

Total Pancreatectomy for End-stage Chronic Pancreatitis

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The metabolic consequences and the clinical results of total pancreatectomy for end-stage chronic pancreatitis are detailed. This experience, accumulated between the years 1952 and 1976, adds 26 cases to the world's literature, which now contains 53 cases reported singly or in small series. The patients were selected on the basis of far-advanced, incapacitating disease in three patients and the failure of 62 previous related operations in 23 patients. Total pancreatectomy was performed with a zero hospital mortality but with serious inhospital morbidity. After discharge, 24 patients required 55 hospital readmissions and 18 related surgical operations; 12 patients have died, five of unrelated causes. Of 14 living patients, five consider themselves to be in good to excellent condition, six in fair condition, and three in poor condition. Twelve thought they were improved over their preoperative state. Our estimate of the result in living patients was similar. In those 12 who died, only four had satisfactory results. The results are also evaluated relative to level of activity, presence of abdominal pain, use of narcotics, weight, alcohol consumption, and the efficiency of endocrine and exocrine replacement. In general, the procedure is effective for relief or amelioration of pain, but the patients' personalities preclude complete adaptation to the apantcreatic state and rehabilitation. A failure to thrive is the common denominator.

TOTAL PANCREATECTOMY remains a formidable procedure both from a technical standpoint and from the point of view of management of the metabolic consequences. Most reported total pancreatectomies have been performed for malignant disease,^{2,3,6,15} which implies a limited follow-up. The world's literature now contains 53 instances of total pancreatectomy performed for pancreatitis reported singly or in small groups, and with a limited follow-up period.^{1,4,5,8,10,11,13-15,17-22} We report 26 patients with chronic pancreatitis treated by total pancreatectomy performed by members of our surgical department between the years 1952 and 1976. Survival, effectiveness of the procedure for relief of pain, results of replacement therapy for metabolic consequences, and quality of life will be assessed.

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Clinical Material

Of the 26 patients, 16 were men and ten were women; mean age was 47 years. Fifteen admitted to alcohol abuse, nine had a cholecystectomy for cholelithiasis in the treatment of pancreatitis, and five had neither alcohol abuse, biliary tract calculi, hyperlipidemia, hyperparathyroidism, trauma, infection, or related drug exposure.

Only three patients had not had a previous operative procedure for pancreatitis. The other 23 had had a total of 62 operations. Thirty-six of these procedures were extrapancreatic, mostly involving the biliary tract. Twenty patients had a previous partial pancreatectomy, and six had had pancreatic duct or pancreatic cyst drainage.

The severity of the disease is evident from these statistics and from the data derived from preoperative clinical characteristics. All patients had severe pain and were using narcotics regularly. Nine had experienced jaundice, 11 had loose, greasy, frothy movements suggestive of steatorrhea, 25 had marked weight loss (average, 37 pounds), and 12 were diabetic (two requiring insulin). The pathologic findings at total resection supported the impression of severe chronic disease in that ten had pancreatolithiasis and the others showed extensive fibrosis.

All living patients have recently been contacted by telephone (seven patients) or were seen in pancreatic clinic (six patients) with one exception. This patient was studied at intervals for six years until contact was lost. Thus, the follow-up in this group is from nine months to 12 years with a mean of 4.1 years. Of those patients who are dead, the follow-up information was obtained from multiple sources and is complete from 0.2 to 16.7 years (mean, 4.9 years).

TABLE 1. *Extent of Operation Up To and Including Time of Total Pancreatectomy (26 Patients)*

Procedure	Number of Patients
Gastrectomy	
0%	1
25%	7
50%	5
75%	13
100%	0
Cholecystectomy	
Yes	25
No	1
Vagotomy	
Yes	6
No	20
Splenectomy	
Yes	19
No	7

Results

The extent of associated procedures that were performed previous to or concomitant with total pancreatectomy is shown in Table 1. Thus, the majority of patients had a 50% or greater distal gastrectomy without truncal vagotomy but with a cholecystectomy and splenectomy. Reconstruction was by end-to-side choledochojejunostomy with a distal gastrojejunostomy.

