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Modified Pancreatojejunostomy in Pancreaticoduodenectomy for the Treatment of Periampullary Tumor: 8 Years of Surgical Experience

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Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
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Background: We modified the anastomosis surgical method based on the Blumgart anastomosis in pancreaticoduodenectomy. This study aimed to compare patient outcomes with regards to clinically relevant postoperative pancreatic fistula (CR-POPF) and other postoperative complications among patients receiving traditional anastomosis, classical Blumgart anastomosis, and our modified-Blumgart anastomosis.

Material/Methods: Data were reviewed from 229 consecutive patients with periampullary tumors who underwent pancreaticoduodenectomy administered by a single surgeon at the Tianjin Medical University Cancer Institute and Hospital between January 2010 and December 2017. Subsequently, clinical factors potentially associated with CR-POPF were analyzed.

Results: During the study period, the incidence of overall CR-POPF was 31 out of 229 patients (13.5%). Using Blumgart anastomosis (BA), the incidence of CR-POPF was lower at 15 out of 148 patients (10.1%), significantly lower than that of traditional anastomosis (invagination technique or "duct-to-mucosa" anastomosis) (15 out of 148 patients versus 16 out of 81 patients, *P*=0.042). Compared with classical Blumgart anastomosis (c-B), our modified-Blumgart anastomosis (m-BA) method had similar outcomes in terms of CR-POPF (9 out of 73 patients versus 6 out of 75 patients, *P*=0.383), CR-POPF-related intra-abdominal hemorrhage rate (0 out of 73 patients versus 1 out of 75 patients, *P*=0.322), and median length of postoperative hospital stay (19 days versus 19 days, *P*=0.752). There were no fatalities as a result of CR-POPF in the BA group.

Conclusions: Upon review of a single surgeon's experience over 8 years, Blumgart anastomosis might be more effective in the prevention of CR-POPF than traditional anastomosis. Our modified-Blumgart anastomosis method maintained a low rate of morbidity and mortality but with simplified procedures that can be easily put into practice. This technique can be used widely with excellent safety for pancreatojejunostomy as a part of pancreaticoduodenectomy.

MeSH Keywords: Anastomosis, Surgical • Pancreatic Fistula • Pancreaticoduodenectomy

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Background

Successful pancreaticoduodenectomy was first reported by Whipple in 1935 for the treatment of periampullary tumor [1], however, this procedure has been widely used only since 1990 due to its previously high mortality rate. Although the perioperative mortality rate observed at experienced surgical centers has decreased from 25% in the 1960s to less than 3% today, morbidity due to postoperative complications is still higher than our ideal, especially for the development of postoperative pancreatic fistula (POPF) [2–5]. The incidence of clinically relevant POPF is still higher than 10% at most centers [6–9] and is a condition which can directly or indirectly lead to serious complications such as infection, hemorrhage, and even death [10–12]. Among the factors that influence postoperative pancreatic fistula, a surgeon's experience and the choice of anastomosis have been shown to be the most important controllable factors [13,14].

Since 2010 [15], several studies reported on the efficacy of mattress sutures for pancreatic parenchyma and the jejunal seromuscular layer during pancreatojejunostomy (PJ) which was proposed as the Blumgart anastomosis. Its modification can decrease POPF incidence [16,17]. Recently published evidence showed that there were no significant differences among the variance methods in the prevention of POPF [18,19]. However, in these studies, most data were derived from multiple surgeons with different surgical experiences. Since 2012, we have used Blumgart anastomosis, and have made innovations to this procedure ourselves. This study retrospectively analyzed patient outcomes from those pancreaticoduodenectomies performed by a single surgeon over an 8-year period. Specifically, we aimed to compare the postoperative pancreatic fistula incidence rate between traditional anastomosis (invagination technique or "duct-to-mucosa" anastomosis), classical Blumgart anastomosis (c-BA) and our modified-Blumgart anastomosis (m-BA).

Material and Methods

Patients and data

This study was approved by the Ethics Committee of the Tianjin Medical University Cancer Institute and Hospital (approval number bc2019019).

