

A Long-term Appraisal of Pancreaticoduodenal Resection for Peri-ampullary Carcinoma *

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IT is particularly appropriate at this time, approximately a quarter of a century following the classic report by Whipple⁴ and his associates, to pause and to appraise the current status of pancreaticoduodenectomy in the management of peri-ampullary carcinomas. This and subsequent publications by Whipple aroused a wave of optimism among surgeons which led to an aggressive application of this operation in a large number of patients with peri-ampullary malignant tumors. Initially, the limits of operability were vague and the technical hazards of the operation were not fully appreciated. The operative mortality was high, the extent of palliation was meager when the tumor could not be completely removed, and instances of long-term control of the disease or cure were distressingly few. These unfavorable aspects of pancreaticoduodenectomy led to a wave of pessimism of such proportion that it appeared for a while that the operation for the treatment of peri-ampullary carcinoma would be abandoned entirely.

Gradually, sufficient experience in the surgical management of these tumors accumulated in some centers to permit an objective evaluation of this procedure. With this concentrated experience, the proper range of resectability was determined, fundamental technical requirements

of the operation were defined, the morbidity and mortality rates were reduced to reasonable limits, and the range of palliation and rates of cure were enlarged.

Carcinomas arising in the head of the pancreas, the ampulla of Vater, the intrapancreatic portion of the common bile duct, or the duodenal mucosa adjacent to the papilla of Vater are similar in their clinical history, physical manifestations, associated laboratory findings and in the nature of the surgical procedures required for their treatment. When considered together, it is important to point out their similarities and their differences. A knowledge of their similarities aids in their general recognition, and an appreciation of their differences is necessary to their proper differential diagnosis during surgical exploration and to the determination of the wisdom of their removal.

Clinical Features

A detailed description of the clinical features of peri-ampullary carcinoma is not germane to this discussion, but certain misconceptions which have been thoroughly recorded in the medical literature may lead to incorrect diagnosis. The delusion that malignant tumors arising in the peri-ampullary area are characterized by the presence of painless jaundice and a palpable gallbladder is difficult to eradicate. In 218 resectable cases of peri-ampullary carcinoma at the Lahey Clinic, abdominal pain was present in 73 per cent. In nonresectable

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TABLE 1. *Peri-ampullary Malignant Tumors,
Site of Origin*

Location	Cases	
	No.	%
Pancreas	89	41
Ampulla of Vater	81	37
Duodenum	27	12
Common bile duct	21	10
	218	100

cases this incidence of pain is much higher. The combination of painless jaundice and a palpable gallbladder occurred in only 26 per cent of patients with resectable peri-ampullary tumors. Jaundice occurs in about 90 per cent of malignant tumors of the peri-ampullary area. The incidence of jaundice is 100 per cent in carcinomas arising in the intrapancreatic portion of the common duct, 95 per cent in resectable carcinomas of the ampulla of Vater, 89 per cent in resectable malignant lesions of the head of the pancreas, and in only 25 per cent of patients with carcinomas arising in the duodenal mucosa adjacent to the papilla of Vater. Weight loss is almost as common in the presence of these tumors as is jaundice. Diabetes mellitus occurs in from 5.0 to 10 per cent. Although diarrhea may be a prominent and distressing symptom of peri-ampullary carcinoma, and particularly of primary ductal carcinoma arising in the head of the pancreas, this symptom occurs in less than one-third of resectable tumors.

Carcinoma of the pancreas, which characteristically is of ductal origin, is an insidious growth with vague initial symptoms, including mild epigastric distress, anorexia, constipation or diarrhea, weight loss and increasing fatigue. These symptoms progress slowly for several weeks or a few months before the onset of jaundice. Jaundice, once it appears, is relentlessly progressive. Carcinoma of the ampulla of Vater, on the other hand, has a more dramatic history with a lower incidence of

abdominal pain. Pain may occur when the common duct becomes completely obstructed and vague abdominal distress may appear after meals. Because jaundice, which is rarely remittent, occurs early in the course of the disease, it is frequently responsible for bringing the patient to the physician before local extension or metastatic spread of the tumors occurs. Carcinomas arising in the intrapancreatic portion of the common bile duct resemble, in historical detail, carcinomas of the ampulla of Vater more closely than primary carcinoma of the head of the pancreas. Since these tumors produce a sclerosing stricture of the bile duct, jaundice is progressive and, ultimately, obstruction of the duct is complete. Malignant tumors arising in peri-ampullary duodenal mucosa produce a more variable clinical picture. The history is frequently prolonged and significant anemia is much more common than in other varieties of peri-ampullary carcinomas. Jaundice is a late manifestation.

