



## Review Article

# Paradigm shift away from open surgical necrosectomy toward endoscopic interventions for necrotizing pancreatitis



Jae Hee Cho,\* Yoon Jae Kim, Yeon Suk Kim

## A B S T R A C T

Interventions for infected and symptomatic walled-off pancreatic necrosis (WOPN) have undergone a paradigm shift away from open surgical necrosectomy toward endoscopic intervention such as transmural drainage and necrosectomy. Recent multicenter studies and evidence-based guidelines have suggested the safety and efficacy of endoscopic transmural necrosectomy (ETN) for management of complicated WOPN. In consideration of the inherent properties and the risks associated with this procedure, ETN should be performed by expert endoscopists who are well-versed in management of necrotizing pancreatitis and supported by a special multidisciplinary team. Although there have been limited data to define the selection criteria and the techniques regarding ETN, this comprehensive review focuses on the current indications, therapeutic outcomes, complications, and controversies of ETN for management of WOPN.

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## Introduction

Acute pancreatitis (AP) is a dynamic inflammatory process with a benign clinical course and low mortality. However, 10–20% of patients experience severe AP, which can result in an intense inflammatory response, a prolonged hospital course, and variety of local and systemic complications that carry a significant risk of morbidity and mortality.<sup>1–4</sup> Necrosis of the pancreas itself is defined by nonenhancement of the parenchyma on dynamic computed tomography scan, and approximately 5–10% of patients with AP develop necrotizing pancreatitis. Necrosis of peripancreatic/pancreatic tissue can progress to liquefaction with subsequent organization without epithelial lining, and eventual evolution into a walled-off pancreatic necrosis (WOPN) over 4 weeks. This may be related to secondary infection or symptomatic sterile necrosis. Because the mortality rate of infected WOPN is as much as approximately 39% compared to 15% of sterile WOPN, patients with infection generally need to undergo an intervention, which has shifted from primary open necrosectomy to a step-up approach. Currently, step-up approach is a widely used treatment modality consisting of percutaneous catheter drainage (PCD), endoscopic transmural drainage (ETD), and endoscopic transmural necrosectomy (ETN). Of these, ETN provides a targeted approach with a reduction in the systemic inflammatory response and avoidance of wound complications<sup>5</sup>; its use is increasingly widespread and now

accepted as a first line treatment for this condition. In this review, we aim to determine the risk and benefits of ETN for management of necrotizing pancreatitis.

## Indications and strategies of intervention for WOPN

The primary indications for intervention in WOPN are similar regardless of different intervention routes, such as endoscopic, percutaneous, or surgical approach. The indications for intervention in WOPN are as follows: (1) clinical suspicion or documented infected WOPN with clinical deterioration; (2) ongoing organ failure in the several weeks after the onset of acute pancreatitis; (3) symptomatic sterile WOPN including intractable pain, persistent unwellness, ongoing gastrointestinal obstruction; and (4) disconnected pancreatic duct syndrome with WOPN.

Among various treatment modalities, surgical debridement, either open or laparoscopic, may be associated with prolonged recovery, the need for repeat operations, external fistula, and abdominal wall hernias.<sup>6,7</sup> Percutaneous debridement techniques have been used as an alternative to operative management; however, these methods are not universally successful and additional combination treatment is required.<sup>8–10</sup> Endoscopic interventions, such as ETD and ETN, have also been introduced in an effort to overcome the aforementioned limitations; however, there are some problems of accessibility and complication. Therefore, combination

Division of Gastroenterology, Department of Internal Medicine, Gachon University Gil Medical Center, Incheon, Korea

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\* Corresponding author. Division of Gastroenterology, Department of Internal Medicine, Gachon University Gil Medical Center, 21 Namdong-daero 774 beon-gil, Namdong-gu, Incheon, 405-760, Korea.

E-mail address: [jhcho9328@gmail.com](mailto:jhcho9328@gmail.com) (J.H. Cho).

treatments using PCD, ETD, ETN, and surgery by a step-up manner have recently been advocated. Endoscopic or percutaneous drainage is first recommended, and followed, if necessary, by endoscopic or minimally invasive surgical necrosectomy. As a targeted minimally invasive approach, ETN with mechanical debridement was demonstrated to be an efficacious and reproducible technique with an acceptable safety profile.<sup>11,12</sup> The ideal goal of ETN is excision of all dead and devitalized pancreatic and peripancreatic tissue while preserving a viable functioning pancreas, and controlling surgery related complications.

### Overview of ETN

Necrotizing pancreatitis is a dynamic disease process that evolves in local and systemic inflammation; consequently, endoscopic/percutaneous drainage alone often proves inadequate, and additional endoscopic/surgical necrosectomy is required. The optimal time for intervention of necrotizing pancreatitis is important in order to reduce the occurrence of procedure related complications, and it should be delayed by approximately 4 weeks after the onset of pancreatitis, when vascular inflammation has decreased, organization of the process has occurred, and delineation of live from dead tissue is complete. At this point, the retroperitoneal inflammatory response decreases and the necrotic areas are demarcated from the surrounding viable tissue, which may permit definitive endoscopic debridement.

