



Efficacy of pancreaticojejunostomy of the pancreatic stump during distal or central pancreatectomy

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Abstract

Background A stapler is usually used for transection and closure of the pancreas in distal pancreatectomy (DP) or central pancreatectomy (CP). When the pancreas is transected to the right of the portal vein, it is difficult to use a stapler and clinically relevant postoperative pancreatic fistula (CR-POPF) frequently occurs. We report on the efficacy of pancreaticojejunostomy (PJ) of the pancreatic stump for patients in whom stapler use is difficult.

Methods Patients who underwent DP or CP were enrolled in this study. The pancreas was usually transected by a stapler, and ultrasonic coagulating shears (UCS) were used depending on the tumor situation. When using UCS, hand-sewn closure or PJ was performed for the pancreatic stump. The relationship between clinicopathological factors and the methods of pancreatic transection and closure were investigated.

Results In total, 164 patients underwent DP or CP, and the pancreas was transected with a stapler in 150 patients and UCS in 14 patients. The rate of CR-POPF was higher and the postoperative hospital stay was longer in the UCS group than in the stapler group. PJ of the pancreatic stump, which was performed for 7 patients, did not worsen intraoperative factors. CR-POPF was not seen in these 7 patients, which was significantly less than that with hand-sewn closure.

Conclusions PJ of the pancreatic stump during DP or CP reduces CR-POPF compared with hand-sewn closure and may be useful especially when the pancreas is transected to the right of the portal vein.

Keywords Central pancreatectomy · Distal pancreatectomy · Pancreaticojejunostomy · Pancreatic fistula

Introduction

Postoperative pancreatic fistula (POPF) is a major complication of pancreatectomy and is still the most frequently occurring complication after distal pancreatectomy (DP), with an incidence of 5–30% [1–3]. Clinically relevant POPF (CR-POPF) leads to prolonged hospitalization, increased treatment costs, and death as the worst possible outcome. Many risk factors for POPF following DP have been reported, including high body mass index (BMI), prolonged operation time, large amount of blood loss, soft pancreatic texture, and pancreatic thickness [4, 5].

Central pancreatectomy (CP) is one of the parenchyma-sparing surgeries and is recommended for benign or

low-grade malignant pancreatic neoplasms in the body and neck of the pancreas because it better preserves exocrine and endocrine pancreatic function. However, CP leaves two divided pancreatic remnants, creating more opportunities for CR-POPF formation [6].

There are many reports on various methods of pancreatic stump closure, but the most effective technique to prevent CR-POPF is yet to be proven, and the appropriate technique for closure of the pancreatic stump during DP remains controversial [7]. Although a randomized controlled trial did not show superiority of stapler versus hand-sewn closure for CR-POPF [8], stapler closure has recently become a standard technique because it is convenient and ideal for laparoscopic or robotic DP. However, stapler closure of the pancreatic stump can be difficult when the tumor location extends to the pancreatic neck.

Several studies have reported the efficacy of pancreaticojejunostomy (PJ) of the pancreatic stump for CR-POPF in patients who have undergone DP [9–11]. Kawai et al. [12]

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reported that PJ of the pancreatic stump did not reduce CR-POPF when they examined all patients who underwent DP. However, the usefulness of PJ of the pancreatic stump, which is limited to when stapler closure is difficult, has not been investigated.

The present study investigated the relationship between methods of pancreatic stump closure and perioperative factors and also compared hand-sewn closure and PJ of the pancreatic stump when it cannot be closed with a stapler.

Patients and methods

Study population

In total, 164 patients who underwent DP or CP in Oita University Faculty of Medicine from January 2011 to December 2023 were enrolled in this study. Patient characteristics were retrospectively collected from the patients' charts. This study was approved by the Ethics Committee of Oita University Faculty of Medicine (approval number: 2744).

