

Cancer of the Pancreas in 125 Patients

Shunichi TANABE, Noboru HARADA,
Takatoshi NODA, Toshimitsu MIYAMOTO,
Tsutomu TOMIOKA, Takashi YAMAGUCHI,
Kensuke YAMAMOTO, Kunihide IZAWA,
Tsukasa TSUNODA, Ryozo YOSHINO,
Toshiya ITO, and Ryoichi TSUCHIYA

*The Second Department of Surgery,
Nagasaki University School of Medicine
Nagasaki, Japan*

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In this report, we did a retrospective study of 125 patients with cancer of the pancreas. Seventeen (36.2%) of the 47 patients with cancer of the pancreatic head underwent resection; 11.2% died within 30 days of surgery, 33.3 survived the first year, and 13.3 survived the first three years. The longest survival was for five years. Nine (23%) of the 39 patients with cancer of the pancreatic body and tail underwent resection; 11.1% died within 30 days, 37.5% survived the first year, and none survived more than three years. The longest survival was for 35 months. Important factors affecting the prognosis were invasion by the cancer of veins or lymph vessels in the surrounding tissues, and metastasis to regional lymph nodes. Lymphatic drainage of small cancers of the pancreatic head were established early. Invasion to the retroperitoneal tissue in cancer of the pancreatic body and tail was more common than in cancer of the pancreatic head.

For the patient of early cancer of the pancreas, we strongly recommend total pancreatectomy over WHIPPLE's pancreatoduodenectomy, based on results of our analysis of the outcome in our patients following these two operations.

Key words: Cancer of the pancreas, Total pancreatectomy, WHIPPLE's pancreatoduodenectomy

INTRODUCTION

The incidence of pancreatic cancer is gradually and steadily increasing, according to the Annals of the Pathological Autopsy in Japan¹⁾. The survival rate is very low, and

田辺篤一, 原田 昇, 野田剛稔, 宮本峻光, 富岡 勉, 山口 孝, 山本賢輔, 井沢邦英, 角田 司, 吉野泰三, 伊藤俊哉, 土屋涼一,

this disease is challenging to gastroenterological surgeons. Here, we reviewed a series of patients with cancer of the pancreas seen in our department.

SUBJECTS AND METHODS

At the 2nd Department of Surgery of Nagasaki University Hospital, we have seen 125 patients diagnosed as having pancreatic cancer between November 1969 and September 1982. All patients has passed more than three years after their initial treatment.

Seventy-eight patients were male and 47 were female. The mean age was 59.7, with a range from 2 to 80 years.

Each patient's record was reviewed to collect information on early symptoms, location of the cancer, treatment, factors in survival, and operative management.

The cancers were evaluated using the General Rules for Surgical and Pathological Studies of Cancer of the Pancreas, published by the Japanese Pancreatic Society²⁾.

RESULTS

EARLY SYMPTOMS

In the order of decreasing frequency, the initial symptoms were epigastralgia, anorexia, general malaise, jaundice, nausea, vomiting, and weight loss.

Early symptoms are described for each of the four sites of cancer in Table 1. Upper abdominal pain was the most frequent in all locations. There are no specific early symptoms of cancer of the pancreas, which cause difficulty in its early detection and diagnosis.

Table 1. Early Symptoms by Location of Cancer

Symptoms	No. of Patients	Head	Body and Tail	Entire	Peri-ampullary
Epigastralgia	78	32	25	14	7
General Malaise	18	10	2	3	3
Anorexia	24	9	6	4	5
Jaundice	12	6	0	1	5
Weight Loss	8	3	4	0	1
Nausea and Vomiting	10	3	4	3	0

LOCATION OF CANCER

The carcinoma was classified as being in one of four sites: the head of the pancreas, the body and tail of the pancreas, the entire pancreas, or the periampullary region. Forty-seven patients had carcinoma in the head of the pancreas, 39 in the body and tail

of the pancreas, 20 in the entire pancreas, and 19 in the periampullary region. There was no correlation between age and the location of the carcinoma (Table 2).

