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# The significance of pancreatic head plexuses dissection in pancreaticoduodenectomy for pancreatic adenocarcinoma

## — Surgery for achieving pathological curative (R0) resection —

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## ABSTRACT

**Background/Aims:** We aimed to histopathologically examine the significance of intraoperative histological diagnosis of pancreatic head plexus stumps in patients with pancreatic cancer.
**Methodology:** We included 94 patients (including 39 with pancreatic adenocarcinoma) who underwent dissection of pancreatic head nerve plexus (PLph) I and II in addition to pancreaticoduodenectomy between 2003 and 2011. The pancreatic nerve plexus dissection was performed en bloc with pancreaticoduodenectomy and resection of the anterior nerve tissue of the pancreas, including PLph I and II to the right of the celiac artery and superior mesenteric plexus. Intraoperative histopathological diagnoses were performed on all PLph I and II stumps. If malignancy was confirmed, partial resection of PLph II toward the left rear of the superior mesenteric artery (SMA) and/or the nerve plexuses surrounding SMA were additionally resected. In the absence of malignancy, R0 resection was performed.
**Results:** Intraoperative histopathological diagnoses of all patients were performed on a total of 1456 sites (PLph I: 542 sites, PLph II: 914 sites) with an average of 16 sites per patient. Cancer was discovered in part of the pancreatic nerve plexuses with high frequency: 15 of 94 patients (16%); 10 of 39 patients (25.6%) were diagnosed as pancreatic adenocarcinoma. In the 39 cases of pancreatic adenocarcinoma, the group with positive resection stumps that were later confirmed to be negative for cancer [PLph (+)→(-)], i.e., those with nerve plexus stumps positive for cancer initially but were negative for cancer after additional resection, showed no statistical difference from the [PLph (-)] group, in which all resection stumps were negative for cancer initially ($p = 0.51$).
**Conclusion:** It was important to perform R0 pancreaticoduodenectomy for pancreatic adenocarcinoma.

**Key words:** pancreatic head plexuses (extrapancreatic nerve plexuses), pancreatic adenocarcinoma, pathological curative resection, pancreaticoduodenectomy

## Introduction

Although there are various treatment strategies for pancreatic adenocarcinoma, the basic strategy is curative resection, which surgically eliminates pancreatic cancer. In other words, of the patients with pancreatic adenocarcinoma who undergo curative resection, some survive the disease, but none can achieve survival by undergoing noncurative resection or no resection at all. Therefore, the goal of the surgical treatment of pancreatic adenocarcinoma is complete resection of the cancer site[1), 2)].

One of the important mechanisms of cancer

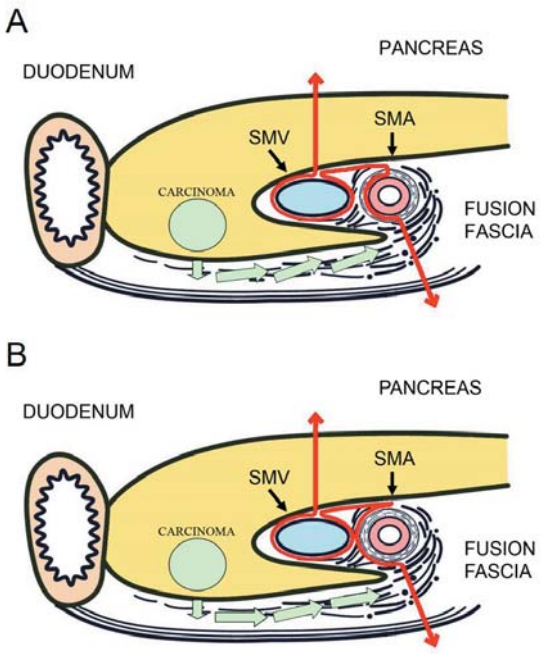


**Figure 1.** Invasion pattern of pancreatic adenocarcinoma occurring in the pancreatic head observed in an axial cross-section (green arrows) and line of resection en bloc of pancreatic head nerve plexuses I and II and posterior nerve connective tissue (red arrow).
During 2003-2006, the nerve plexsus of SMA were completely dissected from the adventitia of SMA (Fig. 1A). Nerve dissection was done a few millimeter apart from the adventitia of SMA during 2007-2011 (Fig. 1B).
Pancreatic head nerve plexus resection stumps that were positive for cancer via intraoperative histological diagnosis were subjected to partial additional resection of PLph II and/or SMA perivascular nerve plexus above and on the left side of the dorsal SMA. However, the vertical nerve plexuses were not resected along a vertical axis and the perivascular SMA nerve plexuses on the left side were not resected along their entire lengths. Instead, the resections were restricted to an area surrounding the cancerous site measuring approximately 1 × 1 cm.

