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ORIGINAL ARTICLE

The rate of postoperative pancreatic fistula after distal pancreatectomy is independent of the pancreatic stump closure technique – A retrospective analysis of 284 cases



(2) (2) (3)

Asian

Journal of Surgery

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Received 9 January 2019; received in revised form 6 February 2019; accepted 7 March 2019 Available online 11 April 2019

KEYWORDS

Distal pancreatectomy; Postoperative pancreatic fistula; Hand-sewn; Stapler closure **Summary** Background: Many techniques have been developed to prevent postoperative pancreatic fistula (POPF) after distal pancreatectomy, but POPF rates remain high. The aim of our study was to analyze POPF occurrence after closure of the pancreatic remnant by different operative techniques.

Methods: Between 2006 and 2017, 284 patients underwent distal pancreatectomy in our institution. For subgroup analysis the patients were divided into hand-sewn (n = 201) and stapler closure (n = 52) groups. The hand-sewn closure was performed in three different ways (fishmouth-technique, n = 27; interrupted transpancreatic U-suture technique, n = 77; common interrupted suture, n = 97). All other techniques were summarized in a separate group (n = 31). Results were gained by analysis of our prospective pancreatic database. *Results:* The median age was 63 (range 23–88) years. 74 of 284 patients (26%) were operated with spleen preservation (similar rates in subgroups). ASA-classes, median BMI as well as

frequencies of malignant diseases, chronic pancreatitis, alcohol and nicotine abuse were also comparable in the subgroups. Neither the rates of overall POPF (fishmouth-technique 30%, common interrupted suture 40%, stapler closure 33% and interrupted U-suture 38%) nor the rates of POPF grades B and C showed significant differences in the subgroups. However is shown to be associated with pancreatic function and parenchymal texture.

https://doi.org/10.1016/j.asjsur.2019.03.009

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Conclusion: In our experience the technique of pancreatic stump closure after distal resection did not influence postoperative pancreatic fistula rate. As a consequence patient specific reasons rather than surgical techniques may be responsible for POPF formation after distal pancreatectomy.

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1. Background

Distal pancreatectomy is a common procedure for benign and malignant diseases of the pancreatic body and tail. Most distal pancreatectomies are done electively, about one fifth for pancreatic adenocarcinoma and one fourth for chronic pancreatitis. The procedure can be performed with or without splenectomy. Although the rate of spleen preserving distal pancreatectomies is increasing, over 80% of distal pancreatectomies include a splenectomy.^{1,2}

Recent advances in pancreatic surgery have reduced postoperative mortality, which is now reported to be less than 3% after pancreatic resections,³⁻⁵ but morbidity due to postoperative pancreatic fistula (POPF) remains essentially unchanged and is observed in 16%–44% of cases.⁶⁻¹⁰ Pancreatic fistula is associated with further complications such as abscesses, sepsis, intraabdominal bleeding, prolonged hospitalization and increased costs of care.^{11–13}

Many surgical techniques to close the pancreatic stump have been developed to reduce pancreatic fistula rate after distal pancreatectomy. These include hand-sewn suture techniques, stapler closure, pancreatoenteric anastomoses or seromuscular/serosal patches. The application of meshes, sealing with fibrin glue, absorbable sealants, or even the combination of multiple techniques did not show any substantial reduction in fistula rate. All these methods are still controversial and are applied by each surgeon empirically.^{14–20}

In older reports the incidence of POPF varied greatly between publications due to different definitions being used to classify pancreatic fistulas. Currently, the definition of the International Study Group of Pancreatic Fistula (ISGPF) is applied, which divides POPF into biochemical leak (BL) as well as B and C fistulas. While the biochemical leak does not require further action, grade B and C fistulas require therapeutic measures making these fistulas clinically relevant.²¹

The aim of this study was to retrospectively compare relevant morbidity and investigate postoperative complications after distal pancreatectomy with different techniques of pancreatic stump closure.

