

Surgical Management of Failed Endoscopic Treatment of Pancreatic Disease

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Abstract

Introduction Endoscopic therapy of acute and chronic pancreatitis has decreased the need for operative intervention. However, a significant proportion of patients treated endoscopically require definitive surgical management for persistent symptoms.

Objective Our aim was to determine which patients are likely to fail with endoscopic therapy, and to assess the clinical outcome of surgical management. Patients were identified using ICD-9 codes for pancreatic disease as well as CPT codes for endoscopic therapy followed by surgery.

Material and Methods Patients with documented acute or chronic pancreatitis treated endoscopically prior to surgical therapy were included ($N=88$). The majority of patients (65%) exhibited chronic pancreatitis due to alcohol abuse. Common indicators for surgery were: persistent symptoms, anatomy not amenable to endoscopic treatment and unresolved common bile duct or pancreatic duct strictures. Surgical salvage procedures included internal drainage of a pseudocyst or an obstructed pancreatic duct (46%), debridement of peripancreatic fluid collections (25%), and pancreatic resection (31%).

Results Death occurred in 3% of patients. The most common complications were hemorrhage (16%), wound infection (13%), and pulmonary complications (11%). Chronic pancreatitis with persistent symptoms is the most common reason for pancreatic surgery following endoscopic therapy. Surgical salvage therapy can largely be accomplished by drainage procedures, but pancreatic resection is common.

Conclusion These complex procedures can be performed with acceptable mortality but also with significant risk for morbidity.

Keywords Endoscopic retrograde
cholangiopancreatography (ERCP) · Endoscopic therapy ·
Acute and chronic pancreatitis · Salvage surgery

Introduction

Pancreatitis is an expansive disease that may be debilitating and managed medically, endoscopically or by surgical approaches. In acute pancreatitis, up to 20% of patients suffer considerable morbidity and/or mortality.¹ Acute severe pancreatitis is characterized by a robust systemic inflammatory response that may result in pulmonary, renal, and hepatic compromise that progresses to multi-system organ failure and decreased immune function.^{2–9} This impaired host response may result in infected pancreatic necrosis that can be treated by either endoscopic or surgical management; however, either approach has significant complications.^{1,10,11} In contrast to the dramatic presentation

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of severe acute pancreatitis, chronic pancreatitis is associated with waxing and waning abdominal pain, steatorrhea, anorexia, malabsorption, weight loss, and diabetes mellitus.¹² Although the course of disease and the clinical presentation of chronic pancreatitis differs markedly from acute pancreatitis, both endoscopic and surgical management may effectively reduce recalcitrant abdominal pain and effectively treat complications such as pseudocysts in select patient populations.^{13–18} However, recent randomized trials have demonstrated that the surgical management of chronic pancreatitis results in improved outcomes compared to endoscopic treatment.^{19,20}

Endoscopic approaches to acute and chronic pancreatitis are varied and include sphincterotomy and stone extraction for gallstone pancreatitis,²¹ pancreatic duct stenting in acute recurrent and chronic pancreatitis,^{22–24} and endoscopic ultrasound (EUS)-guided transmural or transpapillary drainage of fluid collections and pseudocysts. Previous work has demonstrated that pancreatic duct stenting can decrease recurrence rates of acute pancreatitis²³ and reduce the pain associated with chronic pancreatitis.²⁵ However, abatement of symptoms too frequently has a short duration following endoscopic therapy, and the underlying pathophysiology of a fibrotic pancreatic duct is not significantly altered by endoscopic therapy. Conversely, EUS-guided pseudocyst drainage has low complication and mortality rates and is highly successful.¹⁵

Surgical therapy for pancreatitis includes procedures that decompress the pancreatic duct or resect the diseased parenchyma. In the past, decompressive and pancreatic parenchyma-sparing procedures were favored; however, resection of an enlarged, inflamed pancreatic head accompanied by duct drainage has been a valuable addition to decrease neurogenic pancreatic pain in patients with chronic pancreatitis. Decompressive procedures include cystgastrostomy, cystenterostomy, lateral pancreatojejunostomy, and sphincteroplasty. Pancreatic resection is accomplished by pancreatoduodenectomy, distal pancreatectomy, local resection of the pancreatic head, and total pancreatectomy with islet cell transplantation. Puestow and Gillesby described the first widely effective drainage procedure in 1958.²⁶ This procedure was modified by Partington and Rochelle by sparing the spleen and tail of the pancreas.¹⁷ In chronic pancreatitis, short-term pain relief is achieved in 60–95% of patients with a reported 0–5% mortality rate using decompression procedures.^{18,27–29} Alternatively, a resection that preserves substantial pancreatic tissue can be performed.³⁰ Furthermore, patients with a non-dilated pancreatic duct and/or refractory pain are candidates for pancreatic resection.²⁷ Complete pain relief with resection can be achieved in 70–100% of patients with a mortality of 0–4%.^{31–35}

