



# Superior Mesenteric Artery Plexus-Preserving Pancreatoduodenectomy with Circumferential Dissection of Lymph Nodes

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## Introduction

Pancreatic ductal adenocarcinoma (PDAC) is one of the most lethal human cancers worldwide and is the fourth leading cause of cancer-related deaths in Japan,<sup>1</sup> the United States,<sup>2</sup> and Europe.<sup>3</sup> Complete surgical resection offers the only opportunity to cure patients with PDAC and pancreatoduodenectomy with standard lymphadenectomy is commonly performed to achieve a curative surgical resection for resectable pancreatic head cancer; however, one of the factors which impairs the postoperative long-term survival of patients with resectable PDAC is high frequency of lymph node metastasis. Especially, optimal lymphadenectomy of lymph nodes around the superior mesenteric artery (SMA) in cases of pancreatoduodenectomy for pancreas head cancer is controversial. The right side of the SMA lymph nodes is commonly dissected as a standard lymphadenectomy during pancreatoduodenectomy because previous randomized control trials revealed that a complete resection of the SMA lymph nodes is not beneficial and leads to greater morbidity, such as postoperative diarrhea.<sup>4–8</sup> Nevertheless, metastases and recurrence on the left-sided SMA lymph nodes are sometimes found<sup>9</sup> and some surgeons have preferred dissection. A complete resection of the lymph nodes around the SMA as part of an extended lymphadenectomy in previous studies may include

dissection of the SMA plexus, which is strongly associated with postoperative severe diarrhea.<sup>6–8</sup> Therefore, we developed a pancreatoduodenectomy with circumferential dissection of SMA lymph nodes, as well as complete preservation of the SMA plexus for resectable PDAC. The goal of this report was to describe the technical details of a SMA plexus-preserving pancreatoduodenectomy (SMAPP-PD) with circumferential dissection of the SMA lymph nodes and demonstrate the short- and long-term outcomes of this procedure. Our intention was to share the details of the procedure, which might help surgeons in challenging SMAPP-PDs. Therefore, we introduce the simple SMAPP-PD procedure for resectable PDAC herein, which does not include a portal vein (PV)/superior mesenteric vein (SMV) resection and reconstruction.

## Methods

### Preoperative Work-Up and Indication of SMAPP-PD

All patients who were candidates for SMAPP-PD underwent a full clinical evaluation to assess overall health and medical comorbidities. The resectability status, which is defined in the National Comprehensive Cancer Network Pancreatic Cancer (NCCN) guidelines (version 1.2020<sup>10</sup>) based on pretreatment multi-detector computed tomography, was also assessed for each patient. SMAPP-PD was indicated for patients with PDAC in the pancreas head without SMA contact, which is commonly classified into resectable or borderline resectable with venous contact based on the resectability status. SMAPP-PD with PV/SMV resection could be performed in case of PDAC contact with PV/SMV. Preoperative probe laparoscopy was performed only in the selected patients suspected of having an intraabdominal distant metastasis on preoperative imaging examinations. The study protocol was consistent with

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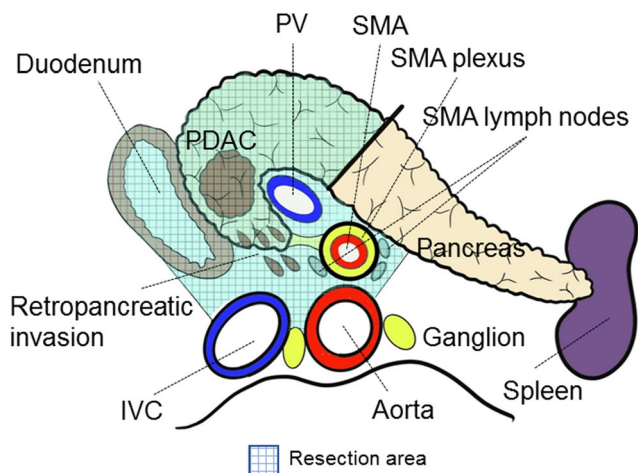
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the recommendations of the Declaration of Helsinki and approved as retrospective study by the Institutional Review Board of Hiroshima University (E-1914).

