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Safety and efficacy of pancreaticogastrostomy for hepatopancreatoduodenectomy compared to pancreaticojejunostomy for perihilar cholangiocarcinoma

Yutaka Nakano[1], Yuta Abe[1*], Daisuke Udagawa[1], Minoru Kitago[1], Yasushi Hasegawa[1], Shutaro Hori[1], Masayuki Tanaka[1], Sho Uemura[1], Masanori Odaira[2], Kisyo Mihara[3], Ryo Nishiyama[4], Naokazu Chiba[5], Shigeo Hayatsu[6], Shigeyuki Kawachi[6] and Yuko Kitagawa[1]

Abstract

Background Hepatopancreatoduodenectomy (HPD) is one of the most challenging surgeries for perihilar cholangiocarcinoma. Postoperative pancreatic fistula (POPF) is a critical and fatal complication. The safety and efficacy of pancreaticogastrostomy (PG) for HPD compared to pancreaticojejunostomy (PJ) remain unclear. In this study, we aimed to investigate and compare the short-term outcomes of PG and PJ for HPD in terms of the POPF rate.

Methods Two groups of patients (PG group vs. PJ group) were retrospectively compared between January 2013 and January 2024. The reconstruction method was changed from PJ to PG in March 2021.

Results A total of 50 patients were enrolled in this study. The PG and PJ groups comprised 15 (30.0%) and 35 (70.0%) patients, respectively. In the PJ group, three (8.6%) patients died after surgery because of clinically relevant POPF (CR-POPF), intraabdominal bleeding, and post-hepatectomy liver failure. The operative time was longer in the PG group (909 min vs. 706 min, $P=0.020$); however, the CR-POPF rate was lower in the PG group than in the PJ group (0 [0%] vs. 19 [54.3%], $P<0.001$). Moreover, the number of patients who developed massive postoperative ascites (≥ 1,500 mL/day) was lower in the PG group than in the PJ group (3 [20.0%] vs. 16 [45.7%] patients, $P=0.028$).

Conclusions Changing the method of pancreatic reconstruction for HPD from PJ to PG improved the short-term outcomes of patients at our institution. PG reconstruction is safe and effective for HPD as it reduces the incidence of CR-POPF.

Keywords Hepatopancreatoduodenectomy, Pancreaticoduodenectomy, Pancreaticogastrostomy, Perihilar cholangiocarcinoma, Postoperative pancreatic fistula

*Correspondence:
Yuta Abe
abey3666@gmail.com
[1]Department of Surgery, Keio University School of Medicine, 35 Shinanomachi, Shinju-ku, Tokyo 160-8582, Japan
[2]Department of Surgery, Tokyo Saiseikai Central Hospital, 1-4-17 Mita, Minato-ku, Tokyo 108- 0073, Japan
[3]Department of Surgery, Kawasaki Municipal Hospital, 12-1 Shinkawadori, Kawasaki-ku, Kawasaki-shi, Kanagawa 210-0013, Japan
[4]Department of Surgery, Saiseikai Yokohamashi Tobu Hospital, 3-6-1 Shimosueyoshi, Tsurumi- ku, Yokohama, Kanagawa 230-0012, Japan
[5]Department of Surgery, Tokyo Medical University Hachioji Medical Center, 1163, Tatemachi, Hachioji, Tokyo 193-0998, Japan
[6]Department of Surgery, National Hospital Organization Saitama Hospital, 2-1 Suwa, Wako-shi, Saitama 351-0102, Japan

Background

Hepatopancreatoduodenectomy (HPD) is one of the most challenging surgeries for perihilar cholangiocarcinoma. HPD was first introduced by Takasaki et al. [1] in 1980 as a treatment for locally advanced gallbladder cancer. Although HPD is curative for perihilar cholangiocarcinoma spreading from the hepatic hilum to the intrapancreatic bile duct, it has high morbidity and mortality rates even after advancements in hepatobiliary and pancreatoduodenal anatomies, surgical techniques, and perioperative management [2–6].

Postoperative pancreatic fistula (POPF) is the most critical and lethal complication of HPD. The clinically relevant POPF (CR-POPF) rate (grades B and C, according to the definition of the International Study Group of Pancreatic Surgery) [7] ranges from 26.3 to 67.0% [2–6], and it is associated with intraabdominal hemorrhage and abscesses. To prevent POPF, wrapping an omental flap around the dissected intraabdominal vessels [8], external drainage of pancreatic juice [9], and external drainage of pancreatic juice followed by second-stage pancreaticojejunostomy (PJ) [10] may be performed [4]; however, HPD remains controversial owing to postoperative complications.

The modified Child's method is routinely selected for HPD for perihilar cholangiocarcinoma [2–6]. At our institution, the modified Child's method was performed from January 2013 to March 2021; however, we also encountered cases of POPF after HPD. Therefore, we changed the method from PJ to pancreaticogastrostomy (PG), based on PG for pancreaticoduodenectomy (PD) [11], in March 2021. PG and PJ have similar incidence rates of POPF in patients with PD, but the safety and efficacy of PG in patients with HPD remain unclear.

