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Pancreaticoduodenectomy With Total Meso-Pancreatoduodenum Excision for Periampullary Carcinoma

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Pancreaticoduodenectomy（PD）is the only curative treatment for periampullary carcinomas, including the ampulla of Vater, the distal common bile duct, and the pancreas. Because positive resection margin and insufficient lymph node dissection around the superior mesenteric artery（SMA）result in a dismal outcome, we devised a new surgical technique called "total meso-pancreatoduodenum excision（tMPDe）" when performing a PD. Between June 2009 and July 2011, 24 consecutive patients with periampullary carcinoma underwent PD with tMPDe and the surgical outcomes were evaluated. Cancer-free resection was achieved in all patients, except for one with R1 in the retropancreatic tissue. Lymph node metastasis around the SMA was found in 5 patients（21%）, while no locoregional recurrence was recognized during a median follow-up period of 18.2 months. From the results, it was found that PD performed with tMPDe is the most effective surgical-oncological treatment for patients with periampullary carcinoma.

Key words: Pancreaticoduodenectomy; Pancreas cancer; Periampullary carcinoma; Meso-pancreatoduodenum; R0 resection.

INTRODUCTION

Periampullary carcinoma（PAC）, arising in the ampulla of Vater, the distal common bile duct, or the head of the pancreas, is one of the most dismal neoplasms among the various gastroenterological malignancies, and pancreaticoduodenectomy（PD）offers the only chance of a cure［1, 2］. However, most patients with PAC show tumor relapses within 5 years after PD［1-3］. Local recurrence is the most common after surgical resection［1-3］. Also, it is often identified when a resection margin is involved in cancer cells［4］.

The limbus of soft connective tissue between the superior mesenteric artery（SMA）and the region from the pancreas head to the uncinate process is the most frequent site for a positive resection margin（R1）in PACs following a PD［4-8］. Recently, Gockel *et al*.［5］identified this anatomical connective tissue structure as a "mesopancreas" and emphasized that complete resection of the mesopancreas was an effective therapy to reduce of R1 resection［6, 7］. On the other hand, the incidence of lymph node metastasis around the SMA is similar to that of the hepatoduodenal ligament in advanced PACs［9, 10］. Thus, local tumor control around the SMA is advocated as an important factor to improve the survival rates of the patients with PAC［4-8, 11］. However an extended lymphadenectomy in PACs shows no survival benefit［12］.

From these results, it is considered that both the excision of mesopancreas and circumferential lymphadenectomy of the root of the SMA are necessary for local tumor control in performing a PD for PACs. This article will describe a new surgical technique called a "total meso-pancreatoduodenum excision." It is a safe and drastic operative procedure in order to reduce R1 resection and postoperative locoregional recurrence.

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MATERIAL AND METHODS

The subjects of this study included 24 consecutive patients who underwent a PD with total mesopancreatoduodenum excision for PAC at our institute between June 2009 and July 2011. Preoperative examination with three-dimensional CT (3D-CT) angiography was performed in all patients to gain an understanding of the branching of the arteries (i.e., inferior pancreaticoduodenal artery, IPDA; first jejuna artery, FJA; and replaced right hepatic artery, rRHA) from the SMA to the head of the pancreas [13]. Patients diagnosed with direct tumor invasion to the SMA or extrapancreatic nerve plexus around the SMA on preoperative CT examination were excluded from this study.

Demographic data and perioperative outcomes of patients were evaluated. For accurate histological evaluation, surgical margins of the PD specimen were marked by the operative surgeon. After the formalin-fixed and paraffin-embedding procedure, the surgical specimens were assessed by two experienced pathologists. The margin status was defined as follows: no cancer cells are identified microscopically at any of the resection margin of the PD specimen (R0), microscopic tumor present at the margin (s) (R1), and gross residual tumor as determined by the surgeon at the time of surgery (R2). Follow-up data in each patient were collected retrospectively from the hospital electronic records. The study was approved by the institutional review board of the Shimane University Hospital. At the time of the start point of this study, the purpose of the present study was explained to each patient and their families and informed consent was obtained with document. Furthermore, adequate care was taken to protect the privacy of the individuals participating in the study. Each patient was informed of the present study's intent to not use the clinical data from this study for any purpose other than for present study.

