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Modified Blumgart Mattress Suture Versus Conventional Interrupted Suture in Pancreaticojejunostomy During Pancreaticoduodenectomy

Randomized Controlled Trial

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Objective: This study used a randomized controlled trial (RCT) to evaluate whether mattress suture of pancreatic parenchyma and the seromuscular layer of jejunum (modified Blumgart method) during pancreaticojejunostomy (PJ) decreases the incidence of clinically relevant postoperative pancreatic fistula (POPF) after pancreaticoduodenectomy (PD).

Background: Several studies reported that mattress suture of Blumgart anastomosis in PJ could reduce POPF rate. This, however, is the first RCT.

Methods: Between June, 2013 and May, 2017, 224 patients scheduled for PD were enrolled in this study in Wakayama Medical University Hospital. Enrolled patients were randomized to either interrupted suture or modified Blumgart mattress suture. The primary endpoint was the incidence of grade B/C POPF based on the International Study Group on Pancreatic Fistula criteria. This RCT was registered with ClinicalTrials.gov (NCT01898780).

Results: Patients were randomized to either interrupted suture (103 patients) or modified Blumgart mattress suture (107 patients) and were analyzed by intention-to-treat. Grade B/C POPF occurred in 7 patients (6.8%) in the interrupted suture group and 11 (10.3%) in the mattress suture group ($P = 0.367$). Mortality within 90 days was 0 in both groups. There were no significant differences in all postoperative complications between the interrupted suture group and the modified Blumgart mattress suture group.

Conclusions: Mattress suture of pancreatic parenchyma and the jejunal seromuscular layer during PJ (modified Blumgart technique) did not reduce clinically relevant POPF compared with interrupted suture.

Keywords: Blumgart anastomosis, interrupted suture, mattress suture, pancreatic fistula, pancreaticojejunostomy

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All authors declare no conflict of interest concerning this study.

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The mortality rate after pancreaticoduodenectomy (PD) has decreased to less than 5% in high-volume centers—thanks to advances in surgical techniques and perioperative management.[1–3] Postoperative pancreatic fistula (POPF) rates, however, remain higher than 10% in most previous prospective studies.[4–7] POPF is 1 of the most harmful complications of PD, and can cause intra-abdominal abscess, intra-abdominal hemorrhage, and even death.

Numerous studies concerning operative techniques of pancreaticoenteric anastomosis have tried to decrease POPF incidence after PD. Among them, several significant randomized controlled trials (RCTs) comparing invagination versus duct-to-mucosa anastomosis,[8,9] pancreaticojejunostomy (PJ) versus pancreaticogastrostomy (PG),[6,10–16] and internal versus external stent,[17,18] and also no stent versus external stent[19] have been reported.

Recently, several retrospective studies reported the efficacy of mattress sutures for pancreatic parenchyma and the jejunal seromuscular layer during PJ to decrease clinically relevant POPF incidence, compared with interrupted suture as in Cattell-Warren anastomosis[20] or Kakita method,[21] because it was proposed as the Blumgart anastomosis[22] by Memorial Sloan-Kettering Cancer Center, New York, in 2000.[23–26] The original Blumgart method, which included mattress sutures for pancreatic parenchyma and the jejunal seromuscular layer, aimed to eliminate tangential tension and shear forces between fragile pancreatic parenchyma and jejunum,[22,23] and also allow the possibility of covering the pancreatic cut surface completely with jejunal serosa.[22,23]

Our modified Blumgart mattress suture technique differed from the original Blumgart anastomosis in that, whereas the original Blumgart method used more than 4 trans-pancreatic jejunal sutures,[22,23] we used between 1 and 3 sutures depending on the size of the pancreas to prevent leakage of pancreatic juice from needle holes and to maintain blood flow in the pancreatic stump.[21] The original Blumgart method also placed a knot on the pancreatic surface, followed by a suture through the jejunal anterior wall and pancreatic anterior wall; these sutures were then tied over the anterior aspect of the pancreas.[22,23] We never tied the trans-pancreatic sutures on the pancreatic surface, but continued to place each double-armed suture needle through the seromuscular layer of the jejunal anterior wall in the direction of the short axis and placed a knot on the jejunal ventral wall to avoid both redistributing the respective shear forces from the pancreas to the jejunum[27] and laceration of the pancreatic parenchyma during knot tying.

Our modified Blumgart mattress suture technique also differs from other reported modified Blumgart methods. Another modified Blumgart method used mattress suture through the jejunal posterior wall in the direction of the long axis after penetrating the suture through the pancreas, and then placed trans-pancreatic sutures from posterior to anterior.[24–26] We sutured through the seromuscular layer of the jejunal posterior wall in the direction of the short axis, as in the original Blumgart method. Concerning mattress suture of the jejunal posterior wall, we think the original Blumgart method could provide closer contact of the jejunum and the pancreatic cut surface than other modified Blumgart methods, and we have thus accepted the direction of the short axis. Our technique in this RCT, therefore, is a novel anastomosis using mattress sutures.

Previous reports described that the grade B/C POPF incidences after Blumgart anastomosis ranged from 2.5% to 20.5%,[23–27] and our pilot study had 4.4% of grade B/C POPF. However, as these studies had retrospective design, the results could not sufficiently confirm the efficacy of the Blumgart mattress suture to reduce clinically relevant POPF incidence.

In this study, we conducted a RCT to compare modified Blumgart mattress sutures and interrupted sutures during PJ, and we evaluated decrease in clinically relevant POPF incidence after PD.

