

ORIGINAL RESEARCH ARTICLE

Colorectal surgery in patients with prior pancreaticoduodenectomy

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Abstract:

Objectives: Colorectal cancer (CRC) surgery after pancreaticoduodenectomy (PD) is difficult to perform, because PD involves dissection and complex reconstruction of the digestive tract. We evaluated the clinical outcomes of CRC surgery in patients with prior PD. **Methods:** Between January 2008 and March 2018, a total of 1727 patients received CRC surgery at our institution. Of these, 10 had previously undergone PD (PD group). As a control group, 280 patients were collected who had undergone resection without any history of previous abdominal surgery. The PD and control groups were further subdivided into four groups by right or left side. Outcomes of colorectal surgery were investigated in the PD and control groups. **Results:** The number of harvested lymph nodes was significantly lower in the PD group. In the right colectomy group, distance from the surgical margin was significantly shorter in the PD group. The rate of postoperative complications was higher in the PD group. Peritoneal dissemination originating from pancreatic cancer was found during CRC surgery for one patient, and one patient developed refractory ascites. Three patients died of pancreatic cancer, rectal cancer, and other disease. Seven patients were alive without recurrence. **Conclusions:** CRC surgery for patients with prior PD can involve difficulty in dissecting lymph nodes and higher postoperative morbidity rates but can provide sufficiently curative resection for CRC.

Keywords:

colorectal cancer, pancreaticoduodenectomy, dissecting lymph node

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Introduction

Previous abdominal surgery causes intraperitoneal adhesions, with a frequency of 75%-93%^{1,2)}. Therefore, in colorectal cancer (CRC) surgery, previous abdominal surgery is one factor that makes surgery difficult, particularly in laparoscopic surgery^{1,3)}. However, several studies have now reported that even laparoscopic surgery for patients who have undergone abdominal laparotomy can be performed safely and without affecting short-term postoperative outcomes^{2,4-7)}. At the same time, almost no reports of CRC surgery for patients who previously underwent pancreaticoduodenectomy (PD) with extensive dissection and complex reconstruction

of the digestive tract, sometimes with combined resection of the portal vein (PV), describe clinical outcomes after either laparotomy or laparoscopic surgery. PD is performed less often than gastrectomy or colectomy. Furthermore, patients who undergo PD often show poor prognosis, the worst being associated with cancer of the pancreatic head, which has a 5-year survival rate of 5.7%⁸⁾. For these reasons, CRC surgery is rarely considered for patients who have undergone PD surgery. With advances in multidisciplinary therapy, today the 5-year survival rate for resectable pancreatic cancer has reached 57%⁹⁾, so the number of CRC surgeries in a patient with prior PD may increase in the future. However, in addition to the safety issues and complications of CRC sur-

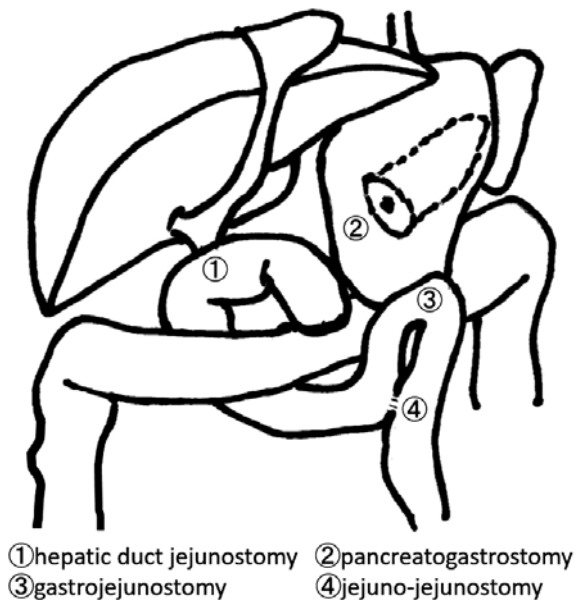


Figure 1. Schema of the reconstruction with digestive tract after PD.

gery, many clinical questions remain regarding whether essential surgical techniques such as complete mesocolic excision (CME) and central vascular ligation (CVL)¹⁰ can actually be performed after PD. Therefore, we designed this retrospective study to evaluate the outcomes of colorectal surgery in patients with prior PD.