Distal and central pancreatectomy

A stapler was used for transection and closure of the pancreas during DP, when the pancreas was transected above or to the left of the portal vein (PV). In CP, the proximal pancreatic stump was also transected with a stapler, and PJ

was performed for the distal stump. Additional treatment or covering of the pancreatic stump was not performed. When the tumor was located around the pancreatic neck or if an accurate pathological diagnosis of the stump was required due to the possibility of cancer infiltration to the stump, the pancreas was divided with ultrasonic coagulating shears (UCS). When using UCS, ligation of the main pancreatic duct and hand-sewn closure of the stump resulted in a high incidence of CR-POPF, so PJ of the stump was performed in all cases from 2022 (Figs. 1, 2, 3) and was performed by board-certified expert surgeons of the Japanese Society of Hepato-Biliary-Pancreatic Surgery.

Definition of postoperative pancreatic fistula

The grade of POPF was defined according to the International Study Group of Pancreatic Fistula (ISGPF) [13]. In this study, POPF grades B and C were defined as clinically relevant POPF (CR-POPF). During this study period starting in 2011, same drain management was implemented with reference to the report by Kawai et al [14]. Drainage tubes were removed within 4 days after surgery when the drain amylase level was less than three times the upper limit of normal range for serum level. Even if the drain amylase level was high, the drainage tubes were removed as soon as possible when the drainage fluid showed no sign of infection and when the drain amylase level continued to decrease.

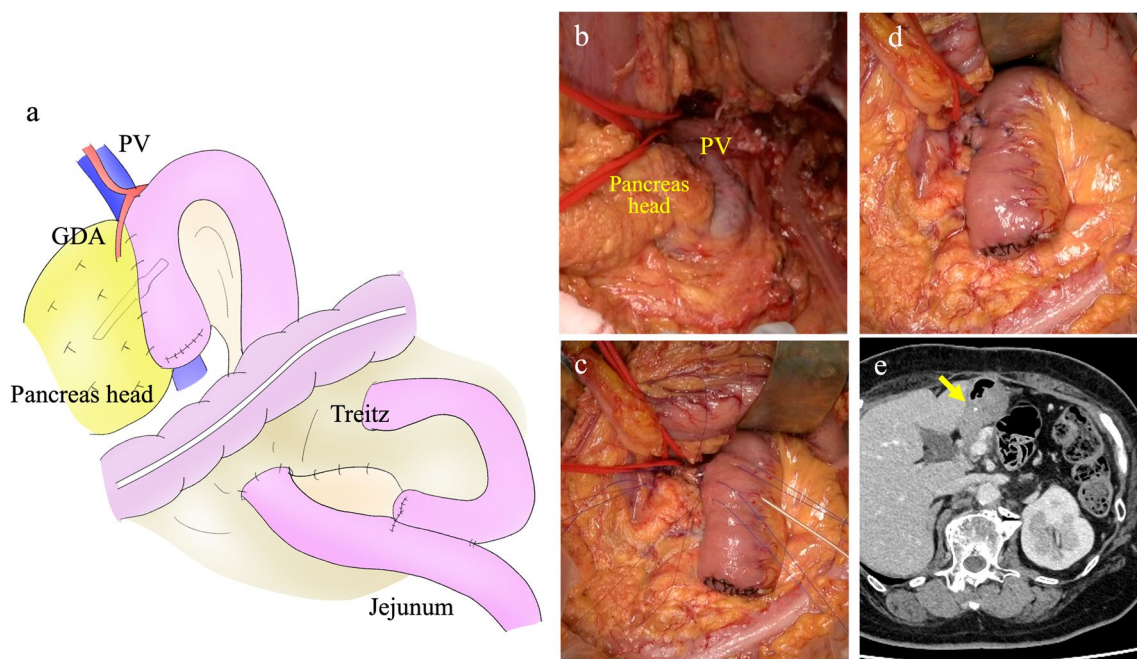


Fig. 1 Schematic of pancreaticojejunostomy of distal pancreatectomy (a). Operative photos after resection of the distal pancreas (b), during pancreaticojejunostomy (c), and after pancreaticojejunostomy (d).

