Reduced Postoperative Pancreatic Fistula Rate After Pancreatogastrostomy Versus Pancreaticojejunostomy

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Received: 5 September 2008 / Accepted: 12 November 2008 / Published online: 13 December 2008 © 2008 The Society for Surgery of the Alimentary Tract

Abstract

Introduction Metaanalysis of retrospective studies employing various definitions of pancreatic fistulas demonstrated a reduced postoperative pancreatic fistula rate after pancreatogastrostomy versus pancreaticojejunostomy. Prospective trials failed to do so, which causes an ongoing debate on the superiority of one or the other procedure. The aim of this study was to compare the two types of anastomosis at our institution with regard to postoperative pancreatic fistula and other complications.

Materials and Methods From 2001 to 2007, 114 pancreatogastrostomies and 115 pancreaticojejunostomies were performed. For retrospective analysis, the ISGPS definitions were employed. Primary endpoint was the occurrence of postoperative pancreatic fistula grade B or C. Secondary endpoints were postpancreatectomy hemorrhage, delayed gastric emptying, intraabdominal fluid collection, reoperation, and mortality. Operative time, intensive care unit stay, and overall hospital stay were also compared.

Results With pancreatogastrostomy, there were significantly less postoperative pancreatic fistulae grade B and C (pancreatogastrostomy (PG) versus pancreaticojejunostomy (PJ), 11.4% versus 22.6%, p=0.03), more intraluminal hemorrhage (PG versus PJ, 10.5% versus 0%, p<0.001) and more delayed gastric emptying grade B and C (PG versus PJ, 18.3% versus 7.9%, p=0.03). Operative time was shorter (PG versus PJ, median 420 versus 450 min, p<0.01), and intensive care unit stay was longer (PG versus PJ, median 4 days versus 5 days, p<0.01), with a tendency toward reduced overall hospital stay (PG versus PJ, median 17 versus 19 days, p=0.08).

Conclusion Surgeons should be aware of a higher rate of delayed gastric emptying and perform meticulous hemostasis to prevent intraluminal bleeding with pancreatogastrostomy. Pancreatogastrostomy is superior to pancreaticojejunostomy in terms of relevant postoperative pancreatic fistula.

Keywords Surgery · Pancreatic surgery ·

Pancreaticoduodenectomy · Postoperative pancreatic fistula · Postpancreatectomy haemorrhage · Delayed gastric emptying

Introduction

nectomy (PD) by Kausch in 1912, there has been a debate

Since the first description of a successful pancreatoduode-

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among surgeons about which anastomotic procedure should be used to reinsert the pancreatic remnant. Among the various methods, only anastomosis to the jejunum or stomach has gained widespread international acceptance.² One, if not the most important, goal of all described procedures has been the reduction of the postoperative pancreatic fistula (POPF) rate to a minimum.

Reported perioperative mortality after pancreatic surgery has decreased to below 5% in centers, while occurrence of pancreatic fistula remains a significant problem, with incidences reported around 30% in the most recent series.^{3–5} A metaanalysis of studies comparing pancreatogastrostomy (PG) and pancreaticojejunostomy (PJ) has shown a significant reduction of the POPF rate in favor of PG when retrospective studies were pooled. However, three prospective randomized trials failed to prove a superiority



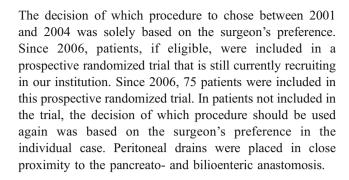
of PG over PJ.⁶ This obvious discrepancy may be attributed to several factors. There may be a publication bias preventing nonsignificant retrospective data from being published. Furthermore, in the past and also for the prospective trials, authors have used many different definitions of POPF, which makes direct comparison of and pooling of data from several studies difficult.⁷ The case number of the prospective trials was around 150,^{8–10} which is lower than that of many retrospective studies and does not provide enough power to prove differences between incidence rates, which are between 10% and 20%. Last but not least, the operative technique varies in detail between the studies. Taken together, there remains an active discussion concerning the optimal anastomotic technique.

A major step toward standardization of perioperative outcome measurement in pancreatic surgery has been the publication of consensus definitions for POPF, delayed gastric emptying (DGE), and postpancreatectomy hemorrhage (PPH) by the International Study Group of Pancreatic Surgery. The aim of this retrospective study was to compare the perioperative outcome of PD with PG versus PJ at our institution by using a large case number and the new consensus definitions.

