Endoscopic treatment of chronic pancreatitis

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Endoscopic therapies, originally utilized for problems in the biliary tree, have been adapted for use in the pancreas. Despite widespread adoption and implementation of these techniques, there are few controlled studies comparing pancreatic endotherapy with either surgery or traditional medical treatment. This review attempts to summarize current endoscopic practice in treating the ductal obstructions and leaks associated with chronic pancreatitis and place these techniques into perspective with respect to alternative management strategies. [Indian J Gastroenterol 2002;21:67-73]

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The consequences of chronic pancreatitis include not only exocrine and endocrine insufficiency, but also relapsing attacks of clinical pancreatitis as well as chronic pain. The etiology of the latter is probably multifactorial and includes ductal or tissue hypertension, tissue ischemia, perhaps as a consequence of chronic cytokine activation, and perineuritis. Chronic pancreatitis may also result in contiguous organ damage to include splenic or portal vein thrombosis, incarceration of the distal biliary duct with chronic cholestasis and secondary biliary cirrhosis, and duodenal or colonic obstruction. Finally, chronic pancreatitis may be associated with ductal disruption. The most common consequences of the latter include pseudocyst formation, but pancreatic ascites, high-amylose pleural effusions as well as pancreatico-enteric and even pancreatic-cutaneous fistulae can occur.

Traditionally, the surgical management of chronic pancreatitis has approached the disease process by attempting to treat local complications as well as resecting or decompressing inflamed or obstructed tissue. As such, patients with an enlarging or symptomatic pseudocyst may undergo a cysto-gastrostomy or cysto-enterostomy, whereas a patient with chronic pain may undergo pancreatic head or tail resection or longitudinal pancreaticojejunostomy. The latter operations presuppose that ductal obstruction, usually a complication of stones or an inflammatory structure, is the cause of chronic pain or relapsing pancreatitis. Support for this view includes duct dilatation due to an inflammatory structure or ductal calculus, the elevated pancreatic ductal and tissue pressures when compared to controls in many cases of chronic pancreatitis, and the symptomatic response that occurs in many patients after surgical decompression.

Comparable to the surgical therapy for chronic pancreatitis, endotherapy attempts similar goals: amelioration of ductal obstruction, resolution of ductal disruption and the treatment of at least a subset of associated complications. Despite the adoption and widespread implementation of endoscopic treatment modalities, a number of disclaimers require emphasis. On the one hand, pancreatic endotherapy has not undergone rigorous trials comparing its results with surgically or even medically treated patients. Results of therapy, therefore, are usually reported by individual centers with both interest and major expertise in therapeutic endoscopy and may not be generalizable to community hospitals who infrequently care for chronic pancreatitis patients. Moreover, it is clear that there are a variety of conditions such as small duct chronic pancreatitis, central pancreatic necrosis with a disconnected gland syndrome, or pseudotumor of the pancreatic head in which there may be multiple strictures and stones within side branches as well as the main pancreatic duct, in which endotherapy has no definitive therapeutic role. Finally, the endoscopic treatment of chronic pancreatitis does not occur in isolation. Access to pain and medical management teams, good interventional radiology support, and an interrelationship with an experienced pancreaticobiliary surgeon are all prerequisites that need to be met prior to initiating pancreatic endotherapy.

Duct obstruction

Major/minor papilla

There are few studies that suggest that sphincter dysfunction influences the development of chronic pancreatitis, even in the setting of pancreatic divisum. However, a significant part of endoscopic pancreatic therapy is facilitated by sphincterotomy of the major or minor papilla. This includes calculus removal, dilation of and prosthesis placement for ductal strictures, and the treatment of both internal and external pancreatic fistulae. We have looked at the risks and benefits of pancreatic sphincterotomy in different situations. Okolo et al retrospectively reviewed all patients undergoing endoscopic pancreatic duct sphincterotomy at Johns Hopkins Hospital over a 4-year period. Fifty of these patients, 40% of whom had chronic pancreatitis, had sphincterotomy for a hypertensive sphincter. Defining clinical improvement as a greater than 50% pain reduction, 60% of this
group had improved pain scores at a median follow-up of 16 months. Although there were a number of complications (pancreatitis 9%, early stent occlusion 9%, and bleeding 3.6%), the authors concluded that the technique was safe and associated with sustained pain relief in this highly selected population. What remains to be defined is the best technique of pancreatic sphincterotomy (pull-type or needle-knife sphincterotomy over a stent) and whether short-term prosthesis placement minimizes the risk of periprocedural pancreatitis. I use a pure cutting current to minimize cautery injury to the pancreatic parenchyma and iatrogenic stricture formation, leaving a stent in place for 1-2 weeks to preclude edematous obstruction of the sphincterotomy site.

