Surgical Oncology 30 (2019) 76–80

Contents lists available at ScienceDirect

Surgical Oncology

journal homepage: www.elsevier.com/locate/suronc

Drainage after distal pancreatectomy: Still an unsolved problem

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ARTICLE INFO

Keywords:
Pancreas fistula
Technique
Drainage

ABSTRACT

Background: The use of intraperitoneal drainage after distal pancreatectomy is still controversial. Its use increases fistula risk, but its absence increases the severity of the fistula. Therefore, since 2014, we have systematically used two drains.

Methods: This study examined consecutive patients undergoing distal pancreatectomy with splenectomy. Two drains were routinely used. One closed-suction-type drain is placed in the left subphrenic space with the aim to avoid the accumulation of any fluid coming from the pancreatic stump. The second is a tubulo-laminar drain placed near the pancreatic stump. These patients were compared with a cohort of patients (n = 94) before the adoption of this strategy (control group).

Results: 127 patients underwent distal pancreatectomy. 48 patients presented no POPF, 60 patients presented biochemical leak and in 19 patients (14.9%), drain amylase level was high and the drain was removed at 4 weeks, classified as grade-B according to the Revised 2016 ISGPS or B1 according to grade-B subclass. No grade-C was observed. The comparison with the 94 patients in the control group with single drainage, the occurrence of POPF was not different. However, in the control group, POPF severity was statistically higher (grade-B 14.9% vs 33%; grade-C 0% vs 3,2%; P = 0.00026).

Conclusions: Since changing the drainage strategy, we have observed a dramatic decrease in pancreatic abscess formation and fluid collections needing percutaneous drainage. The results of this study show that the strategy of double drainage after distal pancreatectomy may reduce the severity of POPF, thus avoiding reoperation or further interventions.

1. Introduction

Distal pancreatectomy is the standard surgical procedure for benign or malignant lesions in the body or tail of the pancreas. Although mortality is decreased considerably after distal pancreatectomy, morbidity remains high. Clinically relevant postoperative pancreatic fistula (CR-POPF) is the most important complication and is responsible for prolonged hospital stays, increased costs, and delayed adjuvant treatment in malignant disease [1].

A recent multicenter study analyzed different strategies used to reduce or avoid CR-POPF, as well as risk factors for its occurrence. Despite the large cohort, the occurrence of CR-POPF could not be reliably predicted. The use of intraperitoneal drainage was significantly associated with increased fistula risk. However, when a fistula occurred in the absence of an operatively placed drain, it was more likely to be severe and require an interventional procedure. Therefore, prophylactic drainage has a potential role in reducing the severity of the fistula [2,3].

Despite several centers performed distal pancreatectomies without any drainage early or late fluid collection are not uncommon even in patients with abdominal cavity drainage. In fact, peri pancreatic fluid collections occur in up to 30% of patients following partial pancreatic resections [4]. Most of these patients are managed via percutaneous drainage or more recently by endoscopic ultrasound guided trans gastric drainage. Both methods have been shown to be effective for the management of these collections. However, fluid collection is mainly located in sub phrenic space usually complicated with pleural effusion pulmonary complication adding a significant burden of suffering to the patients besides additional costs.

According to some authors, routine drainage after pancreatic resection is associated with longer hospital stay and higher rates of pancreatic fistula. Therefore, they advocate abandoning the method, even after pancreaticoduodenectomy [5]. However, a randomized prospective multicenter trial was initiated in 2011 but was stopped early by The Data Safety Monitoring Board because of an increase in mortality from 3% to 12% in the patients who underwent pancreaticoduodenectomy without intraperitoneal drainage [6].