Site of Origin of Peri-ampullary Carcinoma

A review of 218 patients with resectable peri-ampullary carcinoma operated on at the Lahey Clinic from 1942 to 1961 (Table 1) revealed that 89 (41%) of these tumors arose primarily in the pancreas; 81 (37%) were classified as tumors of the ampulla of Vater; 21 (10%) arose in the intrapancreatic portion of the common bile duct and 27 (12%) originated in the duodenal mucosa surrounding the papilla of Vater.

Factors Influencing Prognosis in Malignant Peri-ampullary Tumors

Since the prospects for curing primary pancreatic carcinoma arising in the ducts are small in comparison with the success of treating those arising in the ampulla of Vater, the intrapancreatic portion of the common bile duct or the peri-ampullary

area of the duodenal mucosa, it is important that a precise distinction be made at the operating table regarding the site of origin of peri-ampullary tumors. Failure to discern the importance of this distinction undoubtedly accounts for the widespread pessimism with respect to the value of pancreaticoduodenectomy in the treatment of peri-ampullary tumors.

Differential Diagnosis during Abdominal Exploration

While it is desirable for all physicians to be aware of the variation in prognosis depending upon the precise site of origin of these tumors, it is much more important for the surgeon to make this distinction at the time of abdominal exploration. The bleak prognosis following resection for ductal carcinoma arising in the head of the pancreas, in our opinion, does not justify aggressive surgical treatment of primary pancreatic carcinoma. Rodney Smith,³ who has had a large experience in pancreatic surgery, employs broader indications for pancreaticoduodenectomy in primary pancreatic carcinoma because he believes these patients are more comfortable and their nutrition is better after removal of these tumors despite the fact that the entire tumor cannot be removed. By contrast, the favorable prognosis after radical resection for other peri-ampullary carcinomas warrants an optimistic surgical approach to these tumors, provided the surgeon is able to carry out the operation with reasonable morbidity and mortality rates. With greater experience in the field of pancreatic surgery, one may anticipate that the operative mortality will decrease and that the cure rates will improve. The importance of accurate differential diagnosis of these tumors during abdominal exploration is emphasized by the fact that 14 patients have been operated on at the Lahey Clinic at intervals of one to five years following a previous laparotomy elsewhere, at which

time the tumor in each instance was thought to be inoperable, and only a biliary decompression was performed. In each instance pancreaticoduodenectomy was possible since no significant local spread or distant metastases were demonstrable. The average length of survival in these patients after resection (two years) indicates the tragic consequences of not performing a radical resection at the initial operation.

The gross pathologic features of peri-ampullary carcinoma are sufficiently consistent to permit an accurate diagnosis without resorting to biopsy in most of these tumors provided the surgeon has had sufficient experience with pancreatic surgery. Primary carcinoma of the head of the pancreas produces obstruction of the common bile duct, which accounts for the dilated gallbladder and common duct proximal to the tumor. In addition to the dilatation of these two structures, both the gallbladder and the common bile duct are thinner than normal and a distinct bluish color is apparent when these structures are exposed. Equally prominent features occur in the pancreas itself with carcinoma arising in the proximal portion of the gland. The duct of Wirsung is dilated in 80 per cent of resectable tumors although a lesser number will be frankly palpable at the time of exploration. The body and tail of the pancreas are enlarged, pale and firm. The gland is rounded and the tail is frequently blunt, rounded and withdrawn from the hilus of the spleen. Following mobilization of the head of the pancreas and duodenum, palpation reveals the presence of a tumor in the head. Although the margins of the tumor are indistinct, the gross limit of the distal edge of the tumor is discernible. Immediately beyond the distal limit of the tumor the duct of Wirsung is palpable in the neck and proximal body of the gland. The dilated duct is felt at the junction of the superior and middle third of the gland on the anterior surface of the pancreas.

