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Review Article

Pancreatic Fistula after Pancreatoduodenectomy: Evaluation of Different Surgical Techniques

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ABSTRACT

Postoperative pancreatic fistula (POPF) is one of the most fatal complications of pancreatoduodenectomy. POPF is caused by leakage of pancreatic juice from the pancreatic anastomosis into the abdomen, leading to intra-abdominal complications, such as severe surgical site infections, significant postoperative hemorrhage and multi-organ failure. Many risk factors for POPF have been identified, including patient and surgical technique factors. Our objective was to review the literature on surgical techniques to prevent POPF after pancreatoduodenectomy. Pancreatogastrostomy (PG) has the same incidence of POPF as pancreatojejunostomy (PJ). For PJ anastomosis, the interrupted suture and Blumgart technique also had the same rate of POPF. For soft pancreas it was shown that invagination was better than duct-to-mucosa anastomosis to prevent the POPF. However, a pancreatic duct stent cannot decrease the rate of POPF over the non-stent group. Intraperitoneal drainage cannot prevent POPF, however, it can detect POPF more than the non-drain group. Laparoscopic PD (LPD) and robotic-assisted PD (RAPD) were comparable in rates of POPF with open PD. Overall, no conclusion has been reached regarding the best surgical technique. In any individual case, the surgical technique should be selected based on the surgeon's experience in reducing the incidence of POPF, and other complications.

Keywords: pancreatic fistula; pancreatoduodenectomy; surgical techniques

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INTRODUCTION

The pancreatoduodenectomy (PD) is the surgical procedure of choice for the treatment of pancreatic head and periampullary lesions. This operation was popularized by Whipple in 1935. The overall morbidity after PD reported in a recent large retrospective study was 40.0%[1]. Postoperative pancreatic fistula (POPF) after PD is a dangerous complication that may lead to death. The incidence of POPF grades B and C has been reported at 13.2–16% in various studies[2–6]. One large retrospective study, mentioned above, reported 30–day postoperative and in–hospital mortality rates of POPF at 2.4% and 7.4%, respectively[1]. POPF is significantly associated with life–threatening intra–abdominal conditions, such as severe surgical site infections, significant postoperative hemorrhage, and multi–organ failures, which require further investigations, reoperation, interventions, and/or blood transfusions. POPFs result in prolonged hospital stay, increased therapeutic costs, poor quality of life, and even death[2–6]. Many risk factors for POPF have been identified, primarily divided into patient and surgical technique factors. Techniques to prevent a POPF such as pancreatogastrostomy (PG), duct–to–mucosa procedure, pancreatic duct stent and intraperitoneal, drainage are safe methods for the patient and improve the quality of care. However, there is no consensus on the best surgical technique to prevent POPF. Hence, the objective of this study was to review the literature on surgical techniques to prevent POPF after pancreatoduodenectomy.

Definitions

The International Study Group on Pancreatic Fistula (ISGPF) first defined POPF in 2005[7], with the most recent update in 2016 (Table 1). The updated version defines POPFs into two groups: biochemical (grade A) and clinically significant (grades B and C) POPFs. The term “biochemical, or grade A POPF”, refers to a POPF with observable fluid output having an amylase content greater than three times the upper normal blood level on or after postoperative day 3. Grade A POPFs have no significant clinical effects, and do not require special postoperative care. Grade B or C POPFs are described as clinically relevant POPFs (CR–POPF), and require postoperative management. One of the following is required for the diagnosis of a grade B POPF: an endoscopic or radiological intervention, a drain in place for more than three weeks, and/or clinical infections without organ failure requiring only antibiotic administration. The fistula changes to a grade C POPF whenever a patient requires a significant change in clinical care; such as reintubation, hemodialysis, and/or use of inotropic agents for more than 24 hours, due to respiratory, renal, or cardiac insufficiency, required reoperation, organ failure or death[2,8].

Table 1 Revised classification and grading of postoperative pancreatic fistula

Event	Biochemical	Grade B	Grade C
Drain amylase activity >3 times upper limit of normal serum value	Yes	Yes	Yes
Persisting peripancreatic drainage >3 weeks	No	Yes	Yes
Clinical change and required management for pancreatic fistula	No	Yes	Yes
Percutaneous or endoscopic treatment for collections	No	Yes	Yes
Angiographic procedures for bleeding	No	Yes	Yes
Reoperation	No	Yes	Yes
Intra–abdominal infection	No	Yes	Yes
Organ failure	No	No	Yes
Death	No	No	Yes

Management of POPF grade A is clinical observation, and waiting for spontaneous healing of leakage. If the fistula is not cured by week 3, or if the patients clinical status declines, further investigations are required; such as abdominal computerized tomography (CT) scanning to rule out collection. Specific management of POPF depends on the complications, wherein, antibiotics are required for infections, with percutaneous drainage being the first-line treatment for collection. A CT angiography or angiography followed by embolization is indicated for massive intra-abdominal bleeding. Additionally, nutrition support (enteral via nasojejunal tube or jejunostomy, or parenteral) is most often benefical. Moreover, patients need intensive care unit monitoring when the hemodynamic is unstable or there is multiple organs failure. Reoperation is the last choice for treatment complications and has a high mortality.

Patient factors

Previous publications have identified various risk factors for POPF after PD. A retrospective study in 2016, showed male gender (odds ratio (OR)=1.784; 95% confidence interval (CI): 1.214-2.622), BMI >25 kg/m^2 (OR=1.679; 95% CI: 1.107-2.546), pancreatojejunostomy (PJ) anastomosis (OR=2.102; 95% CI: 1.374-3.216), pancreatic duct diameter ≤3 mm (OR=2.062; 95% CI: 1.416-3.003), and soft pancreatic texture (OR= 3.048; 95% CI: 1.953-4.757) were risk factors for POPF after PD[9]. An observational study in 2018, showed that a soft pancreas (OR=5.275; 95% CI: 2.245-12.395) and a fasting blood glucose level of <108.0 mg/dL (OR=3.011; 95% CI: 1.202-7.540) were risk factors for the development of a POPF[10]. A recent meta-analysis in 2022, included 27 studies (24 retrospective studies and 3 prospective studies) with 24,740 patients, which found that pancreatic adenocarcinoma (OR=0.54; 95% CI: 0.47–0.61), vascular resection (OR=0.57; 95% CI: 0.39–0.83), and preoperative chemoradiotherapy (OR= 0.68; 95% CI: 0.57–0.81) were significantly associated with decreased risk of CR-POPF[11].