The current data suggest that the presence of a drain itself does not protect against the development of a postoperative fluid collection,

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https://doi.org/10.1016/j.suronc.2019.06.002
Received 14 February 2019; Received in revised form 10 April 2019; Accepted 4 June 2019

including pseudocyst and abscess formation. This probably occurs because drains are often isolated from fluid that accumulates after these procedures [7]. There is also evidence that closed suction drains may also promote pancreatic fistula. On the other hand, its absence may lead to a more severe fistula and increased morbidity. We hypothesized that the incorrect installation of the drains and not the presence or absence of drains may be related to complications after distal pancreatectomy. In our opinion, the solution may be to use a drain that does not usually clog and does not promote fistula formation, as well as another drain that prevents the fluid from collecting away from the pancreatic bed (usually the left subphrenic area). Therefore, since 2014, we have systematically used two drains after distal pancreatectomy.

2. Methods

2.1. Study design and setting

This observational study includes a cohort of patients who were treated at an urban referral center for pancreas diseases in São Paulo, Brazil. All patients undergoing pancreas resection at our institution are recorded in a database that is prospectively maintained by our hepato-pancreato-biliary (HPB) fellows and clinical study nurses and is presented to a multidisciplinary tumor board. This study retrospectively examined consecutive patients undergoing distal pancreatectomy with splenectomy for benign or malignant diseases by open or laparoscopic procedures by this team in the period between January 2014 and June 2018. All patients had follow-up with data collection sheets in our surgical clinic. Patients with spleen-preserving distal pancreatectomy and enucleation were excluded from the analysis. This cohort of patients were later compared with historic cases before the adoption of two-drain policy.

2.2. Postoperative pancreatic fistula (POPF) definition

Postoperative pancreatic fistula (POPF) was defined according the International Study Group of Pancreatic Fistula criteria stablished in 2016 [8,9].

According to this new classification, the increase in amylase content of the abdominal fluid alone is no longer enough to define POPF, only if associated with an impaired clinical condition caused by the pancreatic leak. Grade A POPF has been replaced with a new category characterized by an asymptomatic pancreatic leak called “biochemical leak” (BL). The drain *in situ* for an extended period (up to 3 weeks) following the discharge was explicitly approved for this condition.

Since Grade-B POPF is not a homogeneous entity, 3 distinct subclasses with increasing clinical and economic burden were recently identified. This classification framework has potential implications for accurate reporting, comparative research, and performance evaluation [10]. Grade-B POPF was then stratified in three subclasses (B1–B3), according to the recent proposal of Maggino et al. [10] These were: B1, maintenance of abdominal drain over 3 weeks, without the need for any further POPF related treatment; B2, the use of pharmacologic agents for the treatment of POPF, with or without persistent drainage > 3 weeks; and B3, the adoption of any interventional (non-surgical) procedure (percutaneous drainage and/or embolization) [10,11].

2.3. Drainage technique

After open or minimally invasive distal pancreatectomy with splenectomy, the abdominal cavity is drained. Two drains are routinely used. The first drain (drain 1) is a closed-suction-type drain that is inserted in the left subphrenic space in the splenic fossa and is usually exteriorized in the left quadrant. This drain is inserted to avoid the accumulation of any fluid coming from the pancreatic stump in the splenic fossa (Fig. 1A).

The second drain (drain 2) is a tubulo-laminar drain that is placed near the pancreatic stump and exteriorized in the left or right quadrant at the discretion of surgeon. This drain has no negative pressure, so it has no influence in causing or maintaining a pancreatic fistula. This type of drain is also less prone to clogging, and if a pancreatic fistula occurs, it maintains the outflow, which reduces the severity of POPF and avoids further percutaneous drainage (Fig. 1B).

