Follow-up Studies of Radical Resection for Pancreaticoduodenal Cancer

TOSHIO SATO, M.D., YOICHI SAITOH, M.D., NOBORU NOTO, M.D., SEIKI MATSUNO, M.D.

In a study of 66 patients with pancreaticoduodenal cancer with pancreaticoduodenectomy, there were five (7.5%) hospital deaths. Five-year survival rates were 7.8% in 20 patients with carcinoma of the head of the pancreas, 16.7% in 31 patients with carcinoma of the bile duct, and 38.5% in 15 patients with carcinoma of the ampulla of Vater. Fecal fat loss measured was 10 g or less per day in nine of 12 patients. Of the 19 patients having glucose tolerance tests, 13 showed abnormalities including the two who were diabetic. Operative findings which were indicative of a poor prognosis included lymph node metastases, macroscopic invasion of the tumor into the pancreatic capsule in patients with carcinoma of the head of the pancreas, the size of the tumor in those with carcinoma of the common bile duct, and direct invasion of the lesion into the pancreas in patients with carcinoma of the ampulla of Vater.

From the Department of Surgery, Tohoku University School of Medicine, Sendai, Japan

IN PATIENTS WITH pancreaticoduodenal cancer, a marked decrease in the mortality and favorable results of pancreaticoduodenectomy have been reported from several clinics.[1,6,16,19] These favorable results might be attributed to progress in the technique of pancreaticoduodenectomy and improved management of the patients during the postoperative period as well. The present series records the results of pancreaticoduodenectomy in 66 patients with pancreaticoduodenal cancer, with special reference to the pathophysiological aspects at the time of follow-up study and factors influencing the late results of the operation.

Materials

A total of 162 patients with pancreaticoduodenal cancer were operated on from 1960 to 1976. There were 89 patients (61 male and 28 female) with carcinoma of the head of the pancreas; 52 patients (37 male and 15 female) with carcinoma of the common bile duct; and 21 patients (11 male and 10 female) with carcinoma of the ampulla of Vater. Of the 162 patients, 66 were subjected to pancreaticoduodenectomy; 20 with carcinoma of the head of the pancreas including the two subjected to total pancreatectomy, 31 with carcinoma of the common bile duct including the one indicated for total pancreatectomy, and 15 with carcinoma of the ampulla of Vater with the resectability rates of 22.5%, 59.6% and 70.4%, respectively. Reconstruction of the alimentary tract after pancreaticoduodenectomy was performed using a modified Child's method except for the three cases of total pancreatectomy. The methods employed for pancreaticojejunostomy were end-to-end anastomosis in 53 and end-to-side anastomosis in 10 patients. An indwelling plastic catheter was inserted through the pancreaticojejunostomy stoma into the pancreatic duct and the other end of the catheter was led out through the stab wound of the jejunum to the abdominal wall.

Reprint requests: Dr. Toshio Sato, Department of Surgery, Tohoku University School of Medicine, Sendai, Japan, 980.

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Results

Immediate Postoperative Mortality

Of the 66 patients, there were five hospital deaths (7.6%) within one month after pancreaticoduodenectomy. Details of the deaths were two of 20 with carcinoma of the head of the pancreas and three of 31 cases with carcinoma of the common bile duct. There were no hospital deaths in 15 patients with carcinoma of the ampulla of Vater. Classification of these expired cases according to the surgical procedures were; one of 23 cases (4.3%) underwent one-stage operation, and four of 43 cases (9.3%) underwent two-stage operation. The latter 43 cases included those subjected to percutaneous transhepatic biliary drainage.

Postoperative Complications and the Causes of Deaths

Suture breakdown was observed in 10 patients, eight at the site of pancreatico-jejunostomy, and one

TABLE 1. *Postoperative Survival Rates According to the Site of Tumor*

Tumor Site	1-Yr. Survivals	3-Yr. Survivals	5-Yr. Survivals
Pancreas	7/19 (36.8)	3/14 (21.4)	1/13 (7.8)
Common Bile Duct	21/28 (75.0)	8/26 (30.8)	3/18 (16.7)
Ampulla of Vater	9/14 (64.3)	5/13 (38.5)	5/13 (38.5)
Total	37/61 (60.7)	16/53 (30.2)	9/44 (20.5)

Figures in parentheses show percentages.

each at the sites of choledocho-jejunostomy and gastro-jejunostomy. Of these, two patients were directly responsible for the hospital death. Leakage at the site of pancreatico-jejunostomy developed in five of the 53 patients (9.4%) with end-to-end anastomosis and in three of the 10 (30%) with end-to-side anastomosis. Other complications were gastrointestinal bleeding in five, intra-abdominal bleeding and intestinal obstruction in three cases each, and a pulmonary complication and myocardial infarction in two patients each with two deaths. Another patient died of cerebrovascular accident.