SURGICAL TECHNIQUE

An upper midline incision under the umbilicus was made as a standard approach to obtain a good lateral exposure around the SMA. Abdominal cavity was explored to exclude liver and peritoneal metastasis. After lifting the transverse colon toward the cranial side and bringing the upper jejunum to the lower side, the retroperitoneum was opened on the left side of the duodenojejunal flexure, and the inferior vena cava, the left renal vein, and the abdominal aorta were then completely exposed on purpose to mobilize the pancreatic head and body together with the SMA from the retroperitoneum.

To approach the SMA, we made an incision in the jejunal mesentery along the FJA and the transverse mesentery along the middle colic artery (MCA). On the ventral side of the SMA, we started the left-side semicircle lymphadenectomy from the origin of the MCA up to the origin of the SMA in a longitudinal direction. In the process of this procedure, the origin of the common trunk of FJA and IPDA could be easily identified at the left posterior side of the SMA, and taping of these vessels were then carried out (Fig. 1A).

When performing a lymphadenectomy around the SMA, the layer that contains the plexus around the SMA (nerve plexus of the SMA; PLsma) should be preserved to prevent postoperative diarrhea [10, 14-16]. During the right-side semicircle lymphadenectomy, we secured the SMA outside the PLsma layer. Soft connective tissue around the SMA containing lymph nodes, the nerve plexus (PL) around the SMV, and the mesopancreas was dissected up to the origin of the SMA in a longitudinal direction, by pulling a tape of the SMA to the left side. In cases with an rRHA, our technique can secure this artery at the right side of the SMA without the need for the Kocher's maneuver. Moreover, if tumor involvement to the SMA is confirmed at this point, the PD procedure can be interrupted. After completion of circumferential lymphadenectomy, the IPDA and FJA were doubly ligated and divided. The mesopancreas and soft connective tissue around the SMA, including lymph nodes, comprise a part of the "meso-pancreatoduodenum" because they are fed by the IPDA and FJA, which form a common mesentery (Figs. 1B and 1C).

An *en block* lymphadenectomy in the hepatoduodenal ligament and along the common hepatic artery up to the celiac trunk was performed, and the gastroduodenal artery was doubly ligated and divided. The common hepatic duct was transected following

