Int Surg 2019;**104:**244–250
DOI: 10.9738/INTSURG-D-19-00008.1

Prediction of Pancreatic Fistula After Distal Pancreatectomy: Is It Necessary to Place Prophylactic Drain?

Kazuhiro Suzumura, Kenjiro Iida, Hideaki Iwama, Yusuke Kawabata

Department of Surgery, Hyogo College of Medicine, Hyogo, Japan

Background: The aim of this study was to determine the predictive factors for pancreatic fistula (PF) after distal pancreatectomy (DP) among preoperative and intraoperative parameters, and to clarify the patients who did not require drain placement.

Methods: Between July 2009 and April 2017, a total of 102 consecutive patients underwent DP at Hyogo College of Medicine. Preoperative and intraoperative data were collected, and the predictors of PF after DP were identified. PF was identified in 35 patients (34%). In the multivariate analysis, 3 factors [body mass index (BMI) $\geq$22.4, contiguous organ resection, and pancreatic thickness $\geq$11 mm] were found to be independent predictors of PF (odds ratio, 5.7; 95% confidence interval, 1.9–17; $P = 0.002$ odds ratio, 6.7; 95% confidence interval, 1.6–28; $P = 0.009$; odds ratio, 11.6; 95% confidence interval, 3.7–36; $P < 0.001$, respectively).

Results: A scoring scale for the prediction of PF was developed. BMI $\geq$22.4 (score: 1), contiguous organ resection (score: 1), and pancreatic thickness $\geq$11 mm (score: 2) were included in the scoring scale. Patients with a score of 0 never developed PF, whereas PF occurred in all patients with a score of 4.

Conclusions: BMI $\geq$22.4, contiguous organ resection, and pancreatic thickness $\geq$11 mm were predictive factors for PF after DP. No patients with BMI $<$22.4, no contiguous organ resection, and a pancreatic thickness of $<$11 mm developed PF after DP, indicating that such patients may not require drain placement.

Key words: Distal pancreatectomy – Pancreatic fistula – Prediction – Drain

Corresponding author: Kazuhiro Suzumura, MD, PhD, 1-1, Mukogawa, Nishinomiya, Hyogo 663-8501, Japan.
Tel.: +81 798 45 6582; Fax: +81 798 45 6581; E-mail: ssuzumu@hyo-med.ac.jp

The mortality rate of distal pancreatectomy (DP) has fallen to <5%; however, the procedure still has a high morbidity rate (16%–50%) despite recent progress in surgical techniques and perioperative management.[1–7] Pancreatic fistula (PF) is one of the main complications after DP and can be associated with additional complications, such as intra-abdominal hemorrhage and abscess.[8–10] Thus, the prediction of PF after DP is important for postoperative management.

Prophylactic drains after pancreatectomy are useful for monitoring to detect intra-abdominal bleeding, as well as for the detection and drainage of PF.[11,12] Most surgeons use a prophylactic drain after DP. However, the increased risk of intra-abdominal infection is a major disadvantage of drain placement. Recently, some studies demonstrated no benefit for the routine performance of prophylactic drainage after pancreatectomy.[13–16] However, a previous study reported that the postoperative mortality rate in a no-drain group was high (4.5%).[17] Thus, it is important that we precisely select patients without the need for a prophylactic drain. However, studies that consider cases that do not require prophylactic drains, although ensuring safety, have not yet been reported.

The aim of this study was to determine the predictive factors for PF after DP among preoperative and intraoperative parameters, and to clarify the patients who did not require drain placement.

Patients and Methods

Patients

A total of 102 consecutive patients who underwent DP at Hyogo College of Medicine between July 2009 and April 2017 were retrospectively investigated. The following preoperative data were collected: age, sex, body mass index (BMI), comorbidities, blood tests, disease, and neoadjuvant chemotherapy. The intraoperative data, including operative procedure, operative time, intraoperative blood loss, blood transfusion, pancreatic texture, contiguous organ or vessel resection, and pancreas thickness, were also examined. The grading of PF was assessed according to the International Study Group definition.[18] The grade previously defined as grade A was redefined as biochemical leak. Grade B/C PF was considered to be PF. Delayed gastric emptying and postpancreatectomy hemorrhage were also defined according to the definitions proposed by the International Study Group of Pancreatic Surgery.[19,20] The thickness of the pancreatic parenchyma at the resection line was measured on computed tomography before surgery. Mortality was defined as death in the hospital or death within 30 days after surgery.

