World J Surg (2017) 41:552–558
DOI 10.1007/s00268-016-3729-1

ORIGINAL SCIENTIFIC REPORT

Surgical Strategy and Outcome in Patients Undergoing Pancreaticoduodenectomy After Gastric Resection: A Three-Center Experience with 39 Patients

Dooin Lee[1] · Jae Hoon Lee[2] · Dongho Choi[1] · Chang Moo Kang[3] · Jae Uk Chong[3] · Song-Chul Kim[2] · Kyeong Geun Lee[1,4]

Published online: 11 October 2016

Abstract

Background Stomach cancer is the second most commonly diagnosed cancer in Korea. Although the long-term survival outcome has improved, secondary primary tumors from periampullary regions are increasing inevitably and pancreaticoduodenectomy (PD) following gastrectomy is challenging. This study evaluates the surgical outcomes of PD following gastrectomy and suggests the optimum method for reconstruction.

Methods Patients who underwent curative PD with a history of gastric resection between 2005 and 2015 were assessed retrospectively. PD was performed according to the standard fashion, with the aim of creating a new pancreaticobiliary limb with sufficient length (40–50 cm). Different reconstructive methods were employed during PD according to the previous gastrectomy type.

Results A total of 3064 patients underwent PD, 39 of whom had previous gastrectomies including 12 with Billroth I gastrectomy, 20 with Billroth II gastrectomy, and seven patients with total gastrectomy (TG). In patients with Billroth I gastrectomy, all of the previous gastroduodenostomy site was resected for specimen retrieval. All previous esophagojejunostomy site was preserved in seven patients who had TG. In the Billroth II patients, the gastrojejunostomy site was preserved in 17 patients. Re-operation after PD was required in two patients, and 14 patients (36 %) developed pancreatic fistula and five (13 %) of grade B or higher.

Conclusions Our study has been the largest report so far of PD following gastric resection, and we were able to confirm the safety and the feasibility of PD procedure. We therefore suggest standardizing the reconstruction method for PD following gastrectomy based on the type of previous gastrectomy.

Introduction

Despite the fact that the incidence of stomach cancer is decreasing in Eastern and Western countries, it is still the fourth most common cancer in population worldwide and

Dooin Lee and Jae Hoon Lee have contributed equally to this work.

Electronic supplementary material The online version of this article (doi:10.1007/s00268-016-3729-1) contains supplementary material, which is available to authorized users.

✉ Kyeong Geun Lee
hepafel@hanyang.ac.kr

[1] Division of Hepatobiliary and Pancreas Surgery, Department of Surgery, Hanyang University College of Medicine, Seoul, Republic of Korea

[2] Division of Hepatobiliary and Pancreas Surgery, Department of Surgery, Asan Medical Center, Seoul, Republic of Korea

[3] Division of Hepatobiliary and Pancreas, Department of Surgery, Yonsei University College of Medicine, Seoul, Republic of Korea

[4] Department of Surgery, Hanyang Medical Center, Hanyang University School of Medicine, 222 Wangsimni-ro, Seongdong-gu, Seoul, Republic of Korea

second most commonly diagnosed cancer in Korea [1–3]. According to the cancer statistics in Korea, stomach cancer is the most leading primary cancer site in males [2, 3]. However, the number of reasons such as early screening program detection, development of adjuvant chemotherapy, and improved surgical technique has resulted in increased survival of gastric cancer patients [2]. And also second primary cancers after gastric surgery are increasing inevitably [4]. A single center in Korea previously reported an increase in certain second primary malignancies after primary gastric cancer [5]. An increasing incidence of second primary pancreatic cancers was also reported in a 23-year follow-up study [6].

Although patients undergoing pancreaticoduodenectomy (PD) after gastric surgery are relatively rare in Western countries, hepatobiliary and pancreas surgeons in the East, particularly Korea and Japan, often encounter such patients in surgical practice. With high rates of morbidity and mortality in the past [7], PD following gastric surgery has been considered as a challenging task due to various types of gastrointestinal anastomosis, complicated anatomy, and severe adhesions. Although several studies have discussed reconstruction strategies and surgical considerations in case reports [8–11], to the best of our knowledge, there is no general consensus on the most successful PD reconstruction method in patients who have undergone previous gastric surgery. This study was designed to evaluate the surgical outcomes of patients undergoing PD after gastric resection and to suggest the optimal reconstruction method depending on the type of gastrectomy previously performed.

