Pancreaticoduodenectomy for Peri-ampullary Carcinoma *

Analysis of 38 Cases

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Carcinoma of the pancreas causes 1 to 5 per cent of reported cancer deaths and, although considered relatively rare, accounts for 1 to 2 per cent of all forms of cancer. Lancaster [7] showed that the incidence of deaths per unit population from carcinoma of the pancreas increases steadily with each decade. With an expected increase in total population and an expected increase in the percentage of that population reaching older age groups, carcinoma of the pancreas should be seen more commonly.

Almost uniformly, patients with carcinoma of the pancreas die six to nine months following the onset of symptoms. With palliative surgery the average survival is only three to four months. Only four documented cases of five-year survival without curative treatment have been reported.[5]

In 1935, Whipple, Parsons, and Mullins [11] proposed radical pancreaticoduodenectomy for ampullary cancers. The Whipple operation was subsequently extended to include carcinoma of the head of the pancreas.[12]

Dissatisfaction with this operation soon developed as the operative mortality remained high and the five-year survival rate remained low, especially for carcinoma of the pancreas. While most surgeons continue to do pancreaticoduodenectomies for ampullary carcinoma, controversy has arisen over the value of doing such a radical procedure for primary pancreatic malignancies.

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In order to evaluate our own experience in this field, a review of 38 radical pancreaticoduodenectomies performed for peri-ampullary malignancy at the University of Texas Medical Branch from 1947 through 1962 are reviewed.

Clinical Features

In this series of 38 cases of operable peri-ampullary carcinoma, men were encountered 2½ times more commonly than women. The majority of the patients were white, colored patients accounting for only six cases. Age ranged from 38 to 74 years. The average age was 62 years.

Twenty-eight patients gave a history of pain. Jaundice was present in 36 of the 38 patients for an average duration of seven weeks. The gallbladder was palpable in 17 of the patients who had jaundice. Fever was present in only six of the patients. Weight loss was apparent in all but one patient.

Only seven patients were anemic, whereas 14 had leukocytosis on admission. Of 23 cases in which fasting blood sugars or glucose tolerance tests were done, seven revealed a diabetic tendency. Of 24 patients who had amylase determinations performed, six were elevated. Stool occult blood studies on 18 cases revealed nine were positive.

An upper gastro-intestinal series was done on 36 cases, and revealed some abnormality in 17.

TABLE 1. *Diagnostic Biopsy*

Location	No. Cases	Positive No.	Positive %
Ampulla	13	11	85
Pancreas	13	5	38
Common bile duct	5	1	20

Operative Procedures

A variety of approaches are available for obtaining a tissue diagnosis, including specimens of pancreas, duodenotomy, and exploration of the common duct (Table 1).

Pancreas biopsy was performed in 13 cases with only five positive results.

The duodenum was opened in 13 patients and biopsy of the ampulla and adjacent area gave the highest return of positive results in 11 cases.

The common bile duct was explored in five cases, but tissue obtained by scraping the distal duct was positive in only one instance.

Because of the magnitude of pancreaticoduodenectomy, one is reluctant to undertake the procedure without a tissue diagnosis of carcinoma. Biopsy of lymph nodes immediately adjacent to the pancreas was attempted in 17 cases. There were two positive results. Resection was done in these two patients because the lesion was believed to be locally confined. Both patients died in approximately 11 months with carcinomatosis.

Following the practice of Dr. Edgar J. Poth, Chief of General Surgery, it has been customary to obtain a specimen of liver at the time of operation on all patients considered to be suitable candidates for pancreaticoduodenectomy. The specimen is submitted for quick section. This enables one to discover microscopic metastases in what otherwise would be considered an operable situation. This procedure has prevented unnecessary pancreaticoduodenectomy in two patients in the past two years (Fig. 1).

