

Endoscopic transluminal interventions in the management of acute infected necrotizing pancreatitis. Literature review

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Acute necrotizing pancreatitis remains one of the most challenging diseases in general surgery. Infection of necrotic tissue, sepsis, and organ failure are the main determinants of mortality in this pathology. Other life-threatening complications include intestinal obstruction, biliary obstruction, abdominal compartment syndrome, external fistulas, bleeding, and thrombosis of the splenic and portal veins. The formation of walled-off necrosis after the fourth week of disease creates anatomical conditions for a transluminal endoscopic access to the pathological focus when appropriate indications are present. Current management of acute necrotizing pancreatitis is based on a step-up minimally invasive strategy in which endoscopic interventions occupy a leading role. International clinical guidelines, particularly those of ESGE, AGA, and ASGE, support the endoscopic step-up approach as first-line therapy for infected walled-off necrosis. This strategy focuses on controlling septic manifestations rather than performing immediate necrosectomy. Key factors for success include appropriate timing of intervention, a multidisciplinary approach, and individualization of the treatment strategy. The optimal indications for escalation to more invasive procedures remain unresolved and are subject to ongoing debate, often depending on the experience of a particular specialized center. The complexity of clinical decision-making may also be related to differences in treatment approaches between general surgeons and endoscopists, which necessitates a balanced interdisciplinary collaboration.

This literature review highlights the main aspects of managing acute necrotizing pancreatitis with endoscopic transluminal interventions. A comprehensive understanding of the advantages and limitations of this technique promotes its further technical and tactical refinement to improve treatment outcomes.

KEYWORDS

acute necrotizing pancreatitis, acute infected pancreatic necrosis, walled-off necrosis, endoscopic transluminal necrosectomy, direct endoscopic necrosectomy.

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Acute pancreatitis (AP) is the most common disease of the digestive system requiring urgent hospitalization [13]. In most cases (about 80%), AP follows a mild interstitial edematous course and resolves rapidly [69]. Approximately 20% of patients develop acute necrotizing pancreatitis (ANP), which is associated with multiple organ failure (38%), the need for invasive intervention (38%), and a mortality rate of 15–30%, depending on the presence of infected necrosis [9, 50, 78, 86]. In the setting of open surgical procedures, mortality reaches 11–39% [17].

Key aspects in the management of patients with acute pancreatitis include early diagnosis, early pharmacological therapy, and dynamic assessment of the clinical course; in severe forms of AP, early enteral nutrition, antibiotic therapy in the presence of signs of (or proven) infection, and the availability of an appropriate spectrum of minimally invasive interventions, with strict adherence to indications and timing, are essential.

Open surgical necrosectomy historically was the mainstay of treatment for symptomatic necrotic collections; however, management strategies have

evolved. Currently, preference is given to minimally invasive approaches, primarily endoscopic necrosectomy and/or percutaneous catheter drainage (PCD) as the initial step of treatment [62]. Among invasive interventions for complicated AP, endoscopic transluminal interventions are increasingly being applied [3].

Indications for invasive interventions in acute necrotizing pancreatitis

Surgical interest in ANP primarily concerns walled-off necrosis (WON) according to the 2012 Revised Atlanta Classification of acute pancreatitis [8]. WON develops after the fourth week of acute pancreatitis as a result of persistent acute (peri-)pancreatic necrosis and is characterized by a mature, encapsulated collection of both fluid and necrotic material enclosed by a well-defined wall [8, 75].

According to international guidelines for the management of acute pancreatitis, indications for invasive intervention (radiological, endoscopic, or surgical) in acute necrotizing pancreatitis include [3, 13]:

- Documented infected necrotizing pancreatitis (INP).
- Clinical suspicion of INP: in the absence of documented INP, but in the presence of persistent organ dysfunction or ongoing clinical deterioration for several weeks after the onset of acute pancreatitis despite optimal conservative therapy, preferably after the formation of WON; in other words, in the setting of persistent systemic inflammatory response syndrome. A retrospective study by Rodriguez involving 167 patients found that 42 % of such patients had INP [57].
- Compression of adjacent organs without signs of INP, including gastric outlet obstruction, intestinal or biliary obstruction, as well as pain caused by the mass effect of a large WON. Interventions should preferably be performed more than 4–8 weeks after the onset of acute pancreatitis [35, 43]. Secondary infection represents a key risk in this group of indications [3].
- Abdominal compartment syndrome: this condition is less common but may require early decompression (radiological or surgical) during the course of acute pancreatitis. At the same time, revision of the lesser sac or performance of necrosectomy during such a procedure is not recommended due to the risk of bleeding and infection of sterile necrosis [77, 82].
- Fistulas that fail to regress with conservative treatment [3, 12].

Conservative management in acute necrotizing pancreatitis

Recent studies and international guidelines generally support a watchful waiting strategy for

uncomplicated asymptomatic WON and pancreatic pseudocysts, as most of these collections regress spontaneously without the need for intervention [19, 22]. There is substantial evidence that asymptomatic WON should be managed conservatively, regardless of its extent or size [13, 21, 27, 32, 71, 92].

In a study by Jagielski et al., asymptomatic WON was identified in 44 of 168 patients (26 %). The mean follow-up period for patients with asymptomatic WON was 417.02 days (range: 47–1149 days). Complete regression of WON occurred in 30 of the 44 asymptomatic patients. Symptoms related to WON developed in 13 of 44 patients (30 %) during follow-up. The most common indication for interventional treatment of WON was infected pancreatic necrosis, which was diagnosed in 6 of 13 patients (46 %). Overall, 137 of 168 patients (82 %) with WON required interventional treatment [33].

