

Role of endoscopic retrograde cholangiopancreatography in pancreatitis

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Abstract

Endoscopic retrograde cholangiopancreatography (ERCP) has evolved from mainly a diagnostic tool to a treatment method, thanks to newer noninvasive techniques like magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS). This paper looks at how ERCP is used to treat conditions such as acute gallstone pancreatitis, pancreas divisum (PD), sphincter of Oddi dysfunction (SOD), and chronic pancreatitis (CP). For acute gallstone pancreatitis, early ERCP to reduce severity or mortality is now questioned, except when there is cholangitis or ongoing bile duct blockage. For patients with recurring acute pancreatitis due to PD, endoscopic treatment aims to lower duct pressure, but there is not enough strong evidence to support its long-term success. In SOD cases, recent research suggests being more careful with endoscopic sphincterotomy. ERCP plays a clearer role in CP by helping to manage duct stones and strictures in suitable patients. The rising use of pancreatoscopy-assisted lithotripsy as an alternative to ESWL is also discussed.

Key words: endoscopic retrograde cholangiopancreatography; endoscopic sphincterotomy; lithotripsy; pancreas divisum; pancreatitis; stents.

Introduction

Initially introduced in 1968 as a diagnostic innovation, endoscopic retrograde cholangiopancreatography (ERCP) quickly transcended its original purpose following the advent of biliary sphincterotomy, which endowed it with therapeutic capability.¹ Despite its diagnostic significance, the emergence of noninvasive modalities such as magnetic resonance cholangiopancreatography (MRCP) and endoscopic ultrasound (EUS) heralded a paradigm shift, gradually redefining ERCP's utility from diagnostic to predominantly therapeutic applications. Today, ERCP stands at the forefront of therapeutic interventions in the management of pancreatic disorders.

This review aims to elucidate the role of ERCP in the treatment of both acute and chronic pancreatitis (CP).

Acute and recurrent acute pancreatitis

Acute gallstone pancreatitis

Acute gallstone pancreatitis is one of the major indications for ERCP in cases with acute pancreatitis. However, the timing of ERCP ie, urgent (within 24 h) or early (24-72h) has been a subject of debate with contrasting results in several studies. Since most bile duct stones which initiate pancreatitis pass spontaneously into the duodenum the utility of ERCP is questionable in this scenario. The other major question which has been the focus of the majority of the studies is whether urgent or early ERCP would reduce the severity of pancreatitis or mortality.

Early studies in the 1990s suggested that in patients with acute biliary pancreatitis but without obstructive jaundice,

early ERCP and sphincterotomy were not beneficial.²⁻⁴ The Cochrane database systematic review was published in 2012 and included 5 RCTs comprising 644 participants.⁵ This review also concluded that in patients with acute gallstone pancreatitis, there is no evidence that early routine ERCP significantly affects mortality, and local or systemic complications of pancreatitis, regardless of predicted severity. Therefore, early ERCP should only be considered in patients with coexisting cholangitis or biliary obstruction. In contrast, a subsequent systematic review and meta-analysis (11 studies and 1314 patients) concluded a significant decrease in complications in patients with severe gallstone pancreatitis managed with early ERCP/ES compared with conservative management.⁶ Several quality trials published subsequently suggested that urgent ERCP does not reduce major complications or mortality, as compared with conservative treatment in patients with predicted severe acute biliary pancreatitis without cholangitis.^{7,8} On the other hand ERCP may be beneficial in cases with acute biliary pancreatitis and cholestasis. In a multicentre Dutch study, ERCP was associated with fewer complications in cases with cholestasis (25% vs 54%, $P = .020$).⁹ Although, urgent ERCP may not impact major outcomes some reported benefits include a shorter length of hospital stay and a lower rate of hospital readmission.^{10,11}

Pancreas divisum

Pancreas divisum is the most common congenital pancreatic anomaly, occurring in approximately 6%-10% of individuals.¹² Since, the majority of patients with pancreas divisum are asymptomatic; there is considerable controversy as to the clinical significance of pancreas divisum in pancreatic

disease. Nevertheless, a subset of patients with pancreatic divisum may have impaired drainage of pancreatic secretions through the dorsal-dominant system, potentially resulting in increased intraductal pressures, which may precipitate recurrent acute pancreatitis (RAP). Endoscopic therapy (minor papilla sphincterotomy, balloon dilation, and stent placement) for symptomatic PD aims to relieve outflow obstruction by enlarging the minor papilla.