Biopsy of some kind was done in 31 of the 38 cases. A total of 74 specimens were submitted. Positive tissue diagnosis of carcinoma was obtained in only 20. Eighteen operations in this series were performed without a tissue diagnosis of cancer; although cancer was found in all cases, postoperatively.

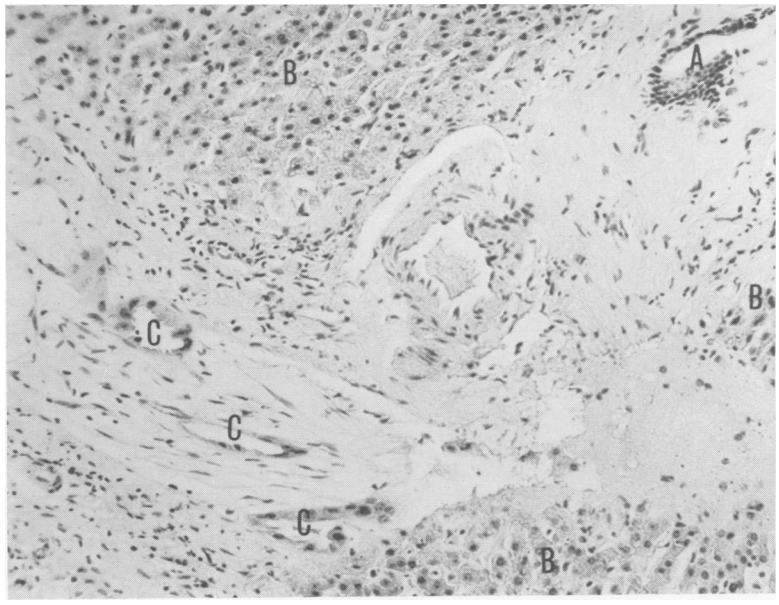

FIG. 1. Liver biopsy demonstrates microscopic metastases which were discovered on quick section and thereby prevented an unnecessary pancreaticoduodenectomy. A, Bile duct cut obliquely; B, Hepatic lobules; C, Metastatic adenocarcinoma from pancreas.

This experience suggests that difficult and time-consuming procedures, to obtain a positive biopsy specimen should not be done routinely. The time saved might contribute to decreasing operative mortality of this extensive surgical procedure.

Twenty patients had a primary resection and the remaining 18 had the two-stage operation. Fourteen of the staged procedures had external biliary drainage and four had internal drainage. External drainage was established by tube cholecystostomy in eight cases and T-tube choledochostomy in six cases.

Two basic methods were used to re-establish the gastro-intestinal tract following pancreaticoduodenectomy (Fig. 2). Twenty-one cases, from the earlier years of this study, had the biliary tract implanted into the end of the jejunum, followed by the pancreas and stomach further down the jejunum. An end-to-end choledochojejunostomy was used in 11 of the above cases, and a cholecystojejunostomy in ten.

In 17 cases, most of which were in the latter part of this study, the pancreas was placed end-to-end into the jejunum and the biliary tract end-to-side some 18 inches below. The gastrojejunostomy was made 18 inches below the biliary anastomosis. The biliary anastomosis was accomplished by choledochojejunostomy in 13 cases, cholecystojejunostomy in one case, and both the gallbladder and the common bile duct were implanted in three cases.

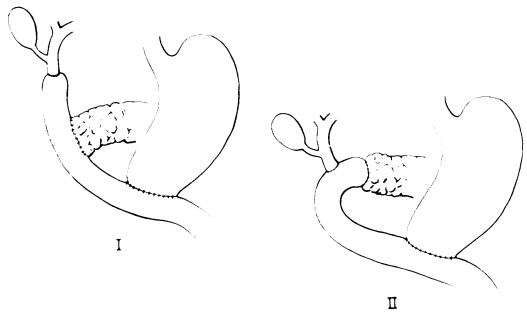

FIG. 2. Methods used to re-establish gastrointestinal system following pancreaticoduodenectomy. I. Biliary anastomosis end-to-end, pancreatic anastomosis end-to-side, gastrojejunostomy distally. II. (Currently preferred method) Pancreatic anastomosis end-to-end, biliary anastomosis, end-to-side, gastrojejunostomy distally.

