Overweight	44 (22.4)	12 (29.3)	
Obese	89 (45.4)	20 (48.8)	
DM, n (%)	58 (26.5)	15 (36.6)	0.1865
Albumin at admission: mean ($\pm$ SD), g/dL	3.7 (0.7)	3.6 (0.7)	0.4939*
Transection (dichotomous), n (%)			
Stapler	73 (34.0)	13 (31.7)	0.7802
Nonstapler	142 (66.0)	28 (68.3)	
Pancreatic closure method, n (%)			
Suture	167 (76.6)	33 (80.5)	0.8594
Stapled	39 (17.9)	6 (14.6)	
None	12 (5.5)	2 (4.9)	
Over sew	71 (32.6)	14 (34.1)	0.8435
Bio glue	96 (44.0)	21 (51.2)	0.3965
Other procedure, n (%)	61 (27.9)	11 (26.8)	0.8930
Splenectomy, n (%)	179 (81.7)	35 (85.4)	0.5761
Drains left, n (%)	76 (35.3)	14 (35.0)	0.9662
EBL: mean ($\pm$ SD), mL	626.6 (688.8)	1109.8 (1520.2)	0.1091*
Blood product transfusion, n (%)			
PRBCs	55 (25.1)	15 (36.6)	0.1286
Platelets	5 (2.3)	4 (9.8)	0.0372**
FFP	12 (5.5)	7 (17.1)	0.0170**
Operative time: mean ($\pm$ SD), min	149.1 (54.1)	155.7 (53.8)	0.4738*
Wound infection, n (%)	1 (0.5)	4 (9.8)	0.0024**
Gross description, duct, n (%)			
Dilated	45 (20.5)	9 (22.0)	0.8295
Not dilated	158 (72.1)	28 (68.3)	
Small	16 (7.3)	4 (9.8)	
Pancreas texture, n (%)			
Soft	127 (58.0)	20 (48.8)	0.3716
Fibrotic/firm	39 (17.8)	11 (26.8)	
Not mentioned	53 (24.2)	10 (24.4)	
Duct size, mean ($\pm$ SD)	3.5 (2.4)	4.5 (3.4)	0.2021*
Laparoscopy vs. open, n (%)			
Open	208 (95.0)	40 (97.6)	1.0000**
Lap	8 (3.7)	1 (2.4)	
Converted	3 (1.4)	0 (0.0)	
Outcomes			
Overall complications, n (%)	40 (18.3)	26 (63.4)	<0.0001
Infectious complications: any, n (%)	25 (11.4)	16 (39.0)	<0.0001
Noninfectious complications: any, n (%)	18 (8.2)	9 (22.0)	0.0209**
VTE, n (%)	1 (0.5)	2 (4.9)	0.0657**
Respiratory failure n (%)	7 (3.2)	4 (9.8)	0.0766**
Reoperation, n (%)	0 (0.0)	7 (17.1)	<0.0001**
Postoperative transfusion, n (%)	27 (12.4)	8 (19.5)	0.2254

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TABLE 6. (Continued)

Variables	Pancreatic Fistula None (A or None)	Pancreatic Fistula Present (B or C)	<i>p</i>
	<i>n</i> = 219	<i>n</i> = 41	
Readmission, <i>n</i> (%)	41 (18.8)	35 (87.5)	<0.0001
Hospital LOS, median (IQR)	6 (2.0)	7 (5.0)	0.0007†
Disposition, <i>n</i> (%)			
Home	210 (95.9)	38 (92.7)	0.4264**
Facility	5 (2.3)	1 (2.4)	
Other	4 (1.8)	2 (4.9)	
30-d Mortality, <i>n</i> (%)	3 (1.4)	0 (0.0)	1.0000**
90-d Mortality, <i>n</i> (%)	3 (1.4)	2 (4.9)	0.1801**

* *p* Value for Student's *t* test.** *p* Value for Fisher's exact test.

† Out of the patients with B and C Fistulas.

Facility: skilled nursing facility, long-term acute care hospital, or physical rehabilitation center; Other: left against medical advice, medical examiner.

DCS was not found to be a risk factor for developing a grade B or C fistula for patients undergoing TDP. In fact, when all trauma patients undergoing DCS (*n* = 10, 26.3%) were excluded, comparing only those with TDP performed at initial operation to EDP, traumatic etiology remained an independent risk factor for developing POPF (OR, 4.63; 95% CI, 2.05–10.45). Taken together, these data suggest that DCS remains an important technique when treating patients with pancreatic injury.

The POPF rates vary throughout the literature; however, these discrepancies have been mitigated by standardizing the definition of a POPF using ISGPF standards.¹² For EDP, after acceptance of ISGPF guidelines, fistula rates range from 5% to 40%.³⁷ POPF rates in the trauma literature trend higher, ranging from 14% to 60% following TDP.^{2,4,6} However, few studies have compared fistula rates in EDPs to TDPs to account for the impact that traumatic etiology has on POPF rates. In a study from 2002, Fahy et al.⁴ compared 15 traumatic with 36 elective DPs and found a significantly higher fistula rate among the trauma population, 60% versus 11%. To our knowledge, our study represents the largest known cohort comparing fistula rates following DPs for trauma to those performed electively. As pancreatic trauma is rare and TDPs are performed infrequently, it seems reasonable to adopt techniques and compare outcomes to EDPs to improve outcomes. However, understanding how traumatic injury affects outcomes is important and may have significant implications for postoperative care.