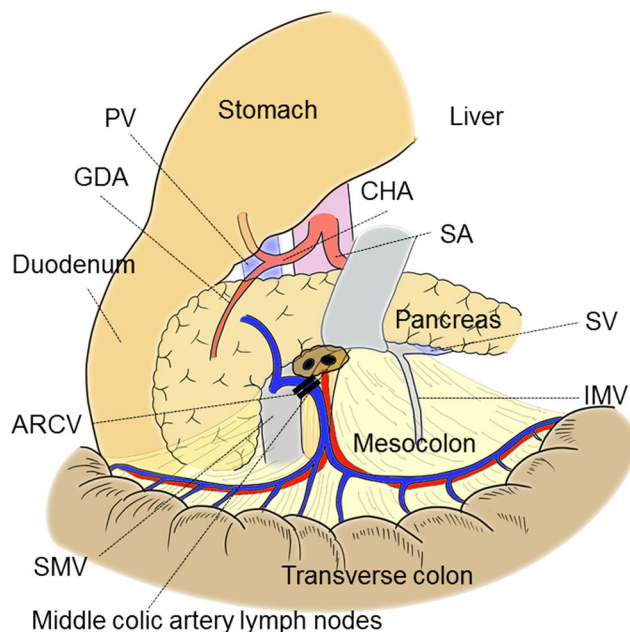
### Surgical Procedure for SMAPP-PD

The basic concept of SMAPP-PD is shown in Fig. 1, which depicts the range of retroperitoneal dissection in SMAPP-PD. Although retroperitoneal organs, including the pancreas head, duodenum, retropancreatic tissue, peripancreatic lymph nodes, SMA lymph nodes, and paraaortic lymph nodes, are removed as an en bloc resection, the SMA plexus is completely preserved in SMAPP-PD.

After an upper abdominal midline incision, the visible peritoneal and visceral surfaces are explored for confirmation of no metastatic disease and peritoneal washing cytology is performed in all cases. The gastrocolic ligament is widely opened until the lesser sac is exposed. Lymph nodes along the middle colic artery are dissected. A few accessory right colic veins are usually divided during this process; however, the middle colic artery is preserved unless tumor invasion is suspected (Fig. 2). The SMV is exposed at the inferior border of pancreas and a tunnel is created behind the neck of the pancreas. This separation is extended to the left side to expose the splenic vein (SV) and the anterior aspects of the SMA lymph nodes are dissected with preservation of the SMA plexus. Then, using the Kocher maneuver, paraaortic lymph nodes are dissected, keeping the lymph nodes attached to the retropancreatic tissue (Fig. 3). The duodenum is mobilized until the left renal and adrenal veins are exposed.

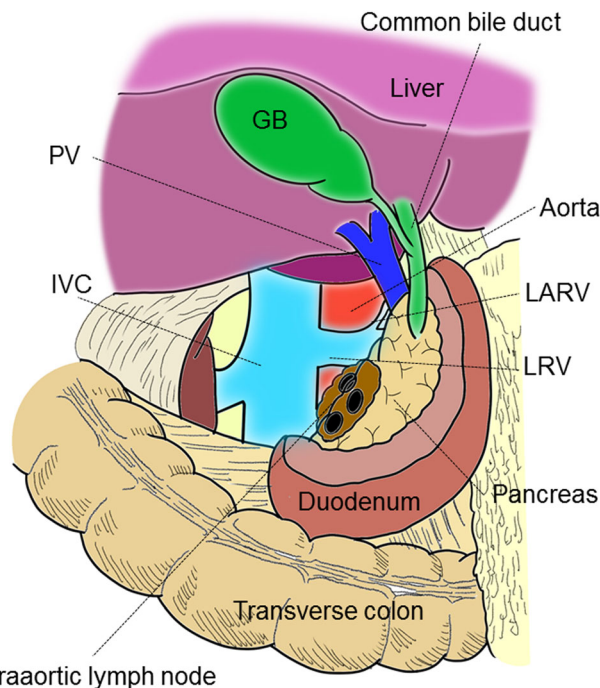


**Fig. 1** The basic concept of SMAPP-PD. The grid indicates the resection area in SMAPP-PD. Pancreas head, duodenum, retropancreatic tissue, peripancreatic lymph nodes, SMA lymph nodes, and paraaortic lymph nodes are removed as an en bloc resection; however, the SMA plexus is completely preserved in SMAPP-PD. SMAPP-PD, superior mesenteric artery plexus-preserving pancreatoduodenectomy; SMA, superior mesenteric artery; PDAC, pancreatic ductal invasive adenocarcinoma; PV, portal vein; IVC, inferior vena cava