Postoperative CT images of pancreaticojejunostomy (e). PV portal vein, GDA gastroduodenal artery, CBD common bile duct

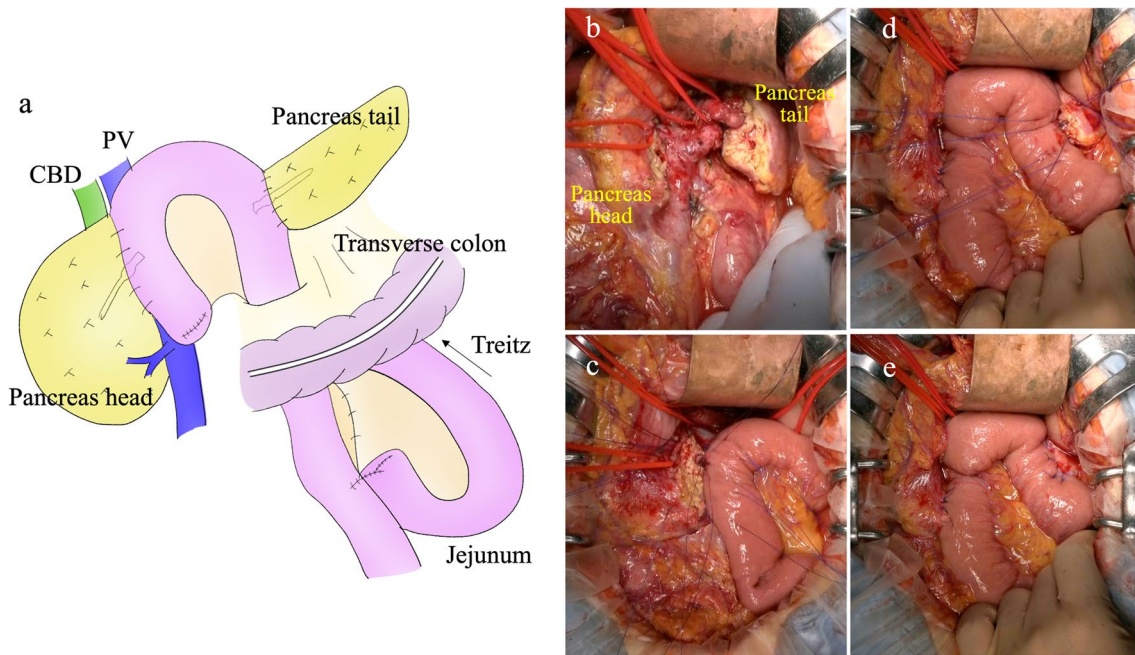
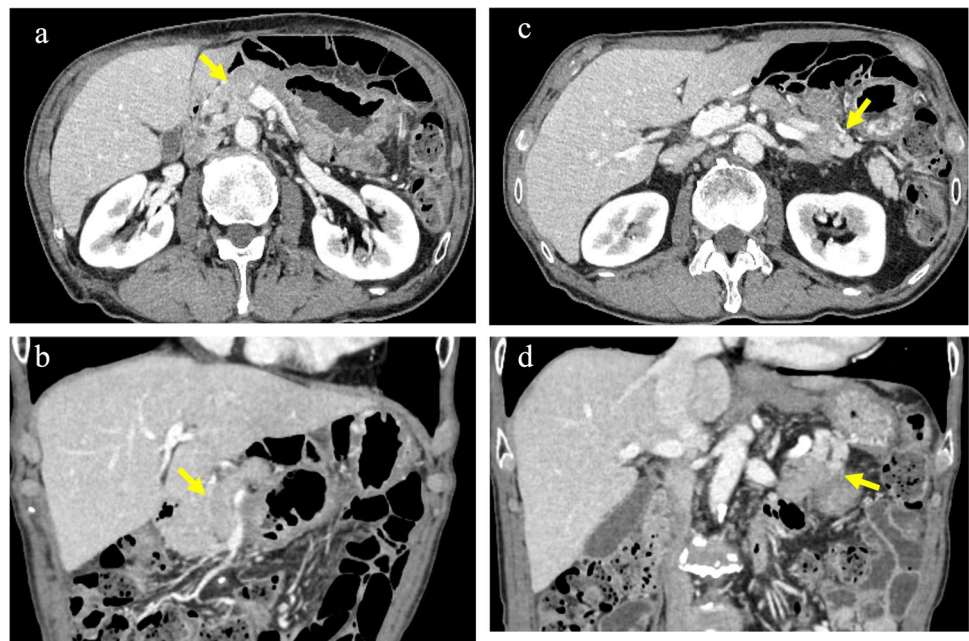