METHODS

Study Design and Participants

This was a single-center RCT with 2 parallel interventions arms, conducted at Wakayama Medical University Hospital (WMUH), between June, 2013 and May, 2017. The study was approved by the Ethical Committee on Clinical Investigation of WMUH (No. 1259) and registered in accordance with ClinicalTrials.gov (NCT01898780), and the University Hospital Medical Information Network Clinical Trials Registry (UMIN000015943). It was conducted in accordance with the Declaration of Helsinki, and preoperative written informed consent was obtained from all participating patients.

Eligible participants were all patients who were scheduled for PD at WMUH for malignant or benign disease of the pancreatic head and periampullary region. This study excluded patients who refused randomization, had severe comorbidity, such as ischemic cardiac disease, respiratory disorders requiring oxygen inhalation, liver cirrhosis, chronic or renal failure requiring hemodialysis, and required combined resection of other organs including colon, liver, and kidney.

Randomization

After providing written informed consent, patients planned for PD were preoperatively randomized to either the modified Blumgart mattress suture group or the interrupted suture group in PJ using a computerized randomization system, in which the permuted block size was 4 in 2 groups, at the coordinating center (Japan Clinical Research Support Unit). To ensure equal distribution between treatment groups, participants were stratified by pancreatic texture (soft or hard), then randomized in a 1:1 ratio to 1 of the 2 groups. Patients with a preoperative diagnosis of pancreatic cancer were assumed to have a hard pancreatic texture.

Operative Procedure

Our standard procedure is that the stomach is divided just proximal to the pylorus, so that more than 95% of the stomach is preserved.[28] In patients with malignant disease, the lymph nodes are dissected at the hepatoduodenal ligament, around the common hepatic artery, around the superior mesenteric artery (SMA), and around the pancreatic head. Concomitant portal vein and/or superior mesenteric vein (PV/SMV) resection is performed in patients with possible or definite tumor invasion.[29] Reconstruction was performed by Billroth II reconstruction. In reconstruction, the retained jejunum is brought through the transverse mesocolon, and then end-to-side PJ performed first, followed by an end-to-side hepaticojejunostomy and by a subsequent antecolic end-to-side gastrojejunostomy.[30]

Interrupted Suture of Pancreatic Parenchyma and Jejunal Seromuscular Layer During PJ

The jejunal seromuscular layer was sutured to the pancreatic parenchyma of the stump in an interrupted penetrating fashion, using 4–0 MONOFLEN (double-armed, polyvinylidene fluoride monofilament; Alfresa Pharma Co., Osaka, Japan) (Fig. 1A-i). The sutures of the jejunal seromuscular layer, in the posterior to anterior direction, were wide enough to contact more closely with the pancreatic cut surface, and to prevent laceration of pancreatic parenchyma, we never tied tightly. Anastomosis was performed in a duct-to-mucosa fashion using a single layer of interrupted 5–0 PDS-II (double-armed, polydioxanone suture; Johnson and Johnson Co., Tokyo, Japan) (Fig. 1A-ii) with 8 or more sutures. We usually used 4 trans-pancreatic jejunal seromuscular sutures based on the Kakita method.[21] However, in the case of thick pancreatic parenchyma, we performed 2-layer sutures of pancreatic parenchyma and the jejunum, in which dorsal pancreas was sutured to the seromuscular layer of the jejunal posterior wall, and the ventral part of the anastomosis was sutured in the same fashion after duct-to-mucosa anastomosis. A 5-Fr polyethylene pancreatic stent tube (Akita Sumitomo Bake, Akita, Japan) was cut to a length of 5 cm and placed at the pancreaticojejunal anastomotic site as an internal stent (Fig. 1A-iii).[17] If the main pancreatic duct was too large or too small for a 5-Fr stent tube, no stent was placed.

Modified Blumgart Mattress Suture of Pancreatic Parenchyma and Jejunal Seromuscular Layer During PJ

The trans-pancreatic suture started from anterior to posterior straight through the pancreas using 4–0 MONOFLEN. A suture was placed through the seromuscular layer of the jejunal posterior wall from back to front in the direction of the short axis, followed by replacement of the mattress suture from front to back of the jejunal posterior wall, and then the trans-pancreatic suture from posterior to anterior was performed (Fig. 1B-i). The needle exited from the pancreas 5 to 7 mm away from the previous entry point of the suture into the pancreas. The needles from these trans-pancreatic sutures were retained and the sutures organized for later completion. After completion of duct-to-mucosa anastomosis (Fig. 1B-ii) and placement of the internal stent, sutures were placed through the seromuscular layer of the jejunal anterior wall in the direction of the short axis. Finally, the jejunum wall was adapted to the pancreatic cut surface, and tying of the knots was performed at the jejunal ventral wall (Fig. 1B-iii). This procedure completely covered the pancreatic stump with jejunal serosa (Fig. 1B-iv).

Postoperative Management

All patients were treated according to the standardized postoperative care pathway for PD. Drain management and checks of the drainage fluid amylase levels were as follows: 1 BLAKE Silicone Drain 10 mm Flat, 3/4 Fluted (Ethicon, Inc., Somerville, NJ) was placed near the pancreatic anastomosis. The drain was removed on postoperative day (POD) 3 or 4 if the drainage fluid was clear, and pancreatic fistula and bacterial contamination were absent.[31] Amylase level in the drainage fluid was routinely measured on POD 1, 3, and 4. In this study, prophylactic octreotide to prevent POPF was not administered.