We hypothesized that the short-term outcomes of PG for HPD in patients with perihilar cholangiocarcinoma are better than those of PJ, especially in terms of CR-POPFP. Therefore, we presented the PG method for HPD and its advantages and investigated and compared the short-term outcomes of PG and PJ for HPD in terms of the POPF rate.

Methods

Patients

Data of patients who underwent HPD for perihilar cholangiocarcinoma between January 2013 and January 2024 were retrospectively reviewed. We included patients who underwent HPD for perihilar cholangiocarcinoma due to tumor invasion into the intrapancreatic bile duct or pancreas preoperatively or intraoperatively, and we excluded those who underwent PD for perihilar cholangiocarcinoma as a two-stage surgery. Patients were divided into two groups according to the procedure for HPD reconstruction (PG group vs. PJ group) and according to the presence or absence of POPF. This multi-center retrospective study included six hospitals in Japan (Keio University Hospital, Tokyo Medical University Hachioji Medical Center, Saiseikai Yokohamashi Tobu Hospital, Tokyo Saiseikai Central Hospital, Kawasaki Municipal Hospital, and National Hospital Organization Saitama Hospital). All hospitals were board-certified training institutions of the Japanese Society of Hepatobiliary-Pancreatic Surgery.

This study was conducted in accordance with the principles embodied in the 1975 Declaration of Helsinki and was approved by the Ethics Committee of Keio University School of Medicine (approval number: 20120443). The requirement for the acquisition of informed consent from patients was waived owing to the retrospective nature of this study.

Surgical procedure of PJ and PG for HPD

For PJ anastomosis, we used the modified Blumgart anastomosis where two or three transpancreatic U-sutures were placed straight through the pancreatic remnant with 3–0 polypropylene sutures. Each of the sutures went through a 10–15-mm longitudinal seromuscular stitch through the back wall of the jejunal loop and then through the pancreatic parenchyma from back to front. For the second suture, one stitch was placed cranially and the other caudal to the main pancreatic duct. The needles of these transpancreatic sutures were retained. After a duct-to-mucosa anastomosis was constructed, the needles of the transpancreatic U-suture were passed through the seromuscular layer of the anterior wall of the jejunal loop in the direction of the short axis. Each of the U-sutures was placed 5–10 mm from the next. These three sutures were tied at the ventral wall of the jejunum. In PJ reconstruction, the specimen must first be removed, and the jejunum is elevated for reconstruction of the pancreas.

Contrarily, PG reconstruction was performed immediately after cutting the pancreas. In PG reconstruction, the specimen may not be removed immediately, thereby expecting that we could prevent the spread of pancreatic juice on the surgical field during specimen removal.

First, we dissected the pancreatic parenchyma above the portal vein, identified the main pancreatic duct, inserted an external drainage stent according to the size of the main pancreatic duct, fixed the stent (Fig. 1a), and sutured the cut pancreatic surface to prevent bleeding and POPF from small branches of the main pancreatic duct and its vessels. Second, we mobilized the pancreatic body and tail at > 3 cm beyond the root of the splenic artery to place the PG anastomosis on the left side of the patient. We then started suturing from the posterior stomach wall to the pancreatic parenchyma anteroposteriorly using 3–0 monofilament polypropylene thread