There are several reasons why a soft pancreatic texture and pancreatic duct diameter <3 mm are associated with increased risk of CR-POPF: the soft pancreas usually has a larger pancreatic body and a smaller pancreatic duct diameter. A recent study reported that a soft pancreas generally has a smaller fibrosis ratio and a larger lobular ratio, which are associated with increased exocrine function[11]. This study also found that patients with POPF usually had significantly increased pancreatic fat and decreased pancreatic fibrosis, Additionally, it also found that a higher BMI was associated with fatty pancreas and soft pancreatic remnants[11]. Pancreatic adenocarcinoma and preoperative chemoradiotherapy have been associated with increased pancreatic fibrosis and decreased exocrine function, which can decrease the risk of CR-POPF[11-13]. Therefore, evaluating significant risk factors for POPF might help a surgeon to identify those with a higher risk, and select appropriate surgical methods as well as postoperative treatment (Table 2). For higher risk patients, it is recommended that treatment be performed in a high-volume center or by an experienced surgeon.

Table 2 Risk factors of postoperative pancreatic fistula

Risk factors	Number of studies	Odd ratio (95% confidence interval)	p-value	Heterogeneity (%)
Male	12	1.56 (1.42-1.70)	<0.001	29
Body mass index >25 kg/m^2	6	1.98 (1.23-3.18)	<0.001	80
Pancreatic duct diameter ≤3 mm	7	1.87 (1.66-2.12)	<0.001	28
Soft pancreas	16	3.49 (2.61-4.67)	<0.001	57
Pancreatic adenocarcinoma	10	0.54 (0.47-0.61)	<0.001	33
Blood transfusion	3	3.10 (2.01-4.77)	<0.001	0
Vascular resection	6	0.57 (0.39-0.83)	0.003	0
Preoperative chemoradiotherapy	5	0.68 (0.57-0.81)	<0.001	49

Surgical techniques

Reconstruction methods

The main reconstruction procedures after PD are pancreatogastrostomy and pancreatojejunostomy. A randomized controlled trial (RCT) in 2015, compared POPF after PD between PG and PJ reconstruction, and the data showed that the rate of CR-POPF was 18% in the PJ group and 25% in the PG group (p-value=0.40). Postoperative complications occurred in 48% and 58% of patients in the PJ and PG groups, respectively (p-value=0.31)[14]. Another RCT in 2016, studied CR-POPF, perioperative outcomes, pancreatic function, and quality of life between PG and PJ reconstruction, and found no significant difference in the rates of CR-POPF after PG versus PJ (20% vs. 22%, p-value=0.617). In addition, there were no significant difference in surgical complications or long-term pancreatic function; such as steatorrhea or diabetes mellitus, between the PG and PJ groups. All participating clinics were high-volume academic centers for pancreatic surgery. However, the data showed that it is technically easier to achieve secure invagination of the pancreatic remnant with PG; especially in the case of a bulky soft pancreas[15]. A recent meta-analysis of seven RCTs showed no significant difference in the rates of POPF in the PG versus PJ groups (relative risk (RR)=0.61; 95% CI: 0.34-1.09; p-value=0.09)[16]. However, the data demonstrated that PJ was significantly superior to PG in decreasing the risk of postoperative intraluminal hemorrhage (RR=1.65; 95% CI: 1.13-2.42; p-value=0.01)[16-17]. Subgroup analysis showed that the incidence of POPF in the PG group was lower than that in the PJ group in multicenter trials. Some potential advantages of PG include that the presence of gastric acid can effectively inhibit the activation of pancreatic enzymes, and an abundant stomach wall vascularization decreases the chance of anastomotic ischemia[17]. It is impossible to decide at this time whether PG or PJ is superior following PD, because the outcome from reconstruction following pancreatic surgery is still unsettled. Therefore, the reconstruction technique still chosen is based on pancreatic features and surgeon experience.

Anastomotic techniques

Treatment of the pancreatic stump is a major problem during PD reconstruction. Many Japanese institutes use Kakita anastomosis (KA); as shown in Figure 1, which was firstly proposed in 1996[18]. However, Western countries generally follow the Blumgart anastomosis (BA); as shown in Figure 2, which was first used in 2009[19]. The BA is intended to entirely cover the pancreatic cut surface to eliminate tension and shear forces. Retrospective studies from to 2014-2015, showed the rates of POPF grades B and C were 37.2% in the Kakita group and 20.5% in a modified Blumgart group (p-value=0.033). The median postoperative hospital stay (POHS) was significantly shorter in the BA group than in the KA group (16 and 23 days, respectively, p-value<0.001)[20-21].