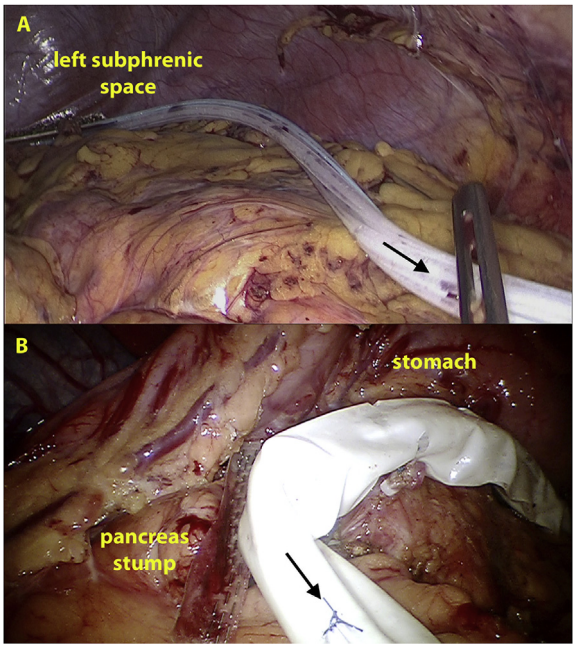

Fig. 1. Double drainage after distal pancreatectomy.
A. Drain 1. Closed-suction drain is placed in the left subphrenic space in front of the stomach and behind the liver left lobe. Arrow shows direction of the fluid.
B. Drain 2. Tubulo-laminar drain near the pancreatic stump, behind the stomach. Arrow shows direction of the fluid.

The fluid from both drains is analyzed, and the amylase level is determined on the 3rd and 5th days post-operation. In cases where the aspect of the drain has changed after this period and the drain is still in place, the drain amylase level is retested. If the result is abnormal, the drain is maintained for 3–4 weeks.

2.4. Drain removal

The first drain is removed 5–7 days after surgery if the fluid amylase content is less than 3 times the normal plasma level. The second drain is removed after 9 days if amylase content is also less than 3 times the normal plasma amylase level. If the amylase level is high, the drain is kept for 3 weeks and removed if the volume drained is less than 20 mL, irrespective of the amylase level. If the volume is greater than 20 ml, the drain is removed after 4 weeks, irrespective of the amylase level. The patient is discharged from the hospital independently of the amylase level or the presence of the drain. The patient is instructed to record the drainage volume and return for drain removal after 3 weeks if the drain volume decreases to less than 20 mL. Otherwise, a return is scheduled after 4 weeks for drain removal.

During follow-up, patients with any abdominal symptoms underwent additional imaging and laboratorial studies.

2.5. Control group

The cohort of patients with two-drains strategy was compared to the patients operated on by the same team before the adoption of this new strategy. Ninety-four patients undergoing distal pancreatectomy were identified in our prospective databank between January 2010 and December 2013. In all patients, a single drain (the same type as drain 2

used in two-drain strategy, previously described) was inserted in the cavity.

2.6. Statistical analysis

Results are reported as mean and standard deviation for numerical variables (after verification of the normality of the distribution) and as counts and percentages for categorical data. Comparison between groups was performed using the student's *t*-test for paired data with equal variance for numerical data (after verification of the normality of the distribution) and with the Chi square for the categorical data. A value of $p < 0.05$ was considered significant.

3. Results

During the study period, 207 patients underwent distal pancreatectomy. Among them, 53 patients who were subjected to spleen-preserving distal pancreatectomy and 27 who underwent enucleation were excluded from the analysis. A total of 127 patients underwent distal pancreatectomy, of which 65 involved a minimally invasive approach and 62 involved conventional open surgery. Two patients underwent conversion to open surgery due to portal vein invasion. There were 76 females and 51 males with a median age of 61.2 years (range: 12–87 years). The main indication for the procedure was ductal adenocarcinoma (PDAC) in 54 patients (42.5%), followed by neuroendocrine tumor [NET; N = 34 (26.8%)], intraductal papillary mucinous neoplasm [IPMN; N = 13 (10.2%)], chronic pancreatitis (8 patients, 6.3%), solid pseudopapillary neoplasm (5 patients, 3.9%), mucinous cystadenoma (5 patients, 3.9%), and other indications (8 patients, 6.3%).

