ARTICLE IN PRESS

Surgery xxx (2020) 1-9



Contents lists available at ScienceDirect

Surgery

journal homepage: www.elsevier.com/locate/surg



Additional modifications to the Blumgart pancreaticojejunostomy: Results of a propensity score-matched analysis versus Cattel-Warren pancreaticojejunostomy

Francesca Menonna, MD^a, Niccolò Napoli, MD^a, Emanuele F. Kauffmann, MD^a, Sara Iacopi, MD^a, Cesare Gianfaldoni, MD^a, Caterina Martinelli, MD^a, Gabriella Amorese, MD^b, Fabio Vistoli, MD^a, Ugo Boggi, MD, FEBS^{a,*}

ARTICLE INFO

Article history: Accepted 7 August 2020 Available online xxx

ABSTRACT

Background: Postoperative pancreatic fistula continues to occur frequently after pancreatoduodenectomy.

Methods: We have described a modification of the Blumgart pancreaticojejunostomy. The modification of the Blumgart pancreaticojejunostomy was compared to the Cattel-Warren pancreaticojejunostomy in cohorts of patients matched by propensity scores based on factors predictive of clinically relevant postoperative pancreatic fistula, which was the primary endpoint of this study. Based on a noninferiority study design, 95 open pancreatoduodenectomies per group were needed. Feasibility of the modification of the Blumgart pancreaticojejunostomy in robotic pancreatoduodenectomy was also shown. All pancreaticojejunostomies were performed by a single surgeon.

Results: Between October 2011 and May 2019, there were 415 pancreatoduodenectomies with either a Cattel-Warren pancreaticojejunostomy (n = 225) or a modification of the Blumgart pancreaticojejunostomy (n = 190). There was 1 grade C postoperative pancreatic fistula in 190 consecutive modification of the Blumgart pancreaticojejunostomies (0.5%). Logistic regression analysis showed that the rate of clinically relevant postoperative pancreatic fistula was not affected by consecutive case number. After exclusion of robotic pancreatoduodenectomies (the Cattel-Warren pancreaticojejunostomy: 82; modification of the Blumgart pancreaticojejunostomy: 66), 267 open pancreatoduodenectomies were left, among which the matching process identified 109 pairs. The modification of the Blumgart pancreaticojejunostomy was shown to be noninferior to the Cattel-Warren pancreaticojejunostomy with respect to clinically relevant postoperative pancreatic fistula (11.9% vs 22.9%; odds ratio: 0.46 [0.21–0.93]; P = .03), grade B postoperative pancreatic fistula (11.9% vs 18.3%; P = .03) .18), and grade C postoperative pancreatic fistula (0 vs 4.6%; P = .05) as well as to all secondary study endpoints. The modification of the Blumgart pancreaticojejunostomy was feasible in 66 robotic pancreatoduodenectomies. In this subgroup with 1 conversion to open surgery (1.5%), a clinically relevant postoperative pancreatic fistula occurred after 9 procedures (13.6%) with no case of grade C postoperative pancreatic fistula and a 90-day mortality of 3%.

Conclusion: The modification of the Blumgart pancreaticojejunostomy described herein is noninferior to the Cattel-Warren pancreaticojejunostomy in open pancreatoduodenectomy. This technique is also feasible in robotic pancreatoduodenectomy.

© 2020 The Authors. Published by Elsevier Inc. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

Introduction

Despite availability of risk scores, ^{1,2} use of mitigation strategies, ³⁻⁵ and definition of tailored treatment strategies, ⁶⁻⁸ post-operative outcome of pancreatoduodenectomy (PD) continues to be influenced primarily by the incidence and severity of

^a Division of General and Transplant Surgery, Azienda Ospedaliero Universitaria Pisana. University of Pisa, Italy

^b Division of Anesthesia and Intensive Care, Azienda Ospedaliero Universitaria Pisana, University of Pisa, Italy

^{*} Reprint requests: Ugo Boggi, MD, FEBS, Professor of Surgery, Head Division of General and Transplant Surgery, University of Pisa, Via Paradisa 2, 56124—Pisa, Italy. E-mail address: u.boggi@med.unipi.it (U. Boggi).

postoperative pancreatic fistula (POPF). ^{9,10} If POPF could be avoided completely, the outcome of PD would improve dramatically, but so far no pancreatic anastomosis has been shown to be flawless. ¹¹ Difficulties in defining the ideal technique for pancreatic anastomosis are probably compounded by the multifactorial origin of POPFs that includes gland texture and duct size, ¹ nutritional factors, ^{12,13} perioperative fluid management, ^{14,15} surgeon's experience and proficiency, ¹⁶ administration of octreotide, ¹⁶ type of sutures, ¹⁷ and patient's specific characteristics, such as previous abdominal operations and central obesity. It is therefore clear that no single anastomosis is suitable for all recipients. ^{11,18}

In 2000, Blumgart et al described a new technique for pancreatic anastomosis. The key innovation of this method was the tension-free approximation of the jejunum to the pancreatic stump using transfixing mattress sutures. The anastomosis was completed by a standard duct-to-mucosa suture. ¹⁹ The original Blumgart technique was modified subsequently by decreasing the number of transpancreatic sutures and by tying the sutures only once over the anterior aspect of the jejunal limb, instead of first tying them on the pancreas before placing the anterior seromuscular suture on the jejunum. ¹⁹⁻²¹ The modified Blumgart pancreaticojejunostomy (PJ) became quickly popular, but the initially encouraging results ^{22,23} were not confirmed in a randomized trial. ²¹

We herein describe an additional modification of the Blumgart PJ (mB-PJ) and provide a propensity score matched comparison with the classic Cattel-Warren PJ (CW-PJ) in open PD. As minimally invasive PD is gaining momentum, we also present the feasibility of mB-PJ in robotic PD.

Materials and methods

This study was approved by the Institutional Review Board of the University of Pisa (study code: 17214_BOGGI). A retrospective analysis of a prospectively maintained database was performed for all PDs performed at a single institution (Division of General and Transplant Surgery, University of Pisa) between October 1, 2011, and May 31, 2019.

Data were collected and analyzed according to the Strengthening the Reporting of Observational Studies in Epidemiology guidelines for observational studies.²⁴

Definition of outcome measures

POPF was defined and graded according to the 2016 update of the International Study Group on Pancreatic Surgery (ISGPS). Grade B and grade C POPFs were considered clinically relevant (CR-POPF). Delayed gastric emptying (DGE) and post-pancreatectomy hemorrhage (PPH) were also defined and graded according to the ISGPS criteria. Postoperative complications were defined and graded according to the Dindo-Demartines-Clavien classification. Complications graded \geq III were considered severe complications. In patients with more than 1 complication, the highest grade was considered. The comprehensive complication index (CCI) was also calculated.