The study was approved by the ethics committee of Hyogo College of Medicine (No. 2672).

Surgical procedure

All surgical procedures were performed by a gastroenterologic surgeon who was board-certified in Japan. The method of pancreatic stump closure and the transection line of the pancreas were selected at the surgeon's discretion. The patients mainly underwent 1 of 3 types of pancreatic stump closure: the clamp-crushing by means of the Child Kelly procedure with main pancreatic duct ligation, or ultrasonic scissors with main pancreatic duct ligation or stapler closure. For malignant tumors, radical resection of the distal pancreas with regional lymph node dissection and splenectomy was performed. For benign or low-grade malignant tumors, we considered laparoscopic surgery [laparoscopic distal pancreatectomy or laparoscopic spleen-preserving distal pancreatectomy (SPDP)]. After DP, a closed drain (20 Fr) was placed near the stump of the remnant pancreas. No patient received octreotide after surgery.

Statistical analysis

The data were expressed as medians. The χ^2 test, Fisher exact test, and Mann-Whitney *U* test were used for the comparison of categoric variables, as appropriate. A receiver-operating characteristics curve was constructed to estimate the optimal cutoff values for age, serum albumin, serum amylase, operative time, intraoperative blood loss, and thickness of the pancreas as predictive factors for PF. *P* values of <0.05 were considered to indicate statistical significance. All statistical analyses were performed using the SPSS software program (version 21.0, SPSS Company, Chicago, Illinois).

Results

Patient characteristics and intraoperative outcomes

The patient characteristics are listed in Table 1. A total of 102 patients [male, n = 53; female, n = 49; median age, 71 years (range, 11–90 years)] were included in the present study. The median BMI was 21.5 (range, 13.8–32.6). The study population in-

Table 1 The patient characteristics and intraoperative outcomes

	Value
Age, y (range)	71 (11–90)
Sex, male/female, n	53/49
BMI (range)	21.5 (13.8–32.6)
Diabetes mellitus, yes/no, n	32/70
Hypertension, yes/no, n	43/59
Hyperlipidemia, yes/no, n	19/83
Serum albumin, g/dL (range)	4.0 (2.7–5.1)
Serum amylase, U/L (range)	77 (26–921)
Disease, n (%)	
PDAC	48 (47)
IPMN	14 (14)
MCN	10 (10)
NET	7 (7)
SPN	5 (5)
Other	18 (17)
Neoadjuvant chemotherapy, yes/no, n	8/94
Surgical procedure, n (%)	
DP	86 (84)
SPDP	16 (16)
Open or laparoscopic DP, n (%)	
Open DP	78 (76)
Laparoscopic DP	24 (24)
Operative time, min (range)	379 (138–769)
Intraoperative blood loss, mL (range)	428 (10–3300)
Intraoperative transfusion, yes/no, n	24/78
Pancreatic texture, soft/hard, n	80/22
Portal vein resection, yes/no, n	3/99
Celiac artery resection, yes/no, n	4/98
Contiguous organ resection, yes/no, n	16/86
Pancreatic thickness, mm (range)	9.8 (3.9–18.6)

IPMN, intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm; NET, neuroendocrine tumor; PDAC, pancreatic ductal adenocarcinoma; SPN, solid pseudopapillary neoplasm.

cluded 32 patients with diabetes mellitus, 43 patients with hypertension, and 19 patients with hyperlipidemia. The most common disease was pancreatic cancer (47%), followed by intraductal papillary mucinous neoplasm (14%). Open surgery and laparoscopic surgery were performed in 78 and 24 cases, respectively. DP and SPDP were performed in 86 cases (84%) and 16 cases (16%), respectively. The median operative time was 379 minutes (range, 138–769 minutes). The median blood loss was 428 mL (range, 10–3300 mL). Eighty patients had a soft pancreatic texture. Portal vein resection and celiac artery resection were performed in 3 and 4 cases, respectively. Contiguous organ resection was performed in 16 cases [stomach, n = 8; colon, n = 7; left adrenal gland, n = 4; left kidney, n = 2; and jejunum, n = 2 (some cases overlapped)]. The median pancreatic thickness was 9.8 mm (range, 3.9–18.6 mm).