The aims of this study were to determine which patients are likely to fail endoscopic therapy and to assess the

clinical outcome of surgical management following initial endoscopic therapy. The findings of this study suggest that patients with chronic pancreatitis may have persistent symptoms following endoscopic therapy and that surgical salvage therapy has low mortality but significant morbidity.

Materials and Methods

Patients were identified by searching institutional databases for ICD-9 pancreatic disease codes (577.0–577.2) and current procedural terminology codes for endoscopic therapy and surgical procedures for pancreatic diseases. Nine hundred twenty-five patients with pancreatic disease and interventional management were identified over the period extending from 28 March 1997 to 14 February 2007. Patients with well-documented acute or chronic pancreatitis treated endoscopically prior to surgical therapies were included for analysis. Patients with neoplastic disease or suspected neoplastic disease preoperatively were excluded. Eighty-eight (10%) patients met the study criteria.

Following patient identification, medical records were retrospectively reviewed for demographic data, etiology of pancreatitis, endoscopic management, and surgical therapy. The etiology of pancreatitis was classified as induced by alcohol, gallstones, hyperlipidemia, pancreatic divisum, trauma, or genetic causes. Additional cases not ascribed to these categories were deemed idiopathic. As documented in the medical record, pancreatitis was described as chronic, acute, or acute necrotizing pancreatitis; acute on chronic pancreatitis; or acute recurrent pancreatitis. Endoscopic management was identified as cystgastrostomy, endoscopic retrograde cholangiopancreatography (ERCP) with stent placement, or sphincterotomy or EUS-guided stent placement. The indications for surgery were persistent symptoms, anatomy not amenable to further endoscopic treatment, common bile duct or pancreatic duct strictures, persistent pseudocysts, infection or clinical deterioration, obstructing pancreatic lithiasis, pancreatic fistula, post-ERCP pancreatitis, hemorrhage, or duodenal stenosis. Each procedure was identified and the medical records were reviewed for complications. Means plus or minus the standard deviation were determined for continuous variables. Other results were summarized as percentages of the patient population.

Results

A summary of the demographic characteristics of the study group is listed in Table 1. Of the 88 patients with pancreatitis that received surgical therapy following endoscopic management, the mean age at time of surgery was

Table 1 Patient Demographics

Characteristics	N	Percent
Age	49±14	
Male/Female	45:43	
Etiology		
Alcohol	40	45.4
Idiopathic	18	20.4
Gallstones	17	19.3
Iatrogenic	4	4.5
Hyperlipidemia	4	4.5
Pancreatic Divisum	3	3.4
Trauma	1	1.0
Genetic	1	1.0
Viral	1	1.0
Type of Pancreatitis		
Chronic	57	64.7
Acute/Acute Necrotizing	14	15.9
Acute on Chronic	9	10.2
Acute Recurrent	7	7.9
Not Documented	1	1.0

49±14 years and the male-to-female ratio was 45:43. Sixty-five percent (65%) of patients had chronic pancreatitis with alcohol-induced disease in 40 of 88 patients. The next most common etiologies were idiopathic causes, gallstones, hyperlipidemia, and pancreatic divisum. Trauma, genetic, and cytomegalovirus-induced pancreatitis were less frequent causes of pancreatitis.

Of the endoscopic therapies that preceded surgical intervention, nearly all (96%) patients were treated with ERCP. In 53% of patients, stents were placed, 10% of patients underwent cystgastrostomy with the remaining patients undergoing ERCP with sphincterotomy of either the bile or pancreatic ducts. Three patients had pancreatic stones extracted while three additional patients had transpapillary pseudocyst drainage (Table 2).