Postoperative mortality was defined as a death within 90 days after operation or during the hospital stay if greater.

Selection criteria and study endpoints

Patients undergoing open PD were included in the study if the pancreatic anastomosis was performed using either the CW-PJ (controls) or the mB-PJ (cases) and if all parameters needed to calculate the clinical risk score for POPF (CRS-POPF)¹ were available. All PJs were performed by a single surgeon (UB), who had

experience with >700 pancreatic anastomoses at the beginning of the study period.

The primary study endpoint was incidence and severity (ie, grade B or grade C) of CR-POPF.

Secondary study endpoints were the incidence and severity of DGE, incidence and severity of PPH, incidence and severity of postoperative complications, median levels of CCI, median levels of drain amylase activity on postoperative days (POD) 3 and 5, need for operative reintervention, need for interventional radiologic procedures, need for interventional endoscopic procedures, duration of hospital stay, hospital readmission, and postoperative mortality.

Study design

This study was designed as a 1:1 propensity scored matched comparison between CW-PJ and mB-PJ with the aim of showing the noninferiority of the mB-PJ with respect to incidence and severity of CR-POPF. Groups were matched based on CRS-POPF and other factors predictive of CR-POPF. Before matching the 2 groups, the importance of each matching parameter was verified in our patient population. Finally, the importance of increasing experience was also assessed to rule out any effect of time-dependent factors on occurrence of CR-POPF.

In an additional analysis, results of mB-PJ in contemporary robotic PDs are presented to show the feasibility of this type of anastomosis under robotic assistance.

Sample size calculation

Based on an estimated incidence of CR-POPF of 15% in CW-PJ, 21,30 we calculated that at least 190 patients (95 per group) were needed to verify the study hypothesis with a power of 85% and an alpha value of 5%.

Operative techniques for pancreaticojejunostomy

With both anastomotic techniques, the pancreatic stump was dissected for 1 to 1.5 cm while paying careful attention to preserve blood supply. Stents were employed selectively at the surgeons' discretion.

CW-PJ was performed using a classic technique. Briefly, the first jejunal loop was gently approximated to the pancreatic stump using interrupted sutures of 5/0 or 4/0 polypropylene placed between the seromuscular layer of the jejunum and the posterior surface of the pancreatic body. A duct-to-mucosa anastomosis was then performed using 5/0 polypropylene sutures. The anastomosis was completed by placing an anterior row of interrupted sutures of 5/0 or 4/0 polypropylene sutures between the jejunum and the pancreas (Fig. 1).

The original Blumgart technique was modified in several respects. First, double-armed 3/0 polypropylene sutures (4/0 expanded polytetrafluoroethylene in robotic PD) were used in place of polyglactin 910 sutures. Second, the number of transpancreatic sutures was decreased from between 4 and 6 to 2. Third, transpancreatic sutures were tied just once over the jejunum. Fourth, a U-shaped suture was placed between the jejunum and the pancreatic capsule posterior to the pancreatic duct. Fifth, a similar U-shaped suture was placed anterior to the pancreatic duct. Sixth, 2 "half-purse string sutures" were placed at the corners of the pancreatic anastomosis. The mB-PJ is shown steps in Fig 2 to 4.

After completion of the pancreatic anastomosis, all retroperitoneal vessels (i.e. hepatic artery, superior mesenteric artery, and superior mesenteric/portal vein) were covered using an omental flap and drains were left near the PJ.

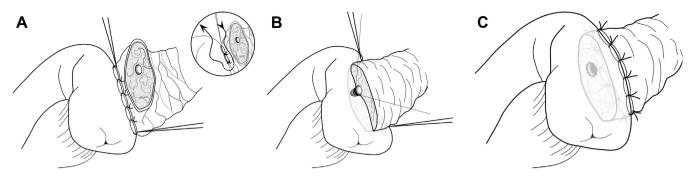


Fig. 1. (A) The proximal jejunum is positioned near to the pancreatic stump. Interrupted sutures are placed between the capsule and tissue of the body of the pancreas and the seromuscular layer of the bowel (details shown in the circle). (B) A small opening is made in the jejunum opposite to the divided pancreatic duct, and a duct-to-mucosa anastomosis is performed. (C) The anastomosis is completed by placing a row of interrupted sutures between the pancreatic tissue and capsule and the seromuscular layer of the jejunum.

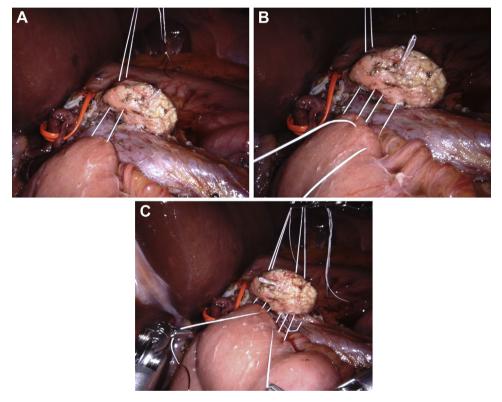


Fig. 2. Posterior anastomotic layer of mB-PJ. (*A*) A temporary stent indicates location and direction of the main pancreatic duct. Using a double-armed suture, a transpancreatic stitch is placed to anchor the jejunum to the pancreatic remnant. (*B*) A U-shaped suture is placed between the seromuscular layer of the jejunum, close to the mesenteric border, and the pancreatic capsule posterior to the pancreatic duct. (*C*) After placing a second transpancreatic suture caudad to the Wirsung's duct, the U-shaped suture placed posterior to the pancreatic duct is tied over the jejunum.

Statistical analysis

Categorical variables are summarized as frequencies, percentages, and rates. Continuous variables are expressed as mean \pm SD if normally distributed or as median and interquartile range if not. The Kolmogorov-Smirnov test was used to assess normality distribution. CRS-POPF was validated in our series using Cochran-Armitage test for trend.

The χ^2 test was used to evaluate the presence of an association between surgical technique (CW-PJ and mB-PJ) and outcome (CR-POPF). As an estimate of the effect size, the odds ratio (OR) was used. Univariate logistic regressions were performed to identify all statistically significant predictors of CR-POPF and their distribution in the 2 study groups.

Propensity score analysis was performed to balance possible confounders between the 2 study groups. Accordingly, linear propensity score values were used to conduct a greedy match by using the nearest-neighbor method and 1-to-1 ratio, with replacement, within a specific caliper width of 0.25 SD of the logit of the estimated propensity score, starting the match from cases with the greatest propensity score. Postmatching covariance analysis and sensitivity analysis were then evaluated using the Rosenbaum test for the Wilcoxon signed rank P value. The ensuing statistical models were used to define the point estimate and 95% confidence intervals (OR \pm 95% CI) of the effect size and to evaluate the efficacy of mB-PJ with respect to CR-POPF. For the statistical significance of the test, a power = 80%, P < .05, 2-tailed significance level was used.