2. Patients and methods

A retrospective analysis of our continuously collected clinical data of all 284 patients, who underwent elective distal pancreatectomy since 2006 at the Clinic of General and Visceral Surgery at University Hospital of Freiburg, Germany, was performed. There were not any special exclusion or inclusion criteria. The surgeons were trained and experienced for all performed operations. We performed distal pancreatectomies in patients with malignant and benign disease located left of the portomesenteric venous axis. Pancreas resections for IPMN were indicated according to the international Fukuoka guidelines and European evidence-based guidelines on pancreatic cystic neoplasms.^{22–24} Patients with chronic pancreatitis and inadequate pain relief or complications from chronic pancreatitis also underwent surgery.

2.1. Surgical technique

Operations were performed laparoscopically, laparoscopically assisted or open via transverse laparotomy.

In all laparoscopically performed cases we used 4-5 ports (two 12 mm ports and 2 or 3×5 mm ports). After severing the lig. gastrocolicum, entrance into the lesser sac was achieved and the lower pancreatic margin was mobilized. Subsequently, the upper pancreatic margin was mobilized and the arterial vessels were localized. The pancreas was tunneled over the portal vein before further dissection. The pancreas was then divided by a stapler or by a high energy device. In cases of splenectomy the spleen was mobilized to be retrieved en bloc with the pancreas and the specimen was removed via a small incision in the epigastrium.

In laparoscopic assisted procedures the dissection was performed in a similar technique. After removal of the specimen with a 4-6 cm median epigastric incision, the pancreatic remnant was covered using a hand-sewn technique.

The open technique was performed using a transverse subcostal laparotomy. After exploration of the abdomen the lesser sac was entered via the lig. gastrocolicum, the left colonic flexure was mobilized, and splenic vessels prepared and either ligated or preserved depending upon whether a splenectomy was performed. The distal pancreas was then mobilized and transected and the remnant was closed using different techniques.

2.2. Closure of the pancreatic remnant after distal resection

For the purpose of our study the surgical techniques used for closure of the pancreatic remnant were categorized into three main groups: I) stapler closure (transection and

remnant closure with a stapling device, n = 52), II) handsewn stump closure (n = 201) and III) other combined techniques like stapler closure combined with suturing, hand-sewn or stapler closure reinforced with fibrin coated collagen fleece or liquid fibrin sealant, serosal patch and pancreatogastrostomy (n = 31).

In hand-sewn techniques the pancreatic duct was always ligated using a polydioxanone 5-0 suture.

The hand-sewn techniques in group II included the Fishmouth-technique (wedge-shaped excision of pancreas cut surface, ligation of the main pancreatic duct and hand sewn interrupted suture of the parenchyma; n = 27) or closure by two different types of seromuscular patch covering of the pancreatic remnant using the second jejunal loop (Omega-loop, without opening the lumen): hereby the fixation of the intestine to the pancreatic remnant was achieved by either three or four interrupted transpancreatic U-sutures (polydioxanone 4-0; n = 77) or by common interrupted seromuscular sutures (polydioxanone 4-0; n = 97) (Fig. 1).

In further sub-analysis the outcome was compared between the five subgroups with stapler closure, hand-sewn closure (three subgroups) and the remaining other closure techniques.

There was no preference given to a single surgical technique. The method of stump closure was purely chosen by the surgeon at the time of the operation and varied over time (Table 4).

2.3. Definition of POPF and statistical analysis

BL, B, and C postoperative pancreatic fistulas were defined in accordance with the ISGPF classification.²¹

Patient characteristics, indications for distal pancreatectomy, surgical technique, and perioperative outcome were continuously documented in a prospectively maintained SPSS database (IBM SPSS Statistics for Windows, Version 22.0. Armonk, NY: IBM Corp). Statistical differences between the subgroups were tested using the Kruskal-Wallis and Chi-square tests.

3. Results

The median age of patients was 63 (23-88) years and was distributed similarly between all groups. Gender was also comparable between the groups (Table 1). In 129 patients (45.4%) histopathological evaluation revealed benign disease while in the remainder of cases primary malignancy of the pancreas or metastases were diagnosed. The detailed histopathological diagnosis was summarized in Table 1. Although there was an observed difference between the number of underlying pathologies, the rate of PDAC patients was similar throughout the groups of surgical techniques. The rate of POPF was not significant different between the surgical techniques in patients with PDAC (PDAC POPF B and C: Fishmouth technique 33%, stapler





Figure. 1 Four different techniques of pancreas remnant closure.

