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NARRATIVE REVIEW

Endoscopic interventions for managing pancreatic fluid collections associated with acute pancreatitis: A state-of-the-art review (with videos)

Randeep Rana[1,2] · **Soumya Jagannath Mahapatra**[1] · **Pramod Kumar Garg**[1]

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Abstract

Acute pancreatitis is an acute inflammatory disease, which may be associated with pancreatic and peri-pancreatic necrosis and development of (peri)pancreatic fluid collections (PFCs). Interventions in acute pancreatitis have evolved over the years with a paradigm shift from open surgical drainage and necrosectomy to minimally invasive approaches. Depending on the presence of necrosis, the PFCs may be acute necrotic collections or acute pancreatic fluid collections, which evolve over a period of three to four weeks to walled-off necrosis and pseudocysts, respectively. Patients with symptomatic and infected PFCs require drainage. In general, drainage should be delayed beyond three to four weeks when the collection wall has matured and the necrotic debris is liquefied. However, some patients may merit early drainage (within the first three to four weeks), if they have suspected infected pancreatic necrosis and worsening organ dysfunction despite antibiotics and supporting therapy. Endoscopic transmural drainage and necrosectomy have now emerged as the most favored treatment modality in suitable pancreatic collections located predominantly in the lesser sac. Being minimally invasive, per-oral endoscopic direct necrosectomy is as effective as surgical necrosectomy in patients with infected necrotic collections but with fewer adverse events. Percutaneous endoscopic necrosectomy is an important addition to our armamentarium for laterally placed collections as an effective alternative to surgical video-assisted retroperitoneal debridement. The current review provides an overview of the evolution, indications, approaches, techniques and outcomes of endoscopic interventions in the management of pancreatic fluid collections associated with acute pancreatitis. Future direction for better outcomes has been highlighted.

Keywords Acute pancreatitis · Endoscopic drainage · Infected pancreatic necrosis · Pancreatic fluid collections · Percutaneous endoscopic necrosectomy

Introduction

Acute pancreatitis (AP) is an acute inflammatory disease of the pancreas which may be associated with systemic as well as local complications. A majority of the patients with AP have mild disease with an uncomplicated course but 20% to 30% patients have a protracted disease course requiring prolonged hospitalization [1, 2]. There has been increasing incidence of emergency admissions of this life-threatening disease in India over the years [3]. The patients with AP are classified as having moderately severe to severe AP depending upon local complications and organ dysfunction according to the revised Atlanta classification [4]. Radiologically, AP can either be acute interstitial pancreatitis (AIP) or be acute necrotising pancreatitis (ANP). Patients with ANP may develop (peri) pancreatic fluid collections (PFCs) in and around the pancreas. In around one-third patients with necrotic collections, secondary infections might develop, which carry a high mortality rate of close to 30%. Infected acute necrotic collections (ANC) are difficult to treat and may lead to delayed organ dysfunction [5, 6]. These patients are also prone to develop systemic inflammation presenting as systemic inflammatory response syndrome (SIRS), which in severe cases leads to organ dysfunction. Persistent organ failure may lead to a high mortality of up to 40%. The role

✉ Pramod Kumar Garg
pgarg@aiims.edu

1 Department of Gastroenterology and Human Nutrition Unit, All India Institute of Medical Sciences, New Delhi 110 029, India

2 Department of Gastroenterology, Govind Ballabh Pant Institute of Postgraduate Medical Education and Research, New Delhi 110 002, India

of endoscopy in managing PFCs associated with AP has evolved dramatically over the past two decades. There has been a major shift from open surgery to minimally invasive approaches particularly endoscopic treatment with the wide availability of endoscopic ultrasound (EUS) and technological advancements in endoscopic accessories and specialized stents. Interventional endoscopy has now developed as an effective treatment modality in the management of various complications of acute pancreatitis. We provide here an overview of the historical perspective, evolution of various approaches, refinement of techniques and outcomes of endoscopic interventions in the management of PFCs associated with acute pancreatitis.

Pancreatic fluid collections: Genesis and classification

Pancreas, a retroperitoneal organ, is anatomically located posterior to the stomach and the head of the pancreas lies in close contact with the C-loop of duodenum. Pancreatic fluid collections localize mostly in the lesser sac, a potential retroperitoneal space between the pancreas and posterior wall of the stomach. PFCs may extend in the retrocolic space to the left paracolic gutter, right paracolic gutter and even pelvis. Smaller fluid collections develop due to inflammatory exudate, vascular leakage and possible leakage of pancreatic secretions while larger fluid collections accumulate primarily due to pancreatic duct leakage as a result of pancreatic necrosis. As per the revised Atlanta classification, PFCs are classified into four categories based on the duration (less than or more than four weeks from the onset of pancreatitis) and absence or presence of necrosis: acute (peri)pancreatic fluid collection and acute necrotic collection (duration < 4 weeks) and pancreatic pseudocyst and walled-off necrosis (duration > 4 weeks) (Fig. 1A–D) [4]. Acute necrotic collections evolve into walled-off necrosis (WON) over time with encapsulation of the collection and partial liquefaction of the necrotic debris. Most of the acute PFCs resolve with expectant management [7]. A quarter of patients with ANC and approximately half of these with WON necrosis need interventions [8, 9].

Most PFCs remain sterile but up to 40% of patients with acute necrotic fluid collections develop secondary infection usually starting from the third week of the illness, known as infected necrotising pancreatitis (INP) but infection could occur even earlier. INP is associated with significant morbidity, prolonged intensive care unit (ICU) stay, prolonged hospitalization and need for intervention and contributes to mortality [5, 6]. INP should be suspected when patients

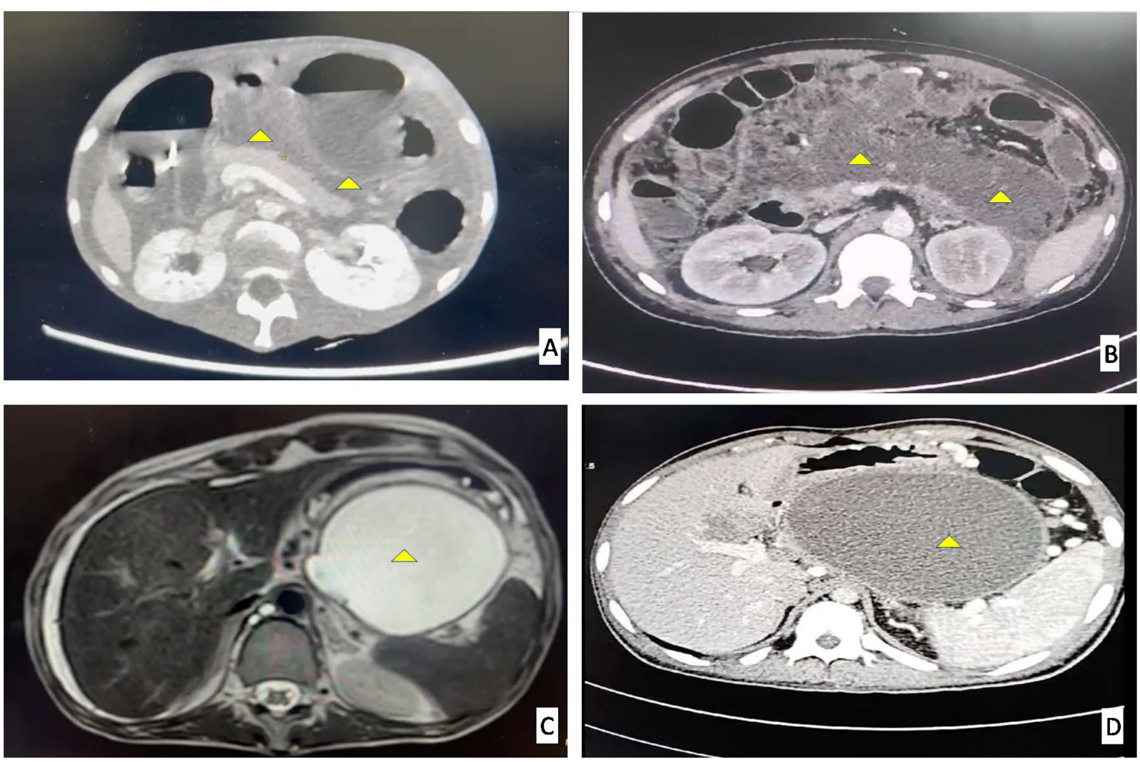

Fig. 1 Classification of different (peri)pancreatic fluid collections based on duration of onset and contents (various collections have been marked with yellow triangle in the given panels). **A** Acute (peri) pancreatic fluid collection. **B** Acute necrotic collection. **C** Pancreatic pseudocyst. **D** Walled-off necrosis (WON)

with ANP manifest with new-onset or persistent fever, leukocytosis, raised procalcitonin and lack of improvement or deterioration in clinical condition beyond the first week of illness. Patients with suspected INP should be subjected to cross-sectional imaging, preferably a contrast-enhanced computed tomography (CECT) of the abdomen to characterize the PFCs in terms of size, number, location, wall maturity, relative amount of necrosis and fluid and presence of gas bubbles, which suggest infection [4, 10]. INP may be confirmed by sampling and culture of the necrotic fluid, but that is generally not advised. It is recommended to manage patients with suspected INP without aspiration of the fluid to confirm the diagnosis.