Fig. 2 Schematic of pancreaticojejunostomy of central pancreatectomy (a). Operative photos after resection of the central pancreas (b), during proximal pancreaticojejunostomy (c), during distal pancreaticojejunostomy (d), and after reconstruction (e). PV portal vein, GDA gastroduodenal artery, CBD common bile duct

cojejunostomy (d), and after reconstruction (e). PV portal vein, GDA gastroduodenal artery, CBD common bile duct

Fig. 3 Postoperative CT images after central pancreatectomy. Transverse (a) and coronal (b) image of proximal pancreaticojejunostomy. Transverse (c) and coronal (d) image of distal pancreaticojejunostomy



Data collection

The following clinicopathological variables were included in the analysis: preoperative factors including age, sex, and BMI; operative factors including DP/CP, open/laparoscopic surgery, level of pancreatic transection (right of the PV/above or left of the PV), instruments for pancreatic

transection (stapler/UCS), operation time, blood loss, and transfusion; postoperative course including CR-POPF, complications, and postoperative hospital stay; and pathological factors, including diagnosis. These variables were compared between the stapler and UCS groups for pancreatic transection and further, between hand-sewn closure and PJ of the pancreatic stump in the UCS group.

Statistical analysis

All variables are expressed as the median (interquartile range) for continuous data. Univariate analyses were performed using the Student *t*-test for continuous variables and chi-squared test for categorical variables. Statistical significance was defined as $P < 0.05$. All statistical analyses were performed with JMP Pro 17 (SAS Institute Inc., Cary, NC, USA).

Results

Patient characteristics

The clinicopathological characteristics of the patients who underwent DP or CP are shown in Table 1. The median patient age was 71 (62-76) years, and of these 164 patients, 78 were women and 86 were men. DP was performed in 158 patients and CP in 6 patients. The pancreas was transected to the right of the PV in 14 (9%) patients. Median operation time was 338 (281-425) min, and median blood loss was 300 (100-665) mL. CR-POPF occurred in 30 (18%) patients, and the median postoperative hospital stay was 16 (12-26) days.

Table 1 Patient characteristics ($n = 164$)

Characteristics	Value
Preoperative factors	
Age, years	71 (62-76)
Sex (female/male)	78 (48%)/86 (52%)
BMI, kg/m ²	22 (21-25)
Diagnosis	
Pancreatic cancer/Others	67 (41%)/97 (59%)
Operative factors	
DP/CP	158 (96%)/6 (4%)
Open/Laparoscopy	80 (49%)/84 (51%)
Pancreatic transection (right of PV/above or left of PV)	14 (9%)/150 (91%)
Pancreatic transection (stapler/UCS)	150 (91%)/14 (9%)
Operation time, min	338 (281-425)
Blood loss, mL	300 (100-665)
Transfusion	26 (16%)
Postoperative course	
POPF (\geq grade B)	30 (18%)
Clavien-Dindo (\geq grade 3)	32 (20%)
Postoperative hospital stay, days	16 (12-26)

BMI body mass index, DP distal pancreatectomy, CP central pancreatectomy, UCS ultrasonic coagulating shear, POPF postoperative pancreatic fistula

Comparison of perioperative factors for pancreatic transection using stapler and ultrasonic dissector

The pancreas was transected with a stapler in 150 patients (stapler group) and UCS in 14 patients (UCS group) (Table 2). There were no significant differences between the two groups in preoperative factors and diagnosis. For operative factors, however, the rate of laparoscopic surgery in the stapler group was higher than that in the UCS group. The pancreas was more frequently transected to the right of the PV in the UCS group versus stapler group. There were no significant differences in operation time and blood loss between the groups. The rate of CR-POPF was higher (50% vs 15%, $P = 0.004$) and the postoperative hospital stay was longer (27 (17-50) vs 15 (12-25) days, $P = 0.014$) in the UCS group than those in the stapler group.