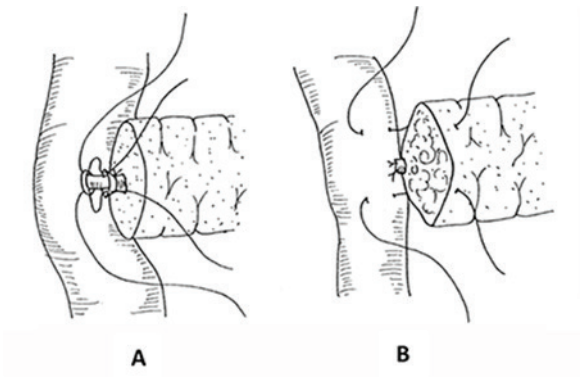

Figure 1 Kakita anastomosis A: Duct to mucosa anastomosis; B: Interrupt suture technique transpancreatic and jejunum[18]

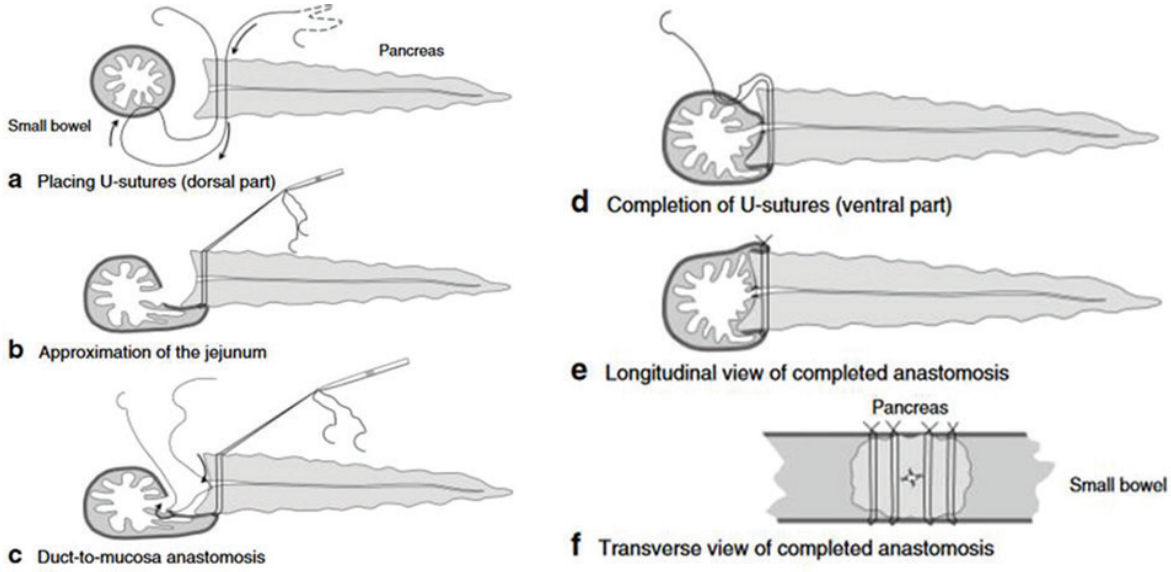

Figure 2 Blumgart anastomosis; a–e longitudinal and f transverse view. The transpancreatic U–sutures were placed straight through the pancreatic remnant about 1 cm distal from the cut end[19]

According to recent data, the incidence of grades B and C POPF following BA varies from 4% to 27.9%, and up to 42.7% in cases with a soft pancreas[19,20,22]. A retrospective study in 2018, comparing a conventional anastomosis (CA) group (Figure 3) with a BA group during PJ, showed there was a significant difference in duration of operation time (473.1±102.0 versus 386.4±58.5 minutes, respectively; p–value<0.001) and intraoperative transfusions (2.2±2.7 versus 0.7±1.5 units, respectively. p–value<0.001) However, there was no significant difference in CR–POPF incidence (43.2% versus 27.9%, respectively; p–value=0.137)[23]. Another retrospective study in 2019, found a significantly lower rate of CR–POPF in the modified BA group compared to a modified KA group (10% versus 19%, respectively; p–value<0.038)[24]. In a recent RCT in 2019, the patients were randomized to either interrupted suture (103 patients) or modified BA suture (107 patients) groups, and were analyzed by intention–to–treat. Grade B/C POPF occurred in 6.8% of the interrupted suture group and 10.3% in the mattress suture group (p–value=0.367)[25].

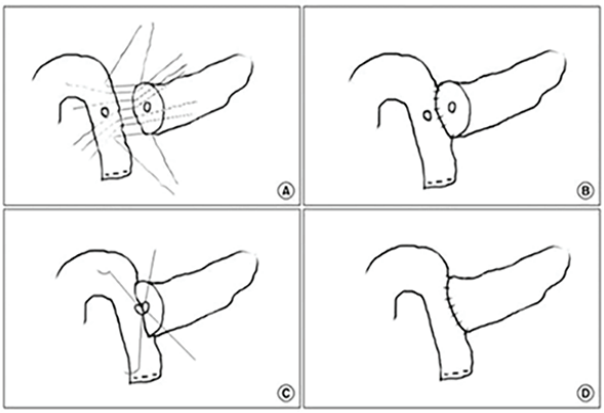

Figure 3 Conventional anastomosis A–B: Six to eight non–absorbable, interrupted sutures between the posterior surface of the pancreas and the seromuscular layer of the jejunum. C: Duct to mucosa anastomosis. D: Six to eight non–absorbable, interrupted sutures between the anterior surface of the pancreas and the seromuscular layer of the jejunum[23]