Table 2 The postoperative outcomes

	No. (%)
Pancreatic fistula	
BL	43 (42)
Grade B	35 (34)
Grade C	0 (0)
Delayed gastric emptying	
Grade A	5 (5)
Grade B	3 (3)
Grade C	1 (1)
Intra-abdominal hemorrhage	
Grade A	0 (0)
Grade B	1 (1)
Grade C	3 (3)
Intra-abdominal abscess	3 (3)
Wound infection	6 (6)
Reoperation	0 (0)
Mortality	1 (1)

BL, biochemical leak.

Postoperative outcomes

The postoperative complications and outcomes are shown in Table 2. Biochemical leak and PF were identified in 43 patients (42%) and 35 patients (34%), respectively. Delayed gastric emptying, intra-abdominal hemorrhage, intra-abdominal abscess, and wound infection were observed in 9 patients (9%), 4 patients (4%), 3 patients (3%), and 6 patients (6%), respectively. No patients underwent reoperation. One death occurred due to cerebral infarction on the ninth postoperative day.

Risk factors for pancreatic fistula after DP

The risk factors for PF after DP are shown in Table 3. Univariate analysis and multivariate analysis were performed to define the predictive factors of PF. The receiver-operating characteristics curve analysis revealed the following cutoff values: age, 66 years [area under the curve (AUC) = 0.449]; BMI, 22.4 (AUC = 0.657); serum albumin, 4.2 g/dL (AUC = 0.552); serum amylase, 97 U/L (AUC = 0.405); operative time, 423 minutes (AUC = 0.602); intraoperative blood loss, 280 mL (AUC = 0.612); and pancreatic thickness, 11 mm (AUC = 0.748). Five risk factors for PF after DP were identified in the univariate analysis: BMI ($P = 0.004$), operative time ($P = 0.028$), intraoperative blood loss ($P = 0.039$), contiguous organ resection ($P = 0.009$), and pancreatic thickness ($P < 0.001$). These 5 risk factors were included in a multivariate analysis. A multivariate logistic regression analysis revealed that BMI ($P = 0.002$; odds ratio, 5.7; 95% confidence interval, 1.9–17), contigu-

Table 3 The risk factors of pancreatic fistula after distal pancreatectomy

	Univariate analysis			Multivariate analysis		
	PF (−) n = 67	PF (+) n = 35	*P* value	Odds ratio	95% confidence interval	*P* value
Age						
<66 y	41	14	0.907			
≥66 y	26	21				
Sex						
Male	32	21	0.24			
Female	35	14				
BMI						
<22.4	43	12	0.004	5.7	1.9–17	0.002
≥22.4	24	23				
Diabetes mellitus						
+	20	12	0.647			
−	47	23				
Hypertension						
+	30	13	0.459			
−	37	22				
Hyperlipidemia						
+	15	4	0.177			
−	52	31				
Serum albumin						
<4.2	46	21	0.382			
≥4.2	21	14				
Serum amylase						
<97	41	24	0.462			
≥97	26	11				
Disease						
Benign	27	11	0.379			
Malignant	40	24				
Neoadjuvant chemotherapy						
+	4	4	0.33			
−	63	31				
Surgical procedure						
DP	55	31	0.393			
SPDP	12	4				
Open or laparoscopic DP						
Open DP	50	28	0.544			
Laparoscopic DP	17	7				
Operative time						
<423 min	49	18	0.028	1.1	0.4–3.4	0.812
≥423 min	18	17				
Intraoperative blood loss						
<280 mL	27	7	0.039	1.7	0.6–5.4	0.333
≥280 mL	40	28				
Intraoperative transfusion						
+	14	10	0.386			
−	53	25				
Pancreatic texture						
Soft	52	28	0.781			
Hard	15	7				
Portal vein resection						
+	1	2	0.231			
−	66	33				
Celiac artery resection						
+	2	2	0.5			
−	65	33				
Contiguous organ resection						
+	6	10	0.009	6.7	1.6–28	0.009
−	61	25				
Thickness of pancreas						
<11 mm	54	13	<0.001	11.6	3.7–36	<0.001
≥11 mm	13	22				

