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ORIGINAL ARTICLE

Prognostic significance of lymph node metastasis in pancreatic tail cancer: A multicenter retrospective study

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Abstract

Background: Distal pancreatectomy (DP) with lymph node (LN) dissection is the standard procedure for pancreatic ductal adenocarcinoma of the tail (Pt-PDAC). However, the optimal surgery including extent of LN dissection is still being debated. The present study investigated the incidence and prognostic impact of LN metastasis on patients suffering from Pt-PDAC.

Patients and method: This multicenter, retrospective study involved 163 patients who underwent DP for resectable Pt-PDAC at 12 institutions between 2013 and 2017. The frequency of LN metastasis and the effect of LN dissection on Pt-PDAC prognosis were investigated.

Results: There were high incidences of metastases to the LNs along the splenic artery in the patients with Pt-PDAC (39%). The rate of metastases in the LNs along the common hepatic, left gastric, and celiac arteries were low, and the therapeutic index for these LNs was zero. In pancreatic tail cancer located more distally, there were no

metastases to the LNs along the common hepatic artery. Multivariate analysis revealed that tumor size was the only independent factor related to recurrence-free survival (HR = 2.01, 95% CI = 1.33–3.05, $p = 0.001$). The level of pancreas division and LN dissection along the common hepatic artery did not affect the site of tumor recurrence or recurrence-free survival.

Conclusions: LN dissection along the hepatic artery for Pt-PDAC has little significance. Distal pancreatic transection may be acceptable in terms of oncological safety, but further examination of short-term outcomes and preservation of pancreatic function is required.

KEYWORDS
distal pancreatectomy, lymph node metastasis, pancreas cancer, pancreatic ductal adenocarcinoma, prognosis

1 | INTRODUCTION

Pancreatic ductal adenocarcinoma (PDAC) is one of the most aggressive and lethal malignancies, and in particular, PDAC located in the pancreatic tail (Pt-PDAC), which is often found at an advanced stage due to the lack of specific symptoms and signs in the early stages, is associated with a poor prognosis.[1] Surgery is the only curative treatment for PDAC, and distal pancreatectomy (DP) with lymph node (LN) dissection is the standard procedure for Pt-PDAC.

Various authors have reported the identification of clinicopathological prognostic factors in pancreatic cancer, of which the presence of LN metastases represents a well-known detrimental prognostic factor.[2] Nevertheless, extended LN dissection for PDAC arising in the pancreatic head has not been shown to be effective in improving long-term outcomes.[3] Regarding LN dissection for Pt-PDAC, the International Study Group on Pancreatic Surgery (ISGPS) defined removal of LNs in the hilum of the spleen, along the splenic artery, and along the inferior border of the body and tail of the pancreas as standard procedure (Figure 1A).[4] The Japanese Pancreatic Society defines the range as slightly wider, adding stations 8a and 9.[5] However, a substantial lack of reliable evidence burdens the strength of these recommendations. As a matter of fact, the range of the LN dissection for Pt-PDAC is still being debated.

Strasberg et al.[6] reported radical antegrade modular pancreatosplenectomy (RAMPS) to be an effective procedure for left-sided PDAC. The benefits of this procedure are negative resection margins and the number of LNs harvested. There are many reports that these are important as prognostic factors[7]; however, prognosis has improved with pre- and postoperative adjuvant therapy in recent years, and it is clear that multidisciplinary treatment plays the key role in improving the prognosis of PDAC. Therefore, it is also important to reduce the surgical invasiveness. Advances in technology such as laparoscopic or robotic surgery are important factors in reducing invasiveness, but it is also necessary to reconsider the current resection range.[8] The present study investigated the incidence and prognostic impact of LN metastasis on patients suffering from Pt-PDAC. To clarify the optimal surgery for the patients suffering from Pt-PDAC, the present study investigated the significance of LN metastasis and prognostic factors including tumor location and operative procedures.

2 | PATIENTS AND METHODS

2.1 | Study design

This multicenter, retrospective study enrolled patients who underwent DP for Pt-PDAC at 12 institutions between January 2013 and December 2017 in Kyushu, Japan. Pancreas between the left border of the aorta and the hilum of the spleen was defined as pancreatic tail according to the 7th AJCC/UICC TNM classification.[9] A pathologist confirmed that all patients had undergone R0 or R1 resection. The pathological data were classified using the 7th AJCC/UICC TNM classification, and we applied the Japan Pancreas Society's General Rules for the Study of Pancreatic Cancer for the LN stations.[5] We investigated the rates of patients with LN metastases at each station. We followed the ethical principles stated in the guidelines of the World Medical Association's Declaration of Helsinki in this study, which was approved by the Ethics Committee of Oita University Faculty of Medicine (approval number: 2446-D10). The acquisition of informed consent from patients was waived owing to the retrospective nature of this study.

