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ORIGINAL ARTICLE

Do Drains Contribute to Pancreatic Fistulae? Analysis of over 5000 Pancreatectomy Patients

R. El Khoury[1,2] · C. Kabir[2] · V.K. Maker[1,2] · M Banulescu[2] · M. Wasserman[2] · A.V. Maker[1,2]

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Abstract

Introduction Conflicting evidence exists from randomized controlled trials supporting both increased complications/fistulae and improved outcomes with drain placement after pancreatectomy. The objective was to determine drain practice patterns in the USA, and to identify if drain placement was associated with fistula formation.

Methods Demographic, perioperative, and patient outcome data were captured from the most recent annual NSQIP pancreatic demonstration project database, including components of the fistula risk score. Significant variables in univariate analysis were entered into adjusted logistic regression models.

Results Of 5013 pancreatectomy patients, 4343 (87%) underwent drain placement and 18% of patients experienced a pancreatic fistula. When controlled for other factors, drain placement was associated with ducts < 3 mm, soft glands, and blood transfusion within 72 h of surgery. Age, obesity, neoadjuvant radiation, preoperative INR level, and malignant histology lost significance in the adjusted model. Drained patients experienced higher readmission rates (17 vs. 14%; $p < 0.05$) and increased (20 vs. 8%; $p < 0.01$) pancreatic fistulae. Fistula was associated with obesity, no neoadjuvant chemotherapy, drain placement, < 3 mm duct diameter, soft gland, and longer operative times. Drain placement remained independently associated with fistula after both distal pancreatectomy (OR = 2.84 (1.70, 4.75); $p < 0.01$) and pancreatoduodenectomy (OR = 2.29 (1.28, 4.11); $p < 0.01$).

Conclusions Despite randomized controlled clinical trial data supporting no drain placement, drains are currently placed in the vast majority (87%) of pancreatectomy patients from > 100 institutions in the USA, particularly those with soft glands, small ducts, and perioperative blood transfusions. When these factors are controlled for, drain placement remains independently associated with fistulae after both distal and proximal pancreatectomy.

Keywords Pancreatectomy · Drain · Fistula · Predictors · Risks

Introduction

Post-operative pancreatic fistula[1] (POPF) is a known complication of pancreatic resection with an incidence of 3–45%.[2] It is associated with increased post-operative morbidity including hemorrhage, retroperitoneal vessel erosion, intra-abdominal sepsis, and increased hospital stay and cost. To mitigate these downstream complications and enable the early recognition and control of pancreatic leak, prophylactic drains are often placed intraoperatively. However, drain placement comes with its own set of drawbacks including retrograde infection, pain, discomfort, and foreign body reaction. While routine drain placement has been discouraged after elective hepatic resection[3] and cholecystectomy,[4] controversy[5] persists after pancreatic surgery regarding their routine placement,[6] type of drain,[7] and timing of removal.[8,9]

Since 1992,[10] randomized controlled trials designed to evaluate routine drain elimination have shown contradictory findings. The Memorial Sloan-Kettering Cancer Center group[11] demonstrated a significant increase in the incidence of fistula in patients receiving drains, while a similar trial by Van Buren et al[12] was closed prematurely due to higher mortality in the no drain group. In the recent PANDRA randomized controlled trial,[13] patients with drains experienced

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✉ A.V. Maker
amaker@uic.edu

1 Department of Surgery, Division of Surgical Oncology, University of Illinois at Chicago, 835 S. Wolcott St. MC790, Chicago, IL, USA

2 Departments of Surgery and Research, Creticos Cancer Center and the Advocate Health Research Institute, Chicago, IL, USA

increased clinically relevant fistulae and fistula-associated complications. Furthermore, while pancreatic fistula risk factors have been defined,[14] questions remain on the optimal clinical setting for selective drain use. With increased availability and expertise in interventional radiology[15] and endoscopy[16] to assist in the management of pancreatic fistula drainage when necessary, there is a need to reassess potential risks of intraoperative drain placement.[17]

In this study, we analyzed the most recent data available from a large pancreas surgery-specific national database. Primary outcomes were determination of the rate of drain placement, the incidence of pancreatic fistula, and assessment of the relationship between drain placement and fistula. Secondary outcomes included identification of risk factors for postoperative fistula, and identification of predictors of intraoperative drain placement.

