

Effect of main pancreatic duct suture ligation on the prevention of clinically relevant pancreatic fistula after distal pancreatectomy: analysis of 82 consecutive patients

A. ULKU¹, U. TOPAL¹, O. ERDOGAN², B. YAVUZ¹, O. YALAV¹, K. DALCI¹, İ.C. ERAY¹, A.G. SARITAS¹, A.T. AKCAM¹

¹Department of General Surgery, Faculty of Medicine, Cukurova University, Adana, Turkey

²Department of Surgical Oncology, Faculty of Medicine, Cukurova University, Adana, Turkey

Abstract. – OBJECTIVE: This study aimed to examine the factors linked to the development of clinically significant pancreatic fistulas following distal pancreatectomy (DP) and to assess the efficacy of suture ligation of the main pancreatic duct.

PATIENTS AND METHODS: A single-center retrospective study was performed on the medical records of 82 patients who underwent DP in our institution between January 2011 and December 2019.

RESULTS: There were 28 males (34.1%) and 54 females (65.9%). The patients' age ranged from 18 to 86 years (median: 55.5 years). Indications for DP included primary pancreatic disease (n=63, 76.8%) and non-pancreatic disease (n=19, 23.2%). Postoperative mortality and morbidity rates were 3.7% and 48%, respectively. Pancreatic parenchymal closure was accomplished by a hand-sewn technique or mechanical stapling in 89 and 13 patients, respectively. Identification of the pancreatic duct and suture ligation was performed in 46 patients (56.1%). Pancreatic fistula was developed in 20 patients (24.4%); 12 fistulas were classified as Grade B, and 8 as Grade C. Biochemical leaks (Grade A) were identified in 8 patients (9.8%). Multivariate analysis indicated that failure to ligate the main pancreatic duct was the only variable associated with an increased risk for pancreatic leak ($p=0.031$; odds ratio=0.233; 95% confidence interval, 0.062-0.879).

CONCLUSIONS: Pancreatic leak remains a common complication after DP. The incidence of leaks is reduced significantly when the main pancreatic duct is identified and directly ligated during DP.

Key Words:

Pancreas, Distal pancreatectomy, Pancreatic fistula, Management.

Introduction

Distal pancreatectomy is a common surgical procedure used to address various neoplastic or non-neoplastic conditions affecting the body and tail of the pancreas. In this surgery, the section of the pancreas to the left is excised, preserving the duodenum and bile ducts. The superior mesenteric vein/portal vein is the landmark for distal pancreatectomy. However, the precise point of pancreatic resection is determined by the tumor's location¹. In recent times, the reasons for performing distal pancreatectomy have expanded to encompass malignant and benign pancreatic conditions, non-pancreatic cancers, chronic pancreatitis, and trauma. The mortality rate post-distal pancreatectomy has seen a decline, now ranging between 0 to 7.3%². Yet, despite advancements in surgical methods and perioperative care, the morbidity rate remains elevated, fluctuating between 36.5% and 50.1% in recent decades³.

The grading system of the 2016 update of the International Study Group of Pancreatic Fistula (ISGPS) classified biochemical leakage as grade A (Table I). Grades B and C are clinically relevant postoperative pancreatic fistulas that require changes in postoperative management and extend the postoperative course⁴. Clinically significant postoperative pancreatic fistula (grade B/C), observed in 14.8-27.7% of patients, stands as the most challenging complication following distal pancreatectomy⁵. It has been shown⁶ to correlate with several severe complications, including intra-abdominal abscesses, hemorrhage, and sepsis. These complications can extend hospital stays and elevate hospitalization expenses. Thus, to enhance short-

Table I. Main parameters for grading of postoperative pancreatic fistula¹⁶.