Follow-up Results

Survival after Operation

Survival rates of the patients after operation are shown in Table 1. There were nine patients who survived more than five years; one with carcinoma of the head of the pancreas, three with carcinoma of the common bile duct, and five with carcinoma of the ampulla of Vater. The longest survival period was six years and one month with carcinoma of the pancreas, nine years and nine months with carcinoma of the common bile duct and 12 years and ten months with carcinoma of the ampulla of Vater.

Late Deaths

Of the 61 patients who survived operation, 47 died after leaving the hospital including the 38 patients who expired within two years. The causes of death were recurrent cancer in 38 and other causes of death included cerebrovascular accident, cardiac failure, hepatitis and gastrointestinal bleeding. Of the nine patients who survived more than five years after operation, only one died of recurrent cancer, four others died of cerebral hemorrhage or acute cardiac failure, while the remaining four patients were still alive without any sign of cancer recurrence.

Pathophysiology at Follow-up

Following examinations were undertaken in 20 patients who were hospitalized for the follow-up study after pancreaticoduodenectomy. Seventeen of the 20 patients were those who had survived more than one year. Any patients visiting the hospital for recurrent cancer were excluded from the follow-up study.

Laboratory Examinations

As shown in Figure 1, the erythrocyte count revealed marked anemia in one, mild anemia in six, and absence of anemia in the remaining 13 patients. One patient with the red cell count of 270 × 10^4 died of pulmonary metastasis one year after the follow-up study. Plasma protein concentration was within the normal range in all except three and AG ratio was above 1.2 in all but five patients. Icterus index was within the

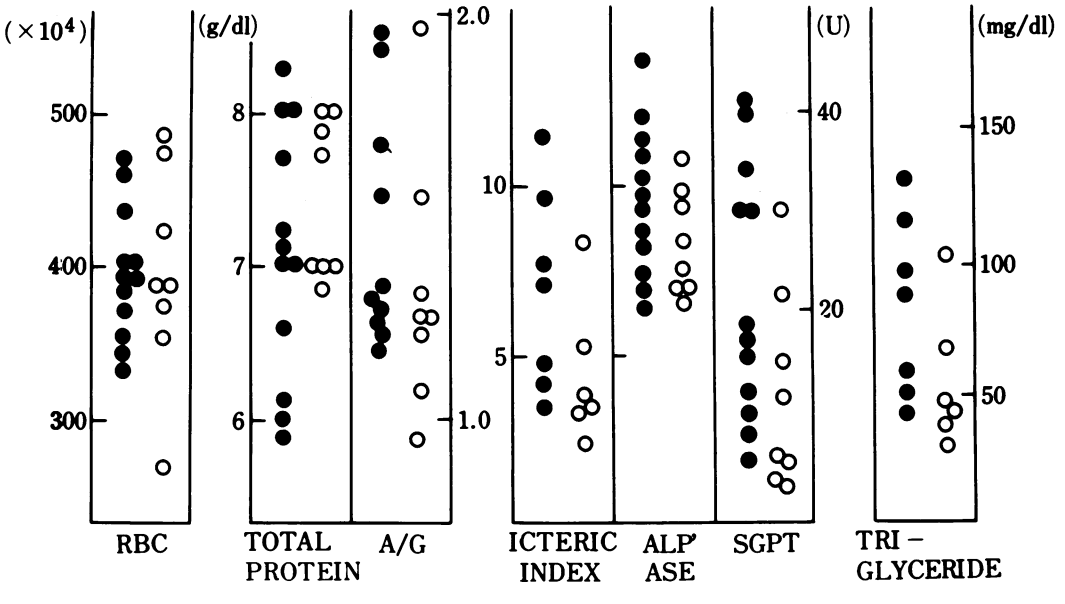

FIG. 1. Results of laboratory examinations in patients with pancreaticoduodenectomy at the time of follow-up. Normal values: Alp'ase, 3 ~ 10 (Armstrong U); SGOT, 4 ~ 35 (Karmen U); Triglyceride, 40 ~ 155 mg/dl (acetylaceton procedure). ● = cases lasted within 5 years after operation. ○ = cases lasted more than 5 years after operation.