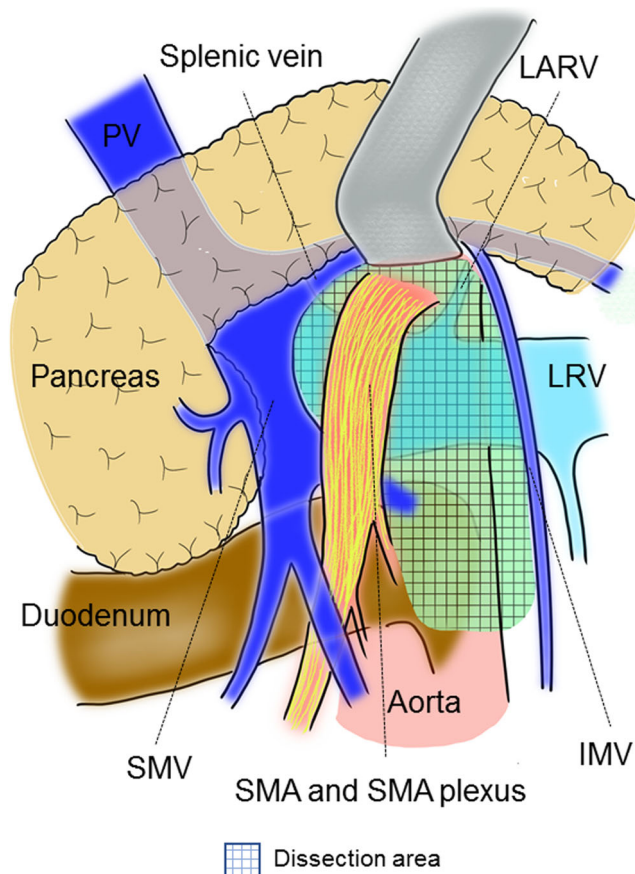
**Fig. 2** Lymph nodes along the middle colic artery are dissected. A few accessory right colic veins are usually divided during this process; however, the middle colic artery is preserved unless tumor invasion is suspected. GDA, gastroduodenal artery; PV, portal vein; CHA, common hepatic artery; SA, splenic artery; IMV, inferior mesenteric vein; SMV, superior mesenteric vein; ARCV, accessory right colic vein

Next, attention is directed below the mesocolon followed by opening the mesocolon on the left side of the middle colic

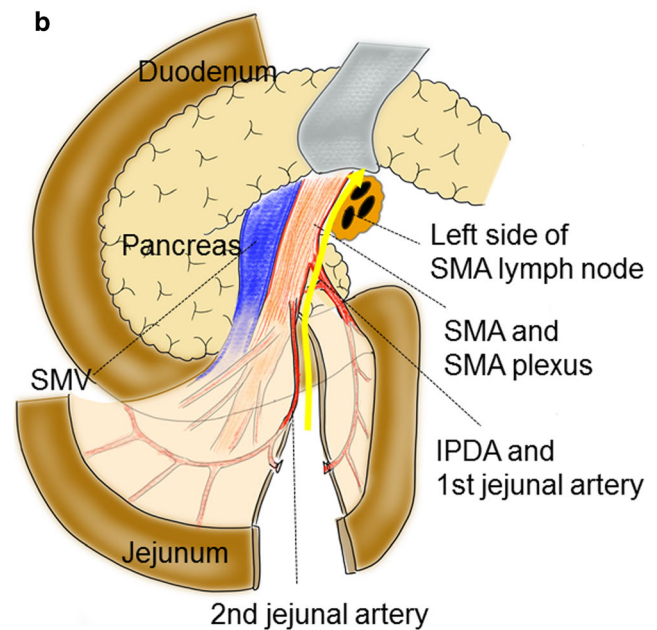
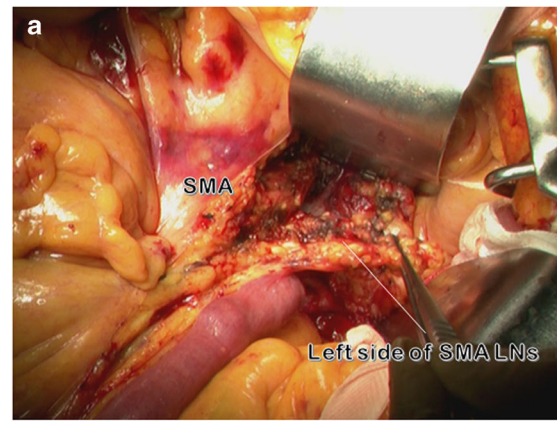


**Fig. 3** The Kocher maneuver is depicted. Paraaortic lymph nodes are dissected, thus keeping the paraaortic lymph nodes attached to the retropancreatic tissue. The duodenum is mobilized until the left renal and adrenal veins are exposed. GB, gall bladder; PV, portal vein; IVC, inferior vena cava; LARV, left adrenal vein; LRV, left renal vein

artery. With cephalad retraction of the transverse colon, the area of the ligament of Treitz is widely visualized. Retroperitoneal dissection, including the left side of the SMA lymph nodes, is performed. In this process, the left renal vein and aorta are already exposed via the Kocher maneuver. The left side margin of this retroperitoneal dissection is the inferior mesenteric vein (Fig. 4). The left side of the SMA lymph nodes is dissected proximally until the root of the SMA, where the left adrenal vein serves as a landmark. With respect to dissection of the left side of the SMA lymph nodes, the SMA plexus can be completely preserved by separating the nerve plexus and outer fatty issue with lymph nodes (Fig. 5a). To investigate the frequency of metastasis on the left side of the SMA lymph nodes, the dissected lymph nodes are removed from the pancreaticoduodenal specimen and sent separately for permanent histologic examination. After transection of the jejunum approximately 20 cm distal to the Treitz



