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ORIGINAL ARTICLE

Modified Blumgart Anastomosis for Pancreaticojejunostomy: Technical Improvement in Matched Historical Control Study

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Abstract
Background Postoperative pancreatic fistula (POPF) is the main cause of fatal complications after pancreatoduodenectomy. There is still no universally accepted technique for pancreaticoenterostomy, especially in patients with soft pancreas.
Methods Between July 2008 and June 2013, 240 patients who underwent pancreatoduodenectomy were enrolled in this single-institution matched historical control study. To approximate the pancreatic parenchyma to the jejunal seromuscular layer, 120 patients underwent anastomosis using the Kakita method (three or four interrupted penetrating sutures) and 120 underwent anastomosis using the modified Blumgart anastomosis (m-BA) method (one to three transpancreatic/jejunal seromuscular sutures to completely cover the pancreatic stump with jejunal serosa).
Results The rate of clinically relevant POPF formation was significantly lower in the m-BA group than that in the Kakita group (2.5 vs 36 %; $p<0.001$). The duration of drain placement and the length of postoperative hospital stay were significantly shorter in the m-BA group. Multivariate analysis showed that m-BA was an independent predictor of non-formation of POPF (hazard ratio, 0.02; 95 % confidence interval, 0.01–0.08; $p<0.001$).
Conclusion The m-BA method is safe and simple and improves postoperative outcomes. We suggest that the m-BA is suitable for use as a standard method of pancreaticojejunostomy after pancreatoduodenectomy.

Keywords Modified Blumgart anastomosis · Kakita method · Pancreaticojejunostomy

Introduction

Pancreatectomy may have serious and potentially lethal complications. Improvements in patient selection and perioperative management have reduced the mortality rate after pancreatectomy to less than 3 % in most centers.[1–3] Despite this substantial decline in operative mortality over the past two decades, even high-volume centers with extensive experience in pancreatic surgery report major complication rates of 20 to 40 % after pancreatectomy.[4–7] The majority of this morbidity results from the development of postoperative pancreatic fistula (POPF) and intra-abdominal hemorrhage from ruptured aneurysms.[5,8] Severe POPF is a social problem because of the prolonged hospitalization and high cost of medical treatment. Since publication of the definitions of POPF grades by the international study group of pancreatic fistula (ISGPF) in 2005,[9] there has been worldwide interest in evaluating the risk factors associated with the development of POPF.[10–17] The main reported risk factors for POPF are soft pancreatic remnant texture, small pancreatic duct diameter, obesity, and preoperative malnutrition.[10,12,13] To try to reduce the rate of this complication, numerous anastomotic techniques[18–20] and methods of reconstruction[20–22] have been proposed and investigated.[23,24] However, there is currently no universally accepted technique for pancreaticoenterostomy, especially in patients with soft pancreas.

In Japan, the Kakita method, originally described by Kakita et al.[25] in 1996, is the most commonly used technique for pancreaticojejunostomy. This simple technique initially

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involved insertion of closed pancreatic duct stenting (ligation of the main pancreatic duct with the external drainage tube) and approximation of the jejunal wall to the pancreatic stump by a single layer of three or four interrupted sutures. A modified Kakita method that involves six to eight interrupted duct-to-mucosa sutures and semi-closed external pancreatic duct stenting (placement of the external drainage tube without ligation) is currently widely used in many high-volume specialist centers in Japan. The Blumgart anastomosis is a U-suture technique described by L. H. Blumgart at the Memorial Sloan–Kettering Cancer Center, New York in 2000.[26] This method involves placement of four to six transpancreatic/jejunal seromuscular sutures to approximate the pancreas and the jejunum and was reported to decrease the incidence of POPF to 4.3 to 6.9 %. We established a simplified version of this technique and found the modified Blumgart anastomosis (m-BA) to be beneficial in several ways. This study evaluated the m-BA by comparing perioperative outcomes between patients who underwent anastomosis using the m-BA method and historical patients who underwent anastomosis using the Kakita method.