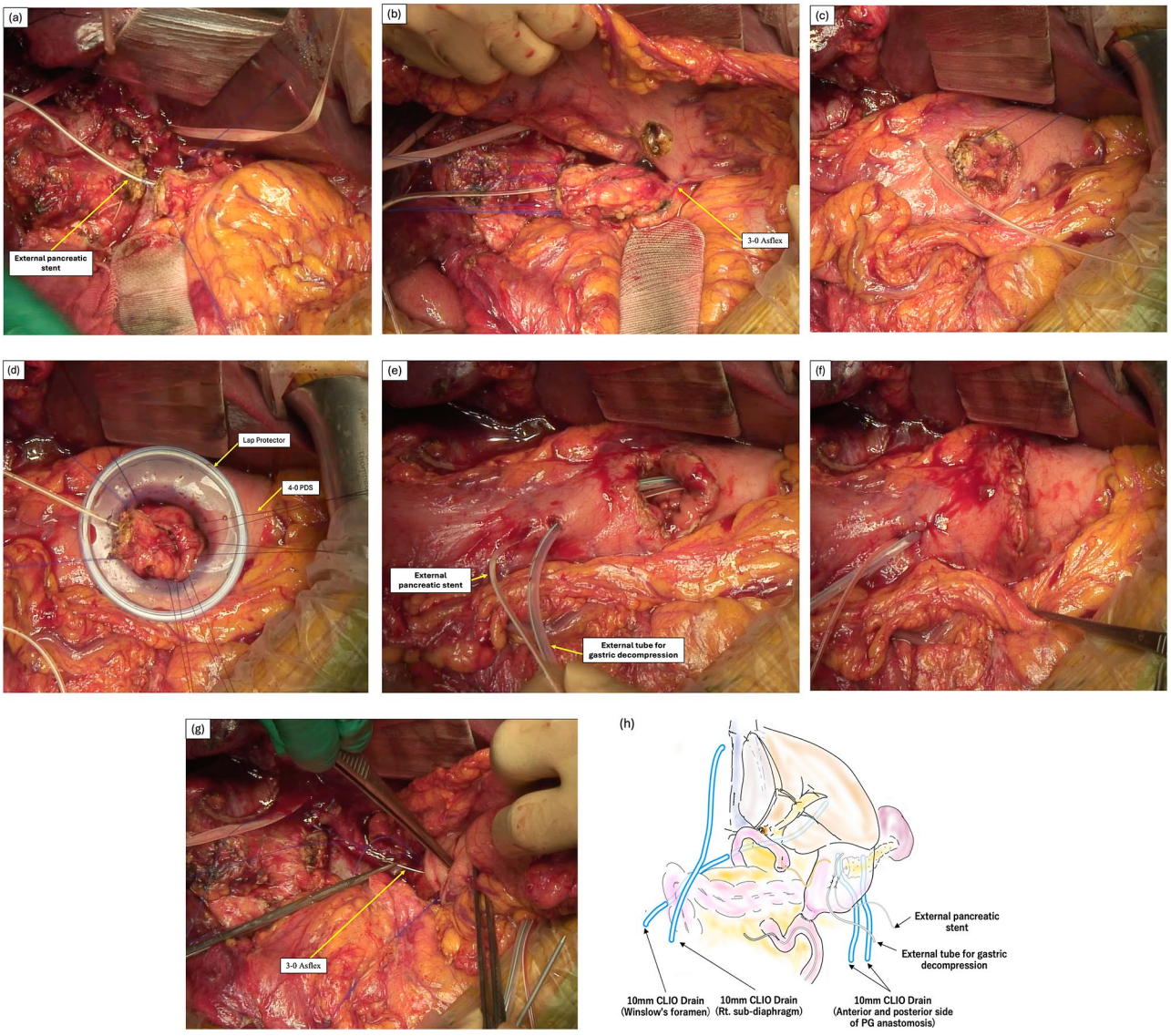

Fig. 1 Surgical procedure of PG for HPD. **a** Insertion of external drainage stent into the main pancreatic duct. **b** Suturing from the posterior stomach wall to the pancreatic parenchyma anteroposteriorly and opening the posterior stomach wall using 3 – 0 monofilament polypropylene. **c** Pulling the pancreatic stump from the posterior side to the anterior side of the stomach. **d** Placement of the Lap Protector™ (Hakko Co., Ltd.) during suturing of the pancreatic parenchyma and stomach into a whole layer using 4 – 0 PDS. **e** Insertion of the external tube for gastric decompression. **f** Closure of the anterior wall of the stomach by layer-to-layer anastomosis using 4 – 0 PDS. **g** Suturing of the posterior stomach wall using 3 – 0 monofilament polypropylene. **h** Drain placement. HPD, hepatopancreatoduodenectomy; PDS, polydioxanone sutures; PG, pancreaticogastrostomy

with double-armed 1/5-circle needles (Asflex, Crownjun Kono Co., Ltd.) (Fig. 1b). Third, the pancreatic stump was pulled from the posterior to the anterior side of the stomach (Fig. 1c). For an optimal surgical field for suturing, we placed a Lap Protector™ (Hakko Co., Ltd.) onto the edge of the anterior side of the stomach and sutured the pancreatic parenchyma and the stomach into a whole layer using 4 – 0 polydioxanone sutures (PDS II®, Ethicon) (Fig. 1d). Finally, the external stent was pulled from the anterior wall of the stomach antrum and inserted into the external tube for gastric decompression (Fig. 1e). After closing the anterior wall of the stomach via layer-to-layer anastomosis using 4 – 0 PDF, the first 3 – 0 monofilament polypropylene thread was sutured to the posterior stomach wall and fixed (Fig. 1e).

After removing the specimen, end-to-side hepaticojejunostomy (HJ) and gastro/duodenojejunostomy followed by Roux-en-Y reconstruction with an end-to-side jejunojejunostomy was performed. Two Clio drains (10 mm; Sumitomo Bakelite, Japan) were placed on the anterior and posterior sides of the PG anastomosis (Fig. 1f). However, the modified Child's method is usually performed for PJ reconstruction. The pancreatic stump, intrahepatic bile duct, and stomach/duodenum were reconstructed

using the Roux-en-Y jejunal limb. After surgery, the external pancreatic drainage tube was pulled from the stomach by esophagogastroduodenoscopy within 2–3 weeks if there were no complications. After discharge, the tube was pulled from outside of the body.

Regarding PG anastomosis, minimizing the risk of pancreatic juice leakage through meticulous suturing and postoperative management is critical for achieving favorable outcomes. Some complications of PG besides POPF include postoperative pancreatitis, gastrointestinal hemorrhage, and delayed gastric emptying. To prevent these complications, the standardization of PG anastomosis methods and proper drain tube placement are needed. We modified this method to perform whole-layer suturing between the posterior gastric wall and the pancreas and allow the insertion of an external tube for gastric decompression.

