# Timing It Right: Endoscopic Necrosectomy for Infected Necrotizing Pancreatitis

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## Abstract

The endoscopic step-up drainage approach involving initial drainage followed by, if required, direct endoscopic necrosectomy (DEN) is the preferred management approach for symptomatic pancreatic necrotic collections. However, limited data suggests that immediate DEN during initial stent placement may hasten clinical recovery by quicker resolution of systemic inflammatory response. However, because of concerns about adverse effects, especially gastric perforation and bleeding, most endoscopists prefer delayed DEN. In this news and views, we discuss a recently published randomized controlled trial that compared upfront necrosectomy at the index intervention versus as a step-up for patients with infected necrotizing pancreatitis.

**Keywords**

- pancreatitis
- lumen-apposing metal stent
- necrosectomy

Acute pancreatitis is one of the most common gastrointestinal causes of hospital admissions, and its spectrum ranges from interstitial pancreatitis to necrotizing pancreatitis.[1] Acute necrotizing pancreatitis is seen in around 5 to 10% of patients where the necrosis can involve the pancreatic parenchyma alone (<1%), the peripancreatic tissue (15%) or both (85%.[2] 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. Initial endoscopic transluminal drainage or image-guided percutaneous drainage is performed as the first step, which, if required, is followed by aggressive interventions, including endoscopic transluminal necrosectomy or minimally invasive surgical necrosectomy.[3–6] After initial successful drainage, 30 to 50% of patients still require step-up therapies in the form of direct endoscopic necrosectomy (DEN) or percutaneous catheter upgradation or video-assisted retroperitoneal debridement due to the presence of significant solid material or large size of the collection.[7,8]

Endoscopic transluminal drainage had been initially performed using multiple double pigtail plastic stents.[6] In this situation, DEN cannot be performed at the time of initial plastic stent placement because of the nonmaturation of the transmural fistula tract. However, the development of lumen-apposing metal stents (LAMS) has revolutionized the management of walled-off necrosis (WON).[9] Apart from making the procedure quicker and safer, LAMS allow endoscopic access to the necrotic cavity during the initial stent placement, thereby permitting upfront DEN. However, most endoscopists prefer delaying DEN even after placing LAMS because immediate DEN risks stent dislodgement and gastric fistula formation with associated complications.[10] Moreover, immediate DEN results in unnecessary necrosectomy and associated complications, as almost one-third of patients with WON recover with endoscopic drainage alone without the need for DEN. However, there is a lack of data comparing the safety and clinical outcomes of immediate DEN versus delayed DEN. A multicenter retrospective study compared the clinical outcomes and predictors of success for endoscopic drainage of WON with LAMS followed by immediate or delayed DEN in 69 and 202 patients, respectively.[11] The authors reported that DEN at the time of initial stent placement reduces the number of necrosectomy sessions required for successful clinical

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resolution of WON with no significant difference in the overall procedural adverse effects. The authors of a recently published multicenter randomized trial evaluated upfront necrosectomy at the index intervention versus as a step-up for patients with infected necrotizing pancreatitis.[12] The authors hypothesized that upfront necrosectomy may reduce the need for reinterventions, resolve systemic inflammatory responses early, and accelerate clinical recovery.

To prove their hypothesis, the authors conducted a multicenter randomized study involving 70 patients with confirmed or suspected infected necrotizing pancreatitis and necrosis extent of at least 33%. The patients were randomized to receive endoscopic ultrasound-guided drainage with upfront necrosectomy ($n = 37$) or step-up treatment ($n = 33$) using LAMS (20 mm diameter; 10 mm saddle length). While in the upfront necrosectomy group, direct necrosectomy was performed immediately after stenting in the same treatment session, in the step-up group, direct necrosectomy or additional drainage was done at a subsequent treatment session if there was no clinical improvement. The primary outcome was the number of reinterventions per patient to achieve treatment success from index intervention to 6 months follow-up, while secondary end-points were treatment success, disease-related adverse events, procedure-related adverse events, clinical improvement at 72 hours after the index intervention, readmissions due to underlying disease or procedure-related symptoms or events, pancreatic exocrine and endocrine status, technical success for endoscopic ultrasound-guided drainage, technical success for endoscopic necrosectomy, and overall treatment costs.

