



# Single-layer versus duct-to-mucosa pancreaticojejunostomy in pyloruspreserving pancreatoduodenectomy for ductal adenocarcinoma – an analysis of a single surgeon's series

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## Summary

**Background** Despite considerable efforts there is no consensus regarding the ideal reconstruction method for the pancreatic remnant after pancreatoduodenectomy (PD).

**Methods** Overall, 86 patients who underwent PD for ductal adenocarcinoma were selected for analysis. One surgeon (RF) took responsibility of all pancreatic resections, either by operating personally or proctoring the procedure. The database was prospectively maintained. End-to-side pancreaticojejunostomy (PJ; Group A) was performed from 01/01 to 10/07 and duct-to-mucosa PJ (Group B) from 10/07 to 12/12. Primary endpoints were 30-day mortality, incidence of pancreatic fistulas, and severe complications. Secondary endpoints were severity of pancreatic fistulas, incidence of unplanned reoperation and reintervention and length of stay (LOS).

**Results** 30-day mortality, pancreatic fistula, complication, unplanned reoperation and reintervention rates showed no significant differences (2.2 vs. 2.4%; 6.7 vs. 0%; 22.2 vs. 29.3%; 6.7 vs. 0%; 11.1 vs. 2.2%). Summarizing unplanned reoperations and reinterventions, the necessity of any unplanned procedure revealed, a significant reduction from 8 (17.8%) in Group A to 1 (2.2%) in Group B ( $p=0.02$ ). Major complications (Dindo–Clavien Grades III–V) were decreased significantly in Group B (Group A: 9/45 (20%) vs. Group B: 2/41 (4.9%);  $p=0.05$ ). LOS was significantly shorter in Group B (15 days,  $\pm 6.01$ ) as compared with Group A (18 days,  $\pm 8.87$ ;  $p<0.05$ ).

**Conclusions** Our data show superior outcomes with duct-to-mucosa PJ as compared with single-layer PJ.

**Keywords** Pancreatoduodenectomy · Duct-to-mucosa pancreaticojejunostomy · Single-layer pancreaticojejunostomy · Complications · Reoperation · Reintervention · Pancreatic fistula

## Introduction

Indisputably, remarkable improvements of surgical results in pancreatoduodenectomy have been achieved due to various reasons in the past two decades [1–4]. Thereof independent, leakage of the pancreatic anastomosis remained the most frequent and dangerous source of life-threatening complications [5, 6]. Despite considerable scientific efforts, no consensus was achieved in defining an ideal anastomosis for reconstruction of the pancreatic remnant yet [7]. Besides the question of whether pancreatogastrostomy or pancreatojejunostomy may be favorable, even randomized controlled trials focusing on different methods of pancreatojejunostomy did not provide convincing data to support a definite technique [8–12]. In homogenous patient cohorts with varying indications for pancreatic resection, additional antisecretory drug therapy, and different surgeons or institutions involved may have affected study results. In fact, it appears that a standardized approach to the pancreatic anastomosis with consistent practice of a single technique could help to reduce the incidence of complications after pancreatoduodenectomy [13]. Restriction to patient series undergoing pancreatoduodenectomy for a single diagnosis and performed by, as far as possible, a standardized technique may be helpful in further research. Therefore, we focused on a comparison of two techniques of pancreatojejunostomy that have been performed in our institution under the responsibility of a single surgeon in patients being operated due to adenocarcinoma, thus being homogenous in terms of surgical technique and diagnosis.

Single-layer versus duct-to-mucosa PJ in PD for DAC

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## Patients and methods

From a prospectively maintained pancreatic database, patients with ductal adenocarcinoma (DAC) undergoing pylorus-preserving pancreatoduodenectomy from 2001 to 2012 were selected for analysis. Amongst others, recorded parameters included tumor stage, age, gender, body mass index, history of coincident chronic pancreatitis, pancreatic duct diameter, pancreatic tissue quality, all complications, unplanned reoperation and reintervention, 30-day mortality, histopathological details, and length of hospital stay.

One single surgeon (RF) took responsibility of all pancreatic resections, either by operating personally or proctoring the procedure. In all patients, pancreatojejunostomy was the method of reconstruction. Overall, 86 patients were selected for this study. In the same period another 134 pancreatoduodenectomies were performed but not included due to resection for another diagnosis than ductal pancreatic adenocarcinoma ( $n=123$ ). In all, 11 patients with pancreatic DAC undergoing Kausch-Whipple pancreatoduodenectomy were also excluded, thus remaining pylorus-preserving pancreatoduodenectomy was the only procedure analyzed.

