Gastrointestinal Intervention

journal homepage: www.gi-intervention.org

Review Article

Is endoscopic necrosectomy the way to go?

James Wei-quan Li, Tiing Leong Ang*

ABSTRACT

Pancreatic necrosis with the formation of walled-off collections is a known complication of severe acute pancreatitis. Infected necrotic pancreatic collections are associated with a high mortality rate. Open necrosectomy and debridement with closed drainage has traditionally been the gold standard for treatment of infected pancreatic necrosis, but carries a high risk of perioperative complications. Direct endoscopic necrosectomy has emerged as a safe and effective modality of treatment for this condition. Careful patient selection and gentle meticulous debridement is important to optimize clinical success. Bleeding is the commonest associated complication with the procedure but most cases can be managed conservatively. Air embolism, although rare, is potentially fatal. The use of fully covered large diameter lumen apposing self-expandable metal stents has further simplified the procedure. These stents optimize drainage, and facilitate endoscopic necrosectomy because repeat insertion of the endoscope into the necrotic cavity can be easily achieved.

Copyright © 2016, Society of Gastrointestinal Intervention. All rights reserved.

Keywords: Acute necrotising pancreatitis; Drainage; Endosonography

Introduction

Approximately 20% of patients with acute pancreatitis are classified as having severe disease, as defined by the presence of persistent organ failure or local complications such as necrosis.¹ Moreover, it is estimated that 33% of patients who have necrotizing pancreatitis go on to develop infected necrosis.^{2,3} Mortality in infected pancreatic necrosis is higher than that of sterile necrosis (approximately 30%–39% vs 12%–15%, respectively)^{1,4} and invasive management of the latter is usually reserved for persistent abdominal pain or if the patient remains symptomatic.¹

Walled-off pancreatic fluid collections (PFC) often occur in the setting of acute pancreatitis, and consist of pseudocysts (PC) and walled-off pancreatic necrosis (WOPN). These typically develop at least four weeks after the acute episode of pancreatitis. WOPN is differentiated from PC by the presence of solid necrotic debris.

Asymptomatic WOPN does not warrant intervention regardless of size as they may resolve spontaneously with time. However, infection of or obstruction by WOPN are indications for therapy as they may impact the clinical course of the disease.⁵ Open necrosectomy for debridement of non-viable and infected pancreatic tissue with closed drainage has traditionally been the gold standard for treatment of pancreatic necrosis.⁶ However,

open surgical debridement is a morbid procedure with perioperative risks, prolonged recovery, need for repeat intervention, and long term complications such as external fistulas, abdominal hernias and pancreatic endocrine and exocrine insufficiency. In addition mortality rates ranged from 11% to 27% depending on the series studied.^{7,8} Over the past two decades or so, there has been a paradigm shift in the management of infected WOPN, with an emphasis on delayed intervention and a step up approach utilizing minimally invasive techniques.⁹ This includes minimally invasive surgical techniques such as video-assisted retroperitoneal debridement (VARD)^{10,11} and laparoscopic debridement.^{12,13} However, complication rates of VARD ranged from 33% to 54%^{11,14} with a mortality of 8% in one series.¹¹ Laparoscopic debridement had little uptake due to the need for a transperitoneal route with a risk of dissemination of infection into the peritoneal cavity. Percutaneous drainage is a non-surgical option but is limited by the inability to clear solid debris, problems with fistula formation, and need for surgical rescue with rates ranging from 53% to 62%.¹⁵

Endoscopic drainage and lavage of WOPN was first described by Baron et al¹⁶ in a series of 11 patients, 9 of whom achieved complete resolution non-operatively. In 2000, the technique of direct endoscopic necrosectomy (DEN) was first described by Seifert et al¹⁷ which consisted of direct entry of an endoscope into the

Department of Gastroenterology and Hepatology, Changi General Hospital, Singapore

Received March 2, 2016; Revised March 31, 2016; Accepted April 8, 2016

* Corresponding author. Department of Gastroenterology and Hepatology, Changi General Hospital, 2 Simei Street 3, Singapore 529889.