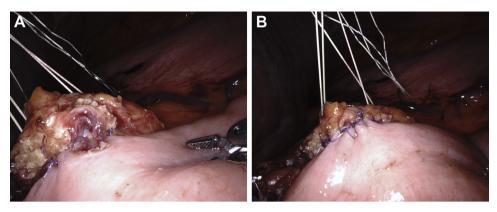


Fig. 3. Duct-to-mucosa anastomosis of mB-PJ. (A) Posterior layer of the duct-to-mucosa anastomosis. (B) Completed duct-to-mucosa anastomosis.

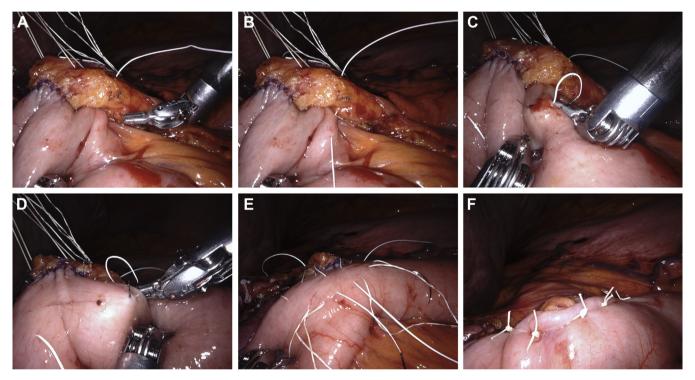


Fig. 4. Anterior anastomotic layer of mB-PJ. Two half purse string sutures are placed at the corners of pancreatic anastomosis, the transpancreatic sutures are placed over the anterior aspect of the jejunum, and a U-shaped suture is placed between the jejunum and the pancreas in front to the pancreatic duct. Half purse string sutures are created in 4 steps. (*A*) First, a transpancreatic suture is placed near the pancreatic margin, approximately 1 cm from the cut end of the pancreatic stump. (*B*) Second, the suture is advanced into the jejunum, close to the mesentery, and in a direction parallel to the long axis of the bowel. (*C*) Third, the suture is further placed on the jejunum in the direction of the short axis, 1 cm from the anastomotic corner. (*D*) Fourth, the suture is placed again on the antimesenteric aspect of the jejunum at the projected level of the anastomotic corner on the same line where all anterior sutures will be placed. (*E*) All anterior sutures are in place. (*F*) Sutures tied over the jejunum.

Propensity score matching was performed using R Package (R Foundation for Statistical Computing, Vienna Austria). Propensity score analysis was carried out using the integrated development environments, RStudio (RStudio, Boston, MA), and Matching, MatchIt, Zelig, and twang packages (R Foundation for Statistical Computing).

The effect of time on occurrence of CR-POPF was assessed by a logistic regression analysis comparing the incidence of CR-POPF to the chronologic order of the procedures.

For sample size calculation PASS 2005 software package (NCSS, and PASS; NCSS Statistical Software, Kaysville, UT) was used.

All statistical analysis, except for propensity score matching and sample size calculation, were carried-out with JMP 9.0.1 software package for Mac (SAS Institute, Inc, Cary, NC) and SPSS Statistics for Mac, Version 20.0 (IBM Corporation, Armonk, NY).

Results

Figure 5 presents the study flow chart. PD with CW-PJ and PD mB-PJ were different for several risk factors known to influence the occurrence of CR-POPF, thus underscoring the need for careful matching. It is worth noting that only 1 grade C POPF was recorded in 190 consecutive mB-PJ (0.5%).

Internal validation of CRS-POPF and identification of other factors predictive for CR-POPF in open PD

As shown in Table I, CRS-POPF was confirmed to predict the occurrence of CR-POPF in open PD. In detail, CR-POPF occurred in 1 of 15 patients (6.6%) in the negligible-risk group, in 4 of 44 patients (9.0%) in

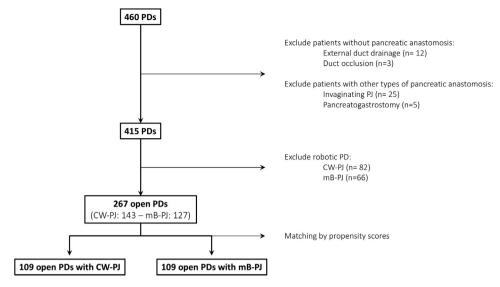


Fig. 5. Study flow chart.

the low-risk group, in 32/157 patients (20.3%) in the intermediate-risk group, and in 21 of 51 patients (41.1%) in the high-risk group (P < .0001).

Individual factors shown to influence the occurrence of CR-POPF were soft gland texture (P=.05), tumor type other than pancreatic cancer (P<.0001), and duct size ≤ 3 mm (P<.0001). Estimated blood loss >1,000 mL did not individually predict occurrence of CR-POPF but was included in the variables used to match the 2 groups, being one of the factors contributing to CRS-POPF.

Other factors shown to predict the occurrence of CR-POPF were mean body mass index (P < .0001), heart disease (P = .01), hypertension (P = .03), diabetes mellitus (P = .05), and vascular resection (P = .0023). Cardiopathy, hypertension, diabetes mellitus, and vascular resection were not included among matching parameters, because these variables were evenly distributed in the 2 groups at the baseline.

Impact of increasing experience on occurrence of CR-POPF

As shown in Fig 6, the rate of CR-POPF remained steady during the study period for either mB-PJ or CW-PJ. As a consequence, increasing experience was not shown to influence the occurrence of CR-POPF in this study.

Comparison of matched cohorts

The matching process identified 2 groups of 109 pairs. As shown in Table II, the 2 groups were matched for all variables shown to predict the occurrence of CR-POPF in this series.

In matched cohorts, CR-POPF occurred in 25 patients (22.9%) after CW-PJ and in 13 patients (11.9%) after mB-PJ, with an OR between mB-PJ and CW-PJ of 0.46 (0.21–0.93; P=.03). In detail, grade-B POPF was recorded in 20 patients (18.3%) after CW-PJ and in 13 patients (11.9%) after mB-PJ (P=.18). Equivalent figures for grade-C POPF were 5 (4.6%) and 0 (P=.05).