**Fig. 4** The grid indicates the retroperitoneal dissection area in SMAPP-PD. The left renal vein and aorta have been exposed by the prior Kocher maneuver. The left side margin of this dissection is the inferior mesenteric vein. Dissection of the left side of SMA lymph nodes with preservation of SMA plexus is performed proximally until the root of SMA where the left adrenal vein appears as a landmark. This dissection of retroperitoneal tissue including the left side of SMA lymph nodes is consistently performed from below the mesocolon. SMA, superior mesenteric artery; SMV, superior mesenteric vein; PV, portal vein; IMV, inferior mesenteric vein; LARV, left adrenal vein; LRV, left renal vein

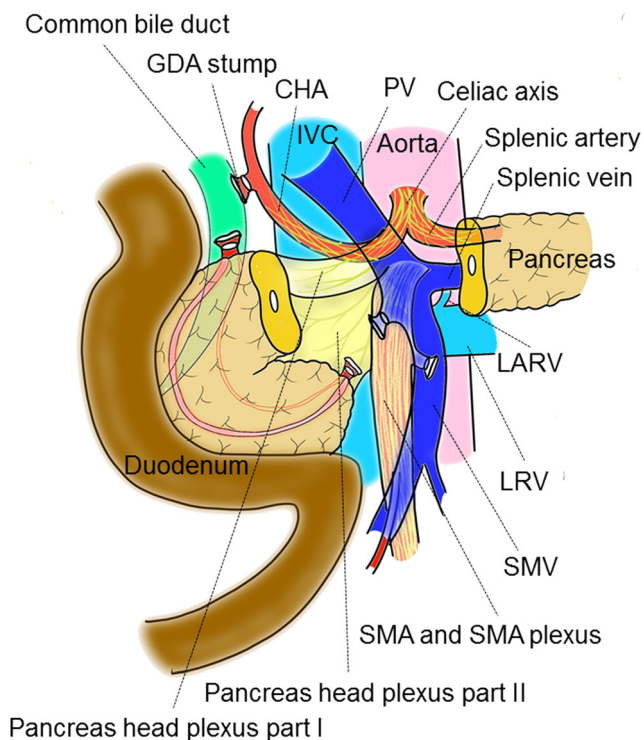


**Fig. 5** Subsequent dissection of the left side of the SMA with preservation of the SMA plexus. **a** The SMA plexus can be completely preserved by separating the nerve plexus and outer fatty issue with lymph nodes. This dissection of the left side of SMA lymph nodes is consistently performed from below the mesocolon. **b** The mesojejunum is divided along the second jejunal artery pedicle (yellow arrow), then dissection of the left side of the SMA is extended to dorsal side with preservation of the SMA plexus. In this process, the IPDA and first jejunal artery are divided and the uncinate process is removed from the SMA plexus. SMA, superior mesenteric artery; SMV, superior mesenteric vein; IPDA, inferior pancreaticoduodenal artery

ligament, the mesojejunum is divided along the second jejunal artery pedicle, then dissection of the left side of the SMA is extended to the dorsal side with preservation of the SMA plexus (Fig. 5b). In this process, the inferior pancreaticoduodenal artery (IPDA) and first jejunal artery are divided and the uncinate process is removed from the SMA plexus. These dissections of retroperitoneal tissues including the left side of SMA lymph nodes are consistently performed from below the mesocolon.

Next, attention is re-directed above the mesocolon. After division of the right gastroepiploic and right gastric arteries

with dissection of the supra- and infra-pyloric lymph nodes, the proximal duodenum is transected 1–2 cm distal to the pylorus. Then, the common hepatic artery lymph nodes are dissected, and the gastroduodenal artery (GDA) is identified and divided. After dissection of the hepatoduodenal ligament is performed, the pancreatic neck is divided by the ultrasonically activated device, with exception of the pancreatic duct which is sharply divided using a scalpel. Based on the processes thus far, all arterial flow to the pancreas head is blocked before ligation of the drainage veins. By reflecting the pancreatic head laterally to the right, the gastroduodenal trunk and superior pancreaticoduodenal veins are identified and divided. When the stump of the jejunum is extricated to the right into the paramesocolic compartment and the SMV is retracted laterally to the left, the pancreatic head plexus (dissection plane) and the right side of the SMA plexus are finely visualized, which thinned owing to the preceding SMA lymph node dissection from the left side (Fig. 6). The pancreatic head plexus is dissected caudad-to-cephalad until the root of the SMA with preservation of the right side of the SMA plexus.