Risk factor	Risk score
BMI ≥ 22.4	1
Contiguous organ resection	1
Pancreatic thickness ≥ 11 mm	2

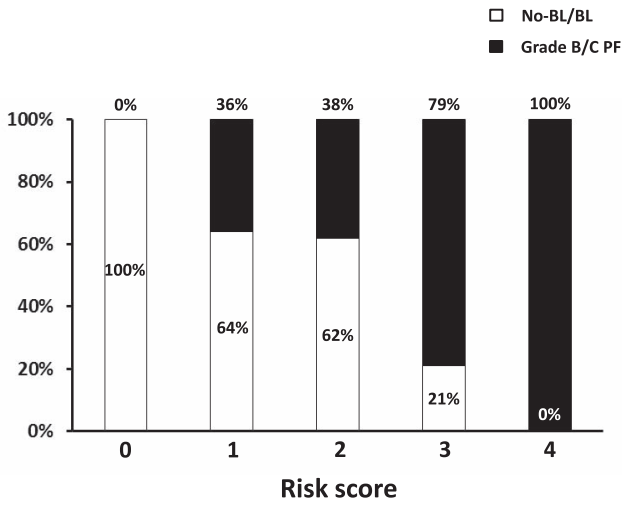

Fig. 1 (a) Parameters with allocated scores. (b) Bar graph of the prevalence of clinically relevant pancreatic fistula.

ous organ resection ($P = 0.009$; odds ratio, 6.7; 95% confidence interval, 1.6–28), and pancreatic thickness ($P < 0.001$; odds ratio, 11.6; 95% confidence interval, 3.7–36) were independent risk factors for PF after DP.

Risk scoring scale analysis for pancreatic fistula

A scoring scale for the prediction of PF was developed. Odds ratios from the multivariate model were translated into corresponding risk scores. Three predictive factors [BMI ≥22.4 (score: 1), contiguous organ resection (score: 1), and pancreatic thickness ≥11 mm (score: 2)] were included in the scoring scale (Fig. 1a). The prevalence of PF gradually increased in proportion with the score, from 0% to 100% (total score 0, 0%; total score 1, 36%; total score 2, 38%; total score 3, 79%; total score 4, 100%; Fig. 1b). No patients with a score of 0 developed PF, whereas PF occurred in all patients with a score of 4.

Discussion

PF, which is one of the main complications after DP, can be associated with additional complications, such as intra-abdominal hemorrhage and abscess.[8–10] Thus, the prediction of PF after DP is important for postoperative management.

As a result we attempted to identify predictive factors for PF after DP among preoperative and intraoperative parameters. Three significant predictors of PF after DP were identified and assigned scores based on odds ratios: BMI ≥22.4 (score: 1), contiguous organ resection (score: 1), and pancreatic thickness ≥11 mm (score: 2). We developed a scoring scale for the prediction of PF. According to our scoring scale, no patients with a score of 0 (BMI <22.4, no contiguous organ resection, and pancreatic thickness <11 mm) developed PF, whereas PF occurred in all patients with a score of 4 (BMI ≥22.4, contiguous organ resection, and pancreatic thickness ≥11 mm). Several studies reported risk factors for PF after DP using patient characteristics and intraoperative factors, such as BMI,[21,22] and thickness of the pancreatic parenchyma.[23,24] These data were thought to support the results of the present study. Regarding contiguous organ resection, Ferrone *et al*[25] reported additional organ resection was a significant predictor of PF, and the incidence rate of PF in patients undergoing additional colon or small-bowel resection was 71%. In the present study, the incidence of PF in patients undergoing additional colon or small-bowel resection was 60%. It was thought that infection made it easier for PF to occur in patients with contiguous organ resection.

