Endoscopic Step-Up Approach in Management of Necrotizing Pancreatitis

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KEYWORDS

• WON • Endoscopic step-up approach • Surgical step-up approach • DEN

KEY POINTS

- Endoscopic step-up approach' in the management of Necrotizing Pancreatitis involves sequential steps of intervention at different time points in the clinical course of the disease.
- Endoscopic ultrasound (EUS)-guided drainage of Pancreatic Walled Off Necrosis (WON) is the first strategic step in Endoscopic step-up approach.
- Lumen Apposing Metal Stent (LAMS) are preferred over plastic stents for providing safe and effective drainage due to their wide calibre.
- Successive steps include Direct Endoscopic necrosectomy (DEN) through LAMS, &/or irrigation using naso-cystic tube (NCT) in select patients, primarily based on characteristics of necrotic debris.
- Minimally invasive percutaneous radiological &/or surgical interventions are considered when endoscopic drainage is not feasible or unsuccessful.

INTRODUCTION

Acute pancreatitis (AP) is one of the most common gastrointestinal emergencies, often requiring hospital admission. The disease is "mild" in about 80% of the patients with favorable outcomes. However, the remaining 20% of patients of AP develop more "severe" acute necrotizing pancreatitis (ANP) associated with morbidity involving one or more organ failures with or without peri-pancreatic fluid collections.[1,2] Pancreatic fluid collections (PFCs) are a frequent complication of AP. A clear-cut distinction between collections associated with acute interstitial pancreatitis and those arising from ANP should be made for an appropriate management strategy. Peri-pancreatic fluid collections arising from acute interstitial pancreatitis are termed "acute peri-pancreatic fluid collection," and those which persist beyond 4 weeks often develop a well-defined

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capsule or wall and are termed "pseudocyst." Similarly, peri-pancreatic fluid collections arising from ANP in the early phase (up to around 4 weeks) when they do not have a mature wall are termed "acute necrotic collection"; and those which develop a mature capsule around the necrotic collection, usually after 4 weeks of the onset of ANP, are termed "walled-off necrosis (WON)." These necrotic collections in ANP can be sterile but can develop infection in about 30% of patients.[3] A conservative management approach is advisable for sterile necrosis unless pressure symptoms are causing persistent abdominal pain or mass effects like gastric outlet biliary obstruction or compartment syndrome, where drainage interventions are required.[4] Whereas infected necrotic collections are an indication for invasive intervention as only a few patients will respond to antibiotics alone.[5]

Historically, open surgical necrosectomy was considered for the management of infected pancreatic necrosis,[6] which went into disrepute due to poor outcomes, including increased morbidity and mortality. Management of infected pancreatic necrosis underwent a paradigm shift after Van Santvoort and colleagues reported that a minimally invasive surgical approach is associated with reduced morbidity and cost when compared with open necrosectomy.[7] This approach was termed a "step-up approach," where a gradual increase from a less invasive procedure to more invasive procedures is performed if needed. Several alternate minimally invasive interventions have emerged, including laparoscopic necrosectomy, video-assisted retroperitoneal debridement (VARD), percutaneous drainage, and endoscopic drainage, which are associated with reduced morbidity and mortality. Selecting a single intervention procedure or even a combined approach is based on the morphology and location of PFC and the patient's clinical condition. Similar to surgery, several recent studies have adopted the "step-up approach" strategy in endoscopy drainage methods. Endoscopic drainage is currently the most preferred intervention for peri-luminal PFC.

This review aims to describe an endoscopic step-up approach in the management of necrotizing pancreatitis, focusing on its evolution, techniques, and recent advances, primarily related to direct endoscopic necrosectomy (DEN).