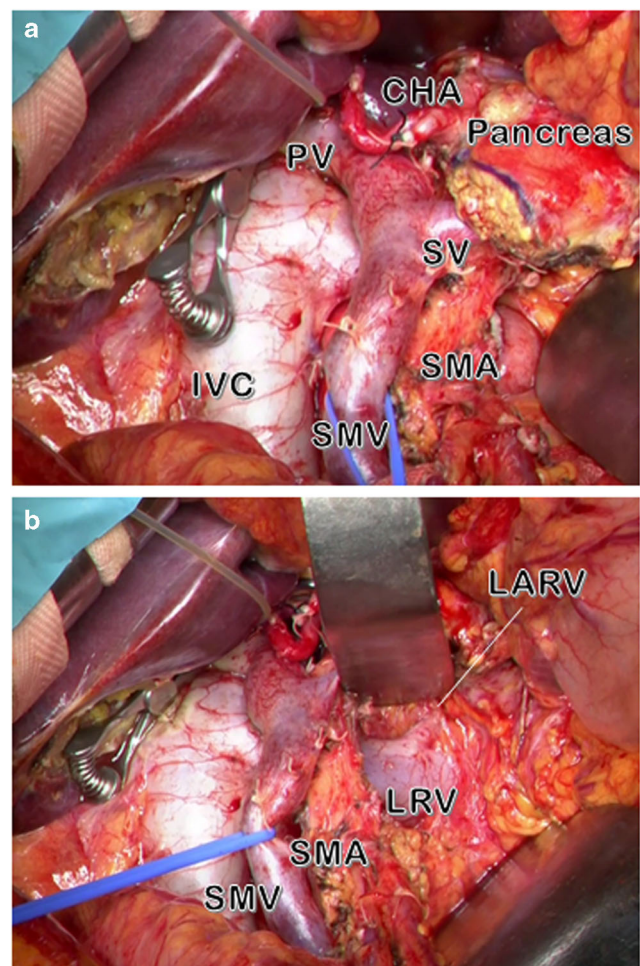


**Fig. 6** The transected jejunum is extricated and the SMV is retracted laterally to the left. The pancreatic head plexus is dissected from caudad-to-cephalad until the root of the SMA (from part II to part I) with preservation of the right side of the SMA plexus. SMA, superior mesenteric artery; GDA, gastroduodenal artery; CHA, common hepatic artery; SMV, superior mesenteric vein; PV, portal vein; IVC, inferior vena cava; LARV, left adrenal vein; LRV, left renal vein. Pancreatic head plexus parts I and II are defined by the Japan Pancreas Society (Classification of pancreatic carcinoma; 7th edition)

Circumferential dissection of the SMA lymph nodes is completed by this right side dissection. After the cholecystectomy and transection of the common hepatic duct, all peripancreatic and lymphatic tissues are removed en bloc with the specimen (Fig. 7).

The portal SMV groove, SMA plexus, and retroperitoneal margins are inked, and separate pancreatic neck margins are obtained prior to sending the specimen for frozen section analysis. Residual tumor status was considered R1 when the pathologic findings demonstrated carcinoma cell was infiltrated in these inked margins.

The reconstructions, including the pancreaticogastrostomy and drain placement, are performed as has been reported previously.<sup>11,12</sup> See also [Electronic Supplementary Material](#).



**Fig. 7** After removal of the pancreaticoduodenal tissue and before reconstruction. En bloc resection of the pancreas head, duodenum, retropancreatic tissue, peripancreatic lymph nodes, SMA lymph nodes, and paraaortic lymph nodes is performed. **a** The SMA plexus is completely preserved. **b** Dissection of the left side of the SMA lymph nodes with preservation of the SMA plexus was performed until the left adrenal vein is exposed. SMA, superior mesenteric artery; CHA, common hepatic artery; SMV, superior mesenteric vein; PV, portal vein; IVC, inferior vena cava; LARV, left adrenal vein; LRV, left renal vein

**Table 1** Patient characteristics, pathologic factors, and postoperative outcomes in patients who underwent SMAPP-PD ( $n = 157$ ; interquartile range where noted, otherwise %)

