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Perianastomotic Irrigation With Passive Drainage Dramatically Decreases POPF Rate After High-risk Pancreaticoduodenectomy

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Objective: To assess whether prophylactic irrigation and passive drainage of pancreatico-jejunal anastomosis could reduce leak and mortality rates after high-risk pancreaticoduodenectomies.

Background: Postoperative pancreatic fistula (POPF) is a life-threatening complication following pancreaticoduodenectomy. Several risk factors have been proposed likewise potential mitigation strategies. Regarding the latter, surgical drain policy remains a "hot topic." We propose an innovative approach to mitigate POPF and POPF-related mortality following high-risk pancreaticoduodenectomies.

Methods: One hundred fifty-seven patients undergoing pancreaticoduodenectomy between January 2012 and November 2021 were included in the study. Subjects with main pancreatic duct ≤ 3 mm and soft parenchyma were classified as high-risk for POPF development. Since August 2015, high-risk patients received prophylactic irrigation and drainage of the perianastomotic area. These patients were compared with risk-matched historical controls.

Results: We identified 73 high-risk patients. Of these, the 47 subjects receiving prophylactic perianastomotic irrigation showed significantly lower POPF rates (12.7% vs 69.2%, $P < 0.001$). Multivariate regression analysis confirmed the significant association between irrigation drainages and POPF (odds ratio 0.014, $P = 0.01$). Although not significant, mortality was lower in the irrigation group (4.2% vs 13.0%, $P = 0.340$). However, none of the fatalities in the irrigation-drainage group were POPF-related. No significant difference in length of hospital stay was observed between the 2 groups (18.0 vs 21.0 days, $P = 0.091$).

Conclusions: Irrigation and drainage of the perianastomotic area represents a powerful approach to reduce POPF and, potentially, mortality after high-risk pancreaticoduodenectomies.

INTRODUCTION

Pancreaticoduodenectomy (PD) for benign or malignant lesions of the pancreatic head, distal bile duct, or duodenum harbors a mortality rate of 1.0% to 5.0%, even at high-volume centers.[1] The incidence of perioperative morbidity, instead, remains between 30.0% and 60.0%.[2] One of the most threatening complications after PD is represented by postoperative pancreatic fistula (POPF). In 2016, the International Study Group in Pancreatic Surgery has updated the POPF definition to "*a drain output with an amylase level more than three-times the upper limit of institutional normal serum amylase activity, regardless its volume, associated with a clinically relevant condition.*"[3] According to this new definition, the "old" grade A POPF has been downgraded to biochemical leak, having no impact on the postoperative clinical course. Therefore, the reported incidence of grade B and C POPF ranges from 1.0% to 36.0%. across the literature.[4]

Several risk factors have been postulated to increase the likelihood of POPF development after PD. Among these, intraoperatively determined small diameter of the main pancreatic duct and soft consistency of the pancreatic parenchyma are believed to play a major role. Moreover, these 2 elements have been repeatedly included in most risk-stratifications scores for predicting the likelihood of POPF development after PD.[5,6]

Together with risk factor assessment, the literature has explored potential perioperative strategies to decrease the POPF rate. In this context, the type, number, and postoperative management of surgical drainages have been thoroughly evaluated in numerous clinical trials, often leading to conflicting conclusions.[7,8]

We believe that patients carrying high-risk pancreatic features for POPF development may benefit from a more aggressive drainage management, which could be potentially associated with lower POPF rates. For this reason, the aims of the present study were to describe our perianastomotic irrigation with passive drainage technique and its management in high-risk patients undergoing PD, and to determine whether this strategy could be associated with lower POPF, mortality and severe complication rates compared with a historical, high-risk patient cohort in the identical setting.

METHODS

A retrospective, observational study was conducted at the Department of General Surgery, Hirslanden Klinik and Klinik Im Park (Zürich, Switzerland). All patients scheduled to undergo PD between January 2012 and November 2021 were included; all surgeries were performed by one of the investigators (J.S.), experienced in pancreatic surgery (>1000 pancreatic resections). The postoperative course was managed according to a standard care

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protocol. Data retrieval and study protocol were approved by the local institutional review board (BASEC-Nr. 2018-00183).