Methods

Patients

Between July 2008 and June 2013, 240 consecutive patients who underwent pancreatoduodenectomy (PD) in the Department of Gastroenterological Surgery (Surgery II) at Nagoya University were identified from the prospective database. The Kakita method was exclusively used before March 2010, and the m-BA method was used after 2010, to approximate the pancreatic parenchyma to the jejunal seromuscular layer. After 120 consecutive patients have underwent anastomosis using the m-BA method (m-BA group), 120 preceding patients who underwent anastomosis using the Kakita method (Kakita group) were enrolled in this study, using a matched historical control design in terms of the ratio of soft to hard pancreatic texture (soft 54, hard 66). Formation of a direct anastomosis between the pancreatic duct and the mucosal layer of the jejunal loop was performed in the same way throughout the 5 years of the study. Written informed consent for inclusion in the current analysis was obtained from all patients, as required by the institutional review board of Nagoya University.

Pancreatoduodenectomy

Most patients underwent subtotal stomach-preserving PD (SSPPD), which involves resection of the pyloric ring with preservation of more than 95 % of the stomach, but conventional PD with distal gastrectomy or pylorus-preserving PD were occasionally performed.[27] Portal vein resection was performed in combination with standard pancreatectomy in patients with possible or definite tumor invasion. Reconstruction was performed by a modified Child's method in conventional PD and SSPPD or by a Traverso method in pylorus-preserving PD. Anastomosis was performed between the jejunum (passed through the mesocolon) and the pancreas, bile duct, and stomach (SSPPD and cPD) or the duodenum (pylorus-preserving PD), in order. Silicone drains (19-Fr, Blake) were routinely placed at the superior and inferior sides of the pancreaticojejunostomy and connected to a continuous-suction device (J-Vac Suction Reservoir; Johnson & Johnson). These drains were placed several centimeters away from the anastomosis. All the operations were performed by the same surgical team, including two experienced surgical operators.

The Kakita Method

The pancreatic duct and the jejunal mucosa were joined in an end-to-side fashion using eight absorbable interrupted sutures, and the pancreatic parenchyma of the stump was approximated to the jejunal seromuscular layer with three or four nonabsorbable interrupted penetrating sutures (Fig. 1a).

Modified Blumgart Anastomosis

We modified the Blumgart anastomosis technique as follows. (1) The original method used four to six transpancreatic/jejunal seromuscular sutures to approximate the pancreas and the jejunum, whereas we used only one to three sutures. (2) The original method used two penetrating sutures through the pancreas that were tied on the pancreas, followed by a suture through the seromuscular layer of the jejunum and the pancreatic capsule. We did not tie the two penetrating sutures on the pancreas but continued them through the seromuscular layer of the jejunum in the direction of the short axis.

Specifically, we used a double-armed 4-0 polypropylene suture to place a U-suture with both arms through the pancreatic stump and a 10–15-mm longitudinal suture through the seromuscular layer of the jejunum (Fig. 1b). Up to three such sutures were placed in a normal pancreas, and only one was placed in a hard or atrophic pancreas. One of these sutures crossed the main pancreatic duct. An anastomosis was then formed between the pancreatic duct and the mucosal layer of the jejunal loop as in the Kakita method. After ligation, of all interrupted duct-to-mucosa sutures (Fig. 1c) were placed through the seromuscular layer of the jejunum 5–7 mm lateral to the previous sutures (Fig. 1d). These sutures were then tied to approximate the pancreas and the jejunum at the ventral wall of the jejunum rather than on the surface of the pancreas to avoid laceration of the pancreas (Fig. 1e). This procedure completely covered the pancreatic stump with jejunal serosa.