Measurement of the Area of Fluid Collection by Postoperative Computed Tomography

Three-phasic contrast-enhanced multidetector computed tomography (CT; GE Healthcare, Milwaukee, WI) was performed on POD 4 to check postoperative disorders and measure accumulation of fluid around the PJ,[28,31] as indicated in the study protocol

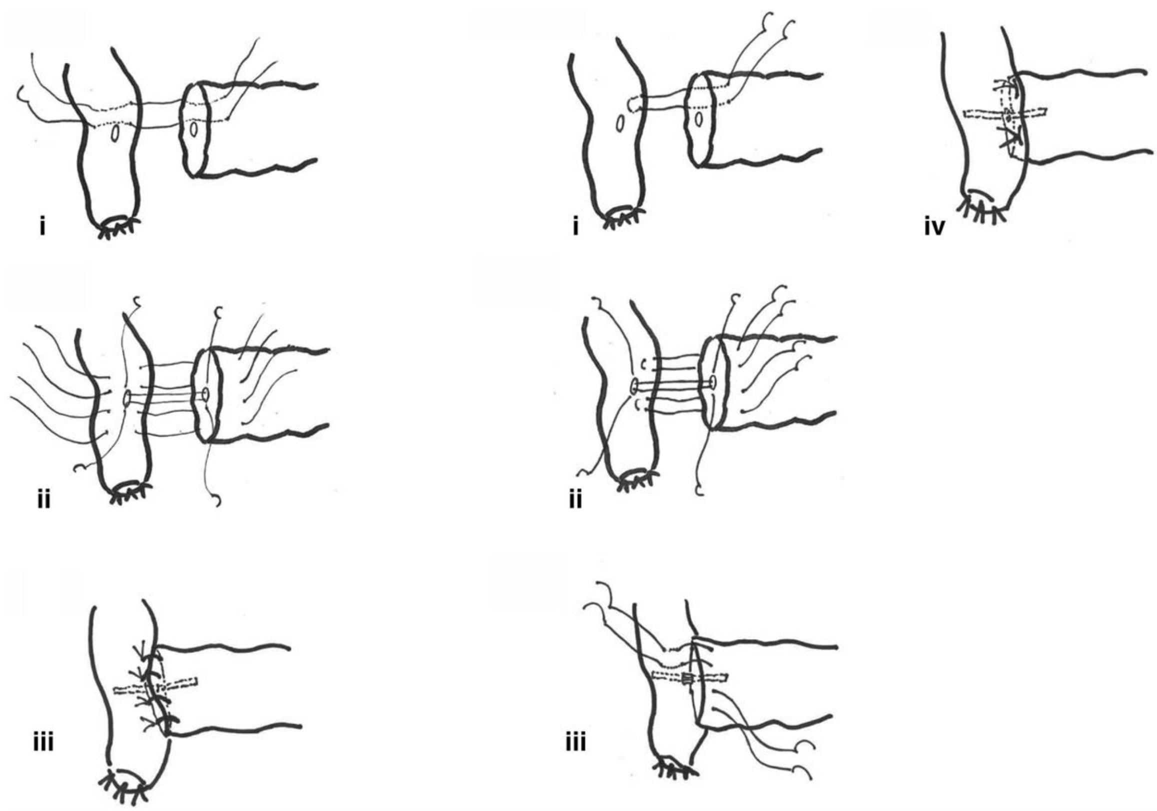

FIGURE 1. (A) Interrupted suture method. (i) The jejunal seromuscular layer was approximated to the pancreatic parenchyma of the stump with interrupted penetrating sutures, using 4–0 MONOFLEN. (ii) Anastomosis was performed in a duct-to-mucosa fashion using a single layer of interrupted 5–0 PDS-II. (iii) After a 5-Fr polyethylene pancreatic stent tube was placed at the pancreaticojejunal anastomotic site during duct-to-mucosa anastomosis, suture of pancreatic parenchyma and seromuscular layer of jejunum was tied. (B) Modified Blumgart mattress suture method; transpancreatic suture starts from anterior to posterior, straight through the pancreas using 4–0 MONOFLEN. Suture was placed through the seromuscular layer of jejunal posterior wall from back to front in the direction of short axis, followed by replacement of mattress suture from front to back of posterior wall of the jejunum in the direction of the short axis, and then a full thickness pancreas bite from posterior to anterior was performed (i). Anastomosis between the pancreatic duct and mucosal layer of the jejunum was then performed (ii), and then after completion of duct-to-mucosa anastomosis and placement of internal stent, sutures were placed through the seromuscular layer of jejunal anterior wall in the direction of short axis (iii). This procedure completely covered the pancreatic stump with jejunal serosa (iv).

(Fig. 2A). CT images were reconstructed and reviewed digitally using Aquarius Net Ver.4 (TeraRecon, San Mateo, CA). We measured maximal areas of interspace between the pancreatic cut surface and the jejunal wall at the PJ (Fig. 2B) and intra-abdominal fluid collection around the PJ (Fig. 2C) by CT findings. Cross-section of these areas on the equilibrium phase was automatically measured by Aquarius Net Viewer (Fig. 2B, C).[32]

Study Endpoints and Definition

The primary endpoint was the incidence of grade B/C POPF within 90 days after operation, either in or out of the hospital. POPF was defined and graded according to the 2017 International Study Group of Pancreatic Surgery (ISGPS) criteria,[4] and was classified as biochemical leak which included amylase-rich fluid more than 3 times greater than the upper limit of the serum amylase level without change in clinical management, grade B (fistula involving increased amylase activity in the drainage fluid in association with clinically relevant conditions), or grade C (fistula causing organ failure or clinical instability such that a reoperation is needed). Secondary endpoints were time required for PJ, cost of sutures required for PJ, and postoperative complications other than POPF within 90 days after operation.