Patients and methods

Patients

Patients who underwent curative PD between January 2005 and March 2015 at three tertiary university-affiliated hospitals were selected from a retrospective PD database. Among total of 3064 patients who underwent PD for periampullary cancers (pancreas, biliary, ampullary, duodenal), IPMN, pancreatitis, and periampullary lesions not amendable to local resection, 39 patients who had previously undergone gastric resection with reconstruction were included in this study. Patients with other synchronous or metachronous cancers or having histories of primary closure of the stomach due to ulcer perforation or trauma were excluded. Thirty-one out of 39 patients had radical gastrectomy due to stomach cancer, and 8 patients underwent gastrectomy due to ulcer perforation. The type of gastrectomy in 39 patients was comprised of 12 Billroth I gastrectomy, 20 Billroth II gastrectomy, and seven total gastrectomy with esophagojejunostomy. There was no patient who underwent Roux-en-Y subtotal gastrectomy in our PD database. This study was approved and overseen by the institutional review boards of each participating hospital and conformed to the ethical guidelines of the Declaration of Helsinki, and informed consent was waived.

Surgical procedures

All surgical procedures were performed by a team of specialized hepato-pancreas-biliary surgeons with over 10 years of experience in each hospital. The operation began with midline or bilateral subcostal laparotomy incision, and prophylactic antibiotics were administered. The abdomen was inspected for signs of metastatic disease, determination of resectability, and confirmation of previous type of gastrointestinal reconstruction. As standard PD fashion [12], removal of extrahepatic biliary tract and pancreatic head portion were performed from lateral aspect of the mesenteric-portal vein axis. Frozen section was performed at the transected remnant pancreas margin and proximal common bile duct margin in most of the patients. Pancreatic anastomosis was performed by duct-to-mucosa or one-layer [13] end-to-side pancreaticojejunostomy with either internal or external [14] drainage in the supracolic compartment. Based on the principle of creating new pancreaticobiliary limb with a sufficient length (40–50 cm), different reconstructive methods were applied during PD according to the previous gastrectomy type.

Postoperative complications

Postoperative data on complications and mortality were collected during the hospital stay and up to 30 days postoperatively, which were ranked in accordance with Clavien–Dindo classification (CDC) [15]. Based on CDC, major complication and minor complication were defined as $\geq$grade III and $\leq$grade II, respectively. Postoperative complications included pancreatic fistula (PF), postpancreatectomy hemorrhage (PPH), delayed gastric emptying (DGE), bile leakage, cholangitis, intra-abdominal abscess, wound problems, and other general complications. PF, PPH, and DGE were diagnosed and graded according to the definition of the International Study Group of Pancreatic Fistula and International Study Group of Pancreatic Surgery [16–18].

Statistical analysis

SPSS version 18.0 (SPSS Inc., Chicago, Illinois, USA) was used for the statistical analyses. Quantitative variables are reported as mean $\pm$ standard deviation and qualitative variables as percentages. The Chi-square test, Fisher's exact test, the independent Student's *t* test, and Mann–

Whitney test were used for comparisons between groups. Data were considered statistically significant at $p \leq 0.05$.

Results

Patient demographics

Between 2005 and 2015, among total of 3064 patients who underwent PD at three tertiary medical centers in Korea, thirty-nine patients who had undergone gastric resection prior to PD were identified. The demographic data including postoperative pathological diagnosis are listed in Table 1. There were 29 men (74 %) and 10 women (26 %) with a mean age of 67.7 years (range 46–82 years) at the time of undergoing PD. The interval between gastrectomy and PD was an average of 161.5 months (range 5–492 months), and mean operation time was 429 min. The previous types of gastrectomy were as follows: subtotal Billroth I ($n = 12$, 31 %); subtotal Billroth II ($n = 20$, 51 %); and total gastrectomy ($n = 7$, 18 %). After PD, 17 out of 39 (43 %) patients were pathologically confirmed as ductal adenocarcinoma, six patients were confirmed as duodenal carcinoma (15 %), and six were confirmed as intra-ductal papillary mucinous neoplasm (IPMN) (15 %); the remaining histopathologies are listed in Table 1.