	Biochemical leak (No POPF)	Grade B POPF*	Grade C POPF*
Increased amylase activity >3 times upper limit institutional normal serum value	Yes	Yes	Yes
Clinically relevant change in management of POPF ¹	No	Yes	Yes
Percutaneous or endoscopic-specific interventions for collections	No	Yes	Yes
Persisting peripancreatic drainage >3 weeks	No	yes	Yes
Reoperation	No	No	Yes
Death related to fistula	No	No	Yes
Signs of infection related to POPF	No	Yes, without organ failure	Yes, with organ failure
Sepsis	No	No	Yes
Reoperation	No	No	Yes
POPF related organ failure ²	No	No	Yes
Angiographic procedures for POPF-related bleeding	No	Yes	Yes

The revised 2016 ISGPS classification and grading of POPF: checklist for clinical use. ISGPS, International Study Group on Pancreatic Surgery; POPF, postoperative pancreatic fistula. *A clinically relevant POPF is defined as a drain output of any measurable volume of fluid with amylase level 3 times greater than the upper Institutional normal serum amylase level, associated with a clinically relevant development/condition related directly to the POPF¹. It suggests prolongation of hospital or ICU stay, including the use of therapeutic agents specifically employed for fistula management or its consequences (of these: somatostatin analogs, TPN/TEN, blood product transfusion, or other medications)². Postoperative organ failure is defined as the need for re-intubation, hemodialysis, and/or inotropic agents >24 hours for respiratory, renal, or cardiac insufficiency, respectively. Reproduced from the study of Bassi et al⁴ 2016.

term outcomes following distal pancreatectomy, identifying the risk factors for clinically significant postoperative pancreatic fistula is crucial.

In recent times, various surgical techniques have been devised and refined to close the pancreatic remnant, aiming to reduce the risk of pancreatic fistula and associated complications. Options for closing the pancreatic remnant encompass the hand-sewn suture method, the stapled closure technique, or a combination of both⁷⁻¹². However, optimal management of the pancreatic remnant remains controversial.

The aim of this study was to analyze factors associated with the occurrence of clinically relevant postoperative pancreatic fistula (grades B and C) in patients who underwent distal pancreatectomy and to determine the effectiveness of main pancreatic duct suture ligation.

Patients and Methods

Design and Subjects

Data for this study were retrospectively gathered from the electronic medical record system, targeting patients who were admitted for distal pancreatectomy between January 2011 and De-

ember 2019. All identified patients were over the age of 18, resulting in an initial cohort of ninety-two patients who underwent distal pancreatic resection. Of these, ten were excluded due to the unavailability of their medical records. As a result, the final study population consisted of 82 patients. This study was approved by the Institutional Review Board of our institute (IRB No. 10.01.2020/95/22), and written informed permission was taken from every patient who registered for the study. Distal pancreatectomy was executed either as the main procedure or within a broader multiorgan removal due to non-pancreatic cancer. The term “contiguous organ resection” refers to the removal of the distal pancreas and spleen along with at least one other organ. Pancreatic parenchymal tissue was evaluated by histopathologic examination. The size of the main pancreatic duct was also measured in preoperative CT or MRI images. Demographic features, indications, surgery and postoperative course and morbidity and mortality were analyzed. Surgical morbidity severity was categorized using the Clavien-Dindo classification¹³. Complications graded III or higher were deemed major. The term “30-day mortality” refers to any death occurring either in-hospital or within 30 days post-distal pancreatectomy.

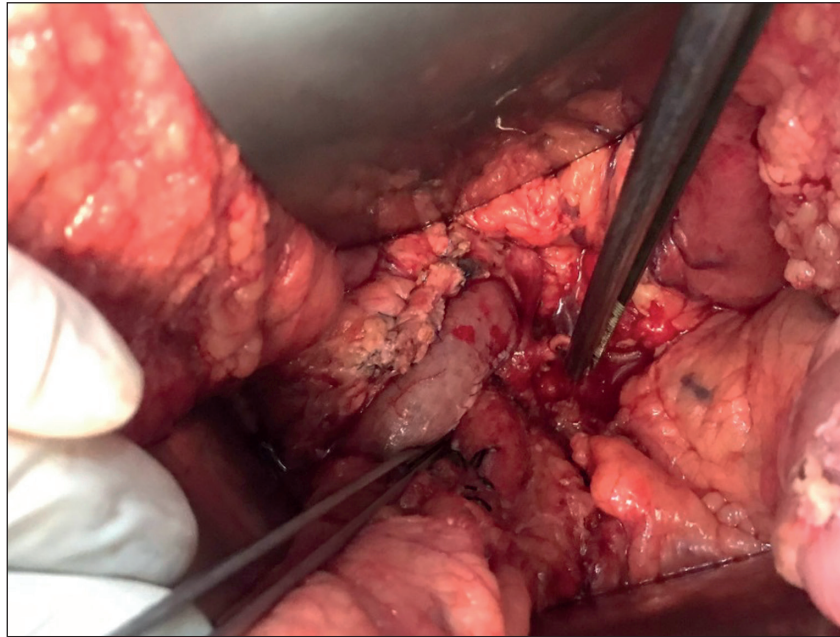


Figure 1. Pancreatic stump.