CONCEPT AND EVOLUTION OF STEP-UP APPROACH

Surgical open necrosectomy was the traditional approach for the management of infected pancreatic necrosis,[8,9] which was associated with very high rates of adverse events (34%–95%) and mortality (11%–39%) along with an increased risk of long-term pancreatic exocrine and endocrine insufficiency.[10,11] The paradigm shift in approach from open necrosectomy to minimally invasive step-up approach was effectively stamped by the landmark publication from the Dutch Pancreatitis Group by Van Santvoort and colleagues in 2010 (PANTER trial), which led to a wider acceptance of the minimally invasive approach. In this study, 88 patients of ANP were randomized to either a direct open necrosectomy or a step-up approach. The latter group had either a percutaneous drain or an endoscopic trans-gastric drainage followed by minimally invasive retroperitoneal necrosectomy, if necessary. Major complications such as new-onset organ failure, perforation, fistula, or bleeding occurred in 12% of patients in the step-up group compared with 40% in the open group. Other outcomes like pancreatic fistula, incisional hernia, and new-onset diabetes were also low in the step-up approach group. The nomenclature of the approach was termed a "step-up approach" because of the sequential increase from less invasive to a more invasive procedure based on the overall clinical scenario. The improved outcomes with the step-up approach (when compared with open necrosectomy) can be attributed to

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reduced provocation from surgical trauma (ie, pro-inflammatory response and tissue injury) by the minimally invasive techniques in patients who are already severely ill. This observation is supported by the decreased frequency of new-onset organ failure in the step-up group.[7]

Later, Bakker and colleagues (2012), in a randomized trial comparing endoscopic trans-gastric with surgical necrosectomy for infected necrotizing pancreatitis, reported that endoscopic necrosectomy reduced the pro-inflammatory response and the composite clinical endpoint. They used an endoscopic step-up approach where initial EUS-guided drainage was performed using double-pigtail plastic stents and a naso-cystic catheter. The necrotic collection was irrigated with 1 L of normal saline per 24 hours. Endoscopic trans-gastric necrosectomy was performed subsequently.[12]

STEP-UP APPROACH

Recent developments have occurred in both the surgical step-up approach and endoscopic step-up approach management of necrotizing pancreatitis.

In the "surgical step-up approach," an image-guided (ultrasound or CT) percutaneous catheter drainage is placed as the first step. The most accessible collection is targeted, and the left retroperitoneum is preferred as this route is the safest and shortest. Here, the drain remains retroperitoneal, and intra-abdominal space remains untouched. If the clinical situation demands, VARD can be performed. Percutaneous drainage (PCD) tract acts as a guide to the deep-seated collections via the retroperitoneal route for minimally invasive necrosectomy thus avoiding the transperitoneal approach and collateral damage to the bowel. The size of the catheter also depends on the relative amount of necrotic debris and the size of the necrotic collection. Laparoscopic necrosectomy can be considered for deeper pockets of infected necrosis.[13]

The "endoscopic step-up approach" includes endoscopic transluminal drainage by endoscopic ultrasound (EUS), with plastic or metal stents as the first step. The choice of stent largely depends on the amount of debris in WON, the collection size, and availability. Currently, large caliber fully covered dedicated stents, including lumen apposing metal stents (LAMS) or bi-flanged metal stents (BFMS), are preferred due to their ease of placement and efficient drainage. Additional naso-cystic catheters can be considered at index drainage or, subsequently, to irrigate the cavity with normal saline regularly. This helps clean up infected material and even loosen the large chunks of adherent debris. If the clinical condition demands an additional step of DEN may be performed using a forward-viewing scope through the LAMS/BFMS[14,15] (**Figs. 1** and **2**A-D). If plastic stents are placed upfront for index drainage, the gastric access route needs dilation with a balloon (12–15 mm) followed by DEN.

Some endoscopists have expanded their reach in managing patients with infected peripheral or para-colic collections that persist after the initial percutaneous drainage. The percutaneous tract (also known as 'sinus tract') is dilated either by increasing the size of the PCD catheter to maximum diameter (up to 30 Fr) or using a large caliber dilating balloon or short length fully covered self-expanding metal stent (FCSEMS) (esophageal), followed then by accessing the cavity using standard forward view endoscope to perform necrosectomy (percutaneous endoscopic necrosectomy).[16]

Timing of Drainage

Among patients with necrotizing pancreatitis, current guidelines recommend delay in drainage until 4 or more weeks to allow collections to mature with defined wall. However, some recent reports suggest that early intervention (<4 weeks) can be attempted for patients with clinical deterioration despite maximal supportive therapy.

