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Endoscopic Intervention in Chronic Pancreatitis

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Abstract

Chronic pancreatitis is an irreversible and progressive disorder of the pancreas characterized by inflammation, fibrosis and scarring. Exocrine and endocrine functions are lost often leading to chronic pain. Its etiology is multifactorial, although alcoholism is the most important risk factor in adults. If chronic pancreatitis is suspected, computed tomography with contrast is the best imaging modality. Although narcotics and antidepressants provide the greatest pain relief, more than half of all patients eventually require intervention by endoscopy or surgery.

Endoscopic retrograde cholangiopancreatography (ERCP) is an effective alternative for a variety of therapies for treating benign and malignant diseases of the pancreas. In the last 50 years, endoscopic treatment has evolved to become the first-line therapy for most acute and chronic inflammatory diseases of the pancreas. As this field progresses, it has become important for gastroenterologists to keep their knowledge of indications for this procedure up-to-date and to perform a sufficient volume of procedures to allow them to manage complex pancreatic endoscopic therapy. Keeping up-to-date should include an understanding of alternative approaches to pancreatic diseases including medical treatment, therapy guided by endoscopic ultrasound, management of symptomatic stenoses and stones, interventions on the celiac plexus, and drainage of pancreatic pseudocysts.

Keywords

Chronic pancreatitis, endoscopic cholangiography, pancreatic stones, pancreatic stenosis, pancreatic pseudocyst, celiac pleural block.

INTRODUCTION

Chronic pancreatitis (CP) is diagnosed more and more frequently in medical practice. It is estimated that the incidence of CP varies between 5 and 14.4 cases per 100,000 inhabitants. (1, 2) Intractable abdominal pain and associated morphological anomalies in the pancreatobiliary system are the main determinants of interventionist endoscopic treatment of CP. (3) There are multiple pain mechanisms in CP, and recent experimental evidence suggests that pancreatic ductal hypertension can activate pancreatic stellate cells which in turn can generate oxidative stress and subsequent inflammation. (4) One source of pain is the sum of chronic inflammation and oxidative stress which induces nociception, mechanical allodynia and inflammatory hyperalgesia, pancreatic neuropathy, peripheral neuroplasticity and central neuroplasticity. (5) In some patients, there are structural abnormalities within the duct or pancreatic parenchyma that may be responsible for, or that may perpetuate, this process. Such abnormalities are often the target for endoscopic or surgical intervention, but correction does not always translate into clinical improvement. This underscores the multimodal nature of the pain syndrome of these patients. Decompression can be performed using endoscopic and surgical approaches, but an endoscopic approach is currently recommended as the first

line modality by the European Gastrointestinal Endoscopy Society (ESGE). (6)

Before any endoscopic treatment is indicated, a meticulous morphological evaluation of the major pancreatic duct (MPD) (also known as the Wirsung duct) is mandatory for assessing the magnitude of the disease and local anatomical alterations that suggest neoplasia. Pancreatic cancer should be ruled out especially in Caucasian women patients over 50 years of age who have jaundice, manifest exocrine insufficiency, and who do not have any pancreatic calcifications. (7) The size and distribution of pancreatic ductal stones can be best assessed by computerized axial tomography (CT scan) although transabdominal ultrasound also provides a fairly good evaluation. Pancreatic ductal stenosis, biliary stenosis and anatomical variants such as pancreas divisum are best identified with magnetic resonance cholangiopancreatography (MRCP). MRCP also has advantages over endoscopic ultrasound (EUS) and CT scans for differentiating pancreatic pseudocysts (PP) from intrapancreatic necrosis (walled-off necrosis) in patients with CP who have had recent acute exacerbations. (8)

CP is responsible for extensive health care use and is associated with disproportionately high socioeconomic costs. (9) Clinical management of this disease is often challenging because it frequently involves prescription of highly regulated opioids for pain control which are associated with numerous side effects and dependency problems. Current approaches to endoscopic CP treatment aim at removing stones that obstruct the pancreatic duct, pancreatic duct stenosis, PP drainage, celiac plexus block (CPB) and benign biliary stenoses. Each technique and its contribution to treatment of CP will be reviewed.

INDICATIONS AND CONTRAINDICATIONS FOR ENDOSCOPIC TREATMENT OF CHRONIC PANCREATITIS

Intractable pain is the most common indication for endoscopic treatment of the pancreas in patients with CP, but the modality of choice depends on morphology:

- Small stones can be extracted using endoscopic retrograde cholangiopancreatography (ERCP) with a pancreatic sphincterotomy using balloons and a Dormia basket. Calculi of more than 5 mm can be best fragmented by extracorporeal shock wave lithotripsy (ESWL) with or without placemtn of a pancreatic duct stent. (10)
- Currently, ESWL is the ESGE's recommended first option. (6)
- Contraindications for ESWL include multiple calculi in the MPD, isolated calculi in the pancreatic tail, multiple MPD restrictions, moderate to massive ascites, pancreatic pseudocysts and masses in the pancreatic head. (11)
- Pancreatic duct stenosis can be treated by pancreatic sphincterotomy and stenting with or without dilation.
- PP should be treated when there is an infection, symptomatic intracystic hemorrhaging, biliary obstruction, obstruction of the gastric outlet, early satiety, abdominal pain, weight loss and increased size of a pseudocyst. It has been suggested that prophylactic treatment of asymptomatic pseudocysts can be considered when the main vessels are compressed, when there is a pancreaticopleural fistula, when a pseudocyst that measures more than 5 cm does not become smaller after 6 weeks, and when a pseudocyst's wall is more than 5 mm thick. (12)
- EUS can be used for drainage of the dilated MPD using rendezvous techniques when transpapillary access is not possible. (13)
- Treatment of pain refractory to standard intervention can be tried with EUS-guided CPB. (14)