No in-hospital postoperative deaths occurred nor did any patient die within 60 days of the operation. Postoperative in-hospital complications were recorded in 14 of 26 patients, however (Table 2). None of the complications were unique to total pancreatectomy, and only one patient required reoperation during that admission.

After hospital discharge, 24 patients had 33 complications that required 55 additional hospitalizations (Table 3); 18 additional related operative procedures were necessary (Table 4), with the majority of these within the

TABLE 2. *In-hospital Complications After Total Pancreatectomy (14 Patients)*

Complication	Number of Complications
Biliary fistula (one patient reoperated)	4
Heart failure, ischemia, or arrhythmia	3
Pneumonia	2
Pulmonary insufficiency	2
Intra-abdominal abscess	2
Urinary tract infection	2
Lower gastrointestinal bleed	1
Hypoglycemia and rib fracture	1
Skin wound infection	1
Ulnar neuropathy	1
Intraperitoneal hemorrhage	1
Septic phlebitis	1
Total	21

TABLE 3. *Reasons for Additional Hospitalizations (24 Patients)*

Reason for Admission	Number of Admissions
Control of diabetes	14
Upper gastrointestinal bleeding	6
Marginal ulcer	2
Esophagitis	1
Unknown	3
Abdominal pain	5
Myocardial infarction	4
Intra-abdominal sepsis	4
Malabsorption, cachexia	4
Viral pneumonia	3
Depression	3
Wound hernia, suture abscess	3
Penetrating marginal ulcer	2
Thrombophlebitis	2
Stricture of choledochojejunostomy	1
Constipation	1
Rectal bleeding	1
Small bowel obstruction	1
Bile gastritis	1
Total	55

first two years. This high rate of complications is further emphasized by the fact that 12 of the 26 patients have subsequently died (Table 5). Of the 12 deaths, four were due to related causes and two to possibly related causes.

Results of the living patients' assessment of their status are shown in Table 6. In general, our evaluations were similar to those of the patients. The six patients whose overall result was classified as fair had minimal or no pain but complained of weakness and anorexia. The three who had a poor result had appreciable pain along with weakness and anorexia. Ten of 14 patients noted a weight gain postoperatively, averaging 15 pounds (Table 7). One patient had no change in weight, two had a loss averaging eight pounds, and no information was available in one patient. Control of diabetes was fairly good in 12 of 14 living patients but poor in two. Twelve of the 14 living patients had satisfactory control of clinical steatorrhea.

TABLE 4. *Additional Operations After Total Pancreatectomy (15 Patients)*

Procedure	Number of Procedures
Drainage of intra-abdominal abscess	5
Operation for upper gastrointestinal bleeding	3
Herniorrhaphy	3
Operation for marginal ulcer	2
Removal of wire wound sutures	2
Revision of choledochojejunostomy	1
Lysis of adhesions	1
Implant of nerve stimulator	1
Total	18

TABLE 5. *Circumstances of Death After Total Pancreatectomy (12 Patients)*

Cause	Number of Cases
Myocardial infarction	4
Marginal ulcer	2
Hypoglycemia, acidosis, cerebral deterioration	2
Fever and seizures	1
Fever and seizures with multiple drug dependencies	1
After pulmonary lobectomy	1
Unknown: Found dead in bed	1
Total	12

Of the 12 patients who died, four had a good to excellent result overall. In six, the result must be classed as poor, and in two it was unknown. Five of those who died had a postoperative weight gain, and eight noted satisfactory control of diabetes (Table 7).

Discussion

As is evident from the number of previous operative procedures in these patients, we are reluctant to carry out total pancreatectomy for chronic pancreatitis. This reluctance is based on an opinion, previously unsupported by data, that the operative mortality would be prohibitive, that substitution therapy was not especially efficient, and that pain requiring narcotics would not be relieved. This report addresses these problems.