Patient Stratification

Patient stratification was achieved according to the classification proposed by Ansorge et al,[9] based on main pancreatic duct size and pancreatic consistency. Both features were assessed intraoperatively by the leading surgeon. Main pancreatic duct diameter cutoff was set at 3 mm; pancreatic parenchyma consistency was graded as "*soft*" or "*hard.*" Patients were classified as "*low-*," "*intermediate-*," and "*high-risk*" according to the presence of none, 1 or 2 risk factors, respectively. From August 2015, patients at high risk for developing POPF routinely received a different drainage policy, as explained later. Clinically relevant pancreatic fistulas (grade B or C according to the International Study Group for Pancreatic Fistula criteria[3]) were recorded and defined as POPF. Complications were recorded and graded according to the Clavien-Dindo classification[10]; complications were classified as "*severe*" when they were found to be equal to or greater than grade 3B.

Surgical Management

A standardized, laparotomic pylorus-preserving pancreaticoduodenectomy with cholecystectomy was planned for all cases. The double-layer, pancreatico-jejunal anastomosis included an inner, duct-to-mucosa layer followed by an external, inverting, intestinal serosa-to-pancreatic capsule layer, both with 5-0 polydioxanone (PDS) (Ethicon Inc., Somerville, NJ) sutures. A single-layer, 5-0 PDS hepatico-jejunostomy and a termino-lateral, double-layer, hand-sewn, 4-0 PDS duodeno-jejunostomy were routinely performed, unless distal gastrectomy was required in case of tumors extending to the distal stomach. At the end of surgery, an extensive peritoneal lavage with 3 to 5 L of saline solution was performed.

Surgical Drainage Policy

Traditionally, both high- and low-risk PD routinely received two 12 Ch Easy Flow (EF) (Websinger, Wolkersdorf, Austria) draining the anterior and posterior aspects of both biliodigestive and pancreatico-jejunal anastomosis. Both EFs entered from a single access in the right upper quadrant. Since August 2015, in high-risk PD, the leading surgeon placed two 20 Ch double-lumen Salem Sump (SS) irrigation tubes with passive drainage (Medtronic Inc., Minneapolis, MN) ventrally and dorsally to the pancreatico-jejunal anastomosis, entering from 2 separate accesses in the left flank. To avoid intra-abdominal misplacement, the tip of each SS was sutured to the parietal peritoneum with 4-0 Vycril Rapide (Ethicon Inc., Somerville, NJ). A drainage catheter (Cystofix, Braun, Melsungen, Germany) was positioned in the lower pelvis via a third, separate access in the left flank, to drain fluids possibly accumulating in the lower pelvis. Drainage policy of the biliodigestive anastomosis, instead, remained unchanged, with 2 EFs draining both anterior and posterior sides. A schematic representation of the new drainages positioning is shown in Figure 1.

Postoperative Management

All subjects were sent to intensive care unit for 24–48 hours to be monitored before being transferred to the ward. Each SS was flushed with 100 ml/h of Ringer solution for 2 postoperative day (PODs); drainage of the collected fluid occurred by passive gravity. The volume and the quality of the drained fluids were inspected every day by the leading surgeon to recognize worrisome appearance. Moreover, biochemical tests were carried out daily on the drained fluids. To obtain the real concentrations of pancreatic enzymes in the drained fluids, irrigation was interrupted every day for 2 hours and bags collecting the drainage fluids were changed before retrieving the samples needed for biochemical analysis. On POD 3, drain amylase, lipase, and bilirubin levels lower than 3 times the upper institutional normal limit allowed for reduction of the flushing speed with Ringer solution to 50 ml/h in each drainage. In case the drainage levels of pancreatic enzymes and bilirubin remained below the aforementioned cutoffs also on POD 4, irrigation was interrupted, and only passive drainage was allowed. New biochemical tests were carried out on drained fluids on POD 5 and 6: SS drainages and pelvic drainage catheter were routinely removed from POD 7 onward in the absence of evidence of any pancreatic fistula. EF drainages were removed the day following SS withdrawal. In case of pancreatic enzymes above 3 times the upper normal limit, irrigation was continued (or even increased to 200 ml/h) for 2 more days and the analysis was repeated.