Medical records of 229 consecutive patients with periampullary tumors who underwent pancreaticoduodenectomy (PD) performed by one surgeon at Tianjin Medical University Cancer Institute and Hospital between January 2010 and December 2017 were reviewed. We collected clinicodemographic characteristics of enrolled patients and their intraoperative data, including final pathological diagnosis, pancreatic texture (firm or soft), main pancreatic duct size, and intraoperative bleeding according to the Prospectively Validated Clinical Risk Score [20,21]. Postoperative data included the length of hospital stay [22], need for percutaneous drainage, POPF-related intra-abdominal hemorrhage, clinically relevant postoperative pancreatic fistula (CR-POPF), reoperation and postoperative mortality. Additionally, we used the International Study Group of Pancreatic Surgery (ISGPS) definition and grading system to evaluate postoperative pancreatic fistula. Clinically relevant postoperative pancreatic fistula was composed of grade B and grade C pancreatic fistula according to the ISGPS. There was no calculation for "biochemical leak" as it has shown no clinical value and is no longer considered to be a real pancreatic fistula [8]. Risk factors for CR-POPF were identified by univariable and multivariable analyses.

Operative procedure

After classical pancreaticoduodenectomy, the jejunal limb was brought through the transverse mesocolon to the right of the middle colic vessels. Then we performed pancreatojejunostomy, hepaticojejunostomy, and gastrojejunostomy in the proper order. From March 2012, we began to use Blumgart pancreatojejunostomy (duct-to-mucosa sutures with full thickness mattress pancreatic/jejunal seromuscular sutures) in pancreaticoduodenectomy. We then further improved the placement of mattress sutures and tried to simplify the procedure by omitting the duct-to-mucosa sutures.

Modified-Blumgart pancreatojejunostomy procedure

We located the pancreatic duct and placed an appropriate internal pancreatic stent. Next, we confirmed that the pancreatic juice could flow throw the duct (Figure 1A). The sutures were placed at full thickness through the pancreas from the anterior to posterior wall. Sutures were then placed through the seromuscular layer of the jejunal from inferior to superior in the direction of the long axis, followed by full thickness pancreas transfixion from posterior to anterior (Figure 1B). The number of the sutures depended on the width of pancreatic transverse section, normally between 3 and 4. We fixed the stent with 3-0 prolene if it was unstable. Then a small enterotomy was performed opposite of the pancreatic duct and a stent was placed into jejunum through it. The 3-0 prolene sutures on the pancreas were tied while being cognizant about the strength of the knots. Needles were still left on these sutures (Figure 1C). Sutures ran along the short axis through the seromuscular layer of the anterior wall of the jejunum (Figure 1D); the knot should be tied on the jejunum surface. We could add some sutures using residual prolene between the excessive gap if needed. If all these steps were done correctly, the pancreas stump was wrapped tightly by the seromuscular edge

