Postobstructive Chronic Pancreatitis

Results With Distal Resection

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Hypothesis: For most patients with chronic obstructive pancreatitis, distal pancreatectomy confers pain relief.

Design: Retrospective case series. Follow-up was complete in 80% of study subjects (mean follow-up, 6.7 years).

Setting: Tertiary care center.

Patients: Among 484 patients with chronic pancreatitis undergoing operation from 1976 to 1997, 40 with postobstructive chronic pancreatitis were identified. Criteria for selection included an isolated, dominant major pancreatic duct stricture or cutoff, changes of chronic pancreatitis in the distal pancreas, and ostensibly normal parenchyma without calcification in the proximal gland. The patients were reviewed with regard to operative procedure, postoperative course, and outcome.

Main Outcome Measures: Outcome measures included degree of pain relief, morbidity and mortality of operation, survival, rates of endocrine and exocrine insufficiency, and ability to return to work and/or normal activities.

Results: All but 1 of the 40 patients had abdominal pain, and 20 (50%) had recurrent episodes of acute pancreatitis. Suspicion of malignancy was a concern in 16 patients (40%). Thirty-eight patients underwent distal pancreatectomy; 1 had a central resection and another a Roux-en-Y cystojejunostomy. There was no operative mortality, but significant morbidity occurred in 15%. Among 31 patients with preoperative pain in whom long-term follow-up was available, complete or significant pain relief was achieved in 25 (81%); 74% returned to normal social function, but about half had some element of pancreatic insufficiency.

Conclusions: Distal pancreatectomy is a safe procedure and achieves pain relief and good quality of life in a large percentage of patients (80%) with presumed postobstructive chronic pancreatitis. However, some of these patients with chronic pancreatitis involving the entire gland have disease masquerading as postobstructive chronic pancreatitis secondary to an ostensibly isolated dominant pancreatic ductal stricture.


The pathogenesis of pain in chronic pancreatitis remains incompletely understood. Although in patients with large-duct disease (main pancreatic duct diameter >7 mm), increased intraductal and interstitial pressures are thought to play a dominant role in causing the pancreatic pain. In small-duct chronic pancreatitis, neuropathic mechanisms of pain seem to dominate. Pancreatic nerves are involved in the inflammatory process that characterizes chronic pancreatitis. Histopathologic changes in the perineural sheath, action of extravasated digestive pancreatic enzymes, release of a variety of noxious agents (eg, histamine, prostaglandins, bradykinins, acidosis), and excitation of afferent, nociceptive nerves contribute to the genesis of chronic pain as a result of the surrounding neural irritation. While ductal drainage procedures performed in large-duct disease will relieve the pain in most of this subgroup of patients, resection of the diseased pancreatic parenchyma harboring the involved inflamed nerves to eliminate the source of pain seems necessary in the more common form of chronic pancreatitis manifesting as small-duct disease.

Obstructive chronic pancreatitis is a particular form of chronic pancreatitis that occurs as a consequence of a primary dominant stenosis or obstruction of the main pancreatic duct, resulting in an apparently localized, segmental inflammation of the distal pancreas. Our objective was to determine the long-term results of distal pancreatectomy in patients with obstructive chronic pancreatitis.
MATERIALS AND METHODS

The medical records of 484 patients with chronic pancreatitis who underwent surgical therapy at the Mayo Clinic, Rochester, Minn, from 1976 to 1997 were reviewed. The diagnosis of obstructive chronic pancreatitis was made in 40 patients (8%), 18 women and 22 men with a mean age of 47 years (age range, 15-77 years). This diagnosis was based on a combination of preoperative findings on diagnostic imaging tests (all had endoscopic retrograde cholangiopancreatography [ERCP] and all but 4 had abdominal computed tomography) and intraoperative findings and were confirmed as chronic pancreatitis by histologic analysis of the resected specimen. Patients were selected who had apparently isolated, dominant major pancreatic ductal stricture or cutoff and changes of chronic pancreatitis in the gland distal to the stricture (Figure 1). In these patients, the head of the pancreas typically appeared normal or relatively normal on imaging tests and lacked parenchymal calcification (Figure 2). Patients with malignancy were excluded from this study.

HOSPITAL COURSE

Complications were defined according to the following criteria: pancreatic fistula, daily drainage of more than 50 mL of amylase-rich fluid (drainage amylase activity >3 x serum activity) after postoperative day 7; intra-abdominal abscess, radiographically or surgically drained fluid collection associated with clinical signs and symptoms of sepsis; and wound infection, need for the wound to be opened.

