

# Endoscopic therapy in chronic pancreatitis: current perspectives

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**Abstract:** Endoscopic therapy in chronic pancreatitis (CP) aims to provide pain relief and to treat local complications, by using the decompression of the pancreatic duct and the drainage of pseudocysts and biliary strictures, respectively. This is the reason for using it as first-line therapy for painful uncomplicated CP. The clinical response has to be evaluated at 6–8 weeks, when surgery may be chosen. This article reviews the main possibilities of endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic ultrasound (EUS) therapies. Endotherapy for pancreatic ductal stones uses ultrasound wave lithotripsy and sometimes additional stone extractions. The treatment of pancreatic duct strictures consists of a single large stenting for 1 year. If the stricture persists, simultaneous multiple stents are applied. In case of unsuccessful ERCP, the EUS-guided drainage of the main pancreatic duct (MPD) or a rendezvous technique can solve the ductal strictures. EUS-guided celiac plexus block has limited efficiency in CP. The drainage of symptomatic or complicated pancreatic pseudocysts can be performed transpapillarily or transgastrically/transduodenally, preferably by EUS guidance. When the biliary stricture is symptomatic or progressive, multiple plastic stents are indicated. In conclusion, as in many fields of symptomatic treatment, endoscopy remains the first choice, either by using ERCP or EUS-guided procedures, after consideration of a multidisciplinary team with endoscopists, surgeons, and radiologists. However, what is crucial is establishing the right timing for surgery.

**Keywords:** chronic pancreatitis, treatment, endoscopy, ERCP, endoscopic ultrasound

## Introduction

Chronic pancreatitis (CP) is an irreversible and progressive inflammatory process, featuring pathological modifications of fibrosis, inflammatory infiltration, and the destruction of exocrine and endocrine tissue. As a result, there are specific morphological changes in the parenchyma and pancreatic ducts.

The most common clinical presentation for patients with CP is abdominal pain,<sup>1</sup> which significantly decreases the quality of life.

Pain is caused by pancreatic hyperstimulation, ischemia, necrosis,<sup>2</sup> oxidative stress, obstruction of pancreatic ducts, and necrosis–fibrosis mechanism.<sup>3–5</sup> Inflammation and damage of the pancreatic nerve is also considered as a cause of pain in CP.<sup>6,7</sup>

Endoscopic therapy in CP aims to provide pain relief and to treat local complications, by using the decompression of the pancreatic duct and the drainage of pseudocysts and biliary strictures, respectively.

The European Society of Gastroenterology (ESGE) recommends endoscopic therapy as the first-line therapy for painful uncomplicated CP. The clinical response has to be evaluated at 6–8 weeks; if it appears to be unsatisfactory, the patient's pancreatic

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problems should be discussed again in a multidisciplinary team with endoscopists, surgeons, and radiologists. Subsequently, the surgical options are to be considered, particularly for patients with a poor outcome following endoscopic therapy.<sup>8</sup> Comparing pain relief by ductal endoscopic procedures to surgery, two of three randomized control trials were favorable to surgery in long-term follow-up.<sup>7,9–11</sup> However, because of the irreversibility of surgery, the current guideline gives priority to endoscopic therapy.

## Endotherapy of pancreatic ductal stones

The decompression of the ducts is the first therapeutic option for patients suffering from pain caused by intraductal obstruction and ductal hypertension. It can be done endoscopically by performing pancreatic sphincterotomy, stones lithotripsy, and extraction or stenting.

Pancreatic sphincterotomy alone is rarely used today as a unique endoscopic method of treatment, because surgical sphincterotomy and sphincteroplasty in CP have been associated with modest results.<sup>12</sup> However, this procedure is indicated in rare cases where the obstruction is located in the papillary orifice, with uniform dilatation of the main pancreatic duct (MPD) above.

Extraction of the pancreatic stones can be done with the Dormia basket or the balloon associated with pancreatic sphincterotomy. It is indicated when the stone is not impacted in the pancreatic duct, in the head of the pancreas, or when there is a small number of stones as the only significant feature of CP.<sup>13–18</sup> Complete or partial pain relief after this type of procedures is 50%–77% (Table 1).