Carcinoma of the ampulla of Vater pro-

duces obstruction of the duct of Wirsung in only 20 to 30 per cent of resectable cases. Thus, the secondary signs of obstruction described above will not be encountered in many of these patients. The biliary tract will show the same degree of dilatation, thinness of the walls of the gallbladder and the common bile duct, and blue color. With the duodenum and head of the pancreas mobilized, the tumor can be felt arising from the mesial wall of the duodenum and projecting into the lumen. Since ampullary carcinomas may spread submucosally, the degree of projection within the lumen of the duodenum varies considerably. Fortunately, the pathologic variety of malignant tumor involving the papilla of Vater which spreads submucosally tends to produce obstruction of the duct of Wirsung so that a diagnosis of carcinoma can usually be made without opening the duodenum. The greatest difficulty in making this diagnosis will occur when the ampullary tumor which projects into the duodenum is extremely soft. Under these circumstances it is easy to confuse such a tumor with a benign polyp. More commonly, the tumor presents as a marblelike projection which is easily palpable and its true nature is frequently apparent. In rare instances the tumor may be deeply ulcerating, with a palpable central crater, thus giving rise to the possibility that one may be dealing with a benign ulcer.

Carcinoma of the intrapancreatic portion of the distal common bile duct produces the same extrahepatic biliary tract signs described above. Obstruction of the duct of Wirsung occurs infrequently. After the duodenum and head of the pancreas are mobilized, a firm tumor is palpable just above the level of the papilla of Vater. This mass does not project into the duodenum. The palpable tumor is slightly more cephalad than is observed in either primary carcinoma of the pancreas or carcinoma of the ampulla of Vater.

Carcinomas arising in the duodenal mucosa in proximity to the papilla of Vater are rarely difficult to diagnose. They tend to be larger, to encircle a considerable portion of the circumference of the duodenum and to have a very large central ulceration. Once they have become sufficiently large to obstruct the common bile duct, the extrahepatic biliary system will have the same characteristics that have been described above.

Frequently it is necessary to distinguish between these various peri-ampullary tumors and benign enlargements of the pancreas. The most common disease which requires this distinction is chronic relapsing pancreatitis. The history frequently is sufficient to make this distinction since patients with chronic relapsing pancreatitis have a long, episodic history of attacks which increase in frequency and severity. When jaundice occurs, it tends to be mild or only moderately severe and is frequently intermittent. The extrahepatic biliary system is occasionally dilated but usually the common duct is normal in size. Because of the inflammatory reaction incidental to the pancreatitis, the common duct and the peritoneum overlying the duct are pale and thickened. In the far-advanced cases of chronic relapsing pancreatitis, it may be difficult to identify the duct because of the induration and edema and because of the absence of the distinctive bluish discoloration which is so characteristic of dilatation of the biliary tree due to the presence of a malignant tumor. The presence of a stone impacted in the intrapancreatic portion of the common bile duct surrounded by edema and induration in the substance of the pancreas may suggest the presence of a peri-ampullary carcinoma. The gallbladder in this circumstance usually will not be dilated and it frequently will contain stones. Furthermore, the pancreatic duct will not be obstructed. The mass in the area of surrounding inflammation in the pancreas is

generally so large that were it a carcinoma, the duct of Wirsung would be obstructed.

Fortunately, peptic ulceration of the duodenum rarely occurs at the level of the papilla of Vater. When such ulceration is present and when there is deep penetration with resultant induration of the head of the pancreas, a primary carcinoma of the pancreas may be suspected. Careful analysis of the history and evaluation of the ulcerating lesion by projecting the lateral wall of the duodenum against the head of the pancreas will usually permit the differential diagnosis between peptic ulceration and a malignant tumor. If the diagnosis remains in doubt, a duodenotomy should be made.