progression in pancreatic adenocarcinoma is perineural invasion because this type of cancer is particularly likely to invade the areas surrounding the nerves[3), 4)]. Invasion to the extrapancreatic nerve plexus is very common in cases of pancreatic adenocarcinoma[5)–7)]. Although developments in diagnostic imaging have led to increasingly accurate diagnoses of extrapancreatic nerve plexus invasion, careful consideration is being made regarding whether complete surgical resection of pancreatic adenocarcinoma with invasion into the extrapancreatic nerve plexus is possible. Furthermore, subsequent multidisciplinary consideration of the optimal course of action will provide important insight, which will be useful in the decision-making process.

The pancreatic body parenchyma, tail tissue, head nerve plexus (PLph) I and II, and the perivascular nerve plexus of the superior mesenteric artery (SMA) are structures that occupy the same space that is covered by the fusion fascia of Treitz during embryological development. Therefore, after invading the nerve fibers or nerve bundles in the posterior tissue, pancreatic adenocarcinoma that develops in the pancreatic head invades laterally into the anterior portion of the fusion fascia of Treitz, i.e., it invades from left to right from PLph I and II into the perivascular area of SMA or celiac artery (Fig. 1)[8)–12)]. Based on this theory, we consider that the dissection of PLph I and II is crucial for radical surgery of pancreatic adenocarcinoma. The purpose of this study was to histopathologically investigate the significance of the dissection of PLph I and II.

pancreatic head plexuses dissection

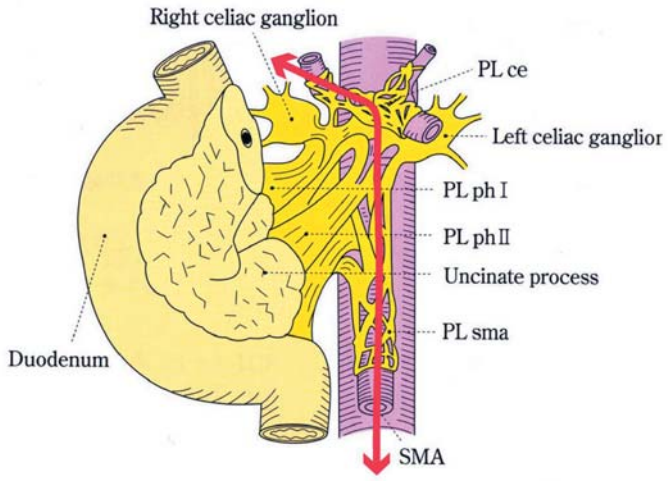


**Figure 2.** Line of resection en bloc of pancreatic head nerve plexuses I and II and posterior nerve tissue seen from a frontal view (red arrow). No resection was performed when the perivascular SMA nerve plexus was negative for cancer.
PL ce: Celiac Plexus, PLph I: Pancreatic head plexus I, PLph II: Pancreatic head plexus II, PL sma: Superior mesenteric arterial plexus
Modified quotation from the Japan Pancreas Society. Classification of Pancreatic Carcinoma. Third English ed. Tokyo: Kanehara, 2011 (16).

## Methodology

1. We included 94 patients (62 men and 32 women) who underwent pancreaticoduodenectomy with dissection of PLph I and II between 2003 and 2011. They had an average age of 68.1 ± 7.9 (range: 39-79) years and were diagnosed with the following conditions: pancreatic adenocarcinoma (39 patients), intraductal papillary mucinous neoplasm (IPMN) of the pancreas (18 patients: adenoma/borderline, 13 patients; carcinoma in situ, 2 patients; and invasive carcinoma derived from IPMN, 3 patients), lower cholangiocarcinoma (24 patients), carcinoma of the ampulla of Vater (12 patients), and endocrine tumor (1 patient).