In case of large impacted intraductal stones >4 mm in diameter, being larger than the duct size, or located above a stenosis, in the head of the pancreas, the ultrasonic lithotripsy procedures (extracorporeal shock wave lithotripsy [ESWL]) should be done as the first procedures<sup>19–22</sup> (Table 2), followed sometimes by the endoscopic extraction of the fragments.<sup>16,17</sup> The aim of ESWL is to obtain fragments less than 3 mm

in diameter to facilitate their expulsion or extraction. Intraductal laser or electrohydraulic lithotripsy through a pancreatoscope or spyscope are technically difficult and are only to be considered as a second-line management after ESWL has failed.<sup>8,23,24</sup>

The complete relief of pain in idiopathic CP after ESWL as a unique method of treatment was seen in 414 of 1,006 patients (42%) in the medium follow-up of 24–36 months. Only 5% of the patients had severe remnant pain.<sup>25</sup> Another long-term study of ESWL as the initial therapy for CP showed that many procedures are needed during a lifetime. However, partial pain relief was seen in 85%, complete pain relief with no narcotic use in 50%, while surgery was avoided in 84% of the patients.<sup>26</sup>

A meta-analysis about ESWL treatment showed that ductal clearance is obtained in 37.5%–100% of the cases.<sup>27</sup> In many studies, there was no correlation between the fragmentation of the stones and the rate of ductal clearance.<sup>27</sup> More than 90% of patients needed less than three sessions of ESWL.<sup>25</sup> Recurrence of stones was seen in 51 patients (14.01%) in the intermediate follow-up group, and in 62 patients (22.8%) in the >60 months long-term group.<sup>28</sup> Secretin administration during ESWL may help the stone fragmentation and it facilitates the excretion of the small pancreatic stones.<sup>29</sup> Also, stopping smoking after ESWL may improve outcomes.<sup>26</sup>

Complications that may occur after ESWL are acute pancreatitis, biliary or pancreatic sepsis, and gastric submucosal hematoma. Although there have been attempts to assess the effect of ESWL on endocrine and exocrine pancreatic insufficiency, the existing data are insufficient for a conclusion.<sup>27</sup>

With the use of all these methods, pain improvement is 95% after procedures and about 40%–76% are painless in 2–4 years (Table 3). It is still doubtful whether the residual pain depends on the number, shape, and location of the remaining stones.<sup>13</sup> The resistance of ductal stenosis or the neurogenic mechanism may be responsible for persistent pain.<sup>17</sup>

ESWL versus ESWL followed by stones extraction and stenting when pancreatic strictures were associated was assessed in a randomized study. Pain recurrence at 2 years was 38% in the first group versus 45% in the second group, with the costs being three times lower in the first group.<sup>30</sup> More than half of the patients had no pain relapse during a median follow-up of 4 years in both groups, with higher costs in the second group.<sup>30</sup>

ESGE recommendations for the treatment of patients with uncomplicated painful CP and intraductal stones  $\geq 5$  mm are ESWL as a first step, immediately followed by endoscopic

**Table 1** Results of pain treatment in chronic pancreatitis after endoscopic sphincterotomy and extraction of pancreatic stones

Author	Number of patients	Ductal clearance (%)	Persistent alleviation (%)	Rate of surgery (%)
Sherman et al <sup>116</sup>	32	72	67.7	–
Smits et al <sup>13</sup>	53	74	77.4	15
Dumonceau et al <sup>117</sup>	70	50	54	–

**Note:** – not reported.

**Table 2** Results of extracorporeal lithotripsy in chronic pancreatitis

Author	Number of patients	Number of sessions	Free of symptoms (%)	Fragments of stones (%)	Ductal clearance (%)
Sauerbruch et al <sup>18</sup>	24	1.6	37	87	50
Ohara et al <sup>19</sup>	32	4.6	79	100	75
Costamagna et al <sup>21</sup>	35	1.9	17	100	80
Delhay et al <sup>20</sup>	123	1.8	53	99	59
Schneider et al <sup>21</sup>	50	2.4	76	85	56
Choi et al <sup>22</sup>	58	2.5	55.2	93.2	46.6
Seven et al <sup>26</sup>	120	1.2	50	—	—
Tandan et al <sup>25</sup>	636	1.6	68.7	—	76