Methods

This retrospective case-control study was conducted at a single center. We obtained approval from the Ethics Committee, Osaka International Cancer Institute (No. 18033).

We reviewed the medical records of 1727 patients who received primary CRC surgery between January 2008 and March 2018 at our institute in Osaka, Japan. Of the 1727 patients, 10 had previously undergone PD (PD group), and 1237 patients had undergone resection for CRC by the same surgical procedure as the PD group. Patients were excluded from the study when there was: 1) a history of previous abdominal surgery, 2) laparoscopic surgery, 3) a history of neoadjuvant chemotherapy or radiotherapy, or 4) CRC surgery with simultaneous or combined resection, including dissection of the para-aortic lymph nodes and lateral pelvic lymph nodes. The control group comprised 280 patients.

Surgical procedures were categorized as PD, ileocecal resection (ICR), right hemicolectomy (RHC), transverse colectomy (TC), sigmoidectomy, anterior resection (AR), low anterior resection (LAR), and abdominoperineal resection (APR).

PD was performed with gastrointestinal reconstruction in the form of hepatic duct jejunostomy, gastrojejunostomy,

pancreatogastrostomy, or jejunio-jejunostomy; if necessary, the PV was resected together with the pancreas at our institution (Figure 1)^{9,11}. ICR, RHC, TC, and sigmoidectomy were defined as tumor-specific CME and CVL (CME/CVL)¹². Procedures for performing tumor-specific mesenteric excision (TSME)¹³ were defined as AR when the anastomosis was located above the peritoneal reflection, and as LAR when the anastomosis was located below the peritoneal reflection.

CRC surgery was categorized as right colectomy (ICR, RHC, and TC) or left group (sigmoidectomy, AR, LAR, APR). Both PD and control groups were subdivided into a total of four groups according to right or left group (Figure 2).

The clinical features of patients including background of PD, age, gender, body mass index (BMI), tumor location, and Union for International Cancer Control (UICC) TNM stage were collected. Surgical outcomes were also reviewed including surgical procedure, operative time, volume of blood loss, number of lymph nodes harvested, the extent of lymph node dissection¹⁴, minimum resection margin of colon in the right group, postoperative complications, Clavien-Dindo classification¹⁵, and the duration of postoperative hospital stay. These data were compared between PD and control groups as well as between subgroups (PD right colectomy group, control right colectomy group, PD left group, and control left group).

Statistical analysis

Data are presented as medians and ranges. Differences between groups were analyzed using the χ^2 test, Fisher's exact test, and the Wilcoxon signed-rank test. Values of $p < 0.05$ were considered statistically significant. Statistical analyses were performed using JMP version 8.0.2 software (SAS Institute, Cary, NC).

Results

The profiles of 10 patients who underwent PD are summarized in Table 1. The most common disease for which PD was performed was cancer of the pancreatic head. PD and portal vein resection (PVR) were performed in three patients (30%). The Roux-en-Y limb was brought up retrocolically in all patients. In five patients (50%), CRC surgery was performed within 5 years after PD. Preoperative chemoradiation therapy for pancreatic cancer was performed in four patients. Table 2 summarizes demographic characteristics of the patients in the two groups. BMI was significantly lower in the PD group than in the control group, and significant between-group differences were observed in the distribution of pathological stages. Surgical outcomes in each subgroup are shown (Table 3, 4). In the right colectomy group, no