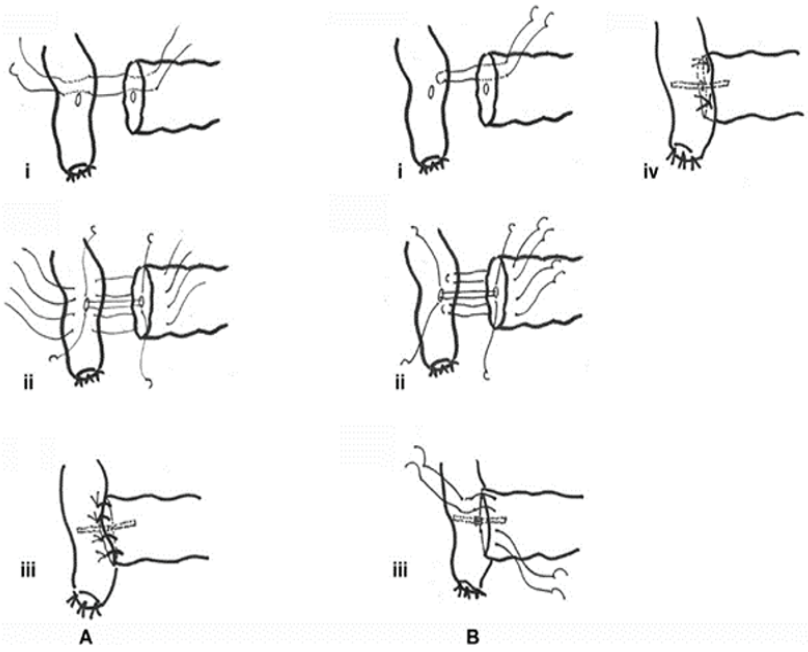

Figure 4 A: Interrupt suture method, B: Modified Blumgart method[25]

A recent meta-analysis published in 2020, included one RCT and ten retrospective comparative studies. There were 2,412 patients, of whom 1,155 (47.9%) underwent BA and 1,257 (52.1%) underwent non-BA. BA was associated with significantly lower rates of CR-POPF than non-BA (OR=0.58; 95% CI: 0.39-0.87; p-value=0.008). However, there were no differences in the rates of POPF (grade B/C) in soft pancreatic texture or grade C POPFs between the two groups (OR 0.46; 95% CI 0.14-1.53; p-value=0.21)[26]. A second report in 2021, included 12 studies (two RCTs, and ten retrospective studies) involving 2,368 patients, 1,075 BA and 1,193 non-BA. The analysis found that BA was superior to non-BA in CR-POPF (risk difference RD=0.10; 95% CI: -0.16-0.04; number needed to treat (NNT)=9), overall morbidity (RD=-0.10; 95% CI: -0.18-0.02; NNT=25), post-pancreatectomy hemorrhage (PPH) (RD=-0.03; 95% CI: -0.06 to -0.01; NNT=33)[27]. The original Blumgart method used four to six transpancreatic jejunal seromuscular U-shaped sutures to approximate the pancreas and the jejunum; whereas, the modified Blumgart method (Figure 4) uses only one to three sutures. In the original method, the sutures were tied at the pancreatic wall, whereas the sutures are tied at the ventral wall of the jejunum in the modified method. This technical aspect was the main difference from other types of non-BA. This modification minimizes the space between the knots, which was a possible source of parenchymal leakage[26,27].

Pancreatic duct sutures

Several previous studies comparing duct-to-mucosa and invagination pancreatojejunostomy (Figure 5) have reported that the overall POPF and morbidity rates were similar in PJ[28-31]. The data from an RCT in 2016, showed that the overall POPF rates in patients treated with invagination versus duct-to-mucosa anastomosis were 30.9% vs. 28.5%, respectively (p-value=0.729). However, respectively, CR-POPF rates were 17.6% versus 3.1% (p-value=0.004), severe complications (27.9% versus 9.4%; p-value<0.013), and POHS (15 versus 13 days; p-value=0.021); all were significantly lower in duct-to-mucosa anastomosis[28].

In contrast, another RCT in 2017, did not demonstrate the superiority of duct-to-mucosa over invagination in the risk of CR-POPF (23% versus 10%, respectively; p-value=0.077). Conversely, in high-risk patients with a soft pancreas, another study reported that invagination may reduce the risk of CR-POPF compared with duct-to-mucosa (10% versus 42%, respectively, p-value=0.010)[29]. Two meta-analyses in 2017 and 2018, found that duct-to-mucosa and invagination in PJ after PD were comparable in rates of postoperative pancreatic fistula (RR=0.78; 95% CI: 0.15-3.96; p-value=0.77)[30,31].

However, in a recent meta-analysis in 2020, which included seven RCT studies involving 1,110 participants, the incidence rate of POPF was significantly lower in the invagination group than in the duct-to-mucosa anastomosis group (OR=1.78; 95% CI: 1.18–2.67; p-value=0.006). Four of the seven trials comparing the rates of CR-POPF in patients with a soft pancreas showed that invagination was significantly better than duct-to-mucosa anastomosis (OR=2.47; 95% CI: 1.57–3.90; p-value<0.0001). Conversely, no significant difference was observed in patients with a hard pancreas (OR=1.06; 95% CI: 0.50–2.27; p-value=0.87). The duct-to-mucosa procedure has a smaller anastomosis, with less leakage than the invagination technique. Additionally, less tissue corrosion is caused by the pancreatic fistula. The pancreatic stump is buried in the jejunum with the pancreatic duct, and the procedure is reasonable for the pancreas having small or unidentified pancreatic ducts, which are the major benefits of invagination for anastomosis. Patients with a soft pancreas and a restricted pancreatic duct should be candidates for this option. However, because the pancreatic stump is exposed to the intestinal lumen, with exposure to digestive juices, it is prone to erosion and bleeding, and the pancreatic duct is easily obstructed. Patients with an excessive pancreatic stump are not suitable for invagination[32].

Pancreatic duct stent

Another issue is whether or not to utilize a stent in PJ anastomosis. The texture of the pancreas and the thickness of the pancreatic duct are two major contributors to pancreatic fistula formation. Intestinal pressure, pancreatic enzyme breakdown, and destruction of the pancreatojejunostomy site contribute to delayed healing. An RCT in 2018, reported that the incidence of CR-POPF was not significantly different between the pancreatic duct in PJ with or without a stent (p-value=0.181)[33]. The same results were reported by an RCT in 2021, in that the internal stenting of PJ did not decrease the rate of CR-POPF after PD; with incidences of CR-POPF in non-stent and internal stent groups of 40% vs 23.8%, respectively (p-value=0.59). However, PD without pancreatic duct stenting is both safe and reliable and can reduce overall operative time and hospital stay. No significant differences were observed in the incidence of postoperative complications in another study[34].