**Note:** — not reported.

extraction of stone fragments. ESWL alone should be preferred over ESWL combined with endoscopic retrograde cholangiopancreatography (ERCP). Endoscopic attempts to extract radiopaque MPD stones without prior stone fragmentation should be considered only for stones <5 mm, preferably in a small number, and located in the head or body of the pancreas. Intraductal lithotripsy is to be attempted only after the failure of ESWL.<sup>8</sup>

## Endoscopic treatment of pancreatic duct stricture

Strictures of the MPD are seen in about half of patients of CP, usually located in the pancreatic head, being caused by inflammation or fibrosis. MPD strictures are defined as a high-grade narrowing of MPD with one of the following: 1) MPD dilatation >6 mm beyond the stricture or when the contrast fails to flow alongside the stricture or 6 Fr nasopancreatic tube. The presence of multiple or tail strictures are the main negative predictors of the relapsing pain.<sup>21,30</sup>

The stenoses are dilated with a balloon or a catheter, followed by the placement of a plastic stent.<sup>18,31</sup> If the stenosis can be overpassed, the MPD is decompressed and the pain is relieved (Table 4). Pancreatic stenting was seen as an alternative to MPD decompression surgery, which is associated with a mortality rate of 2%–5%. Although the sphincterotomy is not necessary in order to place the stent, some authors recommend it for preventing postprocedure pancreatitis. The stent size is chosen to be at least as large

as the pancreatic duct, in order to dilate the stenosis. The 10 Fr is less likely to be obstructed, but its placement is more difficult than a 5 Fr stent. The stents should be long enough to overpass the stenosis, and short enough to minimize the ductal changes.

The protocol concerning the number and the duration of stenting suggested initially the placement of a 10 Fr stent every 6 months with pain relief in 70%–94% of patients. After removing the stent placed for 3 months in patients who stopped drinking alcohol, pain relief was obtained in 58% of patients at 46 months' follow-up.<sup>32</sup> Recurrence of pancreatic strictures was reported in 38% of patients after 2 years of follow-up.<sup>33</sup> Long-term pain relief was obtained in 5 years after stent removal in eight of 14 patients.<sup>34</sup>

When dilation with a single stent is not achieved, the placement of multiple stents for 6–12 months is recommended, resulting in 84% of patients as asymptomatic and 10.5% of patients with symptomatic recurrent stenosis at 38 months' follow-up.<sup>35</sup>

The size of MPD after stenting does not predict the pain response, because pain alleviation can occur when the stent is obstructed, with the pancreatic juice leaking around it.<sup>36,37</sup> After endoscopic clearance of the MPD, the placement of a stent for ductal stenosis causes a slight reduction in the recurrence of symptoms (21% vs 23%). Reversible ductal changes after stenting may occur in most of the patients, thus stenting after complete extraction of ductal stones is not recommended.<sup>38</sup>

**Table 3** Results of pain treatment in chronic pancreatitis after sphincterotomy, endoscopic extraction, and extracorporeal lithotripsy of pancreatic stones

Author	Number of patients	Follow-up (months)	Immediate alleviation (%)	Long-term alleviation (%)	Rate of surgery (%)
Delhay et al <sup>20</sup>	123	14	85	40	8
Sauerbruch et al <sup>23</sup>	24	24	83	68	8
Adamek et al <sup>19</sup>	80	40	—	76	10
Inui et al <sup>24</sup>	504	44	97	78	4
Tadenuma et al <sup>25</sup>	70	36	97	70	0

**Note:** — not reported.

**Table 4** Results of pain treatment in chronic pancreatitis after sphincterotomy, stone extraction, and pancreatic stenting