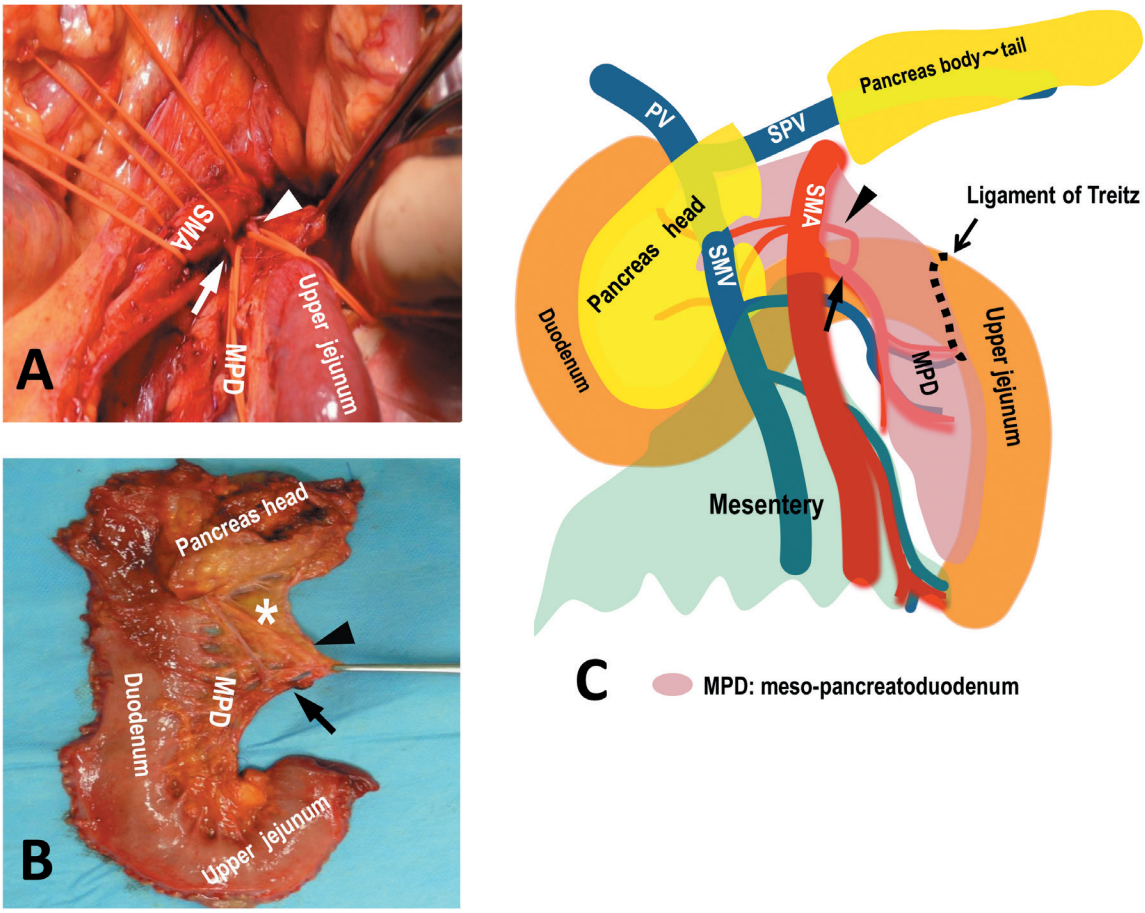

Fig. 1.

(A) An intraoperative view of the total meso-pancreatoduodenum excision.
On the left side of the SMA, the layer of PLsma is preserved, and the "meso-pancreatoduonem" is dissected up to the root of the SMA. The IPDA (*arrowhead*) branched from the FJA (*arrow*) at the left posterior side of the SMA.

(B) A surgical specimen of the total meso-pancreatoduodenum excision with pylorus- preserving pancreaticoduodenectomy.
The retropancreatic connective tissue (*asterisk*), the second, third and fourth portion of the duodenum, and the proximal jejunum form a common mesentery, i.e., the "meso-pancreatoduodenum", which is dominated by the FJA (*arrow*) and IPDA (*arrow head*). The pancreatic head (PH) is turned to the upper right side.

(C) Diagram showing "meso-pancreatoduodenum"
A special image that divides pancreas head and body. Meso-pancreatoduodenum is a united mesentery from duodenum to upper jejunum.
SMA, superior mesenteric artery; PV, portal vein; SMV, superior mesenteric vein; SPV, splenic Vein; MPD, meso-pancreatoduodenum; tMPDe, total meso-pancreatoduodenum excision.

cholecystectomy, and the duodenum and the proximal jejunum were divided with a linear stapler. At this stage, tunneling of the PV was carried out. The pancreas was cut above the PV with sufficient distance from the tumor, and the pancreas head was detached from the retroperitoneum without manipulation of the pancreas head. In cases with cancer involvement to the portal venous system, venous resection followed by an end-to-end anastomosis can be easily conducted. Reconstruction of the digestive system was performed using a modified version of Child's procedure.

Statistical analysis

Continuous variables were dichotomized at their median values for the purpose of statistical analysis. Actuarial survival rate were constructed with Kaplan-Meier method. The JMP software program (ver.9, SAS Institute, Inc., Cary, NC) was used for all statistical analyses.