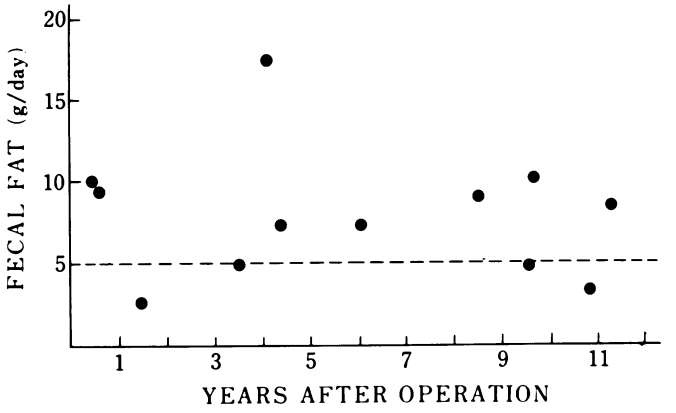

FIG. 2. Fecal fat loss in patients with pancreaticoduodenectomy at the time of follow-up. Normal value of fecal fat is less than five grams per day (method of Van de Kamer).

normal range in all but one and GPT level in all except in two patients. Alkaline phosphatase was slightly elevated in six, and serum triglyceride level was almost normal in all the patients.

Exocrine Function of the Pancreas

In 12 patients, fecal fat loss was measured to study the postoperative exocrine function of the pancreas (Fig. 2). Nine of the 12 patients showed the level of ten grams or less including the four with less than five grams per day. One patient with carcinoma of the head of the pancreas who had had marked fibrosis of the pancreas at the time of operation showed fecal fat loss of 17.8 g per day. In six patients who had survived more than five years, fecal fat loss ranged ten grams or less per day.

Endocrine Function of the Pancreas

To evaluate the postoperative endocrine function of the pancreas, oral glucose tolerance test was performed with simultaneous observation of the insulin secretion. Results of a 50 g glucose tolerance test in 19 patients are shown in Table 2. The normal glucose tolerance type was observed in six of the 19 patients (31.6%), decreased glucose tolerance type in 11 (57.9%) and diabetic type in two patients (10.5%). Only one patient, required administration of insulin. No tendency was noted for an increase in glycoregulation disorders with the passage of time. Of the nine patients who survived more than five years, five showed a decreased glucose tolerance type, but none fell in a diabetic category. Insulin secretion during the oral glucose tolerance test was well maintained in patients with normal or decreased glucose tolerance type, while slight decrease was observed in patient with diabetic type (Fig. 3).

TABLE 2. *Oral Glucose Tolerance Test at the Time of Follow-up*

Pattern of GTT	No. of Patients	No. of Patient, Grouped by Survival Years			
		<1 Yr.	1 to 3 Yr.	3 to 5 Yr.	>5 Yr.
Normal Type	6	0	1	1	4
Decreased glucose tolerance type	11	2	3	1	5
Diabetic type	2	1	1	0	0

Change in Body Weight

Changes in body weight at the time of discharge are shown in Figure 4. A majority of the patients showed a gain in body weight at the time of follow-up which had no correlation to the length of postoperative period. Five showed over ten per cent of gain in weight. One patient who had lost more than 20% died of recurrent cancer one year after the follow-up study.

Histology of the Remaining Pancreas after Pancreaticoduodenectomy

Postoperative examination of the site of pancreaticojejunostomy was possible in seven patients who died and were autopsied one year or more after pancreaticoduodenectomy. Patency of the anastomosis was confirmed in all but one patient.

The parenchymal ratios of the pancreas were determined by the point counting method[20] both at the time of operation and autopsy (Table 3). Comparison with the control ratios determined by Suda et al.[17] which ranged between 94.47 and 93.96% with the