Surgical Technique

Division of the pancreatic parenchyma was by electrocautery or knife or triple-row stapler without reinforcement. The pancreatic stump was closed using the hand-sewn method with pledged polypropylene sutures, either incorporating suture ligation of the main pancreatic duct when feasible or without it (Figure 1). The main pancreatic duct was sutured with a purse-string suture technique using a 5-0 polypropylene suture after catheterization with a stylet or a cannula (Figure 2). Tissue patches or biological sealants for the pancreatic stump were not used during the procedure. Two closed suction drains were positioned along the superior and inferior edges of the pancreatic stump, situated in the bed of the resected pancreas close to the transected edge. If a splenectomy was performed, an additional drain might be placed in the left subphrenic space *via* the left upper abdomen.

Definition of Postoperative Pancreatic Fistula

International Study Group of Pancreatic Fistula (ISGPF)⁴ definition and grading system of postoperative pancreatic fistula were used to define postoperative pancreatic fistula. Pancreatic fistula was classified into four categories. The first was the absence of a fistula. The second, termed biochemical leakage or Grade A, was characterized by a surgical drain amylase level that was three

times greater than the serum level but with no clinical implications. Grade B was defined by biochemical evidence of a fistula that required drainage for more than 3 weeks, interventions like per-



Figure 2. Use of blood cannula for detection of the pancreatic duct.

cutaneous or endoscopic drainage, angiographic procedures due to bleeding, or exhibited signs of infection without organ failure. Grade C involved biochemical evidence of a fistula that resulted in reoperation, organ failure, or death. For the purposes of this study, postoperative pancreatic fistulas of Grades B and C were deemed clinically relevant. Drainage tubes were typically removed within 5 days after surgery if the drain amylase level was three times lower than the serum level. However, even if the drain amylase level was higher, the tubes were removed as soon as possible, provided the drainage fluid was not infected and the amylase level was decreasing.

Statistical Analysis

All statistical analyses were performed using the SPSS Version 24.0 (IBM Corp., Armonk, NY, USA). Data were described as frequencies (percentages of population) and median (interquartile range). We used the Chi-square or Fisher's exact test for univariate analysis to compare categorical data between the patients with PF and the patients without PF. For multivariate analysis, we used the multiple logistic regression analysis. Results are reported as odds ratio (OR) with 95% confidence interval. A p -value < 0.05 was regarded as statistically significant.

Results

Demographic details are provided in Table II. Patients' ages ranged from 18 to 86 years (median: 55.5 years), and the mean BMI was 27.5 ± 3.9 . The mean albumin value of the patients was 3.75 ± 0.55 g/dL. The majority of patients had an ASA score of 2 and 51.2% of patients had at least one additional disease. Of the patients, 63 (76.8%) underwent surgery due to pancreatic disease, while 19 (23.2%) did so for non-pancreatic disease. Cystic neoplasms were the predominant pancreatic indication, while gastric cancer was the leading non-pancreatic cause.

Operative information and technical factors are summarized in Table III. The average operation time was 198.9 ± 46.2 min, and estimated blood loss ranged between 100 mL and 1,400 mL (median: 250 mL). There were 19 (23.2%) patients with fibrotic pancreatic tissue. Distal pancreatectomy was applied to 55 (67.1%) patients with splenectomy, while distal pancreatectomy was applied to 19 (23.2%) patients with splenectomy and one or more additional procedures were per-

Table II. Patient demographics.

