The role of endoscopy in patients with chronic pancreatitis

INTRODUCTION

Chronic pancreatitis (CP) is an inflammatory process characterized by destruction of pancreatic parenchyma and ductal structures with formation of fibrosis. Pain is the predominant symptom of CP and its origin is multifactorial. Treatment is directed toward control of symptoms and management of the structural complications. Medical therapies such as abstinence from alcohol, dietary alterations, analgesics, oral enzyme supplements, and somatostatin analogs are variably effective in relieving pain. In patients for whom medical management fails, surgical and endoscopic options are available.

Endoscopic therapy for CP was introduced more than a decade ago. Endoscopic therapy may reduce or eliminate the need for surgical procedures, may serve as a bridge to surgery in poor operative candidates, and can predict the response to surgical therapy. If endoscopic therapy is unsuccessful, surgical therapy is still a potential option for most patients.

In general, the aim of endoscopic therapy in patients with CP is to alleviate outflow obstruction of the pancreatic duct (PD) or the common bile duct. Endoscopic management should be considered as one management option along with medical, percutaneous, and surgical treatments. This guideline will review the role of endoscopy in the management of CP.

ENDOSCOPIC DIAGNOSIS OF CP

Although radiologic means to assess patients for CP exist in the form of computed tomographic (CT) scans and magnetic resonance imaging (MRI) with or without magnetic resonance cholangiopancreatography (MRCP), the principal endoscopic means of making this assessment include endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasonography (EUS). Both ERCP and EUS can establish the diagnosis of CP. ERCP allows detection of PD changes including ductal dilation, strictures, abnormal side branches, communicating pseudocysts, PD stones, and PD leaks. ERCP is highly effective at visualizing these ductal and duct-related findings, with a sensitivity for the diagnosis of CP of 71% to 93% and a specificity of 89% to 100%. The Cambridge Classification, which assesses the main PD, side branches, and intraductal abnormalities, is a widely accepted system for scoring ductal findings seen on ERCP. Unfortunately, pancreatography is imperfect and care should be taken not to overinterpret minor findings seen on ERCP. Conversely, ERCP may not detect changes of less advanced CP. When the diagnosis of CP is sought, ERCP should be reserved for patients in whom the diagnosis is still unclear after noninvasive pancreatic function testing or other noninvasive (CT, MRI) or less invasive (EUS) imaging studies have been performed.

Although ERCP can be used to obtain information about ductal anatomy to define the levels and degree of obstruction and the presence of strictures and stones, it does not provide information regarding the surrounding pancreatic parenchyma. EUS can provide high-resolution images of both the ductal structures and the parenchyma. EUS allows visualization of parenchymal changes such as alternating hyperechoic and hypoechoic regions (suggesting increased lobularity), hyperechogenic foci and strands, focal areas of hypoechoic tissue, and the presence of cysts. Ductal changes seen at EUS include hyperechogenic duct walls, dilation or irregularity of the main PD, PD stones, and visible side branches.
accuracy of EUS to diagnose CP increases as more of these distinct abnormalities are identified, and EUS may also predict the severity of the disease.\textsuperscript{11,12} There is good interobserver agreement in the diagnosis of CP by EUS, and EUS may detect early CP in a reliable manner compared with ERCP.\textsuperscript{9,10} Although EUS-guided tissue acquisition may allow the histologic diagnosis of CP, it is not recommended for routine use.\textsuperscript{11,12} It may be helpful, however, in diagnosing autoimmune pancreatitis.\textsuperscript{13,14}

**PD STRICTURES**

Benign strictures of the main PD are generally due to inflammation or fibrosis around the main PD. Because ductal obstruction may lead to pain or acute pancreatitis superimposed on CP, endoscopic therapy with balloon dilation or PD stents for the treatment of dominant PD strictures has been evaluated. Stricture dilation may be required to facilitate stent placement or stone removal.

Data regarding the role of endoscopic therapy in treating main PD strictures are inconsistent, and studies addressing this role are heterogeneous. Some authors have reported high success rates (75% to 94%) in treating pain by stenting of PD strictures,\textsuperscript{15-19} although a recent well-designed study was not able to duplicate these results.\textsuperscript{20} In addition, although some authors have correlated clinical improvement to a decrease in the diameter of the main PD upstream to the stent,\textsuperscript{15,16} others have not.\textsuperscript{20} Pancreatic stents are prone to occlusion and patients undergoing endoscopic therapy for PD strictures may require frequent stent exchanges. Symptomatic improvement may persist after pancreatic stent removal despite persistence of the stricture.\textsuperscript{17,18} These data suggest that resolution of the stricture is not a prerequisite for symptomatic improvement. Confounding the literature on PD stent therapy are other therapies performed at the time of stent placement (eg, pancreatic sphincterotomy, pancreatic stone removal) and the tendency of the CP pain to wax and wane and decrease with time as deterioration of pancreas function occurs.\textsuperscript{21} The optimum duration of stent placement, stent number and diameter, and degree of balloon dilation are not known.

