World J Surg (2010) 34:1579–1586
DOI 10.1007/s00268-010-0521-5

World Journal of Surgery

Risk-Adapted Anastomosis for Partial Pancreaticoduodenectomy Reduces the Risk of Pancreatic Fistula: A Pilot Study

Marco Niedergethmann · Niloufar Dusch · Rizky Widyaningsih · Christel Weiss · Peter Kienle · Stefan Post

Published online: 24 March 2010

Abstract

Background Pancreatic fistula (PF) is the main cause of postoperative morbidity and mortality after pancreatectomy. Two reasons for PF are a "soft" pancreatic texture and a narrow pancreatic duct (high-risk gland). Pancreaticojejunostomy (PJ) may lead to a higher fistula rate in such glands. In the literature there are no data available on risk-adapted assignment of pancreatogastrostomy (PG) in a high-risk gland. Therefore, an observational pilot study was conducted to address this issue.

Methods Since January 2007 the concept of a "risk-adapted pancreatic anastomosis" (RAP) was introduced (PG for high-risk glands). The PF rate, morbidity, and mortality during this period (January 2007 to December 2008, $n = 74$) were compared to those between January 2004 and December 2006 ($n = 119$, only PJ). PF was defined according to the International Study Group on Pancreatic Surgery.

Results Through RAP the PF rate was reduced from 22 to 11% ($P = 0.0503$). Grade C PF rate was reduced from 6.7 to 1.4% ($P = 0.1569$) and grade A PF from 6 to 1.4% ($P = 0.2537$). The PF-associated mortality was reduced from 3.4 to 1.4%. PG revealed a PF rate of 7% and PJ accounted for 19% of PFs ($P = 0.1765$). There was no incidence of grade C PF following PG. The incidence of intraluminal hemorrhage ($P = 0.0422$) and delayed gastric emptying ($P = 0.0572$) was higher following PG.

Conclusions The rate of PF could be significantly reduced with the use of RAP. One should be cautious about the indication for PG, since it is associated with a higher rate of intraluminal hemorrhage and delayed gastric emptying. There are no long-term results on PG with respect to its durability and function. A general recommendation for its use cannot currently be made.

Introduction

Pancreatic anastomosis is the "Achilles' heel" in pancreatic surgery [1, 2]. Leakage of the pancreaticointestinal anastomosis is the main trigger for other morbidities following this procedure [2–8]. The two most common reasons for leakage of pancreatic anastomosis are a "soft" texture of the pancreas and a small pancreatic duct size. Chronic pancreatitis leads to fibrotic, "hard" pancreatic tissue. Thus, anastomotic leakage is observed less frequently after resections due to chronic pancreatitis compared to after resections due to solid or cystic neoplasms [9]. The reported incidence of leakage lies between 0 and 30% according to the type of anastomosis performed and may be an underestimation due to selection as well as publication bias [2]. Various techniques are available for the management of the pancreatic remnant such as

M. Niedergethmann and N. Dusch contributed equally to this work.

M. Niedergethmann · N. Dusch · R. Widyaningsih · P. Kienle · S. Post
Department of Surgery, Faculty of Medicine Mannheim, University Medical Center Mannheim, University of Heidelberg, 68135 Mannheim, Germany

C. Weiss
Department of Biomathematics, Faculty of Medicine Mannheim, University Medical Center Mannheim, University of Heidelberg, 68135 Mannheim, Germany

M. Niedergethmann (✉)
Department of Surgery, University Medical Centre Mannheim (UMM), Faculty of Medicine Mannheim/University of Heidelberg, Theodor-Kutzer-Ufer 1-3, 68167 Mannheim, Germany
e-mail: marco.niedergethmann@umm.de

occlusion of the pancreatic duct using fibrin glue [10], simple ligation of the duct [11, 12], optimization of the blood supply to the edge of the pancreatic remnant and meticulous placement of sutures using magnification [13], the application of sealant around the pancreaticojejunostomy [14], various modifications to pancreaticojejunostomy (end-to-end or end-to-side) [15–17], and the pancreatogastrostomy [18–20]. In patients with severe pancreatic fistulas (PF) (grade C), the pancreatogastrostomy has already been suggested as a salvage procedure [21]. The main reconstructed organs following a pancreatic head resection are the jejunum [pancreatojejunostomy and pancreaticojejunostomy with duct-to-mucosa anastomosis (PJ)], and the stomach (pancreatogastrostomy PG) [2, 15, 18–20]. The question of which anastomosis is *generally* the superior one cannot not be answered for the time being. All randomized controlled trials (RCTs) have failed to show an advantage of a particular technique, suggesting that both PJ and PG provide equally good results [19, 22, 23]. Only in some observational clinical studies has PG shown superiority with respect to fistula rates [24]. The influence of a soft gland and/or small duct size, however, has never been stratified in RCTs or observational clinical studies. The high-risk glands (soft texture, narrow duct) tend to have more PF [5–8]. A "one anastomosis fits all" attitude would not reflect the clinical routine.