2.2 | Data collection

The following clinicopathological variables were included in the analysis: preoperative factors including age, sex, body mass index, performance status, American Society of Anesthesiologists physical status, length between the left edge of the aorta and tumor, and neoadjuvant therapy; operative factors including open/laparoscopic

(A)

The station number of the lymph nodes	
No. 7	LNs along the left gastric artery
No. 8a	LNs along the common hepatic artery
No. 9	LNs around the celiac axis
No. 10	LNs at the splenic hilum
No. 11	LNs along the splenic artery
No. 14	LNs along the superior mesenteric artery
No. 15	LNs along the middle colic artery
No. 18	LNs along the inferior margin of the pancreas.

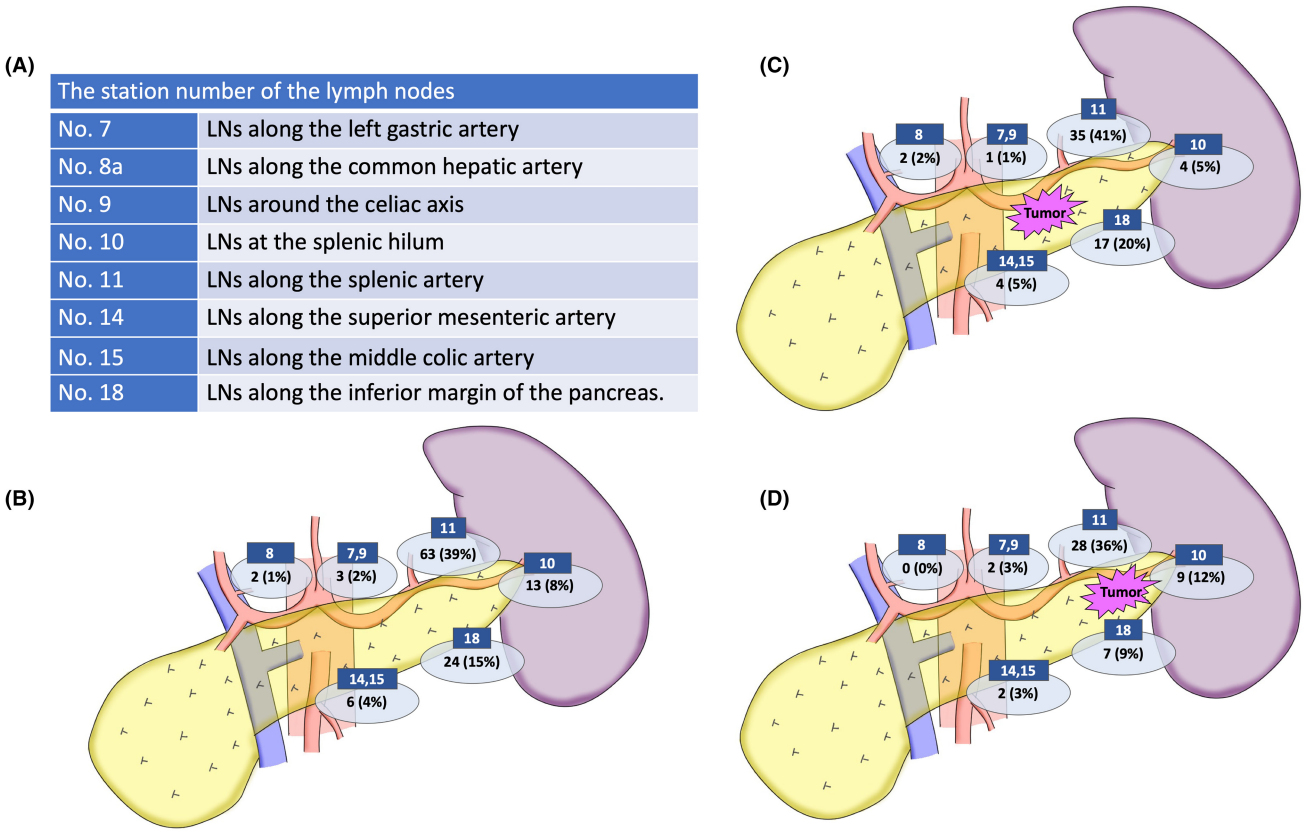

FIGURE 1 Schematics of station numbers of the lymph nodes and frequency of lymph node metastases. (A) Station numbers of the lymph nodes. (B) The rates of patients with lymph node metastases of the pancreatic ductal adenocarcinoma in the pancreas tail at each station. ($n=163$). (C) Lymph node metastases of the pancreatic ductal adenocarcinoma in the proximal pancreas tail ($n=86$). (d) Lymph node metastases of the pancreatic ductal adenocarcinoma in the distal pancreas tail ($n=77$).