	(n=82)
Age (year) (range)	55 (18-86)
Sex	
• Male	28 (34.1%)
• Female	54 (65.9%)
Body mass index (kg/m²)	27.6 (16.9-36.5)
Indications for surgery	
Pancreatic diseases	63 (76.8%)
• Cystic neoplasm of the pancreas	15 (18.3%)
• Pancreatic neuroendocrine tumor	11 (13.4%)
• Pancreatic adenocarcinoma	11 (13.4%)
• Chronic pancreatitis	9 (11%)
• Solid pseudopapillary tumor	7 (8.5%)
• Others	10 (12.2%)
Non-pancreatic diseases	19 (23.2%)
• Gastric adenocarcinoma	8 (9.8%)
• Colonic adenocarcinoma	2 (2.4%)
• Retroperitoneal sarcoma	2 (2.4%)
• Others	7 (8.5%)
Preoperative serum albumin level (g/dL)	3.8 (1.6-5.4)
ASA score	
• 1	19 (23.2%)
• 2	45 (54.9%)
• 3	18 (21.9%)

formed. Spleen-preserving distal pancreatectomy was performed in 8 (9.8%) patients; they all had benign or borderline diseases. The most frequently resected non-pancreatic organ (excluding the spleen) was the stomach (10 patients), followed by the colon (5 patients), gallbladder (2 patients), kidney (2 patients) and surrenal (1 patient).

The pancreatic parenchyma was sealed using a hand-sewn method with ductal ligation in 46 patients (56.1%), hand-sewn without ductal ligation in 23 patients (28%), and solely stapling in 13 patients (15.9%). In 46 patients (56.1%), the pancreatic duct was identified and directly ligated with sutures. Conversely, 36 patients (43.9%) did not have the pancreatic duct ligated. None of the patients had the pancreatic remnant drained into the intestines.

Postoperative complications and mortality are summarized in Table IV. In our study, while the mortality rate was 3.7%, the complication rate was 47.6%. In the postoperative period, death occurred in 3 (3.7%) patients. One of these patients had both pancreatic fistula and esophagojejunal leakage after gastric cancer surgery with total gastrectomy, splenectomy and distal pancreatectomy. He died of sepsis after re-operation. The

Table III. Operative features.

	(n=82)
Operative time (min) (range)	190 (120-330)
Intraoperative blood loss (mL) (range)	250 (100-1,400)
Pancreatic texture	
• Non-fibrotic	63 (76.8%)
• Fibrotic	19 (23.2%)
Type of surgery	
• Distal pancreatectomy with splenectomy	55 (67.1%)
• Distal pancreatectomy with splenectomy and contiguous organ resection	19 (23.2%)
• Spleen-preserving distal pancreatectomy	8 (9.8%)
Pancreatic closure	
• Hand-sewn with ligation of MPD	46 (56.1%)
• Hand-sewn without ligation of MPD	23 (28%)
• Stapler closure	13 (15.9%)
Ligation of MPD	
• Ligation of duct	46 (56.1%)
• No ligation of duct	36 (43.9%)

MPD: Main Pancreatic Duct.

other 2 patients received multi-organ resection for gastric cancer at the age of 70 and 78, respectively. They did not have a pancreatic fistula. In the first case, the reason for death was pulmonary embolism and the second case died of cardiac problems. In our study, the complication rate was 47.6% (n=39). Clavien-Dindo grade III and higher complication rate was 17.1% (n=14). The most common complication was pancreatic fistula, and 20 (24.4%) patients developed pancreatic fistula; 12 (14.6%) of them were classified as grade B and 8 (9.8%) of them were classified as grade C. Eight (9.8%) patients were classified as biochemical leak. Death occurred in one of the patients with pancreatic leakage.

Two patients (2.4%) needed re-operation, one of which had both a pancreatic fistula and esophagojejunal leakage. The first patient died in the intensive care unit due to sepsis after the operation. The second patient underwent a reoperation due to an intra-abdominal abscess resulting from a grade C pancreatic fistula. She was discharged on the 8th day after the operation. Other patients with pancreatic fistula did not require re-operation for intra-abdominal abscess or fluid collection; these patients were treated with percutaneous drainage.

Univariate analysis was performed to investigate the relationship between any risk factor and the development of pancreatic fistula (Table V). None of the variables such as age, gender, ASA score, preoperative albumin level, presence of co-

morbidity, duration of surgery, estimated blood loss, primary pancreatic lesion, pancreatic parenchymal structure (fibrotic), type of surgery performed, and width of the main pancreatic duct showed any significant association with the development of pancreatic fistula.

In the univariate analysis, the failure of the main pancreatic duct suture ligation ($p=0.001$) had a significant relationship with pancreatic fistula. Pancreatic fistula was significantly more common

Table IV. Postoperative 30-day outcomes.