There is no study that examined the implementation of a PG or PJ based on the pancreatic texture and duct size. The aim of this study was to evaluate the concept of a "risk-adapted pancreatic anastomosis" (RAP). According to this concept the surgeon would perform a PG instead of a PJ in all high-risk glands. The results following this concept were compared to the postoperative results following the use of solely PJ as a standard procedure for reconstructing the pancreatic remnant. To obtain preliminary results for a RCT, this investigation was initiated in a prospective observational setting.

Patients and methods

In January 2007 the concept of "risk-adapted pancreatic anastomosis" (RAP) was introduced at the Department of Surgery, University Medical Center Mannheim, Germany, for all pancreatointestinal anastomoses after partial pancreaticoduodenectomy (PD). This implied that during the operation the surgeon (MN, PK, SP) had to decide whether to perform a standard duct-to-mucosa pancreaticojejunostomy (PJ), or a pancreatogastrostomy (PG) (in case of a "soft" pancreas and/or a duct diameter $\leq$ 3 mm). The pancreatic texture was defined as "soft" or "hard" by the surgeon palpating the gland. The pancreatic duct diameter was measured (mm). Patients with a high-risk pancreas (soft pancreas and/or a duct diameter $\leq$ 3 mm) received octreotid perioperatively (intraoperatively 100 μg s.c. and 5 days postoperatively 100 μg s.c. tid). The primary goal of this prospective observational study was to investigate the effect of RAP on the rate of anastomotic leakage. The secondary goal was to evaluate its effects on morbidity and mortality compared to the use of PJ alone. This was a pilot observational study in order to obtain data for the introduction of a prospective RCT.

Data collection

All patients with RAP from January 2007 to December 2008 were recorded in the prospective departmental pancreatic database as described before [25, 26]. During this period (2 years) 74 PD were performed, 47 patients received a PJ, and 27 patients with a high-risk gland received a PG. The period of RAP was compared to the period between January 2004 and December 2006 ($n = 119$), during which patients were also recorded in the prospective departmental pancreatic database. During the latter period (3 years) all PD were reconstructed with a PJ. In case of a soft pancreas and/or small duct size, octreotid was applied perioperatively on demand.

The data of all patients examined included demographics, pathology report, TNM stage and UICC classification, preoperative presenting symptoms, preoperative procedures (e.g., biliary stent), lab work, the American Society of Anesthesiologists (ASA) score, details of the surgical therapy (including blood loss and blood transfusions), the hospital course (including complications and fistula rates), and postoperative survival. Follow-up was performed through personal contact with the patient or patient's primary physician and was terminated on June 1, 2009, or at the patient's death. All deaths occurring within 30 days after surgery or throughout the hospital stay were classified as surgical mortality.

Surgical technique

The reconstruction after partial pancreaticoduodenectomy (classic Kausch-Whipple or pylorus-preserving procedure) was performed as either a duct-to-mucosa pancreaticojejunostomy (since January 2004) or as a pancreatogastrostomy (since January 2007). The two-layer *duct-to-mucosa pancreaticojejunostomy* (PJ, Fig. 1) was standardized as follows [27]: After mobilization of the pancreatic remnant, the inner suture layer was placed on the pancreatic duct. On average eight stitches were required (resorbable monofilament 5-0 sutures). The mesenteric surface of the jejunum was approximated to the pancreas stump and the posterior wall of the outer suture layer was sewn in a running manner (resorbable monofilament 4-0 sutures). A small incision

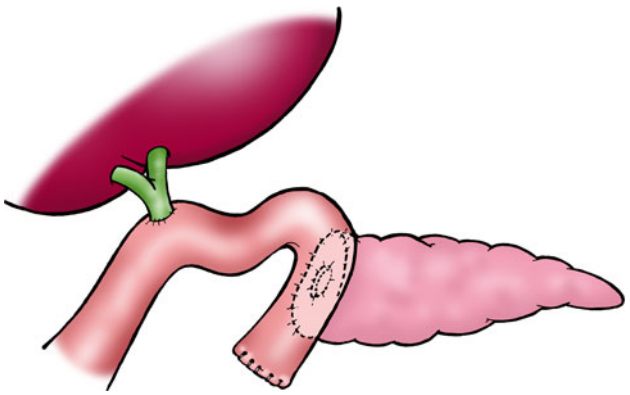

Fig. 1 Pancreaticojejunostomy: after mobilization of the pancreatic remnant, the inner suture layer is placed on the pancreatic duct. The outer suture (posterior and anterior wall) layer is sewn in a running manner

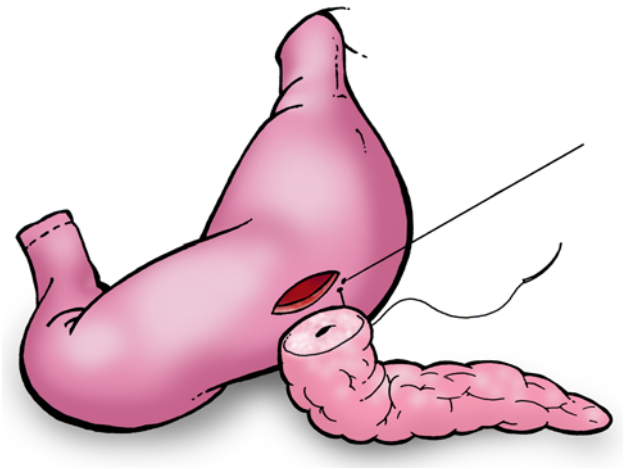

Fig. 2 Pancreatogastrostomy: dorsal small gastrotomy of the stomach for telescoping of mobilized pancreatic stump. Single layers of interrupted sutures are taken from the posterior gastric wall (seromuscular) to the anterior wall of the pancreas