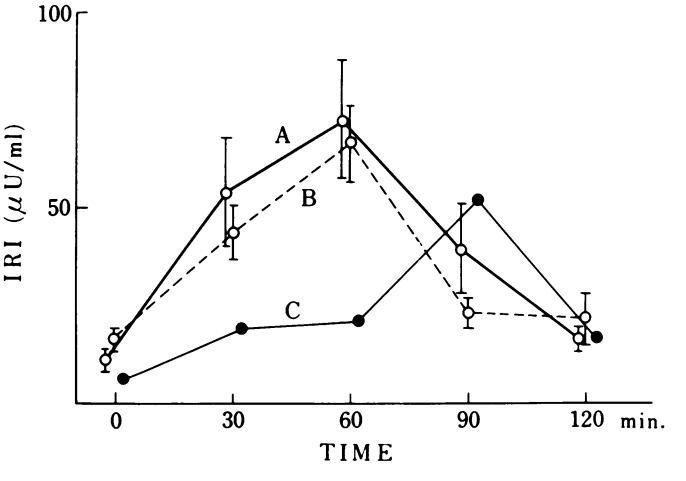

FIG. 3. Plasma levels of IRI during OGTT (50 g) in patients with pancreaticoduodenectomy at the time of follow-up (Mean ± S.E.). A, cases with normal type of OGTT (n = 4); B, cases with decreased glucose tolerance type (n = 4); C, case with diabetic type (n = 1).

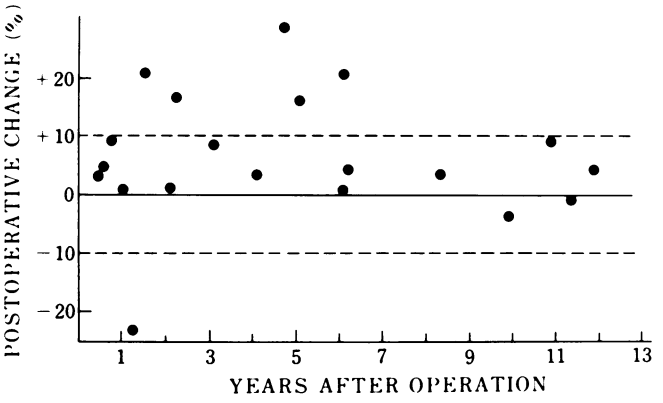

FIG. 4. Postoperative change in body weight in patients with pancreaticoduodenectomy at the time of follow-up. Percentages were calculated referring to the body weight at the time of discharge.

mean of 92.58%, the ratios of the present patients at the time of operation exceeded 93.07% in all but one, and those at autopsy ranged from 82.48 to 95.13%. In one patient who survived eight years and six months after the operation, decrease in the ratio was relatively slight as from 95.45 to 86.35%. However, in another patient who had previously had leakage at the site of pancreatico-jejunostomy, the stoma was found not patent at autopsy and the parenchymal ratio notably decreased from 93.09% at the time of operation to 66.26% at autopsy done eight months after the operation.

Factors influencing Follow-up Results

Factors which were thought to affect the follow-up were studied in relation to the sites of tumors in 61 patients who survived pancreaticoduodenectomy.

Carcinoma of the Head of the Pancreas

Of the 18 patients who survived the operation, 14 died of recurrent cancer within one year and ten months except the one who died three years and two months after the operation. The remaining four patients were still alive with their survival periods of six years and one month, four years and two months,

TABLE 3. *Parenchymal Ratio of the Pancreas at the Time of Operation and at Autopsy*

Case	Age	Sex	Tumor Site	Years after operation	Parenchymal Ratio (%)	
					At Operation	At Autopsy
1	61	M	Bile Duct	8 yr. 6 mo.	95.45	86.35
2	53	M	Bile Duct	3 yr. 7 mo.	94.41	89.65
3	39	M	Pancreatitis	1 yr. 10 mo.	76.43	72.42
4	55	F	Ampulla	1 yr. 6 mo.	95.33	95.13
5	45	F	Bile Duct	1 yr. 3 mo.	93.07	82.48
6	57	M	Pancreas	1 yr.	95.47	90.53
7	51	F	Bile Duct	8 mo.	93.09	66.26

TABLE 4. *Postoperative Survivals According to Findings at Operation in Patients with Carcinoma of the Pancreas*

Findings at Operation		No. of Patients	Survivals			
			<1 Yr.	1 to 3 Yr.	3 to 5 Yr.	5 to 10 Yr.
Tumor Size:	<3 cm	5	2(2)	2(1)	1(1)	
	<5 cm	10	7(6)	2(2)	1	
	>5 cm	3	1(1)	1(1)	1	
No Node Metastasis		6	2(2)	2(1)	2(1)	
With Node Metastasis		12	8(7)	3(3)		1
No Capsular Invasion		9	5(4)	1	2(1)	1
With Capsular Invasion		9	5(5)	4(4)		

Number in parentheses indicates number of fatal cases.

one year and two months, and four months, respectively. Of the two patients who underwent total pancreatectomy, one died of recurrent cancer two years later, and the other died of fulminant hepatitis three months postoperatively.

