

Pancreatectomy for Pancreatic Cancer with Reference to Combined Resection of the Vessels, Twenty Nine Year Experience by a Single Surgeon

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Abstract

Between 1978 and 2007 one hundred and seven patients consecutively underwent resection for primary pancreatic adenocarcinoma. There were 28 pN0 patients, 41 pN1 and 37 pN2 or more (one unknown). Combined resection of the portal vein was performed in 62 out of 107 patients (58%). The hepatic artery in 10 patients, superior mesenteric artery in 8 patients and celiac trunk in 7 patients were also resected additionally to the portal vein. The 5-year survival rate and 10-year survival rate of all 107 cases were 12.1% and 2.8% respectively. The 5-year survival rate of the pN0 group was 37%, significantly better than the 14% 5-year survival rate in the pN1 group ($p=0.043$). Of 69 patients with pN0 or pN1, 38 patients underwent combined resection of the portal vein. There was not significant difference between the 24% 5-year survival rate in the group without the portal vein resection and the 19% 5-year survival rate in the group with portal vein resection. The 20% 5-year survival rate of the portal vein only group and the 5-year survival rate of both the portal vein and hepatic artery group were the same. The groups of the further resection of the superior mesenteric artery and of the celiac trunk showed no long-term survival. It is concluded that aggressive combined resection of the portal vein or additional resection of the hepatic artery be feasible for a survival benefit in pN0 and pN1 diseases. (Keio J Med 58 (2) : 103–109, June 2009)

Keywords: pancreatic cancer, pancreatectomy, portal vein, hepatic artery

Introduction

Nothing else than pancreatic cancer has been so much operated, by so many surgeons, to so few long-term survivors. When pancreatic cancer is detected, the lesion is already grown enough to destroy desmoplastically the surrounding soft tissue, vessels or organs. In Japan combined resection of the portal vein and wide resection of the lymphnode around the aorta have prevailed as feasible in an advanced facility. Despite extended retroperitoneal lymphadenectomy or extended surgery the patient's survival rate was not yet improved.¹ The outcome was

analyzed by focusing on feasibility of combined resection of the major vessels.

Patients and Methods

Between 1978 and 2007 one hundred and seven patients consecutively underwent resection for primary pancreatic adenocarcinoma excluding mucin producing carcinoma, cystadenocarcinoma, endocrine tumor as well as solid pseudopapillary tumor (resectability 50%). There were 69 males and 38 females. The ages ranged from 23 to 79 years (mean 62 ± 10). The procedures were

Table 1

procedure	PV resection and plus α				
	n	PV resection	HA	SMA	Ce
total pancreatectomy	28	23	3	4	7
PD or PpPD	64	35	6	4	0
distal pancreatectomy	15	4	1	0	1*
total	107	62	10	8	8

(HA=hepatic artery, SMA=superior mesenteric artery, Ce=celiac trunk)
(* independent resection)

decided by the location of the main lesion as 64 pancreatoduodenectomies or pylorus preserving pancreatoduodenectomies, 28 total pancreatectomies and 15 distal pancreatectomies (**Table 1**). Four patients died in the hospital, of complication due to surgery (mortality rate 3.7%). All patients underwent lymphadenectomy around the pancreatic head, in the hepatoduodenal ligament, along the common hepatic duct and the right side of superior mesenteric artery. The paraaortic node was picked just behind the pancreatic head. The lymphnode status was classified as pN0: no metastasis, pN1: metastasis only in the local node which attaches to the pancreas parenchyma, pN2: metastasis in the regional node which is able to resect easily by a competent surgeon and pN3: metastasis in the far node which cannot be resected without resection of the organs, due to the location of cancer in the head, body and tail, respectively, modifying the General Rules for Study of Pancreatic Cancer.² There were 28 pN0 patients, 41 pN1 and 37 pN2 or more. Combined resection of the portal vein was performed in 62 out of 107 patients (58%). The portal vein and superior mesenteric vein were resected on grounds of preoperative CT findings and the intraoperative judgment, ligating the distal splenic vein. The superior mesenteric artery and celiac trunk were indicated to resection also on grounds of preoperative CT findings and the intraoperative judgment. Anastomosis of a vessel was done in the end to end fashion using a graft in cases. The hepatic artery was resected when the gastroduodenal artery was impossible to sever from the common hepatic artery for invasion of carcinoma, anastomosing the common hepatic artery and proper hepatic artery. The portal vein was resected in 35 of 64 pancreatoduodenectomies or pylorus preserving pancreatoduodenectomies (55%), 23 of 28 total pancreatectomies (82%) and 4 of 15 distal pancreatectomies (27%). The hepatic artery in 10 patients, superior mesenteric artery in 8 patients and celiac trunk in 7 patients were also resected additionally to the portal vein.