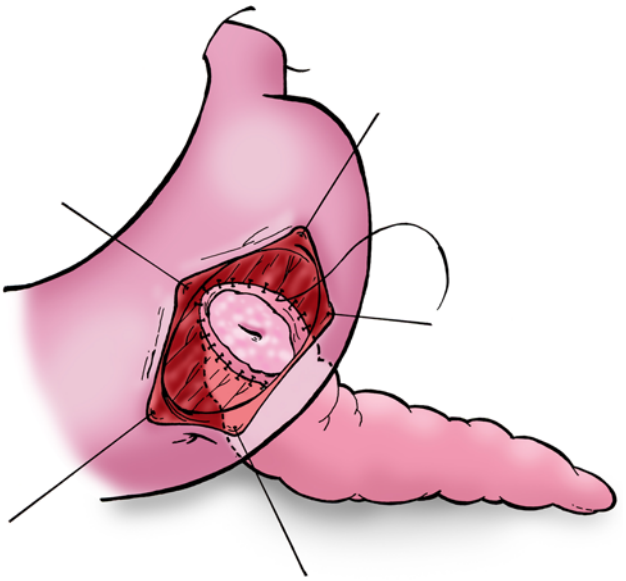

Fig. 3 Pancreatogastrostomy: anterior gastrotomy is performed and 2 cm of the pancreatic remnant is telescoped into the lumen and secured by a running suture

corresponding to the location and diameter of the pancreatic duct was made on the antimesenteric surface of the jejunum. The inner layer (duct-to-mucosa) was completed by stitching the previously placed sutures and tying them gently (Fig. 1). The anastomosis was completed with a running suture of the outer anterior wall.

During the period of RAP (January 2007 to December 2008), a standardized *pancreatogastrostomy* (PG) was performed in all high-risk glands. Small vessels of the cut surface of the pancreatic remnant were sutured with non-resorbable monofilament 4-0 sutures. The pancreatic remnant was mobilized along the splenic vessels for 4 cm. Single layers of interrupted sutures of resorbable monofilament 4-0 sutures went from the posterior gastric wall (seromuscular) to the anterior wall of the pancreas. A small gastrotomy (two thirds of the diameter of the pancreatic remnant) was performed on the posterior wall of the stomach (Fig. 2). Opposite to this incision an anterior gastrotomy was performed. The pancreatic remnant was telescoped over a length of 2 cm into the gastric lumen and secured by a running resorbable monofilament 4-0 inside suture (Fig. 3). A nasogastric tube was placed under vision and the anterior gastric incision was closed (resorbable monofilament 4-0 sutures). After that the posterior surface of the pancreatic remnant was connected to the posterior gastric wall.

Patients with high-risk glands received perioperative octreotid until postoperative day (POD) 5. These patients had a nasogastric tube in place for 48 h as an indicator drain for intraluminal hemorrhage and received a high dose of pantoprazol (40 mg i.v. bid). Patients with a standard anastomosis received neither octreotid nor high-dose pantoprazol. Two soft drains were placed in all patients and they were kept on a fluid diet on POD 2 and 3. Starting on POD 4, they could eat solid meals if tolerated. In all patients the amylase content in the drains was measured daily until POD 7. If the amylase level was less than three times the normal serum amylase level (3×115 U/L = 345 U/L), the drains could be removed on POD 7. If the amylase level was elevated (> 345 U/L), the drain at the pancreatic anastomosis was left *in situ*.

Pancreatic fistula and complications

A PF was defined according to the International Study Group on Pancreatic Surgery (ISGPS) definition [28]. A grade A PF is a so-called "biochemical, transient fistula"

and has no clinical impact. A grade A PF requires little change in management or deviation from the normal clinical pathway. A grade B PF requires a change in patient management or an adjustment in the clinical pathway. It usually leads to a delay in discharge, to readmission, or to discharge of the patient with drains *in situ*. A grade C PF leads to a major change in the clinical management or a deviation from the normal clinical pathway. A deteriorating clinical status with a grade C leakage together with sepsis and organ dysfunction may require re-exploration in an attempt to repair the site of leakage with wide peripancreatic drainage, a conversion to an alternative pancreaticoenteric anastomosis, or a complete pancreatectomy. Other specific surgical complications such as delayed gastric emptying (DGE) or postpancreatectomy hemorrhage (PPH) were assessed following the ISGPS definitions [29, 30].