The only randomized trial (19 patients) published to date suggested a benefit of ERCP and stent placement in cases with RAP and pancreas divisum.¹³ Mean follow-up times in the stent and control groups were 28.6 and 31.5 months, respectively. In this trial, no patients in the stent group required hospitalization or emergency room visits for abdominal pain. Subsequently, other studies also reported the benefits of endotherapy in these cases.¹⁴⁻²² In a systematic review (22 studies and 838 patients), patients with RAP had a response rate ranging from 43% to 100% (median 76%). Reported response rates were lower in the other 2 groups, ranging from 21% to 80% (median 42%) for patients with CP and 11%-55% (median 33%) for patients with chronic abdominal pain.²³ Therefore, endotherapy should be avoided in cases with pancreas divisum and absence of well-documented episodes of pancreatitis (Table 1).

While the majority of the studies embark upon the efficacy of endotherapy it is important to note that there is a lack of quality data on the outcomes of ERCP in pancreas divisum and therefore, the role of ERCP remains debatable in these cases. Moreover, ERCP is associated with its own set of complications especially post-ERCP pancreatitis (15%-20%).²⁴ Therefore, the decision to pursue ERCP in symptomatic cases with pancreas divisum should be preceded by a comprehensive discussion with the individual patient to define expectations before embarking on any medical and/or

interventional therapy.²⁵ Future studies are needed to assess factors predictive for the success of endoscopic therapy and potential risk factors for relapse after ERCP.²⁶ An ongoing randomized single-blind sham-controlled study (SHARP study) is evaluating the efficacy of ERCP in the management of RAP in patients with pancreas divisum.²⁷ The trial aims to provide high-quality evidence on whether ERCP with interventions such as minor papillotomy offers a significant benefit over a sham procedure in reducing the frequency of RAP episodes in this patient population. The results of the SHARP study are anticipated to have important implications for clinical practice, particularly in guiding the management of pancreas divisum-related RAP.

Sphincter of Oddi dysfunction

Sphincter of Oddi dysfunction (SOD) is identified in 40%-50% of patients with idiopathic RAP.²⁸ The evaluation and management of patients with suspected SOD remain complex and nuanced. A thorough history is essential, and it is crucial to rule out other potential causes of upper abdominal pain. If a patient's history and lack of response to empiric treatments suggest SOD, further investigation is warranted.

The Geenen-Hogan (G-H) criteria categorize SOD into 3 subtypes based on the presence of characteristic pain, ductal dilation, and abnormal pancreatic enzyme levels during or shortly after pain episodes. Type I SOD is characterized by objective evidence of impaired biliary or pancreatic drainage and is often associated with structural obstruction. Under the Rome IV criteria, Type I SOD is now recognized as papillary stenosis. Endoscopic sphincterotomy continues to be the primary therapeutic intervention for Type I SOD (papillary stenosis) with a favourable response in approximately 90% of patients. Patients with Type II SOD present with characteristic

Table 1. Outcomes of endotherapy in patients with pancreas divisum and recurrent acute pancreatitis.

Study, year	Study type	n	Classification	Endotherapy	Technical success (%)	Clinical success (%)	Follow-up	Adverse events
Lans, 1992 ¹³	RCT	19	RAP 10, Control 9	Dilatation + stenting	NR	90%	28.6 m	0%
Lehman, 1993 ¹⁴	P	52	CAP 24 RAP 17 CP 11	MiES + stent	NR	26.1% 76.5% 27.3%	1.7 y	15%
Gerke, 2004 ²¹	R	53	RAP 30 CP 14 CAP 9	MiES + stent	NR	RAP 43.3% CP 21.4% CAP 11.1%	29 m	11.2%
Chacko, 2008 ²⁰	R	57	RAP 27 CP 20 CAP 8	Majority MiES (94%)	86%	RAP 76% CP 42% CAP 33%	20 m	11.7%
Borak, 2009 ¹⁹	R	113	RAP 62 CP 22 CAP 29	MiES + stent	NR	RAP 53.2% CP 18.2% CAP 41.4%	43 m	13.3%
Rustagi, 2013 ²²	R	45	RAP 18 CP 7 CAP 13	MiES ± stent (majority)	91.9%	RAP 94% CP 57% CAP 50%	NR	16.1%
Tringali, 2019 ¹⁸	R	48	RAP	MiES ± stent	NR	72.9%	9.7 y	12.9%
De Jong, 2021 ²⁶	Multicentre, R	81	RAP 66 CP 12 CAP 3	MiES + stent	74.1%	RAP 44.4% CP 33.3% CAP 33.3%	≥3 m	37%