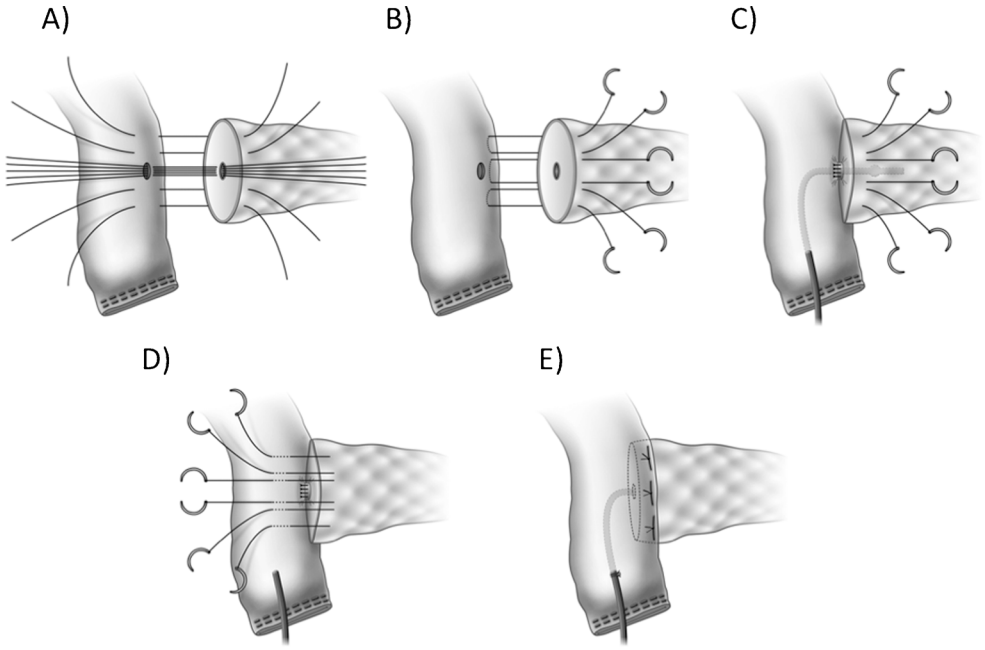

Fig. 1 Schemes of pancreaticojejunostomy. **a** The pancreatic parenchyma of the stump was approximated to the jejunal seromuscular layer with three or four interrupted penetrating sutures in the Kakita method. **b** In the modified Blumgart anastomosis, a U-suture was placed with both arms through the pancreatic stump and a 10–15-mm longitudinal suture through the seromuscular layer of the jejunum. **c** An anastomosis was formed between the pancreatic duct and the mucosal layer of the jejunal loop as in the Kakita method. **d** Sutures were placed through the seromuscular layer of the jejunum 5–7 mm lateral to the previous sutures. **e** These sutures were tied at the ventral wall of the jejunum to completely cover the pancreatic stump with jejunal serosa

Pancreatic Duct Stenting

The diameter of the pancreatic duct was measured intraoperatively. In both techniques, a 4- to 6-Fr polyvinyl catheter was inserted into the main pancreatic duct for external drainage in patients with a non-dilated duct (3 mm or less), and was not inserted in patients with a dilated duct (larger than 3 mm), according to the previous report.[28]

Postoperative Management

Postoperative octreotide was not routinely administered. First- or second-generation cephem antibiotics were administrated immediately before surgery and every 3 hours during surgery. In all patients, administration of antibiotics and H2 blockers was continued routinely by postoperative day 3. Oral intake was routinely started around 4 days after surgery unless postoperative complications such as delayed gastric emptying occurred.

The amylase concentration in the drainage fluid was measured on postoperative days (POD) 1, 3, and 5. POPF was diagnosed and graded in accordance with the ISGPF classification. POPF was diagnosed when the amylase concentration in the drainage fluid on or after POD 3 was more than three times the upper limit of the normal serum level.[9] A fistula of grade B (fistula requiring any therapeutic intervention) or higher was regarded as clinically significant. Abdominal drains were removed on postoperative day 4 in patients without POPF.

Evaluated Factors

The following factors that may be associated with formation of POPF were analyzed in the present study: age, sex, preoperative biliary drainage, blood test results (serum total protein and albumin concentrations), body mass index, pancreatic texture, diameter of the main pancreatic duct, operative time, volume of blood loss, and perioperative blood transfusion.

Statistical Analysis

Differences in the numerical data between the two groups were examined using the χ^2 test or Fisher's exact test when $n<5$. Differences in quantitative variables between the two groups were evaluated using Student's t test or the Mann-Whitney U test if the distribution was abnormal. Predictive factors for POPF were identified by multivariate regression analysis using the Cox proportional hazards model, and variables with a value of $p<0.05$ were entered into the final model. Statistical analysis was performed using JMP® 10 software (SAS Institute Inc.). A value of $p<0.05$ was considered statistically significant.

Results

Patient Characteristics

The patient characteristics are shown in Table 1. There were no significant differences in median age or sex between the Kakita group and the m-BA group. In the Kakita group, the pathological diagnosis was pancreatic cancer in 81 patients, other malignant neoplasm in 14 patients, and cystic neoplasm in 20 patients. In the m-BA group, the pathological diagnosis was pancreatic cancer in 72 patients, other malignant neoplasm in 15 patients, and cystic neoplasm in 23 patients. SSPPD was performed more frequently in the m-BA group than in the Kakita group. The mean operative time, volume of blood loss, and rate of portal vein resection were comparable between the two groups. There were no in-hospital deaths in either groups.