Complications related directly to endoscopic therapy of PD strictures include pain, pancreatitis, stent occlusion, proximal or distal stent migration, duodenal erosions, pancreatic infection, ductal perforation, stone formation, and bleeding (if sphincterotomy is performed). In addition, PD stents may produce ductal damage, including strictures or focal areas of chronic pancreatitis. These changes may improve with time\textsuperscript{22,23} and are more likely to be inconsequential in patients with advanced chronic pancreatitis than those with a relatively normal pancreas.

Patients with CP have an increased risk of pancreatic cancer. The endoscopist must maintain a high index of suspicion of underlying cancer whenever treatment of a pancreatic duct stricture is undertaken, and appropriate tissue sampling should be obtained.\textsuperscript{24} Physicians should have a low threshold to perform EUS to more closely examine the pancreatic parenchyma, with fine-needle aspiration of any areas felt to be suspicious for possible malignancy. Obtaining serum CA 19-9 levels may be helpful in patients considered to harbor a malignancy, although levels can be elevated in patients with chronic pancreatitis in the absence of cancer.

**PANCREATIC DUCT STONES**

Obstructing pancreatic stones may contribute to abdominal pain or acute pancreatitis in patients with CP. ERCP provides direct access to the PD for evaluation and treatment of symptomatic PD stones. In one randomized trial of endoscopic and surgical therapy, surgery was superior for long-term pain reduction in patients with painful obstructive CP.\textsuperscript{25} However, because of its lower degree of invasiveness, endotherapy may be preferred, reserving surgery as second-line therapy for patients in whom endoscopic therapy fails or is ineffective. PD stone removal can be challenging. Frequently the stone configuration and size coupled with PD strictures occludes the lumen. Adjuvant endoscopic approaches such as stricture dilation, intraductal lithotripsy, and pancreatic sphincterotomy may be needed. Even when accessible, PD stones (which are often dense and hardened) may be impacted, requiring extracorporeal shock wave lithotripsy (ESWL) to fragment the stones before endoscopic removal can be achieved. Patients frequently require several ESWL sessions to achieve stone clearance from the duct.\textsuperscript{26} Although some investigators have reported high success rates with this technique\textsuperscript{27} (with or without pancreatic stents), others have had much less impressive results, with improvement in pain seen in as few as 35% of patients, whereas other large series have reported that, despite successful ESWL, most patients experience no improvement in pain.\textsuperscript{20,26} A recent large review of the ESWL literature concluded that ESWL can result in complete duct clearance in as many as 50% of patients and in PD decompression.\textsuperscript{29} Intraductal lithotripsy guided by pancreatoscopy has also been used to fragment PD stones.\textsuperscript{30}

Case series have shown mixed results with regard to improvement in pain with pancreatic endotherapy. Some encouraging short-term and long-term follow-up to 5 years showing improvements in pain (77%-100% and 54%-86%, respectively) have been reported.\textsuperscript{31,32} One large series of 1000 patients with CP with long-term follow-up found that 65% of patients with strictures, stones, or strictures and stones had improvement in pain after endotherapy. Twenty-four percent of patients ultimately required some form of surgery to treat their CP.\textsuperscript{33} Others have found similar outcomes, with clinical improvement rates of approximately 70%.\textsuperscript{29} Although modest, these success rates
are acceptable in the context of a traditionally difficult-to-manage group of patients.

Although most studies suggest that endotherapy does not improve pancreatic function, one recent MRCP-based secretin study suggests that pancreatic exocrine function can improve after endoscopic therapy.40

**PANCREATIC DUCT LEAKS**

PD disruptions or leaks can occur as a result of chronic pancreatitis from a blowout upstream to obstructing strictures or stones. Pancreatic leaks can result in pancreatic ascites, pleural effusions, pseudocyst formation, and internal and external pancreatic fistulas. PD leaks can often be treated with endoscopic placement of transpapillary stents in a manner similar to the use of biliary stents to close biliary duct leaks.35 Endoscopic therapy is successful in closing the leak in approximately 60% of patients.36,37 Factors associated with a better outcome in duct disruption include a partial disruption, successfully bridging the disruption with a stent, and longer duration of stent placement (approximately 6 weeks). There are no comparative studies of surgical, medical, and endoscopic therapy for treatment of PD leaks.