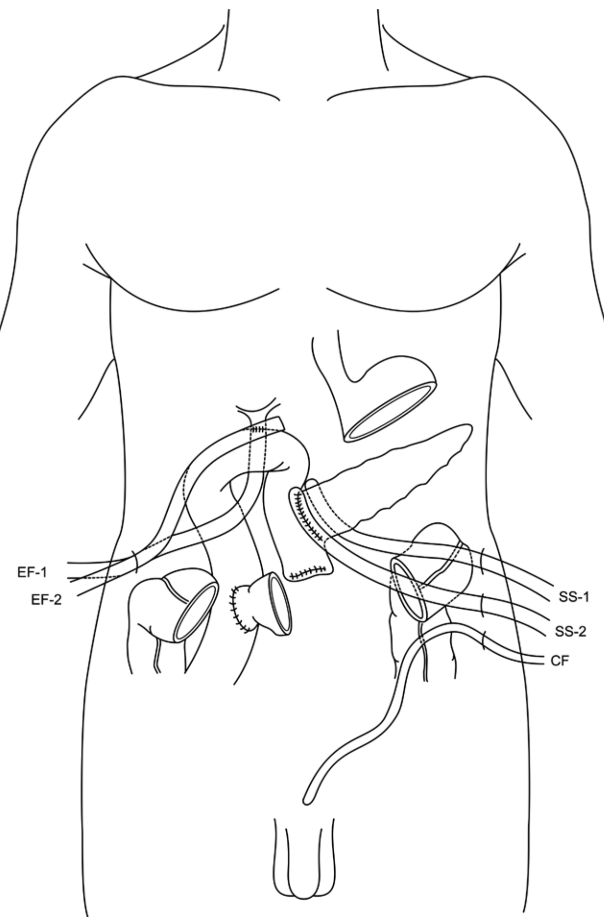

FIGURE 1. Schematic representation of the irrigation-drainage positioning. CF indicates cystofix drainage; EF, easy flow drainage; SS, Salem Sump drainage.

Statistical Analysis

The descriptive statistics for the demographic and clinical characteristics of patients were expressed as mean ± SD or median and interquartile range (IQR) for continuous variables and as absolute frequency (column percentage) for the categorical variables.

Association between categorical variables was investigated using Pearson's Chi-squared test (for cell frequency $n \geq 5$) and Fisher's exact test (for cell frequency $n < 5$). Indeed, Phi (φ) or Cramer's V were reported to highlight the strength of association. The normality assumption was assessed using the Shapiro-Wilk's test. Unpaired Student *t* test was used to assess mean differences; instead, when the assumptions to use a parametric test were not met, the Mann-Whitney *U* test was performed. A multivariate logistic regression model was fitted for high-risk patients performing a backward features selection, that is, gradually excluding variables not improving model fit. Multicollinearity was tested using the variation inflation factor. All statistical tests were 2-sided, with a significance level set at $P < 0.05$. Statistical analysis was performed with SPSS version 24 (IBM, Chicago, IL).

RESULTS

A total of 157 patients underwent PD during the research period and they were included in the study. Patients' demographics, and perioperative data are shown in Table 1. Twenty-three patients (14.6%) had locally advanced tumors that required a vascular resection or resection of one or more additional organs (4 colonic resection, 8 subtotal gastrectomies, 14 hepatic wedge resections). Histological assessment of the surgical specimens showed pancreatic ductal adenocarcinoma in 56.7% of the patients (Table 2). Twenty-six patients developed severe postoperative complications and 7 died (5 in the high- and 2 in the low-/intermediate-risk group), giving an overall morbidity and mortality rates of 16.5% and 4.5%, respectively. Overall, POPF occurred in 25 patients (15.9%, 13 grade B and 12 grade C).

TABLE 1.