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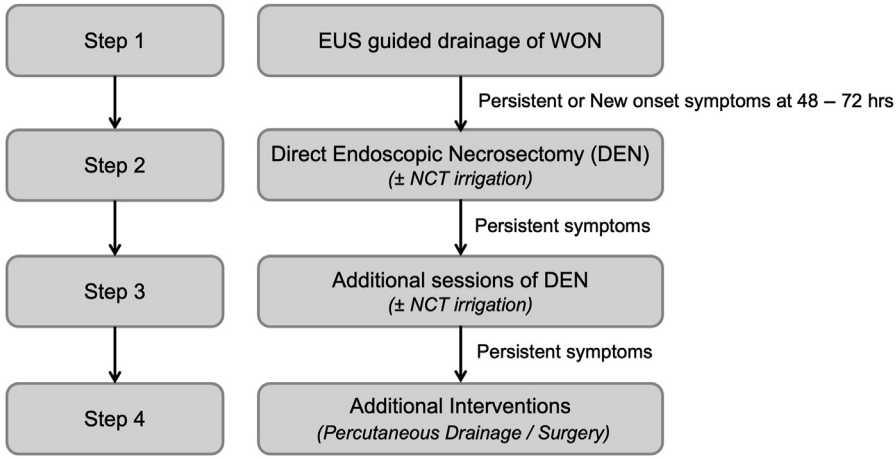

Fig. 1. Flowchart depicting the steps of the endoscopic step-up approach

Endoscopic intervention is technically challenging in the early phase because of the increased proportion of solid debris having immature wall as compared with well-formed relatively liquefied WON in the delayed phase.[17] Trikudanathan and colleagues evaluated early (<4 weeks) interventions that were more often performed in patients with infection and organ failure, with no increase in complications, a similar improvement in organ failure, slightly increased need for surgery, and relatively low mortality.[18] Oblizajek and colleagues and Chantarojanasiri and colleagues also made similar conclusions regarding early drainage in their retrospective studies.[19,20]

Boxhoorn and colleagues evaluated catheter drainage in infected necrosis. They compared immediate catheter drainage within 24 hours after randomization (once infected necrosis was diagnosed) with drainage that was postponed until the stage of WON. This trial reported nonsuperiority of immediate drainage over postponed drainage concerning complications with lesser requirement of invasive interventions in the delayed drainage group.[21]

"Endoscopic STEP-UP APPROACH" VERSUS "SURGICAL STEP-UP APPROACH"

Three randomized controlled trials have compared the endoscopic step-up approach with minimally invasive surgical step-up for the treatment of necrotizing pancreatitis (**Table 1**). The first RCT by Bakker and colleagues (PENGUIN trial), in a small group of 22 patients, showed that the endoscopic approach had lower levels of post-procedure pro-inflammatory marker (interleukin-6) compared with the surgical approach, along with a better composite clinical endpoint (which included new-onset organ failure, pancreatic fistula).[12] Subsequently, Brunschot and colleagues, also from the Dutch Pancreatitis Group, in their multicenter randomized control trial (RCT) (TENSION trial) of 98 patients of infected necrotising pancreatitis (INP), concluded that the endoscopic step-up approach was not superior to the surgical step-up approach in reducing the major complications or death (primary endpoint) at 6-month follow-up. However, the length of hospital stay and incidence of pancreatic fistulas were lower in the endoscopy group.[22] Bang and colleagues, in their RCT (MISER trial) on the same theme that included 66 patients, concluded that the endoscopic step-up approach when compared with minimally invasive surgery, had significantly reduced composite of major complications (including new-onset organ failure, new-onset systemic