E-mail address: tiing_leong_ang@cgh.com.sg (T.L. Ang).pISSN 2213-1795 eISSN 2213-1809 <https://doi.org/10.18528/gii160010>© This is an open-access article distributed under the terms of the Creative Commons Attribution Non-Commercial License (<http://creativecommons.org/licenses/by-nc/3.0/>) which permits unrestricted noncommercial use, distribution, and reproduction in any medium, provided the original work is properly cited.

necrotic cavity and debridement with endoscopic accessories. In 2005 Seewald et al¹⁸ described their experience of using an aggressive endoscopic approach incorporating DEN for treatment of pancreatic necrosis and abscess, generating significant clinical interest in this technique. Alternative methods for obtaining access for drainage and combined modality treatment have also been reported.^{5,19}

This review aims to evaluate the current role of DEN in the treatment of symptomatic WOPN, with an emphasis on DEN in the treatment of infected WOPN.

Literature Search

A rapid literature search strategy was employed for all English language literature published from 2000 (year when the technique of DEN was first published) to December 2015. The search was conducted on the electronic databases PUBMED and EMBASE. The search strategy included the keywords 'endoscopic necrosectomy', 'endoscopic drainage', 'pancreatic necrosis', 'organized pancreatic necrosis', and 'walled-off pancreatic necrosis (WOPN)'. The search strategy was adjusted according to the different requirements for each database.

Technical Aspects of Direct Endoscopic Necrosectomy

The endoscopic approach to establishing transluminal access to the abdominal cavity without the need for surgical incision has been gaining strong interest over almost two decades, with "natural orifice transluminal endoscopic surgery (NOTES)" being explored for a variety of intra-abdominal procedures.²⁰ DEN conceptually represents a clinical application of these transluminal endoscopic interventions.

The key indication is infected WOPN not responding to conservative treatment with appropriate antibiotics. A prerequisite for DEN is the presence of a well-defined mature wall; otherwise any endoscopic access will result in free perforation. This usually requires a time frame of 4–6 weeks from onset of the severe necrotizing pancreatitis. The fluid collection must be accessible endoscopically, such as being located within 1 cm of the duodenal or gastric walls; para-colic collections cannot be accessed and would require adjunctive methods such percutaneous drainage. Coagulopathy, if present, should be corrected. The absence of a mature wall, presence of aneurysmal vessels within the collection, uncorrectable coagulopathy and a predominantly solid, rather

than liquid collection, are contraindications for DEN.

This technique broadly consists of two steps,²¹ namely initial access of the WOPN, which may be performed with or without endoscopic ultrasound (EUS) guidance, and endoscopic necrosectomy if there is a lack of response following transluminal drainage. Both steps are performed in the endoscopy centre using monitored sedation, and general anesthesia is usually not required. EUS-guided access is now the preferred technique of achieving access because it provides real time ultrasonic guidance throughout the procedure, and can be successfully performed in cases of WOPN with and without luminal bulging. Randomized controlled studies performed in context of PC drainage showed that EUS-guidance had significantly higher success rates and could also successfully treat cases that non-EUS guided drainage was unsuccessful, due to its ability to visualize non-bulging PC.^{22,23} It involves utilizing a linear echoendoscope to visualize the WOPN (Fig. 1) and to puncture it with a 19 G needle. This is followed by insertion of guide-wires and dilatation of the puncture tract with co-axial/balloon and cautery devices. Traditionally drainage is then achieved and access maintained through the deployment of double pig-tail plastic stents. In recent years, customized large diameter lumen apposing fully covered self-expandable metallic stents (FCSEMS) have been developed. In contrast to enteral FCSEMS that were previously used, these customized FCSEMS were designed specifically for drainage of PFC and to minimize the risk of migration.²⁴ The lumen-apposing stent (AXIOS™; Boston Scientific, Marlborough, MA, USA) is a fully covered, 10 or 15 mm diameter, nitinol, braided stent with bilateral anchor flanges. When fully expanded, the flange diameter is twice that of the "saddle" section and is designed to hold tissue layers in apposition.²⁵ The Nagi™ stent (TaeWoong Medical Co., Seoul, Korea) is another specially designed FCSEMS with a 10, 12, or 16 mm diameter in the center and 20 mm ends which can reduce the risk of migration.²⁶ The advantages of FCSEMS are their larger diameter (15–16 mm compared to 2.8–3.3 mm [7–10 Fr] for plastic stents) and ability to maintain patency of the dilated tract (Fig. 2). This allows for ease of repeat entry into the necrotic cavity for endoscopic debridement and may even decrease the need for intervention due to more effective drainage.

DEN is carried out if there is a lack of response after conserva-

Fig. 1. Endoscopic ultrasound appearance of walled off pancreatic necrosis.

Fig. 2. Endoscopic view after insertion of Nagi™ fully covered self-expandable metallic stent.

Fig. 3. Endoscopic view of the interior of infected walled off pancreatic necrosis.