Table 2. Sex, Age, and Location of Carcinoma in 125 Patients with Pancreatic Cancer

Location in pancreas	Number of patients	Male		Female	
		No.	Mean age	No.	Mean age
Head	47	30	57.1	17	57.4
Body and Tail	39	22	56.8	17	54.7
Entire	20	14	59.3	6	58.5
Periampullary	19	12	68.5	7	62.1
Total	125	78	60.4	47	58.2

TREATMENT

We did a radical operation on 26 (20.8%) of our 125 patients (pancreatoduodenectomy in 9, total pancreatectomy in 9, and resection of body and tail in 8), a palliative operation on 71 (56.8%), and exploratory laparotomy on 19 (15.2%). Nine patients did not undergo surgery. In only 22.4% of our patients who underwent operation was the cancer resectable. In the palliative operations, biliary enteric bypass operations such as cholecystoduodenostomy, cholecystojejunostomy or external cholecystostomy were done (Table 3).

Table 3. Treatments in 125 Patients

Operation		No. of Patients	Incidence
Resection	PD	9	20.8%
	TP	9	
	DP	8	
Palliative* Operation		71	56.8%
Exploratory Laparotomy		19	15.2%
No Operation		9	7.2%
Total		125	100.0%

PD, Pancreatoduodenectomy

TP, Total pancreatectomy

DP, Distal pancreatectomy

*, Bypass or Drainage operation

SURVIVAL

Of the 47 patients with carcinoma of the head of the pancreas, 17 (36.2%) underwent curative operations, 27 (57.4%) a palliative operation, and 3 (6.4%) an exploratory

laparotomy only. Of the 39 patients with carcinoma of the body and tail of the pancreas, 9 patients (23.1%) had curative operation, 11 (28.2%) a palliative operation, and 12 (30.8%) an exploratory laparotomy. By location, the longest mean survival was 13.6 months for the 8 patients who received distal pancreatectomy, and the longest survival among these patient was 35 months. The mean survival for the 9 patients who received pancreatoduodenectomy for carcinoma of the head of the pancreas was 13.1 months; the longest survival was 4 years. The survival for the 8 patients who received total pancreatectomy for carcinoma of the head of the pancreas was 6.3 months; one patient is still alive, 60 months after. No patient with carcinoma of the entire pancreas or the periampullary region had a curative operation and all died within 6 months except two of 57 (Table 4).

Table 4. Mean Survivals According to Location of Tumors and Surgical Procedures in 125 Patients

			Average Survival (months)	Longest Survival (months)
Head (47)	Laparotomy Only	3(6.4%)	1.2	1.6
	Palliative Operation	27(57.4%)	4.9	24.6
	Resection	17(36.2%)	9.9	52.0
	PD	9(19.1%)	13.1	48.0
TP	8(17.2%)	6.3	60.0, alive	
	No Operation	7(17.9%)	1.2	2.4
Body and Tail (39)	Laparotomy Only	12(30.8%)	3.7	13.0
	Palliative Operation	11(28.2%)	3.3	12.0
	Resection	9(23.1%)	12.6	35.0
	DP	8(20.5%)	13.6	35.0
TP	1(2.6%)	4.0	4.0	
	No Operation	1(5.0%)	0.5	0.5
Entire (20)	Laparotomy Only	4(2.0.%)	3.6	8.0
	Paillative Operation	15(75.0%)	3.5	10.0
	No Operation	1(5.2%)	1.0	1.0
Peri- ampullary (19)	Laparotomy Only	18(94.7%)	2.1	5.0

MORTALITY AND SURVIVAL OF RESECTED CASES

Two of the 17 patients with carcinoma of the head of the pancreas who underwent resection, and one of the 9 such patients with carcinoma of the body and tail of the pancreas died within 30 days of the operation, so the mortality rate was 11.8% and 11.1%, respectively. There was no clear difference between operative mortality depending on the procedure or on the site of the tumor. The overall one-year and three-year survival rates of the 17 patients with resectable lesions of the head of the pancreas were

33.3% and 13.3%, respectively. Of these same 17 patients, nine had pancreatoduodenectomy, and 50.0% survived for one year. Eight had total pancreatectomy, and 14.3% survived for one and three years. The one-year survival rate of patients with resectable carcinoma of the body and tail of the pancreas was 37.3%, and the three-year survival rate, 0% (Table 5).