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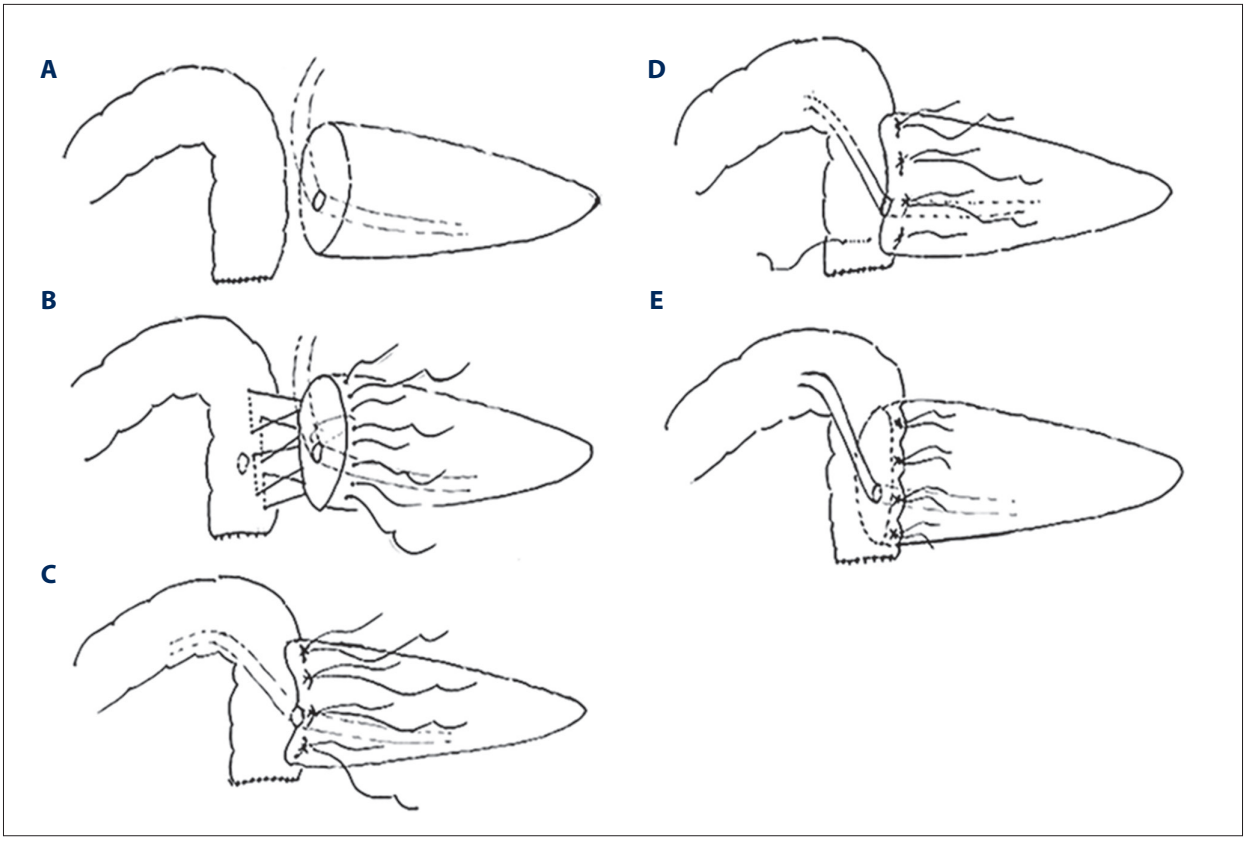

Figure 1. Modified Blumgart pancreatojejunostomy procedure.

of the jejunum on both the anterior and posterior surfaces (Figure 1E). In contrast to c-BA, we superimposed the back-wall sutures on each other (Figure 1B), omitted the "duct-to-mucosa" anastomosis by fixing the stenting and tied the final knot on the jejunum surface (Figure 1E).

Statistical analysis

All categorical data from each group were compared by chi-square statistics and the Fisher' exact test. Differences in continuous variables between the groups were evaluated using Student's *t*-test or the Mann-Whitney U test. Multivariate analysis was carried out with logistic regression analysis. Statistical analysis was performed using SPSS 24.0 software program and statistical significance was defined as $P<0.05$.

Results

A total of 229 patients underwent pancreaticoduodenectomy at our institution from January 2010 to December 2017. The clinical characteristics of enrolled patients are shown in Table 1. Patients were divided into 3 groups according to the type of pancreatojejunostomy received: a traditional group (the invagination technique and the "duct-to-mucosa" anastomosis) and 2 Blumgart anastomosis (BA) subgroups. Since we had improved BA, this method was divided into classical BA (c-BA) and modified BA (m-BA) patient subgroups. There were no significant differences in demographic data, pathologic findings, or preoperational laboratory data between the traditional anastomosis group and the BA group. Similar results were observed between the c-BA and the m-BA groups.

Intraoperative data are shown in Table 2. All patients received conventional Whipple procedure in this study. Four patients accepted portal vein/superior mesenteric vein (PV/SMV) resection in the m-BA group compared with none in the c-BA group (4 versus 0, $P=0.04$). Pancreatic texture, main pancreatic duct size, and intraoperative bleeding were comparable between the c-BA group and the m-BA without significant difference. The minimum time for the operation was 1.5 hours. Finally, there was no significant difference between the groups in terms of the main pancreatic duct size.

Postoperative complications are also shown in Table 3. Overall CR-POPF incidence was 31 out of 229 patients (13.5%) and the incidence of grade C postoperative pancreatic fistula was 5 out of 229 patients (2.2%). The development of CR-POPF in the BA group was significantly lower than that of the traditional group (15 out of 148 patients versus 16 out of 81 patients, $P=0.042$).