Fig. 5. Endoscopic view of the interior of infected walled off pancreatic necrosis after endoscopic necrosectomy.

Fig. 4. Necrotic material removed by Dormia basket.

tive treatment and drainage of the WOPN. It is performed using a gastroscope and preferably with carbon dioxide insufflation. If a large diameter FCSEMS had been inserted, the endoscope can be easily inserted into the WOPN (Fig. 3). If plastic stents had been used, then further balloon dilatation of the fistula opening to 15 to 18 mm has to be performed in order to allow endoscope passage; in fact, in between DEN sessions, there is a tendency for the opening to narrow, and thus repeat balloon dilatation may be needed. The first step in DEN is to irrigate and aspirate the smaller loose debris. Direct irrigation will help to loosen solid material partially adherent to the wall. Accessories such as Dormia basket and retrieval nets are used to gently remove the solid material within the cavity which is deposited within the gastric lumen (Fig. 4). It is crucial to perform gentle debridement, and not to forcibly pull apart solid material adherent to the wall of the WOPN, as this may lead to severe bleeding and perforation. Although it may be ideal to remove all solid material until a pink granulating wall remains (Fig. 5), it is not necessary in all instances.

In fact the use of large diameter FCSEMS may even reduce the need for DEN. When performed, DEN may need to be staged over a few sessions if the amount of solid material is excessive. By performing repeat sessions, solid debris initially adherent to the wall may actually loosen over time and can then be debrided.

Clinical Outcome

A vast majority of published literature to date with regards to DEN comprise of studies which are retrospective in nature, with most early studies following the first report of DEN¹⁷ derived from case series. Seewald et al¹⁸ described a retrospective case series of 13 patients unfit to undergo surgery, with all patients having technical success thus avoiding surgery as the initial treatment; 12 out of 13 patients achieved complete resolution of infected pancreatic necrosis and abscesses with endotherapy alone. In the one patient requiring surgery, it was due to extension of the abscess into the right para-colic gutter, which was inaccessible by endoscopy.

The technical and clinical success rates of DEN were similar in several studies that followed with clinical resolution reported in well over 90% of patients in each of these studies.²⁷⁻²⁹ In addition, none of these earlier studies reported any mortality for DEN. With regards to other complications, bleeding was most commonly described, although majority of cases could be managed conservatively with only one of these early studies reporting uncontrollable hemorrhage during balloon dilatation requiring surgery.²⁸ It should be noted, however, that percutaneous drainage was required for a few patients in addition to DEN where the cavities were inaccessible endoscopically. Recurrence and/or persistence of the necrotic cavity were also one of the issues raised in the early studies. For example, 2 out of the 12 successfully treated patients reported by Seewald et al¹⁸ had recurrent PC from disconnected pancreatic duct syndrome (DPDS). A mean of 4 endoscopic sessions (range, 1-10) was required in the retrospective study by Charnley et al,²⁷ with necrosis successfully treated in 12 out of 13 patients. Escourrou et al²⁹ reported recurrence of infection and/or persistence of a necrotic cavity in a total of 5 patients, with the mean number of DEN sessions performed per patient being 1.8 (range, 1-3) and the mean duration of each session 3.5 hours.

(range, 2.5–4 hours). In this study, there were no reports of recurrence of infection or surgery after an average duration of 19.5 months following adequate endoscopic treatment.

These encouraging results begged the question whether DEN offered an improvement in outcomes compared to endoscopic transmural drainage alone, as both procedures could avoid the need for surgery, and whether there would be a difference in number of procedures required and complication rates with DEN as an additional procedure to transluminal drainage. A retrospective comparative study investigating 25 patients undergoing DEN and 20 patients undergoing standard endoscopic drainage for WOPN reported successful resolution in 88% of the DEN group compared to 45% in the standard drainage group ($P < 0.01$).³⁰ DEN was not associated with an increase in complication rates, which were limited to mild peri-procedural bleeding at similar rates in both groups. There was also no change in the total number of procedures required. Although the number of patients in each group was small, the study still showed a significant difference in the need for surgical drainage (4% vs 30%, $P = 0.034$) and percutaneous drainage (0% vs 20%) after DEN and standard drainage respectively.