The Role of Biopsy in Diagnosis

Controversy continues regarding the proper role of biopsy in establishing the diagnosis of peri-ampullary carcinomas. Any statistical analysis of this problem which includes a high percentage of inoperable cases will show a high degree of accuracy based upon biopsy and frozen section analysis. Securing a positive biopsy diagnosis of favorable operable tumors is much more difficult. The use of the Silverman needle has been recommended in some quarters, but our experience with this method of biopsy has been meager. Practically all ampullary carcinomas can be diagnosed by biopsy if a duodenotomy is performed and a portion of the tumor is secured for frozen section analysis. Experience at this clinic indicates that a correct diagnosis can be made in most instances on the basis of the differential considerations described above. Consequently, direct biopsy of the tumor for confirmation of the diagnosis is rarely performed. Biopsy is not entirely without danger since it may be accompanied by immediate or postoperative hemorrhage, pancreatic fistula, or pancreatitis. There is a possibility that the tumor may be spread by biopsy. The risk of ob-

taining a false-negative report following frozen section analysis of biopsy is considerable in operable carcinoma of the head of the pancreas. Pancreaticoduodenectomy has been performed 218 times at the clinic when the indication for resection was peri-ampullary carcinoma. In six instances no malignant tumor was found. Thus, the margin of error has been less than 3.0 per cent.

Despite our reliance upon the gross characteristics of the pancreas and the biliary tree in arriving at this diagnosis at laparotomy, there are occasional indications for biopsy. If jaundice is relatively mild, if the dilatation of the extrahepatic biliary system is minimal, if the pancreas appears normal by inspection and palpation and no tumor can be felt on the mesial side of the descending portion of the duodenum, the pancreas should not be resected without biopsy. The most suitable avenues for biopsy are through the common bile duct or the duodenum. If the lesion is thought to be in the intrapancreatic portion of the common duct, a choledochostomy is performed in the supraduodenal segment of the common bile duct. If this duct is greatly dilated and if the preponderance of evidence suggests that a malignant tumor will be found in the distal portion of the duct, a transverse incision at the proposed site of division of the bile duct may be utilized. A small scoop is then inserted into the common duct and passed distally until it meets the point of obstruction. With the head of the pancreas and duodenum mobilized, gentle compression is made over the scoop within the duct and the scoop is gently withdrawn. By this maneuver, a fragment of the tumor may be obtained and it may be identified by frozen section analysis. If this method does not resolve the problem, a duodenotomy is performed at the level of the papilla of Vater and a direct biopsy is made of the papilla. If the surgeon still suspects that the tumor is in the intrapancreatic portion of the common

TABLE 2. *Peri-ampullary Carcinoma—
Postoperative Mortality*

Location	No. Operations	Deaths	Mortality, %
Pancreas	89	11	12.4
Ampulla of Vater	81	7	8.6
Duodenum	27	5	18.5
Common bile duct	21	3	14.3
	218	26	11.9

bile duct, a sphincterotomy is performed and a direct biopsy specimen taken.

If a biopsy of the substance of the pancreas is to be made, we prefer to use the scalpel rather than the Silverman needle. It is probably safer in most instances to obtain the biopsy specimen following a duodenotomy regardless of whether the scalpel or Silverman needle is used.

Peripheral biopsies around the head of the pancreas and the distal common bile duct have been frequently used in this clinic, sometimes for the purpose of establishing the diagnosis, and more commonly for determining the feasibility of resection. Suspicious areas in the liver should also be biopsied and analyzed in determining operability.