Two different methods were applied for pancreatojejunostomy. From 2001 to October 2007, an end-to-side pancreatojejunostomy was performed using a single layer of interrupted, absorbable sutures with Maxon 4/0 (Covidien, Dublin, Ireland)—Group A ( $n=45$ ). From October 2007 to 2012, the surgical technique changed to an end-to-side duct-to-mucosa pancreatojejunostomy—Group B ( $n=41$ ). The anastomosis was performed in a standardized technique, starting with interrupted sutures (Maxon 5/0) between the seromuscular layer of the jejunum and the posterior pancreatic capsule, followed by the posterior suture line between the mucosa and the pancreatic duct (interrupted, Maxon 6/0). The anastomosis was completed by the anterior suture lines of jejunal mucosa to the pancreatic duct and the seromuscular layer of the jejunum and the anterior pancreatic capsule, respectively. In case of a narrow pancreatic duct (diameter 3 mm or less), a loose drain (length 7 cm) was inserted for stenting the anastomosis (Climed®, Vienna, Austria). Two drains were routinely left in the abdominal cavity to monitor the pancreatojejunostomy and the biliary anastomosis during the entire study period. A broad-spectrum antibiotic was administered preoperatively as single shot and repeated after 4 h of surgery.

Patient characteristics including risk factors for pancreatic fistula are presented in Table 1. Tumor stage and R status according to final histopathology for Group A and B are summarized in Table 2. Patient characteristics, risk factors for pancreatic fistula, and tumor stage were balanced between groups.

Primary endpoints were 30-day mortality, incidence of pancreatic fistulas, and severe complications. Secondary endpoints were severity of pancreatic fistulas, incidence of unplanned reoperation, and reintervention and length of stay (LOS).

**Table 1** Patient characteristics

	Group A	Group B	<i>p</i>
<i>n</i>	45	41	
Age (median; min–max)	68 (43–85)	71 (39–87)	0.42
Gender f/m	26/19	32/9	0.07
Chronic pancreatitis	4	6	0.32
Pancreatic tissue <sup>a</sup>			0.82
Soft/normal	16	16	
Fibrotic	24	20	
Pancreatic duct <sup>b</sup>			0.65
≤ 3 mm	17	18	
≥ 3 mm	23	19	
BMI (median; min–max)	26.3 (17.2–30.7)	25.1 (17.5–35.4)	0.46
<sup>a</sup> No data in five patients of each group			
<sup>b</sup> No data in five patients of Group A and four patients of Group B			

**Table 2** Histopathology and R status

UICC	Group A	Group B
I	3	6
II	35	30
III	3	2
IV	4	3
R0	33 (73%)	32 (78%)
R1	11 (24%)	8 (20%)
R2	1 (2%)	1 (2%)

## Definitions

Pancreatic tissue quality was graded soft/normal or fibrotic by the responsible surgeon. The diameter of the pancreatic duct was recorded ( $</= 3$  mm or  $> 3$  mm).

For pancreatic fistula, the definition of the Pancreatic Surgery Group was used [14]. Also, patients presenting with intra-abdominal amylase-rich fluid retention after drain removal, who underwent percutaneous ultrasound or computed tomography (CT)-guided drainage, were classified to have pancreatic fistula. Severity of pancreatic fistulas was graded according to the International Study Group Definition for Pancreatic Fistula (ISGPF) proposal [15].

Postoperative bleeding was defined according to the definition of the ISGPS for severe hemorrhage [16]. Unplanned reintervention was defined as any unscheduled percutaneous procedure performed with an intention to treat (e.g., ultrasound or CT-guided drainage of intra-abdominal fluid retention, angiography with intervention in case of bleeding) within 30 days from resection or during hospitalization. Unplanned reoperation was any unscheduled relaparotomy within 30 days of pancreatic surgery, respectively. Postoperative mortality was defined as death during hospitalization or any death within 30 days after surgery. Overall, complications were assessed for clinical severity according to the classification of Dindo–Clavien [17]. Severe complications were defined as Dindo–Clavien Class III or higher. Data are presented as median (minimum—maximum). For uni-

**Table 3** Perioperative results

	Group A	Group B	<i>p</i>
<i>n</i>	45	41	
Overall complications	10	12	0.471
Pancreatic fistula	3	0	0.243
Unplanned reoperation	3	0	0.243
Unplanned reintervention	5	1	0.098
Unplanned reoperation or reintervention	8	1	0.02
30-day mortality	1	1	1.0

variate analysis of categorical variables the Fisher exact test was used. Numerical data were tested for normal distribution by Kolmogorow-Smirnow test, unpaired t-test and Mann-Whitney U-test were applied accordingly. A two-tailed *p*-value < 0.05 was considered as the level of significance.