Case series of patients with pancreatic stump divided with UCS

Details of the patients whose pancreas was transected with UCS are shown in Table 3. Open surgery was performed in all of these patients. As described above, PJ of the pancreatic stump was performed in all cases from 2022 because hand-sewn closure of the stump resulted in a high incidence of CR-POPF, and since then, there have been no cases of CR-POPF. Regarding the patients undergoing CP in the hand-sewn closure group, all two patients developed POPF. These occurred in the proximal pancreatic stump in one patient and both of the proximal pancreatic stump and the distal pancreas with PJ in the other. Among the cases in which PJ of the pancreatic stump was not performed were many cases with pancreatic ductal adenocarcinoma, including two cases of DP with celiac axis resection, and it is possible that many cases involved more difficult surgery.

Comparison of perioperative factors between hand-sewn closure (HS group) and pancreaticojejunostomy of the pancreatic stump (PJ group)

PJ of the pancreatic stump was performed on 7 patients, 4 with DP and 3 with CP. The BMI of the PJ group was lower than that of the HS group (Table 4). The PJ group had shorter operation time (466 (455-556) vs 306 (237-359) min, $P = 0.012$) and less blood loss (1210 (310-1320) vs 170 (100-240) mL, $P = 0.019$) than the HS group. The rate of POPF was zero in the PJ group, and the rates of both CR-POPF and

Table 2 Perioperative factors of pancreatic transection using a stapler vs. ultrasonic coagulation shears (UCS)

	Stapler (n=150)	UCS (n=14)	P value
Preoperative factors			
Age, years	70 (61-76)	75 (72-77)	0.055
Sex (female/male)	71 (47%)/79 (53%)	7 (50%)/7 (50%)	0.849
BMI, kg/m ²	22 (21-26)	22 (20-24)	0.776
Diagnosis			
Pancreas cancer/Others	60 (40%)/90 (60%)	6 (43%)/8 (57%)	0.835
Operative factors			
DP/CP	149 (99%)/1 (1%)	9 (64%)/5 (36%)	<0.001
Open/Laparoscopy	66 (44%)/84 (56%)	14/0	<0.001
Pancreatic transection (right of PV/above or left of PV)	1 (1%)/149 (99%)	13 (93%)/1 (7%)	<0.001
Operation time, min	338 (281-408)	404 (289-467)	0.130
Blood loss, mL	300 (100-613)	275 (133-1223)	0.599
Transfusion	22 (15%)	4 (29%)	0.417
Postoperative course			
POPF (≥ grade B)	23 (15%)	7 (50%)	0.004
Complications (≥ Clavien-Dindo III)	25 (17%)	7 (50%)	0.007
Postoperative hospital stay, days	15 (12-25)	27 (17-50)	0.014

BMI body mass index; DP distal pancreatectomy; CP central pancreatectomy; PV portal vein; POPF postoperative pancreatic fistula

Table 3 Case series of pancreatic stumps divided with an ultrasonic dissector

Case	Age/Sex	Diagnosis	Operation	Pancreato-jejunostomy of pancreatic stump	Operation time (min)	Blood loss (mL)	POPF (≥ grade B)	Complication	Postoperative hospital stay (days)
1	75/F	PDAC	DP	No	455	830	B	PF	61
2	75/M	PDAC	DP	Yes	449	240	None	none	19
3	72/M	PDAC	DP-CAR	No	556	1380	B	PF	46
4	78/F	IPMC	DP	No	466	1210	B	PF	62
5	72/M	PDAC	DP	No	469	1260	C	PF	93
6	73/M	PDAC	DP-CAR	No	585	1320	B	PF	39
7	62/M	PanNET	CP	No	455	310	B	PF	39
8	71/M	Stenosis of MPD	CP	No	267	140	B	PF	32
9	74/M	IPMA	CP	Yes	237	110	None	None	10
10	70/F	RCC metastasis	DP	Yes	306	80	None	None	11
11	77/M	IPMA	CP	Yes	296	170	None	Chylous ascites	18
12	83/M	ITPN	CP	Yes	359	1090	None	Ascites	18
13	78/F	RCC metastasis	DP	Yes	199	100	None	None	14
14	77/F	PDAC	DP	Yes	337	190	None	None	22