Methods

Study Population

The American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) is a national quality improvement program that prospectively gathers patient and outcomes data to assess the quality of surgical care and hospital performance.[18] After Institutional Review Board determination of non-human subject research, the most recent year of complete pathologic data from January 1st to December 31st, 2014, at the time of analysis was queried. Pancreatic resections were identified by the following current procedural terminology (CPT) codes: 48140, 48145, and 48146 for distal pancreatectomy; 48150 and 48152-4 for Whipple-type procedure; and 48155, 48160, 48999, and 49329 for other types of pancreatic resection. The ACS-NSQIP targeted pancreatectomy dataset was linked to the participant user file database and queried for primary and secondary outcome variables. This unique dataset was only made available starting with the queried year with several pancreatic surgery-specific variables from over 100 participating US institutions, including drain placement, post-operative fistula, and the use of postoperative percutaneous drainage. Preoperative demographics and intraoperative findings and outcomes were compared between patients with and without drain placement.

Pancreatic Fistula Definition

The definition of pancreatic fistula was based on the International Study Group on Pancreatic Fistula definitions as best as could be extrapolated from, and within the limitations of, the variables abstracted within the NSQIP pancreatic demonstration project. Based on the NSQIP Variables and Definitions, fistula was assigned to patients with a "yes" value in the post-operative pancreatic fistula category in the following cases: clinical diagnosis of fistula by the attending surgeon associated with drain placement continued longer than 7 days, spontaneous wound drainage, postoperative percutaneous drainage, or reoperation. Patients with persistent drainage defined as a drain output of amylase-rich fluid after postoperative day 3 were also included in the postoperative pancreatic fistula group. As clinical diagnosis with continued drain presence was included in the NSQIP abstraction category with percutaneous drainage and reoperation, there was likely some overlap of patients that also qualified with the category abstracted as experiencing amylase-rich fluid draining after day 3, e.g., "biochemical leak." Therefore, in order to identify clinically relevant postoperative pancreatic fistula, a subgroup analysis was performed excluding postoperative pancreatic fistula diagnoses based only on drain maintenance longer than 7 days from this group. Grade C pancreatic fistulae as defined by the International Study Group for Pancreatic Fistulae (ISGPF)[1] were extrapolated based on the presence of organ space surgical site infection, sepsis, septic shock, reoperation, organ failure, or death.

Statistical Analysis

Values are shown as mean ± standard deviation and percentage. Chi-square and independent Student's *t* test were used to test for non-random associations for categorical and continuous variables. Preoperative and intraoperative variables selected based on components of the fistula risk score[19] were tested in the analysis of risk factors affecting drain placement and pancreatic fistula occurrence. Odds ratios with 95% confidence intervals from univariate and multivariate analyses are reported. A p value < 0.05 was used for significance and entry criteria for the adjusted model. Analyses were completed using SPSS 22.0 (IBM, Armonk, NY) and SAS 9.4 (SAS Institute Inc., Carry, NC).

Results

Population Characteristics, Fistula Incidence, and Mortality

Of 5025 pancreatic resections, 12 cases were excluded due to lack of information on pancreatic drain placement. Of the 5013 patients included, 4343 (87%) received intraoperative drain placement. Patient demographics are presented in Table 1. Forty-nine percent were male with a mean age of 62 years old. Patients who received drains were older ($p < 0.05$), with a higher BMI (27.8 ± 6.3 vs. 27.0 ± 7.0; $p < 0.01$) and presented more often with obstructive jaundice preoperatively (30 vs. 27%; $p < 0.01$).