ENDOSCOPIC TREATMENT OF CALCULI IN THE PANCREATIC DUCT

Pancreatic duct stones are biomineral concretions that can obstruct pancreatic ducts thereby increasing pancreatic duct pressure which can activate the inflammatory process that causes fibrosis. The objective of endoscopic treatment of calculi is to relieve obstruction by removal of stones (Figure 1). (15)

Techniques to fragment and eliminate pancreatic duct stones that have evolved over the years may require intraductal access through mechanical lithotripsy, electrohydraulic lithotripsy, laser-guided lithotripsy or may require an extracorporeal intervention such as ESWL. (16)

Intraductal mechanical lithotripsy is performed with an endoscopic mechanical lithotripter. This technically challenging procedure has a high rate of complications and is rarely used today. Electrohydraulic lithotripsy is performed under direct pancreatoscopic visualization using a mother-child endoscopic system. It has the advantage of supplying energy to a focused area of the calculi. (17) Although technical modifications such as single operator use of the SpyGlass® Direct Visualization System and lithotripsy using a holmium laser have evolved over time, studies published in the literature are limited. (18) In addition, availability, high costs and operator expertise limit widespread use of these techniques.

ESWL is currently the first-line modality for treating painful obstructive pancreatic duct stones that measure more than 5 mm, particularly those located in the pancreatic head and body regions. (6) The objective is to reduce the calculi to fragments smaller than 3 mm which are then usually removed with ERCP and pancreatic sphinctero-

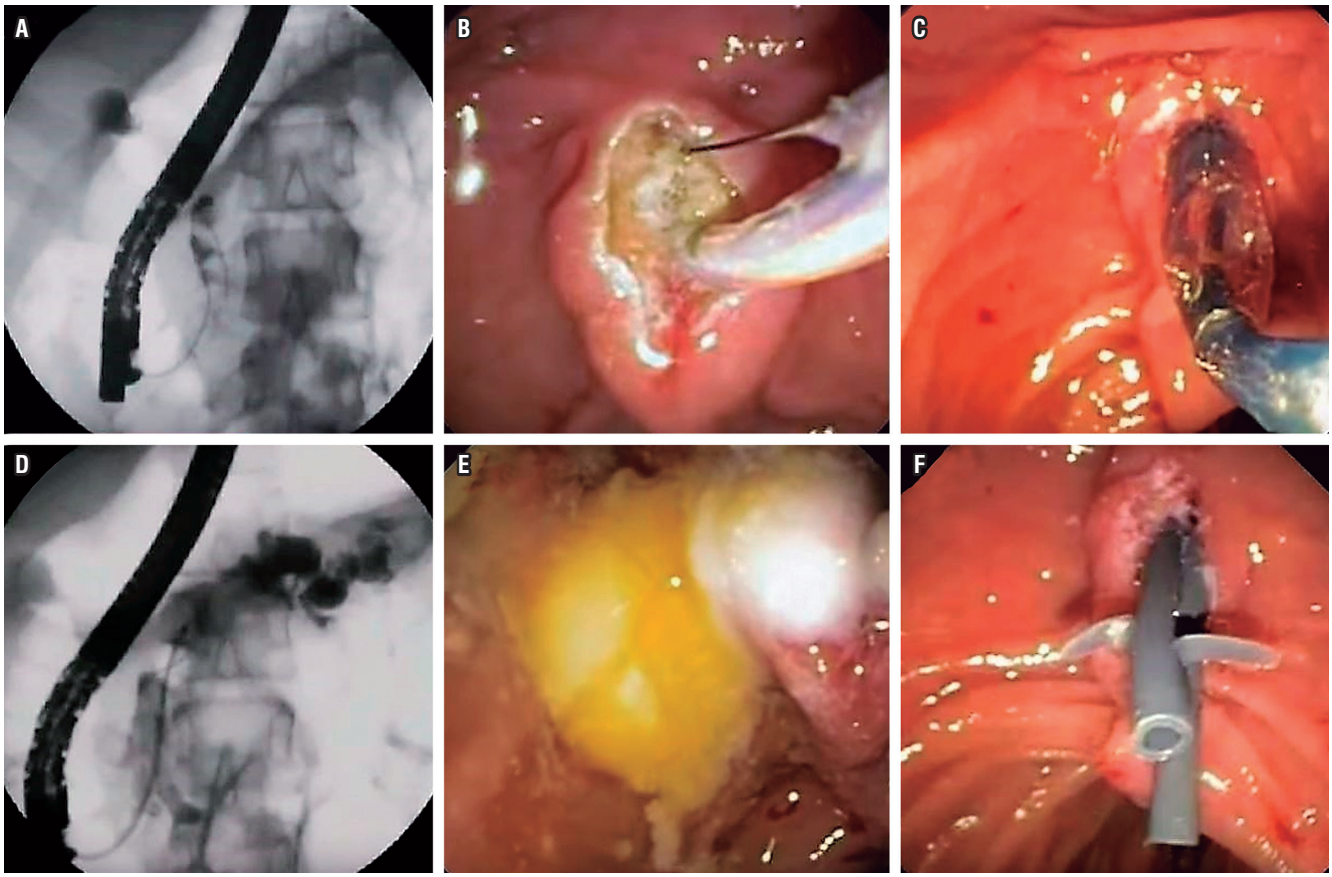

Figure 1. Management of calculi in the MPD in a patient with CP. **A.** Pancreatography shows several calculi in the pancreatic head. **B.** Pancreatic sphincterotomy. **C.** Dilation with sphincterotomy balloon. **D.** Extraction balloon passage. **E.** Extracted pancreatic stones. F. Ten cm passage of two 7 Fr pancreatic stents.

tomy. A concomitant pancreatic ductal stent can be used to treat local stenosis.