## Results

There was one perioperative death in each group, 30-day mortality was 2.2% in Group A and 2.4% in Group B (*p*=1.0). In all, 3 (6.7%) patients in Group A and none in Group B developed pancreatic fistula, the difference not being significant (*p*=0.24). Pancreatic fistulas in Group A were classified as Grade B (*n*=2) and Grade C (*n*=1). Overall, 10 (22.2%) of 45 patients in Group A and 12 (29.3%) of 41 in Group B developed perioperative complications (Table 3). There were no differences with respect to unplanned reoperation (Group A: 3 of 45 (6.7%) patients vs. Group B: none of 41; *p*=0.24) and unplanned radiologic reintervention (Group A: 5 of 45 (11.1%) vs. Group B: 1 of 41 (2.2%); *p*=0.1). Summarizing unplanned reoperations and reinterventions, the necessity of any unplanned procedure revealed a significant reduction from eight (17.8%) in Group A to one (2.2%) in Group B (*p*=0.02). Indications for unplanned reoperations and reinterventions are presented in Table 4. Perioperative complications are summarized and classified according to Dindo-Clavien in Table 5. Major complications (Dindo-Clavien Grades III-V) decreased significantly in Group B (2/41, 4.9%) as compared with Group A (9/45; 20%); *p*=0.05. LOS was significantly shorter in Group B (15 days, +/-6.01 vs. 18 days, +/-8.87; *p*<0.05).

## Discussion

There is strong agreement that the pancreatic anastomosis is the crucial part in reconstruction following pancreatoduodenectomy, thus being the most important and frequent source of surgical complications. Leakage results in pancreatic fistula and may cause intra-abdominal infection and hemorrhage with a need of unplanned reintervention or reoperation and a considerable risk of death [18]. In view of the significant improvements in pancreatic surgery, one may be astonished that a superior

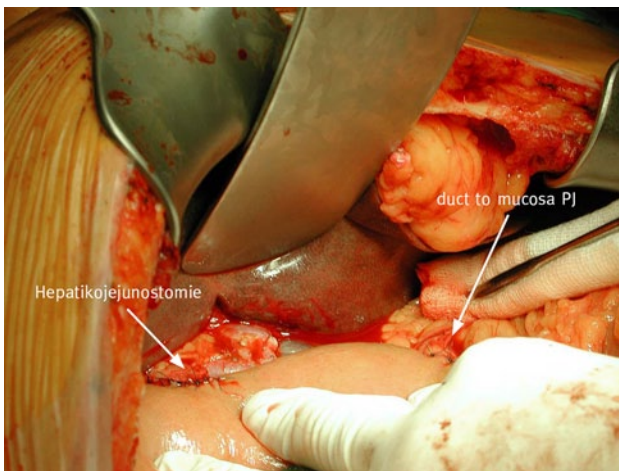
**Table 4** Indications for unplanned reoperations and reinterventions

	A			B		
	<i>n</i>	Reint.	Reop.	<i>n</i>	Reint.	Reop.
Pancreatic fistula	3	2	1	0	0	0
Bleeding	1	1	0	0	0	0
Intra-abdominal abscess	1	1	1	1	1	0
Biliary fistula	1	1	1	0	0	0
Liver failure	0	0	0	1	0	0
Other infections and complications	3	0	0	5	0	0
Other complications	1	0	0	4	0	0
Σ	10	5	3	11	1	0

**Table 5** Comparison of complications according to Dindo-Clavien

	A	B
I	0	1
II	1	8
IIIa	5	1
IIIb	3	0
IVa	0	0
IVb	0	0
V	1	1
Σ	10	11

technique of the pancreatic anastomosis has not been defined. While there exists a wide range of variations, how to connect the pancreatic remnant with the intestinal tract, using the stomach or jejunum, performing one or two suture rows, applying trans-anastomotic loose or external drains or avoiding them, no consistent evidence has been proved for any anastomosis. Even concentration on pancreaticojejunostomy, which is the classic mode of reconstruction, does not reveal clarity despite four prospective randomized trials comparing duct-to-mucosa and invagination pancreaticojejunostomy [9–12]. While Chou, Bassi, and Langrehr did not find significant differences with respect to fistula and mortality, the study by Berger described a significant reduction in fistulas and major complications in the invagination group. Looking more closely at these randomized controlled trials (RCT), variabilities in additional use of routine octreotide medication and internal drain application according to the discretion of the surgeon in the trial from Bassi, different techniques of invagination by Bassi, Langrehr, and Berger, a lack of stratification for risk factors of pancreatic fistula by Langrehr, hinder reliable conclusions. Further differences concern the underlying benign or malign diagnosis of pancreatic disease, a mixture of pyloruspreserving and Kausch-Whipple pancreatoduodenectomies and a potential influence of the surgeons involved. The latter may play a role, despite restriction of surgeons specialized in pancreatic surgery. In his study, Berger described significant differences in pancreatic fistula rate between the two institutions and the eight