Abbreviations: CP, chronic pancreatitis; CAP, chronic abdominal pain; MiES, minor papilla sphincterotomy; NR, nonresponse; RAP, recurrent acute pancreatitis; P, prospective; R, retrospective; RCT, randomized controlled trial.

pain and either ductal dilation or abnormal enzyme levels, and are currently classified as having a functional biliary sphincter disorder according to Rome IV. The response to sphincterotomy is variable in this group of patients. Sphincter of Oddi manometry is recommended in these patients to identify those who are likely to benefit from sphincterotomy. Type III SOD, which involves typical biliary or pancreatic pain without objective evidence of drainage impairment, lacks a definitive causal relationship with RAP, and the utility of endotherapy in these patients remains controversial. In the EPISOD trial, a pivotal randomized study, sphincterotomy offered no benefit over sham treatment in patients with Type III SOD.²⁹ This trial has significantly influenced clinical practice, as evidenced by a marked and sustained decrease in the rates of endoscopic sphincterotomy for newly diagnosed SOD in a large electronic health record dataset following the publication of EPISOD trial results.³⁰ When sphincterotomy is performed, the outcomes of biliary sphincterotomy alone are comparable to those of combined biliary and pancreatic sphincterotomy, suggesting a limited role for pancreatic sphincterotomy in SOD management.³¹

Patients undergoing ERCP for suspected SOD are at high risk for post-ERCP pancreatitis (PEP); therefore, prophylactic measures such as short-term pancreatic stenting and periprocedural NSAIDs should be considered. The challenges in diagnosing SOD, coupled with the high risk of PEP, uncertain benefits of endotherapy, and recurrent pancreatitis after sphincterotomy have led to a decline in the use of endoscopic interventions for SOD.³² Given the complexity and potential risks, the consent process should be thorough. It should ensure that the patient fully understands the benefits, risks, and alternatives to ERCP. This process is vital in managing expectations and fostering shared decision-making.

Chronic pancreatitis

Chronic pancreatitis (CP) affects approximately 50 individuals per 100 000 in the population, with abdominal pain being the predominant symptom.³³ In those with pain due to obstructive causes, such as pancreatic ductal (PD) strictures and calculi, endotherapy offers a viable treatment option. In obstructive CP, endotherapy provides early and sustained pain relief in 88% and 67% of patients, respectively.³⁴ Endotherapy in stenotic disease involves ERCP with PD stenting and/or stricture dilatation. In those with predominant stone disease, endotherapy involves lithotripsy followed by endoscopic clearance of stone fragments. Suitable candidates for endotherapy include those with a single dominant stricture or solitary calculus in the head. On the other hand, those with diffuse disease ie, multifocal strictures or extensive pancreatic calcifications extending from head to body and tail may not respond well to endotherapy.

Endotherapy for pancreatic ductal calculi

While ERCP and extraction of stones are sufficient for clearing *small, non-impacted intraductal calculi (<5 mm)* extracorporeal shock wave lithotripsy (ESWL) is recommended for fragmentation of calculi ≥ 5 mm.^{35,36} Mechanical lithotripsy is not advocated for PD calculi due to high risk for complications, especially trapped basket.³⁷ If ESWL achieves complete fragmentation and the patient is asymptomatic, with no signs of ductal obstruction or pancreatitis, subsequent ERCP may

not be necessary. In this scenario, spontaneous passage of the fragments is expected, and the patient can be monitored with serial imaging and clinical follow-up. On the other hand, If ESWL results in only partial fragmentation of the stone, leading to a significant residual stone burden within the duct, retrieval via ERCP is indicated. This situation is more likely if the stones are large, hard, or located in areas of the duct where they are less likely to pass spontaneously. Pre ESWL sphincterotomy may be performed in cases with a significant ductal stricture or in patients with large stones, to ensure that the ductal orifice is sufficiently open to allow the passage of fragmented stones. This approach helps prevent the accumulation of fragments at the sphincter, which could lead to obstruction and pancreatitis.