For radiolucent calculi, a pancreatic sphincterotomy with placement of a naso-pancreatic drainage tube prior to ESWL can help accurately guide ESWL. (10) When there are multiple duct calculi, the calculi that is closest to the orifice of the MPD should be the main objective. Isolated intraductal stones located in the tail do not need to be treated with ESWL because these concretions are unlikely to result in enough ascending ductal pressure to cause pain. In addition, attempts to fragment duct stones in the tail could cause a collateral splenic lesion.

Derivative surgery is an alternative for managing pain and achieving decompression of ducts. It compares favorably with endoscopic treatment without ESWL. However, due to the morbidity associated with surgical procedures such as Frey's surgery (Figure 2), this is generally reserved for patients for whom non-surgical treatments have failed. (19)

ENDOSCOPIC TREATMENT OF STENOSIS OF THE MAJOR PANCREATIC DUCT

Stenosis is found in the MPD in up to 18% of patients with CP, and the priority is to rule out malignancy. Similar to the principle and problems created by obstructive stones, it is thought that these stenoses contribute to symptoms by causing pancreatic ductal hypertension. For this reason therapy aims at improving these narrow segments in order to decompress the ductal system. The approach usually involves pancreatic sphincterotomy followed by dilation of the stenosis and placement of a stent in the pancreatic duct (Figure 3). Immediate relief of pain with this treatment has been reported in 65% to 95% of cases, and sustained relief of pain has been reported in 32% to 68% of patients. (20)

Currently, the placement of a single 10 Fr polyethylene stent with successive changes yearly, even in the absence of

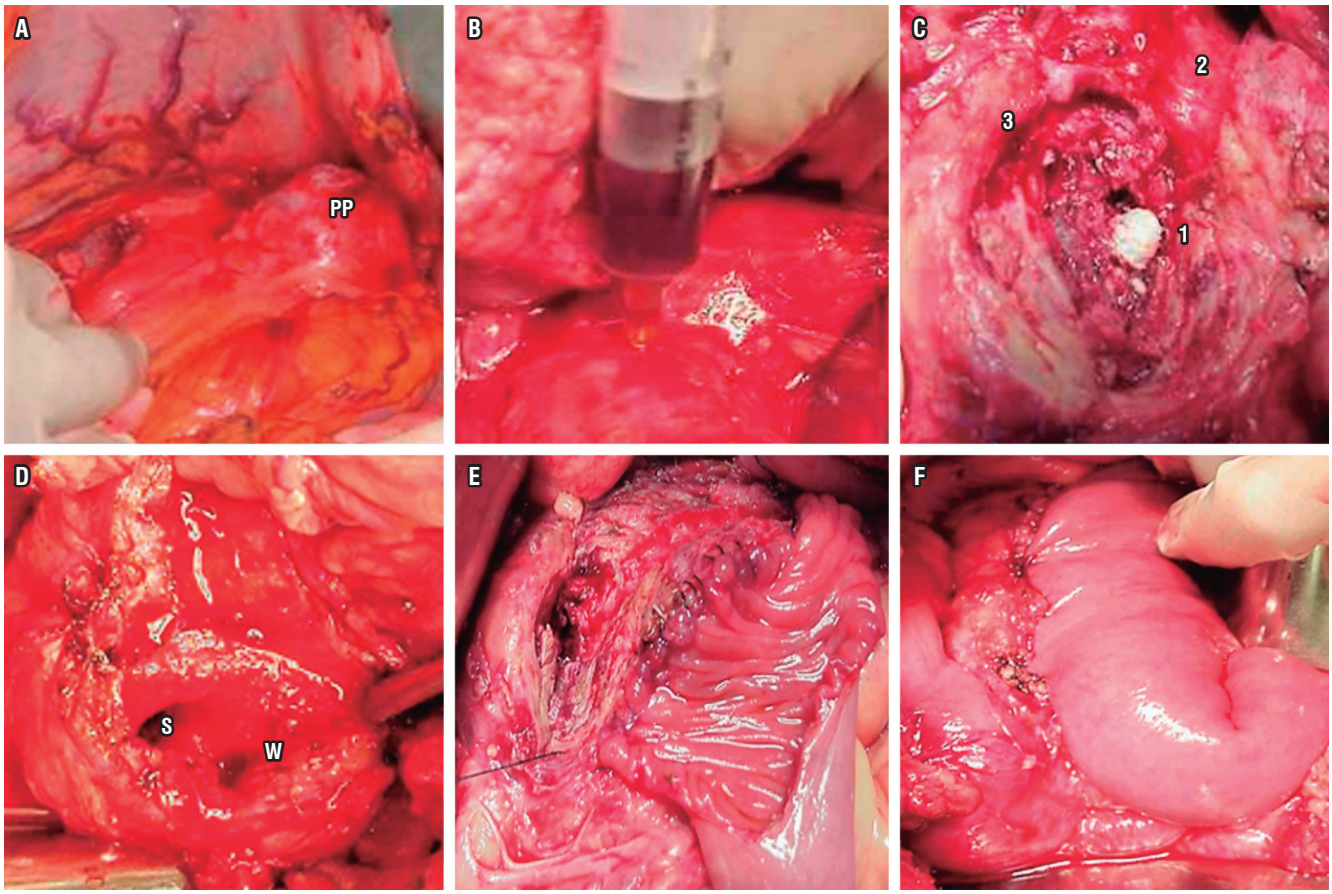

Figure 2. Frey's surgery for CP. **A.** Transcavity approach to PP. **B.** Puncturing anterior pancreatic body to locate main pancreatic duct. **C.** Calculi (1) in the MPD (2), another calculus in the Santorini duct (3). **D.** Open MOD (W) and Santorini duct (S) in the pancreatic head. **E.** Partial anastomosis of the jejunal loop isolated in the anterior pancreas. **F.** Completed anastomosis in two planes.

