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Original Article

Conventional vs pylorus-preserving pancreaticoduodenectomy with pancreaticogastrostomy

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Abstract: Background: Between conventional pancreaticoduodenectomy (CPD) and pylorus-preserving pancreaticoduodenectomy (PPPD), there is still controversy about the superiority of adopting one method over the other in combination with pancreaticogastrostomy (PG). There are few reports about cases of PPPD with PG. Materials and Methods: We studied cases of pancreaticoduodenectomy (PD) with PG for pancreatic head and periampullary carcinoma in our medical center, retrospectively. The data were gathered from 152 patients who underwent CPD/PPPD with PG from January 2010 to April 2015. Cases under study were divided into two groups: CPD group (group A, 101 cases) and PPPD group (group B, 51 cases). The data included preoperative, intraoperative and postoperative conditions of both groups. The outcomes of perioperative data were investigated. Results: No significant statistical difference of the preoperative data was detected between two groups. Despite less blood loss ($p = 0.011$), the overall postoperative complications of group B was significantly higher than that of group A (56.7% vs 34.7%, $p = 0.009$). The single complication, majorly the postoperative pancreatic fistula (POPF) rate, of group B was significantly higher than that of group A (29.4% vs 11.9%, $p = 0.008$). Conclusion: Although PPPD with PG may reduce intraoperative blood loss, it can significantly increase postoperative complications, especially POPF. Therefore, PPPD with PG is not recommended for treatment of pancreatic head and periampullary lesions.

Keywords: Pylorus-preserving, pancreaticoduodenectomy, pancreaticogastrostomy, postoperative complication

Introduction

The conventional pancreaticoduodenectomy (CPD), better known as the Whipple procedure is the standard surgical procedure for pancreatic head and periampullary carcinomas [1]. The pylorus-preserving pancreaticoduodenectomy (PPPD) described by Watson is an alternative procedure performed for ampullary cancer [2]. PPPD has been used widely for the treatment of periampullary tumors since Traverso and Longmire reported its effectiveness in patients with chronic pancreatitis [3]. In some centers, pancreaticogastrostomy (PG) is the routine method for pancreaticoenteric reconstruction following pancreaticoduodenectomy (PD). However, between CPD and PPPD, there is still controversy about the superiority of adopting one method over the other in combination with PG.

In our recent clinical experience of PPPD with PG, one patient died of a severe postoperative pancreatic fistula (POPF). As we reviewed the literature, we found very few reports about cases of PPPD with PG. Therefore, in this study, we reviewed retrospectively 152 cases in which patients underwent PD with PG between January 2010 and April 2015, and studied the short-term complications following PD with PG utilizing retrospectively collected data. The differences of CPD/PPPD with PG were also investigated in terms of early postoperative complications within 30 days after surgery.

Materials and methods

Study population

The data included all cases of pathologically confirmed pancreatic head carcinoma or periampullary carcinoma in patients who received radical resection of PD with PG in our medical center between January 2010 and April 2015 at the Department of Hepatobiliary and Pan-

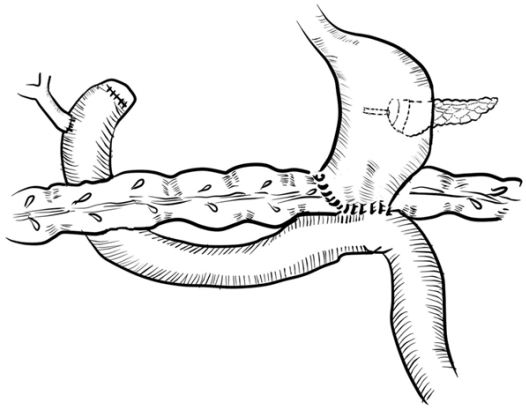

Figure 1. Conventional pancreaticoduodenectomy (CPD): end-to-side gastrojejunostomy in an antecolic route.