Delayed gastric emptying (DGE) and intra-abdominal hemorrhage were defined by ISGPS criteria.[33,34] Other postoperative complications were graded according to the Clavien-Dindo classification, and in this study, severe complications were defined as a condition grade III or more.[35] Discharge was defined as follows: a return to the preoperative activities of daily living, no deep-site infections, normal laboratory data, no drains, and possible oral nutrition above basal metabolism. Mortality was defined as death within 90 days after surgery.

Statistical Methods

The sample size was determined based on the grade B/C POPF rate. Three previous studies[36–38] using the ISGPF POPF definition were used for reference during the design of this protocol to estimate the incidence for interrupted sutures during PJ. In the previous literature, grade B/C POPF rates after PJ with interrupted sutures

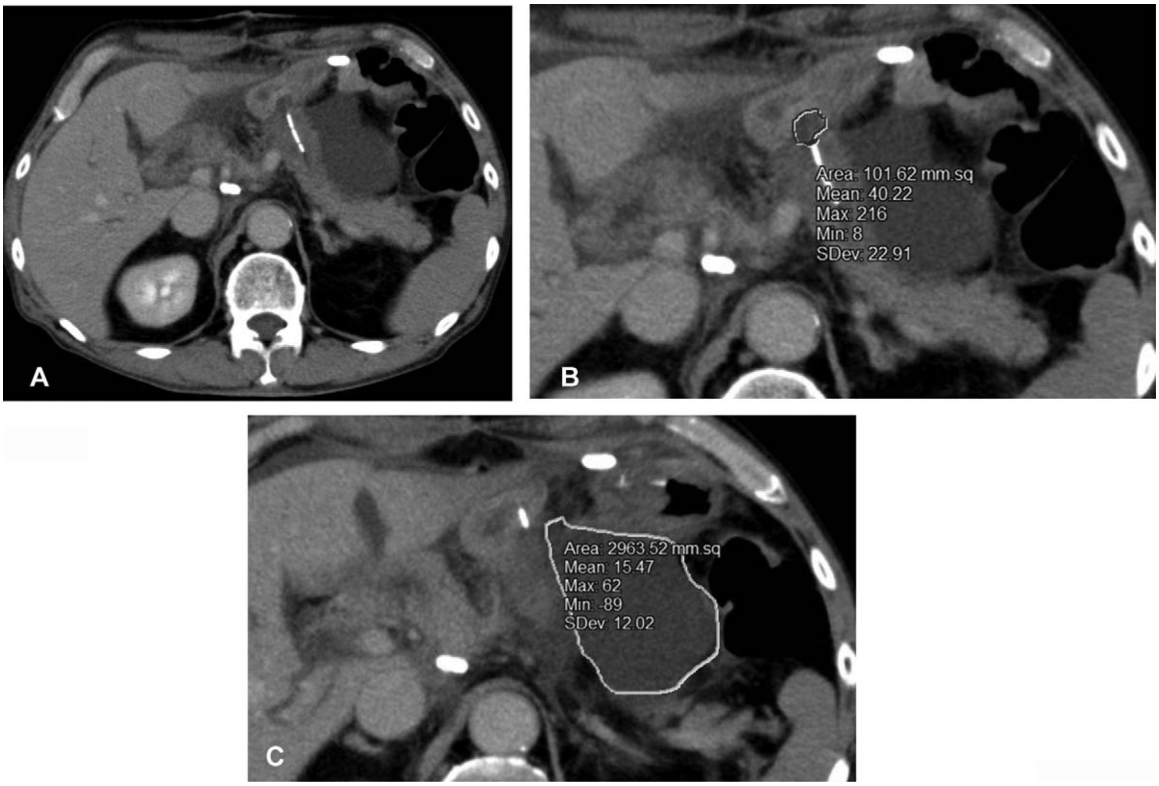

FIGURE 2. (A) Computed tomography (CT) finding around pancreaticojejunostomy (PJ) on postoperative day 4. We measured maximal area of interspace between the cut surface of the pancreas and jejunal wall (B) and maximal areas of intra-abdominal fluid collection around the pancreatic anastomosis at the PJ by CT findings (C).

ranged between 10% and 20%.[36–38] We therefore estimated a grade B/C POPF rate of 15% in the interrupted suture group. Grade B/C POPF rates in PJ using mattress sutures ranged from 4% to 7% in previous studies,[23,24] and previous unpublished data from the authors' institution showed that 4% of 23 consecutive patients who underwent our modified Blumgart mattress suture technique before this study developed grade B/C POPF. The grade B/C POPF rate in the modified Blumgart mattress suture group was expected to be 4%. We therefore suggested that modified Blumgart mattress sutures could reduce the incidence of grade B/C POPF from 15% to 4%. We calculated that this study required 200 patients (100 in each group) to show a difference between the 2 groups at a power of 80% with a significance level of 0.05. Calculating an estimated intraoperative withdrawal rate or postrandomization exclusion of about 10%, it was necessary to enroll a total of 224 patients (112 in each group) to meet the primary endpoint of this study. Furthermore, for intention-to-treat analysis, all randomized patients were analyzed according to the assigned treatment group, except those who did not undergo PD due to peritoneal dissemination or metastasis, or because they were switched to another procedure.

Data were collected prospectively for all patients and included patient demographics, pathologic examinations, perioperative clinical information, and complications. Data are expressed as median with range. Patient characteristics, and perioperative and postoperative factors between the 2 groups were compared by using chi-square statistics, the Fisher exact test, and the Mann-Whitney *U* test. Data were analyzed by intention-to-treat analysis for the primary endpoint. The predictive values of the maximal area of interspace between the pancreatic cut surface and the jejunal wall at PJ or intra-abdominal fluid collection around the PJ for grade B/C POPF were evaluated by analysis of receiver-operating characteristics (ROC). The accuracy of predicting grade B/C POPF was assessed by calculating the area under the curve (AUC). Statistical significance was defined as $P < 0.05$. Statistical analyses were performed using the SPSS 20.0 software program (SPSS Inc., Chicago, IL).