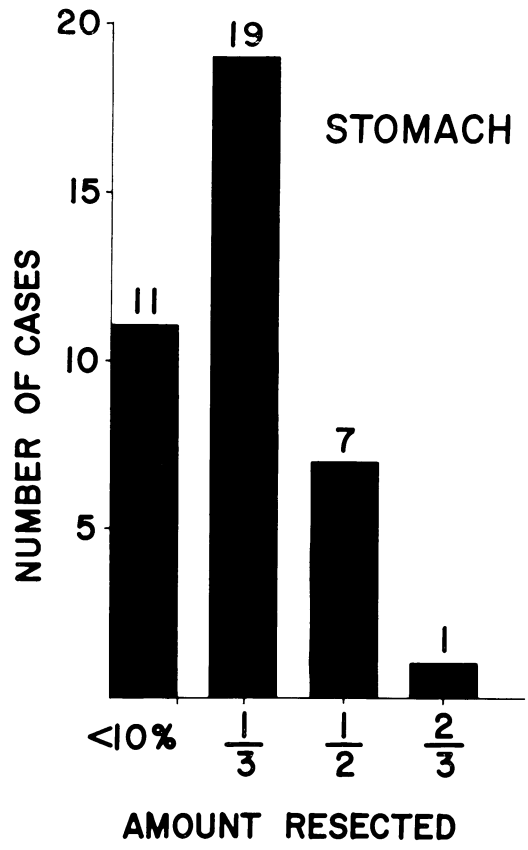

FIG. 3. The amount of stomach resected in conjunction with the pancreaticoduodenectomy.

Since the pancreatic anastomosis is the most precarious, we prefer to have it telescoped into the end of the jejunal loop. If a pancreatic fistula develops, it is less likely to drain activated pancreatic juice since the pancreas has been placed at the end of a defunctionalized limb of jejunum.

In almost half of the cases in which choledochojejunostomy was done a T-tube was placed in the common duct as a safety measure to decompress the biliary system.

In the early years a distal partial gastrectomy was a standard part of the procedure, but with time less and less of the stomach has been removed. In this series, one-half

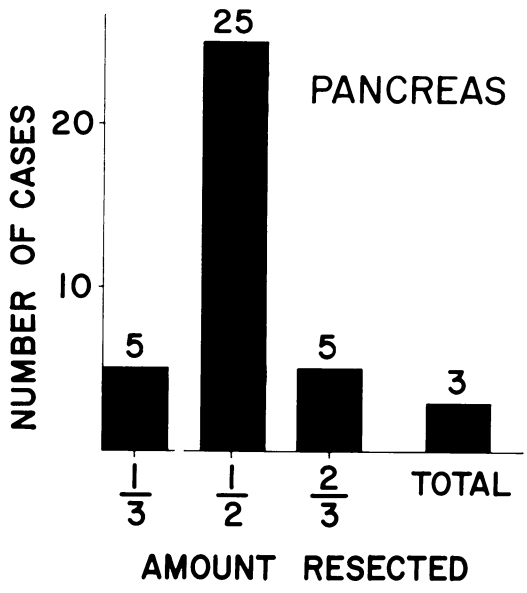

FIG. 4. Amount of pancreas resected.

had only the distal one-third of the stomach resected (Fig. 3).

Usually the pancreas was divided near its mid-point. Total pancreatectomy has been performed on three occasions (Fig. 4).

In all cases in which the gallbladder was not used in the biliary anastomosis, it was removed. This was done on the assumption that removal of the sphincter of Oddi so disturbs the intra-biliary pressure mechanisms that stasis of bile will occur in the gallbladder and stones are likely to form.