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Table 1. Characteristics of enrolled patients.

	Traditional anastomosis	Blumgart anastomosis (BA)				p
		(c-BA)	(m-BA)	p	Total	
No. of patients	81	75	73		148	
Age, yrs, median (range)	60 (27–74)	61 (26–79)	63 (38–86)	0.251	62.5 (26–86)	0.171
Gender, n						
Male	45	46	49	0.463	95	0.2
Female	36	29	24		53	
Diabetes, yes, n	11	14	16	0.632	30	0.207
Hypertension, yes, n	25	15	25	0.051	40	0.538
Jaundice, yes, n	42	46	38	0.255	84	0.476
Preop. biliary drainage	10	12	15	0.191	27	0.333
Final pathological diagnosis, n						
PDAC or pancreatitis	30	36	34	0.862	70	0.134
Others	51	39	39		78	
Preop. laboratory data						
CA19-9 (U/ml), mean ±SD	494±1851	422±1336	423±947	0.996	422±1155	0.719
CEA (ug/l), mean ±SD	3.3±3.5	3.6±2.6	4.1±3.9	0.291	3.9±3.3	0.241
Total bilirubin (umol/L), mean ±SD	117±145	122±117	107±113	0.429	115±115	0.877
Albumin (g/L), mean ±SD	42.3±5.4	44.7±46.1	39.2±5.2	0.323	42.0±33.0	0.942
Hemoglobin (g/L), mean ±SD	127±18	129±19	129±18	0.867	129±19	0.493

c-BA – classical Blumgart anastomosis; m-BA – modified Blumgart anastomosis; PDAC – pancreatic ductal adenocarcinoma.

Table 2. Intraoperative data.

	Traditional anastomosis	Blumgart anastomosis (BA)				p
		(c-BA)	(m-BA)	p	Total	
No. of patients	81	75	73		148	
Operative procedures, n						
Conventional PD	81	75	73	–	148	–
Pylorus-preserving PD	0	0	0		0	
PV/SMV resection	2	0	4	0.04	4	0.916
Pancreatic texture, n						
Soft	36	35	36	0.747	71	0.778
Hard	36	40	37		77	
Main pancreatic duct size, median (range), mm	3 (1–5)	3 (2–11)	4 (1–8)	0.378	4 (1–11)	0.102
Operative time, median (range), hr.	4.5 (1.5–15)	4.5 (1.5–8)	4.5 (2.16–8.05)	0.537	4.5 (1.5–8.05)	0.775
Intraoperative bleeding, median (range), mL	200 (50–1200)	300 (50–1000)	250 (50–1000)	0.95	300 (50–1000)	0.944
Red blood cell transfusion, number, median (range), mL	9,700 (100–1000)	8,400 (300–800)	7,800 (400–1200)	0.082	15,400 (300–1200)	0.685

c-BA – classical Blumgart anastomosis; m-BA – modified Blumgart anastomosis; PD – pancreaticoduodenectomy.

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Table 3. Postoperative course and complications.

	Traditional Anastomosis	Blumgart Anastomosis (BA)				p
		(c-BA)	(m-BA)	p	total	
No. of patients	81	75	73		148	
POPF						
Grade B	13	5	8	0.398	13	0.098
Grade C	3	1	1	0.985	2	0.244
CR-POPF (grade B/C), n	16	6	9	0.383	15	0.042
Biliary leakage, n	0	0	0	–	0	–
Gastric-enteric anastomotic leakage, n	0	0	0	–	0	–
Delayed gastric emptying, n						
Grade B	5	1	6	0.048	7	0.639
Grade C	3	5	8	0.356	13	0.149
Post operation hemorrhage, n	12	4	3	0.726	7	0.008
POPF related intra- abdominal hemorrhage, n	4	1	0	0.322	1	0.035
Reoperation, n	3	2	2	0.978	4	0.674
Intra-abdominal abscess, n	19	11	15	0.347	26	0.525
Percutaneous drainage for Intra-abdominal abscess, n	14	10	11	0.762	21	0.534
Wound infection, n	9	6	6	0.961	12	0.452
Postoperative hospital stay, median (range), d	26 (7–121)	19 (8–77)	19 (7–65)	0.752	19 (7–77)	0.001
Mortality within 90 d, n	3	0	1	0.309	1	0.094
POPF related mortality within 90 d, n	3	0	0	–	0	0.018

c-BA – classical Blumgart anastomosis; m-BA – modified Blumgart anastomosis; CR-POPF – clinically relevant POPF.