The 2024 Chinese multicenter consensus allows observation of pancreatic pseudocysts and WON smaller than 6 cm in the absence of evident symptoms or complications [98].

With regard to INP, data from small cohort studies and a recent meta-analysis (including studies with considerable heterogeneity) suggest that a subset of patients with INP (6/42; 14 % [10]) may be treated with antibiotics alone [10, 25, 53, 60]. However, the exact subgroup of such clinically stable patients has not been clearly defined. Moreover, in some studies, conservative treatment also included PCD, which complicates the identification of patients who received antibiotics as the sole therapy [25, 41].

Diagnosis of infected necrosis

In patients with acute pancreatitis, the absolute impact of infected pancreatic necrosis and organ failure on mortality is comparable; therefore, the presence of either factor indicates severe disease [50]. The relative risk of death doubles when infected pancreatic necrosis and organ failure coexist, indicating a very severe or critical form of acute pancreatitis [50]. Infected necrosis develops in approximately one-third of patients with ANP, on average after the 10th day of disease, and is associated with a mortality rate of about 30 % [9].

INP may be suspected in the presence of clinical signs of sepsis (e.g., temperature > 38 °C, features of persistent systemic inflammatory response syndrome, and clinical deterioration or lack of improvement), or when extraluminal gas is detected within the pancreatic or peripancreatic tissues on computed tomography (CT) [25]. The diagnosis of INP is established when samples of (peri-)pancreatic tissue obtained via percutaneous, endoscopic, or surgical drainage yield positive results for bacteria

and/or fungi on Gram staining or microbiological culture [3].

The additional diagnostic value of fine-needle aspiration (FNA) is limited when clinical and/or imaging findings are already suggestive of infection [79]. Furthermore, a substantial proportion of false-negative (20–29%) and false-positive (4–10%) results has been reported [57, 79].

In a Dutch retrospective analysis involving 208 patients, clinical deterioration (persistent sepsis, new-onset or prolonged organ dysfunction, increasing need for cardiovascular, respiratory, or renal support, leukocytosis, elevated or rising C-reactive protein levels, and fever), despite adequate therapy and in the absence of an alternative source of infection, was attributed to INP in 74 of 92 patients (80.4%); the false-positive rate was 19.6% [3, 79].

A systematic review demonstrated that procalcitonin is the most accurate biomarker for INP. At a cutoff value of 3.5 ng/mL, sensitivity and specificity were 0.90 and 0.89, respectively [94]. Nonetheless, procalcitonin is a nonspecific marker of infectious complications in critically ill patients; therefore, other potential sources of infection must be excluded [39].

The presence of gas within (extra-)parenchymal necrosis on CT showed limited diagnostic value for assessing INP in the aforementioned study (sensitivity 45.9%, specificity 81.5%, accuracy 50.5%) [79]. Magnetic resonance imaging (MRI) is a potential tool for detecting INP; however, large-scale studies evaluating its diagnostic performance remain limited [3].

Fungal colonization of pancreatic necrosis remains poorly studied. It is associated with the development of severe acute pancreatitis, formation of WON, and high mortality, although the benefit of prophylactic antifungal therapy in severe pancreatitis has not been demonstrated. Fungal infection of the pancreas occurs in approximately 40% of patients with severe acute pancreatitis who develop WON [91, 56]. Importantly, patients with positive cultures for pancreatic *Candida* infection exhibited significantly higher mortality compared with those without *Candida* (35.2% vs 13.4%) [56]. A recent meta-analysis of 22 publications evaluating the incidence of *Candida* infection and its impact on mortality in INP further confirmed that local or systemic *Candida* infection is associated with increased mortality in INP [70].

Owing to the diagnostic complexity and the lack of a single sensitive and specific marker for INP, the diagnosis should be based on a comprehensive assessment of the patient's general condition, laboratory parameters, and imaging findings, rather than solely on microbiological findings.

Timing of minimally invasive intervention

European and American guidelines recommend postponing invasive interventions until at least 4 weeks after the onset of pancreatitis to allow maturation of the necrotic collection and liquefaction of necrotic debris [3, 62].

In the randomized controlled trial (RCT) POINTER (104 patients) [15], management of infected necrosis was compared between immediate drainage (percutaneous or endoscopic) within 24 hours after establishing the diagnosis of infected necrosis and postponed drainage after a 4-week waiting period to allow maturation of WON. More than 33% of patients in the postponed-drainage group improved with antibiotic therapy alone and did not require any intervention. Moreover, necrosectomy was performed more frequently in the early-drainage group (51% vs 22%; RR 2.27; 95% CI 1.27–4.06), as were combined endoscopic and radiological drainage procedures (4.4 vs 2.6). Mortality was 13% in the immediate-drainage group and 10% in the postponed-drainage group (relative risk 1.25; 95% CI 0.42–3.68) [15].

The «step-up approach» strategy

In the context of invasive interventions for patients with ANP, the step-up approach should be highlighted. This strategy was first introduced in the publication describing the design and rationale of the PANTER trial in 2006 [14]. In 2010, van Santvoort et al., in a study involving 88 selected patients with INP, demonstrated the effectiveness of this strategy, whereby the least invasive intervention (e.g., percutaneous or endoscopic drainage) is applied first in INP, followed – only in case of failure – by a stepwise escalation to more invasive procedures (e.g., video-assisted retroperitoneal debridement (VARD) or open surgery) [87].