Table 1 Demographic and clinical characteristics of the patients

	Kakita	Modified BA	*p* value
No. of patients	120	120	
Age (years), median (range)	66.0 (18–83)	64.9 (38–84)	0.797
Gender (male/female)	75/45	74/46	0.894
Disease			0.032
Pancreatic cancer	81	72	
Other malignant neoplasms	14	15	
Cystic neoplasms	20	23	
Endocrine neoplasms	1	8	
Pancreatitis	4	0	
Others	0	2	
Operative method			<0.001
cPD	38	9	
SSPPD	64	107	
PPPD	18	4	
Operative time (min), mean±SD	439±103	436±103	0.588
Blood loss (mL), mean±SD	906±836	836±840	0.683
Portal vein resection	40	45	0.500
Pancreatic texture (soft/hard)	54/66	54/66	1.000
MPD (non-dilated/dilated)	50/70	57/63	0.363
Mortality	0	0	1.000

BA Blumgart anastomosis, *cPD* conventional pancreatoduodenectomy with distal gastrectomy, *SSPPD* subtotal stomach-preserving PD, *PPPD* pylorus-preserving PD, *SD* standard deviation, *MPD* main pancreatic duct

Comparisons of the Amylase Concentrations in the Drainage Fluid

The amylase concentration was elevated in 77 (64.2 %) patients on POD 1 and 55 (45.8 %) patients on POD 3 in the Kakita group and 56 (46.7 %) patients on POD 1 and 43 (35.8 %) patients on POD 3 in the m-BA group. The median amylase concentration in the drainage fluid was significantly lower in the m-BA group than in the Kakita group on POD 1 (264 vs 1,380 IU/L, p=0.011) and POD 3 (129 vs 368 IU/L, p=0.003) (Fig. 2). In patients with soft pancreas, the median amylase concentration in the drainage fluid was significantly lower in the m-BA group than in the Kakita group on POD 1 (5,917 vs 10,231 IU/L, p=0.016), POD 3 (790 vs 2,801 IU/L, p=0.047), and POD 5 (317 vs 936 IU/L, p=0.021) (Fig. 3).

Postoperative Complication Rate

The postoperative complications are shown in Table 2. The rate of clinically relevant POPF formation was significantly lower in the m-BA group than in the Kakita group (2.5 vs 36 %), and there were no cases of POPF-related hemorrhage in the m-BA group. The overall postoperative complication

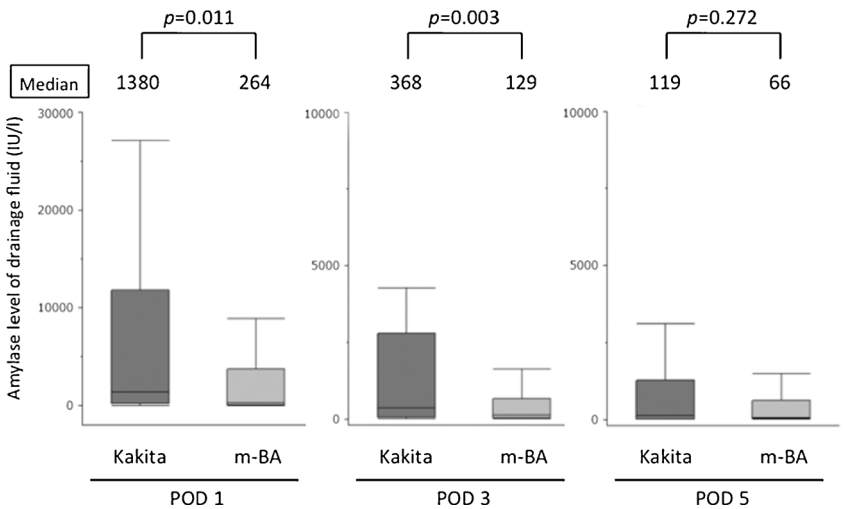

Fig. 2 Comparison of the amylase concentration in drainage fluid in all cases. The median amylase concentrations were significantly lower in the m-BA group than in the Kakita group on POD 1 (264 vs 1,380 IU/L, p=0.011) and POD 3 (129 vs 368 IU/L, p=0.003)