The GEPARD study was the first large multicenter series describing the long-term efficacy of DEN over a median follow-up period of 2 years.³¹ Ninety-three patients from six tertiary centers who underwent DEN between 1999 to 2005 were studied, and it is important to note that all patients included were seriously ill and receiving more than one week of intravenous antibiotics at the time of DEN, with more than half (54 out of 93) having had prior percutaneous and/or transgastric drainage with non-resolution of their necrotic collections. Clinical success was achieved in 81% of patients, with a complication and mortality rate of 26% and 7.5% respectively. The commonest complication was bleeding ($n = 13$), with 2 cases of severe hemorrhage where one patient required surgery and the other died before surgery could be performed. Another reported complication was perforation of necrosis into the abdominal cavity ($n = 5$; one fatal due to the patient's underlying inoperable state, 2 requiring surgery and 2 managed conservatively). There were also 2 cases of air embolism, one resulting in fatal pulmonary embolism and the other causing a stroke due to a patent foramen ovale. Two cases of fistula formation were also reported. The remaining mortalities were due to sepsis and following surgery as a result of multiple organ failure. A mean of 6.2 sessions of DEN were required per patient (range, 1–35), with 18% of patients requiring only one session of DEN. Of the remaining patients in the GEPARD study, clinical success was maintained in the majority of patients who underwent DEN.

In the largest multicenter retrospective chart review to date, Gardner et al³² investigated the primary outcome of resolution of necrotic collections without operative or percutaneous drainage in 104 patients with acute pancreatitis and WOPN from six tertiary US centers. The median length of follow-up was 17.5 months (range, 1–53 months). The overall success rate of DEN in this series was 91.3%, with a complication rate of 32% and mortality rate of 5.8%. Similar to the GEPARD study, the commonest complication was bleeding, with 19 patients having bleeding that resolved with endoscopic intervention during the initial sessions of DEN while 2 patients had severe hemorrhage that could not be controlled endoscopically (one required embolization of a branch of the inferior pancreaticoduodenal artery by interventional radiology and the other patient underwent surgery). Retrogastric perforation occurred during the initial creation of the fistula tract or during repeat tract dilatation in 2 patients, and another 3 cases of pneumoperitoneum were documented on cross-sectional imaging

in patients who reported abdominal pain after initial fistula tract creation. These patients were managed non-operatively and were discharged. The overall complication rate in this series was 14%. Of the 6 mortalities reported, 5 patients died during the follow-up period before resolution and one patient died peri-procedurally. This was a 67-year-old woman who became suddenly hypotensive towards the end of the DEN session after EUS-guided transgastric access was obtained. The clinical suspicion was that of an air embolism, although no autopsy was performed to confirm this. The median number of DEN sessions were 2 (range, 1–13), which differed from the GEPARD study and will be discussed in the next session. The mean duration of the initial procedure was 87 minutes (range, 25–179 minutes), and that of all procedures was 69 minutes, with EUS guidance being used in 45% of cases. The time to cavity resolution after initial intervention was 4.1 months (range, 3.5–4.6 months). Recurrence of fluid collections was also described in 6% of patients, and this will again be touched on in the section on discussion.

Another large retrospective study looked at the immediate and long-term results of endoscopic drainage and DEN in 80 patients with symptomatic PFC.³³ Initial technical success was reported in 97.5%, and clinical resolution was achieved endoscopically in 83.8%. Bleeding was the most common complication (12 out of 80), perforation (7 out of 80, with 4 requiring surgery), and air embolism in one patient. A further 9 patients required surgery for treatment of the fluid collections either due to its location in endoscopically inaccessible areas or inadequate drainage. The long-term success of endoscopic treatment was 72.5%, with surgery required in 4 patients over a mean follow-up of 31 months due to underlying pancreatic duct abnormalities. It should be noted, however, that not all patients in this study had infected WOPN as an indication for endoscopic therapy (24 out of 80 had infected PC with solid debris), and DEN was carried out in 49 patients in this series, the rest of whom had only transluminal drainage as endoscopic therapy.

Another retrospective review of 57 patients across 16 Japanese institutions to evaluate the efficacy and safety of DEN showed that 75% of patients experienced successful resolution after a median of 5 sessions of DEN and 21 days of treatment. The complication rate reported was 33%. Six patients died in this series, 2 from multiple organ failure, one air embolism, one hemorrhage from a Mallory Weiss tear and one from an unknown cause. Recurrent PC formation occurred in 3 out of the 43 patients after clinical resolution during a median follow-up period of 27 months.³⁴