The survival periods of these 18 patients had no correlation to the size of tumors (Table 4). The survival periods, however, were evidently affected by the presence of lymph node metastasis. The survivals more than three years were two out of the six patients without lymph node metastasis, while only one could survive more than three years among the 12 patients with lymph node metastasis. It was also revealed that the macroscopic cancer invasion to the pancreatic capsule apparently affected the survival period. Three of nine patients free from the capsular invasion survived more than three years, but all the nine patients with positive invasion died within two years.

Carcinoma of the Common Bile Duct

Of the 28 patients who tolerated the operation, five were alive with survival periods of four years and seven months, three years and one month, two years and three months, five months, and two months, respectively. The survival periods in those who died were one year or less in four, one to two years in ten, two to three years in two, three to four years in four, and five years or more in three patients.

Of the 12 patients with tumor sizes less than 1.5 cm in diameter, five survived more than three years including the two who were alive more than five years before they died of cerebral hemorrhage and encephalomalacia. Of the ten patients with the size of tumors between 1.5 and 3.0 cm in diamter, three survived more than three years including the one who died of pulmonary metastasis six years and eight months after the operation. All the six patients with the size of tumors more than 3.0 cm in diameter expired within three years after the operation (Table 5). Among the 21 patients without lymph node metastasis,

TABLE 5. *Postoperative Survivals According to Findings at Operation in Patients with Carcinoma of Common Bile Duct*

Findings at Operation		No. of Patients	Survivals			
			<1 Yr.	1 to 3 Yr.	3 to 5 Yr.	5 to 10 Yr.
Tumor Size:	<1.5 cm	12	1	6(5)	3(2)	2(2)
	<3 cm	10	3(2)	4(4)	2(1)	1(1)
	>3 cm	6	3(3)	3(3)		
No Node Metastasis		21	4(2)	11(10)	4(2)	2(2)
With Node Metastasis		7	3(2)	2(2)	1(1)	1(1)

Number in parentheses indicates number of fatal cases.

six survived more than three years including the two who survived more than five years before they died of other than cancer recurrence. Of seven patients with lymph node metastasis, two patients survived more than three years.

Carcinoma of the Ampulla of Vater

Of the 15 patients who survived the operation, six were still alive. Three patients expired within one year after the operation, four expired between one and two years later, one after eight years and eight months, one after nine years and eight months. Five patients survived more than five years and three of them were still alive at the time of follow-up.

It was noted that there was no relationship between the size of the tumors and the survival periods (Table 6). Distinct relationship, however, existed between the presence of lymph node metastasis and the survival period. Six patients with positive lymph node metastasis died within two years except the one who was operated on shortly before the present study. On the other hand, five of the nine patients with negative metastasis survived more than five years.

Histologic examination was performed to reveal the presence or absence of cancer invasion into the pancreatic parenchyma. All the six patients with histologically positive invasion died within two years after the operation, while five of the nine patients who were free from invasion survived more than five years. The causes of death in two patients who survived eight years and nine months and nine years and eight months were encephalomalacia in the former and acute cardiac failure in the latter.

Discussion

Hospital death after pancreaticoduodenectomy has been markedly reduced as evidenced by the reported operative mortality of approximately 20% in the early half of the 1960's which was decreased to 15% in the latter half of the same decade.[1,4,12,16,19] Howard[10] reported no operative deaths in 41 consecutive cases. Aston and Longmire[1,2] reported a mortality of 13.8%, but the mortality for those operated on during the last nine years was 5.1%. Smith[16] reported that a mortality of 7.6% in 224 patients. According to Warren et al.,[19] the mortality was 14.9% for all patients and 10.7% for those operated on after 1962. In Japan, Honjo et al.[9] summarized the operative results of 822 reported cases and found the average hospital death rate to be 20.8%. In our experience, operative death was encountered in 18 of the 34 patients subjected to pancreaticoduodenectomy prior to 1959.[15] After 1960, the number of postoperative death within one month was five of 66 patients (7.6%).

In severely jaundiced patients with pancreaticoduodenal cancer (icterus index over 80), we have made it routine to alleviate jaundice first either by external cholecystostomy or percutaneous biliary drainage prior to performing a radical operation.[15] In our series in which two-stage operations were employed, hospital death was encountered in four out of 43 patients (9.3%), while among those subjected to one-stage operation, one of 23 patients (4.3%) died immediately after the operation. The higher rate of hospital death from the two-stage operation might be attributed to the fact that majority of the cases were highly jaundiced with markedly unfavorable general conditions.