surgery, level of pancreatic division, LN dissection along the common hepatic artery, operation time, and blood loss; postoperative course including postoperative pancreatic fistula (POPF), complications, postoperative hospital stay, and adjuvant chemotherapy; and pathological factors, including tumor size, T stage, LN metastasis, pancreatic cut end margin (PCM), and dissected peripancreatic tissue margin (DPM). The tumor location was divided into two groups: proximal and distal Pt-PDAC, with a median length of 16 mm from the tumor to the left edge of the aorta. In the patients who received neoadjuvant therapy, the data just before surgery was used in this study. Operative and pathological data were obtained from operative and pathological reports from each institution. POPF was defined according to the ISGPF.[10] In this study, POPF grades B and C were defined as clinically relevant POPF.

2.3 | Lymph node dissection and therapeutic value of each lymph node

LN dissection was performed routinely, and the LNs were divided into five groups, Nos. 8 and 9 (common hepatic artery and celiac artery), No. 11 (splenic artery), No. 10 (splenic hilum), Nos. 14 and 15 (superior mesenteric artery), and No. 18 (inferior margin of the pancreas), according to the classification of pancreatic carcinoma by the Japan Pancreas Society.[5] To evaluate the therapeutic value of dissection at each LN station, we used the therapeutic index reported by Sasako et al. for gastric cancer.[11] The therapeutic index of LN dissection (as a percentage) was obtained by multiplying the LN metastasis rate by the 5-year survival rate.

2.4 | Statistical analysis

We investigated the relationship between tumor location and clinicopathological features using univariate analyses. Furthermore, the effect of the level of pancreas division on the operative outcomes was investigated. Prognostic factors of recurrence-free survival (RFS) were analyzed by univariate and multivariate analyses.

All variables are expressed as the median (range) or mean ± standard deviation for continuous data. Univariate analyses were performed using the Student *t*-test for continuous variables and chi-squared test for categorical variables. Survival analysis was performed using Kaplan–Meier estimated survival, and the survival curves were compared using the log-rank test. Statistical significance was defined as $p<0.05$. All statistical analyses were performed with JMP 11 (SAS Institute Inc., Cary, NC, USA).

3 | RESULTS

3.1 | Patient characteristics

During the study period, 163 patients with Pt-PDAC underwent surgery with R0 or R1 resection. The clinicopathological characteristics are shown in Table 1. The pancreas was divided at the superior mesenteric vein (SMV) in 141 patients and to the left of the SMV in 22. The number of patients with LN metastasis was 78 (48%), and the frequency of LN metastasis at each station is summarized in Figure 1B. There were high incidences of metastases to the LNs along the splenic artery (No. 11). Overall, metastases were seldom found in the LNs along the common hepatic, left gastric, and celiac arteries (Nos. 7, 8, 9).

3.2 | Relation between tumor location and characteristics

The numbers of patients with proximal and distal Pt-PDAC were 86 and 77, respectively. As shown in Table 2, the rate of pancreas division at the neck was higher in the proximal Pt-PDAC group than in the distal Pt-PDAC. There were no significant differences between the two groups regarding the postoperative course and pathological findings. The frequency of LN metastasis in the proximal and distal Pt-PDAC is summarized in Figure 1C,D, respectively. Regarding the distal Pt-PDAC, there were no metastases to the LNs along the common hepatic artery (No. 8).

3.3 | Relation between level of pancreatic division and operative outcomes

The pancreas was divided at the neck (neck group) in 140 patients and at the body-tail (body-tail group) in 23 (Table 3). The rate of LN dissection along the common hepatic artery was lower in the neck group than that in the body-tail group. Although there were no significant differences in POPF between the two groups, the postoperative hospital stay in the body-tail group was longer than that in the neck group. Fewer LNs were dissected in the body-tail group than in the neck group. There were no significant differences in the rate of R0 resection.