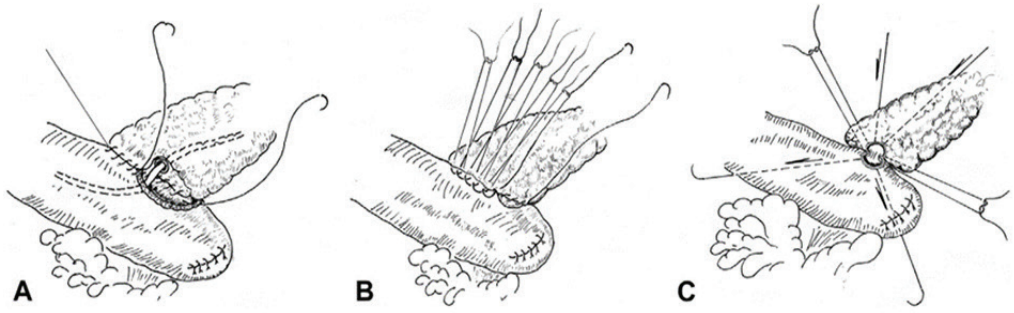

Figure 5 A: Invagination pancreatojejunostomy; B: Out-layer sutures used in both procedures; C: Duct to mucosa pancreatojejunostomy[28]

The data from the RCT in 2018, showed comparable incidences of CR-POPF (28.9% versus 21.6%; p-value=0.256) and overall complications (64.9% vs. 56.8%; p-value=0.257) between external and internal stents, respectively, after PD. However, one study reported lower rates of stent-related complications including stent obstruction, transient peritonitis, and pancreatitis with internal stents, in early clinical outcomes and postoperative drain management; thus, suggesting their superiority[35]. Moreover, data from an RCT in 2022, showed comparable incidences of CR-POPF between non-stent and stent groups in laparoscopic PD (4.9% versus 6.1%, respectively; p-value=1.000)[36]. A recent meta-analysis in 2022, included seven RCTs involving 847 patients, and they found no statistically significant differences between the stent and non-stent groups in POPF (RR=0.85; 95% CI: 0.57–1.26; p-value=0.41), in-hospital mortality, and other complications; although subgroup analysis found that the use of an external stent significantly reduced the incidence of pancreatic fistulas (RR=0.61; 95% CI: 0.43–0.86; p-value=0.005)[37].

However, most of the earlier studies noted above were conducted at a single center, and thus multicenter RCTs evaluating the effectiveness of external pancreatic duct stenting, internal pancreatic duct stenting, and non-stenting needs to be performed; especially those examining the effect of a soft pancreas on the other variables.

Pancreatic duct occlusion

In the 1980s, pancreatic duct occlusion (PDO) was explored as an alternative to PJ anastomosis[38]. An RCT in 2002, assessed postoperative morbidity and pancreatic function after PD with PJ and duct occlusion without PJ anastomosis. The study found that the incidences of POPF in the PJ and occlusion groups were 5% and 17%, respectively (p-value=0.013), and the incidences of diabetes mellitus were 14% and 34%, respectively (p-value=0.001)[39]. A single-center, prospective nonrandomized trial in 2019, assessed the safety and efficacy of pancreatic duct occlusion (PDO) with neoprene-based glue in high-risk POPF cases using the Fistula Risk Score (FRS) after the PDs. The study found that the incidences of CR-POPF were comparable between the PDO and PJ anastomosis procedures (11.8% versus 16.3%, respectively; p-value=0.51). However, new-onset diabetes at 1 and 3 years occurred in 13.7% and 36.7% in the PDO and 4.2% and 12.2% in the PJ anastomosis groups (p-value=0.007)[40]. A meta-analysis in 2022, including 13 studies found that pancreatic anastomosis had a significant benefit over PDO in CR-POPF (RR=2.41; 95% CI: 1.32–4.38; p-value=0.0041). Additionally, diabetes mellitus was more often diagnosed after duct occlusion (RR=1.61; 95% CI: 2.43–3.65; p-value<0.0001). This finding can be explained by the disruptive effect of a PDO on the endocrine pancreatic architecture, resulting in pancreatic anastomosis being the best choice to avoid this specific complication. Although this analysis highlighted that PDO through Wirsung's duct chemical sealing increased the risk of POPF, it was without an increase in postoperative mortality and had a very low prevalence of grade C POPF[41].

Intraperitoneal drainage

Although intraperitoneal drains are frequently placed during pancreatic surgeries, drain insertion and removal time have not been settled. Intraperitoneal drainage is necessary for prophylactic drainage; however, some surgeons believe that routine drain placement is unnecessary after PD. Two RCTs studied the postoperative drain issues. The first, in 2014, included 137 patients with PD, with and without intraperitoneal drainage. The data showed that PD with or without drainage was not significantly associated with CR-POPF at 30-day mortality (10% and 20%; p-value=0.104) and 60-day mortality (12% and 20%, respectively; p-value=0.174). However, this study suggests that abandoning routine intraperitoneal drainage in all patients is unsafe. Another study reported that drains were removed when the amylase concentration was low and/or the volume of output was low, typically about POD

7, the time of discharge from the hospital[42]. Conversely, a recent RCT (the PANDRA trial) in 2016, found that the CR-POPF (grade B/C) in the drain group was 11.9% and the no-drain group was 5.7%; p-value=0.030; furthermore, fistula-associated complications were significantly reduced in the no drain group (drain 26.4% versus no drain 13.0%; p-value=0.0008)[43]. However, there were some patients in whom the clinical of CR-POPF could have been underestimated in the no drain group, which affected the results of this study.