Stump closure with jejunal-loop with

	All	Fishmouth	Stapler	Interrupted	Common	Others	Р
	n = 284	Technique	Closure	U-suture	Interrupted	n = 31	
		n = 27	n = 52	n = 77	n = 97		
Male n, (%)	141 (50%)	12 (44%)	27 (52%)	42 (54%)	40 (41%)	20 (64%)	0.16
Age in y (median)	63 (23-88)	64 (23-83)	61 (28-88)	64 (40-84)	62 (28-83)	64 (23-81)	0.70
BMI (median)	21 (13–35)	21 (13-30)	21 (14–29)	22 (14–34)	21 (15–35)	21 (17-32)	0.99
ASA class (n,%)							0.46
ASA 1	21 (7%)	4 (15%)	3 (6%)	8 (10%)	4 (4%)	2 (6%)	
ASA 2	149 (52.5%)	16 (59%)	27 (52%)	44 (57%)	48 (49%)	14 (45%)	
ASA 3	107 (38%)	7 (26%)	21 (40%)	24 (31%)	42 (43%)	13 (42%)	
ASA 4	7 (2.5%)	0	1 (2%)	1 (1%)	3 (3%)	2 (6%)	
Nicotine abuse (n, %)	65 (23%)	9 (33%)	12 (23%)	15 (19%)	21 (22%)	8 (26%)	0.66
Alcohol abuse (n, %)	25 (9%)	1 (4%)	8 (15%)	4 (5%)	9 (9%)	3 (10%)	0.29
Indication							0.004
PDAC	103 (36%)	15 (56%)	21 (40%)	27 (34%)	31 (32%)	9 (29%)	
Metastasis	24 (8%)	1 (4%)	6 (11%)	8 (10%)	6 (6%)	3 (8%)	
IPMN	32 (11%)	0	7 (13%)	12 (16%)	13 (13%)	0	
NET	28 10%)	0	0	12 (16%)	15 (15%)	1 (3%)	
MCN	13 (5%)	1 (4%)	3 (6%)	0	6 (6%)	3 (10%)	
SCN	32 (11%)	3 (11%)	6 (11%)	8 (10%)	11 (11%)	4 (13%)	
vCP	29 (10%)	5 (18%)	3 (6%)	5 (7%)	7 (7%)	9 (29%)	
Other benign	23 (8%)	2 (7%)	6 (11%)	5 (6%)	8 (8%)	0	

PDAC, pancreatic ductal adenocarcinoma; IPMN, intraductal papillary mucinous neoplasm; NET, neuroendocrine tumor; MCN, mucinous cystic neoplasm; SCN, serous cystic neoplasm; CP, chronic pancreatitis.

closure 33%, interrupted U-suture 32%, common interrupted suture 29%, others 33%). Further demographic data as ASA, BMI, alcohol abuse and smoking were distributed similarly in the groups.

The operative procedure included splenectomy in 210 (74%) patients and adrenalectomy in 73 (26%) patients. The 74 of the 284 patients (26%) that were operated using a spleen preserving technique showed a similar distribution over the five stump closure groups (Table 2). There was no significant differences in the rate of gastric resection (n = 26 (9%)), liver resection (n = 20 (7%)) and resection of colon (n = 36 (13%)) in these groups. 125 patients (44%) were operated laparoscopically or laparoscopically assisted. All patients in the Fishmouth technique group were operated via a laparotomy. The median blood loss was not

significantly different between the groups, while duration of surgery by using a stapler closure of the pancreatic remnant was significantly shorter (Table 2).

One (0.3%) 84 year old Patient died postoperatively due to acute basilar artery thrombosis. There was no postoperative mortality due to surgical complications.

Clinically relevant pancreatic fistulas were detected in 104 Patients (37%). The technique of pancreatic stump closure did not influence the rate of postoperative pancreatic fistula formation (all grades) or the rate of POPF B and C (Table 3). There was not also significant difference between pancreatic stump closure groups in different period of time (Table 4).

