Surgical Treatment of Chronic Pancreatitis

Twenty-two Years' Experience

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Seventy-four patients underwent operation for chronic pancreatitis during a 22 year period at UCLA Hospital. Follow-up data obtained for 60% of these patients an average of 3.2 years postoperation were analyzed by computer for statistically significant benefit between paired operation combinations and the variables of pain relief, stool habits, alcohol use, readmission for pancreatitis, and narcotic use. The combined group of total and cephalic pancreaticoduodenectomy proved more effective with respect to pain relief and readmission ($p < 0.05$) than the group that had pseudocyst drainage. The comparison of groups that underwent resection or ductal drainage showed no statistical differences for the above variables. Regardless of type of operation, if the patient had evidence of pancreatic calcifications and had abstained from alcohol postoperatively, the likelihood of a return to normal activity was more favorable ($p < 0.05$).

THE NATURAL HISTORY of chronic pancreatitis includes a broad spectrum of variables, making treatment decisions difficult. As Spiro states, "We know its associations, we can chart its course, but we know little more."[11] The difficulty is further compounded by the paucity of reports concerning various drainage and resection techniques from relatively few medical centers. While abdominal pain is the typical chief complaint and surgical treatment achieves some benefit in the majority of cases, the kind of operation that provides symptomatic relief for each type and stage of chronic pancreatitis is unclear. With or without treatment, all patients who have smoldering chronic pancreatitis ultimately suffer from progressive exocrine insufficiency and diabetes. During the past 22 years we have developed a plan of surgical treatment aimed at relieving abdominal pain based on the degree of parenchymal inflammation, fibrosis and calcification, as well as the condition of the major ductal system. Although previous reports on the treatment of chronic pancreatitis have yielded considerable data, an in-depth computer analysis of our surgically treated cases might provide further insight into the management of this puzzling disease.

Patients and Methods

Between 1955 and 1977, 419 patients were admitted to UCLA Hospital with a diagnosis of pancreatitis. After reviewing their charts, 279 patients who were identified as having a definite diagnosis of pancreatitis were divided into two groups: acute (22%) and chronic (78%), in accordance with the Marseilles Classification.[7] The etiology, frequency, average age, and male: female ratio for the total group and subgroups are listed in Table 1. The high percentage of chronic patients may reflect the referral pattern of admissions to our hospital. In the operated cases there was a positive correlation with alcohol use (65%) and a negligible incidence of associated biliary tract disease (8%). Although miscellaneous causes of the disease (28% in our series) were usually unknown, they were probably associated with unverified alcoholic intake, rather than stemming from nonpenetrating pancreatic trauma, hyperparathyroidism, hyperlipidemia, or familial pancreatitis. During their hospitalization, 27% of the total group underwent operations for pancreatitis and were diagnosed as having long-standing pancreatitis verified at laparotomy. The specific procedures utilized are listed in Table 2.

The predominant indication for operation was abdominal pain (continuous in half of our patients), followed by the necessity for pseudocyst drainage in 26%, although most of the latter also complained of abdominal pain. Charts of the patients who underwent operation were reviewed in detail for 261 variables in their past medical history, physical examination,

TABLE 1. *Pancreatitis Characteristics*

	Number of Patients			
	279	62	217	74
	Per Cent Total	Per Cent Acute	Per Cent Chronic	Per Cent O.R.
Alcohol	64	34	73	65
Biliary	8	19	5	8
Other	28	47	22	27
Avg. age in yrs.	45	38	47	45
Male:Female	1:1	1:2	1:1	1:1

TABLE 2. *The Pancreatic Operations Performed on 74 Patients*

Pseudocyst drainage		19 (26%)
Drainage		24 (32%)
Lateral	(9)	
Distal	(3)	
Sphincteroplasty alone	(12)	
Biliary bypass		3 (4%)
Resection		28 (38%)
Whipple	(5)	
Total	(8)	
Distal (40–80%)	(7)	
(95%)	(8)	

laboratory studies, and operations performed. Followup information was obtained by using a ten-part questionnaire to indicate postoperative time, abdominal pain, pain medications, alcohol use, appetite, weight, strength, bowel habits, insulin or pancreatic enzymes, and activity or work status. There were 52 variables among the ten categories. A total of 18,792 variables were computer analyzed for frequency. All paired-operation combinations were compared by Chi-square analysis by using the frequency of each variable as listed in Table 3. In addition, all postoperative patients were divided into groups according to the presence of radiographic calcifications or continued use of any amount of alcohol. These groups were then compared to the variables shown in Table 3 via Chi-square analysis.