Table 1 Demographic characteristics, perioperative data, and pathology assessment

Variable	Drain $n = 4343$ (87%)	No drain $n = 670$ (13%)
Demographic characteristics		
Male, no. (%)	2140 (49)	317 (47)
Age*, year ± SD	63 ± 13	61 ± 14
BMI†, kg/m^2 ± SD	27.8 ± 6.3	27.0 ± 7.0
Diabetes, no. (%)	1091 (25)	175 (26)
COPD, no. (%)	183 (4)	28 (4)
CHF within 30 days, no. (%)	13 (0.3)	5 (0.7)
Currently requiring or on hemodialysis within 2 weeks, no. (%)	16 (0.4)	5 (0.7)
Steroid or immunosuppressant use for chronic condition, no. (%)	143 (3)	16 (2)
> 10% weight loss in last 6 months, no. (%)	624 (14)	95 (14)
Preoperative obstructive jaundice†, no. (%)	1323 (30)	178 (27)
Preoperative biliary stent placement, no. (%)	1440 (33)	209 (31)
Neoadjuvant chemotherapy, no. (%)	554 (13)	71 (11)
Neoadjuvant radiation, no. (%)	263 (6)	27 (4)
Neoadjuvant therapy, no. (%)	571 (13)	73 (11)
Preoperative laboratory values		
Creatinine, mg/dL ± SD	0.9 ± 0.5	0.9 ± 0.8
Total bilirubin, mg/dL ± SD	1.3 ± 2.2	1.3 ± 2.3
Albumin, g/dL ± SD	3.8 ± 0.6	3.8 ± 0.6
Leukocytes, × 10^9/L ± SD	7.4 ± 2.8	7.3 ± 2.6
INR, ± SD	1.1 ± 0.2	1.0 ± 0.1
Perioperative data		
Wound class†		
Clean, no. (%)	173 (4)	52 (8)
Clean-contaminated, no. (%)	3636 (83)	535 (80)
Contaminated, no. (%)	413 (10)	62 (9)
Dirty-infected, no. (%)	121 (3)	21 (3)
ASA classification†		
ASA I, no. (%)	30 (0.7)	1 (0.1)
ASA II, no. (%)	1150 (26)	146 (22)
ASA III, no. (%)	2922 (67)	447 (67)
ASA IV, no. (%)	236 (5)	74 (11)
ASA V, no. (%)	1 (0.02)	2 (0.3)
Operative approach		
Open, no. (%)	3360 (77)	534 (80)
Laparoscopic and minimally invasive, no. (%)	983 (23)	136 (20)
Pancreatic resection*		
Distal pancreatectomy, no. (%)	1408 (32)	230 (34)
Whipple-type procedure, no. (%)	2716 (63)	391 (58)
Other: total or subtotal pancreatectomy, unlisted pancreatic resections, no. (%)	219 (5)	49 (7)
Pancreatic duct size		
< 3 mm, no. (%)	855 (35)	115 (33)
> 3 mm, no. (%)	1579 (65)	238 (67)
Pancreatic gland texture*		
Soft, no. (%)	1317 (51)	176 (45)
Intermediate, no. (%)	217 (8)	48 (12)
Hard, no. (%)	1054 (41)	170 (43)
Pancreatic reconstruction†		

Table 1 (continued)

Variable	Drain $n = 4343$ (87%)	No drain $n = 670$ (13%)
Pancreaticojejunal duct-to-mucosa, no. (%)	2291 (53)	290 (43)
Pancreaticojejunal invagination, no. (%)	315 (7)	50 (7)
Pancreaticogastrostomy, no. (%)	90 (3)	8 (1)
Transfusions within 72 h*, no. (%)	852 (20)	104 (16)
Operative time, min ± SD	329 ± 140	322 ± 143
Pathology assessment		
Malignant histology*, no. (%)	3088 (71)	446 (67)

* $p < 0.05$
† $p < 0.01$

One thousand six hundred thirty-eight distal pancreatectomies and 3107 pancreatoduodenectomies were included. Pancreatobiliary reconstructions after Whipple-type procedures were most often a duct-to-mucosa pancreaticojejunostomy (77%) followed by pancreaticojejunal invagination (14%), and pancreaticogastrostomy (2%). Of note, 18% of distal pancreatectomies underwent pancreatoenterostomy.

Patients with drains (Table 2) had a significantly higher incidence of pancreatic fistula (20 vs. 8%; $p < 0.01$) and readmission (17 vs. 14%; $p < 0.05$) compared to patients without drains. There was no difference in grade C POPF rates ($p = 0.69$), delayed gastric emptying, percutaneous drainage, reoperation rates, or length of stay between groups. Seventy-two deaths were recorded, 53 (1.2%) in the drain group and 12 (2.8%) in the no drain group ($p = 0.0026$).