An ongoing debate among pancreatic surgeons is whether or not to leave a postoperative drain. Several studies involving electively resected patients suggest that prophylactic drainage after DP is unnecessary and, in fact, may increase complications.^{38,39} In our study, we performed a subgroup analysis of all EDPs who received prophylactic drain placement and all TDPs that also received drains and compared all grades of POPF, including “grade A” biochemical leaks, between the two groups. On multivariable analysis, we found that TDPs had over an eightfold increased risk of developing any fistula postoperatively compared with EDPs, and over a sixfold increase risk of developing a biochemical leak. Grade A

fistulas may be clinically silent but still represent a pancreatic ductal disruption, which can only be detected if drains are present and may potentially lead to more clinically relevant complications if drains are not in place to evacuate the high amylase fluid. Our results from examination of only grade A fistulas in patients that all had intraoperative drains placed suggests that traumatic etiology is an independent risk factor for stump closure disruption following DP, which may provide a potential explanation for the higher prevalence of POPFs noted in TDPs in this study. Furthermore, while routine drain placement following EDP may arguably be unnecessary, the same conclusions should not be applied to patients undergoing TDP.

Peripancreatic drainage without resection has been used to treat pancreatic injuries in certain clinical scenarios, particularly in low grade injuries (AAST grade I and II). Within our trauma cohort, 8 (21%) patients had grade II injuries, and of those 2 (25%) were initially treated with drainage alone, resulting in persistent pancreatic leaks with progressive lifestyle limiting symptoms alleviated only by definitive resection. Previous studies show similar outcomes in pancreatic injuries treated with resection versus nonoperative management in pediatric and select adult patients.^{40–42} However, nonoperative management often fails in high grade injuries (AAST grades III and IV) as well as some low-grade injuries, requiring subsequent interventions and prolonged hospital stays.⁴³ Current guidelines recommend nonoperative management of AAST grade I and II injuries and operative intervention for high-grade injuries.⁴⁴ Our study was not designed to determine the rate of failure of nonoperative management, but confirms that grade II injuries can indeed fail conservative management.

Our study possesses several limitations. The retrospective nature of data collection inherently limits the scope and quantity of available data, particularly with regards to intraoperative variables such as pancreatic texture and duct size. However, postoperative complications were well documented, especially those requiring subsequent diagnostic work-up, intervention, consultation, or extended hospital stay. While our study represents, to our knowledge, the largest known cohort of patients comparing

TDP to EDPs, due to the low incidence and high mortality associated with pancreatic trauma, our study is still limited by the sample size of our trauma population. More specifically, this limitation precluded us from including variables with multicollinearity in our final multivariable model, namely: age, male sex, and wound infection. Furthermore, the limited sample size of our trauma population prevented us from performing any further multivariable analysis. Lastly, the unequal age distributions among our patient populations limit the applicability of our study. However, most studies involving TDPs have similar age distributions.^{1,2} The younger age of TDP patients is expected and a factor for which it is not easy to control.

CONCLUSION

Pancreatic trauma is rare but associated with high mortality. Operations to treat pancreatic trauma, such as DP, are still associated with high postoperative morbidity, the most common of which is POPF. The purpose of this study was to compare POPF rates following TDP to EDP and to assess how different clinical variables affect fistula rate. On multivariable analysis, we found that pancreatic trauma is a prominent risk factor for clinically significant ISGPF grade B and C POPF following DP. In addition, when analyzing TDPs and EDPs separately, we found that male sex, younger age, and higher rates of infectious complications were all associated with an increased rate of POPFs following EDP, verifying findings from the literature. The TDP patients who developed POPF were less likely to have sutured closure of their pancreatic duct, higher rates of infectious complications, and longer LOS. Lastly, by analyzing a subgroup of patients that were all treated with intraoperative drains, we demonstrated that trauma is an independent risk factor for pancreatic stump disruption following DP. Finally, while we cannot conclude from our analysis that leaving prophylactic drains following TDP clearly improves outcomes, based on the higher rates of pancreatic stump disruption in the trauma population, we feel it imprudent to extrapolate the EDP study data on drain placement to the trauma population. Further studies are needed to determine if intraperitoneal drainage following TDP is associated with a lower rate of grade B and C POPFs.

AUTHORSHIP

N.S.R. was the primary author of the article, was primarily involved in gathering data and creating the database used for the study, and presented the work at the 77th annual AAST meeting. K.T.M. and J.S.L. both oversaw the entire project as co-P.I.s, including data acquisition, statistical analysis, and editing of the abstract, poster, and final article. J.S.L. developed the initial concept for the project. T.G. and Z.S. helped with gathering data, project design, statistical analysis, and authoring of the abstract, poster, and article. A.L., C.B.S., C.S.B., and A.J. were involved in data acquisition and authoring/editing the abstract, poster, and article. B.H.E., P.K.M., and B.C.A. contributed to the project design, offered key clinical input and co-authored/edited the abstract and article.

DISCLOSURE

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