There was considerable variation in the amount of blood required during operation, but on the average 2,000 cc. of whole blood were necessary. Operating time for the pancreaticoduodenectomy ranged from four and one-fourth hours to $11^{3}/_{4}$ hours and averaged $6^{3}/_{4}$ hours.

Site of Origin

In this series (Table 2) carcinoma of the pancreas and carcinoma of the ampulla of Vater each accounted for 16 cases. There were five cases of common bile duct carcinoma and only one case of primary duodenal carcinoma.

There were two cases of epidermoid carcinoma. The first was squamous cell carcinoma of the distal common bile duct which invaded the pancreas and duodenum. Lymph nodes were not invaded. The patient expired six months postoperatively from recurrence of the cancer. The second case was an adenocanthoma of the common bile duct infiltrating the pancreas. Four of 22 lymph nodes were involved with metastatic tumor. The patient ran a progressively downhill course and expired in 11 months. Neither patient received postoperative x-ray therapy.

It is interesting that microscopic examination of the gross specimen revealed local extension of the primary tumor into surrounding peri-ampullary structures in 20 cases.

Complications

Twenty-six cases had at least one major or minor postoperative complication. Pancreatic fistula occurred in seven and biliary

TABLE 2. *Peri-ampullary Carcinoma. Site of Origin*

Location	Cases No.	Cases %
Pancreas	16	42
Ampulla of Vater	16	42
Common bile duct	5	13
Duodenum	1	3
	38	100

TABLE 3. *Peri-ampullary Carcinoma. Postoperative Mortality*

Location	No. Operations	Deaths No.	Deaths %
Pancreas	16	5	31.2
Ampulla of Vater	16	2	12.5
Common bile duct	5	2	40.0
Duodenum	1	0	0.0
	38	9	23.7

fistula in three. Wound infections also occurred in 10 patients.

There were nine hospital deaths, that is, death within 30 days of operation. This resulted in an over-all operative mortality of 23.7 per cent (Table 3, 4). All surviving cases were either followed until death, or are currently being followed.

Survival

Twenty-nine cases are suitable for survival analysis (Fig. 5). Twenty-five are now dead. The longest survival was 76 months and the shortest was three months, with the over-all average of 18 months. Only four patients are still alive; one 29 months, two 18 months and one eight months, postoperatively. All are clinically free of disease at this time.

Of three patients who had total pancreatectomy, one died five days postoperatively from peritonitis, and one died four months postoperatively of unknown cause. A clinic visit two months prior to his death revealed the patient to be well. The third patient had the usual subtotal pancreatectomy done initially, but tumor was found at the line of resection on permanent sections. The remaining pancreas was removed at a second procedure. She lived 4½ years requiring several hospitalizations for management of progressively insulin resistant diabetes and eventually died of bronchopneumonia. Autopsy revealed pulmonary and hepatic metastases.

TABLE 4. *Causes of Postoperative Deaths*

Cause	No. Cases
Shock	3
Hepatic failure*	2
Pancreatic fistula	1
Peritonitis	1
Hemorrhage	1
Renal failure	1
	9

* One of these deaths resulted from ligation of the hepatic artery.

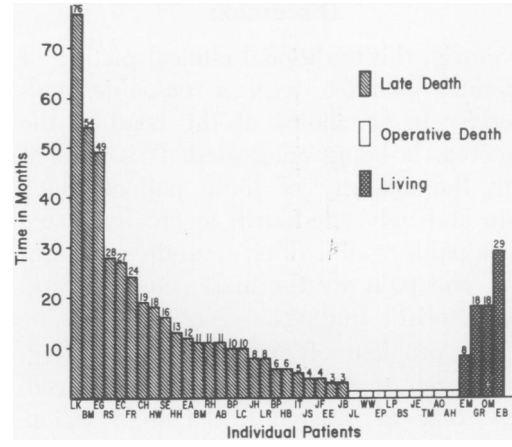

FIG. 5. Vital statistics following pancreaticoduodenectomy for peri-ampullary carcinoma.