	(n=82)
Death	3 (3.7%)
Complications	39 (47.6%)
Re-operation	2 (2.4%)
Clavien-Dindo classification of postoperative complications	
• 0	43 (52.4%)
• 1	14 (17.1%)
• 2	11 (13.4%)
• 3a	8 (9.8%)
• 3b	1 (1.2%)
• 4a	2 (2.4%)
• 4b	0
• 5	3 (3.7%)
Biochemical leak (Grade A)	8 (9.8%)
Pancreatic fistula	20 (24.4%)
• Grade B	12 (14.6%)
• Grade C	8 (9.8%)

Pancreatic fistula after distal pancreatectomy

Table V. Univariate analysis examining clinicopathological and surgical factors potentially linked to clinically significant postoperative pancreatic fistula following distal pancreatectomy.

	POPF ISGPF 2016		<i>p</i>
	Yes	No	
Age (year)			
• <65	17 (29.8%)	40 (70.2%)	0.147
• ≥65	3 (12%)	22 (88%)	
Sex			
• Male	10 (35.7%)	18 (64.3%)	0.075
• Female	10 (18.5%)	44 (81.5%)	
ASA score			
• 1-2	17 (26.6%)	47 (73.4%)	0.298
• 3	3 (16.7%)	15 (83.3%)	
Body mass index (kg/m²)			
• Normal (<25)	5 (21.7%)	18 (78.3%)	0.727
• Overweight - Obese (≥25)	15 (25.4%)	44 (74.6%)	
Serum albumin level (g/dL)			
• ≤3.5	6 (30%)	14 (70%)	0.347
• >3.5	14 (22.6%)	48 (77.4%)	
Operative time (min)			
• <240	16 (23.9%)	51 (76.1%)	0.527
• ≥240	4 (26.7%)	11 (73.3%)	
Blood loss (mL)			
• <500	13 (21.3%)	48 (78.7%)	0.206
• ≥500	7 (33.3%)	14 (66.7%)	
Primary pancreatic pathology			
• Yes	13 (20.3%)	51 (79.7%)	0.105
• No	7 (38.9%)	11 (61.1%)	
Texture of pancreatic parenchyma			
• Non-fibrotic	14 (22.2%)	49 (77.8%)	0.292
• Fibrotic	6 (31.6%)	13 (68.4%)	
Contiguous organ resection			
• Yes	6 (31.6%)	13 (68.4%)	0.292
• No	14 (22.2%)	49 (77.8%)	
Stapler closure			
• Yes	6 (46.2%)	7 (53.8%)	0.055
• No	14 (20.3%)	55 (79.7%)	
Suture ligation of MPD			
• Ligation of duct	5 (10.9%)	41 (89.1%)	0.001
• No ligation of duct	15 (41.7%)	21 (58.3%)	
Pancreatic duct size			
• <3 mm	18 (28.1%)	46 (71.9%)	0.117
• ≥3 mm	2 (11.1%)	16 (88.9%)	

MPD: Main Pancreatic Duct. POPF: Postoperative Pancreatic Fistula. ISGPF: International Study Group of Pancreatic Fistula.

in patients whose main pancreatic duct was not ligated. There was an insignificant but close relationship between stapler closure ($p=0.055$) and pancreatic fistula.

In the multivariate analysis, the sole independent risk factor for clinically relevant pancreatic fistula was the absence of suture ligation of the main pancreatic duct (Table VI) ($p=0.031$; odds ratio=0.233, 95% confidence interval, 0.062-0.876).

Table VI. Multivariate analysis for risk factors for pancreatic fistula after distal pancreatectomy.

	Odds ratio	95% Confidence interval	p-value
Suture ligation of MPD	0.233	0.062-0.876	0.031

MPD: Main Pancreatic Duct.

Discussion

Pancreatic fistula is the most common complication after distal pancreatectomy and is a troublesome problem that can lead to bleeding, abscess formation, sepsis and septic shock, and mortality¹⁴. Complications from pancreatic fistula prolong postoperative hospital stays and increase the use of health resources^{10,15}. It can be managed conservatively today, thereby significantly reducing the incidence of mortality¹¹.