No difference was noted with respect to all secondary study endpoints, except grade-B DGE (CW-PJ: 33 patients; 30.3%) (mB-PJ: 15 patients; 13.8%) (P=.003). The overall rate of DGE, as well as the rate of grade-A and grade-C DGE, were similar in the two study groups. As detailed in Table III, differences were noted in other

outcome variables not included among study endpoints, such as operative time, use of duct stents, and number of surgical drains.

Feasibility of mB-PJ in robotic PD and associated results

During the study period, a total of 148 robotic PDs were performed with either a CW-PJ or a mB-PJ (148 of 415; 35.6%). In 66 patients (44.6%), the pancreatic anastomosis was a mB-PJ. This group included 22 male patients (33.3%) with a mean body mass index of 23.8 \pm 3.5 kg/m² and a median CRS-POPF of 4 (2–5.2). Gland texture was soft in 46 patients (69.7%), duct size was \leq 3 mm in 16 patients (24.2%), tumor type was different from pancreatic cancer in 21 patients (31.8%), and estimated blood loss exceeded 1,000 mL in 17 patients (25.8%).

Considering these risk factors, CR-POPF occurred in 9 patients (13.6%). All CR-POPF were grade B.

DGE occurred in 33 patients (50%) (grade-C DGE: 19.7%) and PPH in 6 patients (9.1%) (grade-C PPH: 7.6%). Severe complications were recorded in 15 patients (22.7%), with a median CCI of 20.9 (0-34.6) and a 90-day mortality of 3%. The median level of drain amylase was 144 U/L (23.5-1,103) on POD 3 and 32 U/L (11.7-291.2) on POD 5. Nine patients (13.6%) required interventional radiology procedures, and 5 patients (7.6%) required repeat surgery. No patient required postoperative endoscopic procedures. Median length of hospital stay was 17 days (12-25.2), and 4 patients (6.1%) required hospital readmission within 90 days.

Discussion

In July 1848 in an issue of the journal *Les Guêpes*, Jean-Baptiste Alphonse Karr wrote "the more things change, the more they stay the same." Although Karr was not discussing pancreatic anastomosis, this epigram perfectly describes the never-ending fight against POPF. Indeed, enthusiastic reports on techniques without failure³¹ were not confirmed in subsequent series.^{32,33} Pancreatic surgeons are now more aware about etiology, mitigation strategies, course, and treatment of POPF, but they cannot completely avoid it.¹¹ Reduction in the frequency and severity of POPF, however, strongly depends on appropriate anastomotic technique.

Table 1Univariate logistic regression analysis of the factors predictive of CR-POPF

	CR-POPF	No CR-POPF	Overall	P (test)
Number of patients (%)	58 (21.7%)	209 (78.3%)	267 (100%)	-
Age (y), median (IQR)	71 (66.7-75.8)	71 (63-78)	71.1 (64-77.1)	.63 (Wilcoxon)
Sex, male (%)	35 (60.3%)	114 (54.5%)	149 (55.8%)	.43 (Pearson)
BMI, kg/m^2 , mean (\pm SD)	26 (± 3.1)	$24 (\pm 3.6)$	$24.5 (\pm 3.6)$	< .0001 (t test)
Prior abdominal operations, number (%)	37 (63.8%)	121 (57.9%)	158 (59.2%)	.42 (Pearson)
ASA score, median (IQR)	3 (3–3)	3 (3–3)	3 (3–3)	.84 (Wilcoxon)
ASA category, number (%)				
I	0 (0%)	0 (0%)	0 (0%)	NA
II	11 (19%)	46 (22%)	57 (21.3%)	.61 (Pearson)
III	41 (70.7%)	138 (66%)	179 (67%)	.50 (Pearson)
IV	6 (10.3%)	25 (12%)	31 (11.6%)	.73 (Pearson)
Neoadjuvant chemotherapy, number (%)	3 (5.2%)	19 (9.1%)	22 (8.2%)	.43 (Fisher)
Cardiovascular disease, number (%)	21 (36.2%)	42 (20.1%)	63 (23.6%)	.01 (Pearson)
COPD, number (%)	8 (13.8%)	17 (8.1%)	25 (9.4)	.19 (Pearson)
Hypertension, number (%)	35 (60.3%)	93 (44.5%)	128 (47.9%)	.03 (Pearson)
Diabetes mellitus, number (%)	8 (13.8%)	54 (25.8%)	62 (23.2%)	.05 (Pearson)
Presence of symptoms, number (%)	46 (79.3%)	187 (89.5%)	233 (87.3%)	.05 (Pearson)
Pain	19 (32.8%)	77 (36.8%)	96 (36%)	.56 (Pearson)
Jaundice	31 (53.4%)	126 (60.3%)	157 (58.8%)	.35 (Pearson)
CRS-POPF, median (IQR)	6 (4–7)	4 (2-6)	4 (3–6)	< .0001 (Wilcoxon)
CRS-POPF risk categories; number (%)	0(1 /)	1(2 0)	1(3 0)	(Toda (Trinconon)
Negligible risk	1 (1.7%)	14 (6.7%)	15 (5.6%)	.20 (Fisher)
Low risk	4 (6.9%)	40 (19.1%)	44 (16.5%)	.03 (Fisher)
Intermediate risk	32 (55.2%)	125 (59.8%)	157 (58.8%)	.52 (Pearson)
High risk	21 (36.2%)	30 (14.3%)	51 (19.1%)	< .0002 (Pearson)
Soft gland texture, number (%)	36 (62.1%)	99 (47.4%)	135 (50.6%)	.05 (Pearson)
Tumor type other than pancreatic cancer, number (%)	34 (58.6%)	61 (29.2%)	95 (35.6%)	< .0001 (Pearson)
Duct size, number (%)	34 (30.0%)	01 (23.2%)	33 (33.0%)	< .0001 (1 car3011)
>5 mm	10 (17.2%)	113 (54.1%)	123 (46.1%)	< .0001 (Pearson)
4 mm	10 (17.2%)	29 (13.9%)	39 (14.6%)	.52 (Pearson)
3 mm	11 (19%)	26 (12.4%)	37 (13.9%)	.2 (Pearson)
2 mm	20 (34.5%)	36 (17.2%)	56 (21%)	.0043 (Pearson)
<1 mm	7 (12.1%)	5 (2.4%)	12 (4.5%)	.005 (Pearson)
STITITI Duct size ≤3 mm, number (%)	38 (65.5%)	67 (32%)	105 (39.3%)	< .001 (Pearson)
Estimated blood loss, number (%)	36 (03.3%)	07 (32%)	105 (59.5%)	< .0001 (Fedison)
≤400 mL (%)	17 (20 2%)	40 (22%)	CE (24.2%)	22 (Doarson)
401–700 mL (%)	17 (29.3%) 9 (15.5%)	48 (23%) 40 (19.1%)	65 (24.3%) 49 (18.3%)	.32 (Pearson)
· ·	` '	` '	` '	.52 (Pearson)
701–1,000 mL (%)	7 (12.1%)	34 (16.3%)	41 (15.4%)	.43 (Pearson)
>1,000 mL (%)	25 (43.1%)	87 (41.6%)	112 (41.9%)	.84 (Pearson)
Estimated blood loss (cc), median (IQR)	899 (332–1340)	842 (446–1332)	848 (432–1335)	.96 (Wilcoxon)
Pylorus preservation, number (%)	48 (82.8%)	143 (68.4%)	191 (71.5%)	.03 (Pearson)
Vascular resection, number (%)	15 (25.9%)	101 (48.3%)	116 (43.4%)	.0023 (Pearson)
Vein resection	14 (24.1%)	94 (45%)	108 (40.4%)	.004 (Pearson)
Arterial resection	1 (1.1%)	2 (1.6%)	3 (1.1%)	.52 (Fisher)
Arterial and vein resection	0 (0%)	5 (2.4%)	5 (1.9%)	.59 (Fisher)
Pathology, number (%)				
Pancreatic cancer	20 (34.5%)	119 (56.9%)	139 (52.1%)	.0025 (Pearson)
Ampullary adenocarcinoma	6 (10.3%)	14 (6.7%)	20 (7.5%)	.35 (Pearson)
Malignant IPMN	3 (5.2%)	24 (11.5%)	27 (10.1%)	.21 (Fisher)
Cholangiocarcinoma	6 (10.3%)	10 (4.8%)	16 (6%)	.11 (Pearson)
Neuroendocrine tumor	4 (6.9%)	5 (2.4%)	9 (3.4%)	.11 (Fisher)
Serous cystoadenoma	1 (1.7%)	3 (1.4%)	4 (1.5%)	1.00 (Fisher)
IPMN	4 (6.9%)	6 (2.9%)	10 (3.7%)	.23 (Fisher)
Chronic pancreatitis	1 (1.7%)	5 (2.4%)	6 (2.2%)	1.00 (Fisher)
Neuroendocrine carcinoma	1 (1.7%)	2 (1%)	3 (1.1%)	.52 (Fisher)