Table 1 Characteristics of patients undergoing PD after gastrectomy

	All patients ($n = 39$) n (%)
Gender	
Male	29 (74 %)
Female	10 (26 %)
Age (years, mean ± SD)	67.7 ± 9.0
BMI	20.79 ± 3.57
Comorbidity	
Diabetes mellitus	7 (18 %)
Hypertension	10 (26 %)
Pulmonary tuberculosis	3 (8 %)
COPD	4 (10 %)
Coronary artery disease	3 (8 %)
Previous gastrectomy type	
Subtotal Billroth I	12 (31 %)
Subtotal Billroth II	20 (51 %)
TG	7 (18 %)
Operation interval (months)	161.5 ± 144.5
Operation time (min)	429.2 ± 124.9
Histopathology after PD	
Ductal adenocarcinoma	17 (43 %)
Ampullary carcinoma	3 (8 %)
Bile duct carcinoma	5 (13 %)
Duodenal carcinoma	6 (15 %)
IPMN	6 (15 %)
Neuroendocrine	1 (3 %)
Chronic pancreatitis	1 (3 %)
Hospital days	24.85 ± 12.8
Postoperative days	18.5 ± 9.7

BMI body mass index, *COPD* chronic obstructive pulmonary disease, *IPMN* intra-ductal papillary mucinous neoplasm, *PD* pancreaticoduodenectomy, *TG* total gastrectomy

Operative reconstruction

Reconstruction methods during PD differed according to the type of previous gastrectomy. In patients with previous Billroth I gastrectomy ($n = 12$, 31 %), all of the previous gastroduodenostomy site was resected for specimen retrieval (Fig. 1a). In the patients with previous Billroth II gastrectomy ($n = 20$, 51 %), 17 of 20 patients had reconstruction that preserved the gastrojejunostomy (GJ) site; the A-loop was resected immediately upward to the GJ site and completely removed with the specimen (Fig. 1b). Instead of using the remnant portion of the A-loop, a new pancreaticobiliary jejunal limb was reconstructed with a sufficient length (40–50 cm) using the distal jejunum, which was transected approximately 10–15 cm distal to the previous jejunojejunostomy (JJ) site. Three patients with previous Billroth II gastrectomy had to undergo resection. In contrast, in the seven (18 %) patients who had previous TG, all previous esophagojejunostomy (EJ) sites were preserved; the JJ site was divided and the afferent limb removed with the specimen, and then, a new pancreaticobiliary jejunal limb was reconstructed of sufficient length (40–50 cm) by transecting a distal portion of the previous JJ site (Fig. 1c).

Postoperative complications

Postoperative morbidity of the 39 patients, as defined by the CDC, is summarized in Table 2; 24 patients (62 %) had one or more adverse events. Minor complications were recorded in 19 (49 %) patients and major complications developed in five (13 %). Three (8 %) patients recorded as CDC grade IIIa required percutaneous drainage due to intra-abdominal abscesses or persistent ascites. Re-operation (CDC grade IIIb) was required in two (5 %) patients, one who had transverse colon resection during PD and underwent re-operation due to disruption at the anastomosis site, and the other who needed re-exploration due to postoperative bleeding. Postoperative complications of the PD after gastrectomy group and overall PD group are summarized in Table 2. In PD gastrectomy group, fourteen patients (36 %) developed a pancreatic fistula (PF)