Classification of complications

Major morbidities were defined as those classified as Clavien–Dindo grades III and IV, and mortality was defined as Clavien–Dindo grade V [12]. Pancreatic fistulas were defined according to the International Study Group of Pancreatic Surgery [7]. Bile leakage and post-hepatectomy liver failure (PHLF) were classified according to the International Study Group of Liver Surgery criteria [13, 14]. PHLF, grade B or C POPF, and ≥ grade 3 bile leakage were considered clinically relevant. In addition to the postoperative 90-day mortality, death during hospital stay was assessed. Pathological findings were analyzed in patients diagnosed with perihilar cholangiocarcinoma. Histopathological diagnosis and TNM staging were performed according to the seventh edition of the Union for International Cancer Control Staging System. Resection margins were evaluated according to the sixth edition of the Japanese Classification of Biliary Tract Carcinomas.

Statistical analyses

The distance between the HJ and PG/PJ anastomoses and that between the PG/PJ anastomosis and the dissected artery closest to the PG/PJ anastomosis (e.g., common hepatic artery, gastroduodenal artery, proper hepatic artery, and left/right hepatic artery) were calculated using postoperative computed tomography (Fig. 2). Normality was assessed by Shapiro-Wilk test. Categorical variables were compared using the chi-squared or Fisher's exact tests, and continuous variables were compared

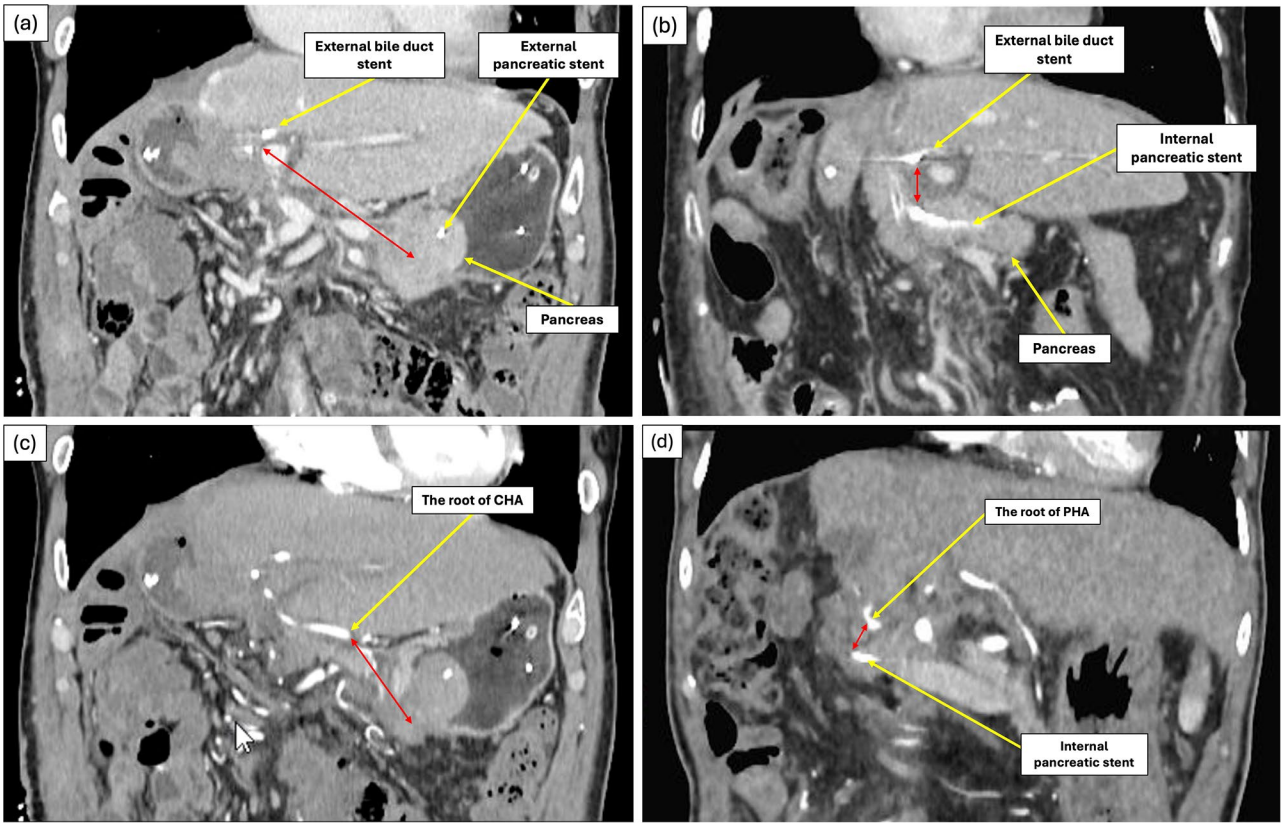

Fig. 2 Distance between the HJ and PG/PJ anastomoses and between the dissected artery and the PG/PJ anastomosis. **a** Distance between the HJ and PG anastomoses (red arrow). **b** Distance between the HJ and PJ anastomoses (red arrow). **c**, **d** Distance between the dissected artery and PG anastomosis (red arrow). CHA, common hepatic artery; HJ, hepaticojejunostomy; PG, pancreaticogastrostomy; PHA, proper hepatic artery; PJ, pancreaticojejunostomy

using the Mann–Whitney U-test. All statistical analyses were conducted using the Statistical Package for the Social Sciences for Macintosh version 29.0 (IBM Corp., Armonk, NY, USA). Differences were considered statistically significant at $P < 0.05$.