In contrast to the technique of stump closure, no difference was observed between the individual underlying

	All	Fishmouth technique	Stapler closure	Interrupted U-suture	Common interrupted	Others	Ρ
Access n, (%) Lap./lap. assisted open	284 125 (44%) 159 (56%)	27 0 27 (100%)	52 27 (52%) 25 (48%)	77 37 (48%) 40 (52%)	97 58 (60%) 49 (40%)	31 3 (10%) 29 (90%)	0.001
Splenectomy n, (%) Duration of surgery in minutes (median, range)	210 (74%) 279 (97–713)	22 (81%) 271 (140–490)	37 (71%) 194 (97–544)	53 (69%) 306 (154–623)	72 (74%) 292 (170–713)	26 (84%) 270 (140–530)	0.46 0.001
ml intraoperative blood transfusion (PRBC; median, range)	0 (0–2100)	0 (0—600)	0 (0—600)	0 (0—2100)	0 (0—1200)	0 (0–2000)	0.48

Table 2 Surgical data: Surgery with the stapler technique was significantly faster. The Fishmouth technique was not done laparoscopically. Blood transfusion and rates of splenectomy were similar in all groups.

	All n (%)	Fishmouth Technique n (%)	Stapler Closure n (%)	Interrupted U-suture n (%)	Common Interrupted n (%)	Others n (%)	Ρ
All (BL-C)	171 (60%)	15 (56%)	36 (69%)	44 (57%)	57 (59.6%)	19 (61%)	
BL	67 (24%)	7 (26%)	19 (36%)	15 (20%)	18 (19%)	8 (26%)	0.51ª
POPF B	87 (31%)	4 (15%)	15 (29%)	23 (30%)	35 (36%)	10 (32%)	
POPF C	17 (6%)	4 (15%)	2 (4%)	6 (8%)	4 (4%)	1 (3%)	0.85 ^b

Table 3 The rate of postoperative pancreatic fistula after distal pancreatectomy was not significantly different between the

omparison POP

^b Comparison only POPF B/C.

pathologies and the rate of POPF. However, when comparing patients with a normal exocrine pancreatic function (IPMN (41%) and SCN (43%)) to an impaired exocrine function (chronic pancreatitis (17%) and adenocarcinoma (22%)), it can be shown that patients with a normal exocrine function develop a significantly higher rate of POPF (p = 0.02). Obesity (BMI > 25 kg/m²) was also a significant risk factor for POPF development (45% vs. 27%, p < 0.05).

The rate of overall postoperative complications (n = 159(56%)) including intraabdominal fluid collections (n = 62(22%)), delayed gastric emptying (DGE) (n = 26 (9%)), hemorrhage (n = 21 (7%)) relaparotomy rate (n = 36 (13%)) wound infection (n = 21 (7%)), burst abdomen (n = 6 (2%)) and sepsis (n = 3 (1%)) were not significantly different between the groups.

4. Discussion

The outcome after pancreatic surgery has improved substantially over the past decades. Despite decreased mortality, postoperative pancreatic fistula formation remains the Achilles' heel of pancreatic surgery. POPF are responsible for a substantial amount of postoperative morbidity. Pancreatic fistula formation is eventually associated with subsequent severe complications and reoperations.²⁵ As a consequence, the development of pancreatic fistula correlates with the duration of hospital stay and costs of treatment.^{12,13}

A common belief is that the closure technique of the pancreatic remnant after distal pancreatectomy can influence POPF. This has driven numerous surgeons to develop novel techniques of pancreatic stump closure. However, many techniques have failed to improve the rate of clinically significant POPFs.^{6,11,26} No improvement could be shown between suture, stapler and radiofrequency ablation.27

Until recently techniques were reported on an anecdotal basis summarizing the results obtained in case series with only a small number of patients.²⁸⁻³⁰ The first prospective trial comparing hand suture with stapler techniques demonstrates new evidence of two different techniques of pancreatic stump closure after distal pancreatectomy.¹¹ In addition to the substantially higher rate of pancreatic fistula after distal pancreatectomy in this prospective randomized trial, when compared to reports by many authors,

Table 4 Rate of pancreatic fistula in different period of time. Despite the difference of surgeons and techniques the rate of POPEs was not significantly affected.