In our study, the mortality rate of the patients was 3.7% and the morbidity rate was 47.6%. The major complication rate of Clavien-Dindo grade III and higher was 17.1%. The morbidity and mortality rates of patients in the present study were higher than previously reported^{7,10,16} rates. However, postoperative complications were graded by using Clavien-Dindo¹³ classification in this study. Therefore, the morbidity and mortality rates of this study were compared to clinical studies using the same criteria. Goh¹⁷ reported a mortality rate of 3% in 232 consecutive patients undergoing distal pancreatectomy and reported 47% morbidity using Clavien-Dindo classification. Kleeff et al¹⁵ reported a mortality rate of 2% in 302 consecutive patients who underwent distal pancreatectomy. As can be seen, our results were consistent with those reported in the literature.

The most common complication was pancreatic fistula in our study and the reported clinically relevant pancreatic fistula incidence (24.4%) was similar to those reported in other studies^{15,18,19}. Of the 20 (24.4%) patients with pancreatic fistulas, 12 (14.6%) had grade B and 8 (9.8%) grade C pancreatic fistulas. Yang et al²⁰ reported a 22.3% grade B and 1% grade C fistula using the 2016 ISGPS criteria in their study. In their published study, Kleeff et al¹⁵ reported that most patients had grade B category. In our study, the grade B fistula rate was higher. In addition, re-operation was necessary only for two patients (2.4%) in our study. This rate was slightly lower than other studies^{15-17,20}, with reported re-operation rates of 3% to 11%.

Previous publications have reported long operation time⁷, stapler closure¹⁵, age ≤ 65 ¹⁹, soft pancreatic texture²¹, hand-sewn closure²², obesity^{7,22},

multivisceral resection²³ and malnutrition²⁴ as risk factors for increased pancreatic fistula rates. However, a reduction in pancreatic fistula formation has also been reported^{8,17,19} after main pancreatic duct ligation. Bilimoria et al⁸ found the incidence of pancreatic fistulas is reduced if the main pancreatic duct is identified and ligated during distal pancreatectomy. In our study, the only predictive factor for clinically relevant postoperative pancreatic fistula formation was the failure of the main pancreatic duct suture ligation.

There was also an insignificant but close relationship between stapler closure and clinically relevant postoperative pancreatic fistula formation in our series ($p=0.055$). Clinically relevant postoperative pancreatic fistula occurred in 6 of the 13 patients in whom a stapler was used, compared to 14 of the 69 patients in whom it was not used. Kleeff et al¹⁵ and Kah Heng et al²⁵ studied the risk factors associated with the formation of postoperative pancreatic fistula. They both determined the use of staplers as a risk factor for pancreatic fistula after distal pancreatectomy. In addition, Martin et al²⁶ identified the diameter of the main pancreatic ductus to be 3 mm below as a risk factor for pancreatic fistula after distal pancreatectomy, but our data does not support this finding.

Limitations

Our study had certain limitations. The sample size was relatively small. In our institution, suture ligation of the main pancreatic duct has not been a standard procedure for every distal pancreatic leak. Additionally, the pool of patients with adequate data for our research was limited. Another limitation was the diverse nature of our patient group, encompassing various benign and malignant pancreatic conditions and tumor sites. Due to the limited patient count, we had to derive conclusions without categorizing them. Lastly, even though all participants underwent distal pancreatectomy, only some had the main pancreatic duct suture ligation. While some patients were able to be compared with different closure modalities, others could be compared between main pancreatic duct suture ligation and existing classical methods.

Conclusions

Pancreatic fistula remains the most common complication after distal pancreatectomy. We identified that the omission of suture ligation of the main pancreatic duct independently increased the risk of clinically significant postoperative pancreatic fistula. It is imperative to make every effort to locate and directly ligate the pancreatic duct with sutures after parenchymal division, irrespective of the chosen method for parenchymal sealing.

Authors' Contributions

AU, OE, AGS, ATA – Conceptualization and methodology; AU, OE, KD, AGS, ATA – Data collection; AU, UT, OE, AGS, ATA – Data analysis and interpretation; AU, UT, OE, BY, KD, AGS, ATA Drafting the article. All authors revised and gave final approval for the manuscript.

Conflicts of Interest

The authors declare no competing interests.

Ethics Approval

The study protocol was approved by the Ethics Committee of the University of Cukurova (Date: 03.12.2021 No.: 117/7).