Materials and Methods

Data The data of our prospectively maintained database for pancreatic surgery was used as a basis to perform a retrospective analysis for PD performed from 2001 to 2007. For correct assessment of POPF, DGE, and PPH grading according to the ISGPS, ^{7,11,12} the patient's records had to be reviewed, which are completely digitalized in our institution after patient discharge.

Operative Technique The technique of completely intragastric pancreatogastrostomy consisted of a purse string suture in the gastric wall (2-0 PDS) and a second intragastric line of interrupted sutures (4-0 PDS). Therefore, an additional anterior gastrotomy was necessary. PJ was performed to a Roux-Y-loop of the jejunum by single layer suture (4-0 PDS; SL-PJ) or with additional duct-mucosa-suture (5-0 PDS; DM-PJ) as described by Cartell. For SL-PJ, a decompression tube was placed in the jejuna limb, and for DM-PJ, pancreatic duct stenting was performed. For hepaticojejunostomy (single layer, interrupted, 5-0 PDS) and gastrojejunostomy (single layer, continuous, 4-0 PDS), the same jejunal Roux-Y-loop was used. In the observed time period, only four surgeons performed all pancreatoduodenectomies, and every surgeon was trained to perform all aforementioned pancreatoenteric anastomoses. The preferred anastomotic techniques were SL-PJ from 2001 to 2003, DM-PJ from 2003 to 2004, and PG from 2004 to 2006.



Standard Postoperative Patient Care All patients were transferred to the intermediate care unit for postoperative surveillance for at least 3 days. Amylase activity in peritoneal drainage fluid was measured daily during the first postoperative week until removal of drains. At the beginning of the observation period, Sandostatin (3× 100 μg s.c.) was administered routinely, but after 2002, only in case of elevated amylase activity (>1,000 U/l) on day 3 or later was it administered routinely. Amylase activity was also measured routinely if fluid samples were obtained by puncture of intraabdominal collections or ascites. Every patient received a double lumen tube for gastric decompression and early jejunal feeding, which was removed depending on tolerance for oral food intake, the goal being removal by postoperative day 3 or 4.

Standard Treatment of Postoperative Complications Abdominal computed tomography was performed in case of clinical suspicion of intraabdominal complication. Intraabdominal collections caused by POPF or other reason were preferably drained interventionally. DGE was treated by application of erythromycin and stepwise increasing oral food intake. In refractory cases, dilatation of the pylorus was the primary invasive treatment option. PPH was treated depending on severity, and first-line management of severe postoperative bleeding consisted of angiographic intervention.

Endpoints The primary endpoint was defined as the occurrence of POPF grade B or C. Secondary endpoints were DGE and PPH, reoperation, intraabdominal collection with the necessity for invasive treatment (IAC), postoperative mortality, length of ICU stay, and overall postoperative hospital stay. Patient demographics, comorbidity, and pathology reports were also evaluated with special regard to known risk factors for POPF. For POPF, DGE, and PPH, definitions and classification of the ISGPS were used.

Briefly, *POPF* is defined as an amylase activity in peritoneal drainage fluid greater than three times the upper serum normal value (300 U/l) on or after postoperative day (POD) 3. Grade A POPF does not require specific medical or invasive therapy or diet restriction, and POPF grade B is managed by specific conservative treatment and typically



Table 1 Patient and Operation Characteristics

	PG	PJ	p
Preoperative parameters			
Number of cases	114	115	ns
Age (median, years)	67.6	65.5	0.02
Male/female ratio	5:6	6:5	ns
Preoperative bilirubin (mg/dl)	3.7	3.3	ns
Preoperative biliary drainage (%)	47.4	59.1	ns
Preoperative creatinine (median, mg/dl)	0.8	0.7	0.04
Preoperative diabetes mellitus (%)	21.1	22.6	ns
Operative technique			
Pylorus-preserving operation (%)	90.4	86.1	ns
Portal vein resection (%)	22.8	26.1	ns
Intraoperative blood transfusion (%)	21.1	27.8	ns
Histopathologic diagnosis			
Adenocarcinoma of the pancreas (%)	41.2	45.2	ns
Ampullary carcinoma (%)	16.7	11.3	ns
Duodenal carcinoma (%)	7.0	3.5	ns
Distal bile duct carcinoma (%)	10.5	16.5	ns
Neuroendocrine tumors (%)	2.6	1.7	ns
IPMN (%)	2.6	0.9	ns
Chronic pancreatitis (%)	11.4	15.7	ns
Other diagnosis (%)	7.9	5.2	ns
Type of lesion			
Benign (%)	16.7	18.3	ns
Malignant (%)	79.8	80.9	ns
Borderline (%)	3.5	0.9	ns