Author	Number of patients	Follow-up	Immediate alleviation (%)	Long-term alleviation (%)	Rate of surgery (%)
Cremer et al <sup>126</sup>	75	37 months	94	52	15
Binmoeller et al <sup>133</sup>	93	45 months	74	38	–
Ponchon et al <sup>152</sup>	23	14 months	74	52.1	–
Dumonceau et al <sup>117</sup>	70	24 months	95	95	–
Smits et al <sup>145</sup>	51	34 months	82	44.8	–
Delhay et al <sup>146</sup>	110	14 years	–	66	21.4
Morgan et al <sup>135</sup>	25		–	45	–
Rösch et al <sup>127</sup>	1,018	59 months	–	65	–
Eleftheriadis et al <sup>147</sup>	100	69 months	–	70	4
Ishihara et al <sup>150</sup>	20	21 months	95	90	–
Weber et al <sup>128</sup>	17	24 months	89	83	–

**Note:** – not reported.

The use of non-covered metal stents for preventing stone recurrence after lithotripsy in patients with pancreatic stricture was accompanied by mucosal hyperplasia inside the stent. But recent studies performed with specially made auto-expandable metal stents showed a partial improvement in pain after stent placement<sup>39</sup> and no migration of the stent.<sup>40</sup> Maintaining the metal stent for 4–7 days produces a dilation of strictures and allows the endoscopic extraction of stones above the stenosis.<sup>41</sup> However, asymptomatic de novo focal pancreatic duct strictures after metal stent retrieval have been noted.<sup>42</sup> New biodegradable stents were tested on animals, but further results are still expected.<sup>43</sup>

Stenting is associated with complications such as: occlusion, ductal stenosis, and stent migration. Stent occlusion (with lithostathine and albumin)<sup>44</sup> may induce local infection and the formation of pseudocysts, with the medium duration to occlusion being 2 months (2–38 months). Since the pain relapses quite rapidly after stent removal, there is a need to repeat the stenting. Some prefer regular replacement every 3 months,<sup>45,46</sup> others only after the stent has been occluded and symptomatic (on demand).<sup>47</sup> The causes of stent occlusion may be: diameter over 8.5 Fr, length of more than 8 cm, or intake of pancreatic enzymes, but the occlusion could be a “scam” because the pancreatic juice may leak around the intraductal precipitates.<sup>48</sup> The ESGE recommends to treat the dominant MPD stricture by inserting a single 10 Fr plastic stent, with stent exchange planned within 1 year even in asymptomatic patients to prevent complications related to longstanding pancreatic stent occlusion.<sup>8</sup> Simultaneous placement of multiple, side-by-side, pancreatic stents could be applied more extensively, particularly in patients with MPD strictures persisting after 12 months of single plastic stenting.

Another complication is the migration of the stent, which can be proximal, into the duodenum (5.2%), or distal, toward

the tail of the pancreas (7.5%). The main way to reduce the migration is to use stents with side wings, especially pigtail stents.<sup>49</sup> The use of S form stents avoids this complication and determines the improvement of duct stenosis in 40% of patients.<sup>50</sup>

Ductal changes, such as ductal stenosis, were described in 54% of stented patients.<sup>51</sup> Some authors claim that the stent itself does not induce ductal changes, but the ductal decompression reveals new stenosis masked previously.<sup>52</sup>

## Endoscopic ultrasound-guided drainage of the MPD

Endoscopic ultrasound (EUS)-guided drainage of the MPD is a second-line procedure indicated when ERCP is unsuccessful, caused by the inability to cannulate the MPD (severe inflammation, previous surgery, postsurgical stricture) or difficult endotherapy (tight stenosis, large stone, MPD rupture, pancreas divisum). In practice, there are only few cases in which ERCP cannot be successfully performed by an experienced endoscopist. Thus, only a very small number of patients, namely those in whom ERCP fails and surgery cannot be performed safely, are good candidates for pancreaticogastrostomy performed by EUS.<sup>8</sup>

The technique consists of puncturing the MPD through the gastric or duodenal wall. It creates a fistula that allows drainage through or near the stent, even in cases of stent occlusion. After advancing the guide wire into the MPD, the transpapillary technique (rendezvous technique) can also be performed.