Results

Overall, 50 patients were enrolled in this study. In the PG and PJ groups, there were 15 (30.0%) and 35 (70.0%) patients, respectively. Demographic and clinical characteristics of the PG and PJ groups are shown in Table 1. There were no differences in baseline characteristics between the two groups. There were no deaths in the PG group, but three patients died after surgery in the PJ group. One patient died due to an intraabdominal abscess (*Enterobacter cloacae* and *Enterococcus faecalis*), anastomotic bleeding of the right hepatic artery, and post-hepatectomy liver failure from hepatic compartment syndrome; CR-POPF did not occur in this patient. However, two patients died due to CR-POPF. One patient underwent multiple percutaneous drainage procedures because pancreatic juice spread throughout the intraabdominal space, and bleeding occurred in the tiny vessels around the jejunum. After bleeding, the patient developed acute exacerbation of interstitial pneumonia and died. Another patient experienced bleeding from the pseudoaneurysm around the right hepatic artery due to CR-POPF. We performed hepatic arterial coil embolization, but the patient developed severe acute cerebral infarction and bacterial pneumonia and died.

Compared with the PJ group, the operative time was longer (911 min vs. 720 min, $P = 0.097$), and the CR-POPF rate was lower (0 [0%] vs. 19 [54.3%], $P < 0.001$) in the PG group. The number of patients who developed massive postoperative ascites (≥ 1,500 mL/day for 7 days) was lower in the PG group than in the PJ group (2 [13.3%] vs. 16 [45.7%], $P = 0.028$). Moreover, patients in the PG group had a lower rate of major morbidity (9 [60.0%] vs. 29 [82.9%], $P = 0.087$) and PHLF (1 [6.7%] vs. 10 [28.6%], $P = 0.085$) than those in the PJ group.

Patients with POPF had lower preoperative albumin levels (3.4 vs. 3.6, $P = 0.033$) and higher rates of PHLF (8 [42.1%] vs. 3 [9.7%], $P = 0.010$) and postoperative arterial bleeding (6 [31.6%] vs. 2 [6.5%), $P = 0.027$) (Table 2). Thus, patients with POPF had longer postoperative hospital stays (59 vs. 40 days, $P = 0.089$).

Discussion

We changed the method of pancreatic reconstruction from PJ to PG for HPD to prevent POPF. Initially, the incidence rate of POPF was > 50%; however, we did not include any patients with POPF after adopting PG in this study. These short-term outcomes are excellent; thus, we decided to report these outcomes first, although an analysis of predictive factors for POPF and PHLF should be performed and evaluated in the future while including more patients who underwent PG or HPD. In this study, no mortality was observed in the PG group, and there were no cases of CR-POPF since March 2021. This finding suggests that preventing CR-POPF is crucial for preventing postoperative mortality following HPD surgery. Moreover, the number of patients who developed post hepatectomy liver failure was lower in the PG than in the PJ group (1 [6.7%] vs. 10 [28.6%] patients, $P = 0.085$) although there was no difference regarding the preoperative estimated future remnant liver function. Thet patients in the PG group had less postoperative ascites than those in the PJ group (830 vs. 1220 mL, $P = 0.147$), and the number of patients who developed massive postoperative ascites (≥ 1,500 mL/day) was lower in the PG than in the PJ group (3 [20.0%] vs. 16 [45.7%] patients, $P = 0.028$). We believe that changing the method of pancreatic reconstruction from PJ to PG for HPD improved short-term outcomes at our institution.

The typical reconstruction method of the pancreas for HPD is PJ, specifically the modified Child's method [2–6]. Meanwhile, several PG techniques are available, including the one-layer invagination technique [15], pancreas-transfixing method with duct-to-mucosa anastomosis [16], and binding invagination techniques [17, 18]. The binding invagination technique with suturing of the pancreas [18] was adopted at our institution. However, we modified this method to perform whole-layer suturing between the posterior gastric wall and the pancreas and allow the insertion of an external tube for gastric decompression. Regarding PG for PD, multiple retrospective studies, randomized controlled trials, and meta-analyses have been conducted, but whether PG prevents POPF better than PJ after PD remains controversial [19–24]. Furthermore, the efficacy and advantages of PG for HPD are unknown because of limited studies. Randomized controlled trials or meta-analyses are required for further studies.

