

## Surgical Treatment for Carcinoma of the Ampulla of Vater and Residual Pancreatic Function before and after Pancreaticoduodenectomy<sup>\*)</sup>

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### ABSTRACT

Examination was made on long-term survival rates of 23 cases on which operation for carcinoma of the ampulla of Vater was performed, as well as on the residual pancreatic functions of the cases on which pancreaticoduodenectomy (PD) was done, by the authors during the period from 1969 to 1982.

PD was done on 17 cases, and the resectability was 74%, without any operative death. The number of survived patients for more than five years was five (42%), and the mean survival period was 45 months. These results of carcinomas of the ampulla were better than those of other periampullary cancers.

The endocrine pancreatic function was determined with the oral glucose tolerance test, and in 79% of the cases, abnormalities of glucose tolerance were observed preoperatively, whereas those aggravated postoperatively were found in 21% of the cases.

The exocrine pancreatic function was determined with the Pancreatic Function Diagnostant test (PFD). The total excretion level of urinary PABA in six hours determined in more than 12 months postoperatively was significantly improved, as compared with that determined preoperatively and within two months postoperatively. The residual function of exocrine pancreas could be expected to recover in more than 12 months after PD, and the PFD proved to be useful for the follow-up.

### INTRODUCTION

Although the diagnosis of periampullary cancers has made remarkable progress, the ratio of unresectable and advanced cancers is still so great that their long-term survival rates have been very poor, as compared with those of other types of cancers in the digestive system. It should be pointed out, however, that carcinoma of the ampulla, among all periampullary cancers, has shown a higher resectability than that of bileduct cancers and pancreatic cancers, showing good prognosis.

The resectability of carcinoma of the ampulla treated by the authors was also high, and a

few patients have been surviving for more than five years, and thus the problem of a postoperative long-term management of patients' nutrition has become important, in addition to the problem of radicality of operation.

In the present paper, reports are made on the examination on the long-term survivals of carcinoma of the ampulla as well as on the changes in the preoperative and postoperative pancreatic functions, which had been treated by the authors.

### MATERIALS AND METHODS

The number of malignant tumors in the biliary tract and pancreas operated by us was

<sup>\*)</sup> 児玉 求, 田中恒夫: 乳頭部癌に対する外科的治療および膵頭十二指腸切除, 術前術後の残存膵機能

192, including 23 of carcinoma of the ampulla, 79 of biliary tract cancers and 90 of pancreatic cancers. Sex ratio of 23 cases of ampullary tumor was 16 male and 7 female patients and their ages ranged from 34 to 80, with the mean of 60.4.

The surgical procedures comprised 17 cases (74%) of pancreaticoduodenectomy (PD), 2 cases (9%) of local resection, 3 cases (13%) of cholecystojejunostomy and 1 case (4%) of cholecystostomy.

The pancreatic function tests were performed on 14 patients who survived for more than one year, out of 17 on whom PD was done. The endocrine pancreatic function was determined with the oral glucose tolerance test (by 50 g OGTT). The exocrine pancreatic function was determined with the Pancreatic Function Diagnostant test (PFD), proposed by Imondi et al.<sup>4)</sup>, using synthetic peptide-N-benzoyl-L-tyrosyl-P-aminobenzoic acid (BTPABA), since the pancreozymin-secretin test, a hitherto most reliable one, is an intubation method so that its postoperative use is not easy. Determination of urinary p-aminobenzoic acid (PABA) was made with modified Bratton-marshall's method by Smith<sup>7)</sup>.

#### Surgical technique of PD:

The head of the pancreas was cut at the left margin of the superior mesenteric vein. Hemostasis at the stump of the residual pancreas was done only to the regions from where arterial hemorrhage was severe, but minor hemorrhage was covered with the oxycel gauze. The stomach was resected within a small range, but truncal vagotomy was added. The biliary tract was cut at the common hepatic duct and cholecystectomy was done. The jejunum was cut on the anal side about 20 cm from the Treitz ligament. The lymph nodes around the celiac axis, common hepatic artery, left gastric

artery, superior mesenteric artery, hepatoduodenal ligament and retropancreas, were cleared out.

The method for the reconstruction of the digestive tract was to pull up the jejunum to the posterior of the colon, and pancreatojejunostomy, choledochojejunostomy, gastrojejunostomy and jejunojejunostomy, was made in this order. During the performance of this procedure, most attention was paid to the anastomosis of the pancreatic duct to the mucosa of the jejunum. The main point of this technique was to cut the jejunal seromuscular layers along with the resected region of the pancreas, and the pancreatic duct and the jejunal mucosa were sutured at four points. Both anterior and posterior walls were sutured in two layers. For all sutures, absorptive threads and atraumatic needles were used.

## RESULTS

Table 1 shows the resectability classified by the region occupied by tumors, and the resectability of carcinoma of the ampulla was found as high as 74%. Likewise, Fig. 1 shows the accumulated rate of survival.