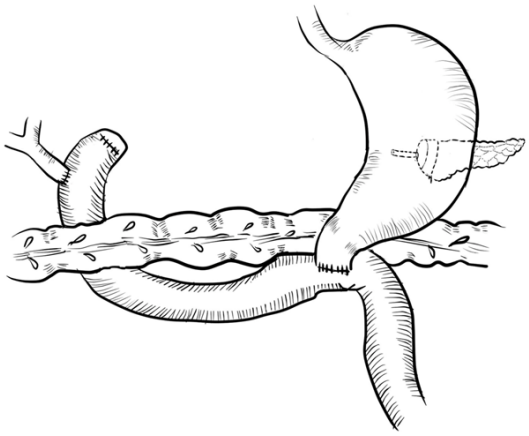

Figure 2. Pylorus-preserving pancreaticoduodenectomy (PPPD): end-to-side duodenojejunostomy in an antecolic route.

creatic Surgery, Lihuili Hospital of Ningbo, Ningbo, China. We excluded the patients who had an upper abdominal surgery history including previous gastrectomy and/or more upper abdominal adhesions to be categorized as poor candidates for PPPD. At the end, 152 cases in total have been included in this analysis. They were divided into two groups: CPD group (group A, 101 cases), and PPPD group (group B, 51 cases). All the operations in this study were performed by Dr. Lu and his team. Data were collected retrospectively on the clinicopathological features of these patients. General information collected from patients included age, sex, previous medical history, and albumin and hemoglobin levels. Intraoperative information included operative time, blood loss and whether it was combined with PV/SMV resection and/or multivisceral organ resection. Postoperative information included mortality, major complications, and length of hospital stay.

Conventional pancreaticoduodenectomy

Following the resection of the Whipple's specimen, Segmental resection of the portal vein or superior mesenteric vein was performed when there was involvement of the venous vasculature. Hepaticojejunostomy was performed using a hand sewn technique with 5-0/6-0 prolene in a retrocolic route, in a continuous fashion, and routine stenting was not performed. The remnant of the pancreas was prepared for the PG anastomosis. For PG, we used a self-designed duct-to-mucosa anastomosis we termed an inserting pancreaticogastrostomy with end-to-side gastrojejunostomy in an antecolic route (**Figure 1**) [4]. A stent was placed in the pancreatic duct and two drains were introduced respectively through the right-sided and left-sided abdominal incisions and placed in the vicinity of the PG.

Pylorus-preserving pancreaticoduodenectomy

In contrast to the CPD, in PPPD, we placed the line of transection on the duodenum approximately 2-4 cm distal to the pyloric ring. The right gastric artery was resected for lymphatic dissection. For better gastric motility, the lesser omentum close to the liver was dissected while the vagus nerve was preserved. We performed an end-to-side duodenojejunostomy in an antecolic route instead of gastrojejunostomy. As for hepaticojejunostomy and pancreaticogastrostomy, we used the same approach as in the CPD (**Figure 2**).

Definition of complications

Major complications were identified in accordance with the consensus by domestic and international experts as well as the definition from the International Study Group of Pancreatic Surgery (ISGPS) [5-8]. The complication of pancreatic fistula was divided into three grades of A, B and C based on the definition from the ISGPS. Biliary fistula was defined as cases what bilirubin levels in the drain fluid exceeded that in plasma when tested three days after the surgery. Biliary fistulas were all confirmed by

Table 1. Patient Characteristics

Contents	PD (n = 101)	PPPD (n = 51)	T or X^2 value	*p* value
Albumin (g/l)	38.3 ± 4.4	39.3 ± 4.4	-1.315	0.190
Serum total bilirubin (umol/l)	104.6 ± 110.6	84.0 ± 99.0	1.121	0.264
Hemoglobin (g/dl)	119.3 ± 15.3	120.0 ± 17.6	-0.240	0.811
Age, year	61.9 ± 11.5	61.9 ± 13.5	0.018	0.985
<60	38 (37.6%)	20 (39.2%)	0.036	0.849
≥60	63 (62.4%)	31 (60.8%)		
Gender				
Male	62 (61.4%)	26 (51.0%)	1.505	0.220
Female	39 (38.6%)	25 (49.0%)		
Preoperative biliary drainage				
Yes	2 (2.0%)	3 (5.9%)	0.627	0.428[a]
No	99 (98.0%)	48 (94.1%)		
Diabetes				
Yes	15 (14.9%)	4 (7.8%)	1.522	0.217
No	86 (85.1%)	47 (92.2%)		
Jaundice				
Yes	55 (54.5%)	23 (45.1%)	1.188	0.276
No	46 (45.5%)	28 (54.9%)		

[a]*p* value adopted with continuous correction.