The actuarial survival rate was calculated with the Ka-

plan Meier method. The difference of the two groups was examined with Logrank test defining the P value less than 0.05 as significant. All 107 cases including deaths in the hospital and later deaths due to other causes than cancer recurrence were used for these statistics.

Results

The 5-year survival rate and 10-year survival rate of all 107 cases were 12.1% and 2.8% respectively. The 5-year survival rate of the pN0 group was 37%, significantly better than the 14% 5-year survival rate in the pN1 group ($p=0.043$). In the patients with positive nodes the pN1 group could live significantly longer than the group with pN2 or more (**Fig. 1**). Of 69 patients with pN0 or pN1, 38 patients underwent combined resection of the portal vein. There was not significant difference between the 24% 5-year survival rate in the group without the portal vein resection and the 19% 5-year survival rate in the group with portal vein resection (**Fig. 2**). Further resection of the hepatic artery was performed in 5 patients out of 69 patients with pN0 or pN1. The 20% 5-year survival rate of the portal vein only group and the 5-year survival rate of both the portal vein and hepatic artery group were the same ($p=0.88$) (**Fig. 3**). A 65 y-o male with pancreatic head cancer lived more than five years. The hepatic artery was combinedly resected as the gastroduodenal artery was difficult to sever from the common hepatic artery for invasion of carcinoma. There was histologic invasion to the gastroduodenal artery but not to the hepatic artery. The groups of the further resection of 6 cases of the superior mesenteric artery and of 5 cases of the celiac trunk showed no long-term survival (**Fig. 4, 5**).

Last fifteen patients of this series have had adjuvant chemotherapy. The results are not yet evaluated for the short observation period. A noteworthy patient is a 62-y-o female who underwent Pylorus preserving Pancreatoduodenectomy and combined resection of the portal vein for pancreatic head carcinoma. The pathology