The step-up approach aims to minimize surgical trauma. In contrast to open necrosectomy, its primary goals are control of the infectious focus and mitigation of sepsis, rather than immediate complete removal of infected necrotic tissue [87]. According to the study, the use of minimally invasive techniques within the step-up approach (percutaneous or endoscopic drainage followed by VARD if required), compared with primary open necrosectomy, allows postponement or avoidance of open surgical necrosectomy, reduces the incidence of recurrent multiple organ failure (12% vs 40%) and late complications (including new-onset pancreatic insufficiency); however, no advantage in terms of mortality was demonstrated (19% vs 16%) [87]. The authors noted that detecting a clinically meaningful difference in mortality would require a trial including several

thousand patients, making such a study unlikely to be conducted [87].

The TENSION trial demonstrated advantages of the endoscopic step-up approach over the surgical step-up approach, including a lower incidence of enteric or pancreatocutaneous fistulas, shorter hospital stay, and reduced treatment costs, without an increase in major complications or mortality [7, 26, 83]. In addition, one meta-analysis [81] and a large international risk-adjusted study including 1980 patients showed reduced mortality when endoscopic or percutaneous drainage was used as the initial step compared with primary minimally invasive surgery [40].

A Cochrane meta-analysis (8 RCTs, 306 patients) demonstrated that: (i) compared with open necrosectomy, the step-up approach was associated with lower rates of both overall and serious complications, as well as lower mean costs; and (ii) compared with the video-assisted minimally invasive step-up approach (VARD), the endoscopically assisted step-up approach resulted in better outcomes in terms of complications, although it required a higher number of procedures (median difference: 2) [27]. The analysis also concluded that differences in short-term mortality among the compared approaches were imprecise.

Effectiveness and limitations of endoscopic transluminal interventions

Outcomes of endoscopic transgastric necrosectomy are encouraging. A systematic review of 10 studies on endoscopic necrosectomy reported complete resolution of WON in 76% of cases, with an overall long-term complication rate of 27% and a mortality rate of 5%, although patient characteristics varied across the included studies [28]. Another systematic review of endoscopic necrosectomy (455 patients) reported a success rate of 81% with endoscopic therapy alone and a complication rate of 36% [80].

The randomized controlled trial by Bakker et al. (22 patients) demonstrated advantages of endoscopic transgastric necrosectomy over VARD and/or open necrosectomy, including a lower risk of recurrent organ failure (0% vs 50%, $p = 0.03$), a reduced incidence of pancreatic fistulas (10% vs 70%, $p = 0.02$), and lower post-procedural interleukin-6 levels ($p = 0.004$) [6].

A retrospective study by Tan et al. confirmed that endoscopic transgastric necrosectomy was associated with fewer complications and a shorter hospital stay compared with surgical necrosectomy [74]. However, a subsequent larger randomized trial (98 patients) [83] comparing the endoscopic step-up approach (drainage followed by necrosectomy if required) with the surgical step-up approach

(PCD followed by VARD if required) did not demonstrate superiority of endoscopic necrosectomy in terms of major complications or mortality. Nevertheless, the endoscopic group showed lower fistula rates and shorter hospitalization [83].

Compared with PCD, a matched cohort study ($n = 24$) found that endoscopic necrosectomy was associated with a higher clinical success rate (92% vs 25%), a shorter hospital stay, and reduced healthcare resource utilization [36].

Limitations of the endoscopic approach include the need for multiple interventions, limited ability to endoscopically assess the full extent of necrotic debris, technical difficulties in removing large volumes of necrotic material, restricted applicability of transgastric endoscopic necrosectomy in cases with extensive retroperitoneal spread, and challenges or inability to adequately treat distally located left-sided necrotic collections [21]. Owing to these limitations, adjunctive PCD is required in approximately 40% of patients, particularly when WON extends into the paracolic gutters or pelvis, and surgical intervention due to failure of endoscopic therapy is necessary in about 20% of patients [47].

Endoscopic ultrasound or conventional endoscopy?

The first description of irrigation of a WON cavity via a transnasal catheter placed endoscopically through a transmural route in combination with endoscopic drainage using two double-pigtail plastic stents (DPPS) 10 Fr, 3 cm was reported by Baron in 1996 in a series of 11 patients [11]. The first direct transluminal endoscopic necrosectomy for WON was described by Seifert in 2000 [66]. Over more than two decades, this technique has undergone substantial evolution. Endoscopic transluminal access to WON can currently be achieved using either a therapeutic gastroscope or an echoendoscope [3, 12].

Selection of the access site to the WON cavity during endoscopic transluminal interventions often represents a challenge for the endoscopist. In approximately 50–60% of cases of acute necrotizing pancreatitis, 4–6 weeks after disease onset, the WON cavity compresses the gastric wall (typically the posterior wall) and/or the duodenal wall [21]. During diagnostic esophagogastroduodenoscopy, a visible bulge into the gastric or duodenal lumen, often accompanied by inflammatory mucosal infiltration, may be observed, indicating close apposition of the WON cavity to the adjacent hollow organ. In such cases, endoscopic transluminal intervention may be performed without endoscopic ultrasound (EUS) at the site of bulging, provided there is no evidence of significant portal hypertension [34, 96].

Two randomized controlled trials confirmed the superiority of EUS-guided access in terms of technical success (100 % vs 33 % and 94 % vs 72 %, respectively) [48, 90]. In cases of «non-bulging» (peri-)pancreatic fluid collections where conventional transmural drainage was not feasible, EUS guidance enabled successful transmural access. Although both studies included only pancreatic pseudocysts, the results can reasonably be extrapolated to patients with WON.