Our study showed that PG is associated with a significantly lower rate of POPF than PJ. Moreover, the distance between the HJ and PG anastomoses was longer than that between the HJ and PJ anastomoses, and the distance between the PG anastomosis and the dissected vessel was longer than that in PJ. There are some advantages of PG for PJ due to the location of the anastomosis. First, the PG anastomosis is farther from the left margin of dissection than the PJ anastomosis; if CR-POPF occurs, there is less possibility of bleeding because there are fewer dissected intraabdominal vessels around the anastomosis. Meanwhile, after performing PJ for HPD, the gastroduodenal artery and some dissected vessels are usually located near the PJ anastomosis site. Second, we can localize leakage from POPF because the stomach

Table 1 Demographic and clinical characteristics between PG group and PJ group

	Total (*N*=50)	PG group (*N*=15)	PJ group (*N*=35)	*P* value
Patient backgrounds				
Age (years)	74 (50–82)	75 (51-82)	73 (50-82)	0.106
Sex (female), n (%)	13 (26.0)	2 (13.3)	11 (31.4)	0.163
Body mass index (kg/m^2/)	20.9 (15.6-28.6)	21.5 (16.9-26.2)	20.4 (15.6-28.6)	0.227
Comorbidities				
Hypertension, n (%)	22 (44.0)	5 (33.3)	17 (48.6)	0.116
Diabetes mellitus, n (%)	14 (28.0)	6 (40.0)	8 (22.9)	0.308
Vascular disease*, n (%)	11 (22.0)	4 (26.7)	7 (20.0)	0.560
Charlson Risk Index	4 (1-7)	4 (2-7)	4 (1-7)	0.171
Serum albumin, (g/dL)	3.5 (2.4–4.3)	3.8 (3.1-4.3)	3.5 (2.4-4.3)	0.180
Serum CEA (ng/mL)	2.4 (0.6–5.6)	3.0 (0.6-4.7)	2.3 (0.6-5.6)	0.847
Serum CA19-9 (U/mL)	45 (2–3716)	42 (10-1386)	53 (2-3716)	0.761
Type of cancer, n (%)				0.173
Bile duct cancer	44 (88.0)	15 (100.0)	29 (82.9)	
Gallbladder cancer	4 (8.0)	0	4 (11.4)	
Intrahepatic cholangiocarcinoma	2 (4.0)	0	2 (5.7)	
NAC or NACRT, n (%)	13 (26.0)	3 (20.0)	10 (28.5)	0.398
Preoperative biliary drainage, n (%)	44 (88.0)	15 (100)	29 (82.9)	0.306
ICG-15R (%)	9.6 (2.0–22.4)	12.0 (6.5-18.2)	8.1 (2-22.4)	0.118
PTPE, n (%)	41 (82.0)	11 (73.3)	30 (85.7)	0.254
Future remnant liver volume (%)	52.1 (33.7–82.0)	46.9 (37.3-69.0)	52.2 (34.4-82.0)	0.403
Remnant ICG-K	0.075 (0.040-0.157)	0.069 (0.049-0.108)	0.080 (0.040-0.157)	0.126
Distance between HJ and PG/PJ (mm)	52.7 (16.3-121.8)	100.2 (78.6-121.8)	42.0 (18.3-87.3)	<0.001
Distance between the dissected artery and PG/PJ (mm)**	24.3 (5.1-72.1)	51.0 (27.3-72.1)	19.4 (5.1-56.5)	<0.001
Operative data				
Type of hepatectomy, L3/C2/L2/R2/R3	1/5/16/27/1	0/3/4/8/0	1/2/12/19/1	0.526
Combined vascular resection, PV/HA/PV+HA	14/2/8	4/1/1	10/1/7	0.581
Operation time (min)	806 (323-1375)	911 (417-1150)	720 (323-1375)	0.097
Blood loss (ml)	625 (195-2368)	520 (240-1905)	740 (195-2368)	0.384
Intraoperative RBC transfusion, n (%)	25 (50.0)	7 (46.7)	18 (51.4)	0.462
Postoperative short-term outcomes				
Major morbidity (CD≧IIIa), n (%)	38 (76.0)	9 (60.0)	29 (82.9)	0.087
postoperative massive ascites (ml)	1076 (160-3971)	830 (168-3280)	1220 (160-3971)	0.147
postoperative massive ascites (≧1,500 ml/day)***	18 (36.0)	2 (13.3)	16 (45.7)	0.028
Postoperative bile leakage, n (%)	6 (12.0)	2 (13.3)	4 (11.4)	0.591
Post hepatectomy liver failure, n (%)	11 (22.0)	1 (6.7)	10 (28.6)	0.085
Postoperative pancreatic fistula, n (%)	19 (38.0)	0 (0)	19 (54.3)	<0.001
Postoperative artery bleeding, n (%)	8 (16.0)	1 (6.7)	7 (20.0)	0.232
Hospital stays (days)	42 (23-168)	39 (31-94)	54 (23-168)	0.415
Postoperative 90-day mortality, n (%)	1 (2.0)	0 (0)	1 (2.9)	0.700
In-hospital death, n (%)	3 (6.0)	0 (0)	3 (8.6)	0.415
Postoperative pathological data				
Lymph node metastasis, n (%)	33 (66.0%)	12 (80.0)	21 (60.0)	0.434
Resection margin, 0/1/2	35/16/1	9/6/0	24/10/1	0.737

Data was presented as median values (minimum-maximum values)

Abbreviations; CD, Clavien-Dindo. CHA, common hepatic artery. C2, central bisectionectomy. HA, hepatic artery. HJ, hepaticojejunostomy. L2, left hepatectomy. L3, left trisectionectomy. NAC, Neoadjuvant chemotherapy. NACRT, neoadjuvant chemoradiotherapy. PG, pancreaticogastrostomy. PJ, pancreaticojesunostomy. PTPE, percutaneous transhepatic portal vein embolization. PV, portal vein. RBC, red blood cell. R2, right hepatectomy. R3, right trisectionectomy

