



Timing of Endoscopic Transmural Drainage for Pancreatic Necrosis: Expanding the Horizon!

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Abstract

Endoscopic transluminal drainage (ETD) has been traditionally performed on collections that have a well-formed enclosing wall and therefore it was advocated for walled-off necrosis. However, recently, retrospective studies have reported that ETD can be safely performed in patients with collections without a well-formed wall also and reported outcomes better than those patients who were treated with percutaneous drainage. The evidence for safety and efficacy of early ETD for infected pancreatic necrosis is scanty and therefore, in this news and views, I will be discussing a recently published systematic review and meta-analysis comparing outcomes after early (<4 weeks) and standard (≥ 4 weeks) drainage of pancreatic necrosis.

Keywords

- ▶ pancreatic necrosis
- ▶ stent
- ▶ acute pancreatitis

Acute necrotizing pancreatitis is associated with significant morbidity and mortality and superadded infection is a sinister event in its natural history as it is associated with increased morbidity and mortality.¹ Surgical debridement along with antibiotics had been the mainstay of management of infected pancreatic necrosis. However, better understanding of pathophysiology of this enigmatic disease along with better understanding of the indications, timing, and type of interventions has led on to paradigm shift in the management of infected pancreatic necrosis.² Minimally invasive endoscopic, percutaneous, and surgical/laparoscopic interventions are associated with lesser inflammatory insult as compared to open surgery and thus improved outcomes. The Minimally Invasive Step Up Approach versus Maximal Necrosectomy in Patients with Acute Necrotising Pancreatitis (PANTER) trial laid the foundation of “step-up” management approach for infected pancreatic necrosis where in initially an endoscopic transluminal drainage (ETD) or image-guided percutaneous drainage (PCD) is performed as first step followed by, if required, to aggressive interventions including endoscopic transluminal necrosectomy (ETN) or minimally invasive surgical necrosectomy.^{3,4}

Over the last one decade, both endoscopic and percutaneous step-up management approach has been the mainstay of treatment of infected pancreatic necrosis. Comparative studies including randomized controlled trials (RCT) as well as systematic reviews/meta-analysis have reported that endoscopic “step-up” approach is associated with reduced occurrence of new onset organ failure as well as external pancreatic fistulae along with shorter hospital stay, lower costs, and better quality of life compared to minimally invasive percutaneous surgical approach.¹ Therefore, endoscopic step-up is the recommended as preferred intervention for the management of endoscopically accessible pancreatic necrotic collections and percutaneous step-up approach reserved for collections that are not accessible endoscopically/when endoscopic expertise is unavailable or has failed.

ETD has been traditionally performed on collections that have a well-formed enclosing wall and therefore it was advocated for walled-off necrosis (WON).⁵ The revised Atlanta guidelines suggested a cutoff of 4 weeks after the onset of illness for the formation of an enclosing wall and therefore the peripancreatic collections beyond 4 weeks of

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illness were called WON. Infected pancreatic necrotic collections earlier than 4 weeks were treated with PCD and endoscopic drainage was not recommended for these collections because of fear of pneumoperitoneum and pneumoretroperitoneum and its infective consequences. However, subsequent studies observed that the cutoff of 4 weeks is arbitrary cutoff and in some collections wall forms earlier than 4 weeks.⁶ Moreover, retrospective studies reported that ETD can be safely performed in patients with collections without a well-formed wall also and reported outcomes better than those patients who were treated with PCD.⁷⁻⁹ The evidence for safety and efficacy of early ETD for infected pancreatic necrosis is scanty and therefore, in this news and views, I will be discussing a recently published systematic review and meta-analysis comparing outcomes after early (<4 weeks) and standard (≥ 4 weeks) drainage of pancreatic necrosis.¹⁰