PG pancreatogastrostomy, PJ pancreatojejunostomy, IPMN intraductal papillary mucinous neoplasia, p derived from statistic tests, ns not significant

leads to prolonged hospital stay or readmission, whereas POPF grade C requires invasive treatment such as percutaneous drainage or reoperation. Because in the beginning of this study Sandostatin treatment was performed routinely as described above, this was not considered a criterion for POPF grade B.

DGE was defined as the necessity of gastric tube decompression after POD 3 or later or the inability to tolerate solid oral intake (SOI) on POD 7 or later. If the gastric tube could only be removed by day 7, 14, or 21 and SOI was only possible by POD 14, 21, or later, DGE was graded A, B, or C, respectively. DGE grade A requires only prokinetic drugs, DGE grade B requires diagnostic measures or prolonged hospital stay, and invasive treatment leads to classification as DGE grade C.

PPH is defined as every bleeding event after pancreatic surgery. PPH grade A does not require specific treatment but only diagnostic measures, PPH grade B requires treatment, and PPH grade C is considered life threatening. Early or late PPH occur within or later than 24 h after the operation. Intraluminal PPH has an intraluminal origin, in contrast to extraluminal PPH.

Statistical Analysis All data were collected and analyzed in a SPSS Version 15.0 database. The two-sided Fishers exact test was used for dichotomous variables, the Mann–Whitney U test for scale variables, Spearman's method for

rank correlation, and binary logistic regression for multivariate analysis.

Results

Patients and Operations From 2001 to 2007, 229 PD were performed at the University Hospital Freiburg. Of these, 114 were reconstructed with PG and 115 with PJ (66 SL-PJ and 49 DM-PJ). Patient characteristics are shown in Table 1. There were no significant differences between the groups PG and PJ except for preoperative creatinine and age at

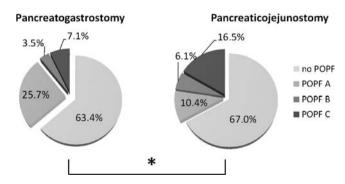


Figure 1 POPF with PG and PJ. PG pancreatogastrostomy, PJ pancreaticojejunostomy. Grade of POPF (A, B, C) is given according to the ISGPS classification. *p=0.03 for POPF grade B or C.



Table 2 Occurrence of the Primary Endpoint with Different Types of Anastomoses

	PG	PJ	p	SL-PJ	DM-PJ	p
POPF grade B or C	11.4%	22.6%	0.03	24.2%	20.4%	ns

Postoperative pancreatic fistula grade B or C (POPF B or C) after pancreatogastrostomy (PG) or pancreatojejunostomy (PJ) SL-PJ PJ with single suture line, DM-PJ PJ with duct-mucosa anastomosis; p derived from statistic tests, ns not significant

operation, which were slightly higher in the PG group. Around 90% of operations were performed with preservation of the pylorus, and in about one fourth of cases, a portal vein resection was carried out because of malignant invasion. Most of the operations were carried out for malignant lesions.

Postoperative Pancreatic Fistula (POPF) The distribution of POPF by definition of the ISGPS is shown in Fig. 1 and Table 2. There were significantly less POPF of grade B and C (PG versus PJ, 11.4% versus 22.6%, p=0.03) in the PG group compared to the PJ group. The overall fistula rate (grade A, B, and C) was not statistically different (PG versus PJ, 36.8% versus 33.0%, p=ns). Intraabdominal collections were associated with POPF (p<0.001) and less frequently with PG (PG versus PJ, 9.6% versus 16.5%), but this reduction did not reach the significance level (p=ns). Comparison of SL-PJ and DM-PJ for the primary endpoint did not show a significant reduction with duct-to-mucosa technique (SL-PJ versus DM-PJ, 24.2% versus 20.4%, p= ns). The underlying pancreatic disease had a significant influence on the rate of POPF grade B and C. There was a negative correlation with pancreatic carcinoma and a positive correlation with ampullary carcinoma, as outlined in Table 3. Univariate analysis for factors known to influence POPF rate also disclosed a significant positive correlation for the preoperative creatinine level. In multivariate analysis, type of anastomosis and pancreatic carcinoma were the only independent predictors of the primary endpoint, as outlined in Table 4.