Evolution of surgical interventions in acute pancreatitis

Over the last two decades, there has been a much better understanding of the pathophysiology and natural course of acute pancreatitis. Open surgical necrosectomy was considered the standard treatment [11] until 1991 when Bradley and Allen showed that conservative management leads to better outcomes in patients with acute sterile necrotising pancreatitis without infection when compared to surgery [12]. Traditionally, open surgical necrosectomy was practiced for infected necrotising pancreatitis and symptomatic sterile PFCs. However, open surgical necrosectomy leads to significant peri-operative stress, collateral damage and long-term complications such as pancreatico-cutaneous fistulas, exocrine and endocrine insufficiencies and surgical site hernias [4, 13–16]. Many parallel developments led to a remarkable shift from traditional open surgical necrosectomy to minimally invasive interventions over the past three decades. First, with the growing expertise, wide availability and technical success, laparoscopic surgical approaches replaced open surgery for many diseases. A landmark study, the PANTER trial [17], showed that minimally invasive 'step-up' approach of percutaneous drainage followed by minimally invasive surgery as needed was superior to open surgical necrosectomy. The second development was a change in thinking about the surgical dogma that all patients with infected necrosis required necrosectomy. A few case reports and case series showed that infected necrosis could be successfully treated without surgery. A comparative study showed that the mortality was lower among patients who were treated with conservative-first approach compared with upfront surgery [18]. A meta-analysis showed that 'conservative first' approach using antibiotics and drainage followed by necrosectomy, if required, was effective in managing INP and 64% patients could be treated without the need for necrosectomy [19]. Table 1 shows the results of various studies on the outcomes in patients undergoing minimally invasive vs. open surgical necrosectomy.

The third simultaneous development was emergence of endoscopic particularly EUS-guided procedures. Endoscopic drainage of pancreatic pseudocyst was first described in 1985 [24]. Endoscopic drainage of WON was first reported in 1996 [25] and direct endoscopic necrosectomy (DEN) was first described in 2000 [26]. A randomized controlled trial (RCT) showed similar efficacy of endoscopic drainage compared to surgery but with lower morbidity, shorter hospital stay, lower cost of management and improved quality of life at two-year follow-up in patients undergoing endoscopic necrosectomy [27]. Table 2 shows a summary of the studies comparing outcomes in patients undergoing endoscopic necrosectomy vs. surgical necrosectomy.

Subsequently, EUS-guided drainage and necrosectomy have been widely adopted as the standard and first line treatment for WON in most patients [10].

Indications and timing of intervention

Patients with INP should be first treated with broad-spectrum antibiotics, adequate nutrition and supportive care. Further intervention is indicated when there is no response to antibiotics [36–38]. The indications for drainage of PFCs include the following [10]:

i) Clinical suspicion or documented infection (INP), preferably after the PFC has evolved into WON.
ii) Clinical deterioration with worsening or new-onset organ failure in patients with acute necrotising pancreatitis preferably when the collection(s) has become at least partially encapsulated.
iii) Symptomatic sterile PFCs causing pressure effect leading to gastric outlet obstruction and/or biliary obstruction.
iv) Sterile WON causing symptoms such as intractable pain or persistent unwellness.
v) Disconnected pancreatic duct syndrome with persistent/recurrent symptomatic PFCs.
vi) The indications of drainage remain the same irrespective of the route of drainage, i.e. endoscopic, surgical or percutaneous (radiological).

Acute necrotic collection Pancreatic collections in the early phase of AP can either be acute (peri)pancreatic fluid collection(s) (APFC) or be ANC, which are mostly sterile. Sterile acute collections do not generally require any intervention and can be managed expectantly. ANCs contain adherent and partially liquefied debris which make them difficult to be drained effectively. A conservative management is thus advised until the ANC gets organized to form a mature WON and the debris may get partially liquefied

Table 1 Studies showing characteristics of open necrosectomy vs. minimally invasive surgery or endoscopic necrosectomy

Author	Type of study	Intervention	Number of patients	Etiology, *n* (%)	Infected necrotizing pancreatitis (INP), *n* (%)	Mortality, *n*	Major complications
Van Santvoort et al. (PANTER Trial), 2005–2008 [17]	RCT	PCD + VARD vs. open necrosectomy	43 vs. 45	Biliary: 26 (60) vs. 29 (64) Alcohol: 3 (7%) vs. 5 (11%) Other: 14 (33%) vs. 11 (24%)	39 (91) vs. 42 (93)	8/43 (18.6%) vs. 7/45 (15.5%)	Abdominal bleeding: 7/43 vs. 10/45 Pancreatico-cutaneous fistula: 12/ 43 vs. 17/45 Endocrine pancreatic insufficiency: 7/43 vs. 17/45
Garg et al. (1997–2008) [18]	Ambispective	Surgical necrosectomy vs. primary conservative treatment	30 vs. 50	Biliary:16 (53.3) vs. 32 (64) Alcohol: 3 (10) vs. 7 (14) Others: 11 (36.7) vs. 11 (22)	30 (100) vs. 50 (100)	13 (43.3%) vs. 14 (28%)	Organ failure at admission in 14 (46.7%) and 28 (56%); APACHE II score and serum creatinine were independent predictors of mortality
Bausch et al. 2002–2010 [20]	Retrospective	PCD + VARD vs. ETN vs. open necrosectomy	14 vs. 18 vs. 30	Biliary: 4 (29) vs. 5 (28) vs. 4 (13) Alcohol: 3 (21) vs. 4 (22) vs. 5 (17) Post-ERCP: 2 (14) vs. 1 (6) vs. 2 (7) Other: 5 (36) vs. 8 (44) vs. 19 (63)	13 (92) vs. 13 (72) vs. 25 (83)	3/14 vs. 3/18 vs. 19/30	Abdominal bleeding: 3/14 vs. 1/18 vs. 8/30 Pancreatico-cutaneous fistula: 2/14 vs. 0/18 vs. 5/30 Endocrine Pancreatic insufficiency: 0/14 vs. 0/18 vs. 5/30
Tan et al. 2011–14 [21]	Retrospective	ETN vs. open necrosectomy	11 vs. 21	Biliary: 5 (45) vs. 6 (29) Alcohol: 4 (36) vs. 6 (29) Other: 2 (18) vs. 9 (43)	10 (91) vs. 19 (90)	0/11 vs. 3/21	Abdominal bleeding: 0/11 vs. 3/21 Pancreatico-cutaneous fistula: 1/11 vs. 4/21 Endocrine Pancreatic insufficiency: 0/11 vs. 8/21
Woo et al. 2011–2016 [22]	Retrospective	PCD + VARD vs. ETN vs. open necrosectomy	8 vs. 12 vs. 10	Biliary: 2 (25) vs. 8 (67) vs. 5 (50) Alcohol: 1 (12.5) vs. 0 (0) vs. 2 (20) Post-ERCP: 1 (12.5) vs. 1 (8) vs. 1 (10) Other: 4 (50) vs. 3 (25) vs. 2 (20)		0/8 vs. 1/12 vs. 1/10	Abdominal bleeding: 0/8 vs. 3/12 vs. 1/10 Pancreatico-cutaneous fistula: 0/8 vs. 0/12 vs. 3/10 Endocrine pancreatic insufficiency: 0/8 vs. 0/12 vs. 3/10

Table 1 (continued)

Author	Type of study	Intervention	Number of patients	Etiology, *n* (%)	Infected necrotizing pancreatitis (INP), *n* (%)	Mortality, *n*	Major complications
Hollemans et al. 2019 [23]	Prospective (long-term (7 years) follow-up of RCT (PANTER Trial))	PCD + VARD vs. open necrosectomy	35 vs. 38			5/35(14%) vs. 2/38 (5%)	Recurrent pancreatitis: 6/30 vs. 8/36 Endocrine insufficiency: 12/30 vs. 23/36 Exocrine insufficiency: 8/28 vs. 18/32 Steatorrhea: 5/28 vs. 0/31

ETN endoscopic transmural necrosectomy, *PCD* percutaneous catheter drainage, *VARD* video-assisted retroperitoneal debridement, *ERCP* endoscopic retrograde cholangiopancreatography, *APACHE II* Acute Physiology and Chronic Health Evaluation II, *RCT* randomized controlled trial