Ramai et al searched MEDLINE (EBSCOhost), Embase (Elsevier), Scopus, and Cochrane from inception through June 2022 with keywords “drainage,” “pancreatic debridement,” “pancreatic drainage,” “direct endoscopic necrosectomy,” “pancreatic fluid collection,” “walled-off necrosis,” “early drainage,” and “delayed drainage.”¹⁰ The authors included studies that evaluated outcomes associated with early and standard drainage of pancreatic necrosis. The exclusion criteria were pediatric (age <18 years) studies, studies not published in the English language, and case reports. The outcomes measured evaluated in the meta-analysis were technical success, defined as successful endoscopic placement of a lumen-apposing metal stent for drainage and clinical success, defined as a reduction in size of necrotic collections. The adverse events and their severity were extracted according to the American Society for Gastrointestinal Endoscopy lexicon whenever reported otherwise, adverse events were extracted as reported in the original studies.

The final analysis included six studies (630 patients) with one study being prospective and the remaining five studies being retrospective and were evaluated to be high quality studies. One hundred and eighty-two patients (28.9%) were enrolled in the early drainage cohort and 448 (71.1%) patients in the standard drainage cohort. Age ranges were similar between groups with alcohol being the main etiology of acute pancreatitis. The mean fluid collection size was 143.4 ± 18.8 mm in early drainage cohort and 128 ± 19.7 mm in the standard drainage cohort with majority of fluid collections being located in the body of the pancreas (86.7%). The technical success was equal in both cohorts and clinical success rates did not favor either standard or early drainage (odds ratio [OR]: 0.39; 95% confidence interval [CI]: 0.13–1.22; $p = 0.11$). The adverse events as well as mortality were not statistically significant different between the two groups (OR: 1.67; 95% CI: 0.63–4.45; $p = 0.31$) and (OR: 1.14; 95% CI: 0.29–4.48; $p = 0.85$), respectively. The incidence of bleeding was higher in early group versus standard group (15 vs. 11, respectively) whereas stent migration (5 vs. 8, respectively) and perforation (0 vs. 5, respectively) were lower in the standard versus early cohort. The hospital stay was reported to be longer for patients

undergoing early drainage compared with standard drainage (23.7 vs. 16.0 days, respectively). The authors concluded that both early (<4 weeks) and standard (≥ 4 weeks) drainage of walled-off pancreatic fluid collections offer similar technical and clinical outcomes.

Commentary

This meta-analysis has reported that early drainage (<4 weeks) of pancreatic fluid collections is associated with similar technical and clinical success rates as well as overall occurrence of adverse events when compared with standard drainage (≥ 4 weeks). This meta-analysis has reinforced the results of previous studies fact that ETD of infected pancreatic necrosis is possible earlier than 4 weeks of onset of acute pancreatitis with good outcomes. Despite several important limitations like small number of studies, heterogeneity in clinical success as well as likelihood inclusion of patients without organ failure and differing study protocols as well as data points, this meta-analysis has provided evidence to perform early ETD in patients with infected pancreatic necrosis and not delay till 4 weeks waiting for the wall to be formed. It is also important to remember that ETD in the early phase is technically challenging especially in solid necrotic collections with poor demarcation of viable and necrotic tissues with increased needs of necrosectomy as compared with liquefied WON in delayed phase that can be managed with drainage alone in majority of patients. One retrospective study has reported that early (<4 weeks) ETD is associated with more frequent requirement of necrosectomy, higher mortality, and need for rescue surgery as compared with ETD in the later phase of illness.¹¹ The current evidence suggests that early ETD should be performed in centers with expertise in advanced endoscopic pancreatic interventions and experienced surgical as well as radiological backup in select group of patients with infected necrotic collections completely refractory to antibiotics and at endoscopically accessible locations. It is also important to remember that retrospective and cohort studies have their important innate limitations and RCTs comparing early versus delayed drainage are needed to provide strong irrefutable evidence supporting early ETD.¹² This systematic review and/or meta-analysis has laid the foundation for the same and it seems that the horizon of ETD is going to expand in future.

Conflict of Interest

None declared.

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