3.4 | Prognostic factors of recurrence-free survival and overall survival in Pt-PDAC

Univariate analyses showed that CA19-9, blood loss, tumor size, LN metastasis, PCM, and DPM were significant factors related to RFS (Table 4). Multivariate analysis revealed that tumor size was the only independent factor related to RFS (hazard ratio = 2.01, 95% confidence interval = 1.33–3.05, $p = 0.001$). Regarding OS, Univariate analyses showed that CA19-9, blood loss, tumor size, LN metastasis, PCM, and DPM were significant factors (Table S1). Multivariate analysis revealed that CA19-9, tumor size, and DPM were the independent

TABLE 1 Characteristics of pancreas tail cancer ($n = 163$).

Characteristics	Value
Preoperative factors	
Age (years)	70.4 (40–87)
Sex (female/male)	78 (48%)/85 (52%)
BMI (kg/m^2)	21.9 (15.1–52.8)
PS (0/1/2)	126 (77%)/30 (18%)/7 (4%)
ASA-PS (0/1/2/3)	3 (2%)/27 (17%)/113 (69%)/20 (12%)
CEA (ng/mL)	3.3 (0.6–240)
CA19-9 (U/mL)	44.6 (0.6–7313)
Length between left edge of aorta and tumor (mm)	16 (0–73)
Neoadjuvant therapy (yes/no)	38 (23%)/125 (77%)
Operative factors	
Open/Laparoscopy	131 (80%)/32 (20%)
Pancreas division (above SMV/left of SMV)	141 (87%)/22 (13%)
LN dissection around common hepatic artery (yes/no)	146 (90%)/17 (10%)
Operation time (min)	279 (120–668)
Blood loss (mL)	327 (0–3741)
Postoperative course	
POPF (≥grade B)	28 (17%)
Complications (≥Clavien–Dindo 3)	36 (22%)
Postoperative hospital stay	18 (7–116)
Adjuvant chemotherapy (yes/no)	134/29
Pathological findings	
Tumor size (mm)	25 (1–88)
UICC T stage (1/2/3/4)	53 (33%)/73 (45%)/37 (23%)
LN metastasis (−/+)	78 (48%)/85 (52%)
Number of harvested LNs	20 (1–77)
Number of positive LNs	2 (0–16)
PCM (−/+)	159 (98%)/4 (2%)
DPM (−/+)	151 (93%)/12 (7%)

Abbreviations: ASA-PS, American Society of Anesthesiologists physical status; BMI, body mass index; DPM, dissected peripancreatic tissue margin; LN, lymph node; PS, performance status; PCM, pancreatic cut end margin; POPF, post operative pancreatic fistula; SMV, superior mesenteric vein.

TABLE 2 Relation between tumor location and characteristics.

Characteristics	Proximal ($n=86$)	Distal ($n=77$)	p Value
Patient characteristics			
Age (years)	70.4 ± 8.2	70.4 ± 8.2	0.990
Sex (female/male)	37 (43%)/49 (57%)	48 (62%)/29 (38%)	0.013
BMI (kg/m^2)	22.4 ± 4.6	22.3 ± 3.1	0.956
PS (0/1/2)	70 (81%)/13 (15%)/3 (3%)	56 (73%)/17 (22%)/4 (5%)	0.419
ASA-PS (0/1/2/3)	2 (2%)/14 (16%)/59 (69%)/11 (13%)	1 (1%)/13 (17%)/54 (70%)/9 (12%)	0.960
CEA (ng/mL)	5.3 ± 6.3	8.6 ± 29.6	0.317
CA19-9 (U/ml)	252 ± 698	398 ± 1103	0.311
Length between left edge of aorta and tumor (mm)	5.8 ± 5.4	31.6 ± 11.5	0.000
Neoadjuvant therapy (yes/no)	22 (26%)/64 (74%)	16 (21%)/61 (79%)	0.468
Operative factors			
Open/Laparoscopy	71 (83%)/15 (17%)	60 (78%)/17 (22%)	0.457
Pancreas division (above SMV/left of SMV)	79 (92%)/7 (8%)	61 (79%)/16 (21%)	0.020
LN dissection around common hepatic artery (yes/no)	79 (92%)/7 (8%)	67 (87%)/10 (13%)	0.312
Operation time (min)	309 ± 107	304 ± 102	0.737
Blood loss (mL)	492 ± 549	544 ± 580	0.554
Postoperative course			
POPF (≥grade B)	13 (15%)	15 (19%)	0.461
Complications (≥Clavien–Dindo 3)	18 (21%)	18 (23%)	0.707
Postoperative hospital stay			
Pathological findings			
Tumor size (mm)	31 ± 17	42 ± 15	0.331
UICC T stage (1/2/3/4)	25 (29%)/41 (48%)/20 (23%)/0	28 (36%)/32 (42%)/17 (22%)/0	0.598
LN metastasis (−/+)	38 (44%)/48 (56%)	40 (52%)/37 (48%)	0.322
PCM (−/+)	83 (97%)/3 (3%)	76 (99%)/1 (1%)	0.354
DPM (−/+)	80 (93%)/6 (7%)	71 (92%)/6 (8%)	0.842

Abbreviations: ASA-PS, American Society of Anesthesiologists physical status; BMI, body mass index; DPM, dissected peripancreatic tissue margin; LN, lymph node; PCM, pancreatic cut end margin; POPF, postoperative pancreatic fistula; PS, performance status; SMV, superior mesenteric vein.