Postpancreatectomy Hemorrhage (PPH) A summary of PPH events is given in Table 5. None of the PPH episodes was considered grade A because there was always a

therapeutic intervention. There were no significant differences between PG and PJ, except for significantly more intraluminal PPH in the PG group than in the PJ group (PG versus PJ, 10.5% versus 0%). This was in part caused by bleeding from the pancreatogastric anastomosis site, which required relaparotomy in four cases (3.5% of PG). There was no case of disruption of the anastomosis by bleeding events as described by other authors. 13 In all four cases that required relaparotomy, the bleeding from the anastomotic site was occurring within the first or second day after the operation, and within the first 20 cases, we performed this procedure. The source of bleeding was in all these cases the cut surface of the pancreas. Since we changed our regimen of bleeding control on this surface intraoperatively from electrocautery to 5-0 PDS sutures, we did not experience this complication any more. Relaparotomy in these cases was preferred to endoscopy as we were worried about additional damage to the pancreatogasrostomy, the gastrojejunostomy, or the ventral gastrostomy.

Delayed Gastric Emptying (DGE) There was a significantly higher rate of DGE of grade B and C in the PG group than in the PJ group (PG versus PJ, 18.3% versus 7.9%, p=0.03), as outlined in Fig. 2. Interestingly, an association of DGE with other complications, namely POPF and IAC, could only be demonstrated for PJ but not for PG (Table 6).

Relaparotomy, Overall Mortality, and Hospital Stay Relaparotomy rates were not statistically different comparing PG and PJ (15.8% versus 10.4%, p=ns). Indications for relaparotomy are shown in Fig. 3. The slightly, but not significantly higher reoperation rate for PG, was for the greatest part caused by relaparotomy for intraluminal bleeding (four cases, 3.5% of PG). Reoperation rates were

Table 3 Occurrence of the Primary Endpoint with Different Histopathologic Diagnoses

Histopathologic diagnosis	Occurrence of POPF grade B or C (%)	Correlation coefficient	p
Pancreatic CA	9.1	-0.18	< 0.01
Ampullary CA	31.3	0.15	0.02
Distal bile duct CA	29.0	0.13	ns
Chronic pancreatitis	19.4	0.02	ns
Other	13.9	-0.04	ns

Shown are the results of correlation analysis for specific histopathologic diagnoses and the occurrence of the primary endpoint POPF grade B or C POPF postoperative pancreatic fistula, CA carcinoma, p derived from statistic tests, ns not significant



Table 4	Analysis	of Factors
Influenci	ng POPF	Rate

Primary endpoint was postoperative pancreatic fistula (POPF) grade B or C (0 = no and 1 = yes). The upper panel shows the results of univariate analysis; the lower panel shows the results of multivariate analysis. *PG* pancreatogastrostomy, *PJ* pancreatojejunostomy, *preop.* preoperative, *intraop.* Intraoperative, *ns* not

significant

Factor		p
Univariate analysis		
	Correlation coefficient	
Type of anastomosis: PG or PJ (=0/1)	0.15	0.02
Age (years)	0.02	ns
Gender $(m/f=0/1)$	0.09	ns
Preop. creatinine (mg/dl)	0.14	0.04
Preop. bilirubin (mg/dl)	0.09	ns
Preop. diabetes mellitus	0.01	ns
Intraop. blood transfusion	0.09	ns
Multivariate analysis		
	Odds ratio	
Type of anastomosis: PG or PJ (=0/1)	2.58	0.01
Pancreatic carcinoma	0.39	0.03
Ampullary carcinoma	2.01	ns
Preop. creatinine (mg/dl)	1.19	ns

high mainly due to postoperative hemorrhage in the pancreatogastrotomy group as specified above. Reoperation rates in general may be higher than in other studies from pancreatic centers. This might reflect our aggressive approach to postoperative complications. We prefer open revisions when we face problems with the pancreatic or biliodigestive anastomosis. We also prefer operative revisions for very early gastrointestinal bleeding from the pancreatic remnant after pancreatogastrostomy. This aggressive approach results in higher reoperation rates but might indeed contribute to our low mortality rates. Overall, perioperative mortality was 2.6%. Causes were late PPH (two cases), peritonitis with sepsis (two cases), liver failure due to stent occlusion after stent placement in the common hepatic artery for arrosion of the gastroduodenal artery (one case), and acute myocardial infarction (one case). There was no significant difference in perioperative mortality between PG (1.8%) and PJ (3.5%).