**Fig.** Intra operative image showing the hepaticojejunostomy and the duct to mucosa pancreaticojejunostomy, as described in the text.

involved surgeons. While institutional fistula rates were 12 and 26%, individual rates of surgeons ranged from 9 to 42% [12]. Not surprisingly, a recent meta-analysis by Bai and a review by Kennedy refer to the importance of meticulous surgical technique for any type of anastomosis and a need for large high-quality trials comparing anastomotic techniques [19–21]. Presumably, the most important factor for inconclusive results is variations in inclusion criteria. The two analyses comparing RCT did not comprise the same studies. Obviously, this is caused by different opinions on what is an invagination anastomosis. While Kennedy includes the studies of Bassi and Berger, Bai summarizes the studies of Langrehr, Chou, Han, and Berger but excludes Bassi [20, 21]. A clear selection of inclusion criteria is mandatory. Therefore, we only included patients with ductal pancreatic adenocarcinoma undergoing pylorus-preserving pancreatoduodenectomy as the only resection type. Furthermore, one experienced pancreatic surgeon was responsible for all resections, either by performing or proctoring the procedure. In compliance with these prerequisites, we found a reduced rate of unplanned radiologic reinterventions and reoperations, as well as a decrease in major complications in the duct-to-mucosa group. Berger used the same definition of major complications, summarizing patients with Dindo–Clavien Grades III–V but came to contrary results in favor of the invagination anastomosis [10]. From the technical aspect, they performed a two-layer “dunking” anastomosis, while we used a single-layer end-to-side technique like Bassi [9, 10]. Obviously, the latter does not provide the same extent of invagination, which may explain the worse results. The impression of insufficient invagination by a single layer end-to-side pancreaticojejunostomy was the reason to change our technique to a duct-to-mucosa anastomosis in 2007. In fact, we were able to decrease our rate of unplanned reinterventions and avoid reoperations after altering the technique.

## Limitations

The most important limitation of our study is the non-randomized nature. Without doubt, the quest of a superior pancreaticojejunostomy can only be achieved by an RCT. However, restriction to a single diagnosis and procedure with one surgeon in charge and a balance in risk factors for pancreatic fistula and patient characteristics in our study allow conclusions for future research. The long study period of 12 years may be seen as another shortcoming. Our restrictions forced us to choose this time frame, especially to include a comparable number of patients with end-to-side anastomosis. In addition, with 86 pancreatoduodenectomies comprising the study population, another 134 pancreatoduodenectomies were performed in this period but excluded from analysis because of other diagnosis than pancreatic adenocarcinoma or another resection technique. A case load of 220 procedures in 12 years together with ongoing dedication in publishing clinical results for quality control reflects a continuous engagement in pancreatic surgery [22, 23]. Certainly, perioperative care also changed during the study period and may influence results. With respect to perioperative death, all quality control-related publications of our institution revealed mortality rates below 5%, as well as data from the senior authors’ former site [22–24]. However, changes over time in complication management partly replaced unplanned reoperation by interventional radiologic drainage or angiographic hemostasis. This trend is also reflected in our results, and it remains unknown to which extent it was caused by changes in anastomotic technique.

Finally, we defined pancreatic fistula according to Sarr [14]. Due to missing drain amylase data of postoperative day 3 in the early years, we were not able to calculate fistula rates according to the more commonly used definition of the ISGPF for the whole study period. A part of the procedures was proctored, which we do not regard as a possible bias. Formerly it was shown that teaching has no negative impact on complication, especially pancreatic fistula rates [24].

In conclusion, our data demonstrate an advantage of duct-to-mucosa pancreaticojejunostomy over end-to-side pancreaticojejunostomy with respect to the combined number of unplanned reoperations and radiologic reinterventions, coincident with a decrease in complications in Dindo–Clavien Classes 3–5. These results were seen in a selected study population with restriction to pancreatic adenocarcinoma as the single diagnosis, pylorus-preserving pancreatoduodenectomy as the single procedure and single surgeon responsibility. Similar close restrictions in patient inclusion, together with clearly defined complications and outcome parameters may be an option for future RCTs searching for the optimal pancreaticojejunostomy.

## Conflict of interest

The authors declare no conflict of interest; the work has not been funded.



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