(usually after four weeks of onset). Infected ANC on the other hand may require drainage even in the early stage if there is clinical deterioration on conservative management. Early drainage has been shown to be effective in such patients. An RCT (POINTER TRIAL) [36] compared early percutaneous catheter drainage with postponed intervention in INP and showed similar outcomes in terms of mortality (13% in the immediate-drainage vs. 10% in the postponed drainage group) but the mean number of interventions was slightly more in the early drainage arm (4.4 vs. 2.6). Adverse event profile was similar in both groups. A retrospective study showed a survival of 73.1% in patients with suspected INP who underwent early drainage in < 21 days (median 14 [8–18]) of illness and showed that 53.8% of patients survived with percutaneous catheter drainage (PCD) alone, while 19.2% required percutaneous endoscopic necrosectomy [39]. A systematic review and meta-analysis assessed the technical success, clinical success and adverse events of early (< 4 weeks) EUS-guided endoscopic drainage vs. delayed (> 4 weeks) drainage [40]. Total 630 patients were included (182 [28.9%] in early drainage arm and 448 [71.1%] in delayed drainage arm). Overall, technical and clinical success (OR, 0.39; 95% CI 0.13–1.22; $p = 0.11$) were similar in both arms with no difference in adverse event profile (OR, 1.67; 95% CI, 0.63–4.45; $p = 0.31$) or mortality (OR, 1.14; 95% CI, 0.29–4.48; $p = 0.85$). Hospital stay was longer in patients undergoing early drainage compared with delayed drainage (23.7 vs. 16.0 days, respectively). In another retrospective study [41], the safety and efficacy of endoscopic transmural drainage (ETD) vs. PCD was assessed in patients with symptomatic necrotic PFCs in early phase of illness (< 4 weeks). In this study, as compared to the ETD group, patients in PCD group took longer time for resolution (61.9 ± 22.9 days vs. 30.9 ± 5.6 days; $p < 0.00001$), increased need for surgery (30% vs. 4%; $p = 0.01$) and a higher frequency of external pancreatic fistula (EPF) (22% vs. nil; $p = 0.02$) but there was no difference in mortality (5 vs. 2, $p = 1.0$).

Surgical intervention in the early phase may be required in emergency situations such as perforation of hollow viscus, severe bleeding not controlled by angiographic intervention and bowel ischemia. Necrosectomy is not advisable during such an emergency laparotomy which could increase complications [10, 13].

Pseudocyst and walled-off necrosis Pancreatic collections beyond four weeks of illness can be either pseudocysts or WON and require drainage if symptomatic or infected. Asymptomatic collections should be managed expectantly and may not require drainage irrespective of size, location and extent. Both pseudocyst and WON are quite similar in terms of indications and technique of drainage but WON

Table 2 Studies showing comparison of endoscopic drainage and/or necrosectomy versus minimally invasive surgical drainage and/or necrosectomy (laparoscopic or VARD) in patients with acute pancreatitis

Author	Type of study	Intervention	Number of patients	Etiology, *n* (%)	Infected necrotizing pancreatitis (INP), *n* (%)	Mortality, *n* (%)	Major complications
Bakker et al. 2008–2010 (PENGUIN Trial) [28]	RCT	Surgical (VARD) vs. endoscopic (ETN)	10 vs. 10	Biliary: 7 (70%) vs. 6 (60%) Alcohol: 2 (20%) vs. 2 (20%) Other: 1 (10%) vs. 2 (20%)	9 (90%) vs. 10 (100%)	4 vs. 1	Bleeding: 0 vs. 0 Perforation: 2 vs. 0 Pancreatic fistula: 7 vs. 1 New-onset organ failure: 5 vs. 0 Incisional Hernia: NA
Kumar et al. 2009–2010 [29]	Prospective	Surgical (PCD + VARD) vs. endoscopic (ETN)	12 vs. 12	Biliary: 5 (42%) vs. 7 (58%) Alcohol: 3 (25%) vs. 3 (25%) Hypertriglyceridemia: 1 (8.3%) vs. 0 (0%) Other: 3 (25%) vs. 2 (16.7%)		1 vs. 0	Bleeding: NA Perforation: NA Pancreatic fistula: NA New-onset organ failure: NA
Khreiss et al. 2008–2013 [30]	Retrospective	Surgical (VARD or LD) vs. endoscopic (ETD + ETN)	20 vs. 20	Biliary: 13 (65%) vs. 9 (45%) Alcohol: 3 (15%) vs. 3 (12%) Idiopathic: 3 (15%) vs. 2 (10%) Other: 1 (5%) vs. 6 (30%)		0 vs. 0	Bleeding: NA Perforation: NA Pancreatic fistula: NA New-onset organ failure: NA
Varadarajulu et al. 2013 [27]	RCT	Surgical vs. endoscopic	20 vs. 20	Biliary: 10 (50%) vs. 6 (30%) Alcohol: 4 (20%) vs. 11 (55%) Others: 6 (30%) vs. 3 (15%)	0 (0%) vs. 0 (0%)	0 vs. 0	Bleeding: 1 vs. 0 Infection: 1 vs. 0
He et al. 2013–2014 [31]	Prospective	Surgical (PCD + VARD) vs. endoscopic (ETD/ETN)	13 vs. 13	Biliary: 7 (53.8%) vs. 5 (45.5%) Alcohol: 2 (15.4%) vs. 4 (36.4%) Other: 4 (30.8%) vs. 2 (18.2%)		3 vs. 3	Bleeding: 2 vs. 1 Perforation: 5 vs. 1 Pancreatic fistula:1 vs. 0 New-onset organ failure: 0 vs. 1

Table 2 (continued)

Author	Type of study	Intervention	Number of patients	Etiology, *n* (%)	Infected necrotizing pancreatitis (INP), *n* (%)	Mortality, *n* (%)	Major complications
van Brunschot et al. 2011–2015 (TENSION Trial) [32]	RCT	Surgical (PCD + VARD) vs. endoscopic (ETD/ETN)	47 vs. 51	Biliary: 30 (64%) vs. 26 (51%) Alcohol: 7 (15%) vs. 7 (14%) Other: 10 (21%) vs. 18 (35%)	27 (57%) vs. 23 (45%)	6 (13%) vs. 9 (18%)	Bleeding: 10 (21%) vs. 11 (22%) Perforation: 8 (17%) vs. 4 (8%) Pancreatic fistula: 13/42 (32%) vs. 2/42 (5%) New-onset organ failure: Single: 13 (28%) vs. 7 (14%) Multiple: 6 (13%) vs. 2 (4%)
Bang et al., 2014–2017 (MISER Trial) [33]	RCT	Surgical (VARD/LD) vs. endsocopic (ETD/ETN)	32 vs. 34	Biliary: 8 (25%) vs. 14 (41.2%) Alcohol: 11 (34.4%) vs. 6 (17.6%) Idiopathic: 11 (34.4%) vs. 14 (41.2%) Hypertriglyceridemia: 1 (3.2%) vs. 0 (0%)	30 (94%) vs. 31 (91%)	2 (6%) vs. 3 (9%)	Bleeding: 3 (9%) vs. 0 (0%) Perforation: 0 vs. 0 Pancreatic fistula: 9 (28%) vs. 0 New-onset organ failure: 3 (9%) vs. 2 (6%)
Garg et al. 2019 [34]	RCT	Surgical (laparoscopic/ open cystogastrostomy) vs. endoscopic (ETD/ ETN)	30 vs. 30	Biliary: 13 (43.3%) vs. 14 (46.6%) Alcohol: 9 (30%) vs. 8 (26.6%) Idiopathic: 8 (26.6%) vs. 8 (26.6%)	2 (6.6%) vs. 4 (13.3%)	0 vs. 0	Bleeding: Perforation: 1 vs. 1 Pancreatic fistula: NA New-onset organ failure: 2 (6.6%) vs. 2 (6.6%) Post-procedural infection: 9/30 vs. 19/30
Angadi et al., 2021 [35]	RCT	Surgical (laparoscopic cystogastrostomy) vs. endoscopic (ETD/ETN)	20 vs. 20	Biliary: 2 (10%) vs. 3 (15%) Alcohol: 8 (40%) vs. 5 (25%) Idiopathic: 9 (45%) vs. 9 (45%) Others: 1 (5%) vs. 3 (15%)	2 (10%) vs. 1 (5%)	0 vs. 1	Bleeding: 1 vs. 1 Perforation: 1 vs. 0 Pancreatic fistula: NA Post procedural infection: 5 vs. 4 New-onset organ failure: 0 vs. 1

ETD endoscopic transmural drainage, *ETN* endoscopic transmural necrosectomy, *LD* laparoscopic debridement, *PCD* percutaneous catheter drainage, *RCT* randomized controlled trial, *VARD* video-assisted retroperitoneal debridement differs significantly with regard to higher complications, particularly infection and the need for necrosectomy.