However, a prospective comparative study found no difference between conventional (n = 53) and EUS-guided drainage (n = 46) in patients with pancreatic pseudocysts with regard to short-term (94 % vs 93 %) and long-term success rates (91 % vs 84 %), or complication rates (18 % vs 19 %) [34]. Notably, the conventional approach was applied exclusively in patients with bulging (peri-)pancreatic collections and in the absence of portal hypertension [34]. It is likely that the principal advantage of EUS-guided transluminal access lies in the ability to access the WON cavity even in the absence of a typical luminal bulge, provided that the collection is within the EUS field of view [89].

In our study involving 28 patients, a 100 % technical success rate for transgastric access to the WON using a duodenoscope was achieved under two combined conditions: supine patient positioning during the procedure and external compression of the stomach by the adjacent WON [52]. These findings suggest that the supine position during endoscopic transluminal interventions allows more accurate endoscopic localization of the WON relative to the stomach, as the intra-abdominal organ configuration more closely matches CT/MRI findings [52]. In contrast, the left lateral position may lead to displacement of intra-abdominal organs, thereby reducing the likelihood of successful access to the WON cavity.

To date, large randomized trials directly comparing transluminal access using a gastroscope versus a therapeutic EUS are lacking. Nevertheless, expert consensus suggests that EUS-guided transluminal intervention is safer with respect to bleeding risk and offers a higher likelihood of access to the WON cavity [3]. Accordingly, the European Society of Gastrointestinal Endoscopy (ESGE) recommends the use of EUS for creating transluminal access to the WON [3].

Technique of endoscopic interventions

Endoscopic transluminal interventions are performed under general anesthesia with endotracheal intubation [7, 52, 51, 62, 65], which protects the airway from aspiration of infected WON contents

and provides better cardiopulmonary control during prolonged procedures.

Current endoscopic options in ANP include [3]:

- Endoscopic transluminal drainage: placement of transmural DPPS or fully covered self-expanding metal stents into the WON cavity;
- Endoscopic drainage using the multiple transluminal gateway technique (MTGT), which involves up to three access points [3, 88];
- Direct endoscopic necrosectomy (DEN): insertion of the endoscope into the WON cavity to remove necrotic debris [64]. In the English-language literature, synonymous terms include peroral endoscopic necrosectomy and endoscopic transluminal necrosectomy;
- Combined interventions (dual-modality drainage, DMD), in which endoscopic transluminal drainage is combined with percutaneous drainage of WON [58]; this approach should be strongly considered when necrosis extends into the paracolic gutters or the pelvis [3, 47, 62].

The endoscopic approach is best suited for the treatment of central necrosis [11], which is predominantly located within the lesser sac, as this region is most readily accessible endoscopically via the stomach or duodenum [47]. Successful endoscopic treatment of WON requires creation of a wide transmural tract and additional irrigation and/or debridement [47]. Depending on the anatomical relationship between the necrotic collection and the gastric or duodenal wall, and considering technical feasibility, access to the WON cavity is achieved via a transgastric or transduodenal route. The transgastric approach is preferred for its technical convenience in endoscopic necrosectomy and for providing the most direct access to the WON cavity [12].

Two main strategies are used during endoscopic transluminal treatment of WON: performing DEN, if required, several days after initial endoscopic drainage (DEN as a secondary procedure) [42, 95], or performing DEN during the primary access session (DEN as a primary procedure) [24, 36, 76]. Several studies have demonstrated the advantages of a step-up endoscopic strategy aimed at avoiding DEN, showing that 20–90 % of patients with WON can be successfully treated with endoscopic drainage alone using plastic stents or large-diameter fully covered metal stents, including dedicated lumen-apposing metal stents (LAMS) [37, 45, 55]. At present, however, studies directly comparing early DEN (during the index procedure) with delayed DEN are lacking [3].

The number of sessions varies and depends on WON size, the amount of solid necrotic debris, use

of cavity lavage, type of stents, endoscopic strategy (primary drainage alone vs immediate necrosectomy), availability of dedicated devices, and the use of combined interventions (DMD) or MTGT. On average, 1–7 DEN sessions per patient may be required to achieve adequate cavity clearance: Ang et al. (8 patients) – 1 (1–3) [2]; Gardner et al. (104 patients) – 3 [24]; Papachristou et al. (53 patients) – 3 (1–12) [47]; Smoczyński et al. (64 patients) – 4.75 (3–9) [72]; Seifert et al. (93 patients) – 6.2 (1–35) [65]; Seewald et al. (13 patients) – 7 (2–23) [64]. Attempts at aggressive cavity debridement may be associated with an increased risk of bleeding. Over time, necrotic sequestra become more clearly demarcated from viable tissue as granulation tissue forms, allowing safer, more controlled removal with a lower risk of injury to viable structures.

With conventional access to the WON cavity, the endoscope is advanced orally, and transmural puncture is performed at the site of luminal compression caused by the adjacent necrotic collection. Gastric wall puncture (fistulotomy) is carried out using a cystotome or a needle-knife papillotome. In EUS-guided access [62]: (1) an optimal puncture site is selected based on (a) absence of large vessels, (b) close apposition to the gastric or duodenal wall (< 1 cm), and (c) favorable orientation for DEN; (2) the WON is punctured using a 19-G FNA needle; (3) cavity contents are aspirated for microbiological analysis; (4) a 0.025–0.035-inch guidewire is advanced into the WON cavity.

The created fistulous tract is then dilated to 4–20 mm, depending on the planned intervention (drainage or DEN), using an endoscopic balloon, dilation catheter, or a guidewire-mounted cystotome [62, 31]. Placement of cautery-enhanced LAMS does not require prior balloon dilation of the tract and allows single-step creation of access to the WON cavity. When multiple DPPS are planned, the fistulous tract is typically dilated to 10–20 mm [62].