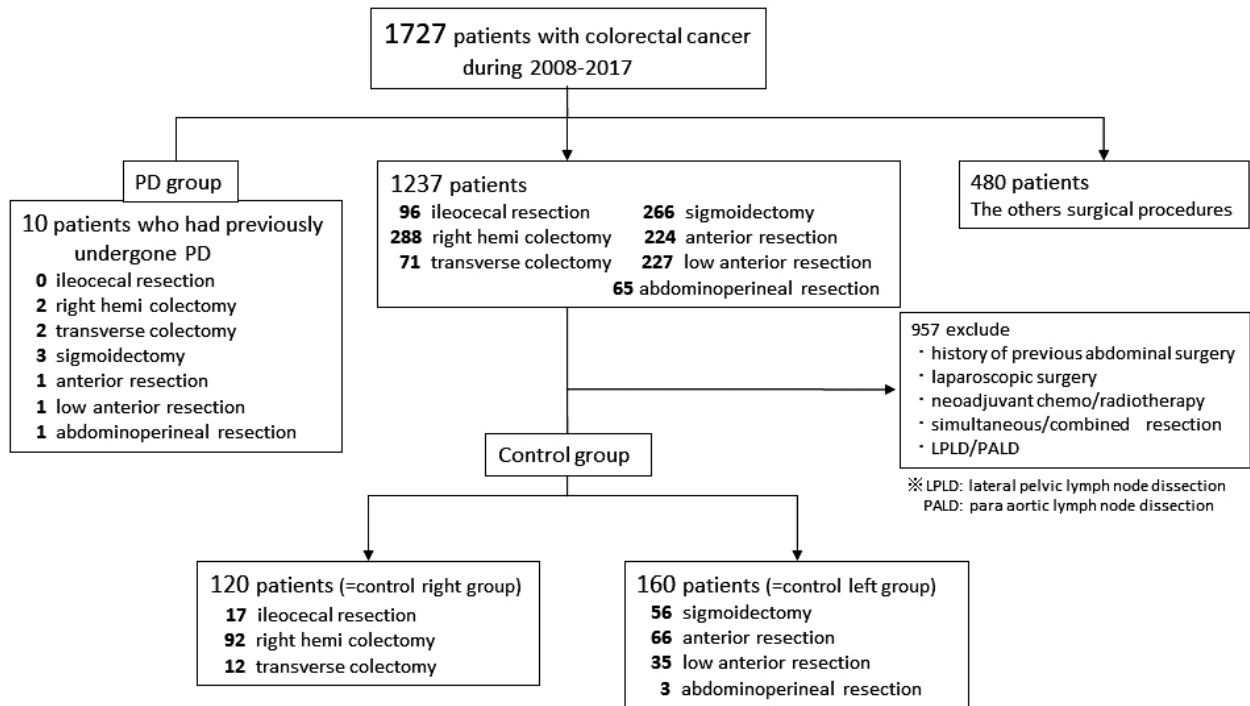


Figure 2. Study design.

Table 1. Background Characteristics of the PD Group.

	n = 10
Primary tumor	
pancreatic head cancer	5
duodenal papilla cancer	2
duodenal cancer	1
intraductal papillary mucinous carcinoma	1
pancreatic neuroendocrine tumor	1
Preoperative CRT	
+	4
-	6
Procedure	
PD	7
PD + PVR	3
RY limb	
antecolic	0
retrocolic	10
Interval from PD to CRC surgery	
1-5 years	5
>5 years	5

※CRT = chemoradiotherapy
 ※PVR = portal vein resection
 ※RY = Roux-en-Y

Table 2. Patient Characteristics.

	PD group (n = 10)	Control group (n = 280)	P
Age	73 (35-84)	66 (31-90)	0.191
Sex (male/female)	8:2	165:115	0.32
Body mass index	19.5 (15.2-21.1)	22.1 (15.2-38.7)	0.0016
Tumor location	Number (%)		
cecum	-	20 (7)	0.116
ascending	2 (20)	58 (21)	
transverse	2 (20)	42 (15)	
sigmoid	3 (30)	60 (21)	
rectum	3 (30)	100 (36)	
Pathological stage			
0	1 (10)	2 (0.7)	0.016
I	4 (40)	37 (13)	
II	1 (10)	85 (31)	
III	3 (30)	114 (41)	
IV	1 (10)	42 (15)	

significant differences in operation time and volume of blood loss were evident between PD right and control right groups. However, the minimum resection margin of colon and the number of harvested LNs were significantly less in the PD right group. D3 lymph node dissection was not performed in PD right group. Laparoscopic surgery was attempted for one patient in the PD right group but required conversion to laparotomy due to severe adhesions (Table 3).

Table 3. Surgical Outcomes in the Right Colectomy Group.