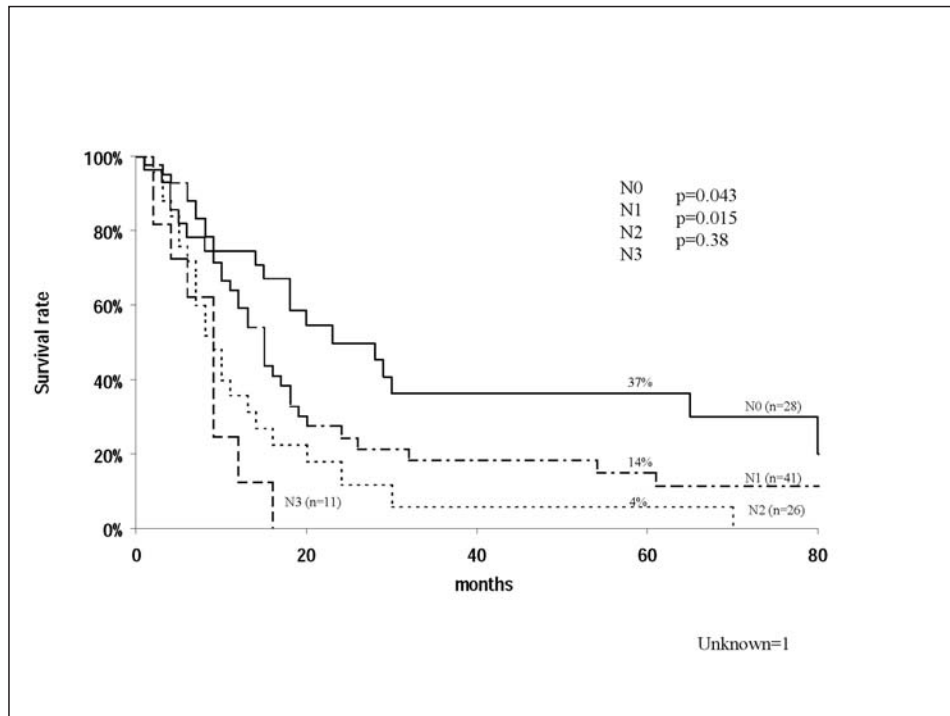


Fig. 1 Survival curves due to pN. The 5-year survival rate of the pN0 group was 37%, significantly better than the 14% 5-year survival rate in the pN1 group ($p=0.043$). In the patients with positive nodes the pN1 group could live significantly longer than the group with pN2 or more ($p=0.015$).

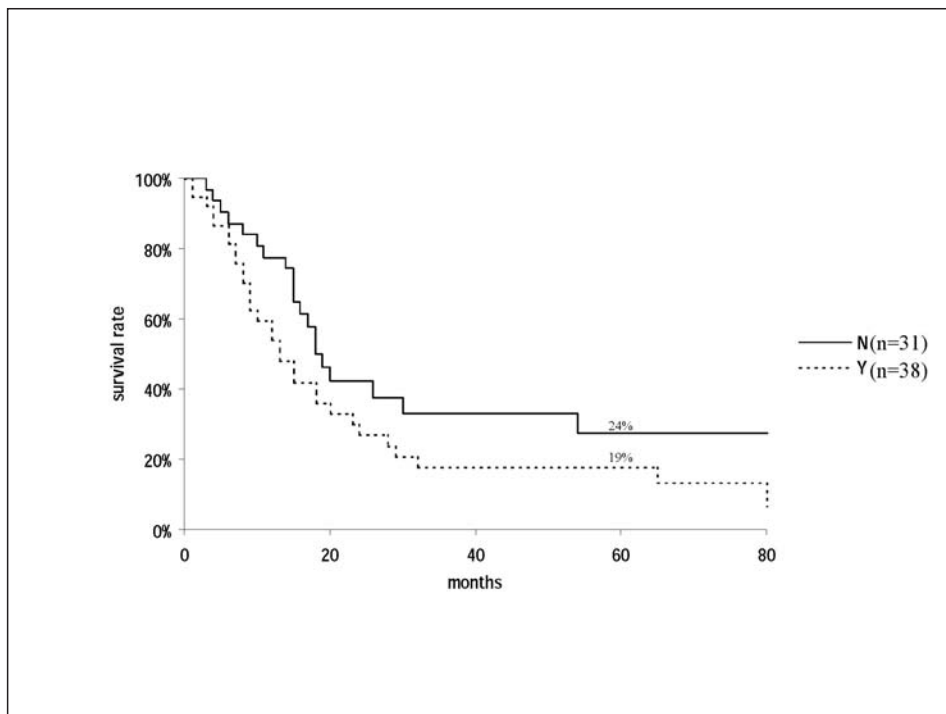


Fig. 2 Of 69 patients with pN0 or pN1, 38 patients underwent resection of the portal vein. There was not significant difference between the 24% 5-year survival rate in the portal vein “No” group (solid line N) and the 19% 5-year survival rate in the portal vein “Yes” group (broken line Y) ($p=0.11$).