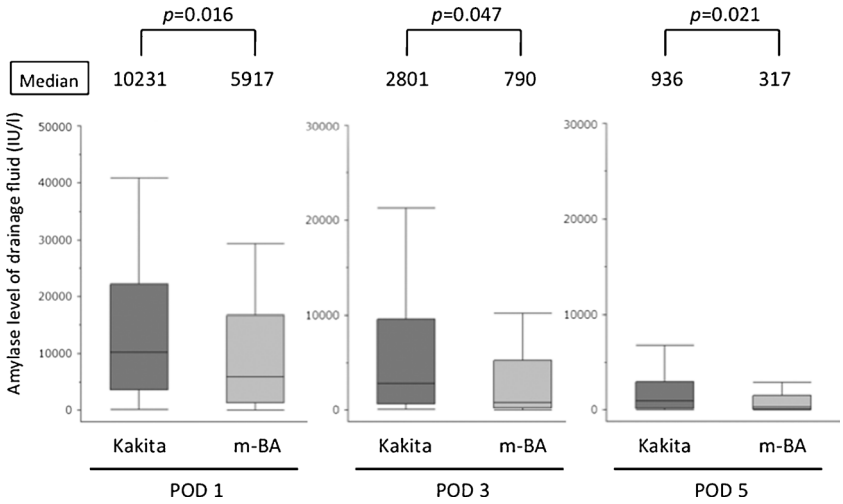

Fig. 3 Comparisons of the amylase concentrations in the drainage fluid in patients with soft pancreas. The median amylase concentrations were significantly lower in the m-BA group than in the Kakita group on POD 1 (5,917 vs 10,231 IU/L, p=0.016), POD 3 (790 vs 2,801 IU/L, p=0.047), and POD 5 (317 vs 936 IU/L, p=0.021)

rate was higher in the Kakita group than in the m-BA group. The median duration of drain placement was significantly shorter (5 vs 8 days, p<0.001) and the median length of postoperative hospital stay was significantly shorter (24 vs 35 days, p<0.001) in the m-BA group than in the Kakita group.

Factors Predicting POPF

The factors predicting POPF are shown in Table 3. Univariate analyses showed that diseases other than pancreatic cancer, soft pancreas and a non-dilated main pancreatic duct (diameter of 3 mm or less) were significantly associated with POPF formation, and that POPF formation was significantly less frequent in the m-BA group than in the Kakita group. Multivariate analysis showed that m-BA was an independent predictor of a lower rate of POPF formation (hazard ratio, 0.02; 95 % confidence interval, 0.01–0.08; p<0.001).

Discussion

POPF formation is the factor most strongly linked with death after pancreatectomy in the majority of case series and remains the leading cause of morbidity after pancreatectomy.[5,8] The rate of POPF formation is still unsatisfactorily high, at about 20 % after pancreatic head resection and 30 % after distal pancreatectomy, even in high-volume centers.[12,29,30] Pancreatic surgeons worldwide have tried to develop techniques to reduce this rate, including various methods of pancreaticoenterostomy formation,[31,32] pancreatic duct stenting,[33] and drain management.[34]

Table 2 Postoperative complication

	Kakita	Modified BA	p value
No. of patients	120	120	
Overall	68 (57)	31 (26)	**<0.001**
POPF (grade B or C)	43 (36)	3 (2.5)	**<0.001**
POPF related hemorrhage	3 (3)	0	0.081
Biliary leakage	2 (2)	2 (2)	1.000
Delayed gastric emptying	4 (3)	2 (2)	0.408
Intra-abdominal abscess	15 (13)	7 (6)	0.074
Peptic ulcer	3 (3)	0	0.081
Cholangitis	9 (8)	6 (5)	0.424
Bacteremia	10 (8)	2 (2)	**0.018**
Wound infection	3 (3)	6 (5)	0.308
Others	4 (3)	8 (7)	0.236
Reoperation	1 (1)	1 (1)	1.000
Mortality	0	0	1.000
Duration of drainage (days), median (range)	8 (4–128)	5 (3–46)	**<0.001**
Length of the hospital stay (days), median (range)	35 (15–139)	24 (12–60)	**<0.001**