RESULTS

During the study period, 239 patients were scheduled to undergo PD in WMUH. A consort flow diagram of this RCT is shown in Fig. 3. Of these 239 patients, 15 patients were excluded from the study before randomization for the following reasons: other organ resection was required (n = 7), presentation of severe cirrhosis (n = 1), presentation of chronic renal failure requiring hemodialysis (n = 1), patient refusal to participate (n = 2), and patients receiving long-term steroid mediation (n = 4). The remaining 224 patients were randomly assigned to the interrupted suture group (n = 112) or the modified Blumgart mattress suture group (n = 112). In the interrupted suture group, 9 patients were subsequently excluded due to liver metastasis (n = 3), peritoneal dissemination (n = 2), or change of procedure (total pancreatectomy, n = 2; and combined colon resection, n = 2). In the modified Blumgart mattress sutures group, 5 patients were subsequently excluded due to peritoneal dissemination (n = 1), or change of procedure (total pancreatectomy, n = 2; and enucleation, n = 2). One patient who was assigned to the modified Blumgart mattress suture group was shifted to PG without duct-to-mucosa anastomosis due to an invisible main pancreatic duct at the pancreatic cut margin, which was caused by severe pancreatitis after endoscopic retrograde cholangiopancreatography.

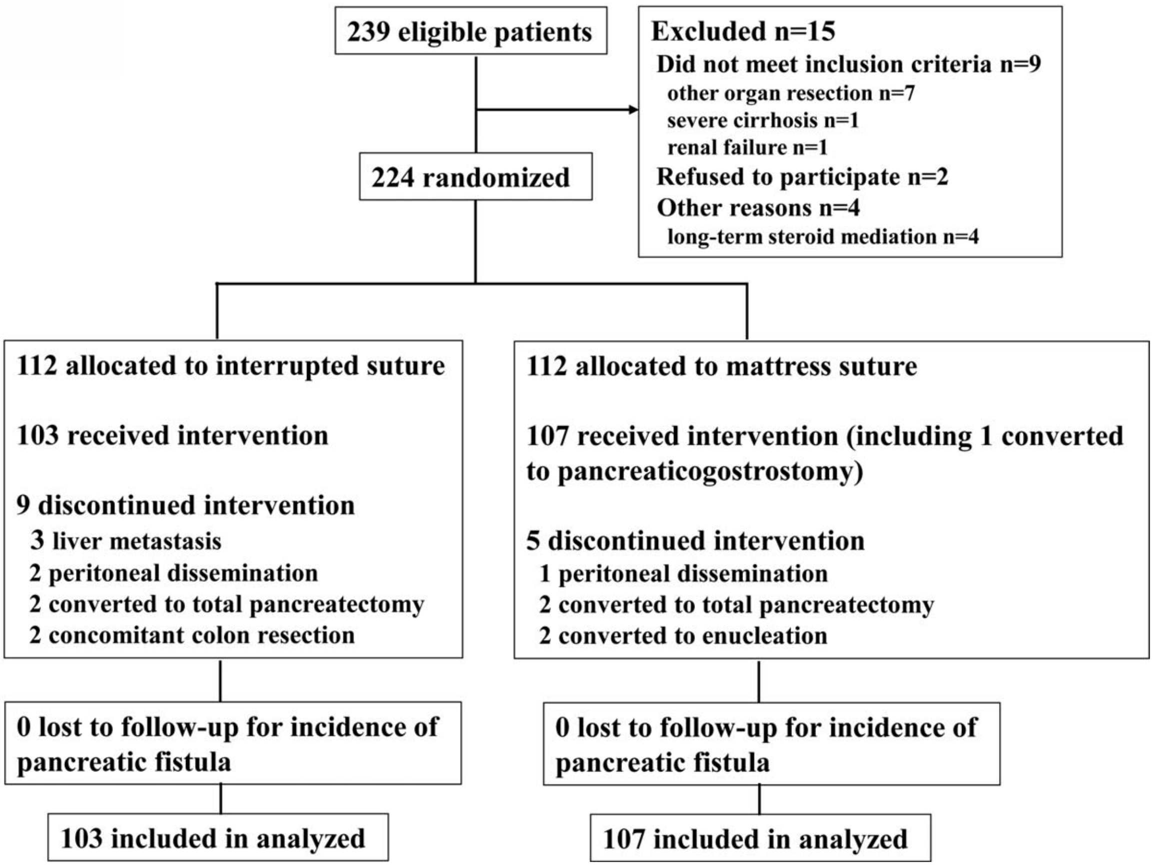

FIGURE 3. Consort flow diagram for the trial.

Table 1 shows patient characteristics and preoperative status. No significant difference was found between the interrupted and modified Blumgart mattress suture groups with regard to any background factors. There was no significant difference in the incidence of neoadjuvant therapy in the 2 groups (Table 1). Moreover, there was no significant difference of grade B/C POPF incidence between the patients with and without neoadjuvant therapy (7.4% vs 8.7%; $P = 0.817$) in this study.