Route of drainage Drainage can be achieved by either percutaneous or per-oral endoscopic transmural route.

Percutaneous catheter drainage is generally used for acute fluid collections and infected collections early in the course of illness when the collections are not well encapsulated or are away from the gastroduodenal wall. Retroperitoneal route is generally preferred. The PCD tract can be used later for video-assisted retroperitoneal debridement (VARD) or percutaneous endoscopic necrosectomy (PEN).

Endoscopic drainage is preferred for mature PFCs with well-defined walls which are located in the lesser sac and are in close proximity to either the stomach or the duodenum. Endoscopic transmural drainage is not preferred for collections that are placed anteriorly and likely to be intraperitoneal (Supplementary Fig. 1A and B).

Techniques of drainage and endoscopic necrosectomy

Endoscopic transmural drainage or percutaneous drainage via retroperitoneal approach is now recommended as the first-line treatment [10, 15] for INP depending on the location of the collection (Tables 1 and 2). Depending on the timing of presentation from the onset of AP, location and wall maturity of the collection and available expertise, either an endoscopic or a percutaneous approach can be employed [4, 13, 14]. Minimally invasive necrosectomy can be performed after the drainage, if required, as a part of the step-up approach.

Per-oral endoscopic approach is suitable for WON in close proximity to the gastroduodenal lumen, ideally, < 1 cm from the posterior gastric wall or medial duodenal wall, but PFCs with a distance of up to 2 cm can be safely punctured under EUS guidance [38]. Percutaneous approach is preferred for necrotic collections located away from the gut lumen and those with poor wall formation/demarcation. Thus, a multimodality team comprising a gastroenterologist, interventional radiologist and surgeon is required for the successful management of these patients.

Endoscopic technique for drainage of pancreatic collections

Endoscopic cystogastrostomy was traditionally done under endoscopic guidance by direct puncture of the gastric wall over the visible bulge due to the underlying collection to create a stoma followed by placement of one or two plastic stents after dilatation of the tract with a balloon. Over the past more than a decade, endoscopic drainage has shifted from the endoscopic vision to EUS guidance. EUS provides many advantages such as (i) direct visualization and proper assessment of the PFC in terms of its wall, content and size; (ii) assessment of the distance between the PFC and the gastric wall; and (iii) avoidance of interposing vessel in the gastric wall [42–44] (Supplementary Fig. 2A-F) and Supplementary Video 1. EUS-guided approach has been shown to have a higher technical success (95% vs. 33% to 66%) and lower adverse events (0% to 4% vs. 13% to 15%) than direct transmural endoscopic drainage as shown in two RCTs [42, 43] and is now the preferred procedure [4, 10, 13].

A 19-G needle is used to puncture the gastric wall to enter the collection and a guidewire (0.025–0.035-in. diameter) is inserted to make two loops inside the collection. The puncture tract is first dilated with the help of a 6F catheter over the guidewire using cautery and then balloon dilatation (12–15 mm) is done followed by placement of two double pigtail plastic stents (7–10 Fr) for continuous drainage (Supplemetary Fig. 2A-F) and Supplementary Video 1. This procedure has shown a technical success of 89% to 100%, a clinical success of 82% to 100% and < 1% procedure-related mortality in patients with pancreatic pseudocysts [45, 46]. The cystogastrostomy tract generally narrows in a few days and plastic stents provide limited flow of cyst contents through and alongside the stents. Direct endoscopic necrosectomy can also be performed through the tract at subsequent sessions which often requires re-dilatation [47–51]. Fully covered self-expandable metal stent (FcSEMS) or lumen apposing metal stent (LAMS) were introduced to provide a wider stoma for drainage and ability to do necrosectomy through the stent. The dumbbell shape of the LAMS prevents its migration providing sufficient axial force for close apposition of the gastric wall and necrotic collection. The wider diameter of the metal stents allows better access for direct endoscopic necrosectomy. Cautery-enhanced lumen apposing metal stent (CE-LAMS) allows easier and faster deployment using a single step access (Fig. 2A–D and Supplementary Video 2) [52].

Metal stents versus plastic stents

Many studies have compared multiple plastic stents with metal stents. A retrospective study showed better clinical success and lesser adverse events with EUS-guided drainage using FcSEMS vs. double pigtail plastic stents for pancreatic pseudocysts [53]. A randomized study by Lee et al. [54] showed equal efficacy, safety and technical success of FcSEMS and plastic stents in managing pancreatic fluid collections. The only difference was shorter procedure time using FcSEMS. For the management of WON, a retrospective study assessed the efficacy and safety of biflanged metal stents (BFMS) against plastic stents and found no statistical difference in technical success, clinical success and adverse events between the two groups. However, BFMS was associated with shorter procedure time and re-intervention durations for the

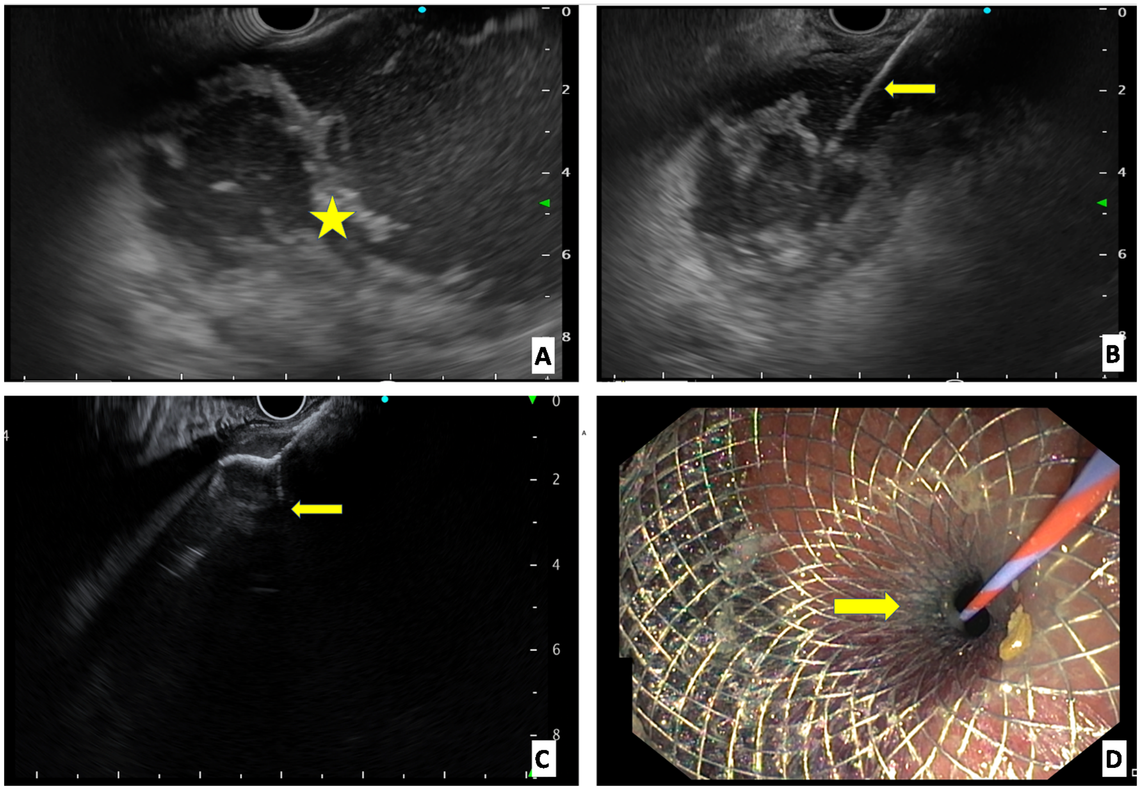

Fig. 2 Endoscopic ultrasound (EUS)-guided cystogastrostomy using cautery-enhanced lumen apposing metal stent (CE-LAMS). **A** EUS identification of the walled-off necrosis (WON) (yellow asterisk). **B** Puncture using cautery enhanced delivery system of LAMS (yellow solid arrow). **C** Deployment of internal/distal flange under EUS vision (yellow solid arrow). **D** Deployment of external/proximal flange under endoscopic vision across the gastric puncture site (yellow solid arrow)

management of residual necrosis using DEN [55]. A systematic review did not find any difference in treatment success, adverse events and recurrence of pancreatic collections when managed using either plastic or metal stents [56].