The consistently high technical and clinical success rates of DEN have spurred interest in how it performs against surgery, which is in general a morbid procedure with high complication rates. A randomized, controlled, assessor-blinded clinical trial held across 3 academic hospitals and 1 regional teaching hospital in the Netherlands compared DEN against surgical necrosectomy.³⁵ It is important to note that the primary endpoint was a reduction in pro-inflammatory response between the 2 groups as measured by the cytokine interleukin-6 (IL-6) levels. This proved to be significant, with IL-6 levels increasing after surgery and decreasing after DEN ($P = 0.004$), and was attributed to avoiding the need for surgical dissection to reach the retroperitoneum or omental sac, as well as the fact that general anesthesia used in surgery is known to induce or prolong systemic inflammation in critically ill patients. Although the primary endpoint for efficacy was a surrogate measure and not clinical resolution, the study nevertheless offered a glimpse into the differences in complication rates between the 2 procedures when compared in a prospective trial. The compos-

ite clinical endpoint of death or major complications (defined as new onset multiple organ failure, bleeding requiring intervention, enterocutaneous fistula, perforation of a visceral organ requiring intervention, and pancreatic fistula) was significantly lower in the group undergoing DEN compared to surgery (20% vs 80%, $P = 0.03$). In particular, there was decreased incidence of multiple organ failure (0% vs 50%, $P = 0.03$) and pancreatic fistulas (10% vs 70%, $P = 0.02$). No patients in the DEN group required pancreatic enzymes at 6 months follow-up, while 50% in the surgery group required pancreatic enzyme replacement ($P = 0.04$). There was one death in the DEN group in this study, compared to 4 in the surgical arm. A median of 3 sessions of DEN were reported in the group receiving endoscopic therapy.

A two-center retrospective comparison of 32 patients comparing 21 surgical necrosectomy cases in one centre with 11 DEN cases in another also showed an increased risk of pancreatic fistula formation following surgical necrosectomy compared to DEN (86% vs 27%, $P = 0.002$).³⁶ This was also associated with a longer intensive care unit (84 days vs 4 days, $P = 0.008$) and hospital (58 days vs 15 days, $P = 0.005$) stay, although long term complications did not differ between groups. This is in keeping with other studies which show a low complication rate with DEN in addition to a high clinical and technical success rate.³⁷

Discussion

The number of cases of DEN reported in the literature has been increasing steadily over the last two decades. The technical and clinical success rates have been consistently high in most case series. However, it is also important to recognize the limitations and risks of DEN. For instance, surgery and percutaneous drainage were required in a few cases where the infected collections were inaccessible endoscopically or when endoscopic therapy proved inadequate to achieve or maintain clinical resolution of the infected WOPN despite initial technical success.^{17,27-31} Many of the studies also reported recurrence and/or persistence of the necrotic cavity or cyst formation on follow-up.^{17,31-34} In cases of pancreatic duct disruption or DPDS the underlying pancreatic duct abnormalities must be addressed to prevent recurrent PFC.

Bleeding is the most commonly reported complication of DEN, but it is assuring that most cases encountered could be controlled endoscopically. It occurs mainly during the necrosectomy process, and not during the initial EUS-guided puncture and fistula creation. It is interesting to note that only the larger case series from multicenter studies reported severe bleeding requiring surgery or angiographic embolization, and in a small number of cases, resulting in mortality.^{31,32,34} This indicates that even though the risk of clinically life-threatening bleeding is currently low from the literature, the numbers may rise as individual centers perform DEN in increasing numbers. Retroperitoneal perforation may occur with DEN^{28,31-33} and conservative treatment may be feasible in selected patients. The reported mortality is much lower than bleeding, with only one mortality in the GEPARD study,³¹ albeit in a patient who had an underlying inoperable state. Thus it is crucial that centers performing DEN should have multi-disciplinary support from both interventional radiologists and pancreaticobiliary surgeons.

Air embolism is another feared complication with DEN,^{31,32,34} accounting for mortality in certain series.^{31,34} This has prompted the use of carbon dioxide insufflation instead of room air in many centers to mitigate this risk. Aggravation of sepsis and multiple organ failure, complications which may not have a direct link to the procedure of DEN, are also reported in many studies, empha-

sizing that the role of DEN in infected WOPN is to control the source of infection. A holistic treatment strategy with goal-directed therapy that encompass medical supportive therapy, systemic antibiotics and intervention, is crucial to achieve good outcomes for patients with sepsis from infected WOPN.³⁸