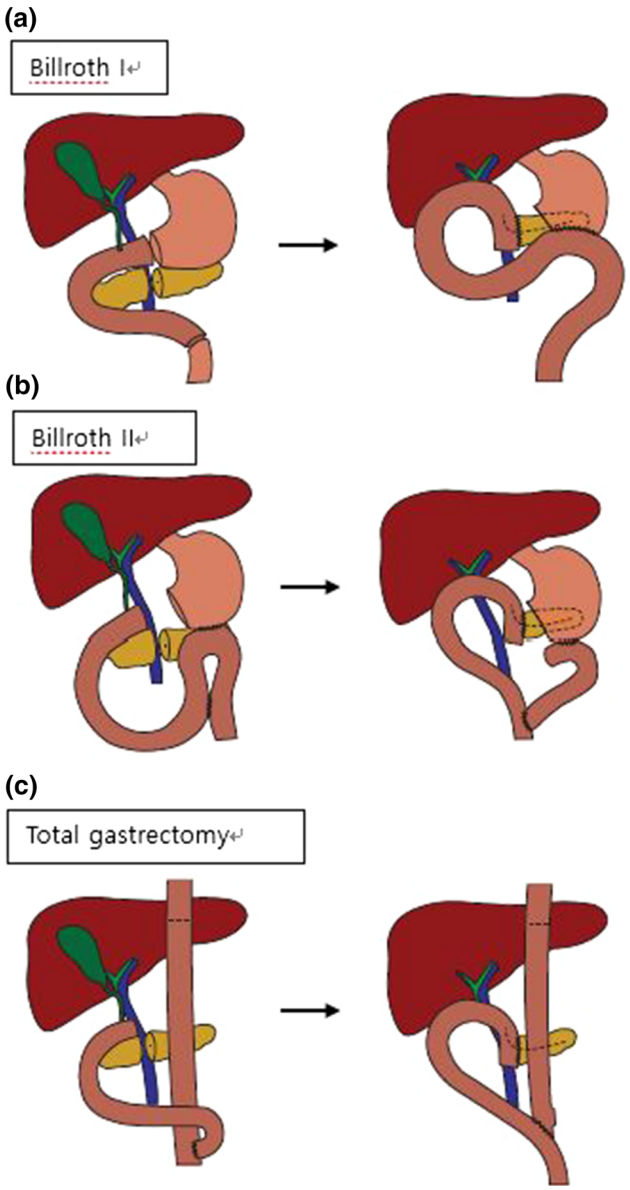

Fig. 1 Schematic configuration of PD following previous gastrectomy. **a** Following Billroth I gastrectomy. **b** Following Billroth II gastrectomy. **c** Following total gastrectomy

according to the International Study Group of Pancreatic Fistula definition. Four patients (10 %) experienced a grade B PF and one patient who experienced transverse colon anastomosis site disruption suffered a grade C PF. The overall frequencies of DGE and PPH were 15 % (6 of 39) and 10 % (4 of 39), respectively (Table 2). One patient suffered recurrent cholangitis during the postoperative period and ultimately underwent re-operation due to afferent loop (A-loop) syndrome.

Table 2 Postoperative complications among PD after gastrectomy group and overall PD group

Adverse event	PD after gastrectomy ($n = 39$) *N* (%)	Overall PD ($n = 3064$) *N* (%)
One or more complication	24 (62 %)	1462 (48 %)
CDC grade		
I–II	19 (49 %)	1093 (36 %)
IIIa	3 (8 %)	158 (5 %)
IIIb	2 (5 %)	93 (3 %)
IV	0 (0)	72 (2 %)
V	0 (0)	46 (1.5 %)
Major complication (≥CDC grade IIIa)	5 (13 %)	369 (12 %)
Mortality	0 (0)	46 (1.5 %)
PF	14 (36 %)	1172 (38 %)
Grade A	9 (23 %)	854 (28 %)
Grade B	4 (10 %)	241 (8 %)
Grade C	1 (3 %)	77 (3 %)
DGE	6 (15 %)	388 (13 %)
PPH	4 (10 %)	267 (9 %)
Grade A	1 (3 %)	172 (6 %)
Grade B	2 (5 %)	75 (2 %)
Grade C	1 (3 %)	20 (1 %)
Bile leakage	2 (5 %)	114 (4 %)
Intra-abdominal abscess	4 (10 %)	231 (8 %)
Wound infection	3 (8 %)	279 (9 %)
Chylous ascites	2 (5 %)	64 (2 %)
Cholangitis	1 (3 %)	122 (4 %)
Postoperative death	0 (0)	46 (1.5 %)
Others	7 (18 %)	351 (11 %)