An international multicenter study showed usefulness of LAMS over plastic stents with higher clinical success, shorter procedural time, lower need for surgery and lower recurrence rates in the setting of WON [57]. However, another RCT of 60 patients comparing LAMS with plastic stents showed no difference in clinical success and higher stent related adverse events such as bleeding and biliary stricture with LAMS (32.3% vs. 6.9%) [58]. It is advisable to remove LAMS at three to four weeks after insertion because of the increased risk of bleeding.

Placement of a coaxial double pigtail plastic stent through the metal stent

A coaxially placed plastic stent within a metal stent may potentially prevent complications pertaining to LAMS including bleeding, stent migration, obstruction and infection of the collection. An RCT compared coaxial double pigtail plastic stent (DPPS) ($n = 34$) with no DPPS ($n = 33$) through the LAMS and showed that the addition of a coaxial DPS within a LAMS was associated with a significantly lower global rate of AEs (20.7% vs. 51.5%, $p = 0.008$) and stent occlusion rate (14.7% vs. 36.3%, $p = 0.042$) in EUS-guided drainage of WON [59]. A systematic review and meta-analysis including 709 patients with pancreatic collections who underwent endoscopic drainage showed no difference in the clinical (OR 0.96, 95% CI, 0.48–1.89; $p = 0.44$) and technical success (OR 1.08, 95% CI, 0.59–1.96; $p = 0.39$) in patients with or without coaxial DPPS through LAMS [60]. However, the overall incidence of stent occlusion and infection was lower in patients who underwent coaxial plastic stent placement and there was no significant difference in the rates of bleeding between the two groups (OR, 0.61; 95% CI, 0.22–1.67; $p = 0.12$) [60]. In general, LAMS may be preferred if there is a significant amount of necrotic debris, i.e. > 30% of the volume of the WON or if it is infected.

Placement of a plastic stent after removal of the metal stent

After successful drainage of the collection, LAMS may be exchanged for a plastic stent at the time of its removal, which can be kept in situ for six months or so. This can be done to prevent the chance of recurrence of collection in patients with suspected DPDS. A retrospective observational study of 53 patients showed increased recurrence of collections and need for re-interventions in patients who did not undergo plastic stent placement after removal of LAMS [61]. However, an RCT of 104 patients did not show any difference in the rates of recurrence of collections and need for reintervention between the plastic stent and no plastic stent groups when assessed until 12 months [62]. A recent systematic review and meta-analysis assessed the outcome of recurrent PFCs in patients with acute pancreatitis and DPDS undergoing either plastic stent or no stent placement after removal of the LAMS [63]. Total 246 patients (143 in the plastic stents group and 103 in the no plastic stents group) were assessed. A lower rate of recurrent PFCs was found in those who received plastic stent insertion after removal of LAMS when compared to no plastic stents (OR 0.15; 95% CI 0.15–1.83; $p = 0.31$). No additional serious adverse events or mortality were noted with stent placement or exchange [63]. There is complete resolution of collection in 20% to 40% cases at the time of LAMS removal precluding the placement of the plastic stent [64]. Some interventional endoscopists also prefer placement of nasocystic drain at the time of LAMS placement for continuous irrigation of the pancreatic cavity but it is usually not required [51].

While drainage alone might be sufficient for managing pseudocysts and WON with < 30% necrosis, most patients with WON having > 30% necrosis and those with infected necrosis require additional necrosectomy.

Direct endoscopic necrosectomy

DEN is usually required for persistent infection after ETD [32]. DEN has traditionally been done using instruments designed for other endoscopic purposes such as stone retrieval baskets, polypectomy snares, Roth-net basket and grasping forceps. It may require many sessions for complete resolution. Newer devices such as Endorotor, waterjet necrosectomy device and over-the-scope grasper (Xcavator, Ovesco AG, Tubingen, Germany) are still in the experimental phase and being tested for endoscopic debridement.

DEN is performed through the LAMS or cystogastrostomy tract [65, 66]. The cavity is entered using a forward-viewing endoscope. The cavity is lavaged and solid debris is removed using the endoscopic accessories. DEN helps in resolution with close to 80% success rate, but may lead to certain complications such as bleeding, perforation and air embolism in 3% to 35% of cases [65, 66]. Necrosectomy can be performed either at the time of initial drainage or in subsequent sessions. In a large multicenter retrospective study [66] comparing immediate DEN ($n = 69$) with delayed DEN ($n = 202$) performed at one week after the initial LAMS-assisted drainage procedure, the clinical success was similar in both groups (91.3% immediate vs. 86.1% delayed, $p = 0.3$). However, the immediate DEN group required fewer necrosectomy sessions (3.1 vs. 3.9, $p < 0.001$). Although the recent DESTIN trial has also shown that upfront endoscopic necrosectomy led to fewer reinterventions and a shorter hospital stay compared with a step-up endoscopic approach in stable patients with INP [67], we however, do not recommend upfront necrosectomy, which requires prolonged procedure time and may lead to complications in sick patients.

Table 3 shows the efficacy and clinical outcomes of endoscopic transmural drainage and necrosectomy in various studies. Supplementary Video 3, provided in supplementary content, shows the procedural details of DEN.

Comparison of per-oral endoscopic and laparoscopic drainage of WON

Another effective minimally invasive modality to drain WON located in the lesser sac is laparoscopic drainage. An RCT comparing laparoscopic vs. endoscopic drainage with plastic stents showed that resolution of WON was similar in both the groups (93.3% in laparoscopic vs. 90% in endoscopic) [34]. Complications were also similar in both groups except post-procedural infection which was more in the endoscopic group (63.3% vs. 30%) requiring endoscopic re-intervention [34]. Another RCT using the metal stents in the endoscopy group for WON with > 30% necrotic debris showed similar outcomes (80% in laparoscopic arm vs. 76% in endoscopic arm) without any difference in the complication rates and need for additional procedures [35]. These studies support equal efficacy of laparoscopic and endoscopic transmural internal drainage of symptomatic pseudocysts and WON.

Percutaneous drainage and percutaneous endoscopic necrosectomy

Percutaneous drainage is indicated in infected necrotic collections which are predominantly laterally placed in the paracolic area (Supplementary Fig. 3A-B) and are not responding to conservative management with intravenous antibiotics. Percutaneous drainage is done by an interventional radiologist generally under computed tomography (CT) guidance. The initial catheter used is usually 12–14 Fr but large bore catheter of size 16 Fr to 20 Fr is generally required for optimum drainage of thick pus and small bits of necrotic debris [87]. Upfront drainage with large bore catheter (> 20 Fr) is not advocated due to increased risk of bleeding [88]. The size of the necrotic collection and amount of debris along with clinical judgement of the gastroenterologist and the interventional radiologist should guide the need of upgradation of the PCD catheter for further

Table 3 Summary of studies in patients with acute pancreatitis and pancreatic fluid collections showing outcomes of endoscopic drainage and necrosectomy

Author	Patients (*n*)	Infected (%)	Timing of intervention (mean/median days after presentation)	Modality	Mean number of repeat interventions	Overall success rate (%)	All-cause mortality	Complications
Baron et al. ***(1996)*** [25]	11	3 (27%)	50	Transmural stents + nasocystic lavage ± transpapillary stenting	2.7	9 (82%)	0	Bleeding—5 Perforation—1 Infection—4
Seifert et al. ***(2000)*** [26]	3	1 (33%)	NA	ETN-first report	NA	3 (100%)	NA	NA
Park et al., ***(2002)*** [68]	9	9 (100%)	42	Transmural stents + nasocystic lavage	NA	8 (89%)	0	Bleeding—1
Seewald et al. ***(2005)*** [69]	13	13 (100%)	NA	ETN + transmural stents + nasocystic lavage ± transpapillary stenting	7	11 (85%)	0	Bleeding—4
Charnley et al. ***(2006)*** [70]	13	11 (85%)	27	ETN	4	9 (69%)	2 (15%)	NA
Voermans et al. ***(2007)*** [71]	25	19 (76%)	84	Transmural stents + nasocystic lavage	2	23 (92%)	0	Major bleeding—1 Minor bleeding—8 Perforation—1
Papachristou et al. ***(2007)*** [72]	53	26 (49%)	49	Transmural stent ± ETN ± transpapillary stenting ± PCD	3	43 (81%)	3 (6%)	Bleeding—9 Gallbladder puncture—1 Stent migration—2
Escourrou et al. ***(2008)*** [73]	13	13 (100%)	28	PCD ± ETN	1.8	13 (100%)	0	Bleeding—3 Infection—3
Hocke et al. ***(2008)*** [74]	30	30 (100%)	NA	ETN	2.7	27 (90%)	2 (6.6)	Bleeding, infection and fistula in 10%
Mathew et al. ***(2008)*** [75]	6	6 (100%)	42	Transmural stents + nasocystic lavage	0	6 (100%)	0	0
Schrover et al. ***(2008)*** [76]	8	8 (100%)	33	Transmural stents + nasocystic lavage	4	6 (75%)	1 (12.5%)	Bleeding—1 Pneumoperitoneum—1 (fatal)
Seifert et al. ***(2009)*** [77]	93	50 (54%)	43	ETN	6.2	75 (81%)	7 (7.5%)	Bleeding—13 Perforation—5 Fistula—2 Infection—1 Air embolism—2
Ross et al. ***(2010)*** [78]	15	9 (60%)	29	PCD ± ETN	1.4	15 (100%)	0	Infection—1