Demographic, Clinical, and Perioperative Data of Patients (N = 157)

Age (y, mean ± SD)	68.0 ± 11.1
Gender, n (%)	
Male	88 (56.1)
Female	69 (43.9)
BMI (kg/m^2, mean ± SD)	237.7 ± 3.7
ASA score, n (%)	
1	4 (2.5)
2	82 (52.3)
3	69 (43.9)
4	2 (1.3)
Diabetes, n (%)	
Yes	26 (16.6)
No	131 (83.4)
COPD, n (%)	
Yes	5 (3.2)
No	152 (96.8)
Smoking, n (%)	
Yes	46 (29.3)
No	111 (70.7)
Neoadjuvant CT, n (%)	
Yes	31 (19.7)
No	126 (80.3)
Neoadjuvant RT, n (%)	
Yes	7 (4.5)
No	150 (95.5)
Preoperative biliary drainage, n (%)	
Yes	60 (38.2)
No	97 (61.8)
Pancreatic texture, n (%)	
Hard	82 (52.5)
Soft	75 (47.8)
Main pancreatic duct diameter (mm, median, IQR)	4.0 (2.0–5.5)
Risk class, n (%)	
Low	79 (50.3)
Intermediate	5 (3.2)
High	73 (46.5)
Vascular resection, n (%)	
Yes	51 (32.5)
No	106 (67.5)
Blood losses (mL, median, IQR)	400.0 (200.0–650.0)
Duration of procedure (min, median, IQR)	240.0 (200.0–274.0)
POPF, n (%)	
Grade B POPF	13 (8.3)
Grade C POPF	12 (7.6)
Severe complications, n (%)	26 (16.5)
Deaths, n (%)	7 (4.5)
Length of stay (d, median, IQR)	16.5 (14.0–21.0)

ASA indicates American Society of Anesthesiologists physical status classification; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CT, chemotherapy; IQR, interquartile range; POPF, postoperative pancreatic fistula; RT, radiotherapy.

TABLE 2.

Postoperative Histology (N = 157)

Postoperative Histology, n (%)	
Pancreatic adenocarcinoma	89 (56.7)
Distal bile duct adenocarcinoma	15 (9.6)
Main duct IPMN	10 (6.4)
Duodenal adenocarcinoma	9 (5.7)
Papillary adenocarcinoma	6 (3.8)
Chronic pancreatitis	6 (3.8)
Neuroendocrine pancreatic tumor	4 (2.5)
Serous cystadenoma	3 (1.9)
Mixed-type IPMN	3 (1.9)
Metastatic renal cell carcinoma	2 (1.3)
Pseudopapillary neoplasia	2 (1.3)
Klatskin tumor	2 (1.3)
Other	6 (3.8)

High-risk Patients

Overall, 73 cases presenting both soft parenchyma and small main pancreatic duct were identified. Of these, 26 received EF and 47 had SS drains. The overall POPF rate among high-risk patients was 32.9%. The 2 populations were homogeneous in terms of age, gender, body mass index (BMI), American Society of Anesthesiologists physical status classification score, comorbidities (eg, diabetes and smoking habits), preoperative neoadjuvant chemo-radiotherapy, biliary decompression, and need for vascular resection (Table 3). The median value of the intraoperative blood losses in the EF group (400.0 ml; IQR: 287.5–525.0) were higher than in the SS group (250.0 ml; IQR: 200.0–450.0, $P = 0.04$). Similarly, the median value of duration of surgery in the EF group (240.0 minutes; IQR: 207.0–300.0) was longer than in the SS group (215.0 minutes; IQR: 184.0–255.0, $P = 0.045$).

Among high-risk patients, there was a strong ($\varphi = 0.58$, $P < 0.001$) statistically significant association between type of drain and POPF onset, $\chi^2(1) = 24.18$, $P < 0.001$ (Figure 2). The relative risk of developing POPF in high-risk patients who received EF versus the SS cohort was 5.4 (95% confidence interval, 2.56–11.95). In this group, we experienced 5 deaths: 3 belonged to the EF group (13.0%) and 2 to the SS group (4.2%). Although not statistically significant, the median length of stay among the SS group was slightly shorter with respect to the historical control group (21 days; IQR: 17.3–26.3 vs 18, IQR: 14.0–25.0, $P = 0.091$). A multivariate logistic regression was performed to assess the effect of gender, age, BMI, diabetes, smoking, neoadjuvant treatment, preoperative biliary decompression, vascular resection, intraoperative blood losses, duration of surgery, and type of drain used on having POPF. Five predictor variables out of 11 were selected by the backward selection process: BMI, the use of SS drains, intraoperative blood losses, preoperative biliary stenting, and history of neoadjuvant treatment (either chemotherapy or radiotherapy) (Table 4). The use of SS irrigation tubes confirmed to be a predictor associated with lower likelihood of POPF; in particular, patients receiving SS irrigation tubes have a reduction of 98.6% in the odds of having POPF (odds ratio = 0.01; 95% confidence interval, 0.00–0.16; $P < 0.001$).