	PD right group (n = 4) n (%)	Control right group (n = 120) n (%)	P
Procedure			0.039
ileocecal resection	0	17 (13)	
right hemicolectomy	2 (50)	92 (77)	
transverse colectomy	2 (50)	12 (10)	
Laparoscopic surgery	1		
conversion to laparotomy	1 (100)		
Operating time (min)	155 (105-350)	130 (87-412)	0.223
Blood loss (ml)	145 (40-585)	177 (0-1015)	0.301
Minimum resection margin of colon (mm)	37.5 (15-130)	100 (50-250)	0.038
The extent of lymph node dissection			0.001
D1	3 (75)	5 (4)	
D2	1 (15)	18 (15)	
D3	0	97 (91)	
Harvested LNs	6 (5-12)	23.5 (4-95)	0.003
Pathological state			0.001
0	1	0	
I	1	18	
II	0	36	
III	3	42	
IV	0	24	

※The final four parameters are presented as median (range)

Table 4. Surgical Outcomes in the Left Group.

	PD left group (n = 6) n (%)	Control left group (n = 160) n (%)	P
Procedure			0.087
sigmoidectomy	3 (50)	56 (35)	
anterior resection	1 (16)	66 (41)	
low anterior resection	1 (16)	35 (22)	
abdominoperineal resection	1 (16)	3 (2)	
Laparoscopic surgery	2		
conversion to laparotomy	1 (50)		
Operating time (min)	197.5 (108-502)	211.5 (103-551)	0.723
Blood loss (ml)	147.5 (20-1210)	157.5 (0-2045)	0.517
The extent of lymph node dissection			0.001
D1	1 (17)	2 (1)	
D2	3 (50)	16 (10)	
D3	2 (33)	142 (89)	
Harvested LNs	10.5 (6-18)	17 (1-67)	0.02
Pathological state			0.091
0	0	2	
I	3	19	
II	1	49	
III	1	72	
IV	1	18	

※The final three parameters are presented as median (range)

Table 5. Postoperative Outcomes.

	PD group (n = 10) n (%)	Control group (n = 280) n (%)	P
Complication	5 (50)	44 (16)	0.03
anastomotic leakage	1 (10)	3 (1)	
intraabdominal abscess	3 (30)	6 (2)	
small bowel obstruction	-	11 (4)	
wound infection	-	16 (6)	
heart failure	1 (10)	-	
duodenal ulcer bleeding	-	1 (1)	
urinary tract infection	-	6 (2)	
pulmonary embolism	-	1 (1)	
Reoperation	2 (20)	4 (1)	0.001
Complication grade (\leq IIIb)	3 (30)	5 (2)	0.001
Postoperative hospital stay	11 (10-43)	14 (7-59)	0.5
Mortality	0	0	

※Complication grade = Clavian-Dindo classification of surgical complications

※Postoperative hospital stay is presented as median (range)

In the left group, only the number of harvested LNs differed significantly between PD left and control left groups. D3 lymph node dissection was performed only for two patients (Table 4). Laparoscopic surgery was achieved for one patient who underwent APR because few adhesions were present at the surgical site (50%, 1 of 2). In one patient who underwent PD due to cancer of the pancreatic head, peritoneal dissemination originating from pancreatic cancer was discovered during CRC surgery. Table 5 compares postoperative outcomes between PD and control groups. Three patients (30%, 3 of 10) showed complication at grade IIIb or higher in the Clavian-Dindo classification. Reoperation was performed for two patients with anastomotic leakage after LAR and intraabdominal abscess after TC. Especially, after TC, intraabdominal abscess developed in all cases (100%, 2 of 2). The complication rate was significantly higher in the PD group than in the control group, but no differences were observed in the length of hospital stay.

One patient who received PD+PVR for cancer of the pancreatic head and developed PV stenosis at the point of PV reconstruction postoperatively underwent RHC. After surgery, a large amount of ascites appeared without recurrence, and medication was necessary for a while. In the PD group, median follow-up was 16.8 months (range, 3.8-116.9 months) after CRC surgery. One patient with peritoneal dissemination found during CRC surgery died of pancreatic cancer, another died of rectal cancer with synchronous liver metastases, and the last one died of other disease. Seven patients remained alive without recurrence.