Drain Placement

Of patients with drains for which the location of drain placement was available, 131 were placed at the biliary anastomosis, 695 by the pancreatic anastomosis, 1833 drained both the pancreatic and biliary anastomoses, and 1074 drained a remnant pancreatic stump after resection. Factors associated with intraoperative drain placement are reported in Table 3. Unadjusted analysis confirmed that drains were more likely to be placed in older and heavier patients, and with a history of neoadjuvant radiation therapy for malignant pancreatic processes. Other risk factors associated with drain placement on univariate analysis included a main pancreatic duct size < 3 mm, a soft gland texture, elevated INR, higher transfusion requirements, and lower ASA classification. Independent factors that remained significant on multivariate analysis were small duct size, lower ASA score, soft gland texture, and blood transfusion. Drains were removed after a mean of 8 postoperative days ± 6 days.

Pancreatic Fistula

Risk factors for pancreatic fistula are reported in Table 4. On multivariate analysis, pancreatic fistula was independently associated with obesity, drain placement (OR = 2.22 (1.37–3.59); $p < 0.01$), soft gland (OR = 1.64 (1.01–2.69);

Table 2 Perioperative outcomes and complications

Variable	Drain $n = 4343$ (87%)	No drain $n = 670$ (13%)
Pancreatic fistula		
Overall†, no. (%)	841 (20)	53 (8)
Grade C ISGPF fistula, no. (%)	227 (5)	13 (2)
Delayed gastric emptying, no. (%)	516 (12)	63 (9)
Percutaneous drain placement, no. (%)	515 (12)	69 (10)
Reoperation, no. (%)	217 (5)	44 (7)
Length of stay, min ± SD	10.4 ± 9.6	9.9 ± 10.1
Readmission*, no. (%)	749 (17)	94 (14)
Mortality†, no. (%)	53 (1)	19 (3)

* $p < 0.05$
† $p < 0.01$

Table 3 Unadjusted and adjusted logistic regression models relating pre- and intraoperative variables to drain placement

	Unadjusted		Adjusted	
Variable	OR (95% CI)	*p*	OR (95% CI)	*p*
Male	1.08 (0.92–1.27)	0.34		
Age	1.008 (1.002–1.015)	*< 0.01*		
Obese	1.22 (1.02–1.48)	*< 0.05*	1.10 (0.80–1.51)	0.54
Underweight	0.92 (0.56–1.49)	0.72	1.27 (0.53–3.04)	0.59
Diabetes	0.95 (0.79–1.14)	0.58		
COPD	1.01 (0.67–1.51)	0.97		
Currently requiring or on hemodialysis within 2 weeks	0.49 (0.18–1.35)	0.17		
Steroid or immunosuppressant use for chronic condition	1.39 (0.82–2.35)	0.22		
> 10% weight loss in last 6 months	1.02 (0.80–1.28)	0.89		
Preoperative obstructive jaundice	1.20 (0.99–1.44)	0.058		
Preoperative biliary stent placement	1.14 (0.95–1.36)	0.15		
Neoadjuvant chemotherapy	1.23 (0.95–1.60)	0.12		
Neoadjuvant radiation	1.54 (1.03–2.30)	*< 0.05*	0.92 (0.50–1.67)	0.77
Creatinine	0.94 (0.82–1.07)	0.34		
Total bilirubin	0.997 (0.959–1.037)	0.89		
Albumin	1.14 (0.99–1.31)	0.062		
Leukocytes	1.02 (0.98–1.05)	0.34		
INR	2.07 (1.06–4.07)	*< 0.05*	2.57 (0.83–8.00)	0.10
Contaminated and dirty-infected vs. clean and clean-contaminated	0.99 (0.77–1.27)	0.95		
ASA classification	0.67 (0.57–0.78)	*< 0.01*	0.68 (0.52–0.89)	*< 0.01*
Laparoscopic and minimally invasive vs. open approach	1.13 (0.98–1.30)	0.10		
Whipple-type procedure vs. distal pancreatectomy	1.14 (0.95–1.35)	0.16		
Other pancreatic resection vs. distal pancreatectomy	0.73 (0.52–1.03)	0.069		
Pancreatic duct size > 3 vs. < 3 mm	0.85 (0.72–0.99)	*< 0.05*	0.74 (0.60–0.91)	*< 0.01*
Pancreatic gland texture hard vs. intermediate	1.37 (0.96–1.95)	0.079	1.44 (0.93–2.25)	0.10
Pancreatic gland texture soft vs. intermediate	1.66 (1.17–2.35)	*< 0.01*	1.59 (1.02–2.48)	*< 0.05*
Pancreaticojejunal duct-to-mucosal vs. not performed	1.57 (1.32–1.87)	*< 0.01*		
Pancreaticojejunal invagination vs. not performed	1.25 (0.91–1.73)	0.17		
Pancreaticogastrostomy vs. not performed	2.24 (1.07–4.66)	*< 0.05*		
Transfusions within 72 h	1.33 (1.06–1.66)	*< 0.05*	1.51 (1.02–2.24)	*< 0.05*
Operative time	1.000 (1.000–1.001)	0.21		
Malignant vs. benign	1.24 (1.04–1.47)	*< 0.05*	1.17 (0.85–1.62)	0.33