Another area which must not be overlooked is patient selection. Although not explored explicitly or in detail from the studies mentioned in this review, it is intuitive that the clinical condition of the patient undergoing DEN has a bearing on the complexity, safety and efficacy of the procedure, and this can be somewhat inferred from the results of the published literature. For example, the GEPARD study³¹ reported clinical success in 81% of patients compared to an overall success rate of 91.3% reported by Gardner et al.³² Moreover, the mean number of sessions of DEN per patient was 6.2 (range, 1-35) and 2.5 (range, 1-13) respectively. When the 18% of patients who had only one session of DEN were removed from the calculation, the mean number of sessions for those requiring repeat DEN was 7.5. This could be explained by the patients included in each study, as the GEPARD study patients were seriously ill with indications for DEN being infected necrosis in patients with constant and intermittent fever, worsening inflammatory markers and deteriorating clinical condition. Moreover, these patients were already receiving intravenous antibiotics for more than one week with at least half of the study population having undergone either transluminal or percutaneous drainage with no improvement.

This can be interpreted both ways. Firstly, careful selection of patients, as with most other procedures, will most likely result in higher clinical success rates with DEN with a need for fewer sessions to achieve clinical resolution of the infected necrotic cavity. Conversely, the GEPARD study highlights that DEN is a viable and efficacious modality of treatment for ill patients whose baseline condition at the time of intervention may preclude them from surgery and for whom other alternatives such as percutaneous drainage have proven ineffective, although a larger number of sessions of DEN may be required to achieve the desired outcome.

While standard double pigtail plastic stents may be adequate for treatment of PC and fully liquefied abscess collections and indeed, may be preferred in view of their lower costs, they may not be sufficient for effective drainage and to maintain access to the necrotic cavity for DEN in the context of infected WOPN. Data is emerging for the utility of FCSEMS in this context.²⁴ Lee et al³⁹ recently demonstrated in a prospective randomized study that FCSEMS could reduce the median procedure time for transmural drainage of PFC under EUS guidance compared to plastic stents (15.0 minutes vs 29.5 minutes, $P < 0.01$). There was also a statistically significant decrease in the number of stents and guide-wires used, pointing indirectly to a more simplified procedure using FCSEMS. A retrospective single centre comparative study showed no statistically significant differences in technical and clinical success rates, as well as adverse events between FCSEMS and plastic stents.⁴⁰ However, there was again a significantly shorter mean procedure time for EUS-guided drainage (28.8 minutes vs 42.6 minutes, $P < 0.001$) and shorter mean procedure time for re-intervention (34.9 minutes vs 41.8 minutes, $P < 0.001$). The total cost of the procedures were similar in both the FCSEMS and plastic stent groups (\$6,274 vs \$5,352, $P = 0.25$).

Lastly, it should also be noted that most of the evidence to date on the topic of DEN is derived from tertiary and academic medical centers, which may also account for their high technical and clinical success rates. The learning curve and quality indicators for DEN have not been formally established. DEN should only be performed by skilled and experienced therapeutic endoscopists

who have a strong foundation in therapeutic endoscopic retrograde cholangiopancreatography and interventional EUS.

Conclusion

DEN has been shown to be an effective and safe minimally invasive option in the treatment of symptomatic WOPN in carefully selected patients. However, these challenging cases should ideally be managed in a multi-disciplinary setting, involving both the interventional radiologists and pancreaticobiliary surgeons, since complementary drainage procedures in context of inaccessible sites, and salvage treatment in context of major complications or inadequate drainage may occur. The greater use of large diameter FCSEMS may potentially reduce the need for aggressive DEN, but will certainly facilitate the process DEN when it is indicated. It is the opinion of the authors that DEN is indeed the way to go in the future.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