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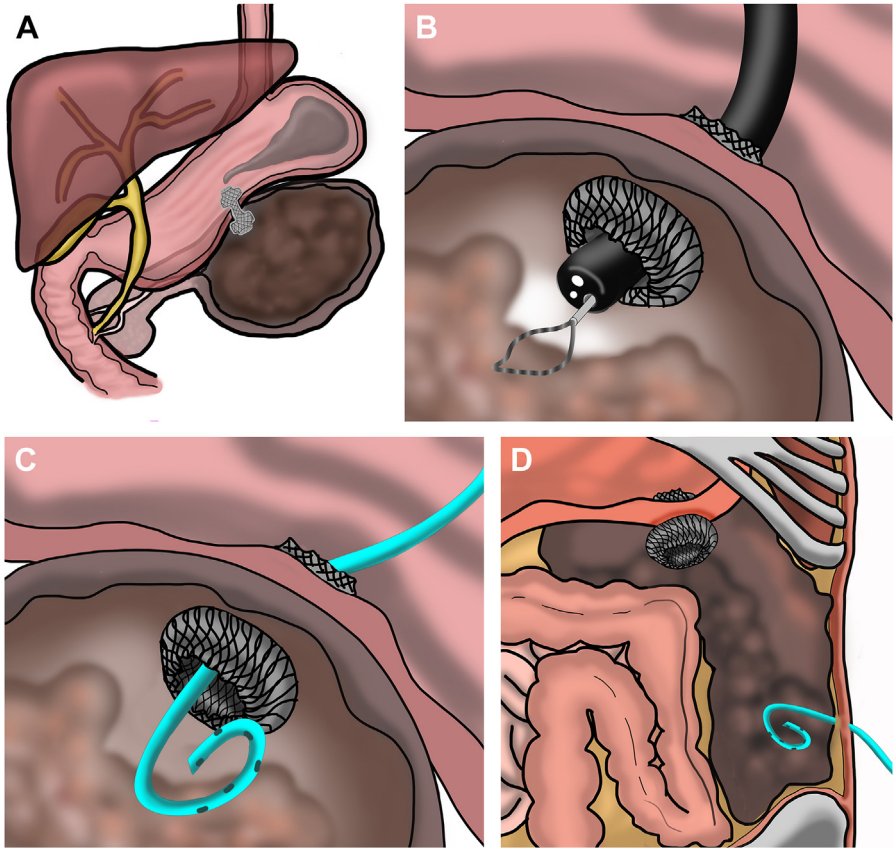

Fig. 2. Diagrammatic illustration showing the endoscopic step-up approach in managing pancreatic necrosis. EUS-guided drainage of WON using LAMS (*A*), DEN through LAMS (*B*), NCT placement through LAMS for irrigation of WON cavity (*C*), percutaneous catheter placement into WON for persistent symptoms after DEN (*D*). DEN, direct endoscopic necrosectomy; LAMS, lumen-apposing metal stent; NCT, naso-cystic tube; WON, walled-off necrosis.

dysfunction, pancreatic fistula), lowered costs, and improved quality of life assessment. The mortality did not differ in both groups.[23]

The meta-analyses of these 3 RCTs concluded that endoscopic intervention was associated with a lower frequency of new-onset organ failure, entero-cutaneous fistula, pancreatic fistula, and shorter hospital stay without any difference in mortality.[24] More recently, Onnekink and colleagues published the long-term follow-up of the *TENSION trial* (also called the *ExTENSION trial*) on clinical outcomes of 83 patients. At 7-year follow-up, the endoscopic step-up approach was not superior to the surgical step-up approach in reducing death or major complications; however, the endoscopic group had fewer pancreatico-cutaneous fistula and re-interventions.[25]

ENDOSCOPIC STEP-UP APPROACH

EUS-guided transmural drainage of periluminal WON is the standard of care. The availability of lumen-apposing metal stents (LAMSs) has revolutionized the efficiency of endoscopic drainage compared with plastic stents. After index drainage, the need

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Table 1
Randomized controlled trials comparing the endoscopic step-up approach with the surgical step-up approach

	Bakker et al, JAMA, 2012 (PENGUIN Trial)	**Van Brunschot et al, Lancet, 2018 (TENSION Trial)**	**Bang et al., Gastroenterology, 2019 (MISER Trial)**
Number of patients	Total—20 Endoscopy—10 Surgical—10	Total—98 Endoscopy—51 Surgical—47	Total—66 Endoscopy—34 Surgical—32
Primary endpoint *(Composite of major complications or death)*	20% vs 80% *(P = .03)*	43% vs 45% *(P = .88)*	11.8% vs 40.6% *(P = .007)*
Pancreatic fistulae	10% vs 70% *(P = .02)*	5% vs 32% *(P = .001)*	0% vs 28.1% *(P = .001)*
Length of hospital	45 d vs 36 d	53 d vs 69 d *(P = .01)*	16.5 d vs 23.3 d
Mortality	10% vs 40%	18% vs 13%	8.8% vs 6.6%

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for subsequent interventions in the step-up approach mainly depends on the patient's clinical condition. Moving up the ladder from simpler to more difficult procedures is practiced in a step-up approach (see Fig. 1).