TABLE 3 Relation between level of pancreas division and operative outcomes.

Outcomes	Neck ($n=140$)	Body-tail ($n=23$)	p Value
Operative factors			
Open/Laparoscopy	113 (81%)/27 (19%)	18 (78%)/5 (22%)	0.786
LN dissection around common hepatic artery (yes/no)	131 (94%)/9 (6%)	15 (65%)/8 (35%)	0.000
Operation time (min)	310 ± 107	283 ± 89	0.253
Blood loss (mL)	514 ± 567	530 ± 551	0.901
Postoperative course			
POPF (≥grade B)	22 (16%)	6 (26%)	0.244
Complications (≥Clavien–Dindo 3)	29 (21%)	7 (30%)	0.313
Postoperative hospital stay (day)	23 ± 16	34 ± 27	0.008
Tumor factors			
Length between left edge of aorta and tumor (mm)	16 ± 15	28 ± 17	0.001
Number of harvested LNs	23.4 ± 14.1	15.5 ± 11.4	0.014
PCM (−/+)	136 (97%)/4 (3%)	23/0	0.267
DPM (−/+)	129 (92%)/11 (8%)	22 (96%)/1 (4%)	0.525

Abbreviations: DPM, dissected peripancreatic tissue margin; LN, lymph node; PCM, pancreatic cut end margin; POPF, postoperative pancreatic fistula.

TABLE 4 Prognostic factors of RFS in Pt-PDAC by univariate and multivariate analyses.

	Univariate analysis		Multivariate analysis	
Factors	HR (95% CI)	*p* Value	HR (95% CI)	*p* Value
Age (>70 years)	1.11 (0.76–1.62)	0.605		
Sex (male)	1.02 (0.70–1.49)	0.927		
BMI (>25 kg/m^2)	0.81 (0.47–1.33)	0.429		
PS (≥1)	0.91 (0.56–1.42)	0.683		
ASA-PS (≥3)	0.94 (0.48–1.68)	0.846		
CEA (>5 ng/mL)	1.34 (0.88–1.99)	0.165		
CA19-9 (>37 U/mL)	1.73 (1.18–2.57)	0.005	1.50 (0.99–2.28)	0.056
Neoadjuvant therapy (no)	0.72 (0.48–1.12)	0.128		
Operative procedure (laparoscopy)	0.98 (0.58–1.57)	0.930		
Pancreas division (left of SMV)	1.08 (0.61–1.78)	0.778		
LN dissection around common hepatic artery (no)	1.21 (0.65–2.10)	0.508		
Operation time (>279 min)	0.98 (0.66–1.43)	0.897		
Blood loss (>327 mL)	1.57 (1.07–2.31)	0.021	1.28 (0.86–1.91)	0.230
POPF (≥grade B)	1.36 (0.84–2.13)	0.188		
Complications (≥Clavien–Dindo 3)	1.45 (0.92–2.20)	0.093		
Postoperative hospital stay (≥18 days)	1.34 (0.92–1.97)	0.131		
Adjuvant chemotherapy (no)	1.07 (0.62–1.76)	0.786		
Tumor size (>25 mm)	2.43 (1.64–3.61)	0.000	2.01 (1.33–3.05)	0.001
LN metastasis (+)	1.82 (1.24–2.71)	0.003	1.30 (0.86–1.99)	0.224
PCM (−/+)	3.57 (1.08–8.74)	0.014	2.25 (0.65–5.79)	0.135
DPM (−/+)	2.26 (1.10–4.14)	0.014	1.73 (0.81–3.35)	0.124

Abbreviations: ASA-PS, American Society of Anesthesiologists physical status; BMI, body mass index; CI, confidence interval; DPM, dissected peripancreatic tissue margin; HR, hazard ratio; LN, lymph node; PCM, pancreatic cut end margin; POPF, postoperative pancreatic fistula; PS, performance status; Pt-PDAC, pancreatic ductal adenocarcinoma of the tail; RFS, recurrence-free survival; SMV, superior mesenteric vein.

factors related to OS. Neoadjuvant and adjuvant therapy did not affect RFS and OS in this study (Figure S1).