RESULTS

The demographic and intraoperative characteristics of this study are shown in Table 1. Thirteen pancreatic head carcinomas, 7 ampullary carcinomas, and 4 extrahepatic bile duct carcinomas were resected. There were 11 males and 13 females with a median age of 72 years (range: 45-82). According to the American Joint Committee on Cancer, seventh edition [17], the tumor stage classification (0/IA/IB/IIA/IIB/III/IV) of the 24 patients with PAC was 1/8/2/5/7/0/1. Five patients (21%) required PV resection, and 8 patients (33%) received blood transfusion.

Table 1. Demographics and intraoperative characteristics details of 24 patients with periampullary carcinomas undergoing a total meso-pancreatoduodenum excision with pancreaticoduodenectomy

Variables	No. of patients
Gender (male/female)	11/13
Age (yr), median (range)	72(45-82)
BTC/PHC	11/13
BMI, median(range)	21.5(15.9-24.9)
Preoperative biliary drainage, (yes/no)	10/14
Diabetes Mellitus, (yes/no)	6/18
TNM stage	
0/IA/IB/IIA/IIB/III/IV	1/8/2/5/7/0/1
Operative procedure	
PD/PPPD	6/18
Portal vein resection rate, (yes/no)	5/19
Operative time (min), median (range)	498 (408-646)
Blood loss (ml), median (range)	1050 (280-1800)
Blood transfusion rate (%)	33

BTC, Biliary tract cancer. PHC, pancreatic head carcinoma.

BMI, body mass index; calculated as weight in kilograms divided by height in meters squared.

PD, pancreaticoduodenectomy. PPPD, pylorus preserving pancreaticoduodenectomy.

Table 2. Surgical outcomes of 24 patients with periampullary carcinomas undergoing a total meso-pancreatoduodenum excision with pancreaticoduodenectomy

Variables	No. of patients
Hospital stay (days), median (range)	31 (12-121)
Length of abdominal drainage (days), median (range)	7 (5-98)
Resumption of oral diet (POD), median (range)	4 (2-19)
Mortality, n. (%)	0 (0)
Postoperative morbidity, n. (%)	9 (38)
Specific complications, n. (%)	
Pancreatic fistula, grade A/B/C	7(29)/2(8)/0(0)
Surgical site infection	4(17)
Gastric stasis, grade A/B/C	0(0)/2(8)/0(0)
Diarrheas	2(8)
Intra-abdominal abscess	1(4)
Recurrence, n. (%)	8(33)

POD, post operative days

Table 2 shows surgical outcomes. The overall morbidity and mortality rates were 38% and 0%, respectively. Postoperative complications were as follows: pancreatic fistula (PF) [18] in 9 patients (38%), which were grade A in 7 and B in 2 cases, surgical site infection in 4 patients (17%), gastric stasis with grade B [19] in 2 patients (8%), diarrhea requiring loperamide hydrochloride in 2 patients (8%) and intra-abdominal abscess without PF in one patients (4%). No patients required reoperation. All postoperative complications were successfully managed with medications or conservative treatments. The median postoperative hospital stay was 31 days. Patients with pancreatic head carcinoma were treated with an adjuvant treatment consisting of gemcitabine-based combination chemoradiotherapy [20] which was introduced immediately after recovery from surgical damage in the same hospitalization, while patients with ampullary or biliary carcinoma received no adjuvant therapy. Follow-up CT examinations were carried out every 3 months to evaluate tumor recurrence after surgery.

The pathological outcomes are shown in Table 3. Definitive pathological reports showed that the total number of dissected lymph nodes was 17 (median, range: 13-32) in the biliary tract carcinomas (BTC), including ampullary and bile duct carcinomas, and 25 (median, range: 13-40) in the pancreatic head carcinomas (PHC), while those around the SMA were 3 (median, range: 0-14) in the BTC and 3 (median, range: 0-9) in the PHC. The incidence of lymph node recognized around the SMA was 9% in the BTC and 31% in the PHC. R0 was achieved in all BTC patients. On the other hand, in PHC,

Table 3. Pathological and survival outcomes of 24 patients with periampullary carcinomas undergoing a total meso-pancreatoduodenum excision with pancreaticoduodenectomy