Fig. 2 shows the postoperative prognosis of 23 cases of carcinoma of the ampulla. No death due to the operation was noted, and five patients survived for more than five years after operation, the longest period of survival being nine years and ten months. The rate of survival for one year was 78%, while the rate for five years, 42%. The mean survival rate of 14 patients receiving PD without metastases to lymph nodes was 48.5 months, whereas that of three patients with metastases was 25.0 months, so that significant difference was observed ( $p < 0.05$ ).

Postoperative complications included four cases of leakage, two cases of hemorrhage, one

Table 1. Patients with carcinoma of the biliary tract and the pancreas

Primary site	Number of patients	Number of resections	Resectability
Ampulla	23	17	74%
Common bile duct	79	30	38%
Pancreas	90	14	16%
Total	192	63	33%

case of hepatic failure, one case of cholangitis and one case of pneumonia.

The endocrine pancreatic function of patients receiving PD determined with the OGTT, comprised preoperatively three cases (21%) of the normal type, five cases (36%) of the border

type and six cases (43%) of the diabetic type, which indicated 79% of the abnormal glucose tolerance test. The results of the postoperative determination included three cases (21%) of some improvement from the previous determination, eight unchanged cases (58%) and three aggravated cases (21%).

The exocrine pancreatic function determined with the PFD revealed that the total excretion level of urinary PABA in six hours (six-hours excretion) in the control group was  $72.7 \pm 3.7\%$  (mean  $\pm$  S. D.). Table 2 shows the results of the PFD determined at each stage of patients receiving PD. Their preoperative levels were significantly below those in the control group ( $p < 0.01$ ). Although the six-hours excretion within two months after operation did not show any difference from that determined before operation, the level determined in more than 12 months after operation was significantly improved, as compared with the levels deter-

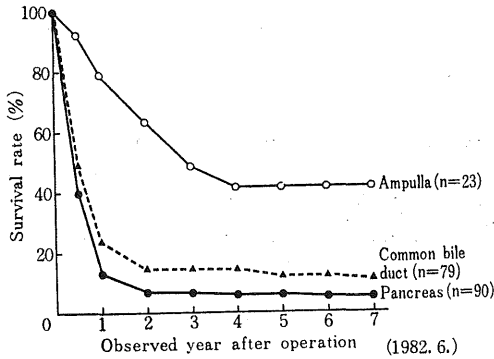


Fig. 1. Accumulated rate of survival in patients with carcinoma of the biliary tract and the pancreas

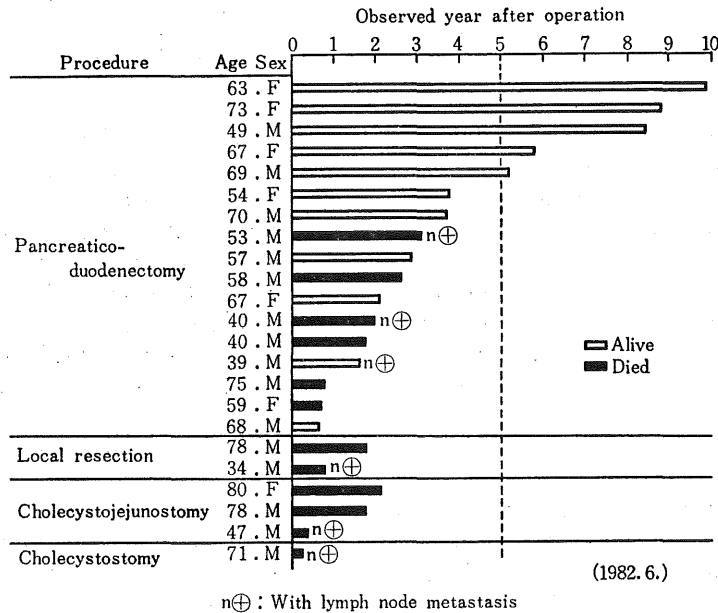


Fig. 2. Prognosis of 23 cases of ampullary carcinoma

Table 2. Pancreatic Function Diagnostant test on patients of pancreaticoduodenectomy

	Number	Total excretion level of urinary PABA in 6 hours (mean $\pm$ S. D.)	
Before operation	8	$24.0 \pm 12.2\%$	$\left. \begin{array}{l} \text{N. S.} \\ \text{P} < 0.01 \end{array} \right\} \text{P} < 0.01$
Within 2 months after operation	12	$30.2 \pm 24.7\%$	
Over 12 months after operation	5	$74.1 \pm 8.5\%$	

**Table 3.** Changes of body weight in patients of pancreaticoduodenectomy

	Decreased group (less than 10%)	Unchanged group (-10%~+10%)	Increased group (more than 10%)	Mean
Within 2 months after operation	9	5	0	-9.5%
Over 12 months after operation	1	12	1	+1.8%

**Table 4.** Reported series of pancreaticoduodenectomy for carcinoma of the ampulla of Vater

Authors	Year	Number of case	Operative mortality	Average survival period	Five-year Number	survivors Rate
Warren, et al. <sup>9)</sup>	1975	112	11%	—	26	32%
Nakase, et al. <sup>5)*</sup>	1977	330	17%	23 mos.	17	6%
Akwari, et al. <sup>1)</sup>	1977	87	13%	—	—	34%
Schlippert, et al. <sup>6)</sup>	1978	31	23%	24 mos.	2	10%
Forrest, et al. <sup>8)</sup>	1979	21	14%	46 mos.	—	24%
Walsh, et al. <sup>9)</sup>	1982	44	16%	—	5	11%
Kodama, et al.	1982	17	0%	45 mos.	5	42%

\* : Cumulative results in 57 institutions in Japan.

mined preoperatively and within two months postoperatively ( $p < 0.01$ ,  $p < 0.01$ ).