TABLE 3.

Demographic, Clinical, and Perioperative Data of High-risk Population

	Easy Flow (n = 26)	Salem Sump (n = 47)	*P*
Age (y, mean± SD)	65.3 ± 10.5	67.5 ± 13.3	0.457*
Gender, n (%)			0.216§
Male	12 (46.1)	30 (63.8)	
Female	14 (53.9)	17 (36.2)	
BMI (kg/m², mean± SD)	24.4 ± 3.6	24.3 ± 3.8	0.886*
ASA, n (%)			0.269§
1	2 (7.7)	1 (2.2)	
2	14 (53.8)	23 (48.9)	
3	9 (34.6)	23 (48.9)	
4	1 (3.9)	0 (0.0)	
Diabetes, n (%)			0.548†
Yes	0 (0.0)	3 (6.4)	
No	26 (100)	44 (93.6)	
COPD, n (%)			0.124†
Yes	2 (7.7)	0 (0.0)	
No	24 (92.3)	47 (100.0)	
Smoking, n (%)			0.147§
Yes	9 (34.6)	8 (17.0)	
No	17 (65.4)	39 (83.0)	
Neoadjuvant CT-RT, n (%)			0.229†
Yes	3 (11.5)	12 (25.5)	
No	23 (88.5)	35 (74.5)	
Preoperative biliary drainage, n (%)			0.075§
Yes	13 (50.0)	13 (27.6)	
No	13 (50.0)	34 (72.4)	
Vascular resection n (%)			0.785§
Yes	8 (30.8)	12 (25.5)	
No	18 (69.2)	35 (74.5)	
Blood losses (ml, median, IQR)	400.0 (287.5–525.0)	250.0 (200.0–450.0)	**0.040**‡
Duration of procedure (min, median, IQR)	240.0 (207.5–300.0)	215.0 (184.0–255.0)	**0.045**‡
POPF, n (%)			**<0.001**§
Yes	18 (69.2)	6 (12.7)	
No	8 (30.8)	41 (87.3)	
Length of stay (days, median, IQR)	21.0 (17.3–26.3)	18.0 (14.0–25.0)	0.091‡
Severe complications, n (%)			0.096§
Yes	10 (38.4)	9 (19.1)	
No	16 (61.6)	38 (80.2)	
Mortality, n (%)			0.340†
Yes	3 (13.0)	2 (4.2)	
No	23 (87.0)	45 (95.8)	

Bold indicates statistically significant values ($P < 0.05$).
*Student *t* test.
†Fischer's exact test.
‡Mann-Whitney *U* test.
§Chi square test.
ASA indicates American Society of Anesthesiologists physical status classification; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CT, chemotherapy; IQR, interquartile range; POPF, postoperative pancreatic fistula; RT, radiotherapy.

The highest-grade complication was recorded for each patient. Although not statistically significant, there was a lower rate of severe complications in the SS group with respect to the traditional drainage group, $\chi^2(1) = 3.24$, $P = 0.096$.

Low- and Intermediate-risk Patients

In our sample, 84 PD showed either none or 1 risk factor for leak development. In the low- and intermediate-risk population, the overall POPF rate was 1.2% throughout the entire study period. Since nothing changed in the management of these patients, we hypothesized that the rate of anastomotic leak remained unchanged along the years. For this purpose, we split the low- and intermediate-risk subjects into patients operated before and after the introduction of irrigation drainages. Populations resulted homogeneous in terms of perioperative characteristics, comorbidities, POPF rates, length of hospital stay, and severe complications. Only the median length of surgical procedure resulted significantly lower in the post-Salem group (238.0 minutes; IQR: 190.0–274.0) with respect to the pre-Salem subsample (270.0 minutes; IQR: 240.0–300.0; $P = 0.012$) (Table 5).

DISCUSSION

Our findings confirmed a significant association between the new drainage policy and lower POPF rates after high-risk PD. Patients undergoing EF drainage have about 70-times higher odds of having POPF than those receiving SS. Moreover, the same data suggest a potential, although not yet significant, reduction in mortality when irrigation drainages were applied in this group of patients.