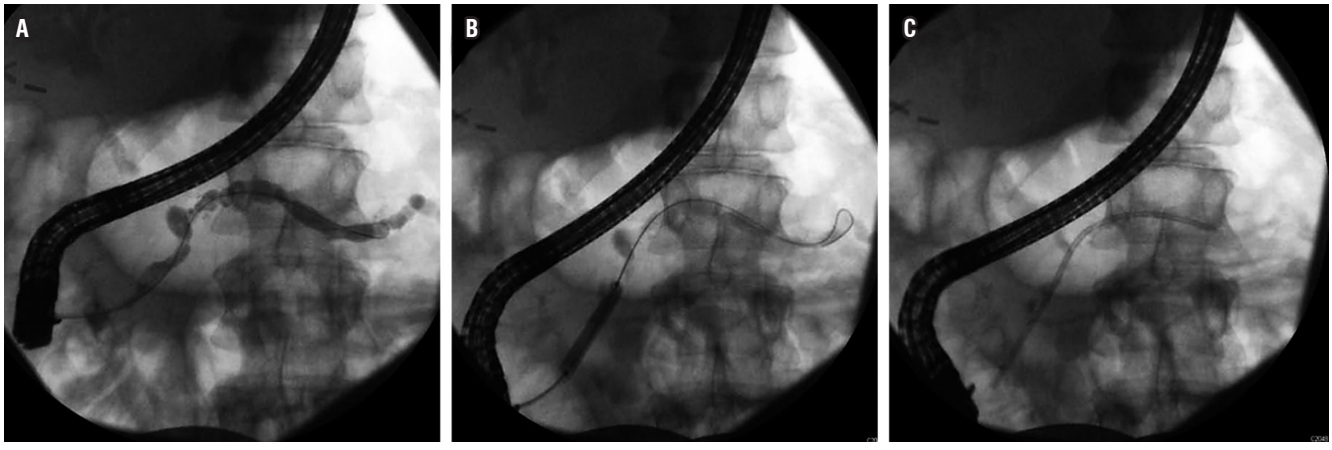

Figure 3. Management of benign stenosis with dilation and stent in a patient with CP. **A.** Stenosis in the head of the pancreas. **B.** Balloon dilation of stenosis. **C.** Passage of pancreatic stent.

symptoms, is the first-line treatment for dominant stenosis of the MPD. (6)

Although straight plastic stents and pig tail stents have been widely used to treat pancreatic duct strictures, there is still no ideal stent. So far, several modifications have been made in pancreatic stent technology: S type stents, stents with lateral flaps, bumpy stents, and even biodegradable stents. (21) Various stents have been tested in animal models and in short-term clinical trials with small sample sizes. Data on the validation of these results and long-term data on efficacy and safety are needed before these stents can be used routinely.

One technique under study for treating main duct stenoses that persist for more than 12 months after treatment with a single plastic stent is the deployment of multiple plastic stents placed side by side simultaneously. (22)

An international multicenter collaborative study has shown that minimally invasive pancreatic duct drainage by EUS in pancreatic stenosis after failed ERCP is safer than surgery and even more effective. (23)

ENDOSCOPIC TREATMENT OF PANCREATIC PSEUDOCYSTS

PPs are collections of encapsulated pancreatic juice with well-defined inflammatory walls. They develop in 20% to 40% of patients with CP. Unlike PP of acute origin, those of CP patients rarely remit spontaneously. Intervention is indicated when symptoms of abdominal pain, nausea, vomiting, early satiety, weight loss or gastric or biliary obstructions or infections persist. Some treatments have been proposed for large, persistent asymptomatic collections, for those that have thick walls (recognizing it is not common to be asymptomatic with cysts> 6 cm), for those associated with fistulas, for changes of the main pancreatic duct, and for calculi of the pancreatic duct. Endoscopic drainage of pseudocysts can be performed by transmural and transpapillary approaches. (24)

It is important to evaluate abnormal ductal anatomy, including ductal leaks and whether or not there is communication with the pseudocyst, with an MRCP or ERCP prior to treatment. An increase in the size of a pseudocyst in images suggests ductal communication with the pseudocyst. Ductal obstruction should be managed prior to endoscopic treatment of pseudocysts in order to achieve a higher success rate and avoid recurrence. Similarly, if arterial pseudoaneurysms are detected, they should be embolized before endoscopic treatment because of the high mortality rate from hemorrhaging of pseudoaneurysms close to pseudocysts. (25)

Transpapillary drainage during ERCP is most useful for small, solitary, communicating pseudocysts located in or near the head and body of the pancreas. This type of drainage is also feasible and useful for treating large and multiple PPs although the results are no better or worse than those of transmural drainage. (26)

Transmural drainage can be done by creating communication between the pseudocyst and the stomach (cystogastrostomy) or the pseudocyst and the duodenum (cystoduodenostomy). After puncture, at least two double pig tail plastic stents should be placed through the puncture to keep the aperture between the pseudocyst and the stomach or duodenum open. The stent must not be removed for at least two months following insertion, and a cross-sectional image must be obtained in order to assess whether the cyst has resolved before the stent can be removed. (27)