sonography in certain cases. Chyle leak was defined as output of milky-colored fluid from a drain, drain site, or wound, on or after postoperative day 3, with a triglyceride content ≥ 110 mg/dL (≥ 1.2 mmol/L). Gastrojejunostomy/duodenojejunostomy leak was verified by gastrointestinal radiography. Intraperitoneal hemorrhage or upper gastrointestinal hemorrhage was defined as the patients who had fluctuation of blood pressure caused by postoperative intraperitoneal hemorrhage or upper gastrointestinal hemorrhage that required blood transfusion at 400 ml or more, or RBC transfusion of 2 U or more. Intraabdominal infections were diagnosed in patients who had sustained fever beyond the 5th postoperative day with an increasing amount of white blood cells (WBC) and local intraabdominal lesion visible on radiological imaging. Abdominal incision infection or dehiscence was patients who had pus and pockets of fluid, excessive serosanguineous drainage, or wound separation that caused delayed healing. For patients with delayed gastric emptying (DGE) complication, the nasogastric tube remained necessary seven days after the surgery, or the nasogastric tube had to be reinstalled three days after the operation. DGE was also diagnosed via upper gastrointestinal radiography. Intractable diarrhea was diagnosed if one week after the surgery, diarrhea exceeded five times per day for three days or more. Pneumonia was diagnosed by radiography. Postoperative hospitalization death or death within 30 days after the surgery was counted as postoperative mortality.

Statistical analysis

The data were presented as the mean and standard deviation or percentage of the group. The statistical analysis was conducted using SPSS 21.0. Two independent samples of t-test were used to compare the means of a normally distributed interval dependent variable for two independent groups. Discrete data were evaluated using Pearson's chi-square test or Fisher's exact test. If a *p* value was less than 0.05, it was considered statistically different.

Results

Preoperative conditions

As mentioned previously, pancreatic cancer patients were divided into two groups based on the application of CPD or PPPD. Overall, 92 cases were for pancreatic head carcinoma and 60 were for periampullary carcinoma. All the cases received radical resection. 57.9% of all the patients were males (n = 88) and 42.1% were females (n = 64), and the mean age was 61.9 ± 12.2 years old (ranging from 21 to 83 years old). Collected data (**Table 1**) showed that the two groups were similar in age and male-female ratios (p = 0.985 and p = 0.220). Preoperative examinations showed that these two groups of patients had similar serum albumin, serum total bilirubin and hemoglobin levels on average (p = 0.190, 0.264 and 0.811, respectively). In group A, 55 out of 101 (54.5%) had jaundice while in group B, it was 45.1% (p = 0.276). Among all 152 patients, 19 had diabetes conditions, which accounted for 14.9% in

Table 2. Operative information, pathology data and postoperative hospitalization

Contents	PD (n = 101)	PPPD (n = 51)	T or X^2 value	*p* value
Operative time (min)	364.3 ± 69.3	362.7 ± 84.5	0.122	0.903
Blood loss (ml)	622.5 ± 506.7	433.3 ± 169.0	2.590	0.011
Postoperative hospital stay (day)	15.6 ± 4.5	14.7 ± 4.5	1.095	0.275
Pancreatic duct diameter (mm)				
<3	24 (23.8%)	10 (19.6%)	0.337	0.562
≥3	77 (76.2%)	41 (80.4%)		
Portal vein resection				
Yes	29 (28.7%)	13 (25.5%)	0.176	0.675
No	72 (71.3%)	38 (74.5%)		
Multivisceral organ resection				
Yes	9 (8.9%)	5 (9.8%)	<0.001	>0.999[a]
No	92 (91.1%)	46 (90.2%)		
Pathology				
Pancreatic head carcinoma	66 (65.3%)	26 (51.0%)	2.927	0.087
Periampullary carcinoma	35 (34.7%)	25 (49.0%)		

[a]*p* value adopted with continuous correction.

group A and 7.8% in group B (p = 0.217). **Table 1** also listed cases with preoperative biliary drainage in both groups (2.0% vs 5.9%, p = 0.428). None of these patients underwent neoadjuvant chemotherapy.