Preoperative Evaluation

The etiology, average age, and male:female ratio of the *operated subgroup* are listed in Table 1. In only 8% was the source considered to be cholelithiasis. Alcohol had been used excessively in the past by 65%, the usual intake being more than four drinks of liquor every day. Although most patients in our series had stopped drinking when first seen, they claimed to have taken their last drink an average of 3.6 years (range 0.18 to 19 years) prior to UCLA Hospital admission. Previous reports in this country and in France also reflect a high incidence of alcohol use—58%,[16] 61%,[3] 62.7%,[17] and 78.5%.[2] In Japan, however, the incidence of alcoholism is lower (30%) and cholelithiasis is likewise infrequent (11%).[10] The 1:1 male:female ratio in our series was similar to the findings of Way et al.,[16] possibly reflecting the social use of alcohol in the United States rather than in France[3] or in Japan,[10] where the ratio is 2:1.

The chief complaint of 94% was pain that began an average 5.6 years prior to admission (range, one month to 35 years). Located in the epigastrium (78%) or back (65%), the pain was described as continuous (chronic pancreatitis) in half of the cases, and intermittent (chronic relapsing pancreatitis) in the other 50%. By the time of admission the average frequency of acute pan-

creatic episodes was every 5.3 months, associated with a high serum amylase in 78% and with alcohol usage in 57% of cases. These exacerbated episodes of pancreatitis had required an average of three hospitalizations before admission to UCLA Hospital. A majority of patients (63%) were taking pain medication at admission; 25% were using codeine or Talwin®, and another 25% were getting Demerol® or morphine by injection or by mouth.

The majority (79%) denied steatorrhea, and only 15% were taking pancreatic enzyme supplements at the time of admission. One-fourth were diabetic, 11% were receiving insulin. The average weight loss since the beginning of illness was 19% of total body weight. Previous pancreatic surgery had been performed on 17%, half of which were pseudocyst drainage procedures. Other major operations, primarily cholecystectomy, had been performed on 49%.

The physical examination was unremarkable except that 48% of patients were thin or cachectic, and 66% evidenced palpable abdominal tenderness or an abdominal mass. Abdominal rigidity or rebound was rarely evident. Admission laboratory studies showed a normal hematocrit, white blood cell count, and platelet count in most patients; 42% had a prolonged prothrombin time associated with a normal partial thromboplastin time. Urine amylase was elevated in 22%, while serum amylase exceeded 200 Somogyi units per deciliter in 37% of patients. Except for serum amylase, the most frequently elevated blood chemistry values were alkaline phosphatase (39%) and fasting blood

TABLE 3. *Outline of Statistical Analysis*

Operation	Variables
Pseudocyst drainage	Narcotics
Ductal drainage—all	Loose stools
lateral drainage	Activity
Resections—all	Pain ↓
Whipple and totals	Readmits
Whipple only	
Totals only	
Distal resections	

TABLE 4. *Follow-up Results (44 Patients)*

Time postop	3.2 yr (.08–12)
Pain decreased or absent	76%
Narcotics	43
Alcohol	36
Insulin (avg. 32 nph units)	30
Pancreatic enzymes	52
Normal activity	80
Gained weight	70

sugar (22%). Preoperative x-ray studies showed pancreatic calcifications in 39% of patients, but in the 41 upper GI series obtained, the typical finding was anterior displacement of the stomach. An ultrasound was performed in 35% of cases; half of these revealed pseudocysts, 88% of which were single, and 75% located in the pancreatic head or neck. The pancreas was enlarged in 52% of cases. ERCP performed in 19% of patients achieved a 64% cannulation rate, and of these, 90% were abnormal. Intraoperative cholangiograms were performed in 29 patients, with 45% showing intrapancreatic bile duct stenosis (18% of the entire surgical group).

Operative Results

Types of operations were equally divided among three categories (Table 2): pseudocyst drainage, ductal drainage, and parenchymal resection. Three patients underwent a choledochojejunostomy only. There were no intraoperative deaths. The 30 day postoperative death rate was 7%, owing to an uncontrolled bleeding ulcer and hepatic failure in one patient each, and myocardial infarction or arrhythmia in three patients undergoing the following operations: pancreaticojejunostomy, cystduodenostomy, total pancreatectomy, 40% distal resection, and 95% distal resection. Major postoperative complications occurred in 11% of cases of which pneumonia occurred in 3%, pulmonary embolus in 1%, myocardial infarction in 3%, and wound infection in 4%.