Statistical analyses

The primary end point of the study was the leakage of the pancreatic anastomosis. A χ^2 test, Fisher's exact test, or Mann-Whitney's U test was performed as appropriate in order to compare the two groups. Statistical significance was accepted at the probability level of 0.05; test results with $0.05 < P < 0.10$ were considered slightly significant. All statistical calculations were performed using SAS software v9.01 (SAS Institute Inc., Cary, NC, USA).

Results

There were no statistically significant differences between the PJ period ($n = 119$, 2004-2006) and the RAP period ($n = 74$, 2007-2008) with respect to the distribution of gender, age, indications, preoperative symptoms and state of health (including jaundice), histopathology results (pancreatic cancer, distal bile duct cancer, cancer of the papilla of Vater, cystic tumors, chronic pancreatitis), stomach reconstruction (pylorus preservation or Kausch-Whipple), and need for perioperative transfusion. The median duration of the surgical procedure was significantly longer for PG than for PJ (390 min vs. 346 min, $P = 0.0001$).

The overall fistula rate was 18% (34/193). The standard use of PJ for reconstruction (2004-2006) was associated with a fistula rate of 22% (26 fistulas/119 resections). After the introduction of RAP, the fistula rate was significantly reduced to 11% (8/74) ($P = 0.0503$). During the RAP period (2007-2008), there was only one case of a grade A fistula (1/74, 1.4%) compared to 6 (6/119, 5%) between 2004 and 2006 ($P = 0.2537$), and 6 cases of grade B fistula (6/74, 8.1%) in the RAP period compared to 12 (12/119, 10.1%) between 2004 and 2006 ($P = 0.6463$) (Table 1). In patients with a grade A leakage, no change or deviation from the normal clinical pathway was necessary. Patients with a grade B fistula were discharged from hospital after an average of 28 days compared to 19 days for those without a fistula ($P = 0.02$). Four patients with a grade B fistula had to be readmitted to hospital compared to none without a fistula. Between 2004 and 2006 five patients were discharged with a drain *in situ* compared to six patients during the RAP period. Between 2004 and 2006 seven patients with grade B leakage required interventional drainage for intra-abdominal abscess caused by the leakage. During the RAP period there was no case of intra-abdominal abscess or interventional drainage (Table 1). During the RAP period the rate of grade C fistula was 1.4% (1/74) compared to 6.7% (8/119) in the period between 2004 and 2006 ($P = 0.1569$) (Table 1). During the latter period four patients died due to the fistula and its subsequent complications. One patient with a grade C fistula during the RAP period also died after septic complications ($P = 0.6508$). Between 2004 and 2006 eight patients with a grade C fistula required re-exploration, three in an attempt to repair the site of leakage with wide peripancreatic drainage and five for completion pancreatectomy. Between 2007 and 2009 one patient with grade C leakage was re-explored for conversion from PJ to PG. There were no cases of grade C fistulas following PG. Focusing on the patients who had a PG, which was performed only for high-risk glands, the PF rate following PG was at 7% (2/27). Following PJ the rate of fistula was 19.5% (32/166) ($P = 0.1765$). Through the introduction of RAP, the fistula-related relaparotomy rate was reduced from 6.7 to 1.4%, reflecting less fistula-associated morbidity during this period. The overall mortality rate during the PJ period was 4/119 (3.4%), including three fistula-associated mortalities. Two patients died during the RAP period but they were not fistula-associated mortalities.

Postoperative hemorrhage (PPH) was observed in 4/74 patients (5%) during the RAP period (2007-2009). There were three PG patients (3/27, 11%) with intraluminal hemorrhage from a cut on the surface of the pancreas. Two patients were treated endoscopically with hemoclipping and fibrin glue (PPH severity grade B), and both did not take their pantoprazol medication. One patient was on high-dose dalteparin anticoagulation medication for atrial fibrillation and was undergoing heparin-based hemodialysis for renal insufficiency. He died during hemodialysis due to massive upper gastrointestinal bleeding on POD 5 before an endoscopy could take place (PPH severity grade C). There was one patient (1/47, 2.1%) with postoperative extraluminal hemorrhage after PJ in the RAP period (PPH severity grade B). Between 2004 and 2006 there were nine patients with PPH: four intraluminal and five extraluminal

Table 1 Results of the concept of risk-adapted pancreatic anastomosis (RAP) compared to the sole use of pancreaticojejunostomy

	PJ 2004	PJ 2005	PJ 2006	PJ period	PJ 2007	PG 2007	PJ 2008	PG 2008	RAP period
PD (*n*)	47	31	41	119	17	11	30	16	74
PF (*n*)	8	6	12	26	4	1	2	1	8
PF rate (%)				22					11
Grade A (*n*)	3	2	1	6	1	0	0	0	1
Grade B (*n*)	3	2	7	12	2	1	2	1	6
d/c w drain[a]	2	1	2		2	1	2	1	
Intervention[b]	1	1	5		0	0	0	0	
Grade C (*n*)	2	2	4	8	1	0	0	0	1
Relaparotomy	2	2	4		1	0	0	0	
Total mortality	2	1	1	4	1	1	0	0	2
Fistula-associated mortality (*n*)				3					0

Fistula grading defined after Bassi et al. [23]

[a] d/c w drain = discharged from hospital with drainage in place

[b] Sonographic or CT-guided drainage

(all PPH severity grade B). There was no significant difference in PPH between the two periods ($P = 0.8658$). The incidence of intraluminal bleeding was, however, significantly higher in PG compared to PJ [3/27 (11%) vs. 4/166 (2.4%), $P = 0.0422$].