PDAC pancreatic ductal adenocarcinoma; IPMC intraductal papillary mucinous carcinoma, PanNET pancreatic neuroendocrine tumor; MPD main pancreatic duct; IPMA intraductal papillary mucinous adenoma; RCC renal cell carcinoma; ITPN intraductal tubulopapillary neoplasm; DP distal pancreatectomy; DP-CAR distal pancreatectomy with celiac axis resection; CP central pancreatectomy; POPF postoperative pancreatic fistula

complications in the PJ group were significantly lower than those in the HS group. The length of postoperative hospital stay was also significantly shorter in the PJ group versus HS group (18 (11-19) vs 46 (39-62) days, $P = 0.001$).

Discussion

This study showed a higher incidence of CR-POPF and longer postoperative hospital stay when the pancreas was

Table 4 Comparison of perioperative factors between hand-sewn closure and pancreaticojejunostomy (PJ) of the pancreatic stump

	Hand-sewn closure (<i>n</i> =7)	PJ of the pancreatic stump (<i>n</i> =7)	<i>P</i> value
Preoperative factors			
Age, years	72 (71-75)	77 (74-78)	0.090
Sex (female/male)	4/3	2/4	0.592
BMI, kg/m ²	24 (22-26)	20 (18-22)	0.010
Diagnosis			
Pancreas cancer/Others	4/3	2/5	0.276
Operative factors			
DP/CP	5/2	4/3	0.576
Open/Laparoscopy	7/0	7/0	1.000
Operation time, min	466 (455-556)	306 (237-359)	0.012
Blood loss, mL	1210 (310-1320)	170 (100-240)	0.019
Transfusion	3/4	7/0	0.007
Postoperative course			
POPF (≥ grade B)	7 (100%)	0	<0.001
Complication (≥ Clavien-Dindo III)	7 (100%)	0	<0.001
Postoperative hospital stay, days	46 (39-62)	18 (11-19)	0.001

BMI body mass index, *DP* distal pancreatectomy, *CP* central pancreatectomy, *POPF* postoperative pancreatic fistula

divided using UCS. One reason for this result is that UCS were only used in special situations. PJ of the pancreatic stump after using UCS decreased the rate of CR-POPF. As PJ was performed for the pancreatic stump to the right of the PV and the pancreas and jejunum used for anastomosis are opposite that in the usual PJ in pancreaticoduodenectomy (PD), the difficulty of this procedure may be higher than that for the usual PJ in PD. However, no CR-POPF occurred after PJ of the pancreatic stump in this patient series. Pancreatic juice was drained to both the duodenum and the jejunum, and all PJ procedures on the stump were performed by board-certified expert surgeons. These may be the reasons for the good outcomes obtained following PJ of the stump.

Several approaches to pancreatic stump closure have been described in the literature, but the most effective method to prevent CR-POPF remains to be proven. In a large series by Ferrone et al. [7], different closure techniques were compared between hand-sewn closure, stapler with or without staple line reinforcement, use of free falciform patches, and pancreatic duct ligation, but there was no significant difference in the rates of CR-POPF. The DISPACT trial [8], in which two groups of patients were randomly assigned to stapler or hand-sewn closure of the pancreatic stump, showed no difference in the rates of CR-POPF. Stapler closure of the pancreatic stump is technically easy and has become popular with many surgeons as the performance of minimally invasive surgery has spread. The incidence of overall CR-POPF in the DISPACT trial was 32%, which was a higher rate than those in other recent studies. Stapler techniques such as pre-firing compression of the pancreas have improved the rate of POPF in DP [15, 16]. Good results with the use of artificial

patches or fibrin-glue sealant have also been described in small series, but thus far, large series have failed to prove their efficacy [17, 18].