Operation time was 30 min shorter when PG was performed (PG versus PJ, median 420 versus 450 min,

 Table 5
 Occurrence of Postpancreatectomy Hemorrhage (PPH)

 According to the ISGPS Classification

	PG (%)	РЈ (%)	p
PPH grade A	0	0	ns
PPH grade B	11.4	4.3	ns
PPH grade C	5.3	4.3	ns
Mild PPH	6.1	2.6	ns
Severe PPH	10.5	6.1	ns
Intraluminal PPH	10.5	0	< 0.001
Extraluminal PPH	6.1	8.7	ns
Early PPH	3.5	0	ns
Late PPH	13.2	8.7	ns

PG pancreatogastrostomy, PJ pancreatojejunostomy, p derived from statistic tests, ns not significant

p<0.01). Postoperative ICU stay was significantly longer after PG than after PJ (PG versus PJ, median 4 days versus 5 days, p<0.01). Length of ICU stay correlated positively with PPH, POPF, and also with occurrence of DGE grade B and C (p<0.05). Overall, postoperative hospital stay was shorter with PG, but this was only a statistic trend (PG versus PJ, 17 versus 19 days, p=0.08).

Discussion

Many retrospective reports have compared PG and PJ, and recent metaanalysis disclosed lower POPF rates in favor of PG. Nevertheless, three prospective, randomized studies failed to demonstrate a better outcome regarding POPF or perioperative mortality, also if pooled for metaanalysis. The results of most of all studies are not directly comparable, as POPF definitions and operative techniques vary. Prospective studies were maybe underpowered to find small differences in POPF rates. Only few recent studies have employed the ISGPS consensus definitions yet. The aim of this

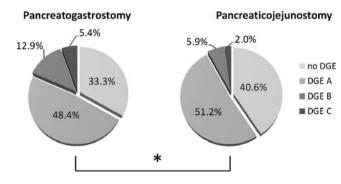


Figure 2 DGE with PG and PJ. PG pancreatogastrostomy, PJ pancreaticojejunostomy. Grade of DGE (A, B, C) is given according to the ISGPS classification. *p=0.03 for DGE grade B or C.



Table 6 Type of Anastomosis Affects the Association of DGE with Other Postoperative Complications

	DGE (%)	p value for association with	
		POPF	IAC
PG	66.7	ns	ns
PJ	59.4	0.03	0.02

PG pancreatogastrostomy, PJ pancreatojejunostomy, DGE delayed gastric emptying (all grades), POPF postoperative pancreatic fistula (all grades), IAC intraabdominal collection requiring invasive treatment, p derived from statistic tests, ns not significant

study was to compare the perioperative outcomes of PG versus PJ at our institution, using the ISGPS definitions and a case number large enough to demonstrate small differences. For proper adherence to these definitions, a review of all patient records was necessary.

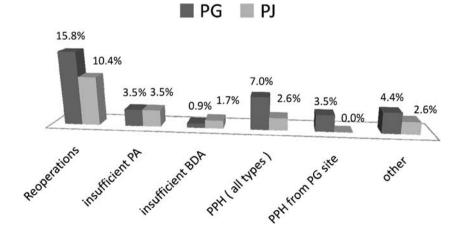
By definition, the clinical impact of POPF grade A is low, as this implies only "biochemical" self-limited fistulae. Therefore, we decided to use POPF grade B and C as the primary endpoint. Our analysis showed a significantly lower rate of the clinically relevant POPF of grade B and C in the PG group, suggesting that PG is superior to PJ in terms of POPF. Of note, the type of anastomosis and pancreatic carcinoma were the only independent factors, which showed an influence on POPF rate, in contrast to other known factors. Pancreatic carcinoma, which is often associated with hard pancreatic texture, was a protective factor; surprisingly, however, chronic pancreatitis, which is well known for its fibrotic pancreatic tissue, was not. Within the PJ group, the duct-to-mucosa technique did not lead to a significant reduction in POPF rate. The lower rate of POPF after PG did not translate into a significantly reduced rate of IAC or reoperations, however. The rationale behind a reduced POPF rate with PG (as performed at our institution) may be the effective inversion of the pancreatic remnant into the stomach and the fact that the complete anastomosis,