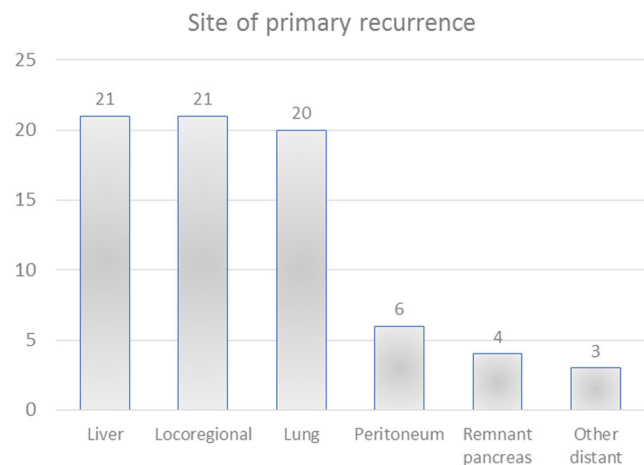
Age, median (IQR)	71 years (63–78 years)
Gender	
Male/female	76 (48)/81 (52)
Body mass index, median (IQR)	20.6 kg/m <sup>2</sup> (18.8–23.0 kg/m <sup>2</sup> )
Performance status	
0/1/2	123 (78)/28 (18)/6 (4)
HgbA1c, median (IQR)	6.1% (5.5–6.9%)
Modified GPS	
0/1/2	135 (86)/10 (6)/12 (8)
Preoperative CA19-9, median (IQR)	88 U/mL (16–421 U/mL)
Neoadjuvant chemotherapy	
Yes/no	10 (6)/147 (94)
Pancreatic texture	
Soft/hard	35 (22)/122 (78)
PV/SMV resection	
Yes/no	38 (24)/119 (76)
Operative time, min, median (IQR)	325 (292–365)
Estimated blood loss, mL, median (IQR)	670 (416–1024)
Blood transfusion	
Yes/no	24 (15)/133 (85)
Postoperative complications	
No/grades I–II/grades III–VI/grade V	127 (81)/14 (9)/15 (9)/1 (1)
Clinically relevant POPF	
No/biochemical leak/grade B/grade C	137 (87)/15 (10)/3 (2)/2 (1)
Peritoneal cytology	
Positive/negative	10 (7)/147 (93)
Tumor size on histologic examination, mm	27 (20–35)
UICC T factor	
T1/T2/T3	38 (24)/98 (63)/21 (13)
UICC N factor	
N0/N1/N2	58 (37)/58 (37)/41 (26)
Metastasis to the left side of SMA lymph nodes	
Yes/no	10 (8)/108 (92)*
Metastasis to paraaortic lymph nodes	
Yes/no	12 (7)/145 (93)
R factor	
R0/R1	127 (80)/30 (20)
Histologic grade	
Grades 1/2/3	51 (32)/90 (58)/16 (10)
Postoperative CA19-9, median (IQR)	9 U/mL (4–27 U/mL)
Use of anti-diarrheal agent	
Yes/no	50 (32)/107 (68)
Initiation adjuvant GS chemotherapy	
Yes/no	113 (72)/44 (28)
Time to initiation of adjuvant GS chemotherapy	17 POD (15–22 POD)
Completion of adjuvant GS chemotherapy	
Yes/no	104 (66)/53 (34)
In-hospital days, median (IQR)	20 (18–24)

SMAPP-PD, superior mesenteric artery plexus-preserving pancreatoduodenectomy; IQR, interquartile range; GPS, Glasgow prognostic score; PV/SMV, portal vein/superior mesenteric vein; UICC indicates Union for International Cancer Control; GS, gemcitabine plus S-1; POD, postoperative days

\*Separated left side of SMA lymph nodes was unavailable in 39 patients

## Results

A total of 157 patients who underwent SMAPP-PD for PDAC at Hiroshima University Hospital (Hiroshima, Japan) from November 2004 to October 2019 were enrolled in the current

**Fig. 8** Incidence of primary recurrence site after SMAPP-PD. Hepatic and locoregional (including the neighbor lymph nodes) recurrences were the most common sites of primary recurrences