FOLLOW-UP

Follow-up information was derived from recent patient visits to our outpatient clinics, from telephone interviews, or from questionnaires sent to the patient or next of kin. Postoperative severity of pain was judged as “complete pain relief” when patients were pain free and no longer required analgesia or “significant improvement” when a decrease in the amount or type of analgesia occurred; for the latter, patients may have still required intermittent analgesic medications, but their pain pattern was better controlled. Those who did not benefit from surgery were considered “unchanged.” Late mortality, cause of death, development of endocrine or exocrine pancreatic insufficiency, and a subjective overall quality of life were recorded.

STATISTICAL METHODS

Diabetes-free survival analysis was performed using the Kaplan-Meier method. The Fisher exact test was used to test for association among pairs of categorical variables. Group differences in ordinal and continuous variables were assessed using the Wilcoxon rank sum test. Preoperative vs postoperative changes were assessed using the McNemar test for matched pairs for categorical variables and the Wilcoxon signed rank test for ordinal or continuous variables. A significance level of .05 was used for all tests.

RESULTS

The cause of chronic pancreatitis in the 40 patients in this study varied with clinical signs and symptoms of sepsis; and wound infection, need for the wound to be opened.

CLINICAL PRESENTATION

The most common clinical presentation was that of abdominal pain, which was constant in 12 (30%) of the 40 patients or characterized by frequent, debilitating attacks in 27 (68%). The pain was severe in 33 patients (83%), with narcotic use documented in all but 1; in addition, 2 patients had undergone percutaneous nerve block. Twenty-four patients (60%) had required hospitalization for pain control, and 20 (50%) had recurrent attacks of acute pancreatitis. Twenty-five patients (63%) were unable to function productively in society (ie, maintain employment or homemaking duties) because of the pain. One patient had only occasional episodes of pain.

Pancreatic endocrine insufficiency, present preoperatively in 2 patients (5%), required only oral hypoglycemic agents. Exocrine insufficiency (manifested as steatorrhea) was present in 3 patients (8%) and was treated with pancreatic enzyme supplements. Weight loss (>5 kg) was present in 13 patients (33%).

PREOPERATIVE EVALUATION

The primary localization of the disease was in the body and/or tail of the pancreas in 40 patients with the head region appearing normal or relatively normal. Pseudocysts (mean diameter, 5 cm), all localized in the pancreatic
body and/or tail, were present in 3 patients (8%). Pancreatic calcifications in the distal gland were evident in 3 patients (8%), while intraductal stones were present in 2 (5%).

Based on the clinical presentation and diagnostic evaluation, a suspicion of malignancy was raised in 16 patients (40%). Typically, these patients presented with pain, an “inflammatory” mass in the body and/or tail region associated with a dominant stricture of the pancreatic duct, and no pancreatic calcifications. Among these 16 patients, 7 had idiopathic pancreatitis. Other concurrent conditions included splenic vein thrombosis (n=4, 10%), active peptic ulcer disease (n=4, 10%), and liver cirrhosis (n=1, 2.5%).

**OPERATIVE MANAGEMENT**

The mean time from onset of symptoms to operation was 4 years (range, 2 weeks to 24 years). A distal pancreatectomy was performed in 38 of 40 patients. In these 38 patients, concomitant splenectomy was performed in 29 and was preserved in the remaining 9. In 2 of these patients, DuVal-type resection was performed with a pancreaticojejunoostomy created to the proximal pancreatic remnant. In 5 patients, more than an 80% resection was required to reach the stricture. Two patients were treated by a different procedure; 1 underwent a central pancreatectomy with closure of the proximal stump and Roux-en-Y drainage of the ductal remnant, while the other underwent a cystojejunoostomy alone without any parenchymal resection. The former patient had complete relief of pain, while the latter required pancreatic resection 4 months following the cystojejunoostomy.

**OPERATIVE MORTALITY AND MORBIDITY**

Among the 40 patients reviewed, there were no postoperative deaths. Significant morbidity occurred in 5 patients (15%), including hemorrhage (n=3) and bowel obstruction (n=2). All 3 patients with bleeding required reoperation, as did 1 with intermittent colonic volvulus. The mean hospital stay was 12 days (median, 11 days; range, 6-48 days).

**LONG-TERM OUTCOME**

**Survival**

Follow-up was complete in 32 patients (80%). Mean follow-up was 6.7 years (range, 9 months to 21 years). Twenty-five patients were alive at the time of follow-up. There were 2 deaths related directly or indirectly to their pancreatic disease.