Our postoperative mortality for this series was most satisfactory, as is the recent experience of others when pancreatectomy was performed for malignancy.¹⁵ On the other hand, considerable morbidity was reported both in the hospital after the procedure and later because of the consequences of major abdominal surgical procedures on the stomach, pancreas, and biliary tract.

An additional price of total pancreatectomy is the steatorrhea and diabetes of the apancreatic state. All of these patients were subject to insulin reactions, as are essentially all patients with diabetes mellitus who use insulin. However, two patients who died had a deteriorated mental state, probably due in part to chronic hypoglycemia. Two others died with seizures and fever of unknown cause. All four of these patients died at a distance from our institution, and we had difficulty obtaining pertinent details of their demise.

The control of clinical steatorrhea is somewhat easier to achieve since appropriate doses of pancreatic replacement can ensure adequate absorption of fat in most patients. In two of the 14 living patients, difficulty was encountered controlling steatorrhea despite an increased dose of enzyme.

Postoperative nutrition, as measured by weight change, can be an indication of absorption and the efficiency of

TABLE 6. *Results in 14 Living Patients (Patients' Assessment)*

General health	
Good to excellent	5
Fair	6
Poor	3
Comparison to preoperative condition	
Better	12
Worse	2
Level of activity	
Very active	4
Moderately active	7
Little activity	3

Specific Information Questions

	Yes	No
Abdominal pain	6	8
Narcotics	3	11
Alcohol consumption	2	12
Employed	3	11

replacement of pancreatic enzyme. Ten of 26 patients failed to gain or lost weight after total pancreatectomy. This record is in a group of patients who had already lost a mean of 37 pounds before operation. However, it is particularly difficult to ascribe any feature of the overall nutritional result to gastrectomy, pancreatectomy, enzyme replacement, or level of caloric intake. It must be remembered that most of these patients are not particularly disciplined or motivated.

To be balanced against the deficiency state and the morbidity of these patients is the result in terms of relief of pain. All patients, including those deceased, reported relief of the severe epigastric pain that brought them to operation, although two of 14 living patients still consumed alcohol and three used narcotics (one demerol, one hydromorphone—Dilaudid®, and one codeine). Of 12 deceased, one was still addicted to demerol at death.

The results of further assessment of the living and dead patients show an improvement over the preoperative state in general but a failure to normalize their life in the majority; thus, the common denominator is a failure to thrive.

Evaluation of the result after surgical therapy of chronic pancreatitis is seriously handicapped by the

TABLE 7. *Metabolic Consequences of Total Pancreatectomy for Pancreatitis*

Metabolic Feature	Living, 14 Patients	Dead, 12 Patients
Postoperative weight gain	10 (average, 15 lbs)	5 (average, 11 lbs)
Satisfactory control of diabetes	12	8
Satisfactory control of clinical steatorrhea	12	—

multiplicity of factors that bear on this result. We have tried to simplify this evaluation with the use of a therapeutic index that assigns arbitrary values to various complications and the presence or absence of pain. In practice, this system did not improve the more usual evaluation employed herein.

Our indications for total pancreatectomy are mainly a failure to control pain with ampullary procedures in patients with ampullary disease, with lateral pancreaticojejunostomy in patients with dilated pancreatic ducts, and with partial or subtotal resection in patients with small duct disease. We are reluctant to perform total pancreatectomy in one stage. Those patients who stop the use of alcohol, who have reasonably stable personalities, and who show some semblance of self-discipline are the preferred candidates for the procedure. They should also have ready access to knowledgeable medical and surgical management for the rest of their life.

The procedure should include an adequate gastric resection with truncal vagotomy to avoid jejunal ulcers and other causes of upper gastrointestinal hemorrhage. In this series, three of the five patients who had antrectomy without vagotomy in earlier years required additional gastric procedures for bleeding, pain, or perforation from marginal ulceration.