Table 3 shows the changes in body weight of patients receiving PD, which were classified to those whose body weight was lost by over 10%, naming them the decreased group, those whose body weight was increased by over 10%, naming them the increased group, and those of the intermediate weight, naming them the unchanged group.

## DISCUSSION

Among the cases of periampullary cancers, the resectability of carcinoma of the ampulla was 74%, a higher percentage than 38% of common bile-duct cancers and 16% of pancreatic cancers. Furthermore, the operative mortality due to PD performed by the authors on the cases of carcinoma of the ampulla proved 0%, and according to the reports made by several researchers<sup>1,3,5,6,8,9)</sup>, the rate was as small as 10 to 20%. The main reason may be attributable to the fact that in carcinoma of the ampulla, as compared with other periampullary cancers, hepatic insufficiency is generally milder, and surgical risks smaller. Cooperman<sup>2)</sup>

observed, "These lesions are favourable because they tend to be papillary and exophytic, and cause jaundice early."

The accumulated rate of survival of carcinoma of the ampulla was very good, as compared with those of common bile-duct cancer or pancreatic cancer (Fig. 1). Examination on the prognosis of each patient with carcinoma of the ampulla revealed that in 17 patients receiving PD, all those who survived for more than five years had no metastases to lymph nodes, and that those who had metastases to lymph nodes showed a shorter survival period than those who had not. Likewise, the prognosis of patients with metastases to lymph nodes who received local resection or palliative operation was poorer. On the other hand, there were several patients who survived for about two years after local resection or after cholecystojejunostomy, which were done on account of old age. These results indicate a similar tendency with the results so far reported by Warren et al.<sup>9)</sup>, Akwari et al.<sup>1)</sup> and Schlippert et al.<sup>6)</sup> and therefore PD is considered to be acceptable as one of the radical treatments for carcinoma of the ampulla. Concerning our

finding, Wise et al.<sup>10</sup> remarked "In elderly and poor risk patients with small localized tumors, local resection may be an acceptable alternative procedure to pancreaticoduodenectomy."

As had been explained so far, several patients with carcinoma of the ampulla have been surviving for over five years, and about 80% of the patients have been alive for one year. This has posed us an important problem how to establish a longterm management program of patients' nutrition and to grasp their conditions of digestive and absorptive function. Although 79% of abnormalities of the endocrine pancreatic function were detected with the OGTT preoperatively, the OGTT conducted postoperatively discovered many unchanged cases as well as some improved cases. There were a few cases where temporary administration of insulin was required postoperatively, but only a few needed a long-term control. Consequently, it is considered that the postoperative pancreatic endocrinic function has been maintained rather well.

Observation on the prognosis of patients who received PD revealed that some of them had been suffering from diarrhea or the loss of body weight until one year after operation, in spite of the large-dose administration of digestive enzyme preparations, but that in more than one year, their body weight had been stable and the symptom of diarrhea was disappearing even though the doses of digestive enzymatic preparations were decreased. The authors therefore have been determining the changes in the exocrine pancreatic function with the PFD, paying particular attention to the postoperative changes in body weight.

In spite of the resection of about 50% of the pancreas when PD was performed, the total excretion level of urinary PABA in six hours within two months after operation did not differ from that determined before operation, and the six-hours excretion determined in later than 12 months after operation showed some improvement, as compared with the levels determined preoperatively and within two months postoperatively, indicating almost similar levels with those of healthy subjects. The authors therefore suspected the presences of four factors in association with the residual exocrine pancreatic function of patients who received PD. These factors are as follows. 1. During the preoper-

ative period, the flow of the pancreatic juice into the digestive tract is hindered by the obstruction of the pancreatic duct, and the results of the PFD show an apparent decline. 2. Exocrine pancreatic function is reversible because the obstruction by the pancreatic duct is not longer than the period of chronic pancreatitis. 3. The reserve capacity of exocrine pancreas is large enough to bear the half resection of the pancreas. 4. At an early stage after operation, patients are at a condition of low nutrition and poor digestion and absorption due to surgical intervention, and the recovery of their exocrine pancreatic function is insufficient. Consequently, the recovery of the excretion level of urinary PABA in 12 months after operation suggests that their digestive and absorptive function are improved, that the opening of the anastomosed pancreatic duct is maintained, and that a good drainage of the pancreatic juice is continued.

When the prognosis of PD is to be followed up, the PFD is a useful method in view of its easy and repeatable determinations after operation.

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