Comparison of Operative Outcomes and Postoperative Complications Between Interrupted and Modified Blumgart Mattress Suture Groups

Operative time, intraoperative bleeding, and transfusion incidence were similar in both the interrupted and the modified Blumgart mattress suture groups (Table 2), and there was no significant difference of the ratio of soft and hard pancreas between the two

TABLE 1. Characteristics of Enrolled Patients

	Interrupted Suture (n = 103)	Modified Blumgart Mattress Suture (n = 107)	*P*
Age, yrs, median (range)	70 (40–86)	68 (24–90)	0.761
Sex, male, n (%)	62 (60.2)	59 (55.1)	0.459
Body mass index, kg/mm^2, median (range)	21.6 (16.1–29.4)	22.2 (14.9–35.1)	0.408
Diabetes, yes, n (%)	21 (20.4)	32 (29.9)	0.112
Jaundice, yes, n (%)	46 (44.7)	39 (36.5)	0.226
Chronic obstructive pulmonary dysfunction, yes, n (%)	20 (19.4)	17 (15.9)	0.502
Restrictive pulmonary dysfunction, yes, n (%)	9 (8.7)	9 (8.4)	0.933
Neoadjuvant therapy, yes, n (%)	15 (14.6)	12 (11.2)	0.469
Final pathological diagnosis, n (%)			0.527
Pancreatic cancer	36 (35.0)	40 (37.4)	
Intraductal papillary mucinous neoplasm	21 (20.8)	27 (25.2)	
Neuroendocrine tumor	1 (1.0)	4 (3.7)	
Bile duct cancer	34 (33.0)	27 (25.2)	
Duodenal cancer	4 (3.9)	2 (1.9)	
Other diseases	7 (6.8)	7 (6.5)	

The cardiovascular, other general condition and laboratory data, were identical for the 2 groups.

TABLE 2. Operative Outcomes Based on Intention-to-treat Analysis

	Interrupted Suture (n = 103)	Modified Blumgart Mattress Suture (n = 107)	P
Operative procedures			
Procedure, classic PD/pylorus-resecting PD, n (%)	6 (5.8)/ 97 (94.2)	4 (3.7)/ 103 (96.3)	0.478
Concomitant PV/SMV resection, n (%)	24 (23.3)	23 (21.5)	0.754
Pancreatic texture of remnant pancreas, soft/hard, n (%)	58 (56.3)/ 45 (43.7)	61 (57.0)/46 (43.0)	0.919
Main pancreatic duct size, median (range), mm	3.0 (1.0–8.0)	3.0 (1.0–6.0)	0.995
Operative time, median (range), min	382 (264–598)	390 (264–637)	0.543
Intraoperative bleeding, median (range), mL	230 (20–2091)	230 (25–3150)	0.783
Red blood cell transfusion, yes, n (%)	5 (4.9)	4 (3.7)	0.690
Time for pancreatic anastomosis, median (range), min	28.5 (19–53)	26 (18–55)	0.026
Number of sutures for pancreatic parenchyma and jejunal seromuscular anastomosis, median (range)	4 (2–10)	2 (1–8)	<0.001
Number of sutures for pancreatic duct and jejunal mucosa anastomosis, median (range)	8 (8–13)	8 (0–12)	0.878
Cost of sutures for pancreatic anastomosis, median (range) (Japanese Yen)	19,136 (16,568–26,840)	16,568 (10,272–22,284)	<0.001

groups ($P = 0.919$; Table 2). Time required for pancreatic anastomosis, however, was significantly shorter in the modified Blumgart mattress suture group than in the interrupted suture group (26 vs 28.5 minutes; $P = 0.026$; Table 2). As the number of sutures for pancreatic parenchyma and the jejunal seromuscular layer was smaller in the modified Blumgart mattress suture group (2 vs 4 sutures; $P < 0.001$), the cost of sutures used during PJ was significantly lower in the modified Blumgart mattress suture group than in the interrupted suture group [¥16,568 vs ¥19,136 (Japanese Yen); $P < 0.001$; Table 2].

There was no significant difference of grade B/C POPF incidence between the interrupted and the modified Blumgart mattress suture groups (6.8% vs 10.3%; $P = 0.367$; Table 3). No patients

TABLE 3. Postoperative Complications Based on Intention-to-treat Analysis

	Interrupted Suture (n = 103)	Modified Blumgart Mattress Suture (n = 107)	P
Pancreatic fistula*, n (%)			0.361
None	70 (68.0)	72 (67.9)	
Biochemical leakage	26 (25.2)	24 (22.4)	
Grade B	7 (6.8)	11 (10.3)	
Grade C	0 (0)	0 (0)	
Clinically relevant pancreatic fistula (grade B/C), n (%)	7 (6.8)	11 (10.3)	0.367
Amylase level of drainage fluid on POD 1, median (range), IU/L	1013 (28–47,983)	1018.5 (10–24,498)	0.920
Amylase level of drainage fluid on POD 3, median (range), IU/L	182 (6–74,135)	131.5 (3–74,135)	0.764
Amylase level of drainage fluid on POD4, median (range), IU/L	79 (4–71,688)	63.5 (3–25,296)	0.638
Maximal area of interspace between pancreas and jejunum at pancreaticojejunostomy based on CT finding on POD 4	45 (0–329)	0 (0–261)	<0.001
Maximal area of intra-abdominal fluid collection around pancreatic anastomosis based on CT finding on POD 4	188 (0–5153)	94 (0–3183)	0.099
Time to drain removal, median (range), d	4 (3–14)	4 (3–44)	0.124
Clavien-Dindo classification, n (%)			0.756
None	61 (59.2)	59 (55.4)	
I	23 (22.3)	24 (22.4)	
II	7 (6.8)	5 (4.7)	
IIIa	11 (10.7)	16 (15.0)	
IIIb	1 (1.0)	2 (1.9)	
Iva	0 (0)	1 (0.9)	
IVb	0 (0)	0 (0)	
V	0 (0)	0 (0)	
Severe complication (IIIa or more)	12 (11.7)	19 (17.8)	0.212
Intra-abdominal hemorrhage†, n (%)	0 (0)	1 (0.9)	0.325
Grade A	0	0	
Grade B	0	1	
Grade C	0	0	
Intraabdominal abscess, n (%)	7 (6.8)	9 (8.4)	0.659
Percutaneous or endoscopic drainage for pancreatic fistula, n (%)	6 (5.8)	9 (8.4)	0.467
Reoperation, n (%)	1 (1.0)	2 (1.9)	0.583
Readmission, n (%)	6 (5.8)	7 (6.5)	0.829
Mortality within 90 d, n (%)	0 (0)	0 (0)	—
Postoperative hospital stay, median (range), d	15 (6–44)	15 (8–52)	0.104