CDC Clavien–Dindo classification, *DGE* delayed gastric emptying, *PD* pancreaticoduodenectomy, *PF* pancreatic fistula, *PPH* postpancreatectomy hemorrhage

Gastric cancer versus gastric ulcer

Among the 39 patients who underwent PD following previous gastric resection, 31 (79 %) had undergone gastrectomy due to stomach cancer and eight (21 %) due to ulcer perforation (Table 3). The mean number of lymph nodes harvested during PD in the previous gastric cancer group (pGC) was 11.8 ± 9.1, somewhat lower than in the previous gastric ulcer group (pGU; 19.9 ± 6.3; $p = 0.023$). The interval between gastrectomy and PD was significantly higher in the pGU group than in the pGC group (342.38 vs 114.84 months, $p < 0.001$). The estimated blood loss during PD was higher in the pGC group ($p = 0.024$), and the mean operation time was also longer ($p = 0.304$) (Table 3).

Table 3 Comparison of PD results in patients undergoing gastrectomy for previous gastric cancer and previous gastric ulcer

	pGC $n = 31$ (79 %)	pGU $n = 8$ (21 %)	p value
Operation interval (m)	114.84 ± 108.4	342.38 ± 126.6	<0.001
No. of lymph nodes harvested during PD	11.8 ± 9.1	19.9 ± 6.3	0.023
Estimated blood loss (ml)	574 ± 554	275 ± 217	0.024
Operation time (min)	437 ± 133	397 ± 82	0.304

PD pancreaticoduodenectomy, *pGC* previous gastrectomy due to gastric cancer, *pGU* previous gastrectomy due to gastric ulcer

Survival

The median cumulative survival after PD was 44.0 months (average 53.2, range 10–87) in 31 patients who previously had gastric cancer (Fig. 2). Until March 2015, of the 31 patients, seventeen (55 %) have survived. Eight patients (26 %) lived for >3 years and two (6 %) of them lived for >5 years after PD. Five-year survival rate was 43.9 % in patients with previous gastric cancer and 28.8 % in overall PD patients without previous gastric cancer ($n = 3025$).

Discussion

In the current era of increased survival rates for stomach cancer, the number of patients undergoing PD due to second primary malignancy is increasing [19], and surgical resection remains the only potentially curative option for these patients. Although PD following gastrectomy is generally considered both complicated and challenging, high-volume hospitals are encountering a growing number of patients who require this procedure. Several previous reports have described cases of PD following gastrectomy in small series and have suggest optimal reconstruction strategies [8–11], but, to the best of our knowledge, this current multicenter study of 39 patients, including diverse types of previous gastrectomy (Billroth I, Billroth II, and TG), is the most extensive study to date. Because PD is a complex procedure, this study was designed to standardize the reconstructive method that should be employed according to the previous type of gastrectomy.