**Pain Control and Quality of Life**

Among the 31 patients with preoperative pain and adequate follow-up, 25 (81%) had complete (n=15, 49%) or partial (n=10, 32%) pain relief. Six patients, however, had inadequate pain relief (ie, inability to work, persistent narcotic use, and/or recurrent hospitalization). Among the 31 patients with preoperative pain, only 9 (29%) were able to work or function normally preop-eratively, while postoperatively 23 (74%) were able to do so (P<.001) (McNemar test). Alcoholic cause was not significantly associated with pain relief (P=.30) (Fisher exact test). Pain relief was achieved in 20 (87%) of 23 patients in whom the head of the gland was deemed normal at operation and 5 (63%) of 8 with an abnormal pancreatic head (P=.16) (Fisher exact test). While there was a trend suggesting that normalcy of the pancreatic head was a predictor of outcome, owing to small patient numbers, it did not achieve statistical significance.

**Pancreatic Function**

Diabetes (preoperative vs postoperative) developed in a significant proportion of patients after surgery (P<.001) (McNemar test). Fourteen patients (45%) went on to develop diabetes during the follow-up (8 requiring insulin, 3 requiring oral drugs, and 3 requiring only dietary management). The diabetes-free survival curve steadily decreased after surgery (Figure 3). The mean time to onset of diabetes among patients who did not have diabetes preoperatively was 2.8 years.

Operative treatment resulted in a significant increase in the proportion of patients with steatorrhea (P<.001) (McNemar test). Postoperative exocrine insufficiency developed in 15 patients (47%).

**COMMENT**

In most patients with chronic pancreatitis, the pancreas is diffusely involved by the inflammatory process. However, in a subgroup of patients, a dominant pancreatic ductal stricture results in what seems to be a postobstructive form of chronic pancreatitis. In this study, postobstructive chronic pancreatitis represented 8% of all patients undergoing surgery for chronic pancreatitis during a 21-year period at our tertiary referral center. Although pancreatic duct strictures are classically described in the setting of a ductal pancreatic adenocarcinoma, a propor-
tion of patients experience symptomatic benign strictures after necrotizing pancreatitis,22 recurrent episodes of pancreatitis,13 pancreatic trauma,10 or other causes.16,17 In this study, recurrent episodes of pancreatitis believed to be secondary to the stricture were documented in 50% of patients. Irrespective of the underlying cause of the pancreatitis, the inciting event is thought to result in injury (chemical or mechanical) to the pancreatic duct, leading to fibrosis and duct stenosis. Consequently, distal obstruction and inflammation in the segment of pancreas drained by the obstructed duct results in postobstructive chronic pancreatitis. The duct distal to the point of stenosis or obstruction is usually dilated to some variable degree. Because the pancreatic parenchyma proximal to the obstruction is drained normally, the proximal pancreas should be normal or relatively normal both on preoperative imaging and at surgery. This proposed pathogenetic mechanism is supported by a study by Austin et al,18 who showed that even a 75% stenosis of the main pancreatic duct in cats leads to postobstructive chronic pancreatitis within 3 months, and once chronic pancreatitis had developed, relief of the obstruction failed to reverse the pancreatic dysfunction in this part of the gland.

With this concept in mind, it seems that removal of the diseased part of the pancreas by distal pancreatectomy should be the treatment of choice. Among the 31 patients with pain preoperatively who were available for long-term follow-up, surgery achieved pain relief in a significant percentage of patients (81%). Similar findings were reported by several groups who found unsatisfactory results with ductal drainage alone.9 Spleen preservation, if technically feasible, is recommended19,20; however, it can be a difficult or impossible undertaking depending on the severity of the fibroinflammatory reaction.

An important consideration in patients with newly diagnosed presumed postobstructive chronic pancreatitis, especially with no known history of pancreatic disease, should be suspicion of malignancy (40% in the present study). This consideration also applies to patients with known chronic pancreatitis because of its well-appreciated association with pancreatic cancer.7,21 Pancreatic cancer can rarely initiate pancreatitis, presumably by obstructing the main pancreatic duct.22 Therefore, the surgeon must maintain a high index of suspicion, especially when facing patients with symptoms believed to be attributable to postobstructive chronic pancreatitis.7,22 In some patients, the uncertainty can only be answered with histologic study of the resected gland.23 When preoperative imaging shows an associated mass in the pancreas, resection should be strongly entertained, even if proof of malignancy is lacking, provided the resection can be done with a reasonable risk in a surgically fit patient.21,23