It is well known that carcinoma of the pancreas has a much worse prognosis than carcinoma of the ampulla. Our experience was no exception (Fig. 6). There were ten cases of carcinoma of the pancreas that survived the operation, but are now dead. The survival ranged from three to 54 months, with an average of 12 months. There were 11 such cases of carcinoma of the ampulla. The survival ranged from four to 76 months, with an average of 24 months.

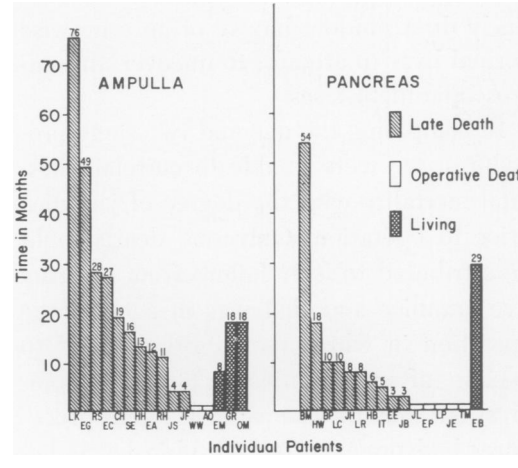

FIG. 6. Comparison of vital statistics following pancreaticoduodenectomy for carcinoma of the ampulla and carcinoma of the pancreas.

Discussion

Slowly, the traditional clinical picture of *painless jaundice with a palpable gallbladder* in carcinoma of the head of the pancreas is being eradicated. It is evident that the majority of these patients have pain and only one-fourth to one-half have a palpable gallbladder. Jaundice, weight loss, and pain are the most consistent and characteristic findings.

The problem of making a tissue diagnosis prior to resection remains unsolved. The fear of resecting a benign lesion, particularly with an operation of this magnitude, makes one reluctant to proceed without a tissue diagnosis. Nevertheless, if radical operation is to be effective, the principles of cancer surgery must be followed as in other areas. Cutting into the neoplasm for diagnosis may on occasion be the deciding factor in local spread and recurrence of the tumor. Warren *et al.*[10] performed diagnostic biopsies rarely, preferring to proceed on the gross characteristics of the pancreas and biliary tree in most cases. In only six of 218 resections for suspected peri-ampullary carcinoma did they fail to find a malignant tumor. Biopsy of suspicious areas in the liver, or of suspicious lymph nodes, to determine resectability is obviously important. In addition we routinely do a random biopsy of an otherwise normal liver to attempt to uncover any microscopic metastases.

In comparing the one and two-stage procedures, we were unable to correlate hospital mortality with the degree of jaundice prior to operation. Only one death could be attributed to liver failure from obstructive jaundice and that was in a two-stage operation in which the bilirubin failed to decline after preliminary T-tube decompression. Six of the single-staged procedures had preoperative bilirubin levels between 30 and 38 mg.% and only one died in the 30 day postoperative period. That patient expired from a gas producing bacterial peritonitis.

Even though operative mortality is unaffected by staging the procedure, because the technical difficulty is considerably greater at the second stage, we believe that primary resection is the procedure of choice.

In our series of 21 cases done five years or more ago, 15 survived operation. Three patients lived at least three years. One of the seven pancreatic tumors lived 54 months and two of the six ampullary tumors lived 76 and 49 months, respectively. The last patient committed suicide and was clinically free of tumor at that time. The remaining cases were all dead in less than three years.

Warren, *et al.*,[10] in reviewing 218 resections at the Lahey Clinic have recently presented encouraging evidence that the operative mortality and long-term survival rates are improving with time and experience. Their over-all operative mortality was 11.9 per cent. In their series of resected cases three of 47 carcinomas of the head of the pancreas, 18 of 48 carcinomas of the ampulla of Vater, four of 10 carcinomas of the duodenum, and four of 11 carcinomas of the common bile duct survived five years or longer.