2. Dissections of PLph I and II in addition to pancreaticoduodenectomy were performed in accordance with methods previously reported[1), 2), 10)]. In brief, the duodenum and posterior surface of the pancreatic head were resected using the Kocher maneuver to remove the parts of the fusion fascia of Treitz adhered to the pancreatic head, and PLph I and II and/or the right of the nerve plexus of SMA were dissected en bloc with the pancreas (Fig. 1-3). During 2003 - 2006, the nerve plexus of SMA were completely dissected from the adventitia of SMA (Fig. 1A). Number of completely dissection was 16 cases out of 39 pancreatic cancer. Since the nerve dissection in front of SMA bleed, and extended dissection of the nerve plexus did not show survival benefit from Japanese randomized control study[13)], nerve dissection was done a few millimeter apart from the adventitia of SMA during 2007 - 2011 (Fig. 1B). Number of later was 23 cases out of 39 pancreatic cancer. That is, all of the small parts of PLph I and II and/or SMA nerve plexuses are ligated and cut (Fig. 3A, B), and the cut ends of the all of the pieces are divided and histopathologically investigated (Fig. 3C). Fig. 3D shows the final view after the resection of PLph I and II and/or SMA nerve plexuses of the pancreatic head.

When the above procedure was performed, both PLph I and PLph II resection stumps were numbered and intraoperative histopathological diagnosis was performed. All resection stumps were ligated, but were so arranged that the numbered stumps used for histopathological diagnosis could be identified (Fig. 4).

PLph resection stumps that were identified as

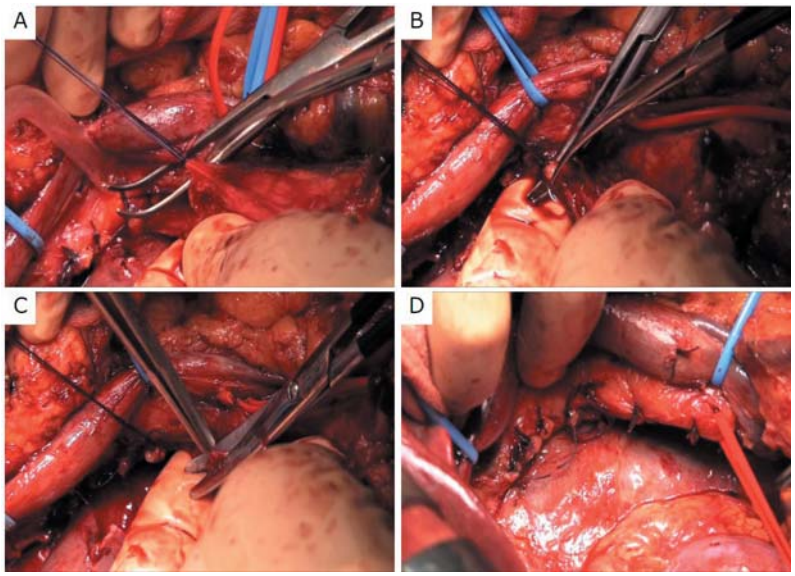


**Figure 3.** Photographs of postresection pancreatic head nerve plexuses I and II
A,B: The upper parts of PLph I are ligated (A) and cut (B).
C: The cut end of the upper parts of PLph I are divided and histopathologically investigated.
D: The final view after the resection of PLph I and II.