TABLE 6. *Postoperative Survivals According to Findings at Operation in Patients with Carcinoma of Ampulla*

Findings at Operation		No. of Patients	Survivals				
			<1 Yr.	1 to 3 Yr.	3 to 5 Yr.	5 to 10 Yr.	>10 Yr.
Tumor Size:	<1.5 cm	5	2(1)	1(1)		2(2)	
	<3 cm	5	1	3(2)			1
	>3 cm	5	2(2)	1(1)			2
No Node Metastasis		9	3(2)	1		2(2)	3
With Node Metastasis		6	2(1)	4(4)			
No Pancreatic Invasion		9	2	2(1)		2(2)	3
With Pancreatic Invasion		6	3(3)	3(3)			

Number in parentheses indicates number of fatal cases.

The procedures of pancreatico-jejunostomy may be divided between end-to-end anastomosis after Child's method and end-to-side anastomosis after Whipple's method of reconstruction. Monge et al.,[12] Howard,[10] Goldsmith et al.[7] and Longmire et al.[2] are in favor of end-to-end anastomosis, while end-to-side anastomosis seems favored by Warren et al.,[18] Fish et al.,[4] Gilsdorf et al.[6] and Smith.[16] Reviewing the literature, one of the following two methods is widely used when pancreatico-jejunostomy is indicated. The first method is invagination of the remaining pancreatic stump into the jejunum and the second is anastomosis between the pancreatic duct and jejunal mucosa. The choice is solely dependent on the degree of dilatation of the pancreatic duct. Aston and Longmire,[1] when the duct of Wirsung is small and thinly walled, usually favor invagination of the pancreatic stump into the jejunum leaving a tube in the duct. In other circumstances with dilated and thickly walled pancreatic duct, they usually perform direct anastomosis between the pancreatic duct and the mucosa of the jejunum. Their data indicate that, pancreatic fistulas developed in eight of 44 patients with end-to-end anastomoses and in two of the 14 patients with end-to-side anastomosis.

Gilsdorf et al.[6] compared to the incidence of pancreatic fistula in a group of 71 patients with end-to-side anastomosis and another group of 17 with end-to-end anastomosis, and found no significant difference in the incidence of pancreatic fistulae (seven per cent in the former and six per cent in the latter group). It seems reasonable to postulate that the occurrence of pancreatic fistula is inevitable in about ten per cent. Therefore, it becomes a matter of importance how to cope with postoperative anastomotic leakage. Howard,[10] in a series of 41 patients with pancreaticoduodenectomy, reported pancreatic leaks in four and biliary leaks in three without mortality. Howard, in an attempt to prevent possible pancreatic or biliary leak from causing a serious outcome, leaves a short polyethylene splint tube in the pancreatic duct, a long arm T-tube through the choledocho-jejunostomy stoma as well as a Levin nasogastric or gastrostomy tube through the gastro-jejunostomy stoma into the proximal jejunal loop. Warren et al.[19] and Aston and Longmire[1] emphasize importance of immediate sump drainage whenever signs of leakage became evident.

In reconstruction of the alimentary tract, the authors usually employ a modified Child's method and invaginate the pancreatic stump into the proximal end of the jejunum. In this series, pancreatic leak was encountered in eight patients and were responsible for death in two. Concerning the necessity of inserting a tube into the pancreatic duct, Gilsdorf et al.[6] hold a negative view citing no distinctly favorable effect of the procedure on the incidence of pancreatic leak. Aston and Longmire,[2] however, are in favor of the use of a tube not only for the pancreatic duct but also for the bile duct. Smith,[16] also, inserts a tube into the pancreatic duct and a T-tube into the bile duct and lead them out of the abdomen.

With marked improvement in the direct result of pancreaticoduodenectomy for pancreaticoduodenal cancer, follow-up result of the operation has become more favorable as well. However, as far as carcinoma of the head of the pancreas is concerned, follow-up results of pancreaticoduodenectomy still present many problems. Reviewing the recent reports of large series,[1,6,16,19] five year survival rates following pancreaticoduodenectomy range from 5.7 to 13% for carcinoma of the head of the pancreas, 23–36.4% for carcinoma of the ampulla of Vater and 19–30% for carcinoma of the bile duct. According to Honjo et al.[9] who reported a collected study in 1975, five year survival rates were 9.5% for carcinoma of the head of the pancreas, 24.1% for carcinoma of the common bile duct and 34.8% for carcinoma of the ampulla of Vater. In the present series, the corresponding rates were 7.8%, 16.7% and 38.5%, respectively. From these data, five year survival rates may be estimated ranging from five to 15% for carcinoma of the head of the pancreas, 20 to 30% for carcinoma of the common bile duct, and 30 to 40% for carcinoma of the ampulla of Vater.