Using the transluminal approach or the transpapillary rendezvous approach, EUS-guided drainage of the MPD remains technically challenging because of the difficulty in orienting the endoscope along the axis of the duct, difficult dilatation of the transmural tract due to pancreatic fibrosis, or the acute angle of the needle in relation to the MPD.

Using this technique, complete or major pain relief occurred in 69% of patients, but the probability of remaining free of pain sharply dropped over time, to 20% after 450 days; a malignant etiology for complete MPD obstruction has been diagnosed in five patients within 1 year after the procedure.<sup>53</sup> Despite success rates of 68%–75%, the complication rates were important in all series published (5%–43%); the complications included perforations, bleeding, pancreatitis, fever, and postprocedural pain.<sup>53–57</sup> Migration and occlusion of stents were frequent (20%–55% of patients) and the placement of stents on each side of the puncture place (side-by-side) was proposed.<sup>53</sup> EUS-guided drainage of the MPD should continue to be confined to tertiary care centers and very experienced endoscopists.

## Endoscopic therapy in the presence of pancreas divisum

Endoscopic therapy in the presence of pancreas divisum includes minor papilla sphincterotomy and stenting using 5–10 Fr stents, depending on the size of the dilated pancreatic duct. It is indicated only in patients with recurrent acute pancreatitis with or without features of CP. The recurrence episodes are reduced in 40–60% of cases.<sup>58</sup> In patients with pancreas divisum and painful symptoms, but no imaging features of CP, pain relief after minor papilla sphincterotomy is better than in patients with CP secondary to pancreas divisum (43% vs 21% after 29 months' follow-up). These findings may be explained by the fact that minor papilla sphincterotomy does not produce the reversibility of CP lesions already done.<sup>59</sup> In the long term, the sphincterotomy has better results than stenting, with a reduced risk of complications. If the dorsal pancreatic duct is not dilated, the stenting is indicated for a period of only 3–6 months.<sup>60,61</sup>

## Endoscopic ultrasound-guided celiac plexus block

In case of pancreatic pain resistant to standard procedure, a solution could be to block the pancreatic sympathetic innervation such as celiac plexus. This is usually situated from the T12-L1 disc space to the middle of the L2 vertebral body and comprising a dense network of ganglia around the aorta. Sympathetic blockade can be achieved by chemical or surgical celiac ganglia or thoracoscopic splanchnicectomy. Chemical sympathectomy can be done using absolute alcohol injected into the celiac plexus under CT or EUS guidance. Analgesia is obtained only for a period of 8–12 months and, therefore, the therapeutic indications for this process are limited.<sup>62,63</sup>

The approach was originally developed transcutaneously by posterior approach, ultrasound- or CT-guided, but it was

associated with paraplegia by affecting the dura mater or with pneumothorax by affecting the pleura. This is the reason for preferring the anterior approach, in the EUS-guided manner. It consists of temporary inhibition of the celiac plexus by using a combination of local anesthesia and steroids, with the aim of reducing pain and improving the quality of life.<sup>64</sup> Sometimes the celiac ganglia can be seen as a unique or concatenate hypoechoic structure, less well-delineated, with some whitish strands inside,<sup>65</sup> situated on the left side of the celiac trunk, usually between the celiac trunk and the left adrenal gland. Sometimes it may be multiple, appearing as a chain.

ESGE recommends considering celiac plexus block (CPB) only as a second-line treatment for pain in CP; EUS-guided CPB should be preferred over percutaneous CPB.<sup>8</sup> The indication is pain in CP, but some studies included pain accompanying moderate pancreatitis<sup>66</sup> or patients with pain that had not responded to other forms of treatment.<sup>67</sup>

The majority of studies used the bilateral injection technique over the central technique, which is considered equally safe, but with close and contradictory results concerning the alleviation of pain,<sup>66,68</sup> with need of a placebo-controlled trial.<sup>69</sup> Direct injection of triamcinolone within the celiac ganglia (13 patients), compared with alcohol injection (five patients), yielded disappointing results regarding pain alleviation (38% vs 80%).<sup>70</sup> In another study using triamcinolone 40 mg injection in each part of the celiac trunk, the improvement of pain was seen in 55% of patients after 8 weeks of follow-up, and in 26% of patients after 12 weeks of follow-up, but with no effect in younger patients or with previous surgery.<sup>71</sup>