Figure 3 Reoperations and indications with PG and PJ. Given are the percentages in the groups of PG and PJ. BDA biliodigestive anastomosis, PPH postpancreatectomy hemorrhage according to the ISGPS classification.

including all suture line stitch channels, are situated intragastric, in contrast to the transmural sutures involved in SL-PJ or DM-PJ. It is noteworthy that for the aforementioned three prospective studies of PG versus PJ, different PG techniques were performed. One also has to reflect that each of the anastomosic procedures has a learning curve that should, as the learning effect occurs for each method, not lead to improved insults of one of these techniques over time. However, we are aware that we are presenting a retrospective study that is not free of this potential bias.

Concerning PPH, analysis showed that there was more intraluminal bleeding in the PG group, which was in part caused by bleeding from the PG site requiring relaparotomy. However, disruption of the pancreatoenteric anastomosis, as described in other series, ¹³ did not occur. Relaparotomy in these cases was considered necessary because air insufflation and gastric distension during gastroscopic hemostatic measures would have constituted a thread to the freshly established PG. Bleeding at the PG site was mainly an initial problem of this technique, which can be circumvented by proper intraoperative hemostasis by small 5-0 sutures on the surface of the pancreatic remnant. In our experience with PG, single stitches rather than electrocoagulation provide sufficient hemostasis at the pancreatic cut surface and pancreatoenteric anastomosis site.

The incidence of clinically relevant DGE (grade B and C) was higher in the PG group. This result seems reasonable, as PG requires more extensive mobilization of the stomach along the lesser curve, which is associated with disruption of autonomous nerve fibers mediating gastric motility. There are also two additional gastrotomies (anterior and posterior) with PG, increasing gastric traumatization. PG furthermore leads to a fixation of the posterior stomach wall to the retroperitoneum, potentially limiting gastric wall motility. However, DGE has also been reported to be less frequent with PG than with PJ in other prospective and retrospective trials. Interestingly, the known association of DGE with other postoperative





complications such as POPF or IAC could only be demonstrated for the PJ group and not for PG. This is important to notice as DGE raises the suspicion for intraabdominal complications especially for PJ, but less so if the anastomosis is a PG. DGE in the PG group might have contributed to the longer ICU stay in this group, as shown by a positive correlation. Nevertheless, there was a trend toward shorter overall postoperative hospital stay with PG.

Perioperative mortality was low in both groups, and lower after PG than after PJ, but not statistically significant. An important factor contributing to postoperative mortality was late extraluminal PPH, as this was the responsible inciting event for 50% of the perioperative mortality. Late PPH leads to lethal hemorrhagic shock in one patient. In the second case, bleeding could be controlled by stent placement in the common hepatic artery, but stent occlusion caused lethal liver failure. The third patient suffered from repeated massive venous intraabdominal bleeding, which led to multiorgan failure and ultimately abdominal sepsis. The potentially fatal role of delayed PPH is in line with the observations of other authors. 12-16 In summary, the pancreatogastrostomy provides a good, simple, and easy to perform anastomosis as an alternative to the pancreaticojejunostomy. We are still including patients for our prospective randomized trial on pancreatic anastomosis. Our preferred technique for patients not eligible for the trial is the pancreatogastrostomy for the soft pancreas and the pancreaticojejunostomy for the hard pancreas. For the soft pancreas, the pancreatogastrostomy is especially easy to perform as the pancreas is invaginated into the stomach. For the hard pancreas, the Warren Cartell anastomosis seems more effective as an extended mobilization of the pancreatic remnant can sometimes be difficult in these patients. Reoperations and complications in the pancreatogastrostomy group were mainly encountered in the beginning of the application of this technique. In our prospective study, which started after the learning curve, we might not anymore encounter these drawbacks of the pancreatogastrostomy as presented in this current retrospective study.

Conclusion

The ISGPS definitions are well suited for comparative studies in pancreatic surgery. In concordance with previous findings, the present study suggests that PG is superior to PJ in terms of POPF. When performing PG, surgeons should be aware of a higher rate of DGE and proper intraoperative hemostasis to prevent intraluminal PPH. Mortality rates for pancreatoduodenectomy are low in centers and did not differ significantly between PG and PJ. These findings have to be confirmed by an additional ongoing prospective trial.

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