Table 3 (continued)

Author	Patients (*n*)	Infected (%)	Timing of intervention (mean/median days after presentation)	Modality	Mean number of repeat interventions	Overall success rate (%)	All-cause mortality	Complications
Gardner et al. *(2011)* [48]	104	40 (39%)	63	ETN	3	95 (91)	2 (1.9%)	Major bleeding—2 Minor bleeding—19 Retrogastric perforation—2 Pneumoperitoneum—3 Air embolism—1
Bakker et al. *(2012)* [28]	10	10 (100%)	59	PCD ± ETN or VARD	3	10 (100)	1 (10%)	Pancreatic fistula—1 Others—1
Rische et al. *(2013)* [79]	31	24 (77%)	NA	ETN + transmural stents + nasocystic lavage ± transpapillary stenting	4	26 (83%)	3 (9.6%)	Perforation of colon—2 Stent dislocation to jejunum—1 Major bleeding—1 (fatal)
Yasuda et al. *(2013)* [80]	57	57 (100%)	50	ETN + transmural stents + nasocystic lavage	5	43 (75%)	6 (11%)	Major bleeding—5 Perforation—3 Air embolism—1
Akshintala et al. (2014) [81]	41	NA	NA	ETD ± ETN ± PCD	4	29 (70.7%)	0 (0%)	Bleeding—3 Infection—3
Keane et al. (2016) [82]	109	22 (20.2%)	NA	ETD ± ETN ± PCD	1.8	(70%)	0(0%)	Clinical signs of infection—55 Major bleeding—2 Perforation—5 Pneumothorax—1 Aspiration—1
Siddiqui et al. (2017) [65]	313	NA	NA	ETD (DPPS, FcSEMS, LAMS) ± ETN	2.5	278 (88.8%)	NA	**Early AE:** Bleeding—8 Infection—7 Perforation—5 Other-6 **Late AE:** Migration—10 Stent occlusion with infection—52

Table 3 (continued)

Author	Patients (*n*)	Infected (%)	Timing of intervention (mean/median days after presentation)	Modality	Mean number of repeat interventions	Overall success rate (%)	All-cause mortality	Complications
Bapaye et al. (2017) [83]	133	90(67.67%)	NA	ETD (DPPS, BFMS) ± ETN	DPPS: 2.74 BFMS: 1.46	Technical success: 133 (100%) Clinical success: 73.7% (DPPS), 94.4% (BFMS)	7 (5.26%)	Bleeding—7 Infection—18 Migration—2
Wang et al. (2018) [84]	160	NA	NA	ETD (DPPS, FcSEMS, LAMS) ± ETN	NA	Technical success: 151 (94.38%) Treatment success: 125 (82.78%)	3 (1.9%)	**Early AE:** Infection—26 Bleeding—9 Migration—4 Other—6 **Late AE:** Occlusion/infection—4 Bleeding—2 Migration—14 Other—2
Chen et al. (2019) [57]	189	50 (26.6%)	NA	ETD (DPPS, LAMS) ± ETN ± PCD	DPPS: 2.6 LAMS: 1.9	Technical success: LAMS (100%), DP PS (98.7%) Clinical success: LAMS (80.4%), DPPS (57.5%)	NA	Bleeding—10 Peritonitis—4 Perforation—1 Misdeployment—1 Other—2
Rana et al. (2021) [85]	170 (Early ETD = 34 Late ETD = 136)	Early: 27 (79.4%) vs. 94 (65.1%)	Mean time to intervention Early: 23.7 (2.6) vs. late: 74.6 (19.7)	ETD ± ETN (LAMS Early—11[32.4%] vs. late—12 [8.8%])	Mean number of repeat interventions: Early: 6 (1.7) vs. 3.1 (1.1)	Clinical success: 94% in early vs. 100% in late arm Need for ETN: early (50%) vs. late; (7.4%); $p < 0.001$ Need for surgical necrosectomy: early (5.7%) vs. late (0%)	5% (early) vs. 0% (Late)	**Bleeding—** **Early—7 (20%) vs. late—2 (1.5%); *p* < 0.001**

Table 3 (continued)

Author	Patients (*n*)	Infected (%)	Timing of intervention (mean/median days after presentation)	Modality	Mean number of repeat interventions	Overall success rate (%)	All-cause mortality	Complications
Shah et al. (2023) [86]	101 (Early—35 [34.7%] vs.)	Early—31 (88.6%) vs. late—12 (18.2%)	NA	ETD ± ETN (Metal stent—early—22 [62.9%] vs. late—41 [62.1%])	Mean number of repeat interventions: early—1.74 (0.872) vs. 1.76 (0.752)	Clinical success: early (85.7%) vs. late (97%) Need for ETN: early (57.1%) vs. late (27.3%) Additional PCD: early (31.4%) vs. late (12.1%)	Early—4 (11.4%) vs. late 1 (1.5%)	**Bleeding: Early—3 (8.5%) vs. late—0 (0%) Peritonitis: early—0 (0%) vs. late—1 (1.5%)**

AE adverse event, *DPPS* double pigtail plastic stent, *BFMS* biflanged metal stent, *ETD* endoscopic transmural drainage, *ETN* endoscopic transmural necrosectomy, *FcSEMS* fully covered self-expandable metal stent, *LAMS* lumen apposing metal stent, *PCD* percutaneous catheter drainage, *VARD* video-assisted retroperitoneal debridement

intervention(s). Minimally invasive techniques such as VARD or minimal access retroperitoneal pancreatic necrosectomy (MARPN) are commonly used surgical modalities for retroperitoneal necrosectomy. VARD is traditionally performed using a surgical incision of size 5 cm for insertion of a laparoscope/nephroscope, irrigation catheter and surgical forceps. Minimally invasive surgery as a part of step-up therapy is advocated as the treatment of choice when compared to open necrosectomy [17]. Percutaneous endoscopic necrosectomy is another minimally invasive approach in which a flexible endoscope is used instead of the rigid laparoscope/nephroscope through the percutaneous tract for debridement of solid necrotic debris. Adequate necrosectomy leads to resolution of necrotic collections and infection in patients with INP [89]. A flexible endoscope allows better access and manipulation in the retroperitoneum. PEN is suitable for (a) predominantly laterally placed infected PFCs, not amenable to per-oral endoscopic drainage; (b) unstable patients who are not fit for general anesthesia and (c) extensive gas in the infected collection resulting in poor visualization on EUS. PEN should be avoided if (i) a large vessel is seen coursing through the cavity; (ii) there is a suspicion of colonic fistula; (iii) there is hemorrhage in the pancreatic bed (a relative contraindication; PEN can be done after angioembolization of the pseudoaneurysm) and (iv) there is extensive (peri) pancreatic necrosis in which case surgical modality should be preferred.

Technique of percutaneous endoscopic necrosectomy

Percutaneous drainage of the laterally placed necrotic pancreatic collection is achieved under radiological guidance preferably through the retroperitoneal approach which avoids peritoneal contamination and risk of bowel injury. After initial drainage, gradual upgradation of the catheter is the prerequisite for PEN with a minimum catheter size of 18 Fr. The procedure can be done under local anesthesia and conscious sedation in the regular endoscopy theatre. PCD is first removed under strict aseptic precautions and an ultrathin flexible endoscope (outer diameter 4.9–5.5 mm) is introduced through the sinus tract after thorough disinfection of the scope using glutaraldehyde and cleaning of biopsy channel using absolute alcohol and betadine. Under endoscopic vision, the sinus tract is entered by instillation of normal saline and CO_2 insufflation at a maximum rate of 1.5–2.0 L/min. After careful inspection of the cavity, liquid pus should be aspirated with gentle suctioning and the cavity should be irrigated using saline. Intermittent withdrawal of the scope is advocated to avoid rise in intracavitary pressure and prevent leakage from the cavity. The size and the content of the cavity determine the need for further sessions of percutaneous endoscopic lavage and necrosectomy. The PCD should be upgraded to a larger bore size catheter

(2–4 Fr more than previous catheter) at each session until a catheter of size 30 Fr is achieved. Percutaneous endoscopic lavage sessions are advised every two to three days. Instead of gradual upgradation of the catheter, a wire guided fully covered SEMS of size 14–18 mm can be placed to achieve early dilation of the tract in patients with sepsis requiring accelerated intervention.