Variables	**No. of patients**	
	BTC (n=11)	PHC (n=13)
TNM stage		
0/IA/IB/IIA/IIB/III/IV	1/5/2/2/1/0/0	0/3/0/3/6/0/1
Total number of LNs dissected		
Median (range)	17(13-32)	25(13-40)
Number of LNs dissected around the SMA		
Median (range)	3(0-14)	3(0-9)
LN metastasis, n (%)	1(9)	7(54)
LN metastasis around the SMA, n (%)	1(9)	4(31)
R0/R1 resection, n (%)	11/0(100/0)	12/1(92/8)
Recurrence, n (%)		
Liver	2(18)	1(8)
Loco-regional	0(0)	0(0)
Peritoneum	0(0)	2(15)
Lymph node	0(0)	1(8)
Others	0(0)	1(8)

BTC, biliary tract carcinoma. PHC, pancreatic head carcinoma.

LN, lymph node. SMA, superior mesenteric artery.

R0, microscopically curative resection margin.

R1, microscopically positive resection margin.

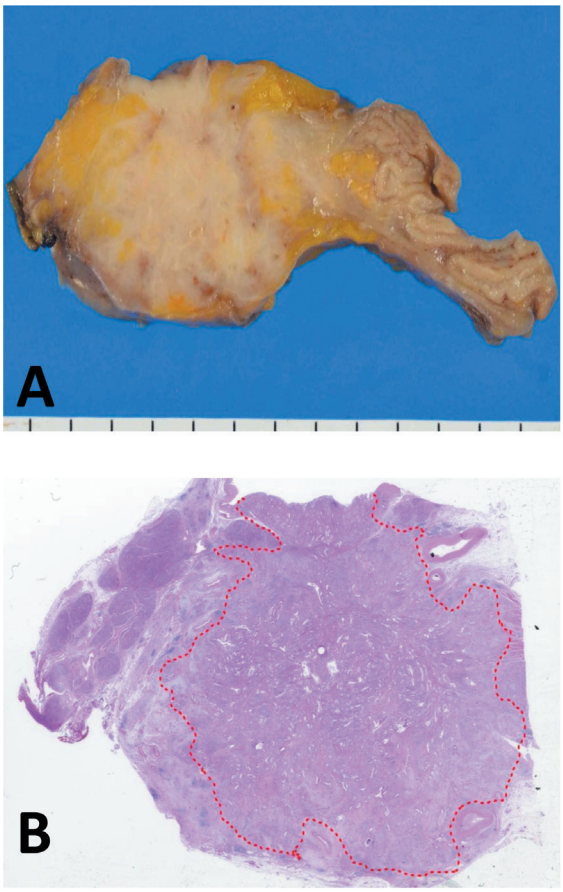

Fig. 2. Total meso-pancreatoduodenum excision have achieved en bloc resection of the peripancreatic retroperitoneal tissue and complete clearance around the SMA without microscopic residue of a tumor cell.
(A) Macroscopic findings. The resected pancreatic head carcinoma specimen showed fibrotic tumor in the cut surface.
(B) Histological findings. The histological findings showed no cancer cells are identified at any of the resection margin (hematoxylin and eosin stain,×0.5).
(C) Invasive ductal carcinoma showed poorly to moderately differentiation containing perineural invasion (hematoxylin and eosin stain,×100).

R0 was accomplished in all cases except for one (8%) with R1 resection due to a microscopic positive margin on the posterior resection limbus [4, 8] (Figs. 2A, 2B and 2C).

During the median follow-up period of 18.2 months, no loco-regional recurrence was observed. One patient with ampullary carcinoma died of liver metastasis. Three patients with pancreatic cancer died of liver metastasis, lymph node metastasis, and peritoneal dissemination. The actuarial survival rate of two year period were 89% and 75% for the BTC and PHC during the median follow-up period of 22.6 months and 17.3 months, respectively.