Intraoperative parameters and postoperative hospitalization

The intraoperative parameters of two groups have been listed in **Table 2**. The blood loss of group A was 622.5 ± 506.7 ml, significantly higher than that of group B which was 433.3 ± 169.0 ml (p = 0.011). There was no significant difference in the operating time and postoperative hospital stay between the two groups. When cases were divided by pancreatic duct diameter with one group < 3 mm and another 3 mm, the distribution of pancreatic duct diameter in these two groups had no significant statistical differences (p = 0.562). The proportion of patients with portal vein/superior mesenteric vein (PV/SMV) resection and reconstruction in both groups were similar (p = 0.675), as was the incidence of other combined multivisceral organ resection (p > 0.999), including partial excision of the colon and liver. In terms of pathology, the proportion of pancreatic head carcinoma in group A was higher than that of group B (65.3% vs 51.0%). However, the periampullary carcinoma rate of group A was lower than that of group B (34.7% vs 49.0%), though this difference was not statistically significant (p = 0.087).

Postoperative complications

In group A, there was no mortality during the perioperative period while in group B one case died. The patient was reoperated on because of grade C POPF. We found that the PG had completely dehisced, leading to severe postoperative intraabdominal infection. The patient died in one week after the reoperation. **Table 3** showed that the total operative complication rate in group A was 34.7% (n = 35), versus 56.7% (n = 29) in group B, which was significantly higher (p = 0.009). Among them, 15.8% in group A and 33.3% in group B were single complications, again significantly higher in group B (p = 0.014). In terms of multiple complications, there were no statistical significance between the two groups (p = 0.496). When itemizing individual complications, the highest incidence in group A was intraabdominal infection (17.8%), which though not statistically significant (p = 0.169), was still lower than that in group B (27.5%). The most common complication in group B was pancreatic fistula, accounting for 29.4%, which was significantly higher than that of group A with 11.9% (p = 0.008). POPF could be divided into three grades. Grade B POPF in group B was 13.7%, significantly higher than 3.0% of group A (p = 0.029) while grade A and C POPF in two groups had no statistical difference. As for DGE, known as the complication most likely to occur in PPPD, the incidence of group B was 13.7%. Although it was still higher than that of group A with an incidence of 9.9%, there was no statistical significance between groups (p = 0.480). Other kinds of complications occurred at a rate lower than 10% in both groups, and there were no statistically significant differences between

Table 3. comparison between postoperative complications

Contents	PD (n = 101) Case number (%)	PPPD (n = 51) Case number (%)	X^2 value	*p* value
Total rate	35 (34.7%)	29 (56.7%)	6.857	0.009
Single complication	16 (15.8%)	17 (33.3%)	6.100	0.014
Multiple complications	19 (18.8%)	12 (23.5%)	0.465	0.496
POPF	12 (11.9%)	15 (29.4%)	7.129	0.008
Grade A	9 (8.9%)	7 (13.7%)	0.834	0.361
Grade B	3 (3.0%)	7 (13.7%)	4.748	0.029[a]
Grade C	0 (0.0%)	1 (2.0%)		0.336[b]
Biliary fistula	4 (4.0%)	0 (0.0%)	0.817	0.366[a]
Chyle leak	7 (6.9%)	0 (0.0%)	2.296	0.130[a]
Gastrojejunostomy/Duodenojejunostomy leak	1 (1.0%)	0 (0.0%)		>0.999[b]
Intra-abdominal hemorrhage	2 (2.0%)	2 (3.9%)	0.029	0.865[a]
Gastrointestinal hemorrhage	1 (1.0%)	0 (0.0%)		>0.999[b]
Intra-abdominal infection	18 (17.8%)	14 (27.5%)	1.891	0.169
Incisional infection	4 (4.0%)	4 (7.8%)	0.394	0.530[a]
Delayed gastric emptying	10 (9.9%)	7 (13.7%)	0.499	0.480
Intractable diarrhea	4 (4.0%)	0 (0.0%)	0.817	0.366[a]
Pneumonia	7 (6.9%)	2 (3.9%)	0.143	0.705[a]
Reoperation	2 (2.0%)	1 (2.0%)	<0.001	>0.999[a]
Postoperative mortality	0 (0.0%)	1 (2.0%)		0.336[b]

[a]*p* value adopted with continuous correction, [b] fisher's exact test.

groups ($p > 0.05$). Two cases in group A and 1 case in group B had to have reoperations, both accounting for 2 % in the respective group.