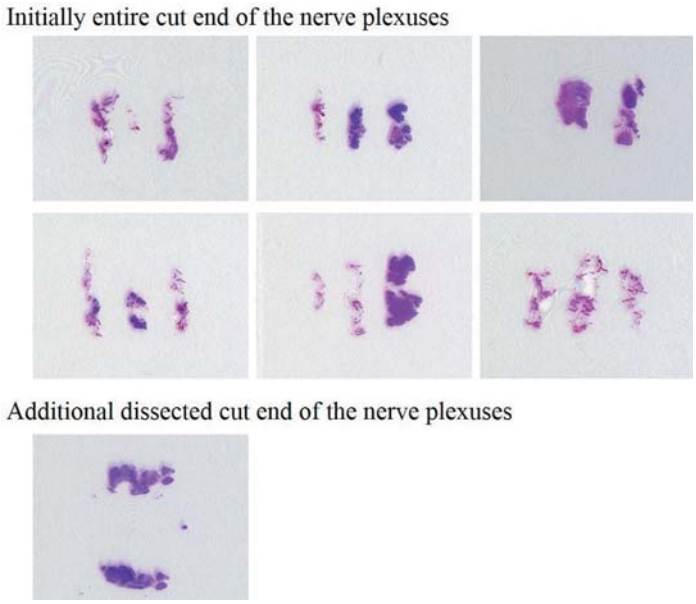


**Figure 4.** Hematoxylin and eosin stained samples during intraoperative pathological diagnoses of the pancreatic head nerve plexus resection stumps.
All PLph I and II resection stumps were subjected to intraoperative histopathological diagnosis. Those that were positive for cancer were subjected to additional partial resection of the nerve plexus on the left side and then resulted negative for cancer histologically [PLph (+)→(-)].

positive for cancer by intraoperative histopathological diagnosis were handled as follows. PLph II and/or SMA perivascular nerve plexus above and on the left side of the dorsal SMA were partially resected and used for intraoperative histopathological diagnoses. However, the vertical nerve plexuses were not resected along a long vertical axis and the perivascular SMA nerve plexuses on the left side were not resected along their entire lengths; rather, the resections were restricted to an area surrounding the

pancreatic head plexuses dissection

**Table 1.** Detailed data on the dissected cut ends of the pancreatic head nerve plexuses in 94 cases

| | PL ph I | PL ph II | Total |
|---|---|---|---|
| Total number of the dissected cut end | 542 | 914 | 1456 |
| Number of the dissected cut end per patient | 5.8 ± 1.9 | 9.7 ± 4.1 | 16.5 ± 4.7 |
| Total number of the first positive cut end | 9 | 15 | 24 |

PL ph I, Pancreas head plexus I; PL ph II, Pancreas head plexus II

**Table 2.** Relationship between pathological diagnosis and the number of PLph(+)→(-) patients.

| Pathological diagnosis | Enrolled patients | PLph(+)→(-) | | |
|---|---|---|---|---|
| | | Only PLph I | Only PLph II | Both PLph |
| Adenocarcinoma of the pancreas | 39 | 3 | 4 | 3 |
| IPMN (adenoma) | 13 | 0 | 0 | 0 |
| IPMN (carcinoma in situ) | 2 | 0 | 0 | 0 |
| IPMN (invasive carcinoma) | 3 | 0 | 1 | 0 |
| Endocrine carcinoma | 1 | 0 | 0 | 0 |
| Adenocarcinoma of the extrabile duct | 24 | 0 | 1 | 0 |
| Adenocarcinoma of the ampullary resion | 12 | 1 | 0 | 0 |
| Total | 94 | 4 | 6 | 3 |

**PLph(+)→(-),** The initial end positive− final cut negative group consists of cases in which the intraoperative histopathological diagnosis of the pancreatic head nerve plexuses were positive, even if only one part, and then were confirmed as negative after additional resection; **Only PLph I,** Cases in which only the initial dissected ends of the pancreatic head nerve plexus I were positive for cancer; **Only PLph II,** Cases in which only the initial dissected ends of the pancreatic head nerve plexus II were positive for cancer.; **Both PLph,** Cases in which the initial dissected ends were positive for cancer for both the pancreatic head nerve plexuses I and II.

IPMN, intraductal papillary mucinous neoplasms of the pancreas; IPMN (adenoma), IPMN with low or intermediate grade dysplasia, adenoma or borderline; IPMN (carcinoma in situ), IPMN with high-grade dysplasia, noninvasive carcinoma; IPMN (invasive carcinoma), IPMN with an associated invasive carcinoma.

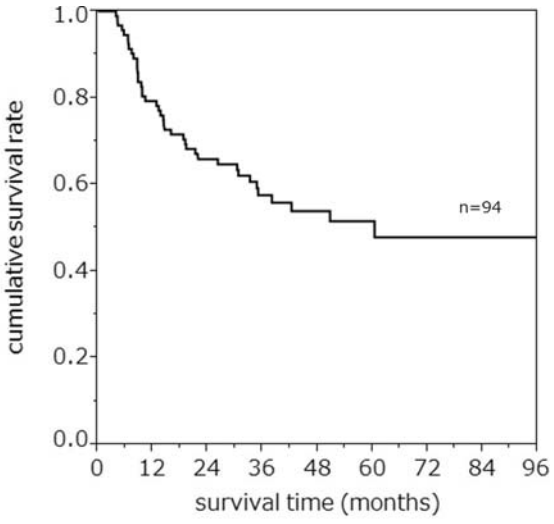


**Figure 5.** Total survival rates for the 94 patients that underwent dissection of pancreatic head nerve plexuses I and II in addition to pancreaticodudodenectomy (Kaplan-Meier)
The average observation period and the median survival time were 29.3 and 60.4 months, respectively. The 1-, 3-, and 5-year total survival rates were 79.3%, 57.8%, and 51.6%, respectively.