In 2018, a retrospective study of patients with postoperative day 1 drain amylase levels <5000 U/L evaluated a high and low risk of POPF by the modified fistula risk. The data showed that high-risk POPF patients with early drain removal had lower rates of CR-POPF (2% versus 15%, respectively; p-value<0.001); including overall morbidity (27% versus 47%; p-value<0.001), than those with late drain removal. Similarly, early drain removal in low-risk POPF patients was associated with decreased rates of CR-POPF (1% vs. 5%; p-value=0.014) and overall morbidity (28% vs. 41%; p-value=0.0003) compared with late drain removal. These findings are indicative of the wide variability in surgical practice and suggest that early drain removal would lead to better outcomes[44].

Surgical approach

Laparoscopic PD (LPD) is very challenging, even for experienced surgeons, because extensive dissection and three intracorporeal anastomoses must be performed[45]. A retrospective study in 2015, compared outcomes between LPD and open PD (OPD), and although the differences were not significant in terms of POPF (48% versus 41%, respectively; p-value=0.52), there was a significantly greater number of grade C POPFs in the LPD group than in the OPD group (24% versus 6%,, respectively' p-value=0.007)[45]. There have been two RCTs comparing the outcomes between LPD and OPD. The first RCT in 2017, found that LPD was comparable to OPD in creating a pancreatic fistula (18.7% versus 15.6%; p-value=0.311). However, LPD was significantly superior to OPD in the duration of POHS (7 versus 13 days, respectively; p-value=0.001) and blood loss (205 versus 401 ml; p-value<0.001)[46]. The second RCT (PADULAP) in 2018, demonstrated that LPD and OPD were comparable in the incidences of CR-POPF (12.5% and 27.6%, respectively; p-value=0.14). LPD was associated with a significantly shorter POHS (median 13.5 versus 17 days; p-value=0.024); however, it had a longer operative time (486 versus 365 minutes, respectively; p-value=0.0001)[47].

A retrospective study in 2017, demonstrated that LPD and robotic-assisted PD (RAPD) were comparable in rates of CR-POPF (18.9% versus 20.8%, respectively; p-value=0.075)[48]. Additionally, another retrospective study in 2018, showed the CR-POPF rates were greater for minimally invasive PD than open PD (15.3% versus 13.0%, respectively; p-value=0.03)[49]. A recent retrospective study in 2021, compared clinical outcomes of robot-assisted minimally invasive (hybrid laparoscopic and robotic) pancreatoduodenectomy (RA-MIPD) and OPD, and found that RA-MIPD was not superior in terms of overall complications (24.7% versus 30.9%; p-value=0.178) or CR-POPF rates (6.7% versus 6.9%; p-value>0.999). Although, the operation time was longer (361.2 versus 305.7 minutes, respectively; p-value<0.001), the average pain score was lower and the POHS was shorter (11.5 versus 17.2 days, respectively; p-value< 0.001) in the RA-MIPD group[50].

Regarding POPF, it remains unclear as to which has a better outcome: MIS-PD or open PD. However, in contrast to open PD, MIS-PD has a smaller surgical incision, decreased inflammation response to trauma and reduced risk of infection during surgery.

CONCLUSION

Postoperative pancreatic fistula is the most fatal complication of pancreatoduodenectomy. This review examined surgical factors related to POPF; especially in soft pancreatic texture and a pancreatic duct diameter of

≤3 mm. Many surgical approaches have been developed to prevent POPF; such as reconstruction methods (PG versus PJ), anastomotic techniques (interrupted suture versus Blumgart mattress PJ), pancreatic duct sutures (invagination versus duct-to-mucosa), pancreatic duct stents (usage versus non-usage), intraperitoneal drainage (with or without drainage, and early versus delayed drain removal) and surgical approaches (LPD, RAPD versus OPD). However, the updated data are still insufficient to arrive at a conclusion concerning the best surgical technique for the prevention of POPF after PD. In any individual case, the surgical technique should be selected based on the surgeon's experience in reducing the incidence of POPF as well as other complications. This review included all practical points of PD for surgeons and mini-conclusions for every topic. It is our opinion that the most favorable PD method is the open technique, interrupted PJ without pancreatic duct stent and early removal of intraperitoneal drainage.