In the final, intention-to-treat analysis of study subjects, the median number of reinterventions was significantly lower for the upfront necrosectomy arm (1 [interquartile range: 0–1] than for the step-up approach arm (2 [1–4]), difference –1 (95% confidence interval [CI]: –2 to 0; $p = 0{\cdot}0027$). Among secondary end-points, patients undergoing upfront necrosectomy showed significant improvement compared to those in step-up approach group in; clinical improvement at 72 hours after the index intervention (upfront necrosectomy (28/37 [76%]) versus step-up approach (17/33 [52%], difference 24.2% points (95% CI: 1.4–44·4); $p = 0{\cdot}035$]; as well as hospital stay from index intervention to discharge (upfront necrosectomy; (9 days [7–20]) versus step-up approach (19 days [9–33], difference – 5 days [95% CI: -13 to 0]; $p = 0{\cdot}048$). Along with clinical improvement, the resolution of SIRS at 72 hours postindex procedure also showed a positive trend toward improvement in the upfront necrosectomy group (19/23, 83% vs. step-up group [12/21, 57%]; difference of 25.5 [95% CI: -2.1 to 49.1], $p = 0{\cdot}064$). The rest of the secondary end-points, procedure-related and disease-related adverse events, including mortality from index to 6-month follow-up, did not differ between groups. The authors concluded that in stabilized patients with infected necrotizing pancreatitis and fully encapsulated collections, upfront necrosectomy safely reduces the number of reinterventions required to achieve treatment success as compared to the step-up treatment approach.

## Commentary

This randomized controlled trial (RCT) has addressed an important question that has been raised by conflicting results of previous retrospective studies regarding the role of upfront endoscopic necrosectomy at the time of index intervention versus as a step-up measure in patients with infected necrotizing pancreatitis. Pawa et al retrospectively compared 43 patients, who underwent immediate DEN, with 37 patients, who underwent delayed DEN.[13] The authors reported that patients undergoing delayed DEN had a shorter index hospital stay and fewer necrosectomies than immediate DEN and immediate DEN was associated with more necrosectomies than delayed DEN regardless of the percentage of necrosis ($p = 0.017$ and 0.0067, respectively).

Yan et al reported the results of a multicenter retrospective study comparing clinical outcomes and predictors of success for endoscopic drainage with LAMS followed by immediate or delayed DEN performed at standard intervals.[11] The mean number of necrosectomy sessions for WON resolution was significantly lower in the immediate DEN group compared to the delayed DEN group (3.1 vs. 3.9, $p < 0.001$) and performing DEN at the time of stent placement was an independent predictor for resolution of WON with lesser number of DEN sessions (odds ratio 2.3; $p = 0.004$). Performing early DEN removes infected solid debris early, resulting in faster resolution of fever, systemic inflammatory response syndrome (SIRS), and organ failure. However, at the same time, many patients with solid debris may not require necrosectomy due to the presence of a large caliber of the metal stent, enabling clinical success with drainage alone. Moreover, DEN immediately after LAMS deployment carries the risk of free gastric perforation consequent to stent dislodgement due to lack of a mature fistulous tract.