There were no significant differences of incidence of delayed gastric emptying, bile leakage, and wound infection in either group.
*Pancreatic fistula was defined and graded according to the 2017 International Study Group of Pancreatic Fistula criteria.
†Intra-abdominal hemorrhage was defined and graded according to the International Study Group of Pancreatic Surgery criteria.

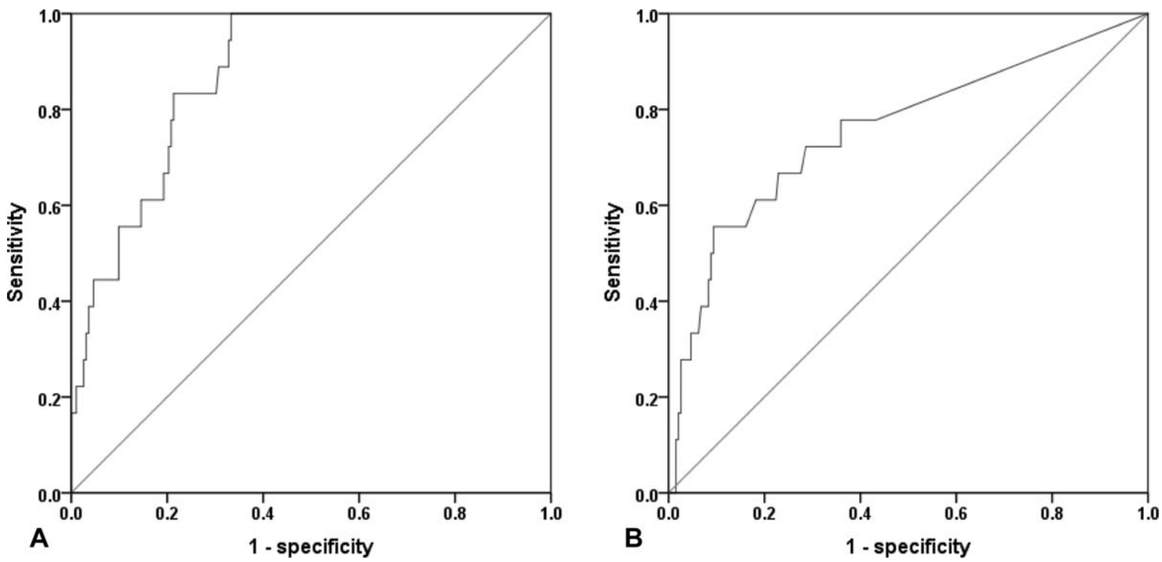

FIGURE 4. Receiver-operating characteristics analyses for prediction of grade B/C postoperative pancreatic fistula (POPF) by assessment of maximal area of intra-abdominal fluid collection around the pancreatic anastomosis (A) and maximal area of interspace between pancreas and jejunum at pancreaticojejunostomy (B). The area under the curve (AUC) of intra-abdominal fluid collection was 0.873 and AUC of interspace between pancreas and jejunum was 0.756.

developed grade C POPF in either group, according to 2017 ISGPF criteria. The amylase levels of the drainage fluid on POD 1, POD 3, and POD 4 were similar between the 2 groups (POD 1: 1013 vs 1018.5 IU/L; $P = 0.920$; POD 3: 182 vs 131.5 IU/L; $P = 0.764$; and POD 4: 79 vs 63.5 IU/L; $P = 0.638$; Table 3). Of the 18 patients who developed grade B/C POPF, 9 received octreotide analog therapeutically, including 5 patients in the interrupted suture group and 4 patients in the modified Blumgart mattress suture group. No patients with hard pancreas developed grade B/C POPF in either group. There was no significant difference of grade B/C POPF incidence in the patients with soft pancreas between the interrupted suture group (n = 7/58, 12.1%) and the modified Blumgart mattress suture group (n = 11/61, 18.0%) in this study ($P = 0.364$).

Mortality rate within 90 days after PD was 0% in both groups. Overall morbidity rate was 42.9% (90 of 210 patients), with no difference between the 2 groups ($P = 0.550$). Incidence of severe complications was 14.8% (31 of 210), with no difference between the 2 groups ($P = 0.212$; Table 3). In this study, 3 patients received reoperation for the following reasons: portal thrombosis (n = 2) and perforation of the colon caused by ischemia with no significant difference between the 2 groups ($P = 0.583$; Table 3).