The mean size of the pancreatic tumor was 4.1 cm (range: 0.8–25.5 cm), and 14.1 (range: 2–68) lymph nodes were removed. The median hospital stay was 6 days (range: 2–36 days). Three patients needed blood transfusion. No mortality was observed. Four patients (3.1%) presented postoperative complications that were unrelated to the pancreatic surgery. Two patients presented pulmonary embolism and had prolonged hospital stays. Two patients presented cardiac complications: one with cardiac congestive heart failure and one with arrhythmia. Surgical complications other than pancreatic fistula occurred in four patients (3.1%). Two of these patients presented delayed gastric emptying, one patient presented asymptomatic portal vein thrombosis, and one patient (87 years old) presented postoperative bleeding due to anticoagulant therapy, which was controlled after suspension of the drug and transfusion. These patients had prolonged hospital stays. Patients demographic data are given in detail in Table 1.

Analysis of the fluid content from drain 1 revealed result in the normal range (up to 2 times the plasma level) in 125 patients, and the drain was removed between the 5th and 7th postoperative days. In two patients, there was communication between both drains, so drain 1 was maintained for three weeks. Analysis of the fluid content from drain 2 revealed results in the normal range in 48 patients (37.8%), and the drain was removed after 9 days. In 79 patients (62.2%), the amylase level was above 3 times the normal plasma level.

In 60 patients, the volume drained was less than 20 mL and drain was removed before three 3 weeks and considered as biochemical leak [8,9]. In 19 patients, the volume drained was greater than 20 mL, and the drain was removed after 4 weeks (Fig. 2).

According to the Revised 2016 ISGPS grading of POPF [8], 48 patients (37.8%) had no POPF, 60 (47.2%) presented biochemical leak and 19 patients (14.9%) presented with grade-B POPF. No grade C POPF was observed.

According to a more recent proposal [10], all 19 patients presented with grade-B1 POPF (maintenance of abdominal drain over 3 weeks, without the need for any further POPF related treatment).

During the 90-day follow-up, no patient needed reoperation or presented persistent abdominal collection. Therefore, no patient needed percutaneous drainage as treatment or additional treatment such as antibiotics. In most patients, the pancreas was divided using a stapler with or without bioabsorbable staple-line reinforcement. In 12 patients (9.4%), the pancreas was too thick to divide it with a stapler and was divided by a harmonic scalpel or conventional scalpel. In all these patients, the amylase fluid content from drain 2 was greater than expected (up to 3 times the normal plasma level). This was significantly higher than those in which the pancreas was divided by a stapler ($p < 0.05$). Furthermore, the average amylase level from these patients (18794 U/L) was significantly higher ($p < 0.05$) than in patients with a stapled pancreas (5718 U/L). When comparing laparoscopic and open operation, there was no significant difference in amylase level or duration of the drainage. The only difference was the hospital stay that was shorter in the minimally invasive group ($p < 0.05$). Operative times and estimated blood loss were equivalent.

3.1. Comparative study with control group

The cohort of patients with two-drain strategy was compared with another cohort of patients undergoing the same surgical procedure before the adoption of this new strategy as a control group for comparison.

Table 2 shows the main clinical and surgical data from both groups. Both groups were comparable in terms of gender distribution, age, BMI, ASA and diagnosis. The number of patients operated on using minimally invasive technique was lower in the control group but not statistically different. The technique of pancreas division did not differ between both groups (Table 2).

Post-operative pancreatic fistula occurrence was not different between both groups (Table 2). However, severity of POPF was greater in the control group. In the two-drain strategy, no grade-C fistula, no grade-B2 or B3 occurred while in the control group there was 3.2% of grade-C POPF and 8.5% of grades B2 and B3 POPF. When comparing no POPF and BL vs occurrence of grade-B and C, between two-drain group vs control group (85.1% and 14.9% vs 63.8% and 36.2%; P = 0.00026) we observed a statistical difference in terms of severity of POPF between both groups. Analysis of the grade-B POPF subclasses (B1 vs B2/B3) showed the same result (P = 0.01508). Comparison between morbidity other than POPF, estimated blood loss, need for transfusion and operative time were similar in both groups (Table 2). However, median hospital stay was longer in the control group (P = 0.127). Mean amylase level (drain 2 vs single drain) was higher in the control group (Table 2).