If there images show a sectioned MPD, the stent should be kept in situ indefinitely to achieve the best results. An attempt to pass the stent through the rupture in the duct is also associated with long-term success. (28)

Before the use of EUS to guide pseudocyst drainage, compression of the gastric or duodenal wall was essential because puncture and drainage was performed through the wall. Under linear echoendoscopic guidance, drainage can be performed with superior results even for pseudocysts that do not bulge and even beyond the gastric or duodenal lumen. (29) EUS can also help delimit an avascular area for puncture which is especially helpful for patients with extensive collateral vascularization secondary to portal hypertension. EUS also helps distinguish pseudocysts from cystic neoplasms. (30)

ENDOSCOPIC TREATMENT OF BILIARY STENOSIS IN PATIENTS WITH CP

Benign biliary stenosis is found in many patients with CP. The clinical estimates of prevalence vary a great deal, ranging from 3% to 46%. (31) In general, benign biliary stenoses present as fibrous calcified circumferential strictures that usually develop within the pancreatic portion of the common bile duct. This makes it possible for biliary obstruction to develop from extrinsic compression related to pancreatic edema and fluid collection. When a stenosis is identified, it is important to exclude malignancy. Patients may experience pain, nausea, weight loss, jaundice, pruritus, and 10% may progress to development of cholangitis or biliary cirrhosis. (32)

Cholangitis is a clear indication that endoscopic intervention should be used to treat a patient with CP, but it is less clear whether it should be used as a preventive procedure. There are numerous observations of patients with cholestasis due to benign biliary stenosis related to CP who were successfully managed without biliary drainage. Nevertheless, it is unclear how to predict who will progress

or develop other complications or whether liver fibrosis will return after successful biliary drainage. The main indications for endoscopic intervention have been adopted from surgery. In addition to the presence of symptoms, indications include secondary biliary cirrhosis, stones in the common bile duct, progression of biliary stenosis based on increased proximal dilation of the biliary ductal, jaundice that persists for more than one month, and alkaline phosphatase greater than two to three times the upper limit of normal. (6)

EUS GUIDED PROCEDURES AFTER ERCP FAILS

The development of linear EUS has allowed new approaches for drainage of the pancreatobiliary system when conventional ERCP fails.

After the initial description by Harada (33), several other studies have evaluated the feasibility and efficacy of pancreatobiliary drainage directed by EUS. The fundamental principle is to use EUS to guide a large gauge needle to perforate the MPD through the gastric or duodenal wall. Once successful access to the MPD is achieved, the duct can be drained using rendezvous techniques or the transmural route. (34) In view of the technical challenge posed by EUS guided rendezvous procedures and the high frequency of complications, this procedure is currently recommended only for selected patients at tertiary care centers which have the appropriate infrastructure and experienced specialists. (35)

EUS GUIDED CPB

CPB is a treatment option aimed at disruption of the afferent pathway of pain transmission from the pancreas. (36) It typically involves injecting a mixture of local anesthetic and a corticosteroid into the celiac plexus. This is different from celiac plexus neurolysis with an ethanol injection, which should not be used to treat benign pancreatic disease. (37) Steroids are used as a substitute for ethanol to prolong the effect of the treatment. The combination of bupivacaine and triamcinolone was also the regimen selected in the largest prospective study on EUS guided CPB. (38)

CPB can be performed percutaneously, but EUS guided CPB has better results and lower risks of complications such as paraplegia which is associated with the percutaneous technique. (14) In view of its dubious efficacy (short-term pain relief, if any) and frequent complications, CPB should be seen as rescue or bridge therapy for patients who do not respond to conventional medical and endoscopic treatment and who are not ideal candidates for surgery. (39) Although EUS guided celiac ganglia neurolysis with absolute alcohol is justified in cases of pancreatic cancer, it should be avoided in cases of CP since the fibrosis resulting from the alcohol injection could hinder subsequent surgery.

Comparative randomized trials have shown that EUS-guided CPB is superior to both fluoroscope-guided CPB and CT-guided CPB in terms of both pain relief and patient preference. Improvement of pain can be expected in 50% to 60% of patients treated with EUS-guided CPBs, but improvement does not usually persist, so many the procedure's benefits disappear after several months. Some patients may respond to sequential CPB, but this management strategy has not been not proven, and risk accumulates with each intervention. (12)

COMPLICATIONS

Although mechanical and electrohydraulic intraductal lithotripsy procedures are associated with increased risk of complications, ESWL is a relatively safe procedure. The usual complications of ESWL include acute pancreatitis, splenic lesions, petechiae, hemorrhaging, cobble stone patterns and perforations. Acute pancreatitis is the most important and occurs most frequently. A recent study of 1,470 procedures found that ESWL had a general complication rate of 6.7%. The study documented an odds ratio (OR) of 1.28 for the development of post-ESWL complications in the presence of pancreatic divisum and the interval between PC diagnosis, respectively. Male gender emerged as a possible independent protective factor against moderate to severe complications, with an OR of 0.19. (40)

Common problems encountered with pancreatic stents include migration and obstruction. Pancreatic stent patency is usually between 6 and 12 months. (41)

Complications of endoscopic drainage of pseudocysts include hemorrhaging, infection, and retroperitoneal leakage. Complications occur in approximately 4% of patients, although mortality is usually low (0.5%). (42) Complications such as hemorrhaging and ruptures are minor with the transpapillary method, but the risk of infection is greater.