Although transection at the pancreatic neck is suggested to be more reasonable [19], pancreatic transection may be performed to the right of the PV depending on the location of the tumor in DP or CP. Stapler closure of the pancreatic stump is not suitable in such a situation, and the surface of the pancreatic stump is often wider. The pancreatic stump is usually closed by ligating or suturing the main pancreatic duct and suturing the pancreatic parenchyma, but the incidence of CR-POPF is very high under these poor conditions [20]. In the present series, the rate of CR-POPF was higher in the UCS group than in the stapler group, partly because surgical conditions such as pancreatic transection performed to the right of the PV and near the tumor in the patients in the UCS group were worse.

Several studies have reported the effect of PJ of the pancreatic stump. Wagner et al. [10] examined the efficacy of PJ of the pancreatic stump compared to hand-sewn closure, and they found a zero rate of CR-POPF in the PJ group compared to a 20% rate of CR-POPF in the hand-sewn group. Meniconi et al. [11] also reported the superiority of PJ, which had a zero rate of CR-POPF compared to hand-sewn closure. Kawai et al. [12] reported on a prospective, randomized, multicenter study of PJ versus stapler closure of the pancreatic stump during DP. The rate of CR-POPF in the PJ group tended to be lower than that in the stapler closure group for patients with a thicker pancreas, although no statistical significance was shown. Furthermore, PJ did not increase postoperative complications including those of

intra-abdominal abscess and ileus, although PJ of the pancreatic stump may have some risks due to intestinal division and contamination with intestinal juice. However, CR-POPF after PJ may become more severe due to activation of pancreatic enzymes and bacterial contamination. Despite this possibility, our series showed good results similar to those of previous reports, and PJ was effective because of decompression of the main pancreatic duct, especially when hand-sewn closure results in a high rate of CR-POPF in poor conditions.

CP is one of the parenchyma-sparing surgeries and is recommended for benign or low-grade malignant pancreatic neoplasms in the body and neck of the pancreas. The size of the remnant pancreas suggests that exocrine and endocrine functions are better preserved. However, CP leaves two divided pancreatic remnants, increasing the opportunities for CR-POPF. Previous meta-analyses showed higher incidences of CR-POPF following CP than after PD or DP [21, 22]. The reported rate of CR-POPF in CP ranged from 26 to 63% [21–23]. Sho et al. [24] reported a low rate of POPF of 8% in CP when using double PJ. In our series, we performed CP in 6 patients, with and without PJ performed for the proximal pancreatic stump in 3 patients each. CR-POPF occurred in 2 (66%) patients without PJ and no patients with PJ. Thus, PJ for the proximal pancreatic stump as an alternative to closure may also be useful in CP.

This study has some limitations. These are the results of a retrospective non-randomized analysis of a small group of patients. Especially, the number of the patients in the hand-sewn closure group with PJ for the pancreatic stump was very small. Furthermore, the recent improvements in the perioperative course may be related to many other factors, such as changes in the operative instruments used and surgeons. It will thus be important to confirm these data in a larger series of patients.

In conclusion, PJ of the pancreatic stump during DP or CP reduces the incidence of CR-POPF compared with hand-sewn closure, especially when the pancreas is transected to the right of the PV.

Authors' contributions Study conception and design: TH, AF, YN, HO, SA, MK, TK, YK, TM, YE, MI. Acquisition of data: TH, AF, YN, HO, SA, MK, TK, YK, TM, YE, MI. Analysis and interpretation of data: TH, AF. Drafting of manuscript: TH, AF. Critical revision of manuscript: MI. All authors read and approved the final manuscript before submission.

Data availability No datasets were generated or analysed during the current study.

Declarations

Ethics approval The protocol for this study was approved by the Ethics Committee of the study center (Oita University, approval number: 2744) and complies with the Declaration of Helsinki and its later amendments.

Consent to participate All participants provided informed consent for participation in this study and for the use of their medical records through an optout form.

Conflict of interest The authors declare no competing interests.

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