The indications for minor papilla sphincterotomy are both more straightforward and more nebulous. On the one hand, minor papilla sphincterotomy in patients with conventional anatomy may simply be the most straightforward way, anatomically, to access the body and tail of the pancreas for other therapeutic maneuvers. Alternatively, divisum anatomy has been postulated to cause attacks of acute relapsing pancreatitis for which minor papilla sphincterotomy or even stent placement alone may prove therapeutic. From the latter standpoint, Ertan described 5-7 Fr stent placement in the minor papilla in 25 divisum patients with relapsing pancreatitis. Exchanging stents every 2-3 months for up to 1 year, 76% remained symptom-free during follow-up approximating 24 months. If these patients did not have ductal changes of chronic pancreatitis prior, they did afterwards, as 84% of the patients were noted to have iatrogenic, stent-induced lesions. The results of endoscopic minor papilla sphincterotomy, in turn, were recently reviewed by Norton and Petersen. These authors compiled an overall response rate of 75% when necessary papilla sphincterotomy is done for acute relapsing pancreatitis but considerably lower rates of improvement in chronic pancreatitis or chronic pancreatobiliary pain without ductographic evidence of chronic pancreatitis.

Pancreatic duct stricture (Fig 1)

Although stents have been placed across ductal strictures to define the patient subset who will respond to decompressive surgery, results have been equivocal. Likewise, long-term stent placement has been associated not only with induction of iatrogenic lesions but also with pancreatic sepsis associated with prosthesis occlusion. Nevertheless, a number of endoscopists have placed 7-10 Fr pancreatic prostheses long-term, often following initial hydrostatic balloon dilatation of the stenosis. The early advocates, Cremer et al., were successful in placing stents in 75 of 76 chronic pancreatitis patients with ductal strictures. Most of these patients had a concomitant major and/or minor pancreatic sphincterotomy and 94% were reported to have initial complete pain relief. Multiple subsequent reports have confirmed pain relief in a majority of patients with stricture who undergo stenting but these same series suggest that less than 25% of patients have resolution of their stenosis. This latter finding suggests that many patients will either be tethered to their endoscopists because of the need for periodic stent exchange or will ultimately need some form of resective or decompressive surgery. Nor will placement of a metallic stent be a long-term answer as mucosal hyperplasia and duct reobstruction is an invariable consequence.

Because of the latter, our group uses prostheses sparingly as definitive treatment of ductal strictures. Moreover, we use long-term prosthesis placement only if an individual refuses surgery or poses an inordinate surgical risk. Finally, we have evolved our technique of stricture treatment, treating pancreatic ductal strictures.
Fig 2: Pancreatography, in a patient who had undergone Whipple procedure for idiopathic chronic calcific pancreatitis/pseudotumor in pancreatic head, demonstrates anastomotic stricture (A) treated with balloon dilation (B), and stone extraction (C).

much like we treat benign biliary strictures. As such, amenable stenoses first undergo balloon dilation followed by placement of two or more parallel prostheses. The latter, in theory, allows not only improved stricture dilation but also lessens the degree of side branch occlusion than occurs with a single large diameter stent. In addition, stent occlusion with the risks of obstructive pancreatitis and pancreatic sepsis seems to be minimized as drainage persists between and alongside the prostheses even after obstruction. Additional studies are required to confirm these personal observations.

Pancreatic calculi (Fig 2)

Pancreatic stones may be both the consequence and the cause of symptoms in chronic pancreatitis. Early work by our group as well as others demonstrated that removal of stones within the main pancreatic duct was associated with decreased ductal diameter as well as improvement in chronic pain and relapsing attacks of pancreatitis in a significant patient subset.27,28 It became clear, however, that more than 50% of stones potentially amenable to endotherapy could not be removed without ancillary maneuvers. Not only were a significant number impacted within a downstream stricture requiring concomitant pancreatic duct sphincterotomy and balloon dilation of the stenosis, but the stones themselves were often exceedingly hard and sharply angulated, precluding mechanical lithotripsy. Moreover, removal attempts were associated with repeated fracture of extraction balloons. Our group described an early experience fracturing these calculi using a tunable dye laser pulse transmitted through a quartz fiber inserted through a mini-scope.26 This technique has largely been abandoned and replaced by electrohydraulic lithotripsy which generates considerably more fragmentation energy.27 Moreover, a rhodamine laser system with an automatic stone-tissue detection system has been developed and studied on pancreatic calculi in vitro and may theoretically preclude the need for direct pancreatoscopy.28