DGE was observed in 44/193 patients (22.8%). Most patients, however, were able to tolerate solid food 1 or 2 weeks after surgery (DGE grades A and B, 37/193, 19.2%). Seven of 193 (3.6%) patients had prolonged problems with solid food intake (>3 weeks) or required reintervention (DGE grade C). Comparing all PJs to all PGs that were performed from January 2007 through December 2008, there were fewer patients with DGE in PJ [34/166 (20%)] than in PG [10/27 (37%)] ($P = 0.0572$). Grade C DGE occurred in two patients with PG (7.4%) compared to five cases with PJ (3%). There was no statistically significant difference with respect to all DGE grades between the two periods (RAP vs. PJ period, $P = 0.1451$).

There was an association between the final histological diagnosis and the incidence of a PF ($P = 0.01$, Table 2). The fistula rate was significantly lower in patients with pancreatic adenocarcinoma (PF 8%, $P = 0.001$) compared to other histologies. There was a tendency for a higher fistula rate in patients with a cystic neoplasm (36%, $P = 0.1063$) or distal bile duct cancer (32%, $P = 0.1117$) compared to those with other histopathologies. The PF rate in patients with chronic pancreatitis, tumors of Vater's papilla, and miscellaneous diagnoses such as NET, GIST, or metastases was not significantly different than that of patients with other histopathological diagnoses (Table 2). In the two groups at risk (cystic neoplasm and distal bile

Table 2 Correlation of histopathology and PF

Histopathology	Total (*n*)	Fistula (*n*)	Grade A	Grade B	Grade C	*P**
ALL	193	34 (18%)	5	19	10	–
Pancreatic adenocarcinoma	95	8 (8%)	2	5	1	0.001
Distal bile duct cancer	19	6 (32%)	2	1	3	0.1117
Carcinoma (23) and adenoma (3) of Vater's papilla	26	5 (19%)	0	4	1	0.7853
Cystic neoplasms (IPMN, SCN, SPN)	11	4 (36%)	1	2	1	0.1063
Chronic pancreatitis[a]	23	6 (26%)	0	4	2	0.2522
Miscellaneous[b]	19	5 (26%)	0	3	2	0.3391

IPMN intraductal mucinous papillary neoplasm, *SCN* serous cystic neoplasm, *SPN* solid pseudopapillary neoplasm

* *P* value for histopathology-specific PF rate in comparison to the specific complementary group

[a] Including two "switch-operations" due to distal bile duct stenosis (Frey procedure to PD)

[b] Miscellaneous includes metastases (3), neuroendocrine tumor (3), gastrointestinal stroma tumor/sarcoma (7), duodenal cancer (3), duodenal ulcer (1), ruptured hepatic aneurysm (1), trauma (1)

duct cancer), the rate of fistula was reduced after the introduction of RAP: In patients with cystic neoplasms, there was one type B fistula (PG) since 2007 compared to three fistulas between January 2004 and December 2006. In patients with distal bile duct cancer, there was one type B fistula (PJ) compared to five in the preceding period. These differences were of no statistical significance.

Discussion

It is still an ongoing debate of whether to use PJ or PG for pancreatoenteric anastomosis. Three RCTs and a recent meta-analysis failed to demonstrate a better outcome with respect to fistula rates or perioperative mortality [22–24, 31]. The definition of PF on one hand and the surgical technique on the other hand were not standardized among the different studies [2]. Prospective studies were probably underpowered to find differences concerning fistula rates. Thus, it is still difficult to recommend one particular anastomosis as a gold standard. Kleespies et al. [32] recently demonstrated that the PF rate is higher following pancreatic head resection for neoplasms of the duodenum, distal bile duct, and ampulla of Vater. The currently available RCTs focus only on short-term results such as PF or DGE. There is no long-term report on durability or function of the anastomoses. It is not important to know which type of anastomosis is generally superior. It is far more crucial to investigate which anastomosis is suitable for which pancreatic texture and/or duct diameter. This might be of a great relevance for the future application of an anastomosis since the number of operations performed for benign or borderline disorders such as intraductal papillary mucinous neoplasms has increased over the past decade [25, 33].

Some retrospective studies have suggested more pancreatic exocrine insufficiency in long-term follow-up in PG compared to PJ [34, 35]. Lemaire et al. [36] described a pancreatic exocrine insufficiency in the follow-up of all 17 patients who underwent a PG in his study. A prospective randomized study, however, demonstrated no difference between the two groups [37]. In summary, based on rare evidence, PG is associated with more severe pancreatic exocrine insufficiency than PJ. There is, however, no evidence that an impaired pancreatic endocrine function would be associated more often with a certain type of reconstruction.