Four decades ago Whipple first advocated pancreaticoduodenectomy for periampullary carcinoma. Since that time, no adequate studies seem to have been made on the pathophysiology after pancreaticoduodenectomy, particularly on the function of the remaining pancreas. Fish et al.[5] studied postoperative changes after pancreaticoduodenectomy, mainly of the absorptive function in six patients who survived from 20 to 84 months postoperatively. They found that half of the patients were disabled by pancreatic insufficiency and none achieved full rehabilitation. Warren et al.[19] reported that the incidence of pancreatic insufficiency was 21.4% among the 89 cases subjected to a Whipple operation. Aston and Longmire[2] noted that of the 31 patients who had survived more than one year, 21 were able to maintain normal pancreatic function and seven showed signs of pancreatic insufficiency. Fish et al.[5] found that the intestinal absorption as surveyed by d-xylose test was normal in all the six cases, while the fecal fat was increased in all but one. In our series, fecal fat loss measured in 12 patients was five grams or less per day in four and ten grams or more in only three. There was no tendency of decrease in the fat absorption with the lapse of time after the operation. A majority showed a gain in body weight.

With regard to disturbance in the pancreatic endocrine function following pancreaticoduodenectomy, Fish et al.[5] reported that all the six patients showed a fasting blood sugar levels in the normal range and none necessitated insulin administration, while GTT was abnormal in all the patients. Similar results were reported by Miyata et al.[11] In the series of Warren et al.,[19] diabetes developed in 12.4% of the total cases. A fifty grams oral glucose tolerance test was performed in 19 patients in this series. Among these, six (31.6%) showed the normal type, 11 (57.9%) were classified as the decreased glucose tolerance type, and two (10.5%) as the diabetic type, of these only one had required insulin administration. No definite correlation was found between the development of a glycoregulation disorder and the length of time after the operation.

In most of the patients with pancreaticoduodenal cancer, the pancreatic duct tends to be obstructed by the tumor. Accordingly, atrophy of the pancreatic parenchyma seems inevitable. In our opinion, however, the most important factor which influences the function of the remaining pancreas is patency of pancreatico-jejunostomy. Comparing the two procedures, namely, invagination of the pancreatic stump into the jejunum and pancreatic duct-jejunal mucosa anastomosis, the latter procedure is generally considered preferable to the former in terms of functional results and patency of the pancreatic duct. In the present investigation, seven patients with invagination of the pancreatic stump into the jejunum could be examined at autopsy as to patency of the pancreatic duct following their survival from one year to eight years and six months. In six, the pancreatic duct remained patent, but in the remaining one case who had shown disruption of pancreatico-jejunostomy stoma immediately after operation, the pancreatic duct was found obstructed.

Goldsmith et al.[7] compared a group of 34 cases subjected to pancreatico-jejunostomy with another group of 45 patients in that the ligation of the pancreatic duct was attempted at the time of pancreaticoduodenectomy and found that there was little difference in the need of supplemental therapy for the pancreatic function between these two groups. Postmortem examination also revealed that histologic findings of the remaining pancreas did not show any significant difference between the two groups with uniform findings of scarring of the pancreas, stenosis of the proximal pancreatic duct as well as dilatation of the distal pancreatic duct in both groups.

In patients subjected to pancreaticoduodenectomy, the most important factor which affected the follow-up results were the presence of regional lymph node metastases. According to Warren et al.,[19] the five year survival rates for patients free of lymph node metastasis were 16.8% in those with carcinoma of the head of the pancreas, 40% with carcinoma of the ampulla of Vater, and 27.5% with carcinoma of the bile duct. The five year survival rates in patients with lymph node metastasis were conspicuously low with the corresponding rates of 7.4%, 9.5% and 0%, respectively. These findings indicate the significant influence of regional lymph node metastasis on the five year survival rate. In our present series with carcinoma of the head of the pancreas, there were two three year survivals out of six patients with negative lymph node metastasis in contrast with only one survival out of 12 patients with positive metastasis. In patients with carcinoma of the ampulla of Vater, there were five five year survivals out of nine patients with negative metastasis, while there was no corresponding survivals in six patients with positive metastasis.