Determination of Operability

The magnitude of pancreaticoduodenal resection with its attendant mortality requires that this operation be reserved for those tumors in which there is a reasonable prospect of eradicating the disease with an acceptable mortality rate. Since cumulative experience indicates that the prognosis following resection for primary carcinoma of the head of the pancreas is poor, the limits of operability should be rigidly defined. The prognosis in cases of carcinoma of the ampulla of Vater and malignant tumors arising in the intrapancreatic portion of the common bile duct or duodenum is more favorable and the range of operability is broader. Pancreaticodu-

denal resection should not be performed when distant metastases are demonstrable except perhaps in the rare instance of hyperfunctioning islet cell carcinoma. Cystadenocarcinomas and nonfunctioning islet cell carcinomas tend to be of low grade malignancy and may attain considerable size without associated metastasis. Indeed, large tumors of the pancreas which grossly appear to be malignant and occurring in patients in whom no evidence of extension or distal spread is demonstrable, suggest the diagnosis of either cystadenocarcinoma or islet cell carcinoma. Because of the good prognosis when these two tumors are excised, attempts should be made to remove them if no distant spread is discernible. Rare instances of bizarre types of malignant tumors occurring in the peri-ampullary area will be encountered. Cattell and Warren¹ have previously published a photograph of a melanoma arising in the ampulla of Vater, which was removed by pancreaticoduodenectomy. This patient is well 39 months after operation. Another patient had a resection for primary leiomyosarcoma arising from the mesial wall of the duodenum. She is well 18 months after operation.

Mortality

The mortality of pancreaticoduodenectomy can be kept at a reasonable level, commensurate with the magnitude of the procedure, with increasing experience in the selection of patients for operation, with careful preoperative preparation and with vigilant attention to the technical details of the procedure.

The mortality following 218 pancreaticoduodenectomies including seven total pancreatectomies performed at the clinic from 1942 to 1961 was 11.9 per cent (Table 2). There were 11 deaths in 89 cases in which pancreaticoduodenectomy (including total pancreatectomy in three cases) was performed for primary carcinoma of the head

of the pancreas, giving a mortality rate of 12.4 per cent. Seven deaths occurred in 81 patients (8.6%) who had resection for carcinoma of the ampulla of Vater. Five deaths occurred in 27 patients (18.5%) who had resection for primary carcinoma of the duodenum. There were three postoperative deaths in 21 cases of resection for primary carcinoma of the common bile duct, giving a mortality of 14.3 per cent. The current mortality rate following resection of carcinoma arising in the ampulla of Vater and distal common duct is approximately 5.0 per cent.

Causes of Death

The factors responsible for postoperative mortality are listed in Table 3. By far the majority of these postoperative deaths resulted from hemorrhage and from renal failure. Pancreatic or biliary fistula was listed as a primary cause of death in four instances but postoperative fistula was also a factor in several instances in which hemorrhage was listed as the primary cause of death. The possibility of delayed hemorrhage is minimized by careful suturing of the pancreatic duct to the jejunum. All patients who died of renal failure had severe jaundice.

While it is our current practice to perform pancreaticoduodenectomy in one stage, it is possible that some of these patients who died of renal failure would have had a better chance of survival if a preliminary decompression of the biliary ob-

TABLE 3. Causes of Postoperative Deaths

Cause	No. Cases
Hemorrhage	8
Renal failure	9
Fistula and peritonitis	4
Coronary occlusion	3
Cerebral thrombosis	1
Liver necrosis and infection	1
	—
	26

TABLE 4. Follow-up of Cases of Carcinoma of Head of Pancreas Resected

Total cases	89	
Operative deaths	11 (12.4%)	
Survived operation	78	
	Died Subsequently	Living
Total	60	18
<3 years	57	15
3-5 years	2	1
5-10 years	1	2
>10 years	0	0
Suitable for 5-year survival study	47	
Lived 5 years or longer	3 (6.4%)	

struction had been accomplished. As related earlier, consideration should be given to this possibility in the older patient who is obese and deeply jaundiced and in whom the prothrombin activity is borderline. Other danger signs include an elevation of the blood urea nitrogen and a reversal of the albumin-globulin ratio. The three patients who died of myocardial infarction were, respectively, 63, 68 and 78 years of age. The 78-year-old patient had a fatal myocardial infarction immediately after the operation; another fatal infarction occurred within 12 hours of operation, and the third patient had a fatal attack on the eighteenth postoperative day.