PEN can be performed through the sinus tract/SEMS once the target catheter size of 30 Fr is achieved to allow access using an adult upper gastrointestinal tract endoscope (~9.2 mm in diameter). Necrosectomy can then be performed similar to DEN using standard endoscopic accessories such as a polypectomy snare, Roth-net basket and grasping forceps [90]. The duration of the procedure usually varies from 30 to 60 minutes and depends on the general condition of the patient, the amount of necrotic debris and the endoscopist's judgement. Complete clearance of the cavity should not be the aim in the first session of necrosectomy. After the cavity is completely cleared, a smaller catheter, usually a 18-Fr nasogastric tube can be placed to observe the quality of drain fluid for a few days. Figure 3A–F and Supplementary Video 4 describe the key steps of PEN. Once clear drain fluid is observed, the catheter is cut short and placed in an ostomy bag to eliminate gravity-assisted drainage. Once the catheter output decreases to below 10–20 mL/day, it can be safely removed and the tract closes spontaneously. A recently conducted meta-analysis of PEN in 284 patients from 16 cohort studies showed a clinical success rate of 82% (95% CI; 77–87%) with no documented procedure-related mortality and a peri-procedure morbidity of 10%. In view of these obervations, PEN can be advocated as a safe and effective endoscopic minimally invasive intervention adding to our armamentarium to treat infected necrotising pancreatitis [91]. Supplementary Table 1 shows various studies describing the outcomes of patients following PEN. Key steps of endoscopic drainage and percutaneous drainage are shown in Fig. 4A–B.

Comparison of endoscopic versus percutaneous drainage

A multicentre study in the US assessed the safety and outcomes of endoscopic drainage and necrosectomy vs. percutaneous necrosectomy and surgical necrosectomy in 2281 patients with ANP (672 in endoscopic, 1338 in percutaneous necrosectomy and 271 in surgical necrosectomy) [92]. The rate of mortality was lower in endoscopic

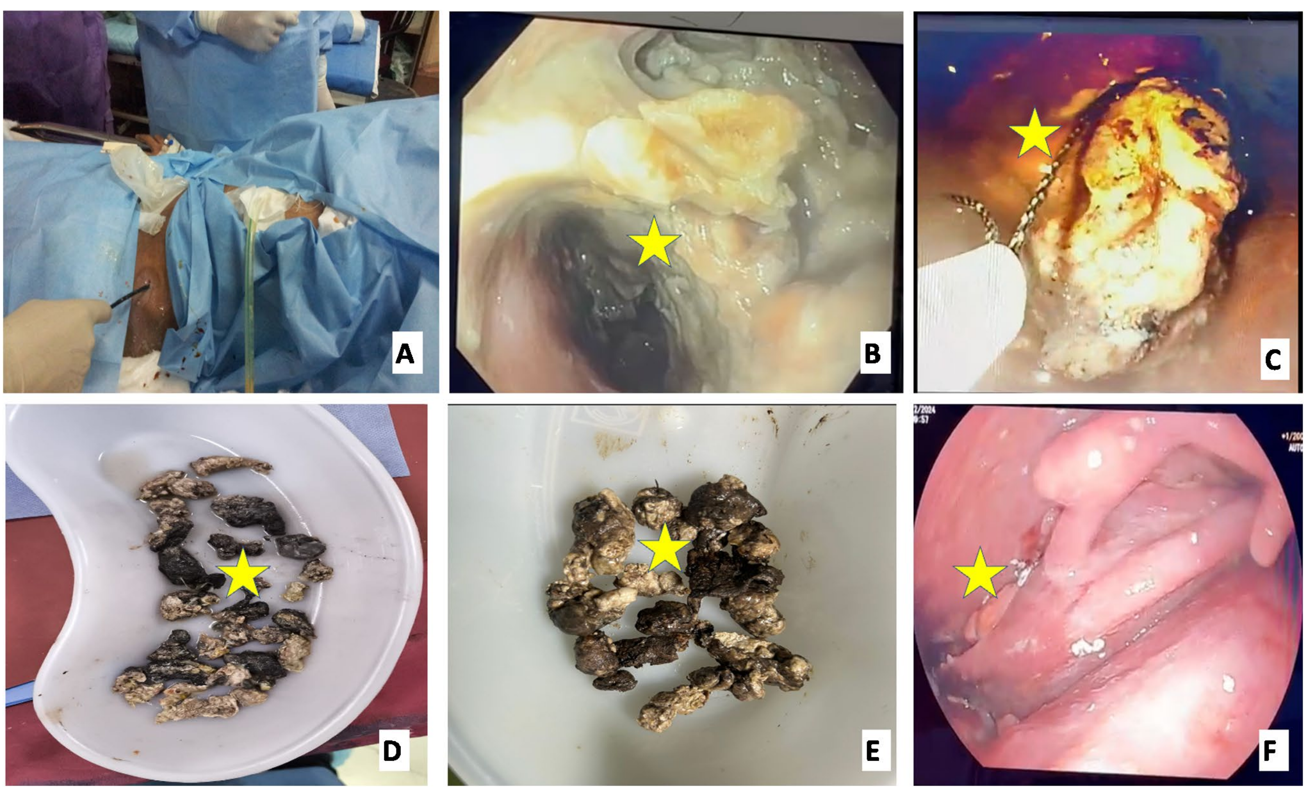

Fig. 3 Percutaneous endoscopic necrosectomy. **A** Insertion of the flexible endoscope through the percutenous drain site. **B** Inspection of the cavity showing extensive necrotic debris (yellow asterisk). **C** Removal of the necrotic debris using snare and Roth-net (yellow asterisk). **D**, **E** Removal of large chunks of necrotic debris in serial sessions (yellow asterisk). **F** Residual clean cavity showing granulation tissue (yellow asterisk)

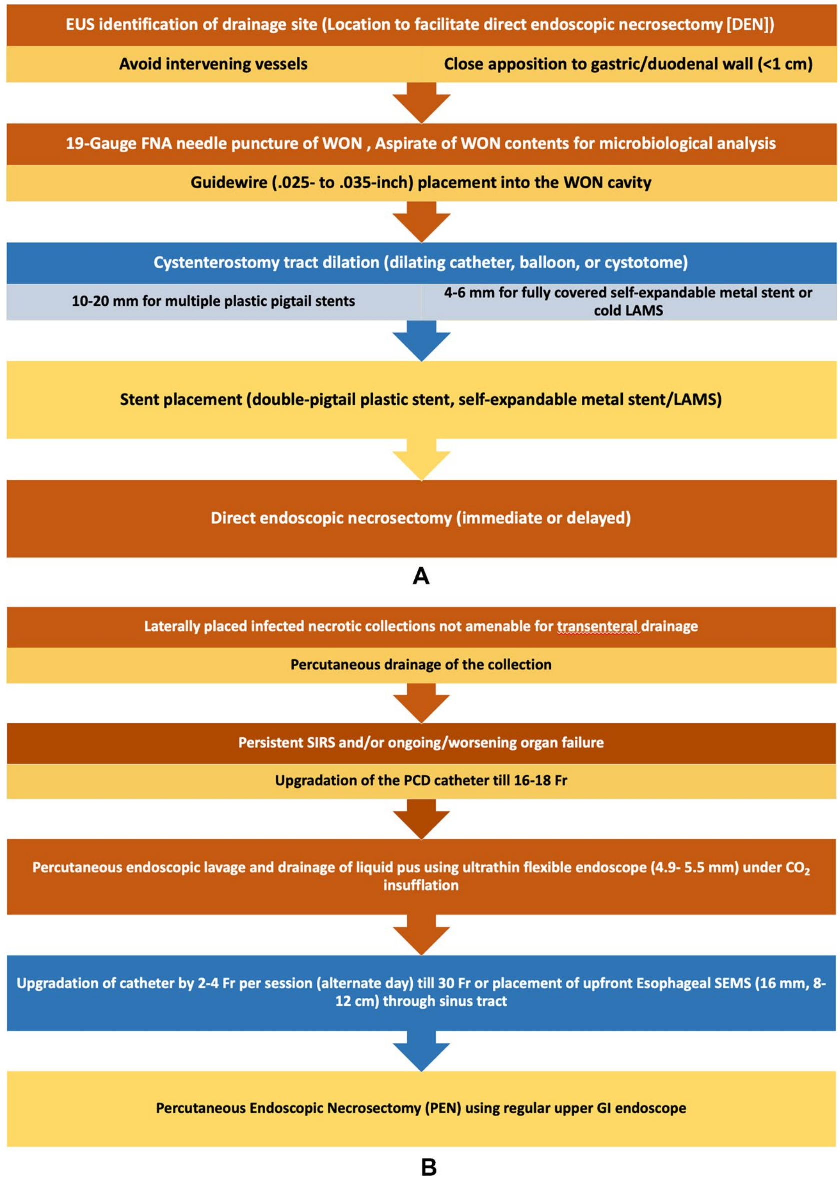

Fig. 4 Key steps of endoscopic drainage (**A**) and percutaneous drainage (**B**) of pancreatic fluid collections. *EUS* endoscopic ultrasound, *FNA* fine-needle aspiration, *WON* walled-off necrosis, *LAMS* lumen apposing metal stent, *SIRS* systemic inflammatory response syndrome, *PCD* percutaneous catheter drainage, *SEMS* self-expandable metal stent, *GI* gastrointestinal

necrosectomy arm as compared to surgery (hazard ratio [HR] 0.27; 95% CI 0.08–0.90; $p = 0.033$) followed by percutaneous necrosectomy (HR 0.44; 95% CI, 0.20–0.98; $p = 0.045$). The endoscopic group had lower adverse events such as procedure-related bleeding ($p < 0.001$), post-procedure organ failure ($p < 0.001$) and shorter hospital stay (20.1 vs. 25.8 vs. 38.3 days; $p < 0.001$) and costs when compared to percutaneous and surgical necrosectomy groups, respectively [92].