3.5 | Relation between prognosis and tumor location or operative procedures

The rates and sites of tumor recurrence are shown in Table 5. The rate of local recurrence for proximal Pt-PDAC was significantly higher than that for distal Pt-PDAC ($p=0.024$), whereas the rate of liver metastasis for distal Pt-PDAC was significantly higher than that for proximal Pt-PDAC ($p=0.014$). The level of pancreas division and LN dissection along the common hepatic artery did not affect the tumor recurrence site. There was no difference in overall survival and RFS in regard to tumor location, level of pancreas division, and LN dissection along the common hepatic artery (Figure 2). Furthermore, laparoscopic surgery did not affect to the number of harvested LNs, the incidence of LN metastasis, and prognosis compared with open surgery.

3.6 | Lymph node metastases and therapeutic index of lymph node dissection

Figure 3 details the therapeutic index of LN dissection. In the analysis of the therapeutic index, regardless of whether proximal or distal Pt-PDAC was performed, the therapeutic index for Nos. 11 and 18 was high, and that for Nos. 7, 8, 9, 14, and 15 was low, with Nos. 7, 8, and 9 being zero.

4 | DISCUSSION

Most PDAC have high malignant potential and metastasize easily to regional LNs. LN dissection for PDAC is performed for therapeutic efficacy and nodal staging of cancer, and many reports have shown LN metastasis to be a prognostic factor.[2,12,13] However, extended LN dissection has been shown to have no prognostic benefit regarding pancreas head cancer.[3] Although there are many reports of LN

TABLE 5 Relation between tumor location or operative procedures and recurrence site.

Tumor location	Proximal ($n=86$)	Distal ($n=77$)	p Value
Recurrence site			
Local recurrence	19 (22%)	7 (9%)	0.024
Liver metastasis	13 (15%)	24 (31%)	0.014
LN metastasis	6 (7%)	8 (10%)	0.438
Peritoneal dissemination	10 (12%)	12 (16%)	0.461
Level of pancreas division	**Neck ($n=140$)**	**Body-tail ($n=23$)**	**p Value**
Recurrence site			
Local recurrence	22 (16%)	4 (17%)	0.839
Liver metastasis	32 (23%)	5 (22%)	0.906
LN metastasis	11 (8%)	3 (13%)	0.411
Peritoneal dissemination	19 (14%)	3 (13%)	0.945
LN dissection along common hepatic artery	**Yes ($n=146$)**	**No ($n=17$)**	**p Value**
Recurrence site			
Local recurrence	25 (17%)	1 (6%)	0.231
Liver metastasis	32 (22%)	5 (29%)	0.485
LN metastasis	11 (8%)	3 (18%)	0.159
Peritoneal dissemination	19 (13%)	3 (18%)	0.597

Abbreviations: LN, lymph node; SMV, superior mesenteric vein.