*Cardiovascular disease, cerebral vascular disease, etc

**The distance between the PG/PJ anastomosis and the dissected artery closest to the PG/PJ anastomosis (e.g., common hepatic artery, gastroduodenal artery, proper hepatic artery, and left/right hepatic artery)

***Intraabdominal drain discharge more than 1,500mL/day during post operative 7 days

Table 2 Demographic and clinical characteristics between POPF (+) vs. POPF (-)

	POPF (+) (*N*=19)	POPF (-) (*N*=31)	*P* value
Patient backgrounds			
Age (years)	70 (58-79)	75 (50-82)	0.016
Sex (female), n (%)	4 (21.1)	9 (29.0)	0.390
Body mass index (kg/m^2/)	21.3 (16.7-28.6)	20.8 (15.6-26.2)	0.803
Comorbidities			
Hypertension, n (%)	9 (47.4)	13 (41.9)	0.466
Diabetes mellitus, n (%)	4 (21.1)	10 (32.2)	0.301
Vascular disease*, n (%)	4 (21.1)	7 (22.6)	0.595
Charlson Risk Index	4 (2-6)	4 (1-7)	0.075
Serum albumin, (g/dL)	3.4 (2.4-4.3)	3.6 (2.4-4.3)	0.033
Serum CEA (ng/mL)	1.7 (0.6-5.6)	3.0 (0.6-5.4)	0.504
Serum CA19-9 (U/mL)	38 (9-3716)	49 (2-1386)	0.608
Type of cancer, n (%)			0.812
Bile duct cancer	16 (84.2)	28 (90.3)	
Gallbladder cancer	2 (10.5)	2 (6.5)	
Intrahepatic cholangiocarcinoma	1 (5.3)	1 (3.2)	
NAC or NACRT, n (%)	4 (21.1)	9 (29.0)	0.390
Preoperative biliary drainage, n (%)	16 (84.2)	28 (90.3)	0.324
ICG-15R (%), median (range)	12.0 (3.3-22.4)	9.1 (2.0-19.0)	0.992
PTPE, n (%)	18 (94.7)	23 (74.2)	0.068
Future remnant liver volume (%)	47.0 (36.5-69.0)	56.1 (33.7-82.0)	0.150
Remnant ICG-K, median (range)	0.073 (0.046-0.133)	0.080 (0.040-0.157)	0.330
Distance between HJ and PG/PJ (mm)	36.3 (16.3-69.0)	78.6 (16.9-121.8)	<0.001
Distance between the dissected artery and PG/PJ (mm)**	19.4 (5.1-33.5)	38.1 (8.0-72.1)	<0.001
Operative data			
Type of hepatectomy, L3/C2/L2/R2/R3	1/1/3/14/0	0/4/13/13/1	0.105
Combined vascular resection, PV/HA/PV+HA	6/0/2	8/2/6	0.577
Operation time (min)	675 (323-1375)	855 (348-1232)	0.181
Blood loss (ml)	911 (255-1990)	472 (195-2368)	0.049
Intraoperative RBC transfusion, n (%)	9 (47.4)	16 (51.6)	0.574
Type of reconstruction (PG/PJ)	0/19	15/16	<0.001
Postoperative short-term outcomes			
Major morbidity (CD≧IIIa), n (%)	17 (89.5)	21 (67.7)	0.077
postoperative massive ascites (ml)	1220 (385-3971)	990 (160-3513)	0.552
postoperative massive ascites (≧1,500 ml/day)***	9 (47.4)	9 (29.0)	0.157
Postoperative bile leakage, n (%)	1 (5.3)	5 (16.1)	0.249
Post hepatectomy liver failure, n (%)	8 (42.1)	3 (9.7)	0.010
Postoperative artery bleeding, n (%)	6 (31.6)	2 (6.5)	0.027
Hospital stays (days)	59 (23-168)	40 (26-153)	0.089
Postoperative 90-day mortality, n (%)	1 (5.3)	0 (0)	0.380
In-hospital death, n (%)	2 (10.5)	1 (3.2)	0.320
Postoperative pathological data, n (%)			
Lymph node metastasis, n (%)	12 (63.2%)	21 (67.7)	0.487
Resection margin, 0/1/2	14/4/1	21/10/0	0.217

Data was presented as median values (minimum-maximum values)

Abbreviations; CD, Clavien-Dindo. CHA, common hepatic artery. C2, central bisectionectomy. HA, hepatic artery. HJ, hepaticojejunostomy. L2, left hepatectomy. L3, left trisectionectomy. NAC, Neoadjuvant chemotherapy. NACRT, neoadjuvant chemoradiotherapy. PG, pancreaticogastrostomy. PJ, pancreaticojesunostomy. POPF, postoperative pancreatic fistula. PTPE, percutaneous transhepatic portal vein embolization. PV, portal vein. RBC, red blood cell. R2, right hepatectomy. R3, right trisectionectomy