cancerous site measuring approximately 1 × 1 cm. The stumps of the partially resected tissue were then confirmed to be negative for cancer via intraoperative histopathological diagnosis (Fig. 4). Partial resection was possible in all patients. While waiting for the results of the intraoperative histopathological diagnosis, we performed pancreaticojejunostomy. Thus, R0 resections were performed on all PLph I and II resection stumps determined to be negative for cancer via intraoperative histopathological diagnosis. Recently, the use of specialized instruments has shortened the operation time for gastrojejunostomy and Braun anastomosis. In this study, these procedures could be performed while waiting for the intraoperative histopathological diagnoses results.

Resected stumps of pancreatic body (1 section) and bile duct (round, cross-sectional slice, 1 section) were subjected to the same intraoperative histopathological diagnoses and additional resections were performed when they were found to be positive for cancer.

3. Cases in which the resected stumps of PLph I and

**Table 3.** Characteristics of patients with ordinary pancreatic adenocarcinoma according to the results of the nerve plexus end.

| | PLph(+)→(-)<br>N = 10 | PLph(-)<br>N = 29 | *p value* |
|---|---|---|---|
| Age (year) | | | |
| Mean ± SD (range) | 68 ± 6 (59-77) | 68 ± 8 (52-79) | 0.84 |
| Gender | | | |
| man | 5 | 18 | 0.71 |
| woman | 5 | 11 | |
| Diabetes (yes/no) | | | |
| yes | 5 | 9 | 0.45 |
| no | 5 | 20 | |
| Jaundice (yes/no) | | | |
| yes | 5 | 13 | 1.00 |
| no | 5 | 16 | |
| CEA (IU/l) | | | |
| Mean ± SD (range) | 4.0 ± 2.9 (0.8-7.0) | 2.6 ± 1.2 (1.29-11.25) | 0.11 |
| CA19-9 (IU/l) | | | |
| Mean ± SD (range) | 124.3 ± 115.5<br>(9.7-371.7) | 363.1 ± 1059.9<br>(11.1-5728) | 0.72 |
| Tumor size (cm) | | | |
| Mean ± SD (range) | 3.3 ± 0.6 (2.3-4.2) | 3.2 ± 1.9 (1.5-11) | 0.17 |
| UICC TNM Classification (7th ed.) | | | |
| T factor | | | |
| T1/T2/T3 | 0/0/10 | 3/3/23 | 0.31* |
| N factor | | | |
| N0 | 3 | 19 | 0.07 |
| N1 | 7 | 10 | |
| Stage | | | |
| ⅠA / Ⅰb/ Ⅱa/ Ⅱb | 0/0/3/7 | 1/2/16/10 | 0.56** |
| Adjuvant Chemotherapy | | | |
| yes | 2 | 13 | 0.26 |
| no | 7 | 15 | |
| Follow-up period (months) | | | |
| Mean ± SD (range) | 21.4 ± 13.5 (6.8-42.3) | 22.5 ± 19.4 (3.7-77.1) | 0.71 |

*, statistically analysis comparing T3 and other T; **, statistically analysis comparing Stage Ⅰ and Ⅱ.
CEA: serum carcinoembryonic antigen, CA19-9: serum carbohydrate antigen 19-9

II were negative for cancer were placed in a group labeled "initial negative resection stump group" [PLph (-)]. Those that had at least one positive cancer site were subjected to additional resection, which then were found to be negative for cancer, and were placed in the group labeled initially positive and ultimately negative for cancer [PLph (+)→(-)].

4. The positive-for-cancer rate of PLph I and II resected stumps for all 94 patients was calculated.

5. The total number of PLph I and II specimens that were resected from all 94 patients and subjected to intraoperative histopathological diagnosis was calculated.