By the time of discharge no patient was taking Demerol or morphine, 31% were receiving insulin, and 81% claimed that their pain had decreased or totally disappeared. Follow-up data obtained from 44 patients an average of three years postoperatively are listed in Table 4. Chi-square analysis of these data indicated no statistically significant difference among the three basic operations or subgroups as listed in Table 3. The subgroup that underwent combined Whipple and total pancreaticoduodenectomy, however, proved to be statistically superior to the group that had pseudocyst drainage in two respects: decreased or absent abdominal pain (p = 0.05) and fewer readmissions for recurrent pancreatitis (p = 0.03). In comparing the

results of these various procedures, it must be remembered that specific operations were selected for specific pathological conditions of the pancreas and the three operative procedures are not necessarily interchangeable nor comparable. For example, a pancreatic resection may have been selected as the treatment of choice for an individual who did not have a pseudocyst suitable for drainage nor a duct sufficiently dilated to be utilized for duct enteric drainage. In general, excisional therapy was utilized for cases with the most severe and extensive pathological changes. Regardless of operation type there was a favorable result and a return to normal activity if the patient had pancreatic calcifications or did not resume use of any quantity of alcohol (Table 5). The other variables in Table 3 were not significantly related to calcifications or alcohol.

Discussion

Preoperative data were remarkably similar to findings in other reports (Table 6), re-emphasizing the fact that we know the associations of chronic pancreatitis and can chart its course.

Our typical patient was severely incapacitated by persistent or recurrent abdominal pain for which pain medication was regularly utilized. Multiple previous hospital admissions had been required during exacerbation of symptoms approximately every five months. Half of our patients were taking narcotics when first seen. Most had stopped drinking prior to admission (average of three and a half years), but had substituted narcotics for liquor. The alcohol history among the majority included at least three hard liquor drinks per day. A small percentage presented with signs and symptoms suggestive of pancreatic endocrine (25%) or exocrine (21%) insufficiency. Loss of appetite combined with some degree of malabsorption may have played a role in the 42% incidence of a prolonged prothrombin time. However, a liver etiology might also be implicated despite the low reported correlation of cirrhosis and chronic pancreatitis. The 39% incidence of elevated serum alkaline phosphatase levels may be an indication of intrapancreatic biliary stenosis; in our series, progressive pancreatic fibrosis in chronic pancreatitis accounted for an 18% cholangiographic incidence of biliary stenosis and in another series documented by ERCP, the figure was 14%.[4]

TABLE 5. *Per Cent Regaining Normal Activity*

Normal Activity	Yes	No	p
Calcifications	73%	27%	0.047
No alcohol	82%	18%	0.041

TABLE 6. *Surgical Treatment of Chronic Pancreatitis —22 Years' Experience Comparison between Series*

Report	No. of Cases	M	F	Mean Age	Calcific	Alcoholism	Cysts	Diabetes	Steatorrhea
Way et al.[16]	57	30	27	42	42.1% (24)	57.9% (33)	28.1% (16)	33.3% (19)	24.6% (14)
Leger et al.[3]	148	135	13	39.8	69.6% (103)	61.5% (91)	19.6% (29)	12.8% (19)	31.8% (47)
Frey et al.[2]	149	101	48	40	48.3% (72)	78.5% (117)	42.3% (63)	26.2% (39)	6.7% (10)
Sato et al.[10]	71	48	23	45.5	56.3% (40)	29.6% (21)	22.5% (16)	29.6% (21)	9.9% (7)
White et al.[17]	142	83	59	43.7	34.5% (49)	62.7% (89)	28.9% (41)	19.0% (27)	16.9% (24)
UCLA Series	74	39	35	44.4	39.2% (29)	64.9% (48)	32.4% (24)	24.3% (18)	27.0% (20)
Total	641	436 (68.0%)	205 (32.0%)	42.1	49.5% (317)	62.2% (399)	29.5% (189)	22.3% (143)	19.0% (122)

Recent studies[5,8,9] propose that persistent alcoholic intake of an unspecified amount over a period of months or years produces a hypersecretory state of pancreatic parenchymal cells with a spotty distribution of intralobular periductal fibrosis and obliteration. Acinar cell hypersecretion of protein is suggested as the initial pathological effect of chronic alcoholic intoxication followed by precipitation of protein plugs in the finer ducts which block the ducts, undergo calcification, and by irritation produce the ductal and lobular lesions of chronic pancreatitis. The involved ducts are irregularly dilated, the epithelium is lost, the periductal connective tissue encroaches on the lumen of the duct to form areas of stenosis, pancreatic cysts, or cause complete disappearance of acini and ducts in the territory drained by a blocked duct. As the disease progresses, these *scattered* areas coalesce to replace pancreatic parenchyma with areas of *sclerotic fibrosis*.