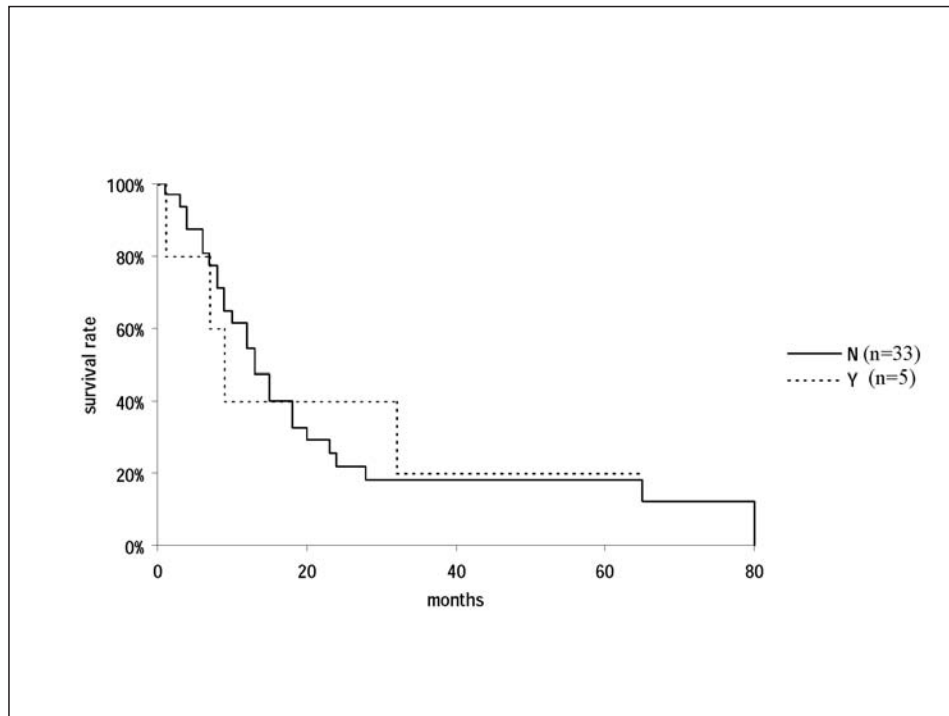


Fig. 3 Further resection of the hepatic artery was performed in 5 patients out of 69 patients with pN0 or pN1. The 5-year survival rate of the portal vein only group (solid line N: Hepatic artery “No”) was 20% while the 5-year survival rate of both the portal vein and hepatic artery group (broken line Y: Hepatic artery “Yes”) was same ($p=0.88$).

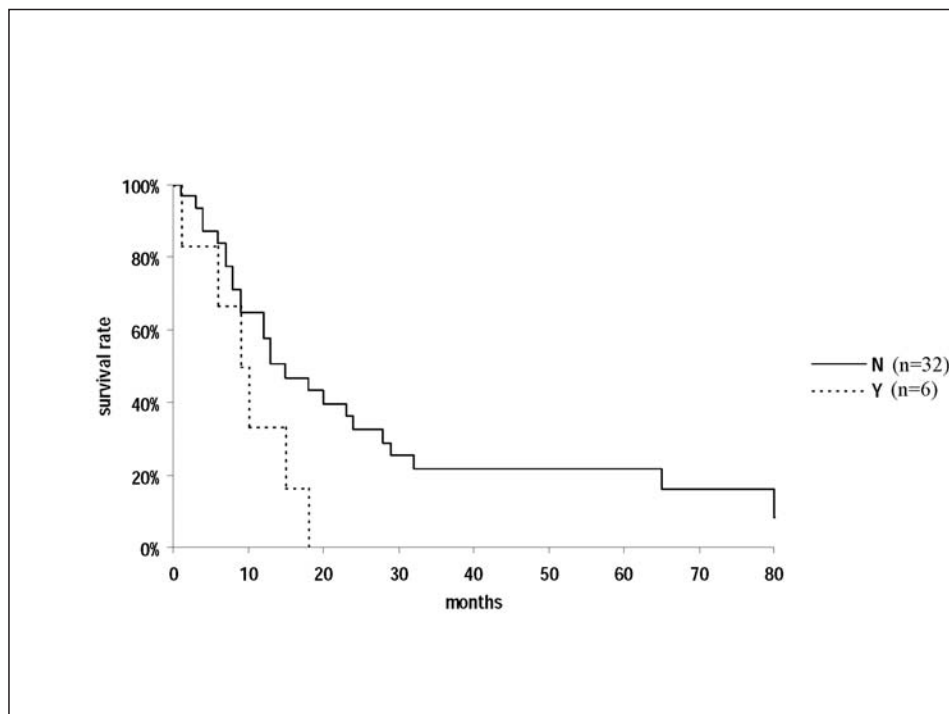


Fig. 4 Further resection of the superior mesenteric artery(SMA) was performed in 6 patients out of 69 patients with pN0 or pN1. Six patients (broken line Y: SMA “Yes”) tended to live less longer than the group of the portal vein only (solid line N: SMA “No”) ($p=0.07$).