$p < 0.05$), and increased operative time. Large pancreatic duct size > 3 mm (OR = 0.62 (0.51–0.77); $p < 0.01$), neoadjuvant chemotherapy within 90 days of resection, and hard pancreatic gland texture (OR = 0.58 (0.35–0.99); $p < 0.05$) were associated with a decreased risk of POPF. When removing patients with fistulae defined only by persistent drainage ($n = 446$) or clinical diagnosis ($n = 136$) with drain placement continued for longer than 7 days, the incidence of fistula in the drain group decreased from 20 to 6% ($n = 259$).

A separate analysis of risk factors for pancreatic fistula was performed for Whipple-type and distal pancreatic resections. The incidence of pancreatic fistula was equivalent in the drain (19%) and no drain groups (8%) after both procedures. Independent risk factors for pancreatic fistula after distal pancreatectomy (Table 5) were drain placement (OR = 2.84 (1.70–4.75); $p < 0.01$) and perioperative transfusions (OR = 1.48 (1.04–2.10); $p < 0.05$). In the Whipple-type procedure group (Table 6), obesity (OR = 1.47 (1.08–2.00); $p < 0.05$), drain placement (OR = 2.29 (1.28–4.11); $p < 0.01$), soft pancreatic gland texture (OR = 1.76 (1.02–3.04); $p < 0.05$), and longer operative time (OR = 1.002 (1.001–1.003); $p < 0.01$) were significantly associated with the development of pancreatic fistula. Conversely, larger pancreatic ducts were associated with a decreased risk of fistulae (OR = 0.59 (0.47–0.74); $p < 0.01$).

Table 4 Unadjusted and adjusted logistic regression models relating risk factors to the incidence of pancreatic fistula