The management of the apancreatic state requires careful attention after operation and for the life of the patient. Twenty to 40 units of insulin are usually required, adjusted to the calories required to support the patient's usual activity. Blood sugar levels ranging between 150 and 250 mg/100 ml are satisfactory. The greatest hazard in the management of apancreatic diabetes is insulin shock. Patients should not be discharged from the hospital until the caloric intake and the insulin dose are stabilized, and the patient thoroughly understands the fine points of control. During the last days of the hospital stay, patients should be encouraged to be physically active. Frequent outpatient visits are essential for the first few months.

The dose of pancreatic enzyme⁹ is adjusted by the characteristics of the stool studies in the short term and the weight curve in the long view. Usually four tablets of pancreatin (Viokase®) or pancreatic lipase (Cotazyme®) are given with each meal and three tablets with snacks. The use of an antacid or cimetidine (Tagamet®) may increase the proportion of enzyme that reaches the duodenum and jejunum in patients in whom control is difficult.¹⁶ Decreasing the amount of fat in the diet may also have a salutary effect on steatorrhea in problem cases.

It is interesting to compare the results of this operative procedure to those of 80 to 95% pancreatectomy as reported by Frey et al.⁷ In their follow-up study of

77 patients having a major resection, 22 were in pain but alive, converted to total pancreatectomy, institutionalized, lost to follow-up when in pain, or dead with the cause related to pancreatitis. In addition, 56 of the 77 were diabetic (45 were taking insulin) and 29 had clinically troublesome steatorrhea. Preservation of 5–20% of the gland does not, in the majority of cases, prevent the deficiencies of total pancreatectomy. Furthermore, the postoperative morbidity after the lesser procedures of 40 to 95% pancreatectomy⁷ is likewise appreciable.

A significant source of postoperative problems is the diabetes, which can be most difficult to control in this clinical setting. The reimplantation of the patients' own islet cells¹² is an intriguing prospect since no immunosuppression would be necessary. Advances in this direction await refinements in the harvesting or culture of human islet tissue. If this technique becomes clinically useful, subtotal or total pancreatectomy in one stage would be the preferred approach.

Interest in total pancreatectomy for adenocarcinoma of the pancreas^{2,3,6,15} has been intensified mainly in an effort to improve the dismal long-term survival rate. Whether possible intrapancreatic spread of tumor cells or multicentricity of tumor genesis is a factor in this poor survival is not known. Also unknown are the long-term results of total pancreatectomy in this setting. The limited survival of patients with carcinoma of the pancreas precludes the gathering of information on this point. For these reasons, we cannot predict whether total pancreatectomy for carcinoma will achieve the desired result, and more follow-up time is necessary. We have not embraced the concept of total pancreatectomy for malignancy as strongly as some but believe that total pancreatectomy is useful in patients in whom anastomosis of the pancreas remaining after the Whipple procedure is hazardous because of the small size of the pancreatic duct and softness of pancreatic tissue. Proof of extension of the neoplastic process into the body of the gland, of course, is an additional impetus to total resection.

References

1. Blackburn, G. L., Williams, L. F., Bistran, B., et al.: New Approaches to the Management of Severe Acute Pancreatitis. *Am. J. Surg.*, 131:114, 1976.
2. Brooks, J. R. and Culebras, J. M.: Cancer of the Pancreas. Palliative Operation, Whipple Procedure, or Total Pancreatectomy? *Am. J. Surg.*, 131:516, 1976.
3. Castellanos, J., Manifacio, G., Lillehei, R. C. and Shatney, C. H.: Total Pancreatectomy for Ductal Carcinoma of the Head of the Pancreas: Current Status. *Am. J. Surg.*, 131:595, 1976.
4. Clagett, O. T.: Total Pancreatectomy for Chronic Pancreatitis with Calcification. *Proc. Staff Meet. Mayo Clin.*, 21:32, 1946.
5. Curchod, B. and Ryncki, P. V.: Contrôle de 3 Cas de Pan-