Bolded values mean that statistical significance was reached.

ASA, American Society of Anesthesia, BMI, body mass index; COPD, chronic obstructive pulmonary disease; IPMN, intraductal papillary mucinous neoplasm.

In the year 2000, Blumgart described a new technique for PJ after PD.³⁴ Results were first reported in 2010 showing a rate of 3.7% of grade-B POPF and 3.2% of grade-C POPF.¹⁹ One year earlier, a German group had reported the results of the "modified Blumgart technique," demonstrating excellent results in comparison with CW-PJ.²⁰ However, while Blumgart PJ is clearly a good anastomotic technique,^{22,23,35} there is still no high-level evidence supporting the preferential use of this type of pancreatic anastomosis.²¹

Our additional modifications to the Blumgart PJ have not eliminated the occurrence of CR-POPF after PD. Honestly, we believe that no surgical technique can do so. At least having further simplified the Blumgart PJ allowed us to achieve acceptable results that were noninferior to those obtained with the CW-PJ. We believe that 2 of our modifications are particularly relevant. First, as described also by Hirono²¹ and Satoi,³⁶ 2 mattress sutures are sufficient to join the jejunal loop to the pancreatic remnant. Second, application of 2 "half purse string" sutures at the corners of the

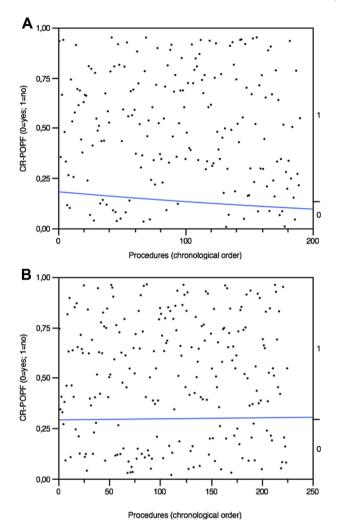


Fig. 6. Logistic regression analysis for probability of CR-POPF versus number of procedures (in chronological order) for mB-PJ (*A*) and CW-PJ (*B*) groups.

anastomosis further improves coverage of the cut end of the pancreatic stump. These modifications ensure tight approximation of the jejunal limb to the pancreatic stump and minimize the possibility of unintentional transfixion of the pancreatic duct. The nonsutured area that is left posterior and anterior to the pancreatic duct is fixed by 2. U-shaped, nonmattress sutures between the seromuscular layer of the jejunum and the pancreatic remnant. Indeed, as in the original Blumgart technique ¹⁹ and at a difference from several descriptions of modified Blumgart anastomosis, 22,37 we do not place transpancreatic sutures straddling the pancreatic duct, as it could result in compression of the duct especially in soft pancreases with small ducts. To the best of our knowledge, this occurrence has never been described, possibly because authors using this technique routinely place duct stents. 22,37 If a stent is not placed, especially in robotic PD where there is no tactile feedback,³⁸ excessive tension on the central transpancreatic suture could result in strangulation of the pancreatic duct.

In 190 consecutive PDs in which the pancreatic anastomosis was a mB-PJ, we recorded 1 case of grade-C POPF (0.5%). Only Hirono et al reported no grade-C POPF in 107 PDs using a modified Blumgart anastomosis. ²¹ In other series, the rate of grade-C POPF ranged from 1.5 to 5.5%. ^{19,22,36,37,39,40}

In the matched comparison, mB-PJ was noninferior to CW-PJ. Secondary outcomes measures were also in keeping with the noninferiority hypothesis.

In an additional analysis, we have shown that mB-PJ is feasible also in robotic PD and is associated with acceptable results. In particular, despite reporting only on 66 consecutive procedures, we had no case of grade-C POPF. Although we believe that robotic assistance permits all types of pancreatic reconstructions, having a simplified the technique of pancreatic anastomosis could be rewarding at the end of a complex and demanding procedure such as robotic PD.