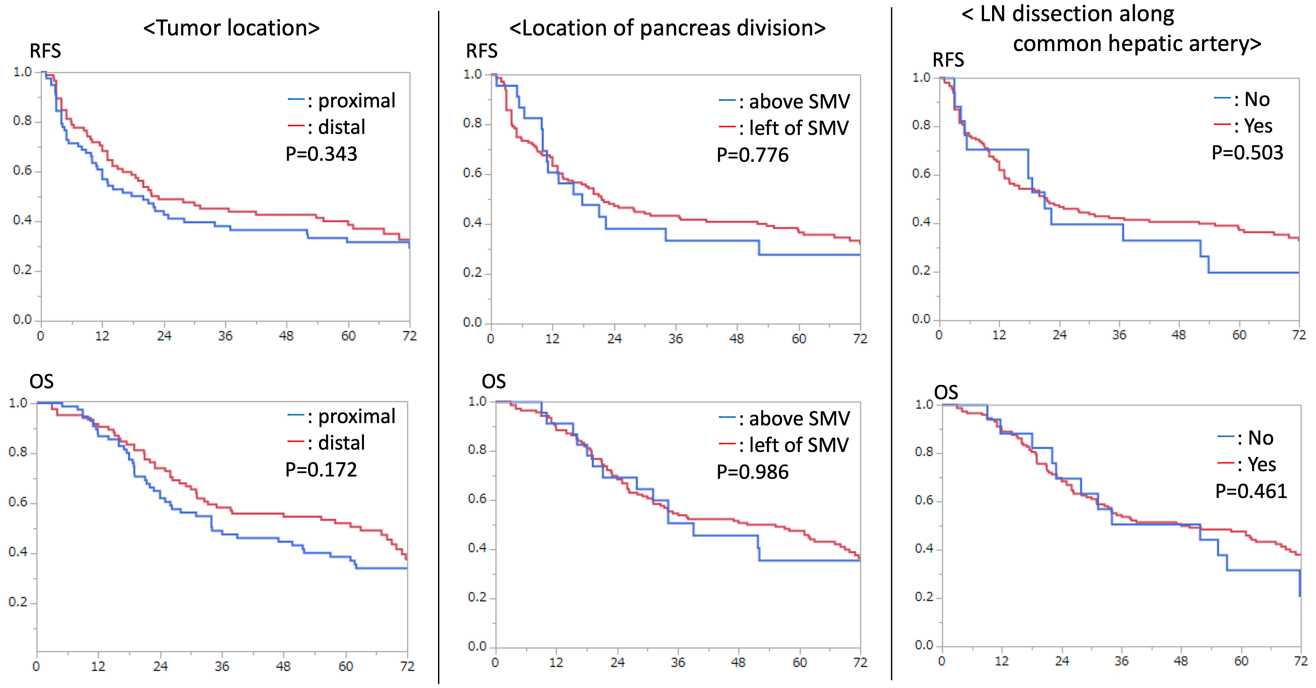

FIGURE 2 Kaplan–Meier curves of recurrence-free survival (RFS) and overall survival (OS) for tumor location, level of pancreas division, and lymph node (LN) dissection around the common hepatic artery. SMV, superior mesenteric vein.

dissection for left-sided PDAC, the ideal range has been controversial. Some investigators have emphasized the effectiveness of extended resections for adenocarcinoma of the body and tail of the pancreas, but the limited number of patients observed in these studies prevented a definitive result.[14,15] The ISGPS defined dissection of LN Nos. 10, 11, and 18 as standard in DP. Whilst some reports showed that left-sided PDAC sometimes metastasizes to LN No. 8,[16] the Japan Pancreas Society defined LN Nos. 8a and 9 in addition to those of the ISGPS as regional LNs to be the standard LN dissection for PDAC localized at the pancreas tail. In the present study,

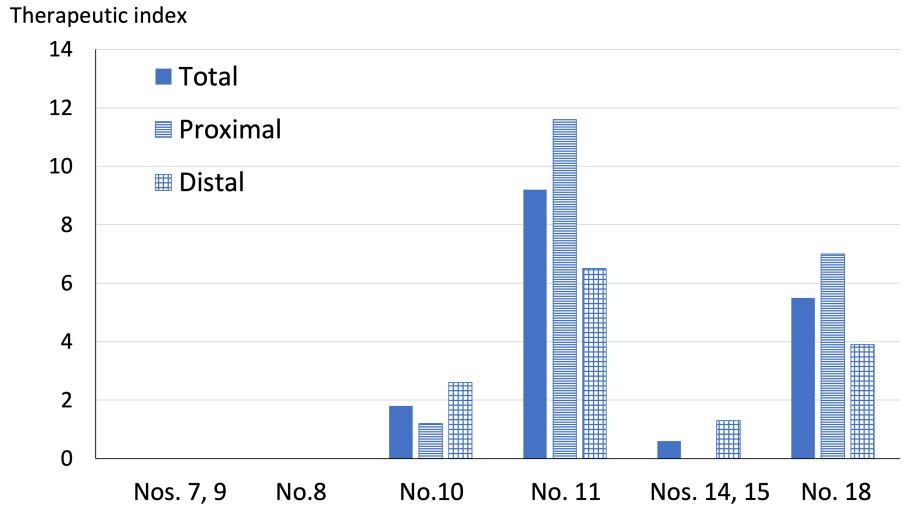

FIGURE 3 Therapeutic index of lymph node dissection. The therapeutic index of lymph node dissection (as a percentage) was obtained by multiplying the lymph node metastasis rate by the 5-year survival rate.

the rate of No. 8 LN metastasis was 1% for Pt-PDAC, and 0% for distal Pt-PDAC. Regarding the therapeutic index of LN dissection, LN dissection of Nos. 7, 8, and 9 for Pt-PDAC is of little significance. Therefore, dissection of these LNs may be unnecessary in PDAC localized to the pancreas tail. As this retrospective study alone cannot conclude that dissection of these LNs is not necessary, further research is required.