During the index session (access session), regardless of whether DEN is performed, a 7–8 Fr transnasal catheter may be placed into the WON cavity for continuous lavage (Fig. 1), provided the patient tolerates nasal tubes [3, 12, 47, 62, 63].

Duration of direct endoscopic necrosectomy session

The duration of a single DEN session should be limited. Prolonged necrosectomy in patients weakened by a long-standing infectious-toxic process, under general anesthesia and mechanical ventilation, may impose significant pathophysiological stress, increase the risk of complications, and predispose

to bleeding. Based on original studies, the optimal duration of a single DEN session is 60–90 minutes [47, 52, 65].

Irrigation of walled-off necrosis

In the interval between sessions, the necrotic cavity may be irrigated via an endoscopically placed transnasal drain into the WON cavity (see Fig. 1) or via PCD. The type of irrigating solution, volume, duration, and frequency are not standardized and vary between centers. Most commonly, 500–1000 mL of normal saline is used daily, administered either in divided doses 3–6 times per day or as a continuous instillation.

Some authors recommend administering antibiotics through the drain during intersession intervals for WON irrigation, guided by microbiological culture results [38, 63, 76], or using antiseptic solutions. In addition, during necrosectomy, some specialists advocate lavage of the WON cavity with large volumes of warm bacitracin solution (1–2 L at 25,000 IU/L) or with 100–300 mL of 0.1%–0.3% hydrogen peroxide (H₂O₂) delivered through the endoscope channel [1, 36, 76].

In the ASGE Technology Review (2023), data are presented on the safety and effectiveness of using 3% hydrogen peroxide (H₂O₂), diluted with normal saline at ratios ranging from 1:2 to 1:10, for irrigation of the WON cavity, both during DEN

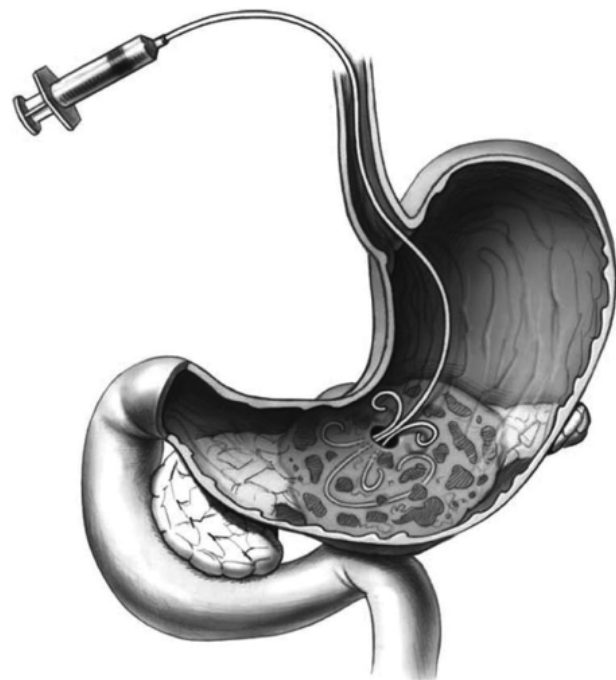


Figure 1. A 7-Fr pigtail-type nasobiliary drain placed adjacent to transmural internal pigtail stents within the WON cavity for the purpose of intensive irrigation and/or debridement [47]



Figure 2. **Solus® double-pigtail plastic stent, Cook Medical™, USA**

sessions and via a transnasal drain. However, there is insufficient prospective evidence to support routine use of H₂O₂ for this indication [12, 62].

The choice between irrigation of the necrotic cavity and DEN remains controversial. The need for DEN should be justified by the amount of solid necrotic debris present within the WON cavity [12]. Routine DEN at the time of LAMS placement is also controversial, and it remains unclear whether it should be performed on a scheduled or on-demand basis [12]. Some data suggest that DEN improves outcomes of endoscopic therapy compared with irrigation alone when plastic stents are used [12, 23]. Experienced endoscopists who perform a high volume of endoscopic necrosectomies recommend avoiding antisecretory therapy after transluminal drainage, as gastric acid secretion may facilitate spontaneous cleansing of the WON cavity [12].

Endoscopic stents

For endoscopic drainage of the WON cavity, 10 Fr double-pigtail plastic stents (Fig. 2) or fully covered self-expandable metal stents (SEMS) are most

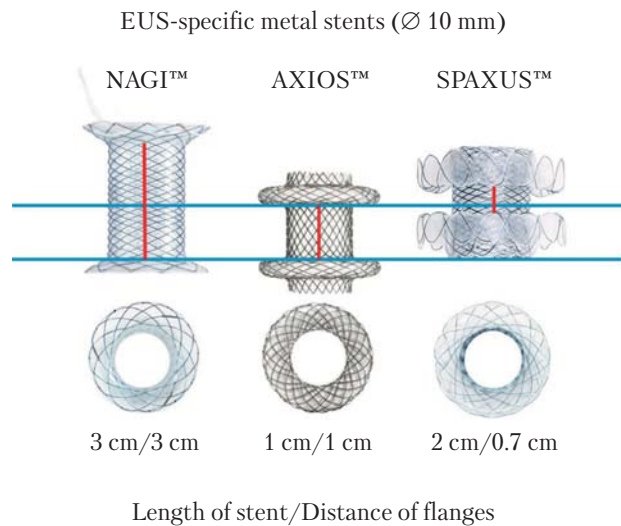


Figure 3. **Examples of specialized covered lumen-apposing metal stents (LAMS) [73]**

commonly used. Specialized LAMS (Fig. 3) are being used with increasing frequency.