Table 5. Mortality and Survival Rate in Resected Cases

Location	Operation	No. of Patients	Operative* Death	Survival for One Year	Survival for Three Years
Head	Resection	17	2/17(11.2%)	5/15(33.3%)	2/15(13.3%)
	PD	9	1/9(11.1%)	4/8(50.0%)	1/8(12.5%)
	TP	8	1/8(12.5%)	1/7(14.3%)	1/7(14.3%)
Body and Tail	Resection	9	1/9(11.9%)	3/8(37.5%)	0/8(0%)
	DP	8	1/8(12.5%)	3/7(42.9%)	0/7(0%)
	TP	1	0/1(0%)	0/1(0%)	0/1(0%)

*, within 30days

FACTORS IN SURVIVAL

To evaluate prognostic factors in carcinoma of the pancreas, macroscopic findings about the size of the tumor, the degree of capsular infiltration, the mode of infiltration, the degree of invasion of lymph vessels or veins of the adjacent tissue, and metastasis to regional lymph nodes were examined, and to clarify the relationship between each factor and survival in our 26 patients with resectable cancer, the 21 who lived more than 3 months after the operation were studied. The three factors that had statistical significance

Table 6. Factors in Survival

Factors	No. of Patients	Survival Period mean month \pm SEM	
Invasion into Veins	(-) 3	30.0 \pm 20.9] P < 0.01
	(+) 18	10.0 \pm 6.2	
Invasion into Lymph vessels	(-) 2	41.5 \pm 9.2] P < 0.001
	(+) 19	10.2 \pm 6.1	
Metastasis to Regional Lymph Nodes	(-) 6	21.2 \pm 17.6] P < 0.05
	(+) 15	10.0 \pm 5.6	

(-), no invasion or metastasis

(+), invasion or metastasis

were invasion to veins, invasion to lymph vessels, and metastasis to regional lymph nodes. Especially, invasion to lymph vessel of the adjacent tissue was evaluated as the most important factor responsible for the prognosis. The mean survival month of resected cases was 41.5 ± 9.2 without invasion to lymph vessels and 10.2 ± 6.1 with invasion to lymph vessels (Table 6).

On patients having resectable cancer of the head or body and tail of the pancreas taken separately, we examined histopathologically invasion of the superficial capsule of the pancreas [positive: S(+), negative: S(-)], invasion of the retroperitoneal tissue of the pancreas [positive: Rp(+), negative: Rp(-)], and metastasis to lymph nodes [positive: N(+), negative: N(-)].

Results are shown in Table 7. Rp(+) was much more common (77.8%) in cancer of the pancreatic body and tail than in cancer of the pancreatic head (23.5%). The incidence of S(+), S(-) and Rp(+), and S(-) and Rp(-) did not show any significant difference.