6. The frequencies of initially positive-for-cancer resection stumps for all 94 patients by disease were calculated.

7. Our analysis of the increased number (10 of 39 patients) of patients with pancreatic adenocarcinoma that were positive is as follows. We first calculated the total survival rate of all 39 patients of pancreatic adenocarcinoma. Thereafter, we compared the survival rate of the PLph (-) group with that of the PLph (+)→(-) group.

### Statistical analysis

We used JMP version 10.0.2 statistical software (SAS Institute Inc., Cary, NC, USA) for the statistical

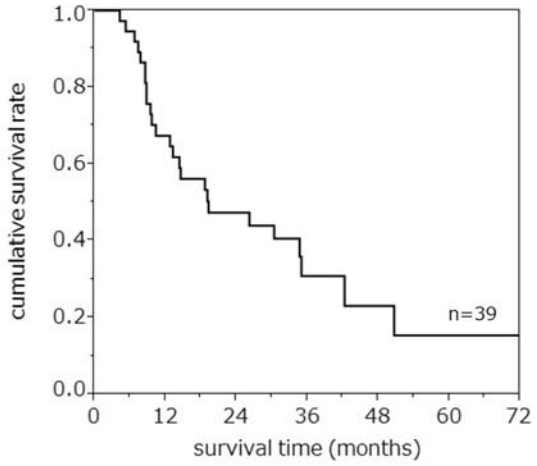


**Figure 6.** Total survival rates for the 39 patients with pancreatic adenocarcinoma (Kaplan-Meier)
The average observation period and the median survival time were 19.3 and 19.1 months, respectively. The 1-, 3-, and 5-year total survival rates were 67.3%, 36.8%, and 18.5%, respectively.

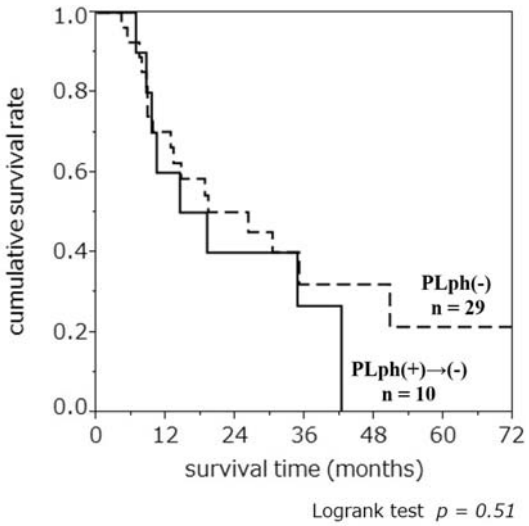


**Figure 7.** Total survival rates by initial resection stump result for pancreatic head nerve plexuses I and II with pancreatic adenocarcinoma (Kaplan-Meier)
PLph (+)→(-): PLph I and PLph II resection stumps that had even one site that was positive for cancer via intraoperative histopathological diagnosis were subjected to additional resection and then confirmed to be negative for cancer. These patients were classified in a group of patients who were initially positive and ultimately negative for cancer.
PLph (-): PLph I and PLph II resection stumps that were negative for cancer at the time of initial resection via intraoperative histopathological diagnosis. These patients were classified in a group of patients who were initially negative for cancer.

analysis. Continuous data is presented as the mean ± standard deviation (range). We used the Wilcoxon test for intergroup comparison of continuous data and the Fisher's exact test to determine the intergroup differences in frequency. Total survival rates were calculated using Kaplan− Meier survival curves, and compared using the log-rank test. Statistical significance was set at $p < 0.05$.