- créatectomie Totale pour Pancréatite Chronique Diffuse Après 3 Ans. *Schweiz Med. Wochenschr.*, 100:1205, 1970.
6. Fortner, J. G., Kim, D. K., Cubilla, A., et al.: Regional Pancreatectomy: En Bloc Pancreatic, Portal Vein and Lymph Node Resection. *Ann. Surg.*, 186:42, 1977.
 7. Frey, C. F., Child, C. G. and Fry, W.: Pancreatectomy for Chronic Pancreatitis. *Ann. Surg.*, 184:403, 1976.
 8. Gourevitch, A. and Whitfield, A. G.: Total Pancreatectomy. *Br. J. Surg.*, 40:104, 1952.
 9. Graham, D. Y.: Enzyme Replacement Therapy of Exocrine Pancreatic Insufficiency in Man. Relation Between In Vitro Enzyme Activities and In Vivo Potency in Commercial Pancreatic Extracts. *N. Engl. J. Med.*, 296:1314, 1977.
 10. Jordan, P. H., Jr. and Grossman, M. I.: Pancreaticoduodenectomy for Chronic Relapsing Pancreatitis; Metabolic Defects Created by Total and Subtotal Ablations. *Arch. Surg.*, 74:871, 1957.
 11. Mangold, G., Neher, M., Oswald, B., et al.: Ergebnisse der Resektionsbehandlung der Chronischen Pankreatitis. *Dtsch. Med. Wochenschr.*, 102:229, 1977.
 12. Matas, A. J., Sutherland, D. E., Steffes, M. W. and Najarian, J. S.: Islet Transplantation. *Surg. Gynecol. Obstet.*, 145:757, 1977.
 13. Miyamori, A., Takebe, T. and Yamagata, S.: Clinical Evaluation of Iron Metabolism in Pancreatic Disease. *Contemp. Top. Immunobiol.* 5:159, 1976.
 14. Miyata, M., Yamamoyo, T., Yamaguchi, M., et al.: Plasma Glucagon After Total Resection of the Pancreas in Man. *Proc. Soc. Exp. Biol. Med.*, 152:540, 1976.
 15. Pliam, M. B. and ReMine, W. H.: Further Evaluation of Total Pancreatectomy. *Arch. Surg.*, 110:506, 1975.
 16. Regan, P. T., Malagelada, J. R., DiMugno, E. P., et al.: Comparative Effects of Antacids, Cimetidine and Enteric Coating of the Therapeutic Response to Oral Enzymes in Severe Pancreatic Insufficiency. *N. Engl. J. Med.*, 297:854, 1977.
 17. Sato, T., Saitoh, Y., Noto, N., et al.: Appraisal of Operative Treatment for Chronic Pancreatitis. With Special Reference to Side to Side Pancreaticojejunostomy. *Am. J. Surg.*, 129:621, 1975.
 18. Warren, K. W., Poulantzas, J. K. and Kune, G. A.: Life After Total Pancreatectomy for Chronic Pancreatitis: Clinical Study of Eight Cases. *Ann. Surg.*, 164:830, 1966.
 19. Waugh, J. M.: Radical Resection of Head of Pancreas and Total Pancreatectomy. *JAMA*, 137:141, 1948.
 20. Whipple, A. O.: Radical Surgery for Certain Cases of Pancreatic Fibrosis Associated with Calcareous Deposits. *Ann. Surg.*, 124:991, 1946.
 21. Yung-K'Ang, F., Shu-Fang, W., Shih-Chih, Y., et al.: Metabolic Observations Following Total Pancreatectomy. *Chin. Med. J.*, 85:236, 1966.
 22. Zininger, M. M.: Personal Communication to Whipple, A. O. (Ref. 20).