Variable	Unadjusted		Adjusted	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Male	1.16 (1.00–1.34)	*< 0.05*	1.06 (0.82–1.37)	0.64
Age	0.999 (0.993–1.01)	0.71		
Obese	1.36 (1.17–1.59)	*< 0.01*	1.41 (1.08–1.86)	*< 0.05*
Underweight	1.00 (0.64–1.56)	0.99	0.43 (0.15–1.25)	0.12
Diabetes	0.76 (0.63–0.90)	*< 0.01*	0.78 (0.57–1.06)	0.11
COPD	0.99 (0.69–1.41)	0.94		
Currently requiring or on hemodialysis within 2 weeks	0.76 (0.22–2.57)	0.65		
Steroid or immunosuppressant use for chronic condition	1.54 (1.06–2.22)	*< 0.05*	1.45 (0.73–2.89)	0.29
> 10% weight loss in last 6 months	0.82 (0.66–1.02)	0.068		
Preoperative obstructive jaundice	0.84 (0.71–0.99)	*< 0.05*	0.97 (0.66–1.42)	0.87
Preoperative biliary stent placement	0.88 (0.76–0.99)	*< 0.05*	1.02 (0.71–1.46)	0.92
Neoadjuvant chemotherapy	0.55 (0.43–0.72)	*< 0.01*	0.56 (0.32–0.96)	*< 0.05*
Neoadjuvant radiation	0.62 (0.43–0.88)	*< 0.01*	1.49 (0.74–2.99)	0.27
Creatinine	1.02 (0.89–1.16)	0.81		
Total bilirubin	0.94 (0.90–0.98)	*< 0.01*	0.94 (0.87–1.01)	0.07
Albumin	1.13 (1.00–1.29)	*< 0.05*	1.04 (0.82–1.32)	0.74
Leukocytes	1.01 (0.98–1.03)	0.70		
INR	1.07 (0.78–1.49)	0.67		
Contaminated and dirty-infected vs. clean and clean-contaminated	1.03 (0.83–1.28)	0.82		
ASA classification	1.08 (0.95–1.23)	0.26		
Laparoscopic and minimally-invasive vs. open approach	1.14 (1.01–1.27)	*< 0.05*	1.12 (0.90–1.41)	0.32
Whipple-type procedure vs. distal pancreatectomy	1.00 (0.86–1.17)	0.97		
Other pancreatic resection vs. distal pancreatectomy	0.95 (0.68–1.34)	0.78		
Drain placement	2.83 (2.11–3.78)	*< 0.01*	2.22 (1.37–3.59)	*< 0.01*
Pancreatic duct size > 3 vs. < 3 mm	0.57 (0.49–0.66)	*< 0.01*	0.62 (0.51–0.77)	*< 0.01*
Pancreatic gland texture hard vs. intermediate	0.77 (0.52–1.15)	0.20	0.58 (0.35–0.99)	*< 0.05*
Pancreatic gland texture soft vs. intermediate	2.01 (1.39–2.92)	*< 0.01*	1.64 (1.01–2.69)	*< 0.05*
Pancreaticojejunal duct-to-mucosal vs. not performed	1.05 (0.89–1.23)	0.55		
Pancreaticojejunal invagination vs. not performed	1.42 (1.08–1.88)	*< 0.05*		
Pancreaticogastrostomy vs. not performed	1.37 (0.83–2.27)	0.21		
Transfusions within 72 h	1.19 (0.99–1.42)	0.06		
Operative time	1.001 (1.00–1.001)	*< 0.01*	1.002 (1.001–1.003)	*< 0.01*
Malignant vs. benign	0.83 (0.71–0.97)	*< 0.05*	0.98 (0.71–1.34)	0.88

Discussion

In this large national database of over 5000 pancreatic resections accrued in a single year, we found the majority (87%) of patients received drains and an incidence of postoperative pancreatic fistula of 18%. Drain placement was independently associated with pancreatic fistula after any pancreatectomy surgery, in Whipple-type resections as well as and distal pancreatectomies. BMI > 30 kg/m^2, soft gland, and higher operative time were associated with an increased risk of pancreatic fistula while main pancreatic duct size > 3 mm and hard gland were protective. Surgeons were more likely to place a drain in patients with main pancreatic duct size < 3 mm, soft gland texture, and significant intraoperative blood loss.

To our knowledge, this study constitutes one of the largest datasets[20] focused on the relationship between drain placement and postoperative pancreatic fistula. We confirmed that drains are placed in the vast majority of cases in the USA[21] even in light of randomized controlled trials supporting no drain placement,[11,13] and demonstrated that components of the fistula risk score were associated with the decision to place drains. [19,22] Importantly, the data supported the contention that drain placement was associated with increased fistula incidence.[23] Interestingly, when clinically relevant fistula

Table 5 Unadjusted and adjusted logistic regression models relating risk factors to the incidence of pancreatic fistula for distal pancreatectomy