Complications of CPB commonly include transient diarrhea, exacerbation of pain, hypotension, and occasional infections. Death is rare. (43)

RESULTS

Extracorporeal Shock Wave Lithotripsy (ESWL)

The effectiveness of ESWL is usually measured in terms of complete stone fragmentation, stone removal and pain relief. Recently, it has been shown that solitary and low density calculi are independent predictors of complete clearance by ESWL. (44) Table 1 lists studies that have

Table 1. 21st century studies showing the results of ESWL with or without ERCP to relieve pain and clear calculi from the major pancreatic duct in cases of CP

Author/year	n	Months	Treatment	Initial relief % (total relief %)	Clearance (%)
Brand, 2000 (45)	48	7	ESWL + ERCP	82	44
Kozarek, 2002 (46)	40	30	ESWL + ERCP	80	ND
Fernbacher, 2004 (47)	125	29	ESWL + ERCP	(48)	64
Delahaye, 2004 (48)	56	173	ESWL + ERCP	85 (45)	48
Iniu, 2005 (49)	237 318	44	ESWL + ERCP ESWL	91	73 70
Dumonceau, 2007 (50)	29 26	52	ESWL + ERCP ESWL	52	ND ND
Seven, 2012 (51)	120	51	ESWL + ERCP	51	ND
Tandan, 2013 (52)	636	96	ESWL + ERCP	96	77
Vaysse, 2016 (53)	91 41	6	ESWL + ERCP ESWL	76	ND
Korpela, 2016 (10)	83	53	ESWL + ERCP	89 (73)	ND

ND: no data.

reported complete removal of calculi from the duct and pain relief in response to ESWL with or without ERCP.

A study of cohort of 636 patients by Tandan has recently demonstrated complete pain relief in 68.7% of patients followed up for two to five years and 60.3% of patients followed up for more than five years after ESWL. (52) Complete clearance of the ducts was observed in 77.5% and 76% of patients in the intermediate and long-term follow-up groups, respectively. Although stones recurred 14.1% of patients in the intermediate follow-up group and 22.8% in the long-term group, none of the patients in the long-term follow-up group required repetition of ESWL, and only 3.8% of the patients in the intermediate follow-up group did. This study suggests that when ESWL is performed when stones are first diagnosed, pain relief is likely to persist for a longer time.

A study of 120 patients by Seven et al. demonstrated pain relief in 85% of patients after a mean follow-up time of 4.3 years. (51) Complete pain relief was seen in 50% of the patients, and there were significant improvements in quality of life scores (visual analogue scale 7.3 [2.7] versus 3.7 [2.4], p <0.001). The proportion of patients without pain after four years of follow-up was significantly higher than for those who underwent surgery (61% vs. 21%, p = 0.009). The longest follow-up period in this study was more than 7 years.

A study by Choi et al. has shown that the use of secretin before ESWL results in greater elimination of stones. (54) That study found that intravenous administration of 16 μg of secretin before ESWL resulted in 63% stone clearance compared to 46% when secretin was not used. Multiple logistic regression suggested that the use of secretin and pancreatic stenting prior to ESWL are independent predictors of complete or near total clearance of the MPD.

Stenting the Pancreatic Duct to Treat Stenosis

Table 2 lists the most important 21st century studies that have evaluated the role of the pancreatic duct stents for treating stenosis of the MPD.

Long-term clinical success after stent placement in MPD stenosis is measured by the absence of pain one year after stent removal. An additional stent is not necessary if the contrast has been eliminated one or two minutes prior to the anastomosis and if a 6 Fr catheter can easily pass through the stenosis. (11)

Pancreatic stenting is technically successful in 85% to 98% of cases and is associated with immediate pain relief in 65% to 95% of patients. Pain relief was maintained for 32% to 68% of patients in 14 to 58 months follow-ups. (66) A recent study of 17 patients who underwent endoscopic pancreatic stenting found that 57% remained completely free of pain (without relapse) after 5 years. (64)

It has been shown that the placement of multiple plastic stents to treat pancreatic stenoses relieved pain in 84.2% of cases and had technical and functional success rates of 100% and 94.7%, respectively. Stent migration and reoperation were observed in 10.5% and 15.8% of cases, respectively. (67)

The use of metal stents was associated with 100% technical and functional success. Although 85.2% of patients did not present pain in the short-term follow-up, complications were observed in 26.8%. These included stent migration in

Table 2. 21st century studies with management by endoscopic cholangiography of pancreatic stenoses with stents in patients with CP

Author/year	n	Months	Type of stent	Relief of stenosis/pain (%)	Need for surgery (%)
Morgan, 2003 (55)	25	ND	Plastic	70/65	ND
Vitale, 2004 (56)	89	43	Plastic	ND/68	12
Eleftherladis, 2005 (57)	100	69	Plastic	ND/62	4
Ishihara, 2006 (58)	20	21	Plastic	40/90	ND
Weber, 2007 (59)	17	24	Plastic	ND/83	ND
Park, 2008 (60)	13	ND	Metal	100/ND	ND
Moon, 2010 (61)	32	ND	Metal	100/ND	0
Seza, 2011 (62)	20	36	Plastic	ND/85	0
Giacino, 2012 (63)	10	19	Metal	100/60	0
Weber, 2013 (64)	17	60	Plastic	ND/57	7
Ogura, 2016 (65)	13	8	Metal	85/92	0
Cahen, 2017 (21)	19	12	Resorbable	58/52	10
Actual series	11	48	Plastic	45/45	36

ND: no data.

8.2% and reoperation in 9.8% of patients. (66) Currently, the use of metal stents is recommended only in clinical trials with planned exchanges within one year because metal stent permeability lasts only one year in the MPD.