Warren et al.[19] reported that 75% of their patients with pancreaticoduodenal cancer were subjected to radical operation and the majority of the cases expired within five years despite the fact that there was absence of lymphatic or blood-borne spread of cancer at the time of operation. Their results indicate the possible presence of some other factors besides the lymph node metastasis which significantly affect the long-term results as well. In the present series, macroscopic cancer invasion to the pancreatic capsule was investigated in relation to the survival rates in patients with carcinoma of the head of the pancreas. There were no long-term survivors with capsular invasion, but three patients without capsular invasion survived more than three years. In patients with carcinoma of the ampulla of Vater, there was little correlation between the sizes of tumor and the survival rate. In contrast to these findings, a factor of cancer invasion to the pancreas markedly affected the prognosis and none survived for a long-term in those with positive invasion while five patients with negative invasion survived more than five years. These findings suggest that patients with carcinoma of the ampulla of Vater with invasion to the pancreas are likely to show poor prognosis similar to those with carcinoma of the pancreas.

In view of the unsatisfactory follow-up results of pancreaticoduodenectomy for carcinoma of the head of the pancreas, the indications for total pancreatectomy require evaluation. Total pancreatectomy is advocated for three reasons: 1) avoidance of leaving cancer foci in the remaining pancreas, 2) en masse removal of the areas of lymphatic drainage, and 3) avoidance of pancreatico-jejunostomy. Possible cancer lesions in the remaining pancreas are residual tumor on the resection line, implantation and growth of cancer cells in the ductal system and development of new tu-

mors from multicentric sites. Hicks et al.[8] identified cancer cells on the resection line in six of the 11 patients who were subjected to pancreaticoduodenectomy for carcinoma of the pancreas. Brooks et al.[3] studied the specimens of the 16 patients who underwent total pancreatectomy and, in seven, detected cancer cells on the usual resection line of the pancreas in pancreaticoduodenectomy. Another purpose of total pancreatectomy for carcinoma of the head of the pancreas is dissection of all areas of lymphatic drainage including the lymph nodes at the distal portion of the pancreas where metastases often occur.

Regarding the results of total pancreatectomy for carcinoma of the pancreas, ReMine et al.[14] reported a hospital death rate of 21.7% among 23 cases. Survival periods exceeded two years in seven, over four years in four and more than five years in two patients. In their consecutive report of 13 other cases with total pancreatectomy, they emphasized the validity of this type of operation.[13] Brooks et al.[3] compared 11 cases who were subjected to pancreaticoduodenectomy with 16 cases subjected to total pancreatectomy both for carcinoma of the pancreas, and found a hospital death rate of 21.0% in the former and 12.5% in the latter as well as a mean survival period of 7.6 months in the former and 23 months in the latter group. ReMine et al. as well as Brooks et al. advocate total pancreatectomy for carcinoma of the head of the pancreas emphasizing little difficulty in postoperative pancreatic insufficiency and citing effectiveness of recently available supplementary therapy.

However, Aston and Longmire[2] autopsied 14 out of 36 expired cases after pancreaticoduodenectomy for carcinoma of the head of the pancreas and detected recurrent cancer in the remaining pancreas in only three cases. With the findings of multiple intra-abdominal and distant metastases observed in most of the cases, they stated that total pancreatectomy would not significantly improve the follow-up result of the cases with carcinoma of the head of the pancreas, though they conceded that the operation might have certain advantages in some selected cases. Smith,[16] studying his fatal cases with recurrent cancer after pancreaticoduodenectomy, also observed that recurrence in the remaining pancreas was not a prominent feature. Warren et al.[18] also contended with the total pancreatectomy might not be justifiable for ductal carcinoma of the pancreas except in unusual circumstances and should probably be indicated for massive cytoadenocarcinoma or large islet cell tumors.

Of our three patients subjected to total pancreatectomy for pancreaticoduodenal cancer, two died of recurrent cancer one year and ten months, and four months after operation, respectively. Another remaining case died of fulminant hepatitis three months after the operation. Our data are too limited to allow any comment on the follow-up results of total pancreatectomy. Nevertheless, it seems likely that not all the problems concerning the treatment of carcinoma of the pancreas can be solved even with the employment of total pancreatectomy.

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