Table 4. Risk factors for clinically relevant postoperative pancreatic fistula.

Variable	Univariable			Multivariable		
	OR	95% CI	p	OR	95% CI	p
Age (>70 years)	0.899	0.292–2.767	0.853			
Sex (male)	1.657	0.726–3.785	0.231			
Preoperative diabetes mellitus (yes)	1.118	0.427–2.928	0.821			
Preoperative obstructive jaundice (yes)	0.991	0.463–2.122	0.982			
Preoperative serum albumin (<40 g/l)	0.782	0.360–1.699	0.535			
Preoperative hemoglobin (<120 umol/L)	0.778	0.317–1.909	0.583			
Duration of operation (>4.5 h)	1.297	0.559–3.010	0.545			
Intraoperative blood loss (>400 ml)	3.083	1.190–7.989	0.02	2.607	0.897–7.582	0.078
Pancreatic texture (soft)	2.368	1.052–5.328	0.037	1.257	0.242–6.537	0.786
Main pancreatic duct (≤3mm)	2.063	0.716–5.947	0.18			
PDAC or pancreatitis	0.401	0.171–0.939	0.035	0.482	0.081–2.881	0.424
Blumgart anastomosis	0.458	0.213–0.984	0.045	0.314	0.123–0.804	0.016

CI – confidence interval; OR – odds ratio.

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Compared with the traditional group, the BA group had a low POPF-related intra-abdominal hemorrhage rate (1 out of 148 patients versus 4 out of 81 patients, *P*=0.035), median length of postoperative hospital stay (26 days versus 19 days, *P*=0.001), POPF-related mortality within 90 days (0 deaths versus 3 deaths, *P*=0.018). Compared with the classical Blumgart pancreatojejunostomy, our modified-Blumgart type was similar in terms of clinically relevant postoperative pancreatic fistula (9 out of 73 patients versus 6 out of 75 patients, *P*=0.383), POPF-related intra-abdominal hemorrhage rate (0 out of 73 patients versus 1 out of 75 patients, *P*=0.322), median length of postoperative hospital (19 days versus 19 days, *P*=0.752). There were no deaths caused by POPF in the BA group.

The risk factors for clinically relevant post-operative pancreatic fistula are summarized in Table 4. Univariable analysis showed that soft pancreas, more than 400 mL intraoperative blood loss, diagnosis of pancreatic ductal adenocarcinoma (PDAC) or pancreatitis and Blumgart anastomosis were significantly associated with CR-POPF. There were no significant factors such as age, gender, preoperative diabetes mellitus, serum albumin level, hemoglobin level, main pancreatic duct diameters, and duration of operation. Multivariable analysis showed that Blumgart anastomosis was the only independent predictor of a lower rate of CR-POPF (*P*=0.016).

Discussion

Of all the potential postoperative complications of Whipple procedure, POPF has received the most attention [23–25]. Several studies have identified many factors contributing to POPF including the hardness of the pancreatic parenchyma, diameter of the main pancreatic duct, and final pathological diagnosis [2,26]. Associated procedure-related factors include intraoperative bleeding, operative time, and surgical technique were possible to improve independently [27,28].

Surgeons are continuously making efforts to develop pancreatic anastomosis to improve the safety of the Whipple procedure. Three aspects must be considered for satisfactory anastomosis: the procedure should be easy to understand, suitable for all patients, and most importantly, cause no destructive CR-POPF. As most grade B pancreatic fistula can be healed with sufficient drainage and supportive treatment, avoiding catastrophic pancreatic fistula was our primary focus as it is a prognostic factor of fatal bleeding, organ failure, and even death. In order to eliminate catastrophic CR-POPF, we must ensure the pancreatic juice is flowing into the intestine cavity successfully, keep the blood supply abundant and make the anastomosis unbreakable between the pancreatic stump and jejunum wall.