Drainage of Pancreatic Pseudocysts

Although endoscopic and long-term surgical drainage of pseudocysts have similar morbidity and recurrence, the mortality rate of endoscopic drainage is only 0.2% while that of surgical drainage is 2.5%. Endoscopic treatment has also been found to be significantly better than surgery in terms of cost, hospital stay and patient quality of life up to 3 months after drainage. (68)

Transpapillary and transmural drainage of PP have been found to have a similar long-term success rates, but the former has a lower morbidity rate (1.8% versus 15.4%, p <0.008). Although transmural drainage of pseudocysts can be performed by conventional drainage or EUS-guided, the success rate is greater with drainage guided by EUS because it does not require intraluminal compression. Results are most favorable for pseudocysts located in the head of the pancreas (Figure 4). (11)

A retrospective study has found that therapeutic failure of endoscopic drainage of the PP is independently associated with the placement of a single stent and with stent durations of less than 6 weeks. A recent randomized controlled trial has shown that recurrence of pseudocysts is associated with early removal of stents. (69)

Most studies have evaluated the role of endoscopic pseudocyst drainage for treating both acute and chronic pancreatitis. Since the revision of the Atlanta classification, (70) it is increasingly recognized that PP are uncommon in cases of acute pancreatitis. (71) It is likely that many cases diagnosed as pseudocysts in patients with acute pancreatitis were actually instances of walled necrosis. Consequently, results obtained from studies with pseudocyst drainage are currently better when only CP patients with true PP are considered.

Biliary Stenosis due to CP

Endoscopic management of benign biliary stenosis due to CP usually involves placement of a biliary stent through ERCP. Balloon-only dilation performs poorly because these stenoses are not easily resolved and because clinical relapse with restenosis is not uncommon after stent removal. The current options are placement of one or several plastic stents or placement of a self-expanding metal stent (SEMS). One review found that the average long-term success, usually defined as resolution of the stenosis, with the placement of a plastic endoscopic biliary stent may be around 37% at 32 months. (72) The same review found that the permeability range of SEMS was 37% to 100% over a 45-month follow-up average. A broad systematic review that compared these two approaches found the greatest success with uncovered SEMS (80%). The success rate for use of a single plastic stent was 36%, but the selected studies did not present sufficient data about the use of multiple stents. (73) Other experiences have shown high success rate with multiple plastic stents. Expert opinion favors this approach but does not support the routine use of biliary SEMS for this indication. (6). Obstruction and infection

are some of the biggest problems with biliary stent placement. (Figure 5).

How frequently stents need to be replaced is also a common question, and patient adherence to recommended replacement also varies. Patients are often asked to return at intervals of three to four months, but the low rate of occlusion with multiple plastic stents may prolong the replacement interval. (74) There is also no consensus on