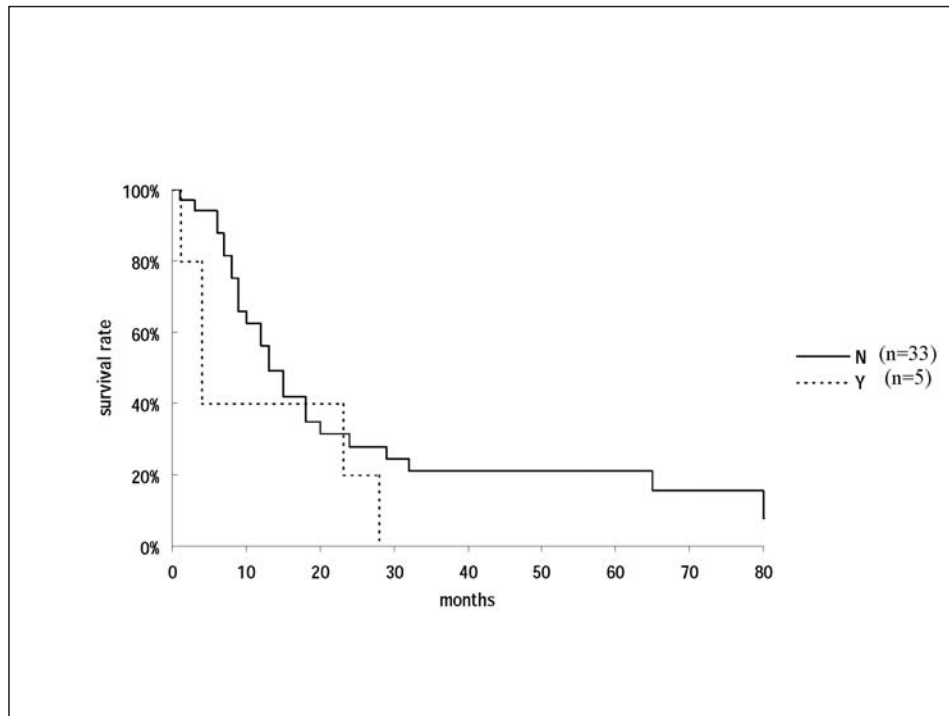


Fig. 5 Further resection of the celiac artery(CA) was performed in 5 patients out of 69 patients with pN0 or pN1. The survival curve of the 5 patients (broken line Y: CA“Yes”) showed no long-term survival as compared to the group of the portal vein only (solid line N: CA“No”). There was no significance.

was invasive duct carcinoma invading the adventitia of the superior mesenteric vein. One lymphnode behind the pancreatic head was involved. As two years later Carcinoembryonic Antigen was elevated, Gemcitabine of ten courses was administered for 14 months and the tumor marker was decreased. However, five years later the patient complained of back pain. A PET scan revealed a mass on the abdominal aorta. After the S1 and Gemcitabine combination therapy for six months, the mass was diminished on a PET scan.

Discussion

Why does a surgeon majoring in pancreatic cancer continue to resect pancreatic cancer despite the miserable postoperative outcome? One answer is that an advanced cancer of the pancreas has never been reported to be cured with chemotherapy only so far, thus we have paid an effort to resect 37 cases of pN2 or more diseases and 62 cases of portal vein infiltration. Since ten years ago gemcitabine has been used for unresectable pancreatic cancer with a safety.³ The clinical response was recognized as relieving consistent painful complaints, however, long-term survivors have hardly been reported.⁴ A patient could live for a few years at the longest.⁵ Various

combinations of chemotherapy were developed. In Japan combination therapy using T-S1 and Gemcitabine is noteworthy to have a high response rate at the present time.^{6,7} Antecedent T-S1 given everyday for seven days and gemcitabine infused at the eighth day prolonged the patient's survival rate to 47.7% at one year and 20.7% at two years. Although a surgeon may be relieved to know that among the various choices of treatment, such as palliative surgery, radical surgery, chemotherapy or radiotherapy, results following resection with adjuvant chemoradiation therapy were the best,⁸ adjuvant chemoradiation was not widely adopted in Japan.