For the creation of the pancreatojejunostomy, invagination technique and "duct-to-mucosa" anastomosis appear to be the 2 most common approaches [27,29] and it seems that the processing of pancreatic duct and blood supply must be done very well to avoid catastrophic POPF. In 2010, Blumgart [15] first proposed mattress sutures between the pancreatic parenchyma and small intestinal wall, which provided the anastomosis a real sense of being unbreakable. Based on his theory, several retrospective studies reported that the Blumgart anastomosis (BA) and its modified type m-BA can decrease the incidence of CR-POPF with a rate from 2.5% to 20.5%, which is superior to the traditional method [16,28,30,31]. A recent study by Lee et al. [32] demonstrated there was no significant difference between Blumgart and conventional duct-to-mucosa anastomosis in the incidence of postoperative pancreatic fistula. Hirono et al. [33] observed in a randomized controlled trial that their m-Blumgart technique did not reduce the CR-POPF compared with interrupted sutures.

It is clear that the ability of the surgeon plays a crucial role in successful surgical outcomes. The success of an operation and the severity of postoperative complications are dependent upon a surgeon's clinical experience, understanding of local anatomy, and surgical techniques. Therefore, differences in ability between surgeons is the biggest bias among surgical studies as all of the aforementioned studies that analyzed outcomes associated with more than 1 surgeon. Contrastingly, in our research, all surgical procedures were performed under the guidance of the same surgeon with extensive experience (more than 25 years of clinical operation experience, performing more than 25 Whipple procedure annually) making our research more reliable and stable.

From 2012, our department began to use Blumgart anastomosis and improve it cautiously. Based on the mattress suture of c-BA, we superimposed the back-wall sutures on each other. And the gap between the posterior wall was completely eliminated, greatly reducing the risk of direct corrosion to the SMV and residual gastroduodenal artery (GDA) by pancreatic juice. Unlike c-BA, we omitted the "duct-to-mucosa" anastomosis by fixing the stent because of the narrow operating space. Also, this can minimize the anastomotic stenosis, which always leads to atrophy of residual pancreas and pancreatitis.

After using this method, the incidence of CR-POPF was not statistically different from before, but this improvement simplified the operation process and made our anastomosis applicable to almost all situations. Compared with the traditional anastomosis (invagination technique and the "duct-to-mucosa" anastomosis), BA had an obvious advantage in prevention of grade B/C postoperative pancreatic fistula, which was similar to previous reports. At the same time, BA also had advantages in terms of post operation hemorrhage, POPF-related intra-abdominal hemorrhage, postoperative hospital stays, and POPF-related

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mortality within 90 day. Our m-BA was similar to our c-BA in terms of post operation complications.

In the m-BA group, only 1 patient developed grade C pancreatic leakage, which was concluded to be a result of reoperation caused by uncinate process stump bleeding on the day of operation. There was no death caused by POPF in the BA group. Additionally, the incidence of CR-POPF was higher in males than in females, but without statistical difference (OR=1.657; 95% CI: 0.726–3.785; *P*=0.231). Although there a soft pancreas, intraoperative blood loss more than 400 mL and diagnosis of PDAC or pancreatitis related to CR-POPF in our study, Blumgart anastomosis was the only independent predictor of a lower rate of CR-POPF in multivariable analysis (OR=0.314; 95% CI: 0.123–0.804; *P*=0.016).

The reliability and stability of our operational results were superior as they were performed under the leadership of a single surgeon. At the same time, intergroup confounding factors were balanced as shown in Table 1, so selection bias was reduced to the greatest extent possible [34]. However, since this was a single-center, retrospective analysis, our evidence base might be considered relatively limited. We plan to conduct a randomized controlled trial to confirm our conclusions about our m-BA procedure.

Conclusions

Examination of an expert surgeon's experience using the Blumgart pancreatojejunostomy over 8 years showed this procedure to be of great preventative value against clinically relevant postoperative pancreatic fistula compared with traditional anastomosis. Importantly, our modified-Blumgart anastomosis procedure also maintained a low rate of morbidity and mortality while simplifying the procedure for easy adoption. We firmly believe that such a modified procedure can be widely used in surgical settings with excellent safety.

Conflicts of interest

None.

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