As the pancreatic parenchyma of the head and uncinate should be normal or relatively normal in patients with postobstructive chronic pancreatitis, one would anticipate that distal pancreatectomy should be more efficient in relieving the pain in these patients undergoing distal pancreatectomy. For the same reasons, it seems reasonable to expect that distal pancreatectomy in postobstructive chronic pancreatitis should not result in pancreatic insufficiency because only 10% of the pancreas is needed to remain eupancreatic.24 Our results, however, showed that distal pancreatectomy in patients with presumed postobstructive chronic pancreatitis failed to significantly relieve pain in 19% of patients and led to some element of pancreatic exocrine or endocrine insufficiency in about half the patients. These findings can be explained by the fact that stricture formation, resulting in an ostensibly “dominant,” isolated pancreatic duct stenosis or obstruction with presumed chronic pancreatitis, often occurs in patients with chronic pancreatitis involving the entire gland. In these patients, a dominant-appearing stricture is an epiphenomenon in the natural history of chronic pancreatitis. After resection of what appears to be the diseased portion of the gland, chronic pancreatitis progresses in the proximal gland as evidenced by the progressive development over time of diabetes in about one half of the 32 patients available for long-term follow-up (Figure 3). This development should not be a major surprise since 10 of our patients were alcoholics preoperatively. This process is not uncommon after all types of resective procedures for chronic pancreatitis.25 In the subgroup of 6 patients who had postobstructive chronic pancreatitis of presumed traumatic origins, pain relief was achieved in only 4 of the 6 patients after a mean follow-up of 10.6 years; one patient developed insulin-dependent diabetes. Interpretation of these results should be cautious because the numbers are small (n=6).

Our results suggest that the surgeon should carefully evaluate the proximal pancreas before undertaking a distal pancreatectomy for presumed postobstructive pancreatitis. Prior to operation, the status of the secondary ducts on ERCP, presence of calcifications, the texture of the gland on endoscopic ultrasonography, and especially the underlying cause of the stricture should be considered when planning the resection and when discussing presumed outcome with the patient. With the recent shift from distal-based resections to proximal resections,20 a more prudent operative consideration in some of these patients, especially those who abuse alcohol, might be the Frey26 or Buchler28 procedure.

In conclusion, in the present study, distal pancreatectomy achieved pain relief in a significant percentage...
of patients (81%) with low morbidity and no mortality. Given the presumed localized nature of the disease at the time of operation, targeted distal pancreatic resections should be the procedure of choice, even in the presence of poststenotic duct dilatation. Distal pancreatectomy is also appropriate when there is suspicion for malignancy, which was a consideration in a high percentage of patients (40%) in our study.

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REFERENCES


DISCUSSION

Theodore X. O'Connell, MD, Los Angeles, Calif. Over the years there has been much discussion and controversy regarding the best operative treatment for chronic pancreatitis. This has ranged from various drainage procedures, including sphincteroplasty, lateral pancreaticojejunostomy, and distal drainage of the tail of the gland. Also, resections of the pancreas have been advocated as effective treatment, including distal pancreatectomy, Whipple or Beger operations, and total or near-total pancreatectomy. While there has been disagreement on the best treatment, it really depends on the etiology of the pancreatitis and the status of the pancreas, especially the duct as seen on ERCP or more recently MRCP [magnetic resonance cholangiopancreatography]. If there is a proximal stricture with distal dilatation, then either sphincteroplasty or lateral pancreaticojejunostomy adequately relieves pain and preserves pancreatic function. In a chain-of-lakes configuration, usually secondary to alcoholism, a lateral pancreaticojejunostomy is usually the best treatment. In a fibrotic duct with pancreatitis confined to the head, the Whipple or Beger operation is ideally suited. With a nondilated pancreatic duct associated with significant pain, the near-total or total pancreatectomy can be considered, especially if the patient has no evidence of pancreatic endocrine or exocrine function. Distal resection is usually limited to single-duct strictures, which in my experience has usually been due to trauma. Obviously, one must be selective in doing the type of operative therapy consistent with the condition seen in the pancreatic duct. No one operation fits all patients. Obviously, in this study the authors have been extremely selective. They have done over 484 operative cases on the pancreas, but only 40 of them have been distal resections. Over the 20-year period, this is only 2 per year. The first question is, how do they select the patients for this? Forty percent of the patients had indications because of presumed malignancy, which only leaves 24 patients or only 1 per year who had it for chronic pancreatitis indications alone.