References

1. Banks PA, Freeman ML; Practice Parameters Committee of the American College of Gastroenterology. Practice guidelines in acute pancreatitis. *Am J Gastroenterol*. 2006;101:2379–400.
2. de Beaux AC, Palmer KR, Carter DC. Factors influencing morbidity and mortality in acute pancreatitis; an analysis of 279 cases. *Gut*. 1995;37:121–6.
3. Isenmann R, Rau B, Beger HG. Bacterial infection and extent of necrosis are determinants of organ failure in patients with acute necrotizing pancreatitis. *Br J Surg*. 1999;86:1020–4.
4. Beger HG, Rau B, Mayer J, Pralle U. Natural course of acute pancreatitis. *World J Surg*. 1997;21:130–5.
5. Gluck M, Ross A, Irani S, Lin O, Hauptmann E, Siegal J, et al. Endoscopic and percutaneous drainage of symptomatic walled-off pancreatic necrosis reduces hospital stay and radiographic resources. *Clin Gastroenterol Hepatol*. 2010;8:1083–8.
6. Traverso LW, Kozarek RA. Pancreatic necrosectomy: definitions and technique. *J Gastrointest Surg*. 2005;9:436–9.
7. Fernández-del Castillo C, Rattner DW, Makary MA, Mostafavi A, McGrath D, Warshaw AL. Débridement and closed packing for the treatment of necrotizing pancreatitis. *Ann Surg*. 1998;228:676–84.
8. Rau B, Bothe A, Beger HG. Surgical treatment of necrotizing pancreatitis by necrosectomy and closed lavage: changing patient characteristics and outcome in a 19-year, single-center series. *Surgery*. 2005;138:28–39.
9. Donald G, Donahue T, Reber HA, Hines OJ. The evolving management of infected pancreatic necrosis. *Am Surg*. 2012;78:1151–5.
10. Horvath K, Freeny P, Escallon J, Heagerty P, Comstock B, Glickerman DJ, et al. Safety and efficacy of video-assisted retroperitoneal debridement for infected pancreatic collections: a multicenter, prospective, single-arm phase 2 study. *Arch Surg*. 2010;145:817–25.
11. van Santvoort HC, Besselink MG, Horvath KD, Sinanan MN, Bollen TL, van Ramshorst B, et al; Dutch Acute Pancreatitis Study Group. Videoscopic assisted retroperitoneal debridement in infected necrotizing pancreatitis. *HPB (Oxford)*. 2007;9:156–9.
12. Bucher P, Pugin F, Morel P. Minimally invasive necrosectomy for infected necrotizing pancreatitis. *Pancreas*. 2008;36:113–9.
13. Parekh D. Laparoscopic-assisted pancreatic necrosectomy: a new surgical option for treatment of severe necrotizing pancreatitis. *Arch Surg*. 2006;141:895–902.
14. Horvath KD, Kao LS, Ali A, Wherry KL, Pellegrini CA, Sinanan MN. Laparoscopic assisted percutaneous drainage of infected pancreatic necrosis. *Surg Endosc*. 2001;15:677–82.
15. Bradley EL 3rd, Howard TJ, van Sonnenberg E, Fotoohi M. Intervention in necrotizing pancreatitis: an evidence-based review of surgical and percutaneous alternatives. *J Gastrointest Surg*. 2008;12:634–9.
16. Baron TH, Thaggard WG, Morgan DE, Stanley RJ. Endoscopic therapy for organized pancreatic necrosis. *Gastroenterology*. 1996;111:755–64.
17. Seifert H, Wehrmann T, Schmitt T, Zeuzem S, Caspary WF. Retroperitoneal endoscopic debridement for infected peripancreatic necrosis. *Lancet*. 2000;356:653–5.
18. Seewald S, Groth S, Omar S, Imazu H, Seitz U, de Weerth A, et al. Aggressive endoscopic therapy for pancreatic necrosis and pancreatic abscess: a new safe and effective treatment algorithm (videos). *Gastrointest Endosc*. 2005;62:92–100.
19. Varadarajulu S, Phadnis MA, Christein JD, Wilcox CM. Multiple transluminal gateway technique for EUS-guided drainage of symptomatic walled-off pancreatic necrosis. *Gastrointest Endosc*. 2011;74:74–80.
20. de la Fuente SG, Demaria EJ, Reynolds JD, Portenier DD, Pryor AD. New developments in surgery: Natural Orifice Transluminal Endoscopic Surgery (NOTES). *Arch Surg*. 2007;142:295–7.
21. Seewald S, Ang TL, Kida M, Teng KY, Soehendra N; EUS 2008 Working Group. EUS 2008 working group document: evaluation of EUS-guided drainage of pancreatic fluid collections (with video). *Gastrointest Endosc*. 2009;69(2 Suppl):S13–21.
22. Park DH, Lee SS, Moon SH, Choi SY, Jung SW, Seo DW, et al. Endoscopic ultrasound-guided versus conventional transmural drainage for pancreatic pseudocysts: a prospective randomized trial. *Endoscopy*. 2009;41:842–8.