STEP 1: EUS-GUIDED DRAINAGE OF PANCREATIC FLUID COLLECTION

The first step of the endoscopic step-up approach is EUS-guided drainage, which is performed using a therapeutic linear echoendoscope (see Fig. 2A). The standard sequential steps in EUS-guided drainage include—puncture of WON with 19G needle, aspiration of content for microbial analysis, passage of guidewire through the needle, coaxial passage of 6Fr cystotome for fistula creation, tract dilation with balloon catheter (12–15 mm for plastic stents; 4–6 mm for metal stents), and finally deployment of greater than 1 double pigtail stent or metals stent (LAMS, BFMS) into WON. Some experts prefer direct puncture of WON using a combined 6Fr/10Fr cystotome for initial puncture and fistula creation. Needle knife should be avoided during EUS-guided drainage of WON.

Cautery-enhanced LAMS (Hot Axios, Boston Scientific, Marlborough, MA; Hot Spaxus Taewoong Medical Co, Gimpo, Korea) have become the game changer in EUS-guided drainage of WON. These stents have a specialized delivery system that enables quicker placement of LAMS without requiring multiple drainage steps. Hot Axios requires only one operator, unlike Hot Spaxus, which requires two. Some endoscopists prefer to place an additional short double pigtail plastic stent through the LAMS to prevent complications, including bleeding and stent blockade by debris in WON. However, the impact of these plastic stents on the step-up approach has not been specifically evaluated. Vanek and colleagues in their RCT reported that the addition of a coaxial DPS within a LAMS was associated with a significantly lower global rate of adverse events and stent occlusion rate.[26]

Metal stents, unlike plastic stents, have to be removed after a finite indwell time of 3 to 4 weeks because of associated adverse events.[27] A major concern at this stage is the recurrence of PFC due to underlying disconnected pancreatic duct (DPD), a common observation after ANP after the removal of metal stents.[28] Our recent RCT comparing the frequency of recurrent PFC after replacing the transmural metal stent with or without plastic stent in patients with DPD showed no difference at 3 months. However, a beneficial trend was observed in plastic stent arm around 1-year period.[29] There is a technical challenge in replacing metal with plastic stents after the near-complete resolution of WON with frequent external migration. Wang and colleagues' study observed disconnected pancreatic duct syndrome (DPDS) is associated with an increased PFC recurrence after stent removal observed around 6 months.[30]

Plastic versus Metal Stents in Endoscopic Step-up Approach

Multiple plastic stents (MPSs) were earlier used for endoscopic drainage. However, due to their small caliber, the WON drainage can be inefficient, leading to delayed resolution and even complications. These challenges have been largely overcome with dedicated short fully covered large caliber metal stents. These include BFMS (Nagi, Niti-S, Taewoong Medical, Gyeonggi-do, South Korea); Plumber (M.I.Tech, Gyeonggi-do, Republic of Korea, etc.) and LAMS (Axios, Boston Scientific, Marlborough, MA; Spaxus, Niti-S, Taewoong Medical, Gyeonggi-do, South Korea) and their cautery enhanced versions. They provide more effective drainage of WON and facilitate DEN.[31] LAMS have a reduced chance of spontaneous migration compared with BFMS.

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Multiple comparative studies reported conflicting results. There are studies favoring metal stents[32,33] and those showing equal results.[34] Bang and colleagues reported non-superiority of LAMS over plastic stents for drainage of WON in their randomized trial.[35] Meta-analysis by Saunders and colleagues showed improved clinical success, fewer interventions, and adverse events with metal stents compared with plastic stents.[36] Recent RCT by Koduri and colleagues compared BFMSs versus plastic stents in WON drainage, reported that the BFMS group had a significantly lower number of re-interventions and reduced length of hospital stay compared with plastic stents.[37] The major advantage of LAMS over plastic stents in the management of WON drainage is the spontaneous efflux of liquid and even solid contents (loose debris) into the gastric lumen after index drainage.[15] Other benefits include tamponade preventing bleed, coverage preventing perforation, and access route for future DEN.