The common indications for surgery were: persistent symptoms (28%), anatomy not amenable to further endoscopic therapy (26%), common bile duct or pancreatic duct strictures (18%), infection or clinical deterioration (16%), and a persistent pseudocyst (15%) (Table 3).

Surgical salvage procedures included internal drainage of a pseudocyst or an obstructed pancreatic duct in 40

Table 2 Endoscopic Procedures

Endoscopic Treatment	N	Percent
ERCP	84	95.5
Stent Placement	47	53.4
Cystgastrostomy	9	10.2
Stone extraction	3	3.4
Transpapillary drainage of pseudocyst	3	3.4
Celiac plexus nerve Block	1	1.0

Table 3 Indications for Surgery Following Endoscopic Treatment

Indication	N	Percent
Persistent/new onset symptoms	25	28.4
Unacceptable anatomy	23	26.1
CBD/PD Stricture	16	18.2
Persistent pseudocyst	13	14.7
Infection or clinical deterioration	14	15.9
Impacted stones	5	5.7
Pancreatic fistula	2	2.3
Post ERCP pancreatitis	1	1.0
Hemorrhage	1	1.0
Duodenal stenosis	1	1.0

(46%) patients, debridement or pancreatic abscess drainage in 22 (25%) patients, and pancreatic resection in 27 (30%) patients (Table 4). The most common drainage procedures were lateral pancreaticojejunostomy (22%) and cystojejunostomy (19%). Eight (9%) patients had duodenal-sparing pancreatic head resections, while 15% of patients had associated procedures such as cholecystectomy or cholecystojejunostomy performed.

An overall complication rate of 56% was observed (Table 5). There were three deaths in the series. One death resulted after a lesser sac marsupialization for pancreatic and retroperitoneal abscess drainage requiring a repeat operation for drainage of a pelvic abscess. This patient developed multi-system organ failure manifested by *Pseudomonas* pneumonia, renal failure, sepsis, and adult respiratory distress syndrome. Another death resulted after external drainage. This patient had bleeding postoperative day 6 requiring reoperation and transfusion of 10 units of

Table 4 Spectrum of Operations

Operation	N	Percent
Internal Drainage	40	45.5
Pancreaticojejunostomy	19	21.6
Cystjejunostomy	17	19.3
Cholecystojejunostomy	14	15.9
Hepaticojejunostomy	6	6.8
Choledochojejunostomy	3	3.4
Transduodenal sphincteroplasty	2	2.3
Pancreatocystojejunostomy	1	1.0
Debridement/Drainage	22	24.7
Pancreatic Resection	27	30.7
Distal pancreatectomy with Splenectomy	13	14.8
Distal pancreatectomy without Splenectomy	1	1.0
Local pancreatic head resection	8	9.1
Subtotal Pancreatectomy	4	4.5
Pancreatoduodenectomy	1	1.0
Associated Procedures		
Cholecystectomy	13	14.8
Gastrojejunostomy	10	11.4

Table 5 Complications

Complications	N	Percent
All Complications	50	56.8
Hemorrhage	14	15.9
Wound infection	11	12.5
Pulmonary	10	11.4
Sepsis	6	6.8
Reoperation	4	4.5
Ileus	3	3.4
UTI	3	3.4
Dehiscence	2	2.3
Infected pancreatic fluid	2	2.3
GI bleed	2	2.3
Urinary retention	2	2.3
Colitis	2	2.3
Neurologic	2	2.3
Thoracic duct injury	1	1.0
DVT	1	1.0
Stroke	1	1.0
Renal Failure	1	1.0
Death	3	3.4

red blood cells, but he subsequently died. The third death resulted after an operation including splenectomy and drainage of a fluid collection. The operation was complicated by bleeding followed by respiratory insufficiency, sepsis, and multi-organ failure in the postoperative period. Overall, repeat operations were necessary in 4% of patients.