Variable	Unadjusted		Adjusted	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Male	1.26 (0.98–1.63)	0.074		
Age	1.00 (0.99–1.01)	0.92		
Obese	1.33 (1.03–1.74)	*< 0.05*	1.02 (0.99–1.04)	0.071
Underweight	1.41 (0.63–3.14)	0.39		
Diabetes	0.99 (0.74–1.34)	0.97		
COPD	1.50 (0.79–2.83)	0.22		
Steroid or immunosuppressant use for chronic condition	1.54 (0.86–2.75)	0.14		
>10% weight loss in last 6 months	0.99 (0.61–1.62)	0.97		
Preoperative obstructive jaundice	0.68 (0.41–1.14)	0.15		
Preoperative biliary stent placement	0.79 (0.50–1.24)	0.30		
Neoadjuvant chemotherapy	0.66 (0.42–1.06)	0.09		
Neoadjuvant radiation	0.79 (0.41–1.52)	0.48		
Creatinine	0.90 (0.69–1.18)	0.45		
Total bilirubin	1.11 (0.84–1.48)	0.46		
Albumin	1.09 (0.86–1.39)	0.50		
Leukocytes	0.99 (0.95–1.04)	0.78		
INR	1.34 (0.77–2.33)	0.31		
Contaminated and dirty-infected vs. clean and clean-contaminated	1.42 (0.96–2.11)	0.08		
ASA classification	1.14 (0.91–1.42)	0.25		
Laparoscopic and minimally-invasive vs. open approach	1.06 (0.89–1.27)	0.49		
Drain placement	2.73 (1.67–4.44)	*< 0.01*	2.84 (1.70–4.75)	*< 0.01*
Pancreatic duct size > 3 vs. < 3 mm	0.76 (0.54–1.06)	0.11		
Pancreatic gland texture hard vs. intermediate	1.01 (0.48–2.16)	0.97		
Pancreatic gland texture soft vs. intermediate	1.31 (0.64–2.68)	0.46		
Transfusions within 72 h	1.43 (1.02–2.01)	*< 0.05*	1.48 (1.04–2.10)	*< 0.05*
Operative time	1.002 (1.001–1.003)	*< 0.01*		
Malignant vs. benign	0.99 (0.76–1.28)	0.91		

was considered alone, there was no difference in POPF between the drain and no drain groups.[20] Thus, at least part of the association between drains and fistula may be the ability to measure and monitor peripancreatic fluid in the post-operative setting. The difference in POPF rates when patients with drains left in place for longer than 7 days were excluded from the fistula group supports the hypothesis that duration of drain may contribute to fistula.[9] Drain placement was also associated in univariate analysis with decreased mortality. As there was no difference in type C fistula between drained and non-drained patients nor a difference in need for percutaneous drain placement, it is difficult to attribute this difference in mortality to an uncontrolled fistula. Nonetheless, the findings are similar to those found by Van Buren et al. in the recently reported randomized controlled trial,[12] though the mortality rate in the non-drained group in that trial was 12%, whereas in this study, overall mortality was 1.4% and 1.2 and 2.8%, respectively in the drain and no drain groups, which are well within the lowest tier of mortality rates for the highest volume programs.[24,25]

Obesity was an independent predictor for pancreatic fistula. This seldom reported association[26] reinforces the need for refinement of risk factors for fistulae. In contrast to recent literature, this group of patients did not experience a reduction in length of hospital stay[27] or an increase in operative time[28] with drain placement. Interestingly, neoadjuvant chemotherapy within 90 days of pancreatic resection for malignancy was associated with a decreased risk of fistula. Intuitively, this may be related to selection of patients with obstructed ducts, pancreatic gland fibrosis, desmoplasia, or post-treatment changes in gland texture.

Our study is limited by its retrospective nature, the absence of randomization or matching, and a heterogeneous sample with an inability to control for surgeon selection biases related to the intraoperative decision to place a prophylactic drain; however, the large number of patients able to be assessed over

Table 6 Unadjusted and adjusted logistic regression models relating risk factors to the incidence of pancreatic fistula for Whipple-type procedure