LAMS reduce procedure time by facilitating faster access to the WON cavity and making necrosectomy through the stent lumen more convenient [67].

In a large retrospective multicenter study involving 124 patients with WON who underwent EUS-guided transmural drainage using LAMS, the authors reported a technical success rate of 100%, a clinical success rate of 86%, and the need for DEN in 30.6% of patients, with a median number of procedures of 2 [67].

Available data suggest that placement of one or two plastic stents coaxially within the lumen of a LAMS (Fig. 4) improves WON drainage and LAMS patency, prevents early occlusion by necrotic debris, and reduces the risk of bleeding and stent migration [30].

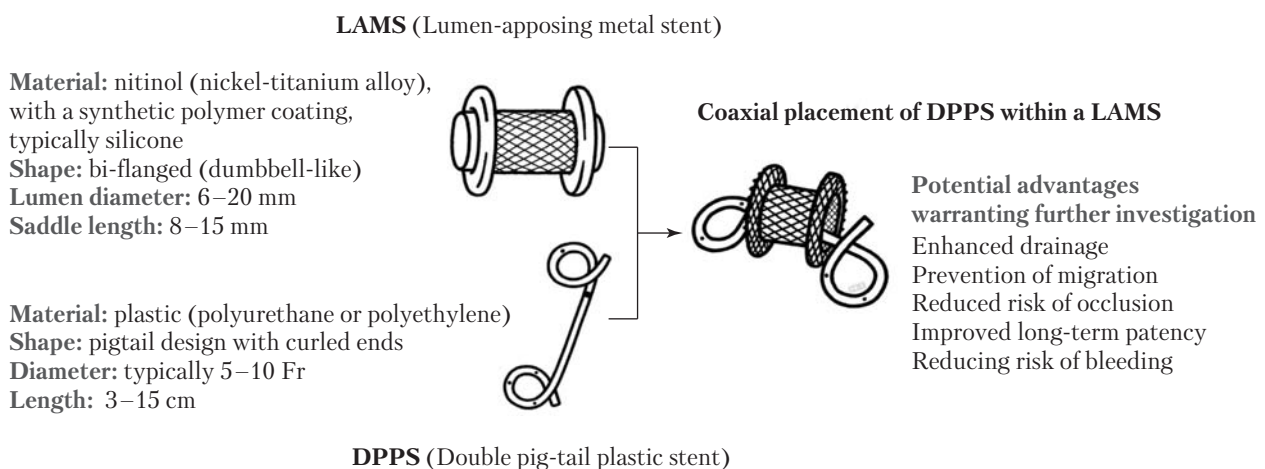


Figure 4. **Schematic illustration of coaxial placement of a double-pigtail plastic stent (DPPS) within a LAMS [30]**

Endoscopic instruments for direct endoscopic necrosectomy

Mechanical endoscopic removal of necrotic sequestra is performed using lavage and devices such as tripod grasper, grasping forceps, polypectomy snares, baskets, and retrieval nets. Recently, promising results of DEN have been reported with the use of innovative endoscopic devices:

- the motorized EndoRotor device (Micro-Tech™, Germany) (Fig. 5), which consists of a rotating blade for resection of necrotic tissue with simultaneous suction; the device is available in two diameters, 3.0 mm and 5.0 mm, for use with endoscopes with different working channel sizes [46, 85];
- an over-the-scope grasper (Xcavator™ – Ovesco Endoscopy AG, Germany) (Fig. 6) [16];
- the multifunctional Necrolit® device, which combines a snare and a basket, allowing sequential resection and retrieval of necrotic debris without the need to change instruments (Fig. 7);
- a waterjet necrosectomy device, a prototype single-use instrument that uses a high-pressure water jet to fragment necrotic tissue and can be employed for irrigation, fragmentation, and aspiration (Fig. 8) [93].



Figure 5. EndoRotor®, powered endoscopic debridement catheter (Micro-Tech™, Germany)



Figure 6. Xcavator™, over-the-scope grasper (Ovesco Endoscopy AG, Germany)

Factors predicting the need for necrosectomy

In a retrospective analysis of 53 patients, larger WON size (median diameter 18 cm [12–21 cm] vs 14 cm [3–46 cm]; $p = 0.01$), extension of WON into the paracolic gutters ($p = 0.003$; OR 8.5; 95% CI 1.4–52.2), and a history of diabetes mellitus ($p = 0.035$; OR 4.1; 95% CI 1.0–19.9) were significantly associated with the need for open surgical intervention following primary endoscopic treatment [47]. At the same time, the authors emphasized that patients with extension of WON into the paracolic gutters should not be categorically excluded from endoscopic therapy; on the contrary, aggressive percutaneous treatment (PCD with intensive irrigation) should be considered as an adjunctive modality that complements endoscopic therapy and may be applied concurrently [47].

In a post hoc analysis of a prospective multicenter database including 639 patients with ANP, the need for surgical intervention was lower in patients with isolated extrapancreatic necrosis compared with those with parenchymal or mixed necrosis (18% vs 57%; $p < 0.001$) [5].

In a retrospective study of 43 patients with WON, the extent of necrosis ($r = 0.703$; $p < 0.001$),



Figure 7. Necrolit®, multiaction catheter for necrosectomy, Meditalia S.r.l., Italy)

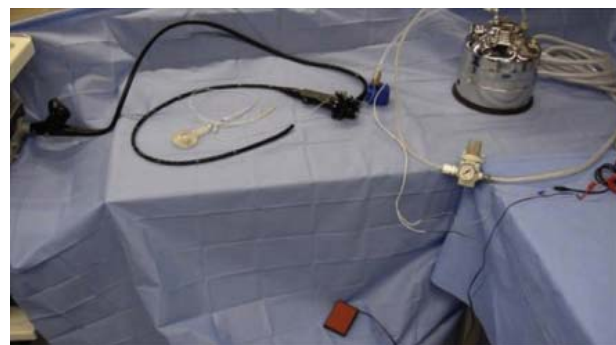


Figure 8. Waterjet necrosectomy device, prototype [93]

increasing WON size ($r = 0.320$; $p = 0.047$), and the amount of solid necrotic debris assessed by EUS ($r = 0.800$; $p < 0.001$) correlated with the need for more aggressive therapeutic interventions [54].