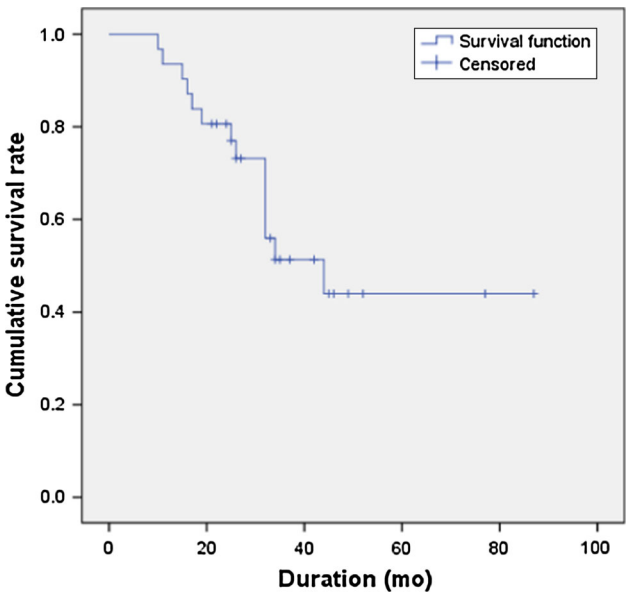

Fig. 2 Overall survival rates after PD followed by gastric cancer surgery

Bechi et al. [11] recently described seven cases of PD following partial gastrectomy (Billroth II and Roux-en-Y) and suggested creating a new pancreaticobiliary limb determined by the length of the A-loop. In patients with a long A-loop (50 cm), they suggested removing the proximal 10 cm of jejunum and using the long A-loop for a pancreaticojejunostomy (PJ) and hepaticojejunostomy (HJ). In the current study, however, 17 out of 20 patients with previous Billroth II gastrectomies had reconstructions that preserved the GJ site; instead of using the remnant portion, the A-loop was resected immediately upward to the GJ site and completely removed with the specimen (Fig. 1). The advantages of this procedure include performing PJ and HJ anastomosis without tension and preventing postoperative complications, such as PF and cholangitis. Only three patients with previous Billroth II gastrectomies underwent resection of the previous GJ site due to severe adhesions and inadequate specimen retrieval.

Yokoyama et al. [10] recently reported a case of A-loop syndrome occurring after PD in a patient who underwent TG. The A-loop syndrome with repeated cholangitis developed due to shortness of the pancreaticobiliary jejunal limb and was resolved by revision of the jejunal limb with sufficient length. In our study, 14 patients (35.8 %) developed PF and only five (12.8 %) had grade B or higher PF. One patient whose reconstruction used the same A-loop as previously used for PJ and HJ anastomosis recovered from postoperative cholangitis without undergoing re-operation.

Although all of the patients who underwent Billroth I gastrectomy ($n = 12$) inevitably underwent GD site resection for specimen retrieval, in the seven patients who underwent TG the EJ sites were all preserved. This procedure enabled the creation of a supracolic, retromesenteric pancreaticobiliary anastomosis of sufficient length and reduced tension. In addition, preserving the EJ anastomosis site resulted in a reduced operation time even in patients with severe adhesions.

All 39 patients who underwent PD after gastrectomy had acceptable rates of postoperative complications in our study. Compared with the overall PD patients, the rates of major complications, PF, DGE, and PPH were not significantly different (Table 2). Compared with the data [20–22] published by our participating institutions since 2000, the overall pancreatic fistula rate in this study was 36 versus 43.4 % [20] versus 38 % [22], and clinically significant PF (Grade B or C) was rated 13 versus 7.5 % [20] versus 17.1 % [22]. Only 15 % (6 of 39) experienced DGE (vs 7.2 % [20] and 33.3 % [22]) in our study, and no mortality was recorded within 12 months of surgery.

In this study, 5-year survival rate was 43.9 % in 31 patients who underwent PD after gastric cancer surgery. Compared with overall PD patients without previous gastric cancer (28.8 % 5-year survival rate), our study showed favorable result in survival outcome. However, statistical comparison with large number of patients would be necessary for further evaluation.

The operation interval between gastrectomy and PD was significantly shorter in the previous pGC group than in the previous gastric ulcer pGU group. The pGU group had more harvested lymph nodes and less estimated bleeding during PD. As the focus on early detection of second primary cancers has intensified in recent years [23], careful follow-up is increasingly important for even longer than 5 years after gastrectomy.

Although this study is the most comprehensive to date, it has several limitations. First, the data were collected retrospectively from three institutions, and the sample was small. However, as the numbers of patients undergoing PD after gastrectomy are very low, combining data from three high-volume hospitals provided an adequate sample size for meaningful analyses. Second, the long-term outcomes of patients who underwent PD after gastrectomy were not sufficiently analyzed. Because the number of patients undergoing PD after gastrectomy is very low, it is very difficult to obtain prognostic data prospectively, and our study focused instead on the complex surgical procedures and perioperative outcomes.

In conclusion, this multicenter study describes the largest number so far of patients undergoing PD after gastrectomy, and we were able to confirm the safety and feasibility of the PD procedure with different reconstruction procedures depending on the type of previous gastrectomy. We therefore suggest standardizing reconstructive strategy for PD in patients who have had a previous gastrectomy according to the type of gastrectomy.

Compliance with ethical standards

Conflict of interest Dooin Lee, Jae Hoon Lee, Dongho Choi, Chang Moo Kang, Jae Uk Chong, Song-Chul Kim, and Kyeong Geun Lee declare that they have no conflict of interest or financial ties to disclose.

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