In general, in this series we had an acceptable rate of grade-C POPF. Grade-B POPF, instead, occurred more frequently than hoped, especially when a CW-PJ was employed. We believe that this result can be explained by the overall high risk of POPF in our series. Indeed, besides the traditional risk factors for POPF, in our study population a vein resection was required in 40% of the

Table IIBaseline characteristics of matched cohorts of patients undergoing open PD and pancreatic anastomosis by CW-PJ and mB-PJ

	CW-PJ	mB-PJ	Overall	P (test)
Number of patients (%)	109 (50%)	109 (50%)	218	_
Sex, male (%)	61 (56%)	62 (56.9%)	123 (56.4%)	.89 (Pearson)
BMI, kg/m^2 , mean (\pm SD)	$24.2 (\pm 3.5)$	$24.6 (\pm 3.8)$	$24.5 (\pm 3.7)$.4 (t test)
CRS-POPF, median (IQR)	4 (3-6)	4 (2-6)	4 (3-6)	.97 (Wilcoxon)
Soft gland texture, number (%)	56 (51.4%)	54 (49.5)	110 (50.5%)	.78 (Pearson)
Tumor type other than pancreatic cancer, number (%)	38 (34.9%)	35 (32.1%)	73 (33.5%)	.67 (Pearson)
Duct size ≤3 mm, number (%)	35 (32.1%)	39 (35.8%)	74 (33.9%)	.57 (Pearson)
Estimated blood loss >1,000 mL, number (%)	41 (37.6%)	41 (37.6%)	82 (37.6%)	1.00 (Pearson)
Age (y), median (IQR)	69 (63-76)	71 (63-77)	70 (63-76)	.59 (Wilcoxon)
ASA score, median (IQR)	3 (3-3)	3 (3-3)	3 (3-3)	.27 (Wilcoxon)
Prior abdominal operation, number (%)	64 (58.7%)	63 (57.8%)	127 (58.3%)	.89 (Pearson)
Cardiovascular disease, number (%)	20 (18.3%)	26 (23.8%)	46 (21.1%)	.32 (Pearson)
COPD, number (%)	12 (11%)	9 (8.3%)	21 (9.6%)	.49 (Pearson)
Hypertension, number (%)	47 (43.1%)	51 (46.8%)	98 (44.9%)	.58 (Pearson)
Diabetes mellitus, number (%)	25 (22.9%)	29 (26.6%)	54 (24.8%)	.53 (Pearson)
Presence of symptoms, number (%)	92 (84.4%)	101 (92.7%)	193 (88.5%)	.06 (Pearson)
Pain	34 (31.2%)	46 (42.2%)	80 (36.7%)	.09 (Pearson)
Jaundice	71 (65.1%)	66 (60.6%)	137 (62.8%)	.48 (Pearson)
Vascular resection, number (%)	43 (39.4%)	53 (48.6%)	96 (44%)	.17 (Pearson)
Neoadjuvant chemotherapy, number (%)	8 (7.3%)	13 (11.9%)	21 (9.6%)	.25 (Pearson)

ASA, American Society of Anesthesia, BMI, body mass index; COPD, chronic obstructive pulmonary disease.

Table IIIPrimary and secondary study endpoints, and other outcome variables, in matched cohorts of patients undergoing open PD with CW-PJ and mb-PJ

	CW-PJ	mB-PJ	Overall	P (test)
Number of patients (%)	109 (50.0%)	109 (50.0%)	218 (100%)	
Primary study endpoint	,	(, , , ,	, , , ,	
CR-POPF, number (%)	25 (22.9%)	13 (11.9%)	38 (17.4%)	.03 (Pearson)
Grade-B POPF	20 (18.3%)	13 (11.9%)	33 (15.1%)	.18 (Pearson)
Grade-C POPF	5 (4.6%)	0 (0%)	5 (2.3%)	.05 (Fisher)
Secondary study endpoints	5 (110/0)	0 (0,0)	5 (21370)	(Tibrier)
DGE, number (%)	64 (58.7%)	53 (48.6%)	117 (53.7%)	.13 (Pearson)
Grade-A DGE	33 (30.3%)	15 (13.8%)	48 (22%)	.003 (Pearson)
Grade-B DGE	23 (21.1%)	23 (21.1%)	46 (21.1%)	1.00 (Pearson)
Grade-C DGE	8 (7.3%)	15 (13.8%)	23 (10.5%)	.12 (Pearson)
PPH, number (%)	10 (9.2%)	9 (8.3%)	19 (8.7%)	.81 (Pearson)
Grade-A PPH	0 (9.2%)	0 (8.5%)	0	NA
	2 (1.8%)	1 (0.9%)	3 (1.4%)	1.00 (Fisher)
Grade-B PPH	` '	` ,	` '	1.00 (Pearson)
Grade-C PPH	8 (7.3%)	8 (7.3%)	16 (7.3%)	1.00 (Pearson)
Postoperative complications, number (%)	40 (44 000)	0 (0 000)	22 (40 4)	27 (P)
Grade I	13 (11.9%)	9 (8.3%)	22 (10.1)	.37 (Pearson)
Grade II	54 (49.5%)	42 (38.5%)	96 (44%)	.10 (Pearson)
Grade IIIa	10 (9.2%)	13 (11.9%)	23 (10.5%)	.51 (Pearson)
Grade IIIb	4 (3.7%)	11 (10.1%)	15 (6.9%)	.11 (Fisher)
Grade IVa	5 (4.6%)	1 (0.9%)	6 (2.7%)	.21 (Fisher)
Grade IVb	0	1 (0.9%)	1 (0.5%)	1.00 (Fisher)
Grade V	5 (4.6%)	9 (8.3%)	14 (6.4%)	.41 (Fisher)
Severe postoperative complications, number (%)	24 (22%)	35 (32.1%)	59 (27.1%)	.10 (Pearson)
CCI, median (IQR)	23 (9-31)	30 (9-42)	24.2 (9-40.5)	.23 (Wilcoxon)
Drain amylase POD 3, median (IQR)	48.5 (13-488)	57.5 (13-1393)	50.5 (13-655.5)	.62 (Wilcoxon)
Drain amylase POD 5, median (IQR)	19 (6-360)	24 (7-533)	20 (6.5-485)	.38 (Wilcoxon)
Reoperation, number (%)	9 (8.3%)	13 (11.9%)	22 (10.1%)	.37 (Pearson)
Interventional radiologic procedures, number (%)	13 (11.9%)	15 (13.8)	28 (12.8%)	.68 (Pearson)
Endoscopic interventional procedures, number (%)	2 (1.8%)	2 (1.8%)	4 (1.8%)	1.00 (Fisher)
Duration of hospital stay, median (IQR)	18 (13-25)	21 (14-30)	19.5 (13-27)	.10 (Wilcoxon)
Hospital readmission, number (%)	17 (15.6%)	11 (10.1%)	28 (12.8%)	.22 (Pearson)
Other outcome variables	(,	()		, , , , ,
Biochemical leak, number (%)	10 (9.2%)	17 (15.6%)	27 (12.4%)	.15 (Pearson)
Operative time (min), median (IQR)	450 (370–515)	545 (460–605)	485 (420–575)	< .0001 (Wilcoxon)
Estimated blood loss (mL), median (IQR)	842 (378–1,307)	758 (435–1,306)	762 (388–1,304)	.98 (Wilcoxon)
Patients receiving RBC transfusions, number (%)	49 (45.4%)	38 (34.9%)	87 (40.1%)	.11 (Pearson)
Transfused RBC units, median (IQR)	0 (0-1)	0 (0-1)	0 (0-1)	.18 (Wilcoxon)
Use of duct stents, number (%)*	68 (74.7%)	13 (11.9%)	81 (40.5%)	< .0001 (Pearson)
Surgical drains, median (IQR) [†]	4 (4-4)	3 (2–3)	3 (2-4)	< .0001 (Tearson)
Patients discharged with an abdominal drain, number (%)	17 (15.6%)	15 (13.8%)	32 (14.7%)	.70 (Pearson)
Origin of PPH, number (%)	17 (13.0/0)	13 (13.0%)	J2 (14.1/o)	.70 (FEdisoli)
Intraluminal	0	2 (1 0%)	2 (0.0%)	50 (Ficher)
		2 (1.8%)	2 (0.9%)	.50 (Fisher)
Extraluminal	9 (8.3%)	4 (3.7%)	13 (6%)	.25 (Fisher)
Intraluminal and extraluminal	1 (0.9%)	3 (2.7%)	4 (1.8%)	.62 (Fisher)
GDA pseudoaneurysm, number (%)	0 (0%)	1 (0.9%)	1 (0.5%)	1.00 (Fisher)