In a prospective cohort of 109 patients with acute pancreatitis (80 with ANP and 39 with WON) who underwent contrast-enhanced CT within the first 5–7 days after symptom onset, a blood urea nitrogen level ≥ 20 mg/dL at admission and an initial necrotic collection > 6 cm were associated with subsequent development of WON, with odds ratios of 10.96 (95% CI 2.57–46.73; $p = 0.001$) and 14.57 (95% CI 1.60–132.35; $p = 0.017$), respectively [61].

In a post hoc analysis of 130 patients who underwent catheter drainage (113 percutaneous, 17 endoscopic) for suspected INP, the extent of pancreatic necrosis ($< 30\%$, $30\text{--}50\%$, $> 50\%$; OR 0.44; 95% CI 0.23–0.83; $p = 0.01$) and heterogeneous morphology of the collection (OR 0.19; 95% CI 0.06–0.61; $p = 0.005$) were two imaging-related factors associated with a lower likelihood of success (defined as survival without necrosectomy) [29].

Two additional studies identified predictors of failure of catheter drainage and the need for subsequent surgery, including persistent single- or multiple organ failure, higher C-reactive protein levels, and extensive necrosis involving more than 50% of the pancreas [4, 68].

Based on our experience, documenting the contents of the WON cavity at the end of each endoscopic session in the procedure report and video recording is essential for assessing the completeness of necrosectomy and planning further management during clinical case discussions.

Complications of endoscopic transluminal interventions

Based on a systematic review including 13 retrospective cohort series ($n = 455$) [80] and one randomized controlled trial ($n = 98$) [84], the overall rate of endoscopy-related complications was 36% [3]. The most common complication was bleeding, occurring in 18% of cases. Perforation (excluding gastric or duodenal perforation) occurred in 4% of patients, and pancreatic fistula developed in 5%.

Clinical recommendations

According to international clinical guidelines for the management of patients with acute necrotizing pancreatitis – including those of the European Society of Gastrointestinal Endoscopy (ESGE, 2018) [3], the American Society for Gastrointestinal Endoscopy (ASGE, 2023) [62], the American Gastroenterological Association (AGA, 2020) [12], and other authoritative sources – we summarize the key

recommendations grounded in a multidisciplinary approach. These recommendations are of particular relevance to routine clinical practice for surgeons, interventional endoscopists, and physicians specializing in interventional ultrasonography.

1. For assessment of disease severity, morphological subtype, and the presence or absence of infected necrosis, use of the Revised Atlanta Classification of acute pancreatitis (2012) is recommended [8].

2. Contrast-enhanced CT is recommended, when indicated, as the primary diagnostic modality at hospital admission and within the first 4 weeks of disease, provided no contraindications exist. MRI may be performed instead of CT in patients with contraindications to contrast-enhanced CT and after 4 weeks of disease when invasive intervention is planned, as MRI better characterizes the content of pancreatic collections with respect to fluid and solid components. In addition, secretin-enhanced MRI is recommended to assess the integrity of the main pancreatic duct and to evaluate for disconnected pancreatic duct syndrome, particularly prior to removal of transluminal stents [3]. However, MRI is more susceptible to motion artifacts, and many patients with necrotizing pancreatitis are unable to adequately hold their breath [17].

The following indications for imaging are proposed [3]:

- at hospital admission, if diagnostic uncertainty exists;
- within the first week after disease onset (or after 72 hours from symptom onset) if no clinical improvement occurs despite conservative therapy;
- between weeks 2 and 4 after disease onset to assess the evolution of complications;
- after 4 weeks from disease onset for planning further management, when invasive intervention is required, and for monitoring treatment response.

3. Routine percutaneous FNA of (peri-)pancreatic collections is not recommended and should be reserved for cases with suspected infection, an equivocal clinical course, and inconclusive imaging findings [3].

4. Routine antibiotic or probiotic prophylaxis to prevent infectious complications is not recommended in acute necrotizing pancreatitis [3, 12].

5. In patients with suspected or confirmed infected necrosis, antibiotic therapy targeting enteric bacteria is recommended, guided by microbiological cultures and antibiograms when available [3]. Empirical use of broad-spectrum antibiotics that penetrate necrotic tissue – such as quinolones, carbapenems, metronidazole, and high-dose cephalosporins – is appropriate; routine antifungal therapy is not recommended [12]. Once blood culture or

FNA results become available, antibiotic therapy should be adjusted accordingly [3].

6. Enteral tube feeding with polymeric formulas is recommended in all patients with predicted severe acute pancreatitis who cannot tolerate oral intake after 72 hours. Initial enteral feeding should be started via a nasogastric tube, except in hemodynamically unstable patients, with transition to nasojejunal feeding in cases of intolerance to nasogastric feeding [3]. Multiple randomized controlled trials have shown no advantage of nasojejunal over nasogastric feeding with respect to tolerance or mortality [18, 44, 49, 97]. A 2020 Cochrane meta-analysis also demonstrated no superiority of one feeding route over the other in severe pancreatitis [20].