Prophylactic drains after pancreatectomy allow for monitoring to detect intra-abdominal bleeding, as well as for the detection and drainage of PF.[11,12] Most surgeons use a prophylactic drain. However, a meta-analysis reported that the routine performance of abdominal drainage increases the risk of major complications after DP.[14,15] The major disadvantage of drain usage is the increased risk of intra-abdominal infection. Yamashita *et al*[26] reported that the prevalence of infection in drained abdominal

fluid gradually increased with time and was >10% on postoperative day 7. Adham *et al*[17] reported that routine prophylactic drainage of the abdominal cavity after pancreatic resection did not reduce the frequency or severity of postoperative complications, including PF, but that the postoperative mortality rate was high (4.5%) in a no-drain group. Thus, patients who require drainage are appropriately selected. In this study, patients with BMI <22.4, no contiguous organ resection, and pancreatic thickness <11 mm did not develop PF after DP. Thus, drainage during DP may be unnecessary for these patients. As a result of our findings in this study, we were able to gain new insight into the fact that it is possible to select patients who do not require prophylactic drains, while still ensuring their safety.

The current study had some limitations, including the relatively small study population, the fact that it was performed in a single institute, the application of different stump closure methods, and its retrospective nature. In the future, prospective studies should be performed based on data of this study.

In conclusion, BMI ≥22.4, contiguous organ resection, and pancreatic thickness ≥11 mm were predictive factors for PF after DP. Patients with BMI <22.4, no contiguous organ resection, and pancreatic thickness <11 mm did not develop PF after DP. Thus, these patients may not require drainage during DP.

Acknowledgments

There were no sources of support in the form of grants, equipment, or drugs.

References

1. Lillemoe KD, Kaushal S, Cameron JL, Sohn TA, Pitt HA, Yeo CJ. Distal pancreatectomy: indications and outcomes in 235 patients. *Ann Surg* 1999;**229**(5):693–700
2. Sledzianowski JF, Duffas JP, Muscari F, Suc B, Fourtanier F. Risk factors for mortality and intra-abdominal morbidity after distal pancreatectomy. *Surgery* 2005;**137**(2):180–185
3. Shimada K, Sakamoto Y, Sano T, Kosuge T. Prognostic factors after distal pancreatectomy with extended lymphadenectomy for invasive pancreatic adenocarcinoma of the body and tail. *Surgery* 2006;**139**(3):288–295
4. Hirano S, Kondo S, Hara T, Ambo Y, Tanaka E, Shichinohe T *et al*. Distal pancreatectomy with en bloc celiac axis resection for locally advanced pancreatic body cancer: long-term results. *Ann Surg* 2007;**246**(1):46–51
5. McPhee JT, Hill JS, Whalen GF, Zayaruzny M, Litwin DE, Sullivan ME *et al*. Perioperative mortality for pancreatectomy: a national perspective. *Ann Surg* 2007;**246**(2):246–253
6. Goh BK, Tan YM, Chung YF, Cheow PC, Ong HS, Chan WH *et al*. Critical appraisal of 232 consecutive distal pancreatectomies with emphasis on risk factors, outcome, and management of the postoperative pancreatic fistula: a 21-year experience at a single institution. *Arch Surg* 2008;**143**(10):956–965
7. 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**(12):2449–2458
8. Balcom JH, Rattner DW, Warshaw AL, Chang Y, Fernandez-del Castillo C. Ten-year experience with 733 pancreatic resections: changing indications, older patients, and decreasing length of hospitalization. *Arch Surg* 2001;**136**(4):391–398
9. Büchler MW, Wagner M, Schmied BM, Uhl W, Friess H, Z'graggen K. Changes in morbidity after pancreatic resection: toward the end of completion pancreatectomy. *Arch Surg* 2003;**138**(12):1310–1314
10. Tani M, Terasawa H, Kawai M, Ina S, Hirono S, Uchiyama K *et al*. Improvement of delayed gastric emptying in pylorus-preserving pancreaticoduodenectomy: results of a prospective, randomized, controlled trial. *Ann Surg* 2006;**243**(3):316–320
11. Cullen JJ, Sarr MG, Ilstrup DM. Pancreatic anastomotic leak after pancreaticoduodenectomy; incidence, significance, and management. *Am J Surg* 1994;**168**(4):295–298
12. Yamaguchi M, Nakano H, Midorikawa T, Yoshizawa Y, Sanada Y, Kumada K. Prediction of pancreatic fistula by amylase levels of drainage fluid on the first day after pancreatectomy. *Hepatogastroenterology* 2003;**50**(52):1155–1158
13. Paulus EM, Zarzaur BL, Behrman SW. Routine peritoneal drainage of the surgical bed after elective distal pancreatectomy: is it necessary? *Am J Surg* 2012;**204**(4):422–427
14. Conlon KC, Labow D, Leung D, Smith A, Jarnagin W, Coit DG *et al*. Prospective randomized clinical trial of the value of intraperitoneal drainage after pancreatic resection. *Ann Surg* 2001;**234**(4):487–493
15. Fisher WE, Hodges SE, Silberfein EJ, Artinyan A, Ahem CH, Jo E *et al*. Pancreatic resection without routine intraperitoneal drainage. *HPB (Oxford)* 2011;**13**(7):503–510
16. Ecker BL, McMillan MT, Allegrini V, Bassi C, Beane JD, Beckman RM *et al*. Risk factors and mitigation strategies for pancreatic fistula after distal pancreatectomy: analysis of 2026 resections from the international, multi-institutional distal pancreatectomy study group. *Ann Surg* 2019;**269**(1):143–149
17. Adham M, Chopin-Lay X, Lepilliez V, Gincul R, Valette PJ, Ponchon T. Pancreatic resection: drain or no drain? *Surgery* 2013;**154**(5):1069–1077

18. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M *et al*. The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. *Surgery* 2017;**161**(3):584–591
19. Wente MN, Bassi C, Dervenis C, Fingerhut A, Gouma DJ, Izbicki JR *et al*. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). *Surgery* 2007;**142**(5):761–768
20. Wente MN, Veit JA, Bassi C, Dervenis C, Fingerhut A, Gouma DJ *et al*. Postpancreatectomy hemorrhage (PPH): an International Study Group of Pancreatic Surgery (ISGPS) definition. *Surgery* 2007;**142**(1):20–25
21. Weber SM, Cho CS, Merchant N, Pinchot S, Rettammel R, Nakeeb A *et al*. Laparoscopic left pancreatectomy: complication risk score correlates with morbidity and risk for pancreatic fistula. *Ann Surg Oncol* 2009;**16**(10):2825–2833
22. Seeliger H, Christians S, Angele MK, Kleespies A, Eichhorn ME, Ischenko I *et al*. Risk factors for surgical complications in distal pancreatectomy. *Am J Surg* 2010;**200**(3):311–317
23. Kawai M, Tani M, Okada K, Hirono S, Miyazawa M, Shimizu A *et al*. Stump closure of a thick pancreas using stapler closure increases pancreatic fistula after distal pancreatectomy. *Am J Surg* 2013;**206**(3):352–359
24. Chang YR, Kang MJ, Kim H, Jang JY, Kim SW. The natural course of pancreatic fistula and fluid collection after distal pancreatectomy: is drain insertion needed? *Ann Surg Treat Res* 2016;**91**(5):247–253
25. Ferrone CR, Warshaw AL, Rattner DW, Berger D, Zheng H, Rawal B *et al*. Pancreatic fistula rates after 462 distal pancreatectomies: staplers do not decrease fistula rates. *J Gastrointest Surg* 2008;**12**(10):1691–1698
26. Yamashita S, Ishizawa T, Ichida A, Kaneko J, Aoki T, Sakamoto Y *et al*. Advantages and disadvantages of proohylactic abdominal drainage in distal pancreatectomy. *World J Surg* 2016;**40**(5):1226–1235