However, metastasis to the lymph nodes was high but 76.5% in cancer of the pancreatic head, but 44.4% in cancer of the pancreatic body and tail. We were surprised that 80% of the patients who were S(-) and Rp(-) had metastasis to the lymph nodes

Table 7. Incidence of Invasion to Surrounding Tissue By Location

Factors	Head	Body and Tail
S(+)	9/17(52.9%)	6/9(66.7%)
N(+)	13/17(76.5%)	4/9(44.4%)
Rp(+)	4/17(23.5%)	7/9(77.8%)
S(-), Rp(-)	5/17(29.4%)	2/9(22.2%)
S(+) on Rp(-)	8/13(61.5%)	0/2(0.0%)
Rp(+) on S(-)	3/ 8(37.5%)	1/3(37.5%)

Table 8. Ratio of Lymph Node Metastasis to Capsular Invasion and/or Retroperitoneal Tissue

	Head	Body and Tail
N(+)/S(-)	6/ 8(75.0%)	1/3(33.3%)
/S(+)	7/ 9(77.7%)	3/6(50.0%)
N(+)/Rp(-)	10/13(76.9%)	0/2(0.0%)
/Rp(+)	3/ 4(75.0%)	4/7(57.1%)
N(+)/S(-), Rp(-)	4/ 5(80.0%)	0/2(0/0%)
/S(-), Rp(+)	2/ 3(66.6%)	1/1(100.0%)
/S(+), Rp(-)	6/ 8(75.0%)	0/2(0.0%)
/S(+), Rp(+)	1/1(100.0%)	3/4(75.0%)

in cancer of the pancreatic head (Table 8).

ASSESSMENT OF OPERATIVE METHODS

WHIPPLE's pancreatoduodenectomy and total pancreatectomy was used for cancer of the pancreatic head. To evaluate these methods, the resected cases of cancer of the pancreatic head were classified into four stages after the classification²⁾ and reviewed the operative procedures, histology of the tumor, the prognosis for the four stages (Table 9). We excluded the patients who died of causes other than recurrence of cancer.

Table 9. Representative List of Patients with Cancer of Head of Pancreas Who died of Recurrence after Resection
(According to Classification of General Rules²⁾)

Stage	Operation	Case	Age	Sex	Macroscopic Stage Factor	Histological Type	Microscopic Staging Factors			Prognosis (months)
							Veins	Lymph Vessels	INF	
I	PD	No. 1	50	M	T ₁ N ₀ S ₀ RP ₀ V ₀	papillary	v ₀	ly ₀	α	48
	PD	∕ 2	63	F	T ₂ N ₁ S ₀ RP ₀ V ₀	tubular	v ₂	ly ₂	γ	19
II	PD	∕ 3	75	M	T ₂ N ₁ S ₀ RP ₀ V ₀	∕	v ₂	ly ₁	β	10
	TP	∕ 4	35	M	T ₁ N ₁ S ₀ RP ₀ V ₀	∕	v ₃	ly ₃	β	11
	TP	∕ 5	54	F	T ₂ N ₁ S ₀ RP ₀ V ₀	papillary	v ₃	ly ₃	β	9
	PD	∕ 6	67	F	T ₁ N ₀ S ₂ RP ₀ V ₀	tubular	v ₂	ly ₂	β	16
III	PD	∕ 7	53	M	T ₂ N ₁ S ₀ RP ₂ V ₂	∕	v ₂	ly ₂	γ	9
	TP	∕ 8	69	F	T ₂ N ₁ S ₂ RP ₀ V ₀	∕	v ₃	ly ₃	γ	11
	TP	∕ 9	49	M	T ₃ N ₁ S ₁ RP ₀ V ₀	∕	v ₂	ly ₂	β	5
	TP	∕ 10	55	F	T ₃ N ₂ S ₀ RP ₂ V ₂	∕	v ₂	ly ₂	γ	5
	TP	∕ 11	67	F	T ₃ N ₂ S ₀ RP ₀ V ₀	papillary	v ₂	ly ₂	γ	60
IV	PD	∕ 12	51	M	T ₂ N ₁ S ₃ RP ₀ V ₀	∕	v ₂	ly ₂	γ	19

Case No. 1--A 50-year-old male patient who had very small cancer in size 0.2 x 0.2 cm and without any local and distant metastasis to the liver or dissemination to the peritoneum underwent pancreatoduodenectomy. But a recurrence arose from the remaining pancreas, in which a multicentric growth was found. He died of recurrence of cancer four years later. This patient would probably have lived longer with a total pancreatectomy. These cases lead us to prefer to do total pancreatectomy for cancer of the pancreas.