Measurement of the Area of Fluid Collection by Postoperative CT

We measured maximal areas of interspace between the pancreatic cut surface and the jejunal wall at PJ, and also intra-abdominal fluid collection around the PJ, by CT findings on POD 4, to evaluate the correlation between these areas and grade B/C POPF incidence. ROC analyses showed that the area of intra-abdominal fluid collection around the pancreatic anastomosis (AUC 0.873, $P < 0.001$; Fig. 4A) had a higher diagnostic accuracy than the area of interspace between the pancreatic cut surface and the jejunal wall at PJ (AUC 0.756, $P = 0.001$; Fig. 4B). The maximal area of interspace between the pancreatic cut surface and jejunal wall at PJ was significantly smaller in the modified Blumgart mattress suture group than in the interrupted suture group (median area; 0 vs 45 mm^2; $P < 0.001$). There was no significant difference, however, in the maximal area of intra-abdominal fluid collection around the PJ between the 2 groups ($P = 0.099$; Table 3).

DISCUSSION

To prevent clinically relevant POPF, 4 important points concerning PJ technique should be considered, based on previous evidence. Pancreatic juice should be completely drained, blood flow should be maintained in the pancreatic stump, laceration of pancreatic parenchyma should be prevented, and the jejunum wall should be in close contact to the pancreatic cut surface. As many reports have shown, duct-to-mucosa anastomosis and placement of an internal stent at pancreatic anastomosis during PJ, our normal practice, might ensure pancreatic juice drainage, and also maintain long-term patency of pancreatic anastomosis.[17–19,39] As Kakita et al[21] suggested, the presence of many sutures and of their being tied too tightly in PJ might reduce blood flow in the pancreatic stump, causing ischemia and necrosis of the pancreatic stump by restriction of tissue blood flow. We therefore used as few sutures as possible, taking care to not tie the suture too tightly, thus maintaining blood flow in the pancreatic stump.

Several retrospective studies reported very low incidence of grade B/C POPF after PJ with the Blumgart mattress suture, ranging between 2.5% and 20.5%, and reported its superiority to the interrupted suture technique.[23–26] Interrupted suture of pancreatic parenchyma and the jejunal seromuscular layer might develop tangential shear forces during the tightening of the knots, and the suture material could easily lacerate pancreatic parenchyma. The Blumgart method, meanwhile, has the advantage of avoiding shear stress on the pancreas by placement of the mattress suture.[22] Although the original Blumgart anastomosis put the knot of penetrating sutures through the pancreas, our technique was modified to tie knots on the ventral wall of the jejunum to make the anastomosis more feasible and safe.[27]

Furthermore, dead space between the pancreatic cut surface and jejunal wall might interfere with proper sealing and healing of anastomosis by retention of effusion from the pancreatic surface.

Although our interrupted suture lifted the jejunal seromuscular layer widely enough to allow the jejunum wall to contact the pancreatic cut surface as closely as possible, our modified Blumgart mattress suture technique could cover the pancreatic surface from both dorsal and ventral sides of the pancreas capsule with jejunal serosa, which theoretically might provide more close contact of the pancreatic surface and jejunal wall, compared with the interrupted suture.

Our hypothesis was that our modified Blumgart mattress suture could reduce POPF incidence compared with interrupted suture, by preventing laceration of the pancreatic parenchyma and more completely covering the pancreatic cut surface. Indeed, our preliminary study before this RCT showed only 4.4% of grade B/C incidence after PJ with our modified Blumgart mattress suture method, which was similar to those of previous reports.[23–27] However, this study showed that the modified Blumgart mattress suture could not reduce the incidence of grade B/C compared with the interrupted suture. The preliminary study was conducted with only 23 patients, and the incidence of grade B/C POPF was 4.4%. However, the grade B/C POPF incidence using the modified Blumgart technique was 10.8% in this RCT. This is yet another instance where one must be careful with the results of a small-scale study. We should also note that the anastomosis in the preliminary study was done by only 1 expert surgeon (HY), and this might be one of the reason for the difference.

When we compared the interspace area between the pancreatic cut surface and the jejunal wall at PJ based on CT findings on POD4, it was indeed smaller in the modified Blumgart mattress suture group than in the interrupted suture group. This result might indicate that covering the pancreatic cut surface with jejunal serosa in mattress suture could create a ‘‘water-tight’’ condition and closer contact of the pancreatic surface and jejunal wall in not only original Blumgart anastomosis, but also in our modified Blumgart anastomosis. ROC analyses, however, showed the area of intra-abdominal fluid collection around the PJ was more significantly associated with grade B/C POPF development than the interspace area between pancreatic cut surface and the jejunal wall in this study. The intra-abdominal fluid collection area was similar between the 2 groups. These results suggested that the modified Blumgart mattress suture might reduce dead space between the pancreatic cut surface and the jejunal wall, and prevent retention of effusion at this area by covering the pancreatic surface with the jejunum; it could not, however, prevent intra-abdominal fluid collection. We thought that simple physical coverage of the pancreatic cut surface might not prevent leakage of pancreatic juice into the abdominal cavity and clinically relevant POPF. This could be the reason that our primary endpoint that modified Blumgart mattress suture could reduce grade B/C POPF incidence has not been met.

Regarding the relationship between the incidence of clinically relevant POPF and neoadjuvant therapy, there was no significant difference of grade B/C POPF rate between the patients with and without receiving neoadjuvant therapy in this study ($P = 0.817$). From the viewpoint of time consumption and the cost required for PJ, we found both shorter times and lower suture costs required for PJ in the modified Blumgart mattress suture group than in the interrupted suture group. The differences between the 2 groups might, however, be clinically insignificant. Other outcomes, including morbidity and mortality (mortality rate was 0 in both groups), were not significantly different between the 2 groups in this study. Therefore, surgeon comfort is likely the most important determinant factor in deciding which method is the best, particularly in the setting of a negative trial like this study.

CONCLUSIONS

In conclusion, this study could not demonstrate the superiority of modified Blumgart mattress suture during PJ to reduce POPF.

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