Some patients had plural complications

Values in parentheses are percentages unless indicated otherwise

Bold characters, statistically significant

BA Blumgart anastomosis, *POPF* postoperative pancreatic fistula

Table 3 Predictive factors of postoperative pancreatic fistula

Variables	Univariate			Multivariate		
	Odds ratio	95 % CI	*p* value	Hazard Ratio	95 % CI	*p* value
Age (≥65 years)	0.99	0.51–1.90	0.975			
Gender (male)	1.71	0.85–3.45	0.133			
Diseases other than pancreatic cancer	2.27	1.18–4.35	**0.012**	1.82	0.71–4.71	0.214
Preoperative biliary drainage	1.67	0.87–3.19	0.120			
Preoperative diabetes mellitus	1.23	0.58–2.60	0.592			
Body mass index (≥25)	2.05	0.90–4.69	0.084			
Preoperative serum total protein (<6.7 g/dl)	0.96	0.49–1.89	0.917			
Preoperative serum albumin (<4.0 g/dl)	0.96	0.50–1.84	0.898			
Operative time (≥450 min)	0.61	0.31–1.23	0.165			
Intraoperative blood loss (≥700 ml)	0.93	0.49–1.78	0.831			
Perioperative blood transfusion	1.05	0.43–2.60	0.909			
Anastomotic method (modified BA)	0.046	0.01–0.15	<**0.001**	0.02	0.01–0.08	<**0.001**
Pancreatic texture (soft)	7.12	3.25–15.61	<**0.001**	6.10	2.30–17.36	<**0.001**
Non-dilated main pancreatic duct	2.28	1.17–4.44	**0.014**	2.23	0.90–5.65	0.085

Bold characters, statistically significant

CI confidence interval, *BA* Blumgart anastomosis

Although randomized controlled trials showed no differences in the complication rates after PD between patients who underwent pancreaticojejunostomy and those who underwent pancreaticogastrostomy,[31,32] pancreaticojejunostomy including duct-to-mucosa anastomosis seems to be the technique most commonly used, and various other techniques have been proposed to minimize the risk of PD-related complications.[31,32,35] Some invagination procedures have been reported but have not been shown to be significantly better.[36,37] Peng et al. reported a POPF rate of 0 % in 106 patients who underwent "binding pancreaticojejunostomy", but the mortality rate was about 3 %.[38]

Recently, the reported rate of POPF has improved to 10–20 % than before. The Kakita method, using two layers of sutures between the pancreatic parenchyma and the seromuscular layer of the jejunum, had at the time been the most frequently used method in several high-volume centers in Japan including our institution. Interestingly, the POPF formation rates reported from two institutions where the original Blumgart anastomosis with sutures between the pancreatic parenchyma and the jejunum was used were outstandingly low at 4.3 and 6.9 %, respectively.[39,40] We therefore replaced the Kakita method with the m-BA in March 2010 and, in the current study, compared short-term outcome between these two methods. The operative time and volume of blood loss were comparable in this series of 120 patients in each group, including 54 patients with soft pancreas in each group. However, the median amylase concentration in the drainage fluid was significantly lower in the m-BA group than in the Kakita group, both in the group overall and in the subgroup of patients with soft pancreas. Moreover, the rate of POPF was significantly lower and the length of postoperative hospital stay was significantly shorter in the m-BA group than in the Kakita group. Multivariate analysis showed that m-BA was an independent predictor of a lower rate of POPF formation.

The main limitation of this study is the very high clinically relevant fistula rate of the control group (36 %). However, the rate of POPF formation itself of the m-BA group was considerably better than that of the previous reports, indicating the usefulness of m-BA.

Conclusion

Placement of sutures between the pancreatic parenchyma and the jejunum risks leakage of pancreatic juice from the needle holes or laceration of the pancreatic parenchyma, especially in patients with soft pancreas. We therefore considered that anastomosis using fewer sutures would be preferable. The original Blumgart anastomosis used four to six transpancreatic/jejunal seromuscular sutures, and our method used only one to three. Our method also completely covered the pancreatic stump with jejunal serosa because of the modified lateral suture through the seromuscular layer of the jejunum. These modifications resulted in more favorable outcomes, and we suggest that the m-BA is suitable for use as a standard method of pancreaticojejunostomy after PD.

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