Theoretically, there are several physiological and technical advantages of PJ. Pancreatic enzymes are inactivated by the acidic gastric secretion. The stomach does not produce enterokinase, which is required for the conversion of trypsinogen to trypsin and the subsequent activation of other proteolytic enzymes [18, 38]. The lack of enzyme activation may prevent autodigestion of the anastomosis [18]. The alkaline pancreatic secretions theoretically may help prevent marginal ulceration. The excellent perfusion of the stomach wall is favorable for anastomotic healing. The thickness of the stomach wall is a good counterfort for the sutures. Proponents of PG argue that the proximity of the pancreas to the posterior wall of the stomach allows for less tension on the anastomosis, making it more favorable, even in soft glands [18]. The Strasbourg group reported a PF rate of 0% after 194 partial pancreaticoduodenectomies with PG [20]. Up to now only retrospective reports and observational studies have demonstrated favorable results with PG with respect to PF rates. However, this has not been proven in a prospective randomized controlled setting [24].

With PJ one could achieve good long-term durability of the anastomosis. However, this would be at a higher risk for PF in high-risk glands. On the other hand, PG might be associated with fewer PFs but with unknown and maybe worse long-term durability and greater secondary exocrine and endocrine insufficiency compared to PJ. Based on current knowledge, we established the "risk-adapted" pancreatic anastomosis. During the operation the surgeon has to decide whether to perform a standard duct-to-mucosa pancreaticojejunostomy or a pancreatogastrostomy in patients with a "soft" pancreas and/or a duct diameter of 3 mm or less.

With the introduction of this concept into the clinical routine, the PF rate was reduced from 22 to 11%. In the patients with high-risk glands, PG had a fistula rate of 7% (2/27). There were no grade C leaks following PG. Relaparotomy and fistula-associated mortality was significantly reduced to 1.4% between 2007 and 2009. In the one patient with a grade C PF after PJ within this period, we performed a conversion to a PG as a salvage procedure, as described by Bachellier et al. [21]. The statistically significant longer operative time for PG (median = 390 min vs. 346 min) is explained by the subtile preparation around the splenic vein in order to mobilize the pancreatic remnant for invagination into the posterior wall of the stomach. Our PG operative time is in contrast to that of other institutions where PG is associated with a shorter operative time compared to PJ. The overall operation time for both procedures, however, is longer in other institutions compared to the presented results [39].

There was significantly more intraluminal postoperative hemorrhage (PPH) with PG versus PJ (11 vs. 2%, $P = 0.0422$). There was, however, no significant difference in the PPH rate between the two periods (2007-2009 at 5.4% vs. 2004-2006 at 7.6%). The standard policy was to apply prolene stitches on the cut surface and not to electrocauterize this surface. Others authors describe the rate of PPH after PG as around 10% [39, 40]. In our study there was no

incidence of anastomotic rupture following PPH and intervention [40]. Primary endoscopic treatment (and diagnosis) upon intraluminal PPH is therefore regarded as safe, even in the case of an early postoperative event. Relaparotomy, as preferred by others [39], is not considered the primary treatment of choice here. Furthermore, a consequent proton-pump inhibitor (e.g., pantoprazol) medication bid with 40 mg as a lifetime medication (initially intravenously and thereafter orally) seems indispensable.

Delayed gastric emptying is a frequently seen complication after PD, with an incidence of 4-70% depending on the definition used [2]. Using the recent ISGPS definition, we found DGE in 44/193 patients (22.8%). Interestingly, there was a tendency for more DGE (37 vs. 20%) and more severe grade C DGE (7.4 vs. 3%) after PG. The reason might be surgical trauma (mobilization, denervation, two gastrotomies) as well as a retroperitoneal fixation by the pancreatic stump, as discussed previously by Wellner et al. [39]. In a recent meta-analysis, there was no difference between the two types of anastomoses with respect to the rate of DGE [24].

In the current series there was a significant association between the final histopathological diagnosis and the incidence of postoperative fistula (Table 2). Pancreatic adenocarcinoma was associated with a PF rate of only 8%, whereas cystic neoplasm and distal bile duct cancer had a PF rate of 36 and 32%, respectively. The risk of having a PF is significantly lower in patients with pancreatic adenocarcinoma ($P = 0.001$). This result is confirmed by other institutions that reported lower PF rates in patients with pancreatic adenocarcinoma and higher rates for those with distal bile duct cancer or other malignancies [20, 41]. This might be due to the fact that pancreatic adenocarcinoma usually occludes the main pancreatic duct, leading to an increase in the duct diameter. It also has a higher stromal component. Distal bile duct cancers and most cystic tumors usually do not affect the remaining pancreatic tissue as much. With the use of RAP the PF rate could be minimized for histopathologies "at risk."

Since duct size is an objective parameter, the surgeon can easily identify an anastomosis being at risk for leakage. The degree of "softness" of the pancreatic tissue and its role in estimating whether an anastomosis is at risk remain a problem. Similar to the prospective randomized study by Berger et al. [42], the stratification for "soft" and "hard" glands was done by the individual surgeon which leads to biased data. As described previously by our group, the pancreatic texture can be estimated reliably by dynamic magnetic resonance imaging (dMRI) preoperatively [27]. This might assist the surgeon in making a decision about an alternative anastomotic technique in so-called high-risk glands in the future.