The majority of centers, however, have used extracorporeal shock wave lithotripsy (ESWL) to fragment pancreatic stones.28-35 In one of the earliest and still largest series to date, the Brussels group treated 123 patients with obstructive pancreatitis with the Lithostar (Siemens, Erlangen, Germany) lithotriptor following an initial PD sphincterotomy and naso-pancreatic drain placement to facilitate stone localization.28 Virtually all stones could be fragmented, 90% of patients had a decrease in major pancreatic duct diameter, and half of the patients had complete clearance of the calculi. Although all patients noted initial pain relief, one-half developed recurrent symptoms felt to be related to migration of stone fragments, residual ductal stenosis, or obstruction of concomitantly placed stents. A third of their patients developed pancreaticobiliary sepsis, suggesting that antibiotic coverage is a requisite for this therapy.

Since this seminal publication, numerous subsequent series have been published confirming these observations.28-34 Brand et al.24 prospectively followed 48 consecutive patients with chronic calcific pancreatitis treated with a median of 13 ESWL sessions (2-74) using a Lithostar prototype. There was complete stone clearance in 21 patients and follow-up at a mean of 7 months showed a significant decrease in pancreatic duct diameter and pain scores. Approximately one-half of the patients were pain-free and several quality-of-life indices demonstrated significant improvement. Our own group has reported 40 patients at a mean follow-up of 28 months after lithotripsy and endotherapy.35 Eighty percent of these patients avoided subsequent surgery and there was a statistically significant decrease in preoperative pain, narcotic ingestion, and yearly hospitalizations.
Data such as the above suggest that certain patients with obstructing calculi respond to stone removal. These studies do not imply that every patient should be treated endoscopically. It is the author’s opinion that patients with multiple calculi and strictures within a pseudotumor of the pancreatic head may be better served by head resection (Beger or Frei procedures or pylorus-preserving Whipple operations).  

**Ductal disruptions (Figs 3, 4)**

Ductal disruptions result in internal or external pancreatic fistulas. The consequence of this leak depends upon its location, whether it occurs in the setting of acute or chronic pancreatitis, and the body’s response. Major ductal disruptions in the setting of acute pancreatitis are associated with acute pancreatic fluid collections or pancreatic necrosis. Both can evolve into a pancreatic pseudocyst or may decompress into a contiguous loop of bowel (pancreatico-enteric fistula). A major leak in the setting of chronic pancreatitis, usually the consequence of ductal obstruction from stricture or stone or a superimposed acute inflammatory process, may also cause a pseudocyst. Other forms of internal fistulae can occur, and include pancreatic ascites, high-amylase pleural effusions, and internal fistulae into the bile duct, small bowel, and even the colon. Percutaneous or surgical drainage of pancreatic fluid collection in the setting of downstream obstruction or central pancreatic necrosis in which there is parenchymal as well as ductal disruption results in an external pancreatic fistula.

The endoscopic treatment of pancreatic duct fistulas in chronic pancreatitis is contingent on their location, the presence of concomitant fluid collections, and whether there is simply a ductal leak as opposed to disconnection of two portions of the gland. Using pseudocyst as an example, fluid collections can be drained transgastrically, transduodenally, or by placement of a transpapillary stent. Initial reports suggested that perhaps 2/3 of patients were potentially drainable by transmucosal fistulization into the cyst cavity using a needle-knife. This latter technique has evolved into tract dilation and placement of multiple pigtail stents or a pigtail stent in conjunction with a nasocystic drain. A meta-analysis of results using these techniques suggests that perhaps 80% of such lesions respond to endotherapy, although there are clearly higher risks of bleeding and iatrogenic infection when draining pseudocysts through the stomach wall. Infectious risks are even higher in patients with evolving necrosis in which significant cavity debris is associated with occlusion of transmurally placed prosthesis. In addition to
the placement of transmural stents, transpapillary endoprostheses can be placed directly into small fluid collections but probably work better when placed beyond the leak into the upstream duct. The pseudocyst can then resolve spontaneously or be treated by endoscopic or percutaneous modalities. Since our initial series of 17 patients treated with pancreatic duct prostheses, 14 of whom resolved their fluid collections, additional studies have been abstracted confirming an 80%-90% definitive procedural efficacy with a 10%-15% minor complication and 10% recurrence rates.