Funding

No funds were received for this study.

Informed Consent

Written informed permission was taken from every patient who registered for the study.

ORCID ID

Abdullah Ulku: 0000-0001-5180-1543
 Ugur Topal: 0000-0003-1305-2056
 Osman Erdogan: 0000-0002-9941-2704
 Burak Yavuz: 0000-0002-5262-0346
 Orçun Yalav: 0000-0001-9239-4163
 Kubilay Dalcı: 0000-0002-3156-4269
 İsmail Cem Eray: 0000-0002-1560-7740
 Ahmet Gökhan Sarıtaş: 0000-0003-2715-6390
 Atılğan Tolga Akçam: 0000-0001-7525-3107

Data Availability

Data supporting the results and analyses presented in this research is available upon reasonable request.

References

- 1) Andrén-Sandberg Å, Wagner M, Tihanyi T, Löfgren P, Friess H. Technical Aspects of Left-Sided Pancreatic Resection for Cancer. *Digestive Surgery* 1999; 16: 305-312.
- 2) Kawai M, Hirono S, Okada KI, Sho M, Nakajima Y, Eguchi H, Nagano H, Ikoma H, Morimura R, Takeda Y, Nakahira S, Suzumura K, Fujimoto J, Yamaue H. Randomized Controlled Trial of Pancreaticojejunostomy versus Stapler Closure of the Pancreatic Stump During Distal Pancreatectomy to Reduce Pancreatic Fistula. *Ann Surg* 2016; 264: 180-187.
- 3) Behrman SW, Zarzaur BL, Parmar A, Riall TS, Hall BL, Pitt HA. Routine drainage of the operative bed following elective distal pancreatectomy does not reduce the occurrence of complications. *J Gastrointest Surg* 2015; 19: 72-79.
- 4) Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, Allen P, Andersson R, Asbun HJ, Besselink MG, Conlon K, Del Chiaro M, Falconi M, Fernandez-Cruz L, Fernandez-Del Castillo C, Fingerhut A, Friess H, Gouma DJ, Hackert T, Izbicki J, Lillemoe KD, Neoptolemos JP, Olah A, Schulick R, Shrikhande SV, Takada T, Takaori K, Traverso W, Vollmer CR, Wolfgang CL, Yeo CJ, Salvia R, Buchler M. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 Years After. *Surgery* 2017; 161: 584-591.
- 5) Van Buren G, Bloomston M, Schmidt CR, Behrman SW, Zyromski NJ, Ball CG, Morgan KA, Hughes SJ, Karanicolas PJ, Allendorf JD, Vollmer CM, Ly Q, Brown KM, Velanovich V, Winter JM, McElhany AL, Muscarella P, Schmidt CM, House MG, Dixon E, Dillhoff ME, Trevino JG, Hallet J, Coburn NSG, Nakeeb A, Behrns KE, Sasson AR, Ceppa EP, Abdel-Misih SRZ, Riall TS, Silberfein EJ, Ellison EC, Adams DB, Hsu C, Tran Cao HS, Mohammed S, Villafañe-Ferriol N, Barakat O, Massarweh NN, Chai C, Mendez-Reyes JE, Fang A, Jo E, Mo Q, Fisher WE. A Prospective Randomized Multicenter Trial of Distal Pancreatectomy With and Without Routine Intraoperative Drainage. *Ann Surg* 2017; 266: 421-431.
- 6) Okano K, Hirao T, Unno M, Fujii T, Yoshitomi H, Suzuki S, Satoi S, Takahashi S, Kainuma O, Suzuki Y. Postoperative infectious complications after pancreatic resection. *Br J Surg* 2015; 102: 1551-1560.
- 7) Fahy BN, Frey CF, Ho HS, Beckett L, Bold RJ. Morbidity, mortality, and technical factors of distal pancreatectomy. *Am J Surg* 2002; 183: 237-241.
- 8) Bilimoria MM, Cormier JN, Mun Y, Lee JE, Evans DB, Pisters PWT. Pancreatic leak after left pancreatectomy is reduced following main pancreatic duct ligation. *Br J Surg* 2003; 90: 190-196.
- 9) Kajiyama Y, Tsurumaru M, Udagawa H, Tsutsumi K, Kinoshita Y, Akiyama H. Quick and simple distal pancreatectomy using the GIA stapler: Report of 35 cases. *Br J Surg* 1996; 83: 1711-1711.