**PANCREATIC PSEUDOCYSTS**

Pancreatic pseudocysts arise as a complication of CP.38,39 Pancreatic pseudocysts complicate the course of CP in 20% to 40% of cases. In general, the indications for drainage of a pseudocyst are symptom driven. Pseudocyst size itself is not an indication for drainage. Pseudocyst drainage should be considered for symptomatic lesions (abdominal pain, gastric outlet obstruction, early satiety, weight loss, or jaundice), infection, or progressive enlargement, even if asymptomatic. Special care must be taken to avoid drainage of cystic neoplasms, duplication cysts, and other noninflammatory fluid collections. EUS can be especially helpful with this determination.40 A guideline on the endoscopic management of pseudocysts has been previously published.39

**BILIARY OBSTRUCTION IN CHRONIC PANCREATITIS**

Distal common bile duct strictures have been reported to occur in 2.7% to 45.6% of patients with CP. These strictures can occur from inflammation, fibrosis, or compression from a pseudocyst or PD stone.5 Because longstanding biliary obstruction can lead to secondary biliary cirrhosis or recurrent cholangitis, biliary decompression is recommended in patients with clinically significant obstruction (eg, cholestasis or jaundice). Surgical biliary bypass is the standard approach for managing chronic common bile duct strictures. Endoscopic therapy has been used as an alternative to surgery.41 Plastic biliary stents are a useful short-term treatment of these CP-induced common bile duct strictures in the setting of cholestasis, jaundice, or cholangitis and may be used as a long-term treatment approach in poor surgical candidates. Unfortunately, long-term success rates are as low as 10% in some studies.42,43 Patients with calcifications of the pancreatic head have the poorest response to endoscopic therapy, with as few as 7.7% of patients achieving clinical success at 1 year when single large-bore stents are used.43

Balloon dilation of biliary strictures in the setting of CP followed by insertion of multiple large-bore plastic stents in an attempt to provide a more effective dilation is a relatively new approach. Unfortunately these strictures tend to be recalcitrant and the restenosis rate after stent removal is high. Despite these drawbacks, the use of multiple stents with frequent stent exchanges and balloon dilations over a long period of time (up to 1-2 years) may be more efficacious than single stents for the treatment these strictures.44,45 Patient selection is critical in this setting because patients need to return frequently for stent changes. Poor compliance with follow-up can lead to biliary sepsis from stent occlusion.46

Uncovered self-expanding metal stents (SEMS) have been used to manage biliary strictures in patients with CP who are poor operative candidates.47,48 At follow-up approaching 3 years, good stent patency has been reported, and most subsequent stent occlusions can be managed nonoperatively, although uncovered stents are not removable. Some patients treated with this approach may still ultimately require surgery. The placement of short-length stents does not appear to preclude operative intervention in the future. More recently, some authors have used covered SEMS because of their potential removability, but results have been mixed.50,51 The routine use of biliary SEMS for this indication is not recommended at this time.

As in the management of PD strictures, the coexistence of pancreatic cancer must be considered when endoscopic therapy of a biliary stricture is undertaken in the setting of CP.

**EUS-GUIDED CELIAC PLEXUS BLOCKADE**

The celiac plexus sits astride the celiac artery and mediates pain impulses from, among other abdominal structures, the pancreas. Chronic inflammation in CP can lead to debilitating pain, although pain in this setting may be multifactorial in origin. Long-term pain management in these patients can be difficult. Patients with CP are rarely considered for celiac plexus neurolysis (ablation) because of the risks of injecting absolute alcohol, which have been addressed in another guideline.52
EUS-guided celiac plexus blockade can be performed in patients with intractable pain from CP. This involves the injection of an anesthetic agent (ie, bupivacaine) in combination with a steroid agent (ie, triamcinolone) in an effort to produce short- to medium-term cessation of pain (typically less than 24 weeks). In the few direct comparisons available, EUS-guided celiac plexus blockade was less expensive and more effective and had a longer duration of action that CT-guided celiac plexus blockade. Because only 50% of patients can be expected to respond to any form of celiac plexus blockade, many patients will still require analgesic medication.  

**SUMMARY**

- ERCP and EUS are useful for the diagnosis of CP and associated pancreatic ductal complications (B).
- ERCP for the diagnosis of CP should be reserved for patients in whom the diagnosis has not been established by noninvasive or less-invasive studies (C).
- Endoscopic therapy of pancreatic ductal obstruction can provide short-term relief of abdominal pain and long-term relief in some patients (B).
- ERCP is effective for the short-term treatment of common bile duct obstruction resulting from CP (B) and long-term treatment in poor operative candidates (C).
- Endoscopically placed pancreatic duct stents are effective for the nonsurgical management of pancreatic strictures, duct leaks, and disruptions (B).
- EUS-guided celiac blockade can effectively provide short-term pain relief in patients with CP (B).

**REFERENCES**


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