Variable	Unadjusted		Adjusted	
	OR (95% CI)	*p*	OR (95% CI)	*p*
Male	1.15 (0.96–1.38)	0.14		
Age	0.99 (0.99–1.01)	0.58		
Obese	1.45 (1.19–1.78)	*< 0.01*	1.47 (1.08–2.00)	*< 0.05*
Underweight	0.72 (0.38–1.38)	0.32	0.38 (0.11–1.28)	0.12
Diabetes	0.63 (0.50–0.79)	*< 0.01*	0.68 (0.48–0.98)	*< 0.05*
COPD	0.88 (0.57–1.38)	0.59		
Currently requiring or on hemodialysis within 2 weeks	1.81 (0.35–9.37)	0.48		
Steroid or immunosuppressant use for chronic condition	1.40 (0.83–2.36)	0.21		
> 10% weight loss in last 6 months	0.78 (0.61–1.003)	0.052		
Preoperative obstructive jaundice	0.83 (0.69–1.002)	0.052		
Preoperative biliary stent placement	0.78 (0.65–0.94)	*< 0.01*	1.01 (0.75–1.38)	0.94
Neoadjuvant chemotherapy	0.51 (0.37–0.71)	*< 0.01*	0.49 (0.26–0.93)	*< 0.05*
Neoadjuvant radiation	0.57 (0.37–0.89)	*< 0.05*	1.52 (0.68–3.41)	0.31
Creatinine	1.01 (0.84–1.22)	0.89		
Total bilirubin	0.93 (0.89–0.97)	*< 0.01*	0.93 (0.86–0.99)	*< 0.05*
Albumin	1.22 (1.04–1.42)	*< 0.05*	1.06 (0.82–1.37)	0.67
Leukocytes	1.02 (0.98–1.05)	0.38		
INR	0.88 (0.51–1.52)	0.65		
Contaminated and dirty-infected vs. clean and clean-contaminated	0.83 (0.63–1.10)	0.20		
ASA classification	1.06 (0.90–1.26)	0.48		
Laparoscopic and minimally-invasive vs. open approach	1.24 (1.05–1.48)	*< 0.05*	1.28 (0.98–1.67)	0.072
Drain placement	2.70 (1.85–3.92)	*< 0.01*	2.29 (1.28–4.11)	*< 0.01*
Pancreatic duct size > 3 vs. < 3 mm	0.50 (0.42–0.59)	*< 0.01*	0.59 (0.47–0.74)	*< 0.01*
Pancreatic gland texture hard vs. intermediate	0.71 (0.44–1.14)	0.15	0.59 (0.47–0.74)	0.077
Pancreatic gland texture soft vs. intermediate	2.30 (1.47–3.58)	*< 0.01*	1.76 (1.02–3.04)	*< 0.05*
Pancreaticojejunal duct-to-mucosal vs. not performed	1.71 (1.19–2.48)	*< 0.01*		
Pancreaticojejunal invagination vs. not performed	2.19 (1.41–3.41)	*< 0.01*		
Pancreaticogastrostomy vs. not performed	1.96 (0.99–3.89)	0.053		
Transfusions within 72 h	1.14 (0.92–1.43)	0.23		
Operative time	1.001 (1.000–1.002)	*< 0.01*	1.002 (1.001–1.003)	*< 0.01*
Malignant vs. benign	0.70 (0.57–0.86)	*< 0.01*	0.91 (0.63–1.30)	0.58

a very short time period of just 1 year using this data source increases the power of the analysis and decreases many other potential sources of bias. The NSQIP variables and definitions also included a clinical diagnosis of fistula with drainage greater than 7 days and amylase-rich drainage greater than 3 days as fistulae. These definitions may continue to be fine-tuned as growing evidence of equivalent clinical outcomes between no fistula and grade A ISGPF fistula[29,30] has prompted an update[2] of the ISGPF grading in 2016 with the renaming[31] of "grade A ISGPF" as "biochemical leak." Additionally, using the captured definitions restricted the precise delineation of grades; however, we used the captured variables to match the ISGPF requisites. Recent techniques to mitigate the risk of fistula including octreotide,[32] fibrin glue,[33] or trans-anastomotic stent placement[34] were also not captured in the NSQIP dataset, though whether these interventions significantly change POPF incidence remains a matter of debate.

In summary, drains are currently placed in the vast majority (87%) of pancreatectomy patients at over 100 institutions in the USA, particularly those with soft glands and small ducts and that received associated blood transfusions. When fistula risk factors are controlled for, drain placement remains independently associated with fistula incidence in both distal and proximal pancreatectomy. These findings contribute important data that may be used when considering the utility of drain placement based on current practice patterns and the possibility of drain-induced fistula.

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Compliance with Ethical Standards

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