7. Parenteral nutrition should be initiated in cases of persistent intolerance to enteral feeding or when adequate caloric intake cannot be achieved enterally [3].

8. Selection of the treatment strategy in necrotizing pancreatitis should follow the widely accepted step-up approach, taking into account the time from disease onset and the dynamics of the clinical course [3, 12].

9. Endoscopic or percutaneous drainage is recommended as the first invasive intervention in patients with (suspected) infected WON, based on collection location and local expertise [3]. An advantage of endoscopic over percutaneous drainage in (suspected) infected WON is the absence of risk for pancreatocutaneous fistula formation [12].

10. When the patient's condition allows, the first intervention for infected necrosis should preferably be delayed for 4 weeks [3, 12].

11. PCD should be strongly considered as an adjunct to endoscopic drainage in cases of WON with deep extension into the paracolic gutters or pelvis [3, 12, 62], or following endoscopic or surgical debridement for additional treatment of residual necrosis [12]. In a prospective study by Ross et al. (107 patients) using DMD for WON, no cases of pancreatocutaneous fistula occurred after successful removal of percutaneous drains during long-term follow-up [59].

12. LAMS are preferred over plastic stents for endoscopic transluminal drainage of necrotic collections according to some guidelines [12]. However, European guidelines consider both plastic stents and LAMS acceptable options for WON management, noting that data on long-term indwelling LAMS are limited [3].

13. As a subsequent step in the absence of clinical improvement after endoscopic transluminal drainage of WON using LAMS or plastic stents combined with irrigation, endoscopic necrosectomy

(DEN) or minimally invasive surgical intervention (if PCD has already been performed) should be prioritized over open surgery, taking into account collection location and institutional expertise [3, 12]. In contemporary management of ANP, open surgical necrosectomy is reserved for patients who are not technically suitable candidates for minimally invasive surgical or endoscopic procedures [12].

14. Long-term placement of transluminal plastic stents is recommended in patients with disconnected pancreatic duct syndrome [3], or distal pancreatectomy may be considered when appropriate in selected candidates [12]. LAMS should be removed within 3–4 weeks to prevent stent-related complications [3, 62].

15. Urgent (≤ 24 hours) endoscopic retrograde cholangiopancreatography (ERCP) with biliary decompression is recommended in patients with acute biliary pancreatitis complicated by cholangitis. ERCP should be performed within 72 hours in patients with persistent biliary obstruction. ERCP is not recommended in patients with acute biliary pancreatitis without evidence of cholangitis or ongoing biliary obstruction [3].

16. Patient management should be individualized, incorporating all available clinical, radiological, and laboratory data, as well as local expertise [3].

17. Optimal management of patients with ANP requires a multidisciplinary approach involving gastroenterologists, surgeons, interventional radiologists, intensivists, infectious disease specialists, and clinical nutrition experts [12]. When local resources are limited, transfer of patients with severe necrotizing pancreatitis to specialized centers with advanced endoscopic capabilities, interventional radiology, and surgical options should be considered [12].

DECLARATION OF INTERESTS

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AUTHORS CONTRIBUTIONS

N. V. Puzyr performed the literature search and selection of relevant sources, conducted data analysis, and prepared the initial draft of the manuscript. A. Y. Tkachenko contributed to the finalization of the review, critical analysis of the selected sources, structuring of the material, and editing of the manuscript.

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Ендоскопічні транслюмінальні втручання в менеджменті гострого інфікованого некротичного панкреатиту. Огляд літератури

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Гострий некротичний панкреатит залишається одним із найскладніших захворювань у загальній хірургії. Інфікування некрозу, сепсис й органна недостатність — визначальні чинники летальності при цій патології. Серед інших загрозливих ускладнень — обструкція кишечника, біліарна обструкція, абдомінальний компартмент-синдром, зовнішні нориці, кровотечі, тромбоз селезінкової та портальної вен. Формування відмежованого некротичного скупчення після 4 тиж від початку захворювання створює анатомічні передумови для транслюмінального ендоскопічного доступу до патологічного вогнища за наявності відповідних показань. Сучасне лікування гострого некротичного панкреатиту ґрунтується на поетапній малоінвазивній стратегії, в якій ендоскопічні втручання посідають провідне місце. Міжнародні клінічні настанови, зокрема Європейського товариства гастроінтестинальної ендоскопії (ESGE), Американського товариства гастроінтестинальної ендоскопії (ASGE), Американської гастроентерологічної асоціації (AGA) підтримують ендоскопічний «ster-up» підхід як терапію першої лінії при інфікованому відмежованому некротичному скупченні. В основі цього підходу лежить контроль виявів сепсису, а не негайне виконання некроектомії. Важливими чинниками успіху є правильний вибір часу втручання, мультидисциплінарний підхід й індивідуалізація стратегії лікування. Досі не визначено оптимальних показань до переходу на більш інвазивні оперативні втручання. Це питання залишається дискусійним і зазвичай вирішується з огляду на досвід спеціалізованого центру. Складність прийняття клінічних рішень також може бути пов'язана з відмінностями в підходах до лікування між загальними хірургами й ендоскопістами, що потребує виваженої міждисциплінарної співпраці.

В огляді літератури висвітлено основні аспекти менеджменту гострого некротичного панкреатиту в контексті ендоскопічних транслюмінальних втручань. Розуміння переваг й обмежень цієї методики сприяє її технічному та тактичному вдосконаленню для поліпшення результатів лікування.

Ключові слова: гострий некротичний панкреатит, гострий інфікований панкреонекроз, обмежене некротичне скупчення, ендоскопічна транслюмінальна некроектомія, пряма ендоскопічна некроектомія.

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