4. Discussion

CR-POPF is the most significant complication after pancreatic resection. In a recent study, several perioperative factors were independently associated with pancreatic fistula, such as obesity, age (< 60 years), hypoalbuminemia, nonmalignant pathology, or a neuroendocrine tumor and a concomitant splenectomy. However, including these factors in a clinical risk score resulted in poor predictive capabilities, which made mitigation strategies ineffective [2]. Moreover, prophylactic drainage reduced the severity of the fistula.

Many methods have been utilized for pancreatic transection and subsequent stump treatment. However, randomized trials have not identified a superior method for either parenchymal division or stump treatment, including the optimal drainage of the remnant pancreas. In our series, the incidence and the severity of fistulas were not different between methods of pancreas transection, but a significantly lower amylase content in the drain fluid was noted when the stapler was used.

CR-POPF grades B and C occur in 9–16% of cases after distal pancreatectomy [12–14]. Several strategies are used to minimize the occurrence of CR-POPF, including an increasing use of minimally invasive techniques. Nevertheless, its incidence has been stable over the years. A recent systematic review with more than 22,000 patients showed an incidence of 15.5% of grades B and C POPF after distal pancreatectomy

Table 1
Patient characteristics.

	All (n = 127)	No POPF (n = 48)	Biochemical leak (n = 60)	Grade-B1 POPF (n = 19)	P value
Sex					0.5197
M	51 (40.2%)	21 (43.8%)	25 (41.7%)	5 (26.3%)	
F	76 (59.8%)	27 (56.2%)	35 (58.3%)	14 (73.7%)	
BMI	24.8	23.9	24.6	27.2	**0.0024**[a]
ASA					0.8402[a]
1 or 2	119	44	57	18	
> 2	8	4	3	1	
Mean age, years	61.2	59.6	62.3	64.4	0.2252
Diagnosis					**0.0147**[b]
PDAC	54 (42.5%)	27 (56.3%)	20 (33.3%)	7 (36.8%)	
NET	34 (26.8%)	10 (20.8%)	19 (31.7%)	5 (26.3%)	
IPMN	13 (10.2%)	3 (6.3%)	8 (13.3%)	2 (10.5%)	
CP	8 (6.3%)	4 (8.3%)	3 (5%)	1 (5.3%)	
Mucinous cystadenoma	5(3.9%)	1 (2.1%)	4 (6.7%)	0	
SPN	5(3.9%)	1 (2.1%)	2 (3.3%)	2 (10.5%)	
Other	8 (6.3%)	2 (4.2%)	4 (6.7%)	2 (10.5%)	
Technique					0.6610
Open	62 (51.2%)	25 (52.1%)	25 (41.7%)	12 (63.2%)	
Laparoscopy	63 (47.3%)	23 (47.9%)	33 (55%)	7 (36.8%)	
Laparoscopy, converted	2 (1.5%)	0	2 (3.3%)	0	
Closure method					0.3367
Stapler	115 (90.6%)	45 (93.8%)	56 (93.3%)	14 (73.7%)	
Harmonic/suture	12 (9.4%)	3 (6.2%)	4 (6.7%)	5 (26.3%)	
Mean amylase level drain 2 (range)	650 (7–145086)	54 (7–368)	1054 (1323–6397)	23210 (8214–145086)	**0.0008**
Morbidity (except POPF)	8 (6.3%)	1 (2.1%)	5 (8.3%)	2 (10.5%)	0.1274
Median Hospital stay, days	6 (2–36)	6 (2–36)	6 (3–34)	9 (3–36)	0.1616
Median blood loss, mL	255	220	255	340	0.2556
Blood Transfusion, n	3	1	1	1	1
Median operative time, min	240	215	258	243	0.4465

[a] Comparison between Grade B1 and others combined.
[b] Comparison between PDAC and other indications.