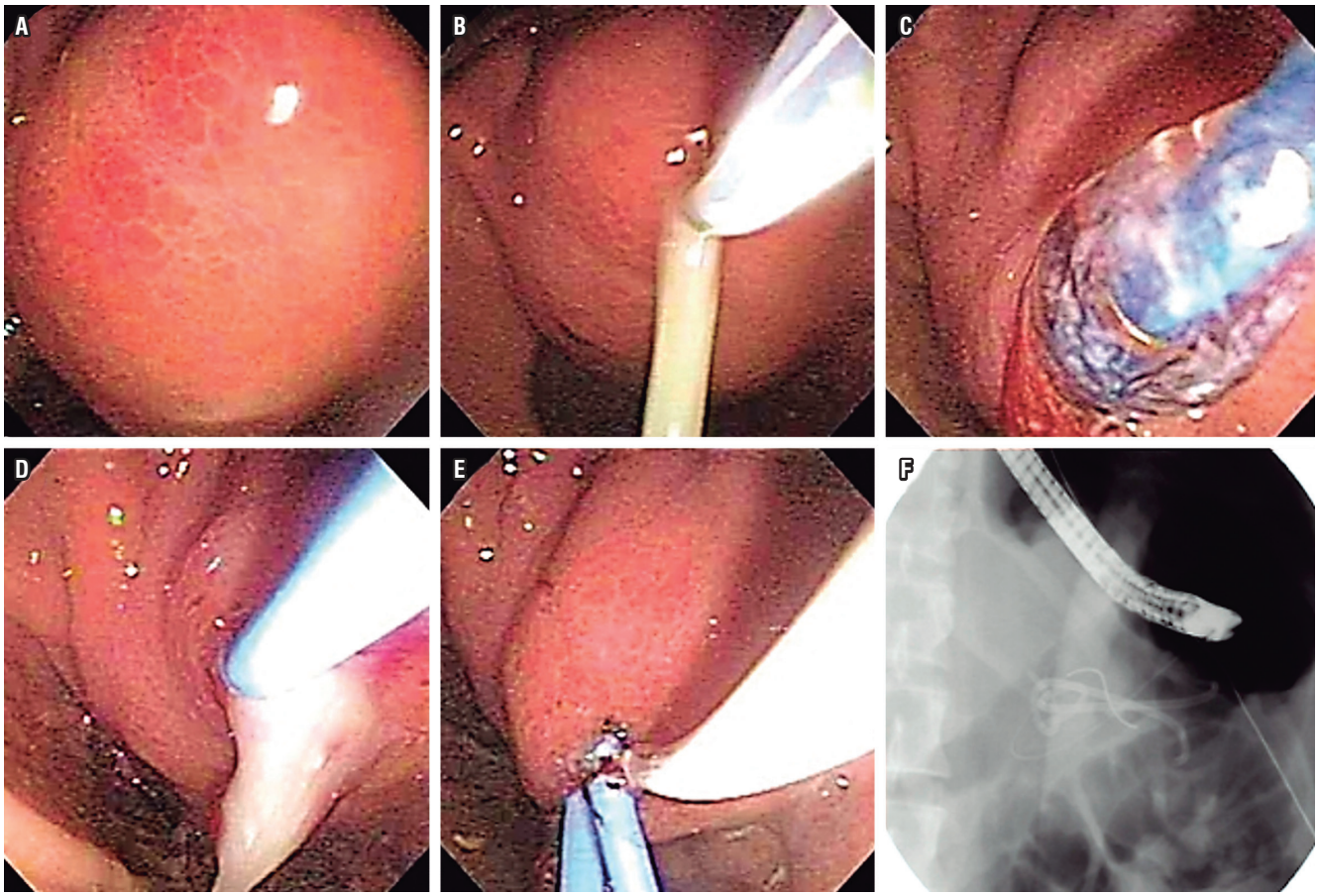

Figure 4. Endoscopic drainage of PP in CP. **A.** PP bulging in the gastric antrum. **B.** Puncture with precut needle with pus output. **C.** Transmural dilation with balloon up to 10 mm. **D.** Passage of first 7 Fr. pig tail catheter **E.** Passage of second pig tail catheter. **F.** Fluoroscopic image of double drainage.

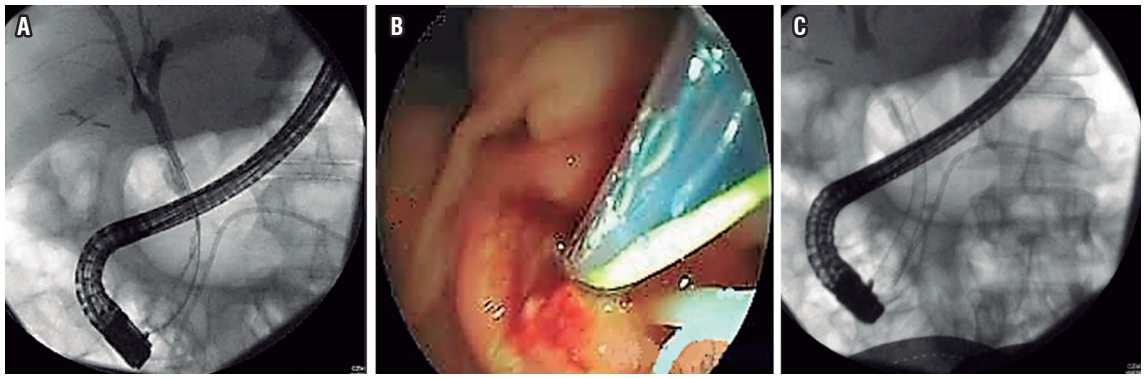

Figure 5. Endoscopic management of biliary stenosis by CP. **A.** Cholangiogram showing distal biliary stenosis. B. Endoscopic passage of metal biliary stent. **C.** Expanded metal biliary stent and plastic stent in the pancreas.

whether and under what conditions endoscopic treatment should be used before considering surgery. Answering this question requires multidisciplinary discussion.

Finally, benign biliary stenoses can be found in many patients with CP, but an important early step is exclusion of malignancy. These stenoses have the potential to cause numerous symptoms including jaundice, cholangitis and secondary biliary cirrhosis. A decision to treat is usually based on development of symptoms or to prevent infection and cirrhosis.

Both endoscopic and surgical options are available, but direct comparisons are needed. Most stenoses recur and may require several endoscopic treatments with balloon dilation and stent replacement every one to two years before a more durable outcome is achieved. Optimal stent selection continues to be evaluated, but the results with the use of multiple plastic stents are equivalent to those of SEMS. Replacement of stents should also be done every few months. Poor patient adherence to scheduled stent replacement increases the risks of adverse events. (75)

EUS Guided Drainage after failed ERCP

A recent study by Shah et al. (76) has reported a success rate of up to 75% for the pancreatic rendezvous procedure guided by EUS. Another Spanish multicenter study of 125 patients showed an overall technical success rate of 67.2% and overall clinical success rate of 63.2% for biliopancreatic access guided by EUS. (77) Another study by Ergun et al. (78) observed significant reductions in the pain score and in the diameter of the MPD during long-term follow-up (median: 38 months [range: 3-120]) of patients whose EUS-guided drainage was successful.

EUS Guided CPB

The roles of percutaneous CPB and EUS-guided CPB to relieve pain in CP patients have been controversial. (14) Even when beneficial, the effects are short-lived. Fifty-five percent of patients improve for the first four to eight weeks, but this proportion falls to 26% after twelve weeks and further to 10% after 24 weeks. (38) The results are even poorer for patients under 45 years of age who had previously undergone pancreatic surgery. (37)

CONCLUSIONS

CP is a challenging disease whose primary symptom is pain. The most commonly described reasons for endoscopic intervention are stones that obstruct the pancreatic duct, pancreatic duct stenosis, PP, celiac nerve plexus blockage, and treatment of benign biliary strictures. Endoscopic Treatment has a role in each of these disorders, and its capacity has been expanded or refined with the development of new technologies such as EUS which allows extra-anatomic approaches.

In summary:

- The primary symptom of CP is pain.
- Pancreatic duct stones should be removed endoscopically if possible even though pain does not always respond to removal of stones.
- Stenosis of the main pancreatic duct can be managed with a stent, but malignancy must always be excluded.
- CPB is rarely effective for long-term pain management in cases of CP.
- Pseudocysts should be operated on only if they are thought to cause pain or intestinal obstruction.
- Compression of the common bile duct is treated with long-term stents.

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