DISCUSSION

Our new surgical procedure, "total meso-pancreatoduodenum excision," was developed to achieve complete clearance of the peripancreatic retroperitoneal tissue and circumferential lymphadenectomy around the SMA, which may promote microscopically curative resection (R0). In this study, we indeed achieved R0 resection in 23 (96%) of 24 patients with PAC, and no loco-regional recurrence was recognized after the surgery, with the median follow-up period of 18.2 months.

One of the principal factors of local recurrence in patients undergoing PD for PAC is R1 resection, and, in most cases, a cancer-positive site is a limbus of the soft connective tissue between the SMA and the region from the pancreas head to the uncinate process, which contains a variety of lymphatic, nervous, and vascular structures [4-8]. Jamieson *et al.* [7] demonstrated that the transection margin status of this soft connective tissue significantly correlates with the survival rate in pancreatic carcinoma after PD. Gockel *et al.* [5] first described the soft connective tissue located from the posterior surface of the pancreatic head to behind the SMV and SMA as "mesopancreas" and proposed a concept of "complete resection of the mesopancreas" in patients with pancreatic carcinoma to reduce loco-regional recur-

rence. In addition, Gaedcke *et al*. [6] clarified that the mesopancreas was also the primary site for R1 resection in PACs. We think that most R1resection cases around the SMA are origin from ventral pancreas in the PHC, whereas our described technique have achieved en bloc resection of the peripancreatic retroperitoneal tissue and complete clearance around the SMA without microscopic residue of a tumor cell.

Another principal factor of loco-regional recurrence is the existence of lymph node metastasis around the SMA. Previous reports have noted a high incidence of lymph node metastasis around the SMA, even in the left side of the SMA, in advanced PACs [9, 10]. In addition, we also demonstrated that lymph node metastasis around the SMA occurred to the high rate in both of PHC and BTC. Although the previous surgical procedure "mesopancreas resection" does not include the concept of lymph node dissection around the SMA, especially on the left side [5, 6], our new surgical procedure, "total meso-pancreatoduodenum excision" include the concept of circumferential lymphadenectomy of the SMA without fatal complications.

The anatomy from the behind the mesentericoportal confluence to the part around the SMA including the mesopancreas is unclear and difficult to understand [5, 6]. Conducting a detailed investigation on surgical specimens of PD, we realized that the retropancreatic connective tissue including the mesopancreas, which is dominated by the IPDA, and the mesentery of the proximal jejunum, which is dominated by the FJA, form a common mesentery; we thus named these structures "meso-pancreatoduodenum". Namely, the meso-pancreatoduodenum tucks the SMA from behind, connects with the third and fourth portions of the duodenum and the proximal jejunum, and contains retropancreatic connective tissue as well as the mesopancreas. Our concept of the "meso-pancreatoduodenum" makes it possible to understand clearly the anatomy from behind the mesenterico-portal confluence to the part around the SMA when performing a PD and makes the PD a safer operation. Indeed, we have reported that total meso-pancreatoduodenum excision procedure significantly reduced the blood transfusion rate than conventional PD and postoperative complication with total meso-pancreatoduodenum excision were the same as that in the conventional PD procedure [14].

Additional advantages of a total meso-pancreatoduodenum excision with PD are as follows: easy identification of arterial or PLsma invasion in the early step of the operation because of the artery-first approach; preceding handling of arterial branches from the SMA, i.e., IPDA and FJA, without manipulation of the pancreas head, which may reduce the risk of squeezing out the cancer cells; and easy identification of the origin of the common trunk of the FJA and IPDA, resulting in a safe operation and certain lymphadenectomy posterior to the SMA. A possible disadvantage of this procedure is intraoperative lymphorrea; to prevent, sure ligation of the soft connective tissue around the SMA is necessary. As mentioned above, we confirmed the safety of this procedure. Operative mortality was null, and operative morbidity was equal to those in previous reports [11, 21].

In conclusion, achievement of R0 operation is the most important factor in successful management of patients with PAC. There are some limitations in this study. Since the number of patients is small in this study, larger prospective study is needed to investigate whether our procedure contributes the improvement of the long-term survival rates of the patients with PAC.

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