The extent of lymphadenectomy in this series might be appropriate. It was never so wide as performed by Nagakawa.⁹ Additional paraaortic lymphnode dissection was also limited just behind the pancreatic head. Patients' recovery is delayed by lymphorrhea due to wide dissection along the aorta none the less patients' survival benefit was not proven.¹⁰ Surgical strategy of the combined resection of the perilesional vessels was based on the results of our previous analysis¹¹ released midway of this series that patients with small tumors invading either to the portal vein or to the hepatic artery but neither to the superior mesenteric artery nor to the celiac artery could have good prognosis if the tumor were completely re-

moved. It does not change at the present time. Imaizumi taught us that combined resection of the vessels gained more radicality in patients of M0 and no metastasis in the further lymphnodes.¹²

The 5-year survival rate of 26 patients of pN2 was 4%. There, what is worse than pN2 patients, were no 5-year survivors in pN3 disease. The stage of pancreatic cancer is dominantly defined by lymphnode metastasis. The most of stage 4 patients are pN3 disease. There are clinically still detectable N3 nodes and more undetectable N3 even with the newest CT. It cannot be clarified for small nodes until a surgeon extirpates them whether they are positive or negative. Another answer to resection of pancreatic cancer despite the miserable postoperative outcome is that the boundary between the stage 4a and 4b among N3 diseases becomes apparent on the histologic examination. Concerning the clinical staging other than using CT and US, Fujioka¹³ reported that the combined preoperative CEA and CA 19-9 levels predicted curability and they would be useful for selection of the patients. Patients whose levels of CEA and CA 19-9 over 5.5ng/ml and 78U/ml respectively would have less curative surgery.

Of the 107 patients finally 13 patients could live over 5 years (12.1%), however, only 3 patients could live over 10 years (2.8%). The behavior of pancreatic cancer seems different from other periampullary carcinomas. Yeo¹⁴ noted that particularly for patients with pancreatic adenocarcinoma, 5-year survival was not equated with cure, because many patients died of recurrent disease over 5 years after resection. Effective adjuvant therapy is eager to be established.

The study analyzing the one year survival rate and the median survival time by Tani¹⁵ clarified that postoperative chemotherapy using 5-fluorouracil via the common hepatic artery or/and gemcitabine systemically was essential for the improvement of survival in patients with locally invasive pancreatic cancer. On the other side a randomized trial for eight years by Kosuge¹⁶ demonstrated no clear survival benefit for the long-term observation period although there were more survivors in the surgery and chemotherapy group after five and six years of surgery. Current adjuvant chemotherapy is to use an agent with less toxicity such as gemcitabine as Oettle¹⁷ showed in the randomized controlled trial. Gemcitabine significantly delayed the development of recurrent disease after complete resection of pancreatic cancer compared with observation alone. A surgeon should not forget adjuvant chemotherapy. Last fifteen patients of this series have had adjuvant chemotherapy not yet analyzed for the short observation period.

How to select an object for adjuvant chemotherapy? Histologic findings, the preoperative levels of tumor markers or the postoperative tumor markers levels checked at intervals at an out-patient clinic are clinically

used. Another method is to utilize some factors correlating to prognostication. One of our colleagues¹⁸ proved the marked correlation between cytoplasmic overexpression of the epidermal growth factor receptor and tumor aggressiveness in patients with pancreatic carcinoma. Another colleague¹⁹ suggested that examination of S-phase kinase-associated protein 2 expression might be clinically useful prognostication in patients with pancreatic carcinoma.

An experienced fighter pilot who has been long time handling a control stick of pancreatic cancer would almost shout may-day, may-day midst of the whirling cloud. However, it is clarified that aggressive combined resection of the portal vein or additional resection of the hepatic artery be feasible for a survival benefit in pN0 and pN1 diseases.

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