Adjunctive therapies for endoscopic necrosectomy and debridement

The main aim of a minimally invasive necrosectomy is near complete debridement, which is generally achieved by mechanical means. However, it is difficult to remove adhered and large amount of debris. In order to facilitate necrosectomy, a few adjunct modalities have been tried as follows.

Mechanical devices for DEN Debridement of necrotic tissue is performed using instruments used primarily for other endoscopic purposes including devices such as stone retrievel baskets, grasping foreceps, polypectomy snares and Roth net. The development of dedicated devices for DEN is aimed at reducing the complexity and time required for debridement.

Endorotor (Interscope, Inc., Northbridge, Mass, USA) is a dedicated instrument for endoscopic necrosectomy cleared by the U.S. Food and Drug Administration (FDA) for the removal of necrotic tissue [93]. The Endorotor system includes a power console, foot control, specimen trap with a preloaded filter and a disposable catheter. The catheter is motorised, compatible with 3.2-mm working channel. It simultaneously cuts with a rotating blade and creates a negative pressure for suctioning of necrotic material. A multicentre, international trial assessed the safety and efficacy of this novel resection system in 30 patients with WON of size ranging between 6 and 22 cm with significant solid necrotic debris of > 30% with a primary endpoint of safety through 21 days after DEN procedure [94]. Fifteen (50%) of the patients achieved complete debridement in one session and 20 (67%) achieved complete debridement in two or fewer sessions with a median of 1.5 sessions (range 1–7) over a median hospital stay of 10 days. Two patients had GI bleed and one patient had pneumoperitoneum following the procedures.

Other techniques include a *Waterjet necrosectomy device* (*WAND*), capable of selective tissue fragmentation for debridement of WON. It allows a controllable waterjet force to fragment necrosis without damage to surrounding healthy tissue. Pre-clinical studies of WAND have shown initial success, but clinical studies are underway for human safety and efficacy [95]. *Over-the-scope-grasper* (Xcavator, Ovesco AG, Tübingen, Germany) is another mechanical device recently developed to remove necrotic debris, blood clots and foreign bodies [96]. It is a plastic transparent cap which is attached over the standard upper GI endoscope and has distal graspers allowing grasping of large pieces of necrotic debris. As of now, however, only a few case reports have described its efficacy.

Hydrogen peroxide Diluted hydrogen peroxide (H_2O_2), an inorganic agent, has been traditionally used for wound management because of its antimicrobial, hemostatic and wound healing attributes. H_2O_2 has also been used to facilitate the debridement of necrotic solid debris in patients with WON. The presence of catalase, an enzyme found in the living tissue, converts H_2O_2 to water and oxygen causing agitation of necrotic debris which is considered to be the potential mechanism of its action. H_2O_2, available in the concentration of 3%, is first diluted with normal saline solution in a ratio from 2:1 to 10:1 [97] and then infused into the cavity during necrosectomy. In a retrospective study, H_2O_2 was associated with a higher clinical success rate (OR, 3.3; $p = 0.03$) and earlier resolution (OR, 2.3; $p < 0.001$) but with a greater number of necrosectomy procedures and no difference in adverse events [97]. Based on the available data, use of hydrogen peroxide may be considered safe in the setting of INP for assisting debridement, but RCTs are needed before any formal recommendation can be made regarding its use.

Nasocystic catheter irrigation A nasocystic catheter (7 Fr) can be inserted at the time of initial drainage, parallel to the plastic stents or through the LAMS. The catheter can be used for constant irrigation of the cavity between DEN sessions at a daily volume of 500 to 1000 mL [98]. Nasocystic lavage with antibiotic irrigation has been used but definite benefit has not been demonstrated. A retrospective study showed no difference in WON resolution (91% vs. 96%, $p = 0.59$), when nasocystic irrigation was used in conjunction with LAMS [51]. Prospective RCTs evaluating the use of a nasocystic catheter in this setting are lacking.

Combined approach—dual modality drainage

Combined approach or dual modality drainage (DMD) refers to combined PCD and ETD for WON. A combined approach is advocated for patients with large collection in the lesser sac with deep extension along paracolic gutter. After both per-oral and percutaneous drainage, necrosectomy may be planned preferably through transgastric route. DMD has been shown to improve patient outcomes in terms of significantly shorter hospitalization (26 vs. 55 days, $p < 0.0026$), duration of external drainage (83.9 days vs. 189 days, $p < 0.002$) and lower rates of external fistulas (0 vs. 3 patients) [78, 99].

Endoscopic interventions for disconnected pancreatic duct syndrome

Pancreatic necrosis involving the central portion of the pancreas may result in transection of the main pancreatic duct with a functioning pancreatic parenchyma on both sides of the transected duct leading to a condition called disconnected pancreatic duct syndrome (DPDS). After initial drainage of the WON, DPDS can lead to either residual or recurrent pancreatic fluid collections. A retrospective study of 149 WON patients demonstrated DPDS to be present in 68% of WON patients [100]. An RCT compared the recurrence of PFCs among 104 patients with DPDS who underwent either plastic stent placement ($n = 52$) or no stent placement ($n = 52$) after removal of SEMS for WON [62]. Recurrent PFCs were seen in seven patients (13%) with stents and in 13 patients (25%) without stents, with the difference not being statistically significant. Most of the recurrent collections were asymptomatic and reintervention was required only in seven patients. The optimal treatment strategy for DPDS in the setting of necrotising pancreatitis is still uncertain and requires prospective studies. Long-term plastic stents may prevent recurrence of collection in patients with DPDS. In patients with a percutaneous fistula due to DPDS or recurrent pancreatitis, EUS-guided pancreaticogastrostomy or placement of a plastic stent between the gastric lumen and fistulous tract may be tried.

Complications associated with endoscopic interventions

Advances in endoscopic interventions in patients with necrotising pancreatitis are not without adverse events. Early complications include intra-abdominal bleeding, stent migration, colonic fistula and air embolism. Pancreatic fistulae may develop following percutaneous and surgical drainage. Various factors known to influence the complications include the severity of pancreatitis, endoscopist's experience and type of endoscopic procedure. The complications associated with interventions are tabulated in Table 3 and Supplementary Table 1. Early identification and management of any procedure-related complication is the key, which includes careful post-procedural monitoring of hemodynamics, symptoms, clinical signs and lab parameters. A multi-disciplinary approach is required to manage these complications such as bleeding, perforation or worsening infection, depending upon the severity of the complications.

Future directions

Despite significant improvement in the management of acute necrotising pancreatitis over the years, the mortality in patients with infected necrosis remains high, varying from 20% to 39%. Infected necrosis is a complex disorder and various parameters determine the outcome, such as the extent of necrosis, presence of multidrug-resistant organisms, pancreatic hemorrhage, bowel fistula, host immunity and nutritional status. In addition to effective drainage and clearance of the necrotic cavity, a better understanding of the pathophysiology of the disease with respect to the host and microbial factors is needed.

To conclude, the management of acute pancreatitis is complex and requires a multipronged strategy. Despite advancements in the management of INP, it is still associated with significant morbidity and mortality. Even though the trend has shifted towards endoscopic management for PFCs, the treatment should be guided by an individual patient's characteristics as one size does not fit all. A multidisciplinary team approach involving intensivists, interventional gastroenterologists, interventional radiologists and pancreatic surgeons is the key for optimum management of patients with acute necrotising pancreatitis.

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Declarations

Conflict of interest RR, SJM and PKG declare no competing interests.

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Consent for publication All authors gave consent to publication.

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