23. Varadarajulu S, Christein JD, Tamhane A, Drelichman ER, Wilcox CM. Prospective randomized trial comparing EUS and EGD for transmural drainage of pancreatic pseudocysts (with videos). *Gastrointest Endosc*. 2008;68:1102–11.
24. Ang TL, Seewald S. Fully covered self-expandable metal stents: the “be all and end all” for pancreatic fluid collections? *Gastrointest Endosc*. 2015;82:1047–50.
25. Itoi T, Binmoeller KF, Shah J, Sofuni A, Itokawa F, Kurihara T, et al. Clinical evaluation of a novel lumen-apposing metal stent for endosonography-guided pancreatic pseudocyst and gallbladder drainage (with videos). *Gastrointest Endosc*. 2012;75:870–6.
26. Itoi T, Nageshwar Reddy D, Yasuda I. New fully-covered self-expandable metal stent for endoscopic ultrasonography-guided intervention in infectious walled-off pancreatic necrosis (with video). *J Hepatobiliary Pancreat Sci*. 2013;20:403–6.
27. Charnley RM, Lochan R, Gray H, O’Sullivan CB, Scott J, Oppong KE. Endoscopic necrosectomy as primary therapy in the management of infected pancreatic necrosis. *Endoscopy*. 2006;38:925–8.
28. Voermans RP, Veldkamp MC, Rauws EA, Bruno MJ, Fockens P. Endoscopic transmural debridement of symptomatic organized pancreatic necrosis (with videos). *Gastrointest Endosc*. 2007;66:909–16.
29. Escourrou J, Shehab H, Buscail L, Bournet B, Andrau P, Moreau J, et al. Peroral transgastric/transduodenal necrosectomy: success in the treatment of infected pancreatic necrosis. *Ann Surg*. 2008;248:1074–80.
30. Gardner TB, Chahal P, Papachristou GI, Vege SS, Petersen BT, Gostout CJ, et al. A comparison of direct endoscopic necrosectomy with transmural endoscopic drainage for the treatment of walled-off pancreatic necrosis. *Gastrointest Endosc*. 2009;69:1085–94.
31. Seifert H, Biermer M, Schmitt W, Jürgensen C, Will U, Gerlach R, et al. Transluminal endoscopic necrosectomy after acute pancreatitis: a multicentre study with long-term follow-up (the GEPARD Study). *Gut*. 2009;58:1260–6.
32. Gardner TB, Coelho-Prabhu N, Gordon SR, Gelrud A, Maple JT, Papachristou GI, et al. Direct endoscopic necrosectomy for the treatment of walled-off pancreatic necrosis: results from a multicenter U.S. series. *Gastrointest Endosc*. 2011;73:718–26.
33. Seewald S, Ang TL, Richter H, Teng KY, Zhong Y, Groth S, et al. Long-term results after endoscopic drainage and necrosectomy of symptomatic pancreatic fluid collections. *Dig Endosc*. 2012;24:36–41.
34. Yasuda I, Nakashima M, Iwai T, Isayama H, Itoi T, Hisai H, et al. Japanese multicenter experience of endoscopic necrosectomy for infected walled-off pancreatic necrosis: the JENIPaN study. *Endoscopy*. 2013;45:627–34.
35. Bakker OJ, van Santvoort HC, van Brunschot S, Gekus RB, Besselink MG, Bollen TL, et al; Dutch Pancreatitis Study Group. Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: a randomized trial. *JAMA*. 2012;307:1053–61.
36. Tan V, Charachon A, Lescot T, Chafai N, Le Baleur Y, Delchier JC, et al. Endoscopic transgastric versus surgical necrosectomy in infected pancreatic necrosis. *Clin Res Hepatol Gastroenterol*. 2014;38:770–6.
37. Ang TL, Kwek AB, Tan SS, Ibrahim S, Fock KM, Teo EK. Direct endoscopic necrosectomy: a minimally invasive endoscopic technique for the treatment of infected walled-off pancreatic necrosis and infected pseudocysts with solid debris. *Singapore Med J*. 2013;54:206–11.
38. Dellinger RP, Levy MM, Rhodes A, Annane D, Gerlach H, Opal SM, et al; Surviving Sepsis Campaign Guidelines Committee including The Pediatric Subgroup. Surviving sepsis campaign: international guidelines for management of severe sepsis and septic shock, 2012. *Intensive Care Med*. 2013;39:165–228.
39. Lee BU, Song TJ, Lee SS, Park do H, Seo DW, Lee SK, et al. Newly designed, fully covered metal stents for endoscopic ultrasound (EUS)-guided transmural drainage of peripancreatic fluid collections: a prospective randomized study. *Endoscopy*. 2014;46:1078–84.
40. Mukai S, Itoi T, Baron TH, Sofuni A, Itokawa F, Kurihara T, et al. Endoscopic ultrasound-guided placement of plastic vs. biflanged metal stents for therapy of walled-off necrosis: a retrospective single-center series. *Endoscopy*. 2015;47:47–55.