Bolded values mean that statistical significance was reached.

GDA, gastroduodenal artery; IOR, interquartile range; PDAC, pancreatic duct adenocarcinoma; RBC, red blood cells.

procedures, whereas neoadjuvant medical treatments were used in only 8% of the patients. Pancreatectomy with vein resection is associated with a higher incidence of several postoperative complications including POPF, 41 whereas the use of neoadjuvant medical therapies is often associated with reduced rates of POPF due to chemotherapy-induced fibrosis on pancreatic parenchyma. 42,43 Additionally, as per institutional policy, until recently we have used octreotide as a prophylaxis against POPF. Recent evidence shows that octreotide, far from being protective, could instead facilitate the occurrence of CR-POPF. 16

This study has several limitations. First, despite prospective collection of data, the retrospective analysis carries the inherent risk of hidden biases mostly related to patient selection. Second, use of mitigation strategies and management of POPF has improved over time thus potentially introducing time-dependent biases in a before-after study. However, we have shown that the date of surgery did not influence the occurrence of CR-POPF in this study, probably because all anastomoses were performed by a single surgeon who had already surpassed the learning curve at the beginning of the study period. Third, despite reporting on a

relatively large number of pancreatic reconstructions, the power of our study may not be sufficient to depict the full spectrum and severity of complications occurring after a mB-PJ. Fourth, this series of PDs was performed at a single institution by a single surgeon, thereby limiting the generalizability of the results.

In conclusion, we have described several additional modifications to the Blumgart anastomosis. mB-PJ was associated with acceptably low rates of CR-POPF, especially of grade-C POPF, and was proven to be noninferior to CW-PJ in open PD. mB-PJ was feasible also in robotic PD.

Conflict of interest/Disclosures

The authors have indicated that they have no conflicts of interest regarding the content of this article.

Funding/Support

None.

^{*} Data missing for 18 CW-PJ.

[†] Data missing for 29 CW-PJ and 2 mB-PJ.

References

- Callery MP, Pratt WB, Kent TS, Chaikof EL, Vollmer Jr CM. A prospectively validated clinical risk score accurately predicts pancreatic fistula after pancreatoduodenectomy. J Am Coll Surg. 2013;216:1–14.
- Mungroop TH, van Rijssen LB, van Klaveren D, et al, and the Dutch Pancreatic Cancer Group. Alternative fistula risk score for pancreatoduodenectomy (a-FRS): Design and international external validation. *Ann Surg.* 2019;269: 937–943.
- Ven Fong Z, Correa-Gallego C, Ferrone CR, et al. Early drain removal—The middle ground between the drain versus no drain debate in patients undergoing pancreaticoduodenectomy: A prospective validation study. *Ann Surg.* 2015;262:378—383.
- Beane JD, House MG, Ceppa EP, Dolejs SC, Pitt HA. Variation in drain management after pancreatoduodenectomy: early versus delayed removal. *Ann Surg.* 2019:269:718–724.
- McMillan MT, Malleo G, Bassi C, et al. Multicenter, prospective trial of selective drain management for pancreatoduodenectomy using risk stratification. Ann Surg. 2017;265:1209–1218.
- Smits FJ, van Santvoort HC, Besselink MG, et al. and the Dutch Pancreatic Cancer Group. Management of severe pancreatic fistula after pancreatoduodenectomy. JAMA Surg. 2017;152:540–548.
- Bouras AF, Marin H, Bouzid C, Pruvot FR, Zerbib P, Truant S. Pancreas-preserving management in reinterventions for severe pancreatic fistula after pancreatoduodenectomy: a systematic review. *Langenbecks Arch Surg.* 2016;401: 141.140.
- Pedrazzoli S, Liessi G, Pasquali C, Ragazzi R, Berselli M, Sperti C. Postoperative pancreatic fistulas: preventing severe complications and reducing reoperation and mortality rate. Ann Surg. 2009;249:97–104.
- Vollmer Jr CM, Sanchez N, Gondek S, et al. and the Pancreatic Surgery Mortality Study Group. A root-cause analysis of mortality following major pancreatectomy. J Gastrointest Surg. 2012;16:89–102.
- Gawlas I, Sethi M, Winner M, et al. Readmission after pancreatic resection is not an appropriate measure of quality. Ann Surg Oncol. 2013;20:1781–1787.
- Shrikhande SV, Sivasanker M, Vollmer CM, et al. and the International Study Group of Pancreatic Surgery (ISGPS). Pancreatic anastomosis after pancreatoduodenectomy: A position statement by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2017;161:1221–1234.
- Gruppo M, Angriman I, Martella B, Spolverato YC, Zingales F, Bardini R. Perioperative albumin ratio is associated with post-operative pancreatic fistula. ANZ J Surg. 2018;88:E602–E605.
- Nishida Y, Kato Y, Kudo M, et al. Preoperative sarcopenia strongly influences the risk of postoperative pancreatic fistula formation after pancreaticoduodenectomy. J Gastrointest Surg. 2016;20:1586–1594.
- Winer LK, Dhar VK, Wima K, et al. Perioperative net fluid balance predicts pancreatic fistula after pancreaticoduodenectomy. J Gastrointest Surg. 2018;22: 1743–1751.
- 15. Fischer M, Matsuo K, Gonen M, et al. Relationship between intraoperative fluid administration and perioperative outcome after pancreaticoduodenectomy: results of a prospective randomized trial of acute normovolemic hemodilution compared with standard intraoperative management. *Ann Surg.* 2010;252:952–958.
- McMillan MT, Soi S, Asbun HJ, et al. Risk-adjusted outcomes of clinically relevant pancreatic fistula following pancreatoduodenectomy: A model for performance evaluation. *Ann Surg.* 2016;264:344–352.
- Andrianello S, Marchegiani G, Malleo G, et al. Polyester sutures for pancreaticojejunostomy protect against postoperative pancreatic fistula: a casecontrol, risk-adjusted analysis. HPB (Oxford). 2018;20:977–983.
- Niedergethmann M, Dusch N, Widyaningsih R, Weiss C, Kienle P, Post S. Riskadapted anastomosis for partial pancreaticoduodenectomy reduces the risk of pancreatic fistula: a pilot study. World J Surg. 2010;34:1579–1586.
- Grobmyer SR, Kooby D, Blumgart LH, Hochwald SN. Novel pancreaticojejunostomy with a low rate of anastomotic failure-related complications. J Am Coll Surg. 2010;210:54–59.
- Kleespies A, Rentsch M, Seeliger H, Albertsmeier M, Jauch KW, Bruns CJ. Blumgart anastomosis for pancreaticojejunostomy minimizes severe complications after pancreatic head resection. *Br J Surg.* 2009;96:741–750.
- 21. Hirono S, Kawai M, Okada KI, et al. Modified Blumgart mattress suture versus conventional interrupted suture in pancreaticojejunostomy during