Pancreatic fistula is an abnormal communication between the pancreatic ductal epithelium and another epithelial surface containing pancreas-derived, enzyme-rich fluid.[11] The International Study Group for Pancreatic Fistula[11] standardized and updated[3] the definition of POPF.

Based on their objective definition, several prognostic scoring systems attempted to predict a patient's risk for developing POPF after PD.[5,6] Historically, small diameter of the main pancreatic duct and soft consistency of the pancreatic parenchyma have always been acknowledged by pancreatic surgeons as risk factors for anastomotic leak. Ansorge et al[9] proved that a standardized intraoperative assessment of pancreatic consistency and duct diameter carried out by experienced pancreatic surgeons could predict the rate of POPF development. Following the first algorithm, several other risk stratification scores have been proposed and some of them have been extensively exploited in the clinical setting and for research purposes.[12,13] Nevertheless, despite the algorithm chosen, pancreatic duct diameter, and pancreatic consistency represented fairly constant variables included among different scores.[5,6] Recently, Adamu et al[5] performed a head-to-head comparison validation of 10 different risk scores for POPF in an independent cohort of patients. Their analysis demonstrated similar performances of the selected models in predicting POPF. Given these premises, in our clinical practice and, thus, for the purpose of this study, we applied the stratification proposed by Ansorge et al,[9] because of its extreme easiness of calculation and good performances with respect to more complex models.

Among the many perioperative strategies proposed to reduce the burden of POPF after PD, the prophylactic use of intraperitoneal, surgical drainages has been thoroughly investigated. Although in the past conflicting results existed between groups supporting the abandoning of surgical drainages[7] and studies claiming their valuable role in decreasing the incidence of POPF,[8] a more patient-tailored solution is the most preferred approach nowadays. Kaminski et al[14] supported the selective placement of drainages in patients at high risk of developing POPF, followed by their removal as soon as the threaten of pancreatic fistula has been avoided. Recently, the review by Brubaker and colleagues[15] concluded that, in intermediate- and high-risk cases, one or more drains appear to mitigate the complication burden of POPF. In line with these results, our clinical practice has recently shifted toward a more careful patients' stratification, thus applying a more invasive drain management only to subjects at highest risk for POPF development.

Continuous irrigation and passive drainage after surgical debridement reduced mortality and need for repeated necrosectomies in case of pancreatic necrosis and subsequent pancreatic abscesses complicating acute pancreatitis.[16–18] We hypothesized that, following PD, irrigation and drainage of the

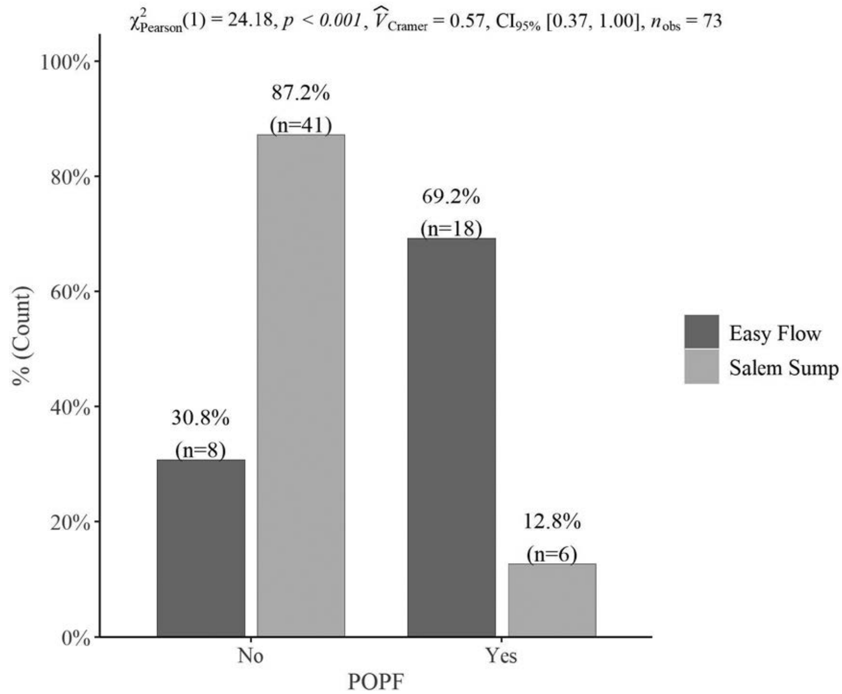

FIGURE 2. Bar plot representing POPF distribution with respect to the use of SS or EF irrigation tubes among high-risk patients. EF indicates easy flow drainage; POPF, postoperative pancreatic fistula; SS, Salem Sump drainage.