This RCT has answered many of the previous unanswered questions on the timing of DEN. There is a concern of increased inflammatory response following immediate necrosectomy, and this could result in worsening organ failure and complications. However, this RCT has demonstrated that the upfront DEN does not provoke any significant inflammatory response. Also, it resulted in a significantly higher proportion of patients having clinical improvement at 72-hour postindex intervention along with resolution of SIRS or sepsis or organ failure and a decrease in the size of the necrotic collection by 25% percentage or more. However, it is important to understand that this immediate DEN approach is unsuitable for all patients with infected pancreatic necrosis. This RCT included stable patients with well-encapsulated necrotic collections, and only 10% of the included patients had organ failure at the time of intervention. Necrosectomy may not be feasible in the early stages of illness when there is poor demarcation between the viable and nonviable tissue. Also, drainage alone may be a safer option initially in unstable patients as it allows patient stabilization and delayed necrosectomy in a more stable condition may be a safer option.

 

Importantly, there was no significant difference in either the treatment success or the adverse events between the two treatment arms, suggesting that both immediate and delayed DEN are equally effective and safe. The only difference observed was in the number of reinterventions, the length of hospital stay, and healthcare costs. In conclusion, this RCT suggests that immediate DEN may be a better treatment option than a step-up endoscopic treatment approach in clinically stable patients with WON having significant necrotic debris.

### Discloser

There are no conflicts of interest and no financial disclosures to be made by any of the authors.

### Conflicts of Interest

None declared.

## References


1 Yadav D, Lowenfels AB. The epidemiology of pancreatitis and pancreatic cancer. Gastroenterology 2013;144(06):1252–1261
2 Sharma V, Rana SS, Bhasin DK. Extra-pancreatic necrosis alone: contours of an emerging entity. J Gastroenterol Hepatol 2016;31 (08):1414–1421
3 van Santvoort HC, Besselink MG, Bakker OJ, et al; Dutch Pancreatitis Study Group. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med 2010;362(16):1491–1502
4 Babu RY, Gupta R, Kang M, Bhasin DK, Rana SS, Singh R. Predictors of surgery in patients with severe acute pancreatitis managed by the step-up approach. Ann Surg 2013;257(04):737–750
5 Jearth V, Rana SS. Endoscopic step up: when and how. Surg Open Sci 2022;10:135–144
6 Rana SS. Endoscopic treatment of pancreatic necrosis: still searching for perfection!. J Gastroenterol Hepatol 2023;38(08): 1252–1258
7 Baron TH, DiMaio CJ, Wang AY, Morgan KA. American Gastroenterological Association clinical practice update: management of pancreatic necrosis. Gastroenterology 2020;158(01):67–75.e1
8 Rana SS, Bhasin DK, Sharma RK, Kathiresan J, Gupta R. Do the morphological features of walled off pancreatic necrosis on endoscopic ultrasound determine the outcome of endoscopic transmural drainage? Endosc Ultrasound 2014;3(02):118–122
9 Rana SS. An overview of walled-off pancreatic necrosis for clinicians. Expert Rev Gastroenterol Hepatol 2019;13(04): 331–343
10 Guo J, Saftoiu A, Vilmann P, et al. A multi-institutional consensus on how to perform endoscopic ultrasound-guided peri-pancreatic fluid collection drainage and endoscopic necrosectomy. Endosc Ultrasound 2017;6(05):285–291
11 Yan L, Dargan A, Nieto J, et al. Direct endoscopic necrosectomy at the time of transmural stent placement results in earlier resolution of complex walled-off pancreatic necrosis: results from a large multicenter United States trial. Endosc Ultrasound 2019;8 (03):172–179
12 Bang JY, Lakhtakia S, Thakkar S, et al; United States Pancreatic Disease Study Group. Upfront endoscopic necrosectomy or step-up endoscopic approach for infected necrotising pancreatitis (DESTIN): a single-blinded, multicentre, randomised trial. Lancet Gastroenterol Hepatol 2024;9(01):22–33
13 Pawa R, Dorrell R, Clark C, Russell G, Gilliam J, Pawa S. Delayed endoscopic necrosectomy improves hospital length of stay and reduces endoscopic interventions in patients with symptomatic walled-off necrosis. DEN Open 2022;3(01):e162


 