Some speculation is required, however, to progress from this well-conceived and specifically documented explanation of the pathological changes occurring in the smaller ducts to the alternating areas of constriction, dilatation and calculi formation frequently found in the duct of Wirsung in patients suffering from chronic pancreatitis. This theory suggests that small duct fibrosis and reaction may be sufficiently intense at some site adjacent to the main duct to provoke stenosis followed by stasis and precipitation of the protein plugs in the duct of Wirsung which subsequently form calculi, thereby promoting the same reaction around the major duct that has been observed in the lesser secondary ducts.

We have attempted to analyze our results of various types of treatment applied to different pathological changes that may accompany chronic pancreatic dis-

ease. Inasmuch as the earliest obstruction usually occurs in the pancreatic head and neck, pancreatic pseudocysts of a few millimeters to 5 cm may frequently develop in this area. In our cases, 75% of pseudocysts located by ultrasound were located in the head or neck of the gland. It is not clear, however, why a few patients with extensive chronic calcifying pancreatitis do not complain of pain. Perhaps pain is produced by obstruction of normal adjacent lobular ducts followed by inflammation and not merely from the presence of fibrosis, duct dilatation and calcification. If one accepts the proposal that the disease process starts in the small ducts and secondarily affects the major duct, it is difficult to explain why extensive drainage of the duct of Wirsung alone provides pain relief. It would appear that the process could only be relieved by excision of that portion of the gland containing the small duct changes. On the other hand, it could be postulated that the frequently occurring small duct disease in the head and neck of the gland produces a secondary stenosis in the proximal portion of the main duct which is then followed by calculus formation and obstruction of the main ductal system in the body and tail. Extensive drainage of this obstructed major duct system could be expected to provide symptomatic relief under these conditions. Our experience leads us to believe that lateral pancreaticojejunostomy is most successful when the duct is incised well down into the head of the gland and out onto the uncinate process. The sphincter of Oddi is then divided through an open duodenostomy, calculi are removed and stenotic areas dilated until there is extensive open drainage laterally into the jejunum and proximally into the duodenum. If adequate drainage cannot be obtained because the ductal system is obliterated by scar or numerous cal-

culi, or if there are persistent subacute inflammatory reactions and multiple pseudocysts in the parenchyma of the gland, a resection is necessary. Indeed, if such changes are present throughout the gland, a total pancreatectomy is required to obtain optimal pain relief. Side-to-side pancreaticojejunostomy has relieved pain more successfully if radiographic pancreatic calcifications are present.[6] The reason is unclear and may possibly be related to the likelihood of a dilated duct when calcifications are present. Our results suggest that all patients, regardless of the type of operation they have, will respond favorably to a pancreatic operation if calcifications are present.

Selection of a particular operation for a specific case was based on the following general principles: large solitary pseudocysts, if attached to the posterior stomach wall, were drained by cystogastrostomy; otherwise, a Roux-en-Y type cystjejunostomy was utilized. Single or multiple small cysts with marked surrounding parenchymal inflammation, a condition typically seen in the head of the gland, were treated by partial pancreatectomy, usually pancreaticoduodenectomy. Pseudocysts that recurred following drainage were treated by partial pancreatectomy.

A sphincteroplasty alone was performed in unusual cases where there was evidence of isolated obstruction at the sphincter of Oddi with uniform diffuse distal duct dilatation, or while searching for the pancreatic duct for a pancreatogram.

The commonly encountered diffusely dilated pancreatic duct with alternating areas of constriction and dilatation (chain of lakes variety) was drained by a lateral pancreaticojejunostomy. We are repeatedly impressed by the observation that persistent inflammation, calcification and duct obstruction in the head of the pancreas serves to initiate and perpetuate inflammatory changes in the more distal portions of the gland, and that symptomatic relief depends on obtaining adequate duct drainage of the head and uncinate portions of the pancreas by widely opening the proximal portion of the duct of Wirsung and the duct to the uncinate process and removing all obstructing calculi or by excision of the involved pancreas by pancreaticoduodenectomy. As a more conservative procedure, this operation was first used even in cases where pancreatic excision might eventually be necessary. Marked parenchymal inflammation with or without small pseudocysts and with extended duct obstruction owing to fibrotic obliteration or impacted calculi was treated by resection of the involved area.