In recent years, there have been several reports on the extent of LN dissection in left-sided PDAC, and there are many opinions that the frequency of metastasis to LN Nos. 8 and 9 is low and that dissection is unnecessary especially in Pt-PDAC.[17–19] Ishida et al.[17] reported that non-peripancreatic LN (Nos. 7, 8, 9, and 14) metastasis was not observed when the tumor is 20 mm away from the portal vein and concluded that non-peripancreatic LN dissection can be avoided in those patients. Matsui et al.[18] reported that only LNs around the splenic artery and splenic hilus should be dissected routinely in patients with Pt-PDAC because there was no LN metastasis at station Nos. 7, 8, 9, and 14 in patients with Pt-PDAC. In contrast, Minagawa et al.[20] reported that metastasis to the LNs along the common hepatic artery or superior mesenteric artery was rare but was a significant prognostic factor in patients with pancreatic body/tail cancer. However, in Pt-PDAC, the frequency of metastasis in LN No. 8 or 14 is very low, and there is no metastasis to those LNs in more distal Pt-PDAC.

Several studies have suggested that the level of pancreatic division during DP has an impact on the risk of POPF.[21] Transection at the pancreatic neck was suggested to be more reasonable than transection at the pancreatic body or tail because the reduced thickness of the pancreatic neck would result in a lower risk of developing a POPF.[22] Regarding glucose tolerance, transection at the pancreatic body or tail may have advantages because several studies have suggested a positive relationship between diabetes and pancreatic volume reduction.[23,24] The results from the present study indicated that the level of pancreas division did not affect the rate of POPF in Pt-PDAC, and we did not examine glucose metabolism. However, although there was no significant difference, the rate of POPF was higher with transection at the pancreatic body or tail, and the length of hospital stay was longer. Furthermore, the low number of yielded LNs in the group of the pancreatic body or tail transection may indicate that the dissection range even at stations 11 and 18 was small. There was no difference between pancreas division of the neck and body-tail in terms of long-term outcomes, but the level of pancreatic division should be further investigated in the future.

Comparing proximal and distal Pt-PDAC, there was no difference in prognosis. Regarding recurrence site, the rates of local recurrence and liver metastasis were different, although there were no differences in the pathological factors. According to a previous report, a relationship between splenic vein invasion and liver metastasis has been shown,[25] but the relationship between tumor location and recurrence site is unclear. Larger studies limited to Pt-PDAC patients may be helpful to identify recurrence patterns in Pt-PDAC.

Multidisciplinary treatment is necessary for long survival, and a smooth transition between pre- and postoperative adjuvant treatment and surgery is important. Based on the results of many reports, including this study, No. 8 LN dissection may not be necessary for Pt-PDAC. To examine the relationship between surgical procedure and prognosis, this study enrolled patients before 2017 when neoadjuvant therapy was not actively performed. We also examined recurrence in these patients but found no difference in the incidence of LN recurrence or local recurrence based on the level of pancreas division. In the future, depending on the management of the pancreatic fistula, it may be possible to preserve the pancreatic parenchyma through more distal resection, and the necessity of RAMPS will need to be reconsidered.

This study has limitations. It is a retrospective study using multicenter data. Specific details of operative procedures might have differed among the institutions. Despite these limitations, this study contains important results for reconsideration of the surgical procedure for Pt-PDAC, including the range of LN dissection and the level of pancreas division.

In conclusion, LN dissection along the hepatic artery for PDAC in the pancreas tail has little significance. Reducing the extent of pancreatic resection may be acceptable in terms of oncological safety, but further examination of the short-term outcomes and the preservation of pancreatic function is required.

AUTHOR CONTRIBUTIONS

All authors substantially contributed to the conception and design of the study and performed the acquisition of data for the study. TH and MK performed analysis and interpretation of the data and drafted the manuscript. MI contributed to the review and/or critical revision of the article. Each author has participated sufficiently to the work to be considered an author and agrees to be accountable for all aspects of the work by ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. All of the authors have read and approved the final version of the manuscript.

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CONFLICT OF INTEREST STATEMENT

The authors declare no conflicts of interest for this article. Susumu Eguchi, Hiroaki Nagano, and Masafumi Inomata are editorial board members of *Annals of Gastroenterological Surgery*.

ETHICS STATEMENT

Approval of the research protocol: The protocol for this study was approved by the Ethics Committee of the study center (Oita University, approval number: 2446-D10) and complies with the Declaration of Helsinki and its later amendments.
Informed Consent: The acquisition of informed consent from patients was waived owing to the retrospective nature of this study.
Registry and the Registration No. of the study/trial: N/A.
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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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