The question of cost-effectiveness remains unresolved. Some studies followed up the patients for only 1–4 weeks.<sup>68,70</sup> The only study with an extended follow-up period showed duration of pain relief even up to 673 days. This raises the question of whether the natural course of the disease may have been responsible, because there were no data indicative of the level of severity of CP: the duration of disease from the onset of pain, presence of diabetes, or calcifications.<sup>66</sup>

In many studies, pain alleviation varied from 55% to 70%, with a short follow-up duration.<sup>66–68,71</sup> While technical success has been high, long-term pain relief is disappointing. Persistence of pain alleviation for as long as 24 weeks was seen in no patients<sup>67</sup> or in only 10% of patients (was 55% after EUS-guided CPB).<sup>71</sup> In addition, about 40% (8-week group follow-up), and 30% (24-week group follow-up) of the EUS-guided CPB had continued benefit, compared to 12% (12-week follow-up) in the CT-guided



CPB, clearly suggesting the superiority of the EUS method.<sup>72</sup> Two meta-analyses showed efficacy in managing chronic abdominal pain with this method in 51.46%<sup>72</sup> and 59.45%<sup>73</sup> of patients, respectively. The remaining pain could have been caused by sympathetic stimulation originating from T9-T11 or from somatic route innervation coming from extrapancreatic tissue.

CPB has the same efficiency compared to thoracoscopic splanchnicectomy for pain treatment in CP, but with a better quality of life.<sup>74</sup>

The side effects of this method are diarrhea and hypotension due to parasympathetic activity. Pain exacerbation for about 48 hours after the procedure may occur in 9% of patients.<sup>75</sup> The risk of paraparesis is reduced for the anterior approach, but peripancreatic abscess and retroperitoneal hemorrhage<sup>76</sup> were noted. More recently, lethal necrosis and perforation of the stomach and the aorta after multiple EUS-guided CPB have been reported,<sup>77</sup> so this method is not as benign as previously believed.

Infectious complications are uncommon, but potentially serious. In a series of 90 patients, only one patient developed an infectious complication (peripancreatic abscess), which was resolved with a 2-week course of antibiotics.<sup>74</sup> Prophylactic antibiotics should be considered in patients who are under acid suppression, but this is not routinely recommended because concentrated alcohol has sufficient bactericidal effect.<sup>64</sup> The rate of major complications seemed very low (0.6%).<sup>78</sup>

## Treatment of pancreatic pseudocysts

Pseudocysts are encountered in about 30% of patients with CP. As spontaneous resolution is seen in less than 10%, some criteria of nonresolution were established, such as: persistence over 6 weeks, pancreatic duct anomaly (except for communication with the pancreatic duct), proven CP, and pseudocyst thick wall.<sup>79</sup>

Pseudocyst treatment can be done percutaneously, endoscopically, or surgically. Endoscopic therapy, as the first-line therapy for uncomplicated chronic pseudocysts for which the treatment is indicated, provides similar long-term results compared to surgery, at a lower cost, with shorter hospitalization and better quality of life during the first months following treatment.

Before choosing the endoscopic treatment, it is necessary to accurately determine the communication with the Wirsung duct by using magnetic resonance imaging (MRI) or ERCP examination and to differentiate potential neoplastic cystic lesions

(MRI and EUS-FNA [fine needle aspiration]). Moreover, to avoid pseudocyst relapse, described in 4%–17% of cases after 6–9 months' of follow-up,<sup>77,78,80</sup> communication with a secondary pancreatic duct should be assessed very carefully.

Indications for treatment are:

1. Complicated pseudocysts (one criterion is sufficient): compression of large vessels, obstruction of the stomach or duodenum, stenosis of MPD due to compression, infected pseudocyst, pleural pancreatic fistula;
2. Symptomatic pseudocysts: nausea, vomiting, pain, early satiety, upper gastrointestinal bleeding (10%–20%).