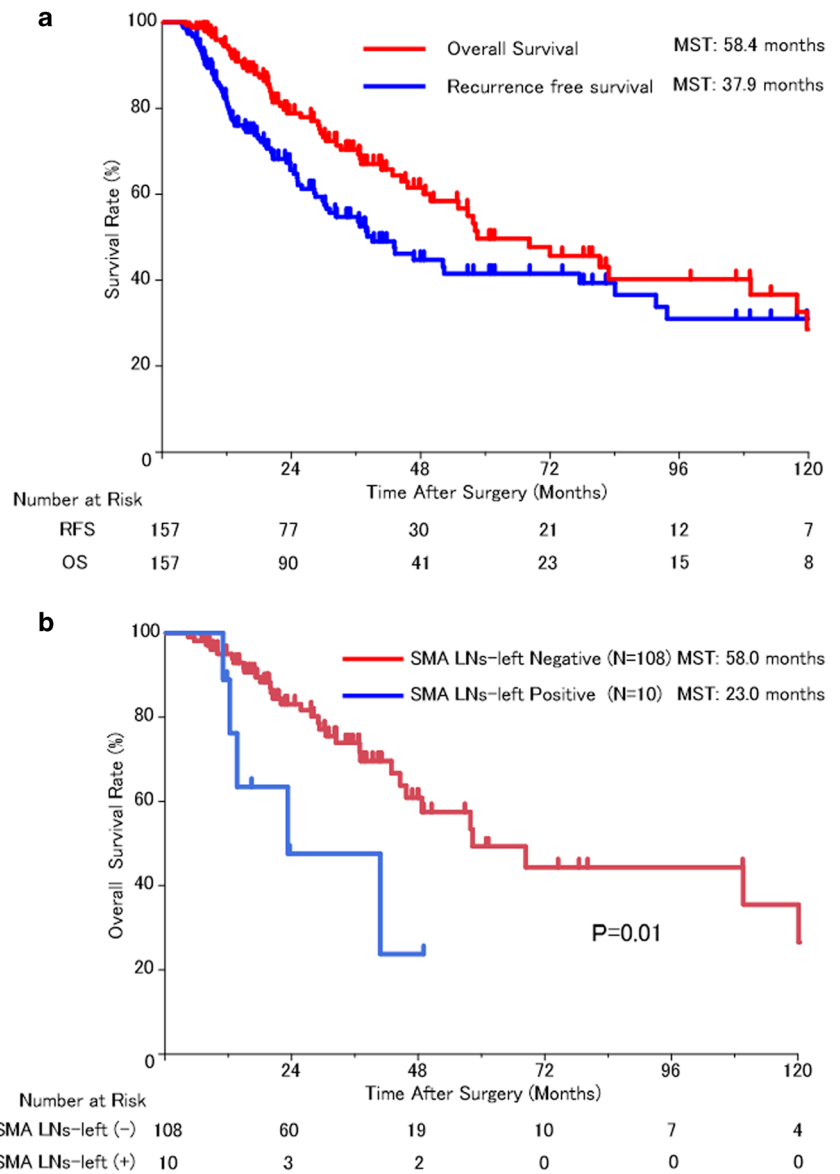
study. All patients were considered to have resectable PDAC based on NCCN guidelines. Patient characteristics, pathologic factors, and postoperative outcomes of all eligible patients are summarized in Table 1.

The median operative time and estimated blood loss in this series were 325 min and 670 mL, respectively. 16 patients (10%) experienced a major complication (> grade III), including one (0.6%) postoperative mortality. R0 resection was performed in 127 patients (80%). After the SMAPP-PD, an anti-diarrheal agent (1–3 mg of loperamide daily in most patients) was required in 50 patients (32%) 1 month postoperatively. Adjuvant gemcitabine plus S-1 chemotherapy, which is the standard adjuvant therapy regimen for PDAC in our institution, was initiated in 113 patients (72%) with a median time to initiation of 17 postoperative days. 10 cycles of adjuvant chemotherapy were completed in 104 patients (66%). With respect to the long-term outcomes, 75 patients (48%) were diagnosed with recurrences on imaging examinations at the time of the last follow-up evaluation (31 December 2019). Hepatic (28%) and locoregional (including neighbor lymph nodes [28%]) recurrences were the most common sites of primary recurrence (Fig. 8). The median recurrence free and overall survival of all eligible patients were 37.9 and 58.4 months, respectively (Fig. 9a). Of the 157 enrolled patients, separated left side of SMA lymph nodes was available in 118 patients (75%). The pathologic findings demonstrated that metastasis on the left side of the SMA lymph nodes existed in 10 (8%) of specimens. Patients with metastasis to the left side of SMA lymph nodes had significantly worse OS than those without ( $P = 0.01$ , Fig. 9b).