Conclusion

Mortality of pancreatic head resections has declined over the past decade. Morbidity remains high and can be decreased only with the use of sophisticated anastomosis techniques for pancreatointestinal reconstruction. RCTs and meta-analyses have failed to demonstrate an anastomosis technique that is generally superior to others. One of the future questions to be answered is "Which technique is suitable for which gland?". The presented risk-adapted concept for pancreatic reconstruction shows advantages for using PG for the so-called high-risk glands in the early postoperative phase. The rate of PPH after PG is clinically relevant, with endoscopy offering adequate diagnosis and treatment. By using high-dose proton-pump inhibitors together with meticulous stitches for hemostasis on the cut surface of the pancreatic remnant, the risk of PPH can be minimized. More clinically relevant problems with DGE have been seen in PG, probably due to pronounced surgical trauma to the stomach. Since there are no long-term results on the durability and function of PG, a recommendation for its use in general currently cannot be made. Nevertheless, it is obvious that PG leads to a lower rate of pancreatic fistula—and fistula-related mortality—particularly for high-risk glands.

Because this study is an observational pilot study, it has a few limitations. First, it is not a randomized controlled trial. However, the results of this study are crucial for the initiation of a stratified prospective randomized controlled trial that will address risk-adapted anastomosis in pancreatic surgery. Second, the results are limited because of the relatively small number of patients in the PG group. Further data from prospective randomized trials are necessary to appropriately investigate this hypothesis.

References

1. Callery MP, Pratt WB, Vollmer CM (2009) Prevention and management of pancreatic fistula. J Gastrointest Surg 13:163–173
2. Niedergethmann M, Farag Soliman M, Post S (2004) Postoperative complications of pancreatic cancer surgery. Minerva Chir 59:175–183
3. Richter A, Niedergethmann M, Sturm JW et al (2003) Long-term results of partial pancreaticoduodenectomy for ductal adenocarcinoma of the pancreatic head: 25-year experience. World J Surg 27:324–329
4. Strasberg SM, Linehan DC, Clavien PA et al (2007) Proposal for definition and severity grading of pancreatic anastomosis failure and pancreatic occlusion failure. Surgery 141:420–426
5. Reid-Lombardo KM, Farnell MB, Crippa S et al (2007) Pancreatic anastomotic leakage after pancreaticoduodenectomy in 1, 507 patients: a report from the pancreatic anastomotic leak study group. J Gastrointest Surg 11:1451–1458 (discussion 1459)