Utilizing these principles and selecting the operative procedure best adapted to the pathological changes in each case as outlined above, lateral pancreaticojejunostomy ductal drainage in our patients provided pain relief as effective as that of the proximal or complete pancreaticoduodenectomy by statistical comparison. Excluding the one death that occurred among the 13 proximal or total pancreatic resections and the one death among the nine extensive side-to-side pancreaticojejunostomies, all of these procedures achieved complete or substantial pain relief. The poor results in the pseudocyst drainage group stem from the fact that only localized drainage of an extensive spotty process was obtained and the progressive natural history of the disease was unchanged. Moreover, the fact that half of the patients had undergone prior pseudocyst drainage procedures before admission to UCLA underscores the temporary relief so frequently accompanying internal pseudocyst drainage in chronic calcific pancreatitis. Frey reports a 31% incidence of reoperation after internal pseudocyst drainage, with a 37.5% reoperation rate for cystgastrostomy.[1] Unless the disease process is confined to the distal portion of the pancreas, a 40–80% distal resection is unlikely to achieve pain relief. An extended resection of 80–95% of the distal gland will remove more of that portion of the pancreas in which the chronic inflammatory changes usually reside and, therefore, the more extensive resections have obtained greater pain relief.[17] However, persistent smoldering pancreatitis and abdominal pain, pancreatic fistulas or bile leak, and subsequent diabetes in 72%[2] have led us away from the 95% distal resection. Instead, we prefer an extended *proximal* 95% resection, leaving the area of the gland with the lowest frequency of pancreatitis and the highest concentration of pancreatic islets. Our experience with pancreaticoduodenectomy or total pancreatectomy has demonstrated complete pain relief in 64% and some relief in the remaining patients, although minimal experience has been reported by others with these extensive resection procedures and do not reflect our favorable results. White et al. report three such patients, all with recurrent symptoms,[17] and Frey et al. reported 19 patients with a 58% incidence of some degree of pain relief commensurate with the 56% rate of pain relief following 80–95% distal pancreatectomy.[2] Many of their patients treated by a Whipple procedure had been lost to followup or had died; possibly the pain relief outcome may have improved in those cases. Leger et al. reported a 50% mortality among 16 patients six years after pancreaticoduodenectomy. Of the remaining survivors, 75% experienced good results.[3]

The assumption has always been that if the patient resumes the use of alcohol, any beneficial effect of an

operative procedure will be compromised, and our data statistically confirm this assumption. Indeed, persistent alcohol consumption subsequent to pancreatectomy has proved to be the only significant prognostic factor associated with a limited period of survival.[3] For this reason, the psychosocial adjustment of all patients must be carefully considered before any operation is performed. Extensive resectional procedures should not be contemplated when the patient does not have the intelligence or motivation to cooperate with appropriate dietary and medical management during the remainder of his life. The possibilities of social and employment rehabilitation must also be carefully evaluated as factors affecting the eventual outcome of treatment.

Encouraged by the results of complete or proximal pancreaticoduodenectomy for pain relief, a pylorus preservation modification of the Whipple operation has been performed[13] whereby the side effects of an extensive gastric resection, a vagotomy or an antrectomy are eliminated. Neither postgastrectomy syndromes nor marginal ulcers have been encountered among the 14 patients who underwent this procedure, although all of the patients, even those with a pancreatic remnant, evidence marked exocrine insufficiency.[14] The disturbed digestive function occasioned by a proximal pancreatic resection seems to be lessened by preserving the pylorus, but intensive oral enzyme replacement must be started. The 50% six year mortality rate subsequent to pancreaticoduodenectomy reported by Leger et al.[3] was considered secondary to metabolic disturbances. Steatorrhea and malnutrition constituted the cause in one fourth of these deaths. Frey et al.[2] noted that clinically troublesome steatorrhea was more likely to occur after pancreaticoduodenectomy (55%) than after other types of resections. We have been encouraged by the effectiveness of Pancrease®* in relieving refractory steatorrhea in our patients. These capsules of enteric coated microspheres have been shown to be superior to other commercial oral pancreatic enzymes using weight gain and fat utilization in a controlled study.[15]

Retaining a portion of the pancreatic tail at surgery is of course the best protection against the development of diabetes,[2] but when the entire gland must be removed, we inject a suspension containing the patient's own mixed pancreatic cells into the portal vein in an effort to prevent diabetes. This technique involves collagenase digestion and has proven 100% successful in our most recent canine model following total pan-

createctomy.[12] Since our first attempt on November 15, 1977, four patients have had transplantation, two of whom had partial success. The inability of the portal system to accept the entire graft suspension owing to a reactive portal hypertension has been a problem. Retrospectively, two of our patients evidenced compromised islet function (decreased insulin response during a preoperative glucose tolerance test) prior to operation as a result of their long-standing pancreatitis. It is hoped that further development of islet cell transplantation techniques will improve the reliability of islet cell reimplantation and minimize the undesirable sequelae of extensive pancreatic resection when required.

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* Johnson & Johnson Company. Piscataway, NJ.