STEP 2: DIRECT ENDOSCOPIC NECROSECTOMY (DEN)

DEN, the next step in the endoscopic step-up approach, is defined as the "physical removal of necrotic or solid debris by passing forward-viewing endoscope either through the earlier placed LAMS or cysto-gastric (-enteric) fistulous tract" (see **Fig. 2**B). The purpose is to mechanically extract the remaining solid debris which can be the focus of persistent (source control) or new-onset infection. Debris within residual WON can be either "loose" or "adherent" or combination of both. The former, as the name suggests, are easy to dislodge and remove in small fragments. The 'adherent debris' is firmly attached to the wall of the remnant cavity and hence its removal is labor-intensive and associated with prolonged procedure time and risk of adverse events. DEN often requires passing the endoscope several times in and out of the necrotic cavity to drag out the pieces of debris, which can be either left in the gastric lumen or extracted out of the mouth.

A combination of endoscopic accessories are utilized for DEN, including braided snare, forceps, net, and baskets.[38] DEN requires airway intubation (often, to prevent aspiration), CO2 insufflation (to prevent air embolism), and water pump irrigation (to clean the field of view). DEN can pose a risk of bleeding due to hidden blood vessels deeper within the necrotic debris. The timing of DEN can be secondary or primary. The former is widely practiced and is part of the step-up approach, where the endoscope is passed via spontaneously expanded LAMS into WON. In "primary DEN," the LAMS is dilated with a balloon at index procedure to allow endoscope entry into WON along with aggressive irrigation.

Seifert and colleagues first described DEN in 2000 on 3 patients with infected WON, who were not fit enough for a surgical intervention. They inserted an endoscope directly into the cavity and used a stone-retrieval basket to debride the necrotic material.[39] In 2009, Gardner and colleagues reported higher rates of resolution with DEN (88%) when compared with conventional transmural endoscopic drainage using plastic stents (45%) for the treatment of WON.[40] Recent innovations in 'mechanical DEN' include over-the-scope grasper (OTSG, OVESCO AG, Tübingen) and powered endoscopic debridement (PED) device (EndoRotor System, Interscope Inc, MA). PED is a through-the-scope device with simultaneous cutting and suction action to remove necrotic debris, thus avoiding frequent removal of the endoscope for clearing solid debris.[41] These novel necrosectomy devices currently appear promising in small series.

Naso-Cystic Tube (NCT) Irrigation

Some endoscopists favor placing a naso-cystic tube (NCT) to irrigate the WON cavity with normal saline to clean the infected material and also loosen the adherent debris

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(see Fig. 2C). Placement of NCT can be primary (at the index drainage) or secondary (at the time of DEN). Some operators prefer to place NCT as an additional step between index drainage and DEN.[15] NCT use has been described both with the use of plastic and LAMS. Puri and colleagues reported the use of NCT at index drainage with a high success rate, in collections with significant debris.[42] Siddiqui and colleagues also showed that PFC with viscous solid debris-laden fluid drained by stents and NCTs had a 3-times higher success rate than those with drainage by stents alone.[43] Although available evidence is limited, NCT irrigation can be considered in large complicated WON with thick necrotic debris and concomitant sepsis is recommended.[44]