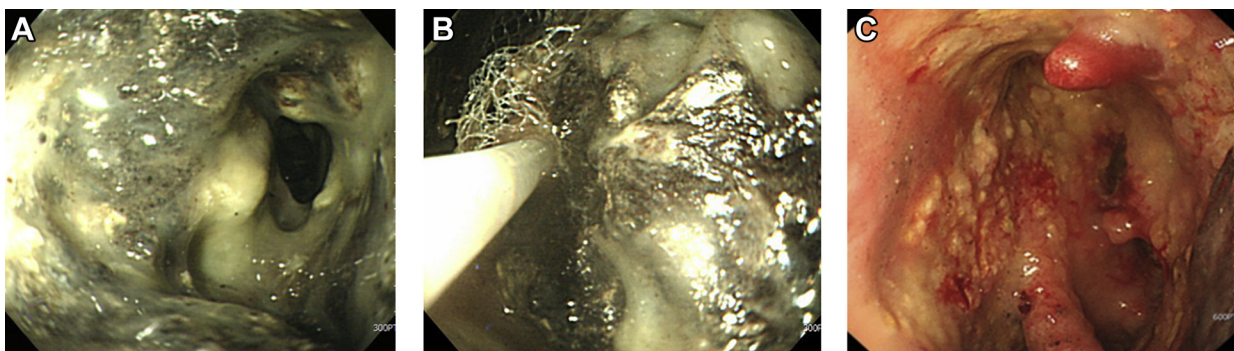
Endoscopic interventions require proximity to the gastroduodenal lumen and WOPN, whereas percutaneous drainage may be suitable for collections distant from the gut lumen and those with less demarcation. Necrosis closely adhering to the posterior gastric wall or medial duodenal wall is considered an ideal access route for ETN; thus it is typically performed via a transgastric or transduodenal approach. Under conscious sedation or anesthesia, a puncture site is identified by locating a bulge into the gastrointestinal lumen using endoscopic ultrasound or visual assessment. The fluid collection is then entered, a sample of fluid is aspirated and cystenterostomy is created using wire-guided balloon dilators up to 15–20 mm. Once the entry site is established, direct endoscopic debridement using endoscopic accessories, including snare, baskets, and stone retrieval balloons, can be performed using a conventional upper or water-jet endoscope. When ETN extends into the fat of the mesocolon or small bowel mesentery, meticulous care should be taken to avoid vascular injury, particularly to the colic, superior, or inferior mesenteric vessels. After mechanical removal of necrotic debris, large-bore double pigtail plastic stents or a fully covered self-expandable metallic stent (SEMS) are inserted into the cavity; a nasocystic tube may occasionally be placed for postinterventional lavage. ETD can be performed during the index procedure, but it is usually repeated on a regular basis until the

cavity is clean by direct visualization. As many as 3–10 sessions may be necessary for complete debridement of the necrotic cavity; however, the number of sessions depends on disease severity (Fig. 1).

### Outcomes of endoscopic intervention

Endoscopic interventions for WOPN carry significant additive risks, and there are a few comparative data to document increased success. Published studies of ETD and ETN are summarized in Table 1.<sup>5,11–23</sup> The Dutch Pancreatitis Group compared endoscopic intervention ( $n = 10$ ) and surgical necrosectomy ( $n = 10$ ), and showed that ETN reduced the proinflammatory response as well as the composite clinical end point compared with surgical necrosectomy.<sup>5</sup> Factors that predict failure of endoscopic therapy have not been well studied. A major determinant for the feasibility of ETN is the location of the target collection and other risk factors for failure of endoscopic intervention are the size of the necrotic cavity (>15 cm), deep retroperitoneal extension, presence of diabetes mellitus, and comorbid conditions. Early aggressive adjuvant therapy, such as PCD with or without sinus tract endoscopy or video-assisted retroperitoneal debridement, in addition to endoscopic treatment, was required in patients with more extensive necrotic debris, severe pancreatic duct disruption, or deep retroperitoneal necrotic extension.<sup>17</sup> In cases of inaccessible necrotic collections, a variety of other minimally invasive retroperitoneal approaches, including PCD, sinus tract endoscopy, and video-assisted retroperitoneal debridement procedure may be either preferable or serve as adjuncts to endoscopic therapy.

Several novel approaches were recently introduced. First, the multigateway approach uses more than one transmural entry site created in order to facilitate rapid drainage in large (>80 mm) symptomatic WOPN.<sup>24</sup> One tract may serve as a channel for irrigation, whereas the other acts as an exit conduit for drainage of necrotic contents.<sup>25</sup> Second, esophageal fully covered SEMS has been used for drainage of peripancreatic/pancreatic collections<sup>26,27</sup>; however, potential stent migration and uncertainty regarding cost-effectiveness preclude widespread adoption in clinical practice. Third, a novel type of antimigration SEMS for cystenterostomy has been developed.<sup>28,29</sup> These stents have a wide lumen (16 mm diameter), allowing insertion of the endoscope through the stent lumen for direct necrosectomy. In addition, novel methods including hydrogen peroxide, vacuum sponge, and newly developed grasping type of scissors for debridement are under continuous investigation.<sup>30–32</sup> Although their advantages and safety are unclear compared to conventional methods, further studies using newly developed devices and accessories for endoscopic necrosectomy are anticipated.



**Fig. 1.** Sequential endoscopic images showing walled off pancreatic necrosis (WOPN) cavity. (A) Initial finding after entry into complicated WOPN; (B) net snare removal of necrotic material; and (C) clean cavity after endoscopic necrosectomy.

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