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**The distance between the PG/PJ anastomosis and the dissected artery closest to the PG/PJ anastomosis (e.g., common hepatic artery, gastroduodenal artery, proper hepatic artery, and left/right hepatic artery)

***Intraabdominal drain discharge more than 1,500mL/day during post operative 7 days

wall is wrapped around the pancreas, the space around the anastomosis is limited, and the distance between the HJ and PG anastomoses is longer than that between the HJ and PJ anastomoses. Moreover, if drain tubes are placed around the PG anastomosis, as in our institution, the space could become smaller, and pancreatic juice would not spread into and throughout the intraabdominal free space, thereby preventing critical complications. According to our data, the PG anastomosis was placed on the left side of the patient unlike the PJ anastomosis, allowing for the division of fluid collection between the PG and HJ anastomoses. Thus, we believe that localizing leakage from POPF is important if it occurs and that performing PG increases the distance from the HJ or the dissected vessel.

Finally, the pancreas was reconstructed immediately after dissection of the pancreatic parenchyma. This is important because a long interval between pancreatic division and reconstruction may result in intraperitoneal saponification around the pancreas and lipolysis due to pancreatic lipases [25]. Sugiura et al. reported that delayed division of the pancreatic parenchyma could reduce the risk of developing CR-POPF after HPD [26]. This technique supports our concept of immediate reconstruction after dissection of the pancreatic parenchyma and prevention of the spread of pancreatic juice on the surgical field. Although the delayed division of the pancreas is important, it is natural to dissect the pancreatic parenchyma first. Thus, PG for HPD has the advantage of preventing the spread of pancreatic juice and ensuring smooth progression of surgery.

This study has some limitations. First, this was a retrospective study with a relatively small number of patients, and the potential for an unbalanced comparison remains due to the lack of matching between the groups. According to a review article on HPD [2–6], 50 patients is not a small sample size, but the number of PG patients should be larger. Second, this study only focused on short-term outcomes and not long-term outcomes such as pancreatic function (i.e., exocrine and endocrine abilities). Although an advantage of this surgery is the prevention of postoperative mortality, long-term outcomes regarding the survival rate or pancreatic function are also important. In future studies, we will discuss whether HPD is controversial in terms of short- and long-term outcomes. Third, owing to the lack of studies on PG in patients with HPD, it is difficult to support our data. Randomized controlled trials or meta-analyses are needed to evaluate whether PG for HPD is effective in reducing the incidence of CR-POPF. Fourth, confounding factors such as differences in surgeon's experience in PG vs. PJ exist. This study included six high-volume centers with hepato-biliary-pancreatic divisions and different surgeon experiences in PJ anastomosis; however, just one surgeon was responsible for PG anastomosis. Moreover, there were no changes in institutional protocols during the study period because one principal investigator checked the institutional protocols of the six high-volume centers and controlled the strategy of perihilar cholangiocarcinoma. Finally, this study focuses not on pancreaticoduodenectomy but rather on HPD for perihilar cholangiocarcinoma. According to previous studies on HPD for perihilar cholangiocarcinoma, the incidence of CR-POPF ranges from 40.0 to 86.8% [2–6], aligning with our findings (54.3%). CR-POPF is a common occurrence in HPD and is significantly different from that observed in pancreaticoduodenectomy. In our study, no cases of CR-POPF were observed in the PG group, and no fistula-related bleeding nor other fistula-related complications occurred. Our data do not allow a definite conclusion that the location of the anastomosis prevents severe consequences after CR-POPF. However, we believe that PG reconstruction holds potential to improve short-term outcomes of HPD. The observed differences in the distance between the HJ and PG anastomoses, compared to PJ anastomoses, may support this hypothesis. Moving forward, we aim to conduct a multi-center study to collect additional data on HPD for perihilar cholangiocarcinoma. This future study will encompass data analysis aimed to determine whether PG reconstruction can serve as a predictive risk factor for CR-POPF and prevent fistula-related bleeding or other fistula-related complications.

Conclusions

Changing the method of pancreatic reconstruction from PJ to PG for HPD improved the short-term outcomes in our institution. PG reconstruction is safe and effective for HPD in reducing the incidence of CR-POPF.

Abbreviations

CR-POPF	Clinically Relevant Postoperative Pancreatic Fistula
HJ	Hepaticojejunostomy
HPD	Hepatopancreatoduodenectomy
PD	Pancreaticoduodenectomy
PG	Pancreaticogastrostomy
PHLF	Post-Hepatectomy Liver Failure
PJ	Pancreaticojejunostomy
POPF	Postoperative Pancreatic Fistula

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Author contributions

YN, YA, DU, and YK conceived and designed the study. YN drafted the manuscript. MK, YA, HY, SH, MT, SU, MO, KM, RN, NC, SH, and SK analyzed the data and critically revised the manuscript. All authors were involved in data interpretation and in drafting the manuscript. All authors have read and approved the final version of the manuscript.

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Data availability
The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the principles embodied in the 1975 Declaration of Helsinki and was approved by the Ethics Committee of Keio University School of Medicine (approval number: 20120443). The requirement for the acquisition of informed consent from patients was waived owing to the retrospective nature of this study.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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