DISCUSSION

DR. WILLIAM P. LONGMIRE, JR. (Los Angeles, California): The experiences reported by Dr. Braasch and his colleagues with their large series of total pancreatectomies add highly important information to the field of pancreatic surgery for chronic pancreatitis. From their experience, it seems that patients must be carefully selected for any type of extensive pancreatic excision, and as they have indicated, the side effects of the operation may be particularly difficult for such a patient to cope with. Moreover, although the pain may be eliminated or significantly reduced, the overall results of the operation may be disappointing.

(Slide) In the past 22 years there have been 217 patients seen at the UCLA Hospital with a diagnosis of chronic pancreatitis, 78 of whom have undergone operation. The majority had a history of alcoholism, although most had stopped drinking for some time prior to the operation. Indeed, we have been particularly insistent on this point before proceeding with any major extirpative surgery.

(Slide) Some type of resection has been performed in 30 of these patients. Twenty were treated by distal pancreatic resection (as indicated in this slide, eight of them with less than an 80% resection), and 12 with greater than 80% distal resection; 10 have undergone a proximal or a total pancreatic resection.

(Slide) Although in the past the majority of our patients have been treated by a lateral pancreaticojejunostomy, or by less than an 80% distal resection, at present it is our impression that once the process has reached the extensive chronic phase that concerns us in this discussion, it is the diseased head of the pancreas that is responsible for maintaining the smoldering inflammation in the gland. Generally, the region of the head in such cases might even be considered the pacemaker of the disease.

On this basis, treatment of our recent patients has usually involved a proximal resection. Two technical steps in this procedure should be emphasized:

(Slide) First, when performing a pancreaticoduodenectomy for benign disease, it is unnecessary to remove an extensive portion of the duodenum, and therefore the pylorus may be preserved, so that the side effects of subtotal gastrectomy are not added to those of pancreatic resection. Dr. Braasch has indicated that the majority of his patients had 50% or more of the stomach resected.

(Slide) Second, whenever possible, the distal portion of the pan-

creas (10–20% of the tail of the pancreas) is preserved. Inasmuch of this portion of the pancreas contains the highest concentration of islet cells, diabetes may not be aggravated or created by an extensive resection of this type.

I also wish to add that in one of our recent cases of total pancreatectomy, the gland was prepared by Dr. L. William Traverso by a technique which he has developed in which the islets are reimplanted through the portal vein. Unfortunately, owing to the extensive scarring and calcification present in this gland, it was difficult to make the proper preparation. In studies performed about a week ago, we could detect no evidence of islet cell activity. Dr. Traverso has experimented on animals that have survived subsequent to this transplantation for as long as two years, and therefore I think that this technique offers possibilities for further treatment in the future.

DR. WILLIAM H. REMINE (Rochester, Minnesota): I have been very interested in total pancreatectomy for some time, but not necessarily for pancreatitis. In our first report of the overall study of total pancreatectomy reported 36 cases. Three of those pancreatectomies were for pancreatitis; two of the patients died of the complications of alcoholism.

In our next report, which brought our total up to 68, there were five patients with pancreatitis who were operated on with total pancreatectomy. Unfortunately, of these five patients who had the entire pancreas removed, the longest survival was eight years, during which time the patient underwent bilateral truncal vagotomy for stomal ulcer and then subsequently died with a massive gastrointestinal hemorrhage which was thought to be from esophageal varices. Two patients died 16 months and four months, after operation, presumably with diffuse cerebral damage. Both patients had courses complicated by persistent alcoholism, drug abuse and psychosis. Two others remain alive at seven and ten years.

It's our policy now not to try to do total pancreatectomy on these patients if we can possibly avoid it. First of all, we're operating entirely for pain. They already have diabetes and they have pancreatic insufficiency, at least by our criteria.

We now try to go to splanchnic block because these people are going to continue drinking. If they are not alcoholics, then it might be safe to try total pancreatectomy.

These patients are not very satisfactory candidates for total pan-