Chemical Necrosectomy

Chemical necrosectomy, as the name suggests, uses chemicals to loosen up thick adherent debris in WON for subsequent ease of removal. Such chemicals can be used to irrigate the WON cavity, either directly through an endoscope or NCT. The most commonly used chemical is *Hydrogen peroxide (H_2O_2)* used as a fresh 3% solution that acts by its rapid decomposition into water and nascent oxygen in the presence of enzyme catalase found in most living cells. As a result of its effervescing action, it helps in the chemical debridement of necrotic tissue which allows dislodging of the debris adherent to the wall.[45] H_20_2 also irritates the wall of WON, leading to the formation of granulation tissue and fibrosis.[46] H_2O_2-assisted necrosectomy is both effective (high technical and clinical success rates) and safe as reported in a recent meta-analysis by Garg and colleagues of 15 studies, including 454 patients along with shorter time to resolution of WON.[47] NCT irrigation through the metal stent of the WON cavity in symptomatic patients after index drainage reduced the need for DEN and improved the resolution. *Streptokinase* is another chemical agent which acts by fibrinolysis and dissolution of necrosum.[48]

STEP 3: ADDITIONAL SESSIONS OF DIRECT ENDOSCOPIC NECROSECTOMY (DEN)

Symptomatic patients with WON containing significant debris usually require multiple sessions of DEN, which increases their anesthesia risk, and associated complications with prolonged hospital stay and cost. The subsequent sessions of DEN are generally scheduled 2 to 3 days apart. Endoscopic visualization of healthy granulation tissue without large chunks of necrosis within WON suggests the completion of DEN and may not require further intervention. Small residual superficial adherent debris need not be aggressively removed. Bang and colleagues (2014) reported that using an algorithmic step-up approach resulted in successful outcomes in 91% of patients with WON, using MPS/NCT and multiple transluminal gateway techniques based on the size and extent of WON.[49] Rana and colleagues (2014), using plastic stents in drainage of WON, reported that large collections and those with significant amounts of solid debris required DEN or surgical necrosectomy.[50] The same authors later published (2017) a series of 86 patients, whose initial drainage using MPS was stepped-up in those with persistent symptoms or non-responders by exchanging plastic stents with FCSEMS and performing DEN, thus avoiding surgery.[15]

Recently, Chandrasekhara and colleagues (2021), using LAMS in a large cohort of 136 patients, concluded that large WON ($\geq$10 cm), greater than or equal to 30% solid necrosis or para-colic extension are more likely to require a step-up approach and should be considered for early endoscopic re-intervention.[51] Seicean and colleagues (2020) reported that 3 or more sessions of DEN were required when estimated debris was greater than 50% in WON, irrespective of its size or location.[52] Lakhtakia and

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colleagues highlighted the "endoscopic step-up approach" in a large cohort of 205 patients having symptomatic WON and drained with BFMS. About three-fourths of patients achieved clinical success with index drainage, and the remaining 25% of symptomatic patients were considered for a step-up approach. In the first step, any loose debris occluding the lumen of BFMS was declogged using endoscopic devices (snare or forceps). Non-responders were considered for second step, that is, the placement of an NCT in residual WON through the BFMS. Each irrigation session was done at 8 hourly intervals using 20 mL 3% hydrogen peroxide, followed 10 minutes later by 100 mL saline solution. Patients still not responding underwent third step (DEN) using a gastroscope with a water jet passed through the BFMS. Using this strategy, each step provided incremental clinical benefit, leading to overall success of 96.5%.[15] All these publications emphasize the importance of endoscopic step-up approach in the management of patients with WON.

STEP 4: PER-CUTANEOUS DRAINAGE (PCD) OR SURGERY

Patients who did not improve after multiple sessions of DEN require additional routes/methods of drainage, which can be percutaneous drainage and/or surgery (see **Fig. 2**D). Bakker and colleagues reported that 20% of patients in the DEN group required minimally invasive surgical re-interventions (VARD).[12] Recently, Zhai and colleagues (2022) reported that 18 out of 101 patients with WON undergoing DEN required additional non-endoscopic interventions (PCD or surgery). Increasing APACHE-II score, more than 50% necrosis, and paracolic gutter extension were negatively associated with the success of DEN.[53] In some select groups of patients having large WON with extension to paracolic gutters, combined modality of drainage with percutaneous drainage immediately followed by endoscopic drainage. Ross and colleagues reported successful management of 15 patients with combined drainage with less procedure-related morbidity.[54] Nemoto and colleagues reported the outcomes of patients with WON when the endoscopic step-up approach was adopted. One-third of patients required combined drainage, and 4% with persistent symptoms with the endoscopic step-up approach required surgery.[55]