In a large study by Tandan and colleagues, complete pain relief was found in 69% at intermediate (2-5 years) and 60% at long-term (>5 years) follow-up.³⁸ Multiple other studies have confirmed the safety and efficacy of ESWL in the management of chronic calcific pancreatitis.³⁹⁻⁴⁷ In a systematic review and meta-analysis (22 studies and 3868 patients), the pooled proportion of patients with complete stone fragmentation was 86.3%, complete ductal clearance was 69.8% and complete absence of pain during follow-up was 64.2%⁴⁸ (Table 2).

Pancreatotomy-assisted laser or electrohydraulic lithotripsy (LL or EHL) is an emerging alternative to ESWL for pulverizing large intraductal calculi. In a recent review, the pooled technical success and overall fragmentation success were 91.2% and 85.8%, respectively.⁵¹ The potential advantages of Pancreatotomy-guided lithotripsy include the ability to target stones under direct visualization. It also allows visualization of radiolucent stones missed on imaging, and confirmation of ductal clearance after lithotripsy.^{51,52} However, the need for expertise, additional costs and the requirement of a dilated duct to allow insertion of pancreatoscope are noteworthy limitations.⁵¹

Endotherapy for PD strictures

The endoscopic management of PD strictures includes pancreatic sphincterotomy, followed by the placement of 1 or more plastic stents. In responders, endotherapy should be continued for at least 1 year before removing the stents.³⁶ Patients with early positive responses to endotherapy tend to experience sustained benefits over the long term.⁵³ Nearly two-thirds of patients report long-term alleviation of pain following endoscopic PD drainage.⁵⁴

In cases with persistent symptomatic stricture, treatment options extend to the placement of multiple plastic stents (MPS), fully covered self-expandable metal stents (FCSEMS) or surgery. Costamagna and colleagues reported the outcomes of MPS in 19 patients with refractory PD strictures.^{55,56} (84%) of patients were symptom-free at an average follow-up of 38 months. In a subsequent follow-up study by the same group including 48 patients, 3-quarters remained asymptomatic 9.5 years post-stent removal, with a recurrence of stricture and symptoms in a minority of cases.⁵⁷

Recent studies have evaluated the utility of FCSEMS and biodegradable stents in cases with refractory PD strictures with clinical success rates varying from 50% to 100% across different studies.⁵⁸⁻⁶³ However, the predominance of these studies is characterized by limited sample sizes and brief follow-up durations, complicating definitive conclusions

Table 2. Outcomes of ESWL in patients with chronic calcific pancreatitis⁴⁹.

Study, year	N	Stone location	ERCP	Complete fragmentation (ductal clearance)	Pain relief: overall (complete relief)	Follow-up, months
Inui et al., 2005 ³⁹	555	NR	42.7%	92.4% (72.6%)	91.1% (NR)	44.3 m
Tadenuma et al., 2005 ⁴¹	117	Head (85.5%), Body-tail (14.5%)	55.6% (55.6%)	96.6%	68.2% (NR)	77.5 ± 30.9 m
Seven et al., 2012 ⁴⁰	120	Head (66.7%), head-body (1.6%), body (2.5%), head-body-tail (29.2%)	100%	NR	85% (50%)	4.3 ± 3.7 years
Suzuki et al., 2013 ⁴³	479	NR	53.2%	92.1% (74.3%)	90.8% (NR)	31.4 m
Ohyama et al., 2015 ⁴²	128	Head (76.6%), Body-tail (23.4%)	100%	NR (51.6%)	89.9% (NR)	42.4 ± 35.8 m
Hu et al., 2016 ⁴⁴	214	Head (75.7%), Head-body (6.1%), body (2.3%), head-body-tail (15.9%)	96.7%	100% (72.4%)	95.4% (71.3%)	18.5 ± 3.3 m
Li et al., 2016 ⁵⁰	849 (PC 59)	Head (23.7%), Head + other location (72.3%), Tail (3.4%)	PC group: 98.3%	PC group: 100% (67.2%)	89.1% (63.6%)	21.9 m
Vaysse et al., 2016 ⁴⁶	146	NR	73.5%	NR (56.8%)	NR	23 m
Tandan 2019 ⁴⁷	5124	Head (55.1%) Body (21.4%) Tail (7.4%) Diffuse (15.9%)	EPS 98% PD stent 69%	72.6%	94.5% (82.6%)	6 m

Abbreviations: ESWL, extracorporeal shock wave lithotripsy; PD, pancreatic duct; NR, not reported.