If arterial pseudoaneurysms are detected in the vicinity of the pancreatic pseudocysts, arterial embolization should be considered prior to pseudocyst drainage.<sup>8</sup>

## Transpapillary/transductal endoscopic drainage

Transpapillary/transductal endoscopic drainage with stent placement for a period of 4–6 weeks is recommended for small pseudocysts communicating to the MPDs located in the head or the body of the pancreas, but this is usually required in a limited number of cases.<sup>81</sup> The immediate success is about 85%. Double-pigtail stents of 10 Fr are preferred to prevent migration. A favorable predictor of successful therapy is a dilated Wirsung duct above a stenosis overpassed by the stent. Morbidity is 6% and mortality is 0%.<sup>80–90</sup> Modest results are obtained when the pseudocyst is older than 6 months, or smaller than 6 cm.<sup>91</sup> Stents should be left in place for a longer duration as their removal within 2 months is associated with a higher incidence of pseudocyst recurrence.<sup>8</sup>

Transmural conventional endoscopic drainage (cystogastrostomy or cystoduodenostomy) is indicated for pseudocysts noncommunicating with the MPD, with ductal wall thickness <1 cm and compressive on the digestive tract. The success rate varies between 74% and 94%; morbidity is about 9%–17% and mortality is 0%. Difficulties occur when gastric portal hypertension is present. EUS-guided drainage has been reported, especially for collections without bulging onto the gut wall or with parietal vessels, due to portal hypertension.<sup>92–94</sup> The success rate is 88%–95%. The main limitation is the location of fluid collection further than 1–1.5 cm from the gut wall.<sup>45,95,96</sup> It is important to avoid these methods for pancreatic cystic neoplasms or for pseudoaneurysms. Technically, cystoduodenostomy should be preferred over cystogastrostomy if both routes are deemed equally feasible. ESGE recommends to insert at least two double-pigtail plastic stents; these should not be retrieved before cyst resolution as determined by cross-sectional imaging and not

before, 2 months of stenting.<sup>8</sup> Unfavorable results are found for infected pseudocysts, with thick wall or for patients with walled off pancreatic necrosis or with portal hypertension.<sup>90</sup>

## EUS-guided drainage

EUS-guided drainage is indicated in the case of portal hypertension or in the absence of luminal bulging. Although known as a technique since 1998, published series of EUS drainage of pseudocysts has reported a success rate of 88%–95%, including infected pseudocysts.<sup>97,98</sup> The puncture site is enlarged either by balloon dilatation or by coagulation. Negative predictors of treatment response are ductal stenosis and rupture of the Wirsung duct.<sup>99</sup> Using the axial echoendoscope appears to facilitate the approach to the pseudocysts, which are difficult to locate.<sup>100</sup> When it is necessary, endoscopic transmural drainage may be combined with EUS drainage.<sup>101</sup> More recently, the success rate for plastic or metallic stents is over 95%, with similar outcome and complete resolution when the stent was removed within 3 months.<sup>102,103</sup> While current evidence suggests that placement of metal stents is technically feasible in patients with pseudocysts, there are no data to prove that metal stents are superior to plastic stents in terms of treatment efficacy, complications, recurrence rates, or cost-effectiveness. Randomized trials with long-term follow-up are needed to compare metal and plastic stents for drainage. The main advantages would be the possibility to create a larger diameter access fistula for drainage, to increase the final success rate, and to reduce the time to resolution. The major disadvantages are stent migration and bleeding. The use of metallic stents with anti-migration systems could avoid this complication.<sup>104</sup>