REFERENCES

1. Kimura W, Miyata H, Gotoh M, Hirai I, Kenjo A, Kitagawa Y, et al. A pancreaticoduodenectomy risk model derived from 8575 cases from a national single-race population (Japanese) using a web-based data entry system: the 30-day and in-hospital mortality rates for pancreaticoduodenectomy. Ann Surg 2014;259:773-80.
2. Bassi C, Marchegiani G, Dervenis C, Sarr M, Abu Hilal M, Adham M, et al. International study group on pancreatic surgery (ISGPS). the 2016 update of the international study group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. Surgery 2017;161:584-91.
3. Cameron JL, He J. Two thousand consecutive pancreaticoduodenectomies. J Am Coll Surg 2015;220:530-6.
4. Aoki S, Miyata H, Konno H, Gotoh M, Motoi F, Kumamaru H, et al. Risk factors of serious postoperative complications after pancreaticoduodenectomy and risk calculators for predicting postoperative complications: a nationwide study of 17,564 patients in Japan. J Hepato-Biliary-Pancreat Sci 2017;24:243–51.
5. Fu SJ, Shen SL, Li SQ, Hu WJ, Hua YP, Kuang M, et al. Risk factors and outcomes of postoperative pancreatic fistula after pancreaticoduodenectomy: an audit of 532 consecutive cases. BMC Surg 2015;15:34.
6. Nakata K, Mori Y, Ikenaga N, Ideno N, Watanabe Y, Miyasaka Y, et al. Management of postoperative pancreatic fistula after pancreatoduodenectomy: analysis of 600 cases of pancreatoduodenectomy patients over a 10-year period at a single institution. Surgery 2021;169:1446–53.
7. Bassi C, Dervenis C, Butturini G, Fingerhut A, Yeo C, Izbicki J, et al. International study group on pancreatic fistula definition. postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 2005;138:8–13.
8. Chen BP, Bennett S, Bertens KA, Balaa FK, Martel G. Use and acceptance of the international study group for pancreatic fistula (ISGPF) definition and criteria in the surgical literature. HPB 2018;20:69–75.
9. Hu BY, Wan T, Zhang WZ, Dong JH. Risk factors for postoperative pancreatic fistula: analysis of 539 successive cases of pancreaticoduodenectomy. World J Gastroenterol 2016;22:7797–805.
10. Ke Z, Cui J, Hu N, Yang Z, Chen H, Hu J, et al. Risk factors for postoperative pancreatic fistula. Medicine (Baltimore) 2018;97:e12151.
11. Zhang B, Yuan Q, Li S, Xu Z, Chen X, Li L, et al. Risk factors of clinically relevant postoperative pancreatic fistula after pancreaticoduodenectomy: a systematic review and meta-analysis. Medicine (Baltimore) 2022;101:e29757.
12. Ellis RJ, Brock Hewitt D, Liu JB, Cohen ME, Merkow RP, Bentrem DJ, et al. Preoperative risk evaluation for pancreatic fistula after pancreaticoduodenectomy. J Surg Oncol 2019;119:1128–34.
13. Kiełbowski K, Bakinowska E, Uciński R. Preoperative and intraoperative risk factors of postoperative pancreatic fistula after pancreaticoduodenectomy – systematic review and meta-analysis. Pol J Surg 2021;93:1–10.
14. Grendar J, Ouellet JF, Sutherland FR, Bathe OF, Ball CG, Dixon E. In search of the best reconstructive technique after pancreaticoduodenectomy: pancreaticojejunostomy versus pancreaticogastrostomy. Can J Surg 2015;58:154–9.
15. Keck T, Wellner UF, Bahra M, Klein F, Sick O, Niedergethmann M, et al. Pancreatogastrostomy versus pancreatojejunostomy for RECOnstruction after PANCreatoduodenectomy (RECOPANC, DRKS 00000767). Ann Surg 2016;263:440–9.
16. Ricci C, Casadei R, Taffurelli G, Pacilio CA, Beltrami D, Minni F. Is pancreaticogastrostomy safer than pancreaticojejunostomy after pancreaticoduodenectomy? a meta-regression analysis of randomized clinical trials. Pancreatology 2017;17:805–13.
17. Lyu Y, Li T, Cheng Y, Wang B, Chen L, Zhao S. Pancreaticojejunostomy versus pancreaticogastrostomy after pancreaticoduodenectomy: an up-to-date meta-analysis of RCTs Applying the ISGPS (2016) Criteria. Surg Laparosc Endosc Percutan Tech 2018;28:39–146.
18. Kakita A, Takahashi T, Yoshida M, Furuta K. A simpler and more reliable technique of pancreatojejunal anastomosis. Surg Today 1996;26:532–5.
19. Kleespies A, Rentsch M, Seeliger H, Albertsmeier M, Jauch KW, Bruns CJ. Blumgart anastomosis for pancreaticojejunostomy minimizes severe complications after pancreatic head resection. Br J Surg 2009;96:741–50.
20. Fujii T, Sugimoto H, Yamada S, Kanda M, Suenaga M, Takami H,