6. Shinchi H, Wada K, Traverso LW (2006) The usefulness of drain data to identify a clinically relevant pancreatic anastomotic leak after pancreaticoduodenectomy? J Gastrointest Surg 10:490–498
7. Traverso LW (2006) Pancreatic cancer: surgery alone is not sufficient. Surg Endosc 20(Suppl 2):S446–S449
8. Yang YM, Tian XD, Zhuang Y et al (2005) Risk factors of pancreatic leakage after pancreaticoduodenectomy. World J Gastroenterol 11:2456–2461
9. Bartoli FG, Arnone GB, Ravera G et al (1991) Pancreatic fistula and relative mortality in malignant disease after pancreaticoduodenectomy. Review and statistical meta-analysis regarding 15 years of literature. Anticancer Res 11:1831–1848
10. Suc B, Msika S, Fingerhut A et al (2003) Temporary fibrin glue occlusion of the main pancreatic duct in the prevention of intra-abdominal complications after pancreatic resection: prospective randomized trial. Ann Surg 237:57–65
11. Goldsmith HS, Ghosh BC, Huvos AG (1971) Ligation versus implantation of the pancreatic duct after pancreaticoduodenectomy. Surg Gynecol Obstet 132:87–92
12. Papachristou DN, Fortner JG (1981) Pancreatic fistula complicating pancreatectomy for malignant disease. Br J Surg 68:238–240
13. Strasberg SM, Drebin JA, Mokadam NA et al (2002) Prospective trial of a blood supply-based technique of pancreaticojejunostomy: effect on anastomotic failure in the Whipple procedure. J Am Coll Surg 194:746–758 (discussion 759-760)
14. Lillemoe KD, Cameron JL, Kim MP et al (2004) Does fibrin glue sealant decrease the rate of pancreatic fistula after pancreaticoduodenectomy? Results of a prospective randomized trial. J Gastrointest Surg 8:766–772 (discussion 772-764)
15. Warshaw AL, Thayer SP (2004) Pancreaticoduodenectomy. J Gastrointest Surg 8:733–741
16. Murr MM, Nagorney DM (1999) An end-to-end pancreaticojejunostomy using a mechanical purse-string device. Am J Surg 177:340–341
17. Landen S (1998) Consolidation of a friable pancreas for pancreaticojejunal anastomosis. Dig Surg 15:297–298
18. Aranha GV, Aaron JM, Shoup M (2006) Critical analysis of a large series of pancreaticogastrostomy after pancreaticoduodenectomy. Arch Surg 141:574–579 (discussion 579-580)
19. Yeo CJ, Cameron JL, Maher MM et al (1995) A prospective randomized trial of pancreaticogastrostomy versus pancreaticojejunostomy after pancreaticoduodenectomy. Ann Surg 222:580–588 (discussion 588-592)
20. Rosso E, Bachellier P, Oussoultzoglou E et al (2006) Toward zero pancreatic fistula after pancreaticoduodenectomy with pancreaticogastrostomy. Am J Surg 191:726–732 (discussion 733-724)
21. Bachellier P, Oussoultzoglou E, Rosso E et al (2008) Pancreatogastrostomy as a salvage procedure to treat severe postoperative pancreatic fistula after pancreatoduodenectomy. Arch Surg 143:966–970 (discussion 971)
22. Duffas JP, Suc B, Msika S et al (2005) A controlled randomized multicenter trial of pancreatogastrostomy or pancreatojejunostomy after pancreatoduodenectomy. Am J Surg 189:720–729
23. Bassi C, Falconi M, Molinari E et al (2005) Reconstruction by pancreaticojejunostomy versus pancreaticogastrostomy following pancreatectomy: results of a comparative study. Ann Surg 242:767–771 (discussion 771-763)
24. Wente MN, Shrikhande SV, Muller MW et al (2007) Pancreaticojejunostomy versus pancreaticogastrostomy: systematic review and meta-analysis. Am J Surg 193:171–183
25. Niedergethmann M, Grutzmann R, Hildenbrand R et al (2008) Outcome of invasive and noninvasive intraductal papillary-mucinous neoplasms of the pancreas (IPMN): a 10-year experience. World J Surg 32:2253–2260
26. Niedergethmann M, Shang E, Farag Soliman M et al (2006) Early and enduring nutritional and functional results of pylorus preservation vs classic Whipple procedure for pancreatic cancer. Langenbecks Arch Surg 391:195–202
27. Dinter DJ, Aramin N, Weiss C et al (2009) Prediction of anastomotic leakage after pancreatic head resections by dynamic magnetic resonance imaging (dMRI). J Gastrointest Surg 13:735–744
28. Bassi C, Dervenis C, Butturini G et al (2005) Postoperative pancreatic fistula: an international study group (ISGPF) definition. Surgery 138:8–13
29. Wente MN, Bassi C, Dervenis C et al (2007) Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery 142:761–768
30. Wente MN, Veit JA, Bassi C et al (2007) Postpancreatectomy hemorrhage (PPH): an International study group of pancreatic surgery (ISGPS) definition. Surgery 142:20–25
31. Yeo CJ (1995) Management of complications following pancreaticoduodenectomy. Surg Clin North Am 75:913–924
32. Kleespies A, Albertsmeier M, Obeidat F et al (2008) The challenge of pancreatic anastomosis. Langenbecks Arch Surg 393: 459–471
33. Tanaka M (2004) Intraductal papillary mucinous neoplasm of the pancreas: diagnosis and treatment. Pancreas 28:282–288
34. Jang JY, Kim SW, Park SJ et al (2002) Comparison of the functional outcome after pylorus-preserving pancreatoduodenectomy: pancreatogastrostomy and pancreatojejunostomy. World J Surg 26:366–371
35. Rault A, SaCunha A, Klopfenstein D et al (2005) Pancreaticojejunal anastomosis is preferable to pancreaticogastrostomy after pancreaticoduodenectomy for long-term outcomes of pancreatic exocrine function. J Am Coll Surg 201:239–244
36. Lemaire E, O'Toole D, Sauvanet A et al (2000) Functional and morphological changes in the pancreatic remnant following pancreaticoduodenectomy with pancreaticogastric anastomosis. Br J Surg 87:434–438
37. Konishi M, Ryu M, Kinoshita T et al (1999) Pathophysiology after pylorus-preserving pancreatoduodenectomy: a comparative study of pancreatogastrostomy and pancreatojejunostomy. Hepatogastroenterology 46:1181–1186
38. Delcore R, Thomas JH, Pierce GE et al (1990) Pancreatogastrostomy: a safe drainage procedure after pancreatoduodenectomy. Surgery 108:641–645 (discussion 645-647)
39. Wellner U, Makowiec F, Fischer E et al (2009) Reduced postoperative pancreatic fistula rate after pancreatogastrostomy versus pancreaticojejunostomy. J Gastrointest Surg 13:745–751
40. Yekebas EF, Wolfram L, Cataldegirmen G et al (2007) Postpancreatectomy hemorrhage: diagnosis and treatment: an analysis in 1669 consecutive pancreatic resections. Ann Surg 246:269–280
41. Aranha GV, Hodul P, Golts E et al (2003) A comparison of pancreaticogastrostomy and pancreaticojejunostomy following pancreaticoduodenectomy. J Gastrointest Surg 7:672–682
42. Berger AC, Howard TJ, Kennedy EP et al (2009) Does type of pancreaticojejunostomy after pancreaticoduodenectomy decrease rate of pancreatic fistula? A randomized, prospective, dual-institution trial. J Am Coll Surg 208:738–747 (discussion 747-739)