In addition to pseudocysts, we have described pancreatic duct stent placement across a ductal disruption for the treatment of pancreatic ascites/pleural effusions, enteric fistulae, and amenable pancreatico-cutaneous fistulae. A recent publication by Bracher et al has confirmed that placement of S-7 Fr stents led to resolution of pancreatic ascites in 7 of 8 patients. Moreover, there was no recurrence at a mean of 14 months. Our data show absence of ascites recurrence in our originally reported patients at a mean follow-up of over 6 years.

The technical ability to place a transpapillary stent for ductal leak, however, does not mean that it is the treatment of choice in all situations. Large fluid collections, particularly those with necrotic debris, as well as disconnected glands, may best be handled with a combination of surgical and interventional radiologic techniques.

**Bile duct obstruction**

There are a plethora of miscellaneous complications of chronic pancreatitis that can be temporized endoscopically. The latter include gastric outlet obstruction or pseudo-obstruction for which a nasojejunal feeding tube or percutaneous endoscopic gastrostomy/jejunostomy tube can be placed. Bile duct obstruction, however, is the complication most commonly approached endoscopically. Given previous experience using stricture dilation and intermittent stent exchange for a variety of benign biliary stenoses, endoscopists have reported using biliary stent insertion for acute cholangitis and cholangitis as well as an attempt to preclude the biliary cirrhosis that can occur in the setting of chronic pancreatitis.

There have been multiple series addressing this complication. Early series by the Brussels and Amsterdam groups, as well as our own experience, suggest that stent placement ameliorates acute cholestasis and cholangitis. Stricture resolution, however, proved infrequent and complications including prosthesis migration and recurrent cholangitis secondary to occlusion were commonplace. A more recent series by Vilain et al reported balloon dilation and >12 months of stenting in 25 patients. Eighty percent of patients remained asymptomatic at a mean of 32 months of stent retrieval, although there were six cases of treatment-related cholangitis and a 36% rate of periprocedural pancreatitis. It is this author's experience that stenting is an excellent temporizing maneuver but that most patients who present with a cicatrized distal bile duct are better served by surgical decompression.

**Conclusions**

Given the preceding data, what can we say with certainty about endoscopic therapy for chronic pancreatitis? On the one hand, I believe strongly that endoscopic therapy should not be undertaken in isolation; access to competent interventional radiology and pancreatic surgery is essential before venturing on it. We cannot, nor should we try, drain all pseudocysts, treat all fistulae or strictures, or attempt to remove all stones endoscopically. Nor should any of these procedures be attempted by the novice.

The following issues are not yet clear: How many biliary sphincterostomies should an endoscopist do before attempting endoscopic pancreatic therapy? How many biliary stones should have been successfully removed first? How many biliary strictures successfully managed prior to attempting these maneuvers in the pancreas? There are no clear data to answer these questions. However, I personally feel that a minimum of several hundred biliary sphincterostomies, as well as concomitant biliary endotherapy sessions, should be undertaken prior to attempting pancreatic duct sphincterotomy. Small cuts and large, the use of coagulative current, and of a conducting wire have all been associated with intragang head strictures that are technically difficult to deal with and may require ultimate resection of the pancreatic head. Small stents occlude, frequently, and soon. Obstructive pancreatitis as well as pancreatic sepsis may be the consequence. Pancreatic stones, even in conjunction with ESWL therapy, are at least a lot more difficult to remove when compared to biliary calculi. A practitioner who endoscopically drains 1-2 pseudocysts per year probably shouldn't attempt endoscopic therapy.

After 15 years of performing endoscopic therapy in the pancreas, I am struck by how much I still do not know. I do know this, however: a patient's local anatomy, one's previous experience, and the alternative treatment modalities within your institution all interact to define the best interventional approach to the symptomatic patient with chronic pancreatitis. Because we can do something technically does not mean that it is invariably right. Endotherapy deserves a major role, however, in amenable patients with obstructive calculi, internal or external fistulae, and the high-risk patient with stricture-associated obstructive pancreatitis. Controlled trials, while desirable, may have less to do with the incorporation of
these approaches into one's practice than outcomes analyses and the compilation of short- and long-term cost-efﬁcacy data.

References


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