## Results

### Results I: All 94 patients

1. Fifteen of the 94 patients (16%) were initially positive for cancer in PLph I and II resection stumps.
2. PLph resection stump specimens subjected to intraoperative histopathological diagnosis were taken from a total of 1,456 sites (PLph I: 542 sites, PLph II: 914 sites) from the 94 patients who underwent pancreaticoduodenectomy (Table 1). The total number of sites per patient ranged from 8 to 30, with an average of 16.5 sites per patient. This included an average of 5.8 PLph I sites (3-13) and 9.7 PLph II sites (4-25). Of the total 1,456 sites, 9 PLph I sites and 15 PLph II sites were initially positive for cancer.
3. As indicated above, resection stumps from PLph I or II that had even one site positive for cancer by intraoperative histopathological diagnosis were placed in the PLph (+)→(-) group. There were 15 patients (16% of the total) in the PLph (+)→(-) group (Table 2). Only 5 patients presented with cancer in PLph I, 7 patients in PLph II, and 3 patients in both the nerve plexuses. Most patients (10) in the PLph (+)→(-) group had pancreatic adenocarcinoma, and all 3 patients that were positive for cancer in both PLph I and II had pancreatic adenocarcinoma. One of the 3 patients had invasive carcinoma derived from IPMN, 1 of the 24 patients had bile duct carcinoma, and 1 of the 12 patients had ampullary carcinoma, respectively.
4. The total survival rates for the 94 patients are shown in Figure 5. The average observation period was 29.3 ± 26.6 (3.7-120.2) months. The mean survival time was 60.4 months, and the 3- and 5-year survival rates were satisfactory (57.6% and 47.9%, respectively).

### Results II: 39 cases of pancreatic adenocarcinoma

5. Most (10) of the patients in the PLph (+)→(-) group were diagnosed with pancreatic adenocarcinoma. We performed detailed examinations of these patients. The average age of the 39 patients with pancreatic adenocarcinoma was 67.9 ± 7.8 (52-79). There were 23 men and 16 women (Table 3). Ten of these 39 patients (25.6%) were placed in the PLph (+)→(-) group and were determined to be negative for cancer after additional resections were performed. While there were no significant differences between the 2 groups for preoperative factors, patients in the PLph (+)→(-) group tended to have high carcinoembryonic antigen (CEA) levels. In terms of postoperative final diagnosis, although there were no significant differences between the groups for tumor size, T-factor, N-factor, or stage according to the UICC TNM classification (7th edition)[14]; patients in the PLph (+)→(-) group tended to have higher scores. Many of the patients that did not undergo postoperative adjuvant chemotherapy were in the PLph (+)→(-) group, but the difference between the 2 groups was not significant.

6. The total survival rates of the 39 patients with pancreatic adenocarcinoma are shown in Figure 6. The average observation period was 22.2 months; the mean survival time (MST) was 19.3 months; and the 1-, 3-, and 5-year survival rates were 67.3%, 30.8%, and 18.5%, respectively. Our comparison of the total survival rates for the 10 patients in the PLph (+)→(-) group and the 29 patients in the PLph (-) group are shown in Figure 7. MST was 14.4 months in the PLph (+)→(-) group and 26.2 months in the PLph (-) group. There were no statistically significant differences between the PLph (+)→(-) and PLph (-) groups ($p = 0.51$). However, long-term survival was not observed in the PLph (+)→(-) group (5-year survival rate: 0% vs. 21.4%) and patients in this group tended to have poor prognosis (Fig. 7).

## Discussion

### 1. Surgical anatomy of the extrapancreatic nerve plexuses

The classification of pancreatic carcinoma[15] divides extrapancreatic nerve plexuses into 7 sites (Fig. 2). Previous studies on the surgical anatomy have identified the following main nerves distributed in the pancreas: 1) Nerve that enters the upper medial margin of the uncinate process from the right celiac ganglion (pancreatic nerve head I), 2) Nerve that enters the medial margin of the uncinate process past SMA from the left and right sides of the celiac ganglion (PLph II), 3) Nerve that enters the pancreatic head along the common hepatic artery and the gastroduodenal artery, 4) Nerve that enters the posterior aspect of the pancreatic tail via the splenic plexus from the left celiac ganglion, and 5) Nerve that runs directly toward the anterior portion of the pancreas from the left celiac ganglia and the celiac plexus. Of these, numbers 1 and 2 are formed from markedly thick nerve bundles and were therefore named PLph I and II, respectively, by Yoshioka & Wakabayashi[16].

### 2. Dissection method of PLph I and II

Classifications of invasion into the posterior pancreas, PLph I and II, and superior mesenteric plexus are important for tumor staging. However, from a surgeon's point of view, all of these require resection[1), 2), 14)]. R0 resection renders a cancer-free resected stump. Therefore, surgeons performing surgery for pancreatic adenocarcinoma essentially consider PLph I and II, posterior nerves, and connective tissue together with the SMA perivascular nerve plexus.