## Discussion

We have described the technical details of SMAPP-PD with circumferential dissection of the SMA lymph nodes for

**Fig. 9** **a** Kaplan–Meier survival cumulative curves for all 157 patients who underwent SMAPP-PD for resectable PDAC. The median recurrence free and overall survival of all eligible patients were 37.9 and 58.4 months, respectively. **b** Comparison of the OS in between patients with and without metastasis to the left side of SMA lymph nodes. Significant worse OS was found on patients with metastasis to the left side of SMA lymph nodes than those without ( $P=0.01$ ), (Separated left side of SMA lymph nodes were unavailable in 39 patients)



resectable PDAC and reported the short- and long-term outcomes. We developed SMAPP-PD expecting some advantages in surgical resection for PDAC. First, the artery-first approach, including a preceding ligation of the IPDA and GDA before ligation of drainage veins from pancreas head, could control bleeding during the procedure, which also contributes to a reduced operative time. The operative time and estimated blood loss during this series were less than the finding reported in a large-scale study in Japan.<sup>13</sup> Second, en bloc dissection of the retropancreatic tissues, including peripancreatic lymph nodes, could help achieve clear retropancreatic margins. In addition, circumferential dissection around the SMA also may help achieve margin clearance at the SMA, which is the most frequent point of R1 resection. We believe these retropancreatic dissections during SMAPP-PD may be associated with a high R0 resection rate in the

current study. Third, the SMA lymph nodes in SMAPP-PD include not only the right side, but also the left side of the SMA. According to the consensus statement from the ISGPS, only lymph node stations along the right side of the SMA are included in a standard lymphadenectomy, but the left side of SMA lymph nodes is not included.<sup>14</sup> The current results revealed that metastasis on the left side of the SMA lymph nodes, which could cause a local recurrence nearby, occurred in 8% of patients with resectable PDAC. All patients with the left side of the SMA lymph node metastases had other lymph node metastases elsewhere. However, the metastatic stations were completely included within the regional lymph nodes which are harvested by standard lymphadenectomy. Therefore, these metastatic lymph nodes on the left side of the SMA would be left if only the right side of the SMA lymph nodes was dissected as a standard lymphadenectomy. Based

on these findings, we believe that circumferential dissection of SMA lymph nodes may contribute to local control of PDAC in this area. Fourth, complete preservation of the SMA plexus helps to prevent severe postoperative diarrhea. A complete resection of the lymph nodes around the SMA is commonly avoided in a standard lymphadenectomy because a complete resection frequently causes severe postoperative diarrhea; however, we suggest that it is technically possible to achieve a good balance between circumferential dissection of the SMA lymph nodes and complete preservation of the SMA nerve plexus in the case of pancreatoduodenectomy for PDAC without tumor contact to the SMA. Postoperative diarrhea after SMAPP-PD was well-controlled with minimal use of anti-diarrheal agents in the current series, which may result in early initiation of adjuvant chemotherapy. We believe these advantages of SMAPP-PD provide a significant benefit of prolonged survival after surgery.

Although the short- and long-term outcomes after SMAPP-PD appear to be favorable, the current study has some inherent limitations due to its retrospective, noncomparative, single-institutional nature. First, we need to consider the racial difference in physique of patients in order for the SMAPP-PD procedure to be accepted worldwide. In general, body mass index of the Japanese patients is smaller than those in western countries. However, we believe that SMAPP-PD is possible and beneficial even for patients with large physique because we have successfully performed SMAPP-PD in dozens of patients whose body mass index was  $>25$  kg/m<sup>2</sup>. Second, some patients who underwent SMAPP-PD experienced unfavorable postoperative outcomes, including R1 resection, locoregional recurrence, and poor prognosis. To improve the prognosis of these patients, further efforts to develop a more effective perioperative therapeutic strategy for resectable PDAC will be needed. Recently, a large-scale randomized control trial from Japan demonstrated significant survival benefits of gemcitabine plus S-1 neoadjuvant chemotherapy for resectable PDAC.<sup>15</sup> Although most of the patients in the current series underwent upfront surgery, we expect that introduction of SMAPP-PD combined with neoadjuvant chemotherapy can lead to a favorable prognosis. Nevertheless, a prospective, large-scale, comparative, global study is required to prove the potential advantages of SMAPP-PD and perioperative treatments.

## Conclusion

In conclusion, SMAPP-PD with circumferential dissection of the SMA lymph nodes can be safely performed with a high rate of R0 resection for resectable PDAC. This procedure maintains a good condition among patients after pancreatoduodenectomy and enables early initiation of adjuvant chemotherapy. SMAPP-PD showed good preliminary

short- and long-term outcomes in the current study. These findings warrant a clinical trial to further investigate the efficacy of SMAPP-PD combined with neoadjuvant chemotherapy for resectable PDAC.

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 Quality control of data and algorithms: Kenichiro Uemura, Shinya Takahashi  
 Data analysis and interpretation: Naru Kondo, Kenjiro Okada  
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 Manuscript preparation: Naru Kondo, Shingo Seo  
 Manuscript editing: Naru Kondo, Kenichiro Uemura  
 Manuscript review: Yoshiaki Murakami, Shinya Takahashi

## Compliance with Ethical Standards

**Conflict of Interest** The authors declare that they have no conflict of interest.

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