Table 3. Summary table of the role of ERCP in pancreatitis.

	Diagnosis	Management
1.	Acute biliary pancreatitis	Early ERCP should be considered only in selected patients with co-existing cholangitis or biliary obstruction
2.	Sphincter of Oddi dysfunction (SOD) Type I SOD (papillary stenosis) Type II SOD (functional) Type III SOD	Endoscopic sphincterotomy Endoscopic sphincterotomy in selected cases with positive SOM Endoscopic sphincterotomy is not indicated
3.	Pancreas divisum	Endotherapy (minor papillotomy ± stenting) should be performed only in cases with well-documented episodes of pancreatitis
4.	Chronic pancreatitis a. Pancreatic ductal calculi b. Pancreatic ductal stricture	Endotherapy is indicated in those with a single dominant stricture or solitary calculus in the head ESWL ± ERCP recommended for large (>5 mm) PD calculi Endotherapy with 1 or more plastic stents for 1 year Multiple plastic stents in symptomatic refractory strictures

regarding the efficacy of metal stents. Issues such as the optimal duration for stent placement, the potential for the development of new strictures, and the risk of stent migration remain critical considerations. These factors necessitate further evaluation before the routine application of FCSEMS can be endorsed for the treatment of recalcitrant PD strictures in routine clinical settings.

Benign biliary strictures

BBS manifest in approximately 10%-15% of individuals with CP, presenting a particular challenge to endotherapy owing to periductal fibrosis and calcification. Initial responses to single plastic stent placement are observed in merely a quarter of BBS patients, highlighting the necessity for alternative strategies, such as the employment of MPS or FCSEMS.⁶⁴⁻⁶⁶

Efficacy rates for MPS in addressing CP-related BBS vary significantly across studies, ranging from 44% to 92%.^{65,67,68}

FCSEMS has been recognized as a viable and effective alternative to MPS for BBS, offering the advantage of requiring fewer endoscopic sessions. A multicentre study focusing primarily on CP-related BBS reported an 80% rate of short-term stricture resolution, with a stent indwelling period defined between 10 and 12 months.⁶⁹ Subsequent long-term follow-ups revealed that 62% of patients remained stent-free after the removal of FCSEMS, over an average duration of 58 months.⁷⁰ Comparative analyses of MPS and FCSEMS suggest nearly identical 2-year stricture-free success rates (MPS 90% vs FCSEMS 92%).⁷¹ Therefore, the choice of stents is largely based on the available expertise and patient's compliance.⁷²

Pseudocyst, PD leaks, and disruptions

Pseudocysts are detected in about one-third of patients with CP. Endoscopic trans-papillary drainage is indicated in cases with small (<5 cm) pseudocysts communicating with the PD.^{73,74} The management of CP-related ascites and pleural effusion includes placement of a trans-papillary plastic stent to bridge the PD leak.

Summary

ERCP has transitioned from a primarily diagnostic tool to a predominantly therapeutic intervention in the management of both acute and chronic pancreatitis (Table 3). In acute pancreatitis, particularly acute gallstone pancreatitis, early ERCP is indicated in cases with cholangitis or cholestasis. The role of ERCP is not well defined in cases with RAP and pancreas divisum, although a subset of carefully selected patients may benefit from minor papilla endotherapy.

In chronic pancreatitis, ERCP serves a critical role in managing pain and addressing complications like pancreatic ductal strictures and calculi. Techniques including stenting, stricture dilatation, and lithotripsy have shown significant efficacy in relieving symptoms and improving the quality of life for patients with chronic pancreatitis. Moreover, ERCP facilitates the management of associated conditions such as benign biliary strictures and pseudocysts through targeted endoscopic interventions.

Author contributions

Zaheer Nabi contributed to the conception of the manuscript and overseeing the literature review. D. Nageshwar Reddy assisted in drafting the manuscript and revising it critically for important intellectual content, ensuring the accuracy and integrity of the work.

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Conflicts of interest

Conflict of interest disclosure forms (ICMJJE) have been collected for all co-authors and can be accessed as supplementary material [here](#).

Data availability

The data underlying this article will be shared on reasonable request to the corresponding author.

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