perianastomotic area dilutes and removes even minimal quantities of leaked pancreatic juices. This, ideally, should prevent any activation of proteases outside the intestinal lumen, which would result in self-digestion of the anastomosis itself together with the perianastomotic tissues and vessels. We tested a similar approach also in high-risk distal pancreatectomies, confirming its safety, feasibility, and promising results in terms of stump leak reduction.[19]

In our high-risk population, almost one-third of subjects experienced POPF. These findings overlap with results from high-risk patients found in the literature, for whom POPF ranges between 20.0% and 100.0%.[5,9,12,13] However, only 12.7% of our high-risk subpopulation receiving perianastomotic irrigation experienced POPF after PD. Moreover, when compared with the traditional drainage policy, data proved a statistically significant association between the SS irrigation drainages and lower rates of POPF among high-risk patients.

Avoiding misplacement represents a key step for the correct management of irrigation drainages. In fact, at the beginning of this new policy, at least 2 POPFs were related to drain misplacement, which was confirmed during surgical revision for grade C anastomotic leak. Therefore, anchoring the SS to the parietal peritoneum from the very beginning could have provided even lower POPF rates.

At multivariate analysis, the odds of developing POPF in high-risk patients receiving EF drainages were more than 70-times higher, even after adjustment for confounders. These findings support the benefits expected by our innovative drainage policy management, which we believe to have a real potential in changing the postoperative course of PD at highest risk to develop POPF.

The analysis performed on low- and intermediate-risk patients did not demonstrate any significant variation in POPF rates across the timespan of this study. This can be considered as a further, albeit indirect proof that the reduction of POPF rate in the high-risk cohort was genuinely related to the new drain management and not influenced by confounders.

These premises let us speculate on the potential of irrigation-drainage in decreasing mortality after PD. In fact, the number of deaths we would have expected to see without SS would have been at least 6, with respect to the only 2 fatalities observed in the 47 patients following the introduction of the new drainage policy. The lack of statistical significance was almost certainly related to the paucity of events in both groups. None of the 2 fatalities in the SS group were attributable to POPF or POPF-related complications, but they were rather caused by aspiration pneumonia. As a matter of fact, since the introduction of irrigation drainages, we did not experience a single case of deadly tryptic erosion among our patients. This represents one of our most important collateral achievements.

Enhanced recovery after surgery protocols are gaining popularity also in major pancreatic resections.[20] Therefore, our approach could appear to some colleagues quite complex, excessively invasive and anachronistic. Major criticisms address the availability of less invasive mitigation bundles (with respect to our approach) leading to acceptable fistula rates, even in high-risk subjects.[21] Other critics could be moved toward having surgical drainages in place for an excessive long time, when recent analyses promote early drain removal

TABLE 4.

Multivariate Logistic Regression Model for POPF

Variable	OR	95% CI	*P*	VIF
BMI (kg/m^2)	1.243	1.00–1.60	0.062	1.50
Preop CT-RT				2.30
No	–	–		
Yes	16.122	1.88–179.70	0.024	
Biliary decompression				1.80
No	–	–		
Yes	12.403	2.25–83.30	0.010	
Drain type				3.10
Easy flow	–	–		
Salem sump	0.014	0.00–0.16	<0.001	
Blood losses (*ml*)	1.002	1.00–1.01	0.040	1.60

CI indicates confidence interval; CT, chemotherapy; OR, odds ratio; RT, radiotherapy; VIF, variance inflation factor.

TABLE 5.