2006–2009	All n = 59	Fishmouth Technique n = 27	Stapler Closure n = 9	Interrupted U-suture n = 1	Common Interrupted n = 14	Others $n = 8$	Ρ
BL n, %	19 (32%)	7 (26%)	6 (67%)	0	5 (36%)	1 (13%)	0.36
POPF B n, %	12 (20%)	4 (15%)	2 (22%)	1 (100%)	3 (21%)	2 (25%)	
POPF C n, %	6 (10%)	4 (15%)	0	0	1 (7%)	1 (13%)	
2010–2013	All n = 87	Fishmouth Technique n = 0	Stapler Closure n = 27	Interrupted U-suture n = 37	Common Interrupted n = 13	Others $n = 10$	Р
BL n, %	19 (22%)	0	6 (22%)	6 (16%)	3 (23%)	4 (40%)	0.55
POPF B n, %	23 (26%)	0	8 (30%)	11 (30%)	1 (8%)	3 (30%)	
POPF C n, %	4 (5%)	0	2 (7%)	2 (5%)	0	0	
2014–2018	All n = 138	Fishmouth Technique n = 0	Stapler Closure n = 16	Interrupted U-suture n = 39	Common Interrupted n = 70	Others $N = 13$	Р
BL n, %	29 (21%)	0	7 (44%)	9 (23%)	10 (14%)	3 (23%)	0.23
POPF B n, %	52 (38%)	0	5 (31%)	11 (28%)	31 (44%)	5 (38%)	
POPF C n, %	7 (5%)	0	0	4 (10%)	3 (4%)	0	

there was also no effect shown when two completely different techniques were utilized. This led us to the idea to study our own population of patients after distal pancreatectomy over time since our technique of pancreas stump closure changed substantially over the years. In the initial resections distal pancreatectomies were performed as open procedures and the pancreatic remnant was closed by the traditional Fishmouth technique. With the development of laparoscopic procedures, the pancreatic remnant was increasingly closed by stapler and thereafter different techniques of parenchyma-serosal patches were performed.

The limitation of the study is its retrospective character despite a continuous data collection. The main finding that could be extracted from our study is that the surgical technique did not influence the rate of pancreatic fistula formation. However, our finding appears to stand in contrast to a multitude of authors that report improved fistula rates after applying a certain technique for stump closures.²⁹⁻³² Even small modifications of established techniques such as comparing stapler closure to a mesh reinforcement stapler technique demonstrated an impressive improvement in the rate of POPF formation.³¹ A decrease in POPF was reported e.g. by Sudo et. al, who examined a duct-to-mucosa pancreatogastrostomy after distal pancreatectomy,²⁹ and Wagner et al. when patients with pancreatojejunostomy and simple suturing of the pancreatic remnant were compared.³⁰ Fujii et al. investigated patients with placement of an elevated jejunum patch using the modified Blumgart method after scalpel transection compared to scalpel transection alone.³³ However, all studies were characterized by a small patient collective and the exceptional results could frequently not be reproduced by other surgeons.

We observed clinically relevant postoperative pancreatic fistula formation in 37% of cases, which is higher than the 5–29% previously reported. ^{1,3,26,34,35} To compare fistula rates is difficult since a certain variability of the definition of POPF is applied in the different centers. This was improved by the general acceptance of the ISGPF definition of pancreatic fistula³⁶ rendering the data comparable between centers despite eventual interference with institutional standards. According to this classification the single multicenter, randomized controlled trial revealed POPF in 36% of cases. ¹¹ In our series 87 (31%) patients showed POPF grade B and 17 (6%) POPF grade C. The Fishmouth technique and stapler closure led to a lower fistula rate without statistical significance.

The rate of POPF was independent of the closure technique, however it was associated with pancreatic function and parenchymal texture, depending on the underlying pathology as shown so far by several authors. $^{37-40}$

Conflict of interest

The authors declare no conflict of interest.

Funding

No funding was received for this study.

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