Discussion

This study was conducted to evaluate the clinical outcomes of CRC surgery among patients with prior PD. The results showed that this procedure involves an increase in the difficulty of dissecting lymph nodes and postoperative morbidity rate, but also demonstrated the possibility of curative resection for CRC. We experienced two cases that may have represented specific situations after PD surgery. These findings support strategies for patients with CRC after PD.

Our study showed that the number of harvested LNs was significantly lower in the PD group than in the control group. Moreover, in the subdivided right colectomy group, the minimum resection margin of the colon was also significantly shorter and D3 lymph node dissection was not performed. These findings indicated that complete CME/CVL in the right colectomy group was difficult to perform after PD. In our study in particular, the Roux-en-Y limb was brought up retrocolically in all patients, which leads to very difficult dissection around the transverse colon, and this was also one of the causes of incomplete CME/CVL. Although some reports have shown that right colectomy was unaffected by open surgery^{4,7)}, right colectomy with CME/CVL after PD was still difficult to perform because of extensive dissection mainly around the SMV and reconstruction of the digestive tract which should not be damaged.

Because the surgical sites differed, most patients in the PD left group showed few adhesions in the lower abdomen. However, in the PD group the number of harvested LNs was also significantly lower and D3 lymph node dissection was performed only for 33%. This finding showed that performing CME/CVL with ligation of the root of inferior mesen-

teric artery (IMA) might still be difficult because of adhesions around the extent IMA, and incomplete CME/CVL led to the smaller number of dissecting LNs also in the PD left group.

We expected that the operation time would be longer, and the amount of blood loss would be increased in the PD group; however, no differences in either characteristic were observed between the PD and control groups in this study. BMI was lower in the PD group, which might have contributed to the short operation time. Incomplete CME/CVL might also have led to shorter operation times and reduced blood loss. In terms of the possibility of laparoscopic surgery, one patient (33%, 1 of 3) underwent laparoscopic APR without conversion to laparotomy. Although the indications for laparoscopic surgery for colon cancer are limited, laparoscopic surgery may be worth a try for rectal cancer.

We also showed that the rate of postoperative complications was significantly higher in the PD group, and in particular, after TC which was most affected by PD, intra-abdominal abscess developed in all cases. While Ikeda⁴⁾ showed the feasibility of right colectomy after gastrectomy, our results indicated that CRC surgery after PD remained difficult because of the presence of severe adhesions and troublesome reconstruction of the digestive tract, and the safety of this procedure has not been established. So, to prevent complications in CRC surgery after PD, we should perform CRC surgery more carefully recognizing the potential of postoperative complications.

Although two patients (20%, 2 of 10) who had distant metastases at the time of CRC surgery died of pancreatic cancer and CRC, respectively, seven patients remained alive without recurrence. These results showed that CRC surgery may allow curative resection in the patient with prior PD without distant metastasis.

We also experienced two cases that may have represented specific situations after PD surgery. One case at 21 months after PD involved peritoneal dissemination from pancreatic cancer found during CRC surgery. We did not expect any recurrences and could not detect disseminations in preoperative examinations. The other case involved the appearance of large amount of ascites after CRC surgery. This patient received PD+PVR for cancer of the pancreatic head and developed PV stenosis at the point of PV reconstruction postoperatively. However, no ascites was observed before CRC surgery, possibly because of the development of collateral circulation around the SMV^{16,17)}. The patient developed refractory ascites after CRC surgery, which might have been induced by the dissection of collateral vessels during CRC surgery. These rare findings represent valuable information for future CRC surgery after PD.

Some limitations must be considered when interpreting the results of this study. First, this study was a single center, retrospective analysis. Second, this study involved a small

number of patients. Third, selection bias was present in the control groups. In recent years, laparotomies have mostly been performed for advanced-stage CRC, because laparoscopic surgeries have typically been performed for early-stage CRC. The control group thus contained more cases of advanced-stage CRC, which may have influenced the background characteristics of patients.

In summary, although CRC surgery for patients with prior PD involved difficulty with dissecting lymph nodes, a higher postoperative morbidity rate, and some unexpected situations, curative resection is possible for CRC without distant metastasis.

Conflicts of Interest

There are no conflicts of interest.

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