All of these structures are present within the same space covered by the fusion fascia of Treitz[8], together with the pancreatic parenchyma, nerves, and arteries. Therefore, cancer can easily invade adjacent structures and continue to expand without resistance. In effect, when cancer developing in the pancreatic head expands, it invades the nerve bundles anterior to the pancreas. Instead of invading vertically, it does so laterally, i.e., it invades toward the left side of the patient's body, toward SMA (Fig. 1). Therefore, determination of whether resection of pancreatic adenocarcinoma in the pancreatic head is possible or not does not depend on whether the cancer has invaded the inferior vena cava because invasion to the perivascular SMA is the most commonly observed scenario. Pancreatic adenocarcinoma appears to have

an affinity for nerve invasion; therefore, invasion along nerve plexuses is common. Because this type of infiltration cannot be observed by the naked eye, it is important to perform a pathological examination[1].

The tissue that reaches PLph and SMA from the tissue of the anterior pancreatic head that is surrounded by the fusion fascia of Treitz serves as vehicle for the progression of pancreatic adenocarcinoma (Fig.1)[1), 2)].

There are reports[18), 19)] indicating that imaging diagnosis is possible for invasion of PLph I and II. However, in the present study, cases in which preoperative imaging diagnosis and intraoperative clinical examination did not reveal perineural invasion were later discovered to have perineural invasion via pathological examination. Resection of nerve plexuses that have been diagnosed with pancreatic adenocarcinoma is essential to the goal of surgery that will render the resection stump histopathologically negative for cancer (ew [-]).

### 3. Determination of positive-for-cancer or negative-for-cancer in the resection stumps of PLph I and II when pancreaticoduodenectomy was performed

The importance of determining sites that may have microscopic residual tumor (R1) in the area defined as PLph to the right of SMA is now recognized[1), 2), 20)−26)]. R1 resections reportedly have poor prognosis[20), 23), 25), 27)−29)], especially R1 resection of SMA stumps[27)]. Therefore, it is extremely important to perform R0 resections in this area.

Postoperative pathological examination and handling of the samples were not considered sufficient to investigate all PLph I and II resection stumps to determine whether samples were negative or positive for cancer along the length and width of PLph I and II. Samples deform and shrink after formalin fixation, and this makes it impossible for the surgeon to determine the location of the resection stump. Further, this would be impossible for a pathologist who did not observe the surgery being performed. In recent years, inking of resection stumps has been shown to be a pathologically effective method; as a result, the number of R1 resections have surprisingly increased[26), 29)]. Furthermore, the AJCC cancer manual indicates that pathological examinations should be conducted after the SMA margin is inked[30)]. However, the inking method allows one to determine if a R0 resection was performed only after surgery; it cannot be known during surgery if an actual R0 resection was performed. A major difference in our method is that it allows the surgeon to know during surgery whether an actual R0 was performed and allows an additional resection to be performed during surgery.

A study[25)] reported subjecting part of the PLph resection stump to intraoperative histopathological examination with the intention of performing additional resection if found to be positive for cancer, but the stump was histopathologically determined to be negative for cancer. However, this study comprised one patient and examined only part of the nerve plexus. To the best of our knowledge, there are no studies reporting on the performance of intraoperative pathological examination of each PLph resection stump along the vertical axis in cases in which there is no clear invasion into PLph I and II with additional resection of the nerve plexuses that were positive for cancer as well as histological complete resection, similar to our study.

Many studies report on R0 resections based on naked eye assessment. However, these did not include intraoperative histopathological examinations of all resection stumps; thus, it is difficult to call these "actual R0 resections." They were simply referred to using this term because the results seem to indicate it.

The detailed investigation performed in this study indicated that even in cases in which localized complete resections were performed, there were no significant differences between the prognosis of cases with initial invasion into PLph I and II and those without such invasion. Therefore, this indicates the importance of performing R0 resection along the length and width of PLph I and II to render them cancer-free.

However, long-term survival was not observed in the PLph (+)→(-) group (5-year survival rate: 0% vs. 21.4%). Median survival time for the 10 patients with adenocarcinoma [PLph (+)→(-) group] was 14.4 months, whereas it was 26.2 months for the 29 patients in the PLph (-) group. These results indicate the possibility that the number of patients used in this study was too small to produce statistically

significant differences. This aspect requires further research.

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