- 10) Sheehan MK, Beck K, Creech S, Pickleman J, Aranha GV. Distal Pancreatectomy: Does the Method of Closure Influence Fistula Formation? *Am Surg* 2002; 68: 264-268.
- 11) Balzano G, Zerbi A, Cristallo M, Dicarolo V. The Unsolved Problem of Fistula After Left Pancreatectomy: The Benefit of Cautious Drain Management. *J Gastrointest Surg* 2005; 9: 837-842.
- 12) Takeuchi K, Tsuzuki Y, Ando T, Sekihara M, Hara T, Kori T, Nakajima H, Kuwano H. Distal pancreatectomy: is staple closure beneficial? *ANZ J Surg* 2003; 73: 922-925.
- 13) Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg* 2004; 240: 205-213.
- 14) Jiwani A, Chawla T. Risk Factors of Pancreatic Fistula in Distal Pancreatectomy Patients. *Surg Res Pract* 2019; 2019: 4940508.
- 15) Kleeff J, Diener MK, Z'Graggen K, Hinz U, Wagner M, Bachmann J, Zehetner J, Müller MW, Friess H, Büchler MW. Distal pancreatectomy: risk factors for surgical failure in 302 consecutive cases. *Ann Surg* 2007; 245: 573-582.
- 16) Hutchins RR, Hart RS, Pacifico M, Bradley NJ, Williamson RCN. Long-term results of distal pancreatectomy for chronic pancreatitis in 90 patients. *Ann Surg* 2002; 236: 612-618.
- 17) Goh BKP. Critical Appraisal of 232 Consecutive Distal Pancreatectomies With Emphasis on Risk Factors, Outcome, and Management of the Postoperative Pancreatic Fistula. *Arch Surg* 2008; 143: 956-965.
- 18) Balcom Iv JH. Ten-Year Experience With 733 Pancreatic Resections. *Arch Surg* 2001; 136: 391.
- 19) Yoshioka R, Saiura A, Koga R, Seki M, Kishi Y, Morimura R, Yamamoto J, Yamaguchi T. Risk Factors for Clinical Pancreatic Fistula After Distal Pancreatectomy: Analysis of Consecutive 100 Patients. *World J Surg* 2009; 34: 121-125.
- 20) Yang F, Jin C, Hao S, Fu D. Drain Contamination after Distal Pancreatectomy: Incidence, Risk Factors, and Association with Postoperative Pancreatic Fistula. *J Gastrointest Surg* 2019; 23: 2449-2458.
- 21) Ridolfini MP, Alfieri S, Gourgiotis S, Di Miceli D, Rotondi F, Quero G, Manghi R, Doglietto GB. Risk factors associated with pancreatic fistula after distal pancreatectomy, which technique of pancreatic stump closure is more beneficial? *World J Gastroenterol* 2007; 13: 5096-5100.
- 22) Wellner UF, Makowiec F, Sick O, Hopt UT, Keck T. Arguments for an individualized closure of the pancreatic remnant after distal pancreatic resection. *World J Gastrointest Surg* 2012; 4: 114-120.
- 23) Paye F, Micelli Lupinacci R, Bachellier P, Boher JM, Delpero JR. Distal pancreatectomy for pancreatic carcinoma in the era of multimodal treatment. *Br J Surg* 2014; 102: 229-236.
- 24) Sierzega M, Niekowal B, Kulig J, Popiela T. Nutritional Status Affects the Rate of Pancreatic Fistula after Distal Pancreatectomy: A Multivariate Analysis of 132 Patients. *J Am Coll Surg* 2007; 205: 52-59.
- 25) Kah Heng CA, Salleh I, San TS, Ying F, Su-Ming T. Pancreatic fistula after distal pancreatectomy: incidence, risk factors and management. *ANZ J Surg* 2010; 80: 619-623.
- 26) Martin AN, Narayanan S, Turrentine FE, Bauer TW, Adams RB, Zaydfudim VM. Pancreatic duct size and gland texture are associated with pancreatic fistula after pancreaticoduodenectomy but not after distal pancreatectomy. *PLoS One* 2018; 13: e0203841-e0203841.