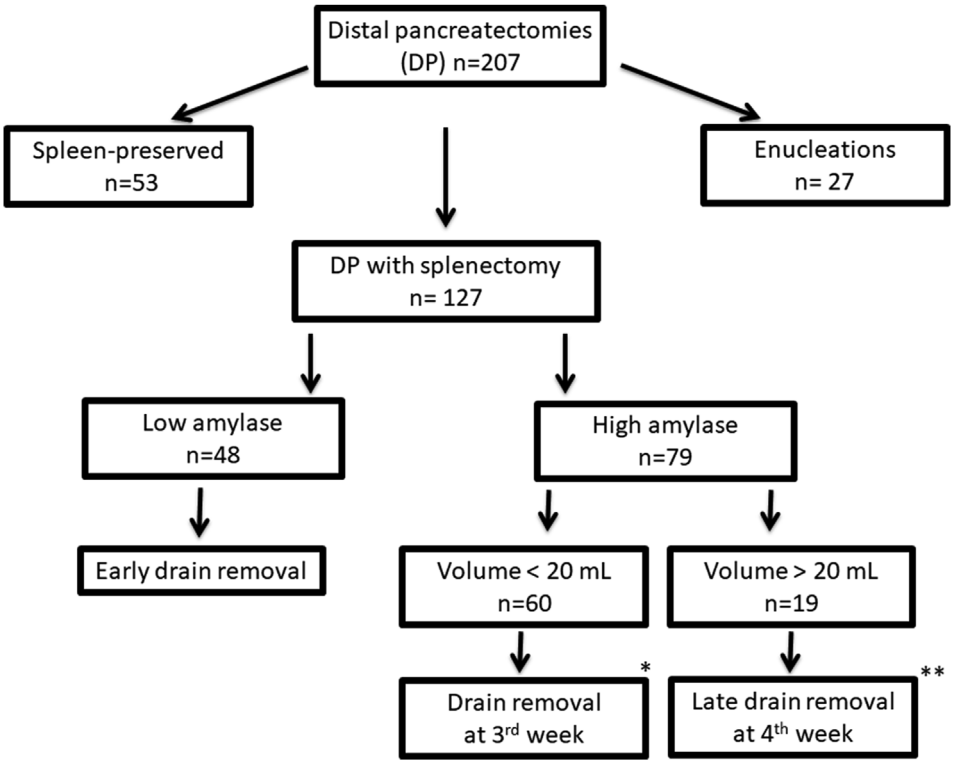

Fig. 2. Drain removal flow chart. * considered as biochemical leakage; ** Grade-B POPF - According to the Revised 2016 ISGPS grading of POPF [8] or Grade-B1 POPF - According to Maggino et al. [10].

Table 2
Clinical and surgical data from double drainage vs single drainage patients.