Case No. 9--A 49-year-old man in stage III underwent total pancreatectomy. Histological investigation of the resected specimen disclosed a skip lesion confined to the duct of the pancreas 2 cm apart from the main focus pancreatic cancer. Total pancreatectomy was a fortunate choice for this patient. For patients in stage III, total pancreatectomy seems not to have any advantage in prognosis if the lymph nodes were already involved.

Of our four patients in stage II with S₀, RP₀, V₀, but with metastasis to lymph

nodes, the survival in the two by pancreatoduodenectomy was 19 and 10 months, and the other two by total pancreatectomy, 11 and 9 months. Histological extension showed more progressive finding in the patients with the total pancreatectomy compared with the pancreatoduodenectomy. For the patients in this stage, total pancreatectomy failed to show any difference in survival.

DISCUSSION

High diagnostic accuracy for pancreatic cancer is made possible by improvement of imaging diagnostic aids such as endoscopic retrograde cholangio-pancreatography, percutaneous transhepatic cholangiography, selective celiac arteriography, ultrasound sonography, computed tomography, and aspiration cytology. However, these diagnostic aids are still not able to diagnose early pancreatic cancer. In fact, most of our patients were diagnosed in an advanced stage. Poor prognosis of pancreatic cancer mainly depend on the delay of diagnosis due to vague and non-specific early symptoms and on the tendency of early drainage of cancer into regional lymph nodes even in small pancreatic cancer. To settle these problems of diagnostic delay and poor prognosis, more reliable routine screening tests for early detection of cancer of the pancreas are needed. The usual operation in this disease is WHIPPLE's pancreatoduodenectomy, but prognosis with this operation is poor. MONGÉ⁸⁾ reported 21% operative mortality and 18.2% five-year survival. WARREN⁴⁾, SMITH⁵⁾, and others⁶⁾⁹⁾ reported similar or worse results. To increase survival, since 1977 we have utilized total pancreatectomy as a radical operation for cancer of the pancreas. For the reasons of that we encountered patients with multicentric growths and with metastatic skip lesions in the pancreatic duct, and that possibility of dissemination of free-floating cancer cells⁷⁾ or direct spread of cancer along the pancreatic ducts⁸⁾, we have utilized total pancreatectomy as a radical operation for cancer of the pancreas. BROOKS⁸⁾ showed the necessity of selection of patients for total pancreatectomy in his results of 19% five-year survival. REMINE⁹⁾ reported a 4.7% mortality rate and improvement in the five-year survival rate from 12 to 25% by using total pancreatectomy instead of pancreatoduodenectomy. LONGMIRE⁸⁾¹⁰⁾ found a 12% mortality rate and 20 months average survival with the WHIPPLE procedure, and a 17% mortality and 26 months average survival with total pancreatectomy. IHSE⁷⁾ reported 21% five-year survival for sixty-five patients who had undergone total pancreatectomy. However, HERMAN⁹⁾ made comparisons studies of the two operations, and doubted that total pancreatectomy gave longer survival. In our series, total pancreatectomy has not still achieved improvement in survival in patients in stage II or more advanced stages, especially when they had a metastasis to the lymph nodes. However for the patients in stage I, no metastasis to lymph nodes, total pancreatectomy seem to be a reasonable curative operation to avoid a recurrence from intraductal dissemination or multicentric growth of the cancer. In other attempts to make a more radical dissection of pancreatic cancer, FORTNER¹¹⁾¹²⁾¹⁸⁾ has tried regional pancreatectomy. In this recent result, of the 29 patients who underwent this operation, ten

are alive one to 53 months later, and eleven died of recurrences after 5 to 30 months, but follow up period is not enough for evaluation of this operation for the patient of pancreatic cancer.

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