The authors state that the patients are selected because they have a single stricture or cutoff and distal pancreatitis with a normal-appearing head. I agree with this indication. However, in the data on pain relief, they state that a good outcome was seen in only 5 of 8 patients with an abnormal pancreatic head, which is one third of the remaining 24 patients. How were these patients selected for this operation, and should they be in the future?

Although alcohol is a presumed cause in 25% of the patients and trauma in only 15%, this has not been my experience. The question is, could some of the alcoholics really have had a traumatic pancreatitis secondary to mid duct strictures due to alcoholics injuring themselves without a history and having a traumatic pancreatitis on top of their alcoholism? Secondarily, could some of those 8 patients with pancreatitis in the head be due to alcoholism and really be skewing the data toward the alcoholic etiology?
It is stated that approximately 50% of the patients develop pancreatic insufficiency. Obviously, exocrine insufficiency is not much of a problem, and that could easily be taken care of by oral pancreatic enzymes. But endocrine insufficiency requiring insulin therapy is much more of a problem and causes serious quality of life issues. This occurred in approximately 50% of the patients. It is stated that 5 patients had resections of over 80% of the gland. Were these patients more likely to develop diabetes than those with more limited resection, and should they have had a drainage procedure rather than a resection? Similarly, were those patients with pancreatitis in the head more likely to develop diabetes? Are there any other identifying characteristics of disease, presentation, extent of operation, which would predict the development of diabetes and perhaps avoid the resection? Also, is the development of the diabetes secondary to resection or progression of the disease, or a combination of both?

Interestingly, the patients presented have a decreased long-term survival that is independent of the most obvious factor of alcoholism. Do the authors have any explanation for this finding? Although I agree with the authors that this is a satisfactory operation for selected patients, I cannot necessarily agree with their conclusion that it is “the treatment of choice” since there is no comparison with a control group of patients with other procedures such as the drainage procedure through the dilated duct to come to such a firm conclusion.

Richard A. Prinz, MD, Chicago, Ill: This paper makes some very relevant points for surgeons handling chronic pancreatitis. I understood that there were actually 102 patients who had a distal pancreatectomy in your overall group. Can you share with us how those patients did and why you didn’t include them in this group of 40? Alcohol is obviously the most common etiology for chronic pancreatitis in this country. You piqued my interest when you said that alcohol had no effect on outcome. Certainly, alcohol is likely to affect the entire gland, and many patients continue to drink afterward. Both of these factors make a poorer outcome more likely. Your results in having no pancreatic leaks are certainly outstanding; can you share with us how you handled the stump to achieve this, especially since many of these patients had normal pancreas to the right?

Hung Ho, MD, Sacramento, Calif: First, you managed to preserve the spleen in 9 cases and proceed with splenectomy in 29 cases. Did you always attempt to preserve the spleen, and when would you not? The second question is related to the leak rate. I would like to know how you managed the stump as well. Specifically, how do you assure yourself intraoperatively that you actually closed the pancreatic duct?

G. Robert Mason, MD, Maywood, Ill: Dr Farnell was kind enough to show us one CT scan with a dilated duct distal to the stricture. This actually is usually an indication for a drainage procedure. I wonder why the choice for resection was made in a patient like that. Perhaps he has more. I would like to know how many patients have pancreatic remnant and not the resection alone as the cause of diabetes?

Dr O’Connell commented that it couldn’t be concluded that distal pancreatectomy is the treatment of choice because we have not performed a comparative analysis. His point is well made. Dr Madura is here in the audience, and he and his colleagues published a nice paper that addressed postobstructive pancreatitis and compared drainage, Whipple procedure, and distal pancreatectomy and concluded that the results were clearly superior in the group undergoing distal pancreatectomy (Surgery. 1995;118:727-733).

Dr Prinz asked about the 102 patients who had distal pancreatectomy for chronic pancreatitis who served as the denominator for this study. We are currently in the process of analyzing that group of patients. He also asked about the effect of alcoholic etiology on outcome. While alcoholic etiology did not significantly predict a poorer outcome in this study, the number of alcoholic patients was small (10 patients). Alcoholic etiology may well have been shown to correlate with outcome if the study cohort was larger.

There were a couple of questions about how we handle the pancreatic stump. We felt fortunate that there were no leaks in this particular group of patients. In some of these patients, there was already a complete occlusion of the duct due to ne-