Results

Carcinoma of the Head of the Pancreas. Seventy-eight of 89 patients survived pancreaticoduodenectomy for primary carcinoma of the head of the pancreas (Table 4). There were 11 deaths (12.4%). Of the 78 patients who survived operation, 60 have subsequently died: 57 patients survived less than three years, two lived three to five years, and one from five to ten years following operation. Eighteen patients are living: 15 of these were operated upon less than three years ago, one patient has sur-

TABLE 5. *Follow-up Cases of Carinoma of Ampulla of Vater Resected*

Total cases	81	
Operative deaths	7 (8.6%)	
Survived operation	74	
	Died Subsequently	Living
Total	46	28
<3 years	36	11
3- 5 years	6	6
5-10 years	4	5
>10 years	0	6
Suitable for 5-year survival study	48	
Lived 5 years or longer	18 (37.5%)	

vived four years, and two are living from five to ten years after operation. One of the two current survivors had a nonfunctioning invasive islet cell carcinoma and is living eight years after resection and the other had a total pancreatectomy for a cystadenocarcinoma. Of 47 patients suitable for five year follow up, three (6.4%) lived five years or longer.

Carcinoma of the Ampulla of Vater. Of 81 patients who had resections for primary carcinoma of the ampulla of Vater, 74 survived operation (Table 5). There were seven postoperative deaths (8.6%). Of the 74 patients who survived, 46 died subsequently: 36 lived less than three years, six lived from three to five years, and four lived from five to 12 years. Twenty-eight patients are living: 11 were operated on less than three years ago, six have survived from three to five years, five from five to ten years, and six more than ten years after operation. Of 48 patients suitable for five year follow up, 18 (37.5%) have lived five years or longer.

Carcinoma of the Duodenum. Resection was performed in 27 patients for carcinoma of the duodenum (Table 6). There were five deaths (18.5%). Ten of the 22 patients who survived operation died subsequently: nine lived less than three years, and one

lived 11 years after operation. Twelve patients are living: eight were operated on less than three years ago, one was operated on five years, and three between five and ten years ago. Of ten patients suitable for five year follow up, four (40%) have survived five years or longer after operation.

Carcinoma of the Common Bile Duct. Twenty-one resections were performed for carcinoma of the intrapancreatic portion of the common bile duct (Table 7). There were three postoperative deaths (14.3%). Of the 18 patients who survived operation, nine have subsequently died: eight survived less than three years, and one lived for four years. Nine patients are living: four were operated on less than three years ago, one was operated on four years ago, three from five to ten years ago, and one is living 11 years after resection. Of 11 patients suitable for five year follow up, four (36.4%) have survived five years or longer.

Long-Term Survivals. Twenty-nine patients have survived five years or longer, as shown in Table 8. The significance of distinguishing between primary carcinoma of the pancreas, on the one hand, and carcinoma arising in the duodenum, the intrapancreatic portion of the common bile duct and the ampulla of Vater, on the other, is indicated by an analysis of the long-term survival

TABLE 6. *Follow-up of Cases of Carcinoma of Duodenum Resected*

Total cases	27	
Operative deaths	5 (18.5%)	
Survived operation	22	
	Died Subsequently	Living
Total	10	12
<3 years	9	8
3- 5 years	0	1
5-10 years	0	3
>10 years	1	0
Suitable for 5-year survival study	10	
Lived 5 years or longer	4 (40%)	

rates. Only three of the 29 patients who survived five years or longer had primary carcinoma of the pancreas and the tumors in these patients were either cystadenocarcinomas or nonfunctioning islet cell carcinomas. In contrast, there were four patients with long-term survival following resection of primary carcinoma of the duodenum, four with carcinoma of the distal common bile duct and 18 with carcinoma of the ampulla of Vater.