STEP-UP APPROACH VERSUS PRIMARY DEN

The optimal timing to perform DEN is still a matter of debate. And definite recommendations are lacking. Secondary DEN, as part of the step-up approach, is preferred by most. Metal stent rapidly allows the liquid content to drain out at index drainage. LAMS, after placement, expand gradually over a few days, thus creating a more mature tract which allows solid debris to drain out spontaneously through the LAMS if it is loose and small, thereby avoiding the need for future DEN in a significant proportion of patients. Lakhtakia and colleagues reported that 75% of patients with WON improve following drainage with metallic stent alone.[15] Guo and colleagues, in a multicenter survey among experts, reported that 86.4% of respondents would prefer a step-up approach.[56] Pawa and colleagues, in their retrospective analysis using LAMS for WON, concluded that the step-up approach group (n = 37) had a shorter hospital stay and fewer sessions of necrosectomy than primary DEN (n = 43).[57]

Primary DEN is based on the premise that early debridement and extraction of necrotic debris leads to rapid clinical improvement. This approach may require fewer reinterventions, thus reducing hospital stay and cost. In a retrospective analysis, Yan and colleagues, comparing primary DEN (n = 69) versus step-up approach (n = 202) using 10 or 15 mm LAMS for WON, reported no difference in clinical success, technical success, and overall adverse events. However, the number of endoscopic

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sessions for resolution of WON was significantly lower in the primary DEN group, with stent dislodgment observed at 4.3%.[58] In a recent prospective multicenter RCT (DESTIN trial), Bang and colleagues compared primary necrosectomy versus a step-up approach in patients with infected WON using 20-mm LAMS. They reported a significantly lower number of reinterventions in primary DEN. Other outcome measures (mortality, procedure-related adverse events, overall disease-related adverse events) remained similar.[59]

However, the strategy of primary DEN poses several challenges. It requires rapid stent dilation with the balloon, which carries a risk of bleeding and also stent dislodgement with its inherent risk of perforation due to an immature tract. The rapidly exiting turbid fluid may interfere with the visualization of debris and its removal. Also, loose debris can be removed, however firm, large, and adherent debris require aggressive attempts for removal, which may be ineffective or can have serious consequences, such as bleeding. In sick patients, prolonged procedure under sedation carries additional risk of serious outcomes.[60] With the advent of LAMS and technological advances in its deployment, large prospective RCTs are needed to standardize the criteria for early or delayed DEN for better outcomes in the management of symptomatic or infected WON. Most experts recommend an interval of 2 to 3 days between stent placement and first session of DEN, based on the clinical condition of the patient, size of the WON, amount of solid debris, and degree of adhesion to the adjacent wall.

SUMMARY

The endoscopic step-up approach in the management of necrotizing pancreatitis involves sequential steps of intervention at different time points in the clinical course of the disease. This widely popular strategy involves index drainage of WON by EUS. LAMS are preferred over plastic stents for safe and effective drainage due to their wide caliber. Additionally, LAMS can provide a conduit for subsequent endoscopic interventions. Successive steps in the endoscopic step-up approach include DEN and/or irrigation using NCT in symptomatic patients, primarily based on necrotic debris characteristics. The recently proposed primary DEN is based on the premise that it requires fewer reinterventions, associated with reduced hospital stay and cost. A judicious selection of strategy is warranted as primary DEN poses several challenges. Minimally invasive percutaneous radiological and/or surgical drainage are considered when endoscopic drainage is not feasible or successful.

CLINICS CARE POINTS

- Early endoscopic drainage of PFC (<4 weeks), having immature or partially matured wall, may be considered in select patients (ongoing sepsis, persistent organ failure).
- Large calibre metal stents are preferred in index drainage of WON having significant debris.
- Conceptually, endoscopic step-up approach (similar to surgical step-up approach) in management of pancreatic WON is associated with reduced major complications (perforation, bleeding).
- Endoscopic step-up approach avoids unnecessary interventions, especially DEN, in patients who are clinically recovering.
- The use of 'Primary DEN' is controversial and requires judicious selection of subject. More studies are needed to identify the ideal candidates.

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DISCLOSURE

None.

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