Discussion

In this study, our aim was to examine the outcome of patients that had initial endoscopic treatment but required surgical salvage therapy for ongoing symptoms from pancreatic disease. Both acute and chronic pancreatitis may result in extensive tissue destruction with difficult-to-treat symptoms and complications. Both endoscopic and surgical approaches may result in resolution of symptoms, but often endoscopic therapy is chosen because it is less invasive and has a limited recovery period compared to surgery. Few data exist to determine whether endoscopy or surgery is most appropriate for advanced pancreatic disease. Moreover, the outcome of surgical therapy after failed endoscopic therapy has not been documented. In this study, the findings indicate that chronic pancreatitis with persistent or newly developed symptoms is the most common reason for pancreatic surgery following endoscopic therapy. While pancreatic resection may be required, surgical salvage therapy can often be accomplished by drainage procedures. These complex procedures can be performed with acceptable mortality but significant risk for morbidity.

The results of our study suggest that patients with chronic pancreatitis that are treated with endotherapy are

the most likely patients that will require salvage surgery. These findings are in agreement with recent randomized trials that demonstrated surgical therapy for obstructive chronic pancreatitis resulting in more durable pain relief.^{19,20} Dite et al. concluded that endotherapy may remain the first line therapy and that surgery should be performed following failed endotherapy. However, their study does not completely address the risks associated with complex procedures in a group of patients with chronic illness and substantial co-morbidities. The current study suggests that overall mortality rates are low (3.4%), but that the overall complication rates are high (56.8%) and that some of the complications may result in permanent sequelae. It is also important to note that many of the patients undergoing endotherapy require multiple procedures that extend over several months. Furthermore, a Dutch trial reported a 58% complication rate in patients treated endoscopically.¹⁹ Without correction of the underlying pancreatic pathology, many of these patients are unable to obtain adequate nutrition and over time, lose significant weight and further increase their risk of postoperative complications.³⁶ In addition, even though this work does not provide direct evidence that early initial operative therapy will decrease patient morbidity, Cahen et al. illustrates a morbidity rate of 35% in a group of surgical patients that had a duration of symptoms of only 21 months.¹⁹ In our study, nearly all surgical patients had two to five endoscopic procedures performed over 2–3 years prior to surgery. Thus, extended endoscopic therapy may affect the morbidity of salvage surgery for chronic pancreatitis. Given these findings, we suggest that surgery be considered as a first-line therapy for select patients with chronic pancreatitis.

While successful long-term outcomes following endotherapy for patients with chronic pancreatitis have been difficult to achieve, endotherapy for the complications of acute pancreatitis has been employed with increasing success. Pancreatic pseudocyst drainage by either the transpapillary or transmural approach has replaced surgical therapy and percutaneous drainage as the first-line treatment option in appropriately selected patients.^{37,38} Furthermore, aggressive endotherapy with transmural stent placement and vigorous irrigation of lesser sac pancreatic abscesses has been increasingly successful.³⁷ Pancreatic fistulae are readily identified and treated with ERCP followed by transpapillary stenting.³⁷ In years past, each of these complications of acute pancreatitis was thought to be best managed by surgical therapy, yet these operations were difficult and associated with high morbidity. Therefore, endotherapy for appropriately selected patients with pancreatic pseudocysts and fistulae is appropriate. Although some patients with pancreatic abscesses or necrosis may be successfully treated by skilled, dedicated endoscopic therapists, these complications of acute pancreatitis require

long-term therapy with multiple interventions that can result in treatment over several months. In patients with significant necrosis and tissue destruction, surgical pancreatic debridement remains the mainstay of therapy.

Surgical outcomes for pancreatic resection and drainage procedures have improved markedly in the last decade with significantly decreased mortality rates. However, despite the improved mortality in these ill patients, the risks of complications remain significant. More recent complete reporting has demonstrated that over 50% of patients undergoing pancreatic surgery have complications.³⁹ Furthermore, evidence suggests that thorough preoperative evaluation and preparation of patients may decrease the risk of complications.⁴⁰ Therefore, assessment of patients for endotherapy or surgical therapy for pancreatic disease must include a complete risk assessment and evaluation of the likely long-term outcomes of either an endotherapeutic approach or surgical management. Failed endotherapy may not be a prerequisite for surgical therapy of acute or chronic pancreatitis.

Conclusion

In conclusion, because of the significant risk of complications, only patients who are likely to have a long-lasting beneficial effect from endotherapy should undergo this type of therapy initially for chronic pancreatitis or pancreatic necrosis. Patients with complex disease and are unlikely to respond to endotherapy should have primary surgical therapy. This approach may decrease cost, treatment duration, patient discomfort, and potentially limit subsequent surgical complications.

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