Demographic, Clinical, and Perioperative Data of Low- and Middle-risk Population

	Pre-Salem Sump (n = 37)	Post-Salem Sump (n = 47)	*P*
Age (y, mean ± SD)	68.9 ± 8.6	69.4 ± 10.7	0.825*
Gender, n (%)			0.380§
Male	18 (48.6)	28 (59.6)	
Female	19 (51.4)	19 (40.4)	
BMI (kg/m^2, mean ± SD)	23.5 ± 3.9	23.1 ± 3.5	0.571*
ASA, n (%)			0.382§
1	0 (0.0)	1 (2.1)	
2	22 (59.4)	23 (48.9)	
3	14 (37.8)	23 (48.9)	
4	1 (2.8)	0 (0.0)	
Diabetes, n (%)			0.806§
Yes	11 (29.7)	12 (25.5)	
No	26 (70.3)	35 (74.5)	
COPD, n (%)			1.000†
Yes	1 (2.8)	2 (4.2)	
No	36 (97.2)	45 (95.8)	
Smoking, n (%)			1.000§
Yes	13 (35.1)	16 (33.6)	
No	24 (64.9)	31 (66.4)	
Neoadjuvant CT-RT, n (%)			0.427§
Yes	9 (24.3)	8 (16.8)	
No	28 (75.7)	39 (83.2)	
Preoperative biliary drainage, n (%)			0.662§
Yes	16 (43.2)	18 (38.2)	
No	21 (56.8)	29 (61.8)	
Vascular resection, n (%)			0.650§
Yes	15 (40.5)	16 (34.0)	
No	22 (59.5)	31 (66.0)	
Blood losses (ml, median, IQR)	600.0 (475.0–700.0)	600.0 (100.0–650.0)	0.096‡
Duration of procedure (min, median, IQR)	270.0 (240.0–300.0)	238.0 (190.0–274.0)	**0.012**‡
POPF, n (%)			0.440†
Yes	1 (2.8)	0 (0.0)	
No	36 (97.2)	47 (100)	
Length of stay (days, median, IQR)	16.0 (14.0–19.5)	15.0 (12.0–18-0)	0.162‡
Severe complications, n (%)			0.083†
Yes	5 (13.5)	1 (2.1)	
No	32 (86.5)	46 (97.9)	
Mortality, n (%)			0.191†
Yes	2 (5.4)	0 (0.0)	
No	35 (94.6)	47 (100.0)	

Bold indicates statistically significant values ($P < 0.05$).
*Student *t* test.
†Fischer's exact test.
‡Mann-Whitney *U* test.
§Chi square test.
ASA indicates American Society of Anesthesiologists physical status classification; BMI, body mass index; COPD, chronic obstructive pulmonary disease; CT, chemotherapy; IQR, interquartile range; POPF, postoperative pancreatic fistula; RT, radiotherapy.

once amylase levels on POD 1 set below certain thresholds.[22] Despite these potential criticisms, it is worth to remind that our drainages have both a diagnostic and therapeutic function. In fact, along with the qualitative and quantitative analysis of drained fluids mandatory for POPF diagnosis, irrigation can be modulated during the hospital stay to mitigate POPF severity and its associated complications. In a population whose risk to develop anastomotic leak is above 65%, our approach aims at minimizing the need for further invasive procedures, such as radiological drainage of newly formed fluid collections. So far, none of our patients experienced any drainage-related complication. Moreover, although not assessed in a structured way, overall patients' satisfaction was high, and they did not encounter any restriction to an early mobilization.

All procedures were carried out by the same leading surgeon, with a long-lasting expertise in pancreatic surgery. Surgical technique, patients' selection, drain positioning and postoperative management were all standardized and performed by the same surgeon, as well. To our knowledge, there are no comparable cohorts of patients minimizing the perioperative variability to this extent.

Despite the encouraging results, our study is mainly limited by its retrospective nature, which harbors inferior level of evidence with respect to prospective studies. However, given the relevance of our findings, we believe that these results will be undoubtedly confirmed in the setting of future randomized trials.

CONCLUSIONS

To the authors' knowledge, this is the first study reporting the results of prophylactic irrigation of perianastomotic area after systematic stratification of high-risk patients undergoing PD. We aimed to provide a thorough description of the drainage technique and management to allow reproducibility of our approach. These encouraging results may represent the starting point for replication of our technique in similar settings of pancreatic surgery to confirm the benefits expected in terms of POPF reduction and its associated complications in patients at high risk. We hope that our initial experience could lead to the assessment of the potentiality of such drainage policy in the context of larger, randomized clinical trials.

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