et al. Modified Blumgart anastomosis for pancreaticojejunostomy: technical improvement in matched historical control study. J Gastrointest Surg 2014;18:1108–15.
21. Oda T, Hashimoto S, Miyamoto R, Shimomura O, Fukunaga K, Kohno K, et al. The tight adaptation at pancreatic anastomosis without parenchymal laceration: an institutional experience in introducing and modifying the new procedure. World J Surg 2015;39:2014–22.
22. Kawakatsu S, Inoue Y, Mise Y, Ishizawa T, Ito H, Takahashi Y, et al. Comparison of pancreatojejunostomy techniques in patients with a soft pancreas: Kakita anastomosis and Blumgart anastomosis. BMC Surg 2018;18:88.
23. Lee YN, Kim WY. Comparison of Blumgart versus conventional duct-to-mucosa anastomosis for pancreaticojejunostomy after pancreaticoduodenectomy. Ann Hepato-Biliary-Pancreat Surg 2018;22:253–60.
24. Satoi S, Yamamoto T, Yanagimoto H, Yamaki S, Kosaka H, Hirooka S, et al. Does modified blumgart anastomosis without intra-pancreatic ductal stenting reduce post-operative pancreatic fistula after pancreaticojejunostomy?. Asian J Surg 2019;42:343–9.
25. Hirono S, Kawai M, Okada KI, Miyazawa M, Kitahata Y, Hayami S, et al. Modified Blumgart mattress suture versus conventional interrupted suture in pancreaticojejunostomy during pancreaticoduodenectomy: randomized controlled trial. Ann Surg 2019;269:243.
26. Li Z, Wei A, Xia N, Zheng L, Yang D, Ye J, et al. Blumgart anastomosis reduces the incidence of pancreatic fistula after pancreaticoduodenectomy: a systematic review and meta-analysis. Sci Rep 2020;10:17896.
27. Ricci C, Ingaldi C, Alberici L, Pagano N, Mosconi C, Marasco G, et al. Blumgart anastomosis after pancreaticoduodenectomy. a comprehensive systematic review, meta-analysis, and meta-regression. World J Surg 2021;45:1929–39.
28. Bai X, Zhang Q, Gao S, Lou J, Li G, Zhang Y, et al. Duct-to-mucosa vs invagination for pancreaticojejunostomy after pancreaticoduodenectomy: a prospective, randomized controlled trial from a single surgeon. J Am Coll Surg 2016;222:10–8.
29. Senda Y, Shimizu Y, Natsume S, Ito S, Komori K, Abe T, et al. Randomized clinical trial of duct-to-mucosa versus invagination pancreaticojejunostomy after pancreatoduodenectomy. Br J Surg 2017;105:48–57.
30. Zhang S, Lan Z, Zhang J, Chen Y, Xu Q, Jiang Q, et al. Duct-to-mucosa versus invagination pancreaticojejunostomy after pancreaticoduodenectomy: a meta-analysis. Oncotarget 2017;8:46449–60.
31. Lyu Y, Li T, Wang B, Cheng Y, Zhao S. Selection of pancreaticojejunostomy technique after pancreaticoduodenectomy: duct-to-mucosa anastomosis is not better than invagination anastomosis. Medicine (Baltimore) 2018;97:e12621.
32. Cao Z, Luo W, Qiu J, Liu Y, Zheng L, Zhang T. Is invagination anastomosis more effective in reducing clinically relevant pancreatic fistula for soft pancreas after pancreaticoduodenectomy under novel fistula criteria: a systematic review and meta-analysis. Front Oncol 2020;10:1637.
33. Bin X, Lian B, Jianping G, Bin T. Comparison of patient outcomes with and without stenting tube in pancreaticoduodenectomy. J Int Med Res 2018;46:403–10.
34. Singh K, Kaman L, Tandup C, Raypattanaik N, Dahiya D, Behera A. Internal stenting across the pancreaticojejunostomy anastomosis and main pancreatic duct after pancreaticoduodenectomy. Pol Przegl Chir 2021;93:1–5.
35. Shin YC, Jang JY, Chang YR, Jung W, Kwon W, Kim H, et al. Comparison of long-term clinical outcomes of external and internal pancreatic stents in pancreaticoduodenectomy: randomized controlled study. HPB 2019;21:51–9.
36. Cai H, Lu F, Zhang M, Cai Y, Wang X, Li Y, et al. Pancreaticojejunostomy without pancreatic duct stent after laparoscopic pancreatoduodenectomy: preliminary outcomes from a prospective randomized controlled trial. Surg Endosc 2022;36:3629–36.
37. Guo C, Xie B, Guo D. Does pancreatic duct stent placement lead to decreased postoperative pancreatic fistula rates after pancreaticoduodenectomy? a meta-analysis. Int J Surg 2022;103:106707.
38. Di Carlo V, Chiesa R, Pontiroli AE, Carlucci M, Staudacher C, Zerbi A, et al. Pancreatoduodenectomy with occlusion of the residual stump by Neoprene injection. World J Surg 1989;13:105–11.
39. Tran K, Van Eijck C, Di Carlo V, Hop WCJ, Zerbi A, Balzano G, et al. Occlusion of the pancreatic duct versus pancreaticojejunostomy: a prospective randomized trial. Ann Surg 2002;236:422–8.
40. Mazzaferro V, Virdis M, Sposito C, Cotsoglou C, Droz Dit Busset M, Bongini M, et al. Permanent pancreatic duct occlusion with neoprene-based glue injection after pancreatoduodenectomy at high risk of pancreatic fistula: a prospective clinical study. Ann Surg 2019;270:791.
41. Chierici A, Frontali A, Granieri S, Facciorusso A, de' Angelis N, Cotsoglou C. Postoperative morbidity and mortality after pancreatoduodenectomy with pancreatic duct occlusion compared to pancreatic anastomosis: a systematic review and meta-analysis. HPB 2022;24:1395–404.
42. Van Buren GI, Bloomston M, Hughes SJ, Winter J, Behrman SW, Zyromski NJ, et al. A randomized prospective multicenter trial of pancreaticoduodenectomy with and without routine intraperitoneal drainage. Ann Surg 2014;259:605.
43. Witzigmann H, Diener MK, Kienkötter S, Rossion I, Bruckner T, Bärbel Werner, et al. No need for routine drainage after pancreatic head resection: the dual-center, randomized, controlled PANDRA trial (ISRCTN04937707). Ann Surg 2016;264:528–37.
44. Xourafas D, Ejaz A, Tsung A, Dillhoff M, Pawlik TM, Cloyd JM. Validation of early drain removal after pancreatoduodenectomy based on modified fistula risk score stratification: a population-based assessment. HPB 2019;21:1303–11.

45. Dokmak S, Ftériche FS, Aussilhou B, Bensafta Y, Lévy P, Ruszniewski P, et al. Laparoscopic pancreaticoduodenectomy should not be routine for resection of periampullary tumors. J Am Coll Surg 2015;220:831–8.
46. Palanivelu C, Senthilnathan P, Sabnis SC, Babu NS, Srivatsan Gurumurthy S, Anand Vijai N, et al. Randomized clinical trial of laparoscopic versus open pancreatoduodenectomy for periampullary tumours. Br J Surg 2017;104:1443–50.
47. Poves I, Burdío F, Morató O, Iglesias M, Radosevic A, Ilzarbe L, et al. Comparison of perioperative outcomes between laparoscopic and open approach for pancreatoduodenectomy: the PADULAP randomized controlled trial. Ann Surg 2018;268:731.
48. Nassour I, Wang SC, Porembka MR, Yopp AC, Choti MA, Augustine MM, et al. Robotic versus laparoscopic pancreaticoduodenectomy: a NSQIP analysis. J Gastrointest Surg 2017;21:1784–92.
49. Kantor O, Pitt HA, Talamonti MS, Roggin KK, Bentrem DJ, Prinz RA, et al. Minimally invasive pancreatoduodenectomy: is the incidence of clinically relevant postoperative pancreatic fistula comparable to that after open pancreatoduodenectomy? Surgery 2018;163:587–93.
50. Kim HS, Kim H, Kwon W, Han Y, Byun Y, Kang JS, et al. Perioperative and oncologic outcome of robot–assisted minimally invasive (hybrid laparoscopic and robotic) pancreatoduodenectomy: based on pancreatic fistula risk score and cancer/staging matched comparison with open pancreatoduodenectomy. Surg Endosc 2021;20:364–9.