	Double drainage (n = 127)	Single drainage (n = 94)	P value
Sex			0.1935
M	51 (40.2%)	46 (48.9%)	
F	76 (59.8%)	48 (51.1%)	
BMI	24.8	23.9	
ASA			0.5073
1 or 2	119	90	
> 2	8	4	
Mean age, years	61.2	60.7	0.2408
Diagnosis			0.4288
PDAC	54 (42.5%)	45 (47.9%)	
NET	34 (26.8%)	23 (24.5)	
IPMN	13 (10.2%)	8 (8.5%)	
CP	8 (6.3%)	4 (4.3%)	
Mucinous cystadenoma	5(3.9%)	3 (3.2%)	
SPN	5(3.9%)	5 (5.3%)	
Other	8 (6.3%)	6 (6.4%)	
Technique			0.2657
Open	62 (48.8%)	53 (56.4%)	
Laparoscopy	63 (49.6%)	40 (42.6%)	
Laparoscopy, converted	2 (1.5%)	1 (1.0%)	
Closure method			0.5875
Stapler	115 (90.6%)	83 (88.3%)	
Harmonic/suture	12 (9.4%)	11 (11.7%)	
POPF			
No^{0}	48 (37.8%)	28 (29.8%)	0.2153$^{0\ vs\ bl,b,c}$
BL^{bl}	60 (47.2%)	32 (34.0%)	
B1^{b,b1}	19 (14.9%)	23 (24.5%)	0.00026$^{0,bl\ vsb,c}$
(B2 or B3)^{b,b23}	0	8 (8.5%)	0.01569$^{b1\ vsb23}$
C^{c}	0	3 (3.2%)	0.00535$^{b1\ vsb23,c}$
Mean amylase level drain[a]	650	1327	**0.0016**
Morbidity (except POPF)	8 (6.3%)	9 (9.6%)	0.3663
Median Hospital stay, days	6 (2–36)	8 (2–59)	**0.0127**
Median blood loss, mL	255	330	0.06476
Blood Transfusion, n	3	6	0.1348
Median operative time, min	240	220	0.05273

[a] Drain 2 vs single drain.

[15,16].

Pancreatic fluid collection in the subphrenic space is usually complicated with pleural effusion and pulmonary complication. If a unique drain is used to drain the pancreatic stump, it should be anchored in the left subphrenic space so that the pancreatic effusion will be directed from the pancreas to the drainage bag without passing through the subphrenic space. If it is inserted in the opposite direction, any pancreatic fluid will pass through the subphrenic space. Indeed, in a recent report from Korea, the drain was intraoperatively placed and anchored onto the pancreatic stump via the left subphrenic space systematically [5]. The study reported a high CR-POPF incidence of 27.3%, where 22.8% needed percutaneous drainage, and an endoscopic drainage procedure was performed in 2.7% [5].

Based on the high incidence of CR-POPF and the greater severity of subphrenic abscesses than those in other peritoneal locations, we designed a method of drainage for use after distal pancreatectomy with splenectomy. This method could minimize the effects of pancreatic fistulas after distal pancreatectomy, thus reducing the incidence of subphrenic fluid collection and pancreatic abscess. Therefore, the need for reoperation and radiologic or endoscopic interventions is decreased. Distal pancreatectomy without splenectomy does not require double drainage since the subphrenic space is occupied by the spleen.

The rationale for this strategy is ensuring effective drainage of both the pancreatic stump and the left subphrenic space with no fluid exchange. This task can be achieved with the insertion of two drains. One closed-type drain is inserted in the left subphrenic space and exteriorized away from the path of the pancreatic drain. The second drain is anchored onto the pancreatic stump and exteriorized away from the left subphrenic space. The timing (3–4 weeks, irrespective of volume and amylase level) of the removal of the drain 2 assumes that, after this period, this drain is completely encircled by cicatricial process that makes any abdominal collection unlikely.

In our historic series of distal pancreatectomy without double drainage, several cases of fluid collection needed reoperation or intervention radiology (Table 2). Since changing the drainage strategy, we have observed a dramatic decrease in pancreatic abscess formation and fluid collections needing percutaneous drainage. Indeed, while some patients had grade B POPF due to prolonged drainage (part of our strategy and not a complication *per se*), no one needed reoperation, radiologic or endoscopic interventions. If a subclass of grade-B classification is used, these patients are re-classified as being grade-B1 [10]. When we compare both groups, two-drain vs one drain, the number of POPF is not different but the severity of POPF is higher in the one-drain patients (Table 2).

In summary, the results of this study show that the strategy of double drainage after distal pancreatectomy may reduce the severity of POPF, thus avoiding reoperation or further interventions.

Conflicts of interest

The authors declare no conflicts of interest.

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