From the literature, Jordan[5] collected 955 cases of pancreaticoduodenectomy for peri-ampullary cancer through 1959. An additional 214 cases have been reported through 1962.[1, 2, 4, 6, 8-10] The reported cases plus this series make a combined total of 1,169 cases. The combined operative mortality is 19.9 per cent (Table 5). Also, Jordan[5] collected the reported five-year survivors through 1959 and found 23 carcinomas of the pancreas, 51 carcinomas of the ampulla of Vater, 13 carcinomas of the duodenum and six carcinomas of the common bile duct. It is obvious from the collected data that carcinoma of the pancreas carries an operative mortality twice that

of ampullary while the incidence of long-term survival is six times as great for ampullary cancer.

A number of factors contribute to the failure of this operation in the vast majority of pancreatic cancers. Jaundice develops much later in the pancreatic tumors by virtue of location.

Ninety per cent of pancreatic cancers are ductile in origin and most eventually obstruct the pancreatic duct to produce ductal dilatation. This stagnant pancreatic fluid may contain cancer cells and contribute to the high local recurrence rate when subtotal pancreatectomy is performed.

Normally only 2 cm. of pancreatic tissue separate the intra-pancreatic common bile duct and the portal or superior mesenteric vein. Since the duct must be compressed to produce jaundice for recognition of the disease, yet the vein must be totally uninvolved for a surgical cure, it is no small wonder that the survival rate of carcinoma of the pancreas is small.

In five per cent of patients, the pancreas is diffusely involved with tumor. This diffuse involvement may be due to implantation along the ductile route, or from true multicentric origin of the tumor, but argues well the case for total pancreatectomy.

Even if total pancreatectomy and *en bloc* portal vein resection could be done without significantly altering the morbidity and mortality rate, the cure rate for carcinoma of the pancreas might remain low. Malignant characteristics of this tumor are such that even an extended radical procedure might not alter the ultimate outcome. When survival times are examined for pancreatic cancer, untreated or following palliative operation, it is apparent that this tumor is rapidly growing and highly lethal in all but a few instances.

TABLE 5. *Peri-ampullary Malignancy. Postoperative Mortality*

Collected Series

Location	No. Operations	Deaths	
		No.	%
Pancreas	514	109	21.2
Ampulla of Vater	370	46	12.4
Common bile duct	104	22	21.2
Duodenum	101	20	19.8
Unclassified	80	35	43.7
	1,169	232	19.9

Summary

Thirty-eight cases of pancreaticoduodenectomy performed for peri-ampullary malignancy at the University of Texas Medical Branch from 1947 through 1962, are presented. There are: 16 instances of pancreatic carcinoma, 16 of ampullary carcinoma, five of common bile duct carcinoma, and one of duodenal carcinoma. The overall operative mortality is 23.7 per cent.

All cases were either autopsied, followed until death, or are under current care. Only four patients are still alive: one 29 months, two 18 months and one eight months postoperatively. All are clinically free of disease at this time.

Eleven hundred sixty-nine cases of pancreaticoduodenectomy for peri-ampullary malignancy are collected through 1962. The combined operative mortality is 19.9 per cent.

We believe that all patients considered suitable candidates for pancreaticoduodenectomy for peri-ampullary cancer should have liver biopsy at the time of operation with quick section. This procedure, by revealing microscopic metastases, has prevented two unnecessary pancreaticoduodenectomies in the past two years.

We believe that primary resection is the procedure of choice.

Radical operation for carcinoma of the pancreas is not satisfactory, but in carefully selected cases may still be worthwhile. Significant cure rates and palliation with reasonable morbidity and mortality can be expected with pancreaticoduodenectomy in cases of carcinoma arising in the

ampulla of Vater, common bile duct, and duodenum.

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