Discussion

Whether to perform CPD or PPPD still remains controversial for pancreatic head and periampullary carcinoma. Most of the current research in this field concerns whether to preserve the pylorus but does not address this specifically in cases of PG pancreaticoenteric reconstruction. Controversies also remain in the preference between Pancreaticojejunostomy (PJ) and PG following PD. PJ has been used more commonly in comparison to PG, yet PG has been gaining favor in recent years. Some retrospective studies and prospective randomized controlled trials (RCTs) have reported lower incidence rate of POPF after PG as compared to PJ [4, 9, 10]. In our medical center, PG has also been the usual practice in recent years. Although according to several RCTs' research findings, PG and PJ had similar complication incidences [11, 12], A lower POPF rate with better healing effects of PG than PJ was found in our practice [4]. However, severe POPF occurred in one case of PD with PG in our center after being performed with PPPD recently, which led us to study the complication incidences of preserving pylorus in PG retrospectively.

Theoretically, due to its simpler of operation, less blood loss, shorter operative time, and the preservation of the entire stomach and pylorus, PPPD has the advantage of achieving good nutritional status postoperatively. The studies from several RCTs and a meta-analysis also indicated consistent results in less blood loss and shorter operative time. Huttner *et al*. [13] have collected 8 recent RCTs comparing CPD vs PPPD which included 512 participants with periampullary or pancreatic carcinoma and found no relevant differences in mortality, morbidity, and survival between the two operations, but less operative time and blood loss with higher incidence of DGE in PPPD. In the RCTs of Taher *et al*. [14], the PPPD group required fewer blood transfusions and shorter hospital stay, with similar morbidity compared to CPD, There was one case of postoperative death in the CPD group while no mortality occurred in PPPD group, which led to his conclusion that PPPD procedure was a more effective treatment for

periampullary carcinoma and cancer of the pancreatic head region than the standard Whipple's operation. In our study, we also found that the intraoperative blood loss of PPPD group was lower than that of the CPD group (622.5 ± 506.7 ml vs 433.3 ± 169.0 ml, p = 0.011), yet there was no statistical significance between two groups from the perspective of operative time (364.3 ± 69.3 min vs 362.7 ± 84.5 min, p = 0.903).

However, some groups advocate that CPD is superior, citing similar nutritional status between PPPD and CPD, and argue that the bad effects of DGE outweigh the benefits of shorter operative time and less blood loss [15, 16]. In Kawai *et al*.'s RCTs [17], 130 patients were randomized to preservation of the pylorus ring (PPPD) or to resection of the pylorus ring with preservation of nearly the entire stomach (PRPD). The incidence of DGE in PRPD was significantly lower than that in PPPD (4.5% vs 17.2%), yet the quality of life, weight loss, and nutritional status were all similar during a 6-month follow-up period. It was then concluded that PRPD significantly reduced the incidence of DGE as compared to PPPD.

All the above studies did not distinguish between PG and PJ. In our separate study of PD with PG, the total complications of PPPD were higher than that of CPD (56.7% vs 34.7%). The incidence rate of DGE in PPPD was higher than that of CPD (13.7% vs 9.9%), but no significant differences were indicated. Oida modified gastrointestinal anastomosis to cases of PD with PG, although SSPPD was observed to have less DGE, but no difference was made as regards to postoperative complications between SSPPD and PPPD [18]. We also noticed that the occurrence rate of POPF in PPPD was higher than that of CPD (29.4% vs 11.9%). It might be due to increased introgastric pressure from pylorus preservation, leading to PG leakage. The mechanism is unclear and still needs to be proved by animal experiments and RCTs. Some scholars believe that DGE is not caused by pylorus preservation but instead by other complications related to POPF [19-21]. Others hold the view that DGE almost exclusively occurs as a consequence of other postoperative complications, which are the most important factor associated with DGE. Therefore, the incidence of DGE could not be simply concluded as the consequence of preserving pylorus, creating a chicken-and-egg conundrum.

Conclusion

There has been no evidence from previous studies to indicate the overwhelming superiority of PPPD over CPD. However, in our retrospective study, preserving pylorus in PG significantly increased the postoperative complications, especially POPF. Therefore, we recommend against performing PG in cases of PPPD. In the future, analyses of long-term survival from multicenter and prospective studies can help to validate the optimal techniques for PD and pancreaticoenteric reconstruction.

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Disclosure of conflict of interest

None.

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