- pancreaticoduodenectomy: Randomized controlled trial. *Ann Surg.* 2019;269: 243–251
- Kojima T, Niguma T, Watanabe N, Sakata T, Mimura T. Modified Blumgart anastomosis with the "complete packing method" reduces the incidence of pancreatic fistula and complications after resection of the head of the pancreas. Am J Surg. 2018:216:941–948.
- Wang SE, Chen SC, Shyr BU, Shyr YM. Comparison of modified Blumgart pancreaticojejunostomy and pancreaticogastrostomy after pancreaticoduodenectomy. HPB (Oxford). 2016;18:229–235.
- 24. von Elm E, Altman DG, Egger M, et al, and the STROBE Initiative. The strengthening the reporting of observational studies in epidemiology (STROBE) statement: guidelines for reporting observational studies. *J Clin Epidemiol*. 2008;61:344–349.
- Bassi C, Marchegiani G, Dervenis C, et al, and the International Study Group on Pancreatic Surgery (ISGPS). The 2016 update of the International Study Group (ISGPS) definition and grading of postoperative pancreatic fistula: 11 years after. Surgery. 2017;161:584–591.
- Wente MN, Bassi C, Dervenis C, et al. Delayed gastric emptying (DGE) after pancreatic surgery: a suggested definition by the International Study Group of Pancreatic Surgery (ISGPS). Surgery. 2007;142:761–768.
- Wente MN, Veit JA, Bassi C, et al. Postpancreatectomy hemorrhage (PPH): An International Study Group of Pancreatic Surgery (ISGPS) definition. Surgery. 2007:142:20—25
- **28.** Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann Surg.* 2004;240:205–213.
- Slankamenac K, Graf R, Barkun J, Puhan MA, Clavien PA. The comprehensive complication index: a novel continuous scale to measure surgical morbidity. *Ann Surg.* 2013;258:1–7.
- Hua J, He Z, Qian D, Meng H, Zhou B, Song Z. Duct-to-mucosa versus invagination pancreaticojejunostomy following pancreaticoduodenectomy: a systematic review and meta-analysis. J Gastrointest Surg. 2015;19:1900–1909.
- Peng S, Mou Y, Cai X, Peng C. Binding pancreaticojejunostomy is a new technique to minimize leakage. Am J Surg. 2002;183:283–285.
- Kawaida H, Kono H, Hosomura N, et al. Surgical techniques and postoperative management to prevent postoperative pancreatic fistula after pancreatic surgery. World J Gastroenterol. 2019;25:3722–3737.
- **33.** Fujii T, Sugimoto H, Yamada S, et al. Modified Blumgart anastomosis for pancreaticojejunostomy: Technical improvement in matched historical control study. *J Gastrointest Surg.* 2014;18:1108–1115.
- **34.** Blumgart LH, Fong Y. *Surgery of the Liver and Biliary Tract.* 3rd ed. Philadelphia (PA): Saunders Ltd; 2000.
- Bassi C, Falconi M, Molinari E, et al. Duct-to-mucosa versus end-to-side pancreaticojejunostomy reconstruction after pancreaticoduodenectomy: results of a prospective randomized trial. Surgery. 2003;134:766–771.
- Mishra PK, Saluja SS, Gupta M, Rajalingam R, Pattnaik P. Blumgart's technique of pancreaticojejunostomy: an appraisal. Dig Surg. 2011;28(4):281–287.
- 37. Kennedy EP, Yeo CJ. Dunking pancreaticojejunostomy versus duct-to-mucosa anastomosis. *J Hepatobiliary Pancreat Sci.* 2011;18:769–774.
- Polanco PM, Zenati MS, Hogg ME, et al. An analysis of risk factors for pancreatic fistula after robotic pancreaticoduodenectomy: outcomes from a consecutive series of standardized pancreatic reconstructions. Surg Endosc. 2016;30: 1523–1529.
- **39.** Napoli N, Kauffmann EF, Menonna F, Perrone VG, Brozzetti S, Boggi U. Indications technique and results of robotic pancreatoduodenectomy. *Updates Surg.* 2016;68:295–305.
- **40.** Boggi U, Signori S, De Lio N, et al. Feasibility of robotic pancreaticoduodenectomy. *Br J Surg.* 2013;100:917–925.
- Peng C, Zhou D, Meng L, et al. The value of combined vein resection in pancreaticoduodenectomy for pancreatic head carcinoma: a meta-analysis. BMC Surg. 2019;19:84.
- Marchegiani G, Andrianello S, Nessi C, et al. Neoadjuvant therapy versus upfront resection for pancreatic cancer: the actual spectrum and clinical burden of postoperative complications. Ann Surg Oncol. 2018;25:626–637.
- Czosnyka NM, Borgert AJ, Smith TJ. Pancreatic adenocarcinoma: effects of neoadjuvant therapy on post-pancreatectomy outcomes - an American College of Surgeons national surgical quality improvement program targeted variable review. HPB (Oxford). 2017;19:927–932.