It is of particular interest to note the long-term survival rate in carcinoma of the ampulla of Vater (Table 9). Four patients who died subsequently lived five, eight, nine and 12 years, respectively. Fourteen patients are living. Four have survived five years, four from seven to eight years, five from 11 to 13 years and one 19 years. Cattell, Warren and Au² have previously reported a five year survival rate of 52 per cent following pancreaticoduodenectomy for carcinoma of the ampulla of Vater in a group of patients who had not had explorations before coming to the clinic. The greater survival rate in this group as compared with the entire group of patients with resectable ampullary carcinomas results from the elimination from statistical consideration of a number of patients in whom prolonged delay (one to five years)

TABLE 7. Follow-up Cases of Carcinoma of Common Bile Duct Resected

Total cases	21	
Operative deaths	3 (14.3%)	
Survived operation	18	
	Died Subsequently	Living
Total	9	9
<3 years	8	4
3- 5 years	1	1
5-10 years	0	3
>10 years	0	1
Suitable for 5-year survival study	11	
Lived 5 years or longer	4 (36.4%)	

TABLE 8. Peri-ampullary Carcinoma, Long-Term Survival—More Than 5 Years

Location	Cases	
	No.	%
Pancreas	3	6.4
Ampulla of Vater	18	37.5
Duodenum	4	40.0
Common bile duct	4	36.4
Total	29	

TABLE 9. Carcinoma of Ampulla of Vater Long-Term Survival

Dead		Living	
Interval	No. Patients	Interval	No. Patients
5 years	1	5 years	4
8 years	1	7- 8 years	4
9 years	1	11-13 years	5
12 years	1	19 years	1
	4		14

occurred between a preliminary biliary decompression elsewhere and subsequent resection at the clinic.

Postoperative Metabolic Status

Two factors contribute to metabolic deficiencies following pancreaticoduodenectomy. Many patients have obstruction of the duct of Wirsung preoperatively with secondary fibrosis and ischemia of the pancreas. The fibrosis and ischemia may destroy part of the acinar and islet cell tissue, thus giving rise to diabetes mellitus or to acinar insufficiency. Diabetes mellitus developed in 22 of 192 patients who survived pancreaticoduodenectomy (Table 10). Recognition of diabetes is more common when survival is prolonged. The diabetes is usually mild and relatively easily controlled. The other factor which contributes to these deficiencies is the surgical removal of approximately one-half of the pancreatic mass.

TABLE 10. *Peri-ampullary Carcinoma*
Late Postoperative Complications

Location	Diabetes Mellitus	Acinar Insufficiency	Jejunal Ulcer
Pancreas	11	19	4
Ampulla of Vater	7	17	8
Duodenum	3	4	2
Common bile duct	1	3	2
Total	22	43	16

Acinar Insufficiency

Forty-three patients who survived operation had acinar insufficiency (Table 10). In many instances this deficiency was mild and was controlled by regulating the amount of fat in the diet. In others, severe degrees of malabsorption occur and require intensive treatment with pancreatic supplements. Viokase, 10 grains every two hours from 7 a.m. to 7 p.m., is the most effective means of improving intestinal absorption in these patients.

Jejunal Ulcer

Only a small segment of the stomach was removed at operation in many of these cases. The increasing incidence of jejunal ulceration among the survivors who lived for a considerable period of time indicates that either a high partial gastric resection or a vagotomy should be performed at the time of pancreaticoduodenectomy. Sixteen jejunal ulcers have been recognized among the survivors (Table 10). These ulcers may appear within a few months or many years after the resection. Serious hemorrhage from the ulcer has occurred in several instances. Perforation occurred in one. If a jejunal ulcer develops, especially if it is associated with massive hemorrhage, operation is indicated. Subtotal gastric resection

has been employed, as a rule, in such cases, because operation has frequently been required during or immediately after an episode of bleeding. Bilateral vagotomy without resection of the ulcer might be satisfactory.

Conclusions

A long-term analysis of pancreaticoduodenectomy for peri-ampullary carcinoma indicates that this is a feasible and valuable procedure in carefully selected cases. The reputation of this operation in the future will depend upon the discrimination with which it is applied, the mastery of the technical requirements for success as judged by reasonable morbidity and mortality rates and by the ultimate demonstration that the procedure so applied will afford significant palliation, and in many instances will result in a permanent cure.

These data indicate the importance of differentiating peri-ampullary carcinomas according to the site of origin and with respect to the pathologic type of tumor. The prognosis in cases of primary carcinoma of the pancreas is poor, while the outlook for significant palliation and for cure is good in carcinoma arising in the distal common duct, the duodenum and the ampulla of Vater.

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