Conventional endoscopic drainage and EUS-guided drainage have been compared in some papers. In a prospective nonrandomized study, the two approaches seemed equally safe and effective,<sup>82</sup> but this was not confirmed by a nonrandomized study of 53 patients, where EUS represented a salvage method in the case of failure of conventional endoscopic drainage (possible only in 57% of patients), owing to non-bulging pseudocysts or the location in the tail of the organ, but it was a more time-consuming procedure.<sup>105</sup> EUS drainage had a duration of 75 minutes and transmural drainage 45 minutes, with similar success rates. The conclusion of this study was that EUS should be reserved for pseudocysts located in the tail of the pancreas, because these are unlikely to cause luminal compression or they are technically difficult to access. Also, EUS assessment would identify a tumor in 5% of pseudocysts.<sup>105</sup> Another randomized clinical trial showed a significantly better success rate for EUS- than for conventional endoscopic-guided drainage (100% vs 33%),

despite the small number of patients (30 patients), even after statistical adjustment for luminal compression, with a lower rate of life-threatening massive bleeding.<sup>106</sup> A different study also confirmed a significant advantage for EUS over conventional endoscopic drainage (94% vs 72%); both were considered first-line methods for the treatment of bulging pseudocysts, but the authors recommended that EUS-guided drainage should be preferred for non-bulging pseudocysts.<sup>107</sup> In a randomized trial, EUS-guided and surgical drainage appear to have the same rates of treatment success, complications, and reinterventions.<sup>108</sup> Also, costs are lower with the EUS procedure compared to surgery.<sup>140</sup>

The rate of complications is about 18%, including bleeding, infection, and pneumoperitoneum or stent migration.<sup>82</sup> Perforation at the site of transmural stenting was more common with pseudocysts involving the uncinate region.<sup>109</sup> Complications seem to be more common in pseudocysts with recent history of acute pancreatitis and the placement of straight stents, but no significant differences were observed between the placement of one or two stents, or between patients with or without nasocystic drainage.<sup>110</sup>

## Common bile duct stenosis treatment

Biliary obstruction occurs during the course of CP in 3%–23% of patients, being related to fibrosis and pseudocyst compression. ESGE recommendations of treatment are for symptomatic strictures, secondary biliary cirrhosis, biliary stones, progression of biliary stricture, or asymptomatic elevation of serum alkaline phosphatase (>2 or 3 times the upper limit of normal values) and/or of serum bilirubin for longer than 1 month.<sup>8</sup>

Stenting with one biliary plastic prosthesis is associated with a low success rate, with frequent relapses, mainly related to the presence of calcifications (Table 5).<sup>111</sup> This is the reason for the recommendation of temporary (1-year)

**Table 5** Biliary stenting in chronic pancreatitis

Author	Number of patients	Follow-up (months)	Success rate (%)
Devière et al <sup>129</sup>	25	14	12
Barthet et al <sup>24</sup>	19	18	10
Smits et al <sup>130</sup>	58	46	28
Born et al <sup>131</sup>	18	23	17
Kiehne et al <sup>132</sup>	14	52	16
Vitale et al <sup>133</sup>	25	32	80
Farnbacher et al <sup>134</sup>	31	28	32
Kahl et al <sup>111</sup>	61	40	26
Cahen et al <sup>135</sup>	58	9	38

placement of multiple, side-by-side, plastic biliary stents. The stents should be exchanged every 3 months, because the risk of cholangitis is very high, but quite often the compliance of alcoholic patients is low. One nonrandomized series has compared long-term results after temporary treatment with single versus multiple simultaneous plastic stents; it showed overall clinical success in 24% vs 92% of patients.<sup>112</sup>

Much hope was invested in metallic biliary stents. Although uncovered stents are not advisable for treating biliary strictures, partially or completely covered stents are promising, with 50%–80% long-term success, with a low recurrence rate (14%); their removal has recently been proved as feasible in 75% of patients.<sup>113–115</sup>

The choice between endoscopic and surgical treatment should rely on local expertise, local or systemic patient comorbidities (eg, portal cavernoma, cirrhosis), and expected patient compliance with repeat endoscopic procedures.<sup>8</sup>

## Conclusion

In conclusion, as in many fields of symptomatic treatment, endoscopy remains the first choice, either by using ERCP or EUS-guided procedures, after consideration of a multidisciplinary team with endoscopists, surgeons, and radiologists. However, what is crucial is establishing the right timing for surgery.

## Author contributions

Andrada Seicean and Simona Vultur had substantial contributions to conception and design, analysis and interpretation of the data; drafting and critical revision of the article; and gave final approval of the version to be published. Both authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

## Disclosure

The authors report no conflicts of interest in this work.

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