

News and Views

Endoscopic Versus Surgical Necrosectomy for Walled-off Pancreatic Necrosis: The Debate Continues!

Acute pancreatitis (AP) is a potentially life-threatening disease which can be associated with various local or systemic complications.^[1,2] Approximately 10%–20% patients of AP develop pancreatic necrosis, and this could be localized either in the pancreatic parenchyma or spread to extrapancreatic tissue as extrapancreatic necrosis.^[1-3] These patients with pancreatic necrosis have increased morbidity as well as mortality because of increased risk of complications such as organ failure, infection, and local complications.^[1-5] Untreated patients with infected pancreatic necrosis (IPN) have very high mortality, and these patients usually require some form of intervention along with antibiotics for a successful outcome.

Over the past decade, there has been a paradigm shift in the management of AP and its local complications with decreasing role of surgery and increasing emphasis on conservative and minimally invasive treatment approaches. Open surgical necrosectomy is no longer considered standard of care as well as no longer considered an absolute requirement for IPN as the metabolic impact of open necrosectomy exceeds the physiologic reserves of critically ill patients with infected necrosis. The minimally invasive step-up approach versus maximal necrosectomy in Patients with Acute Necrotising Pancreatitis trial comparing open necrosectomy versus step-up approach had demonstrated that, using step-up approach, there was a significant decrease in major complications, death, new onset organ failure, and hospital stay.^[6]

Over the past few years, a new less invasive endoscopic step-up approach has also been shown to be safe and effective treatment modality for patients with IPN.^[7,8] This endoscopic step-up approach is similar to step-up approach used for IPN that involves an initial percutaneous drainage (PCD) followed by surgical or laparoscopic or minimally invasive necrosectomy, if required.^[6] The studies have shown that, using an endoscopic step-up approach, 82%–89% of patients with walled-off necrosis (WON) can be successfully treated with drainage techniques only with only a small fraction of patients needing more aggressive direct endoscopic necrosectomy.^[7,8] Moreover, in week 3–4 of illness when the collections are not walled off, an alternative approach of initial PCD in weeks 2–4 of illness followed by endoscopic transluminal drainage, and necrosectomy has also been shown to be safe and effective.^[9] Importantly, endoscopic drainage under endoscopic

ultrasound (EUS) guidance has also been shown to be safe and effective in the presence of venous collaterals as well as after angioembolization of pseudoaneurysm.^[10,11] Furthermore, availability of fully covered metal stents and lumen-apposing metal stents (LAMS) have further improved the results as well as safety profile of endoscopic drainage with recent studies using metal stents showing that the use of metal stents is associated with fewer endoscopic necrosectomy sessions, lesser adverse events, shorter hospital stay, and reduced need for salvage surgery.^[12,13] However, this endoscopic approach has not been compared with the current standard of care of a surgical step approach in patients with IPN. In this news and views, we discuss a high-quality multicenter randomized trial conducted in seven medical centers and 12 teaching hospitals by Dutch pancreatic study group that was done to investigate superior treatment approach amongst the two.^[14]

The patients included in this study were adults >18 years of age, with evidence of infection or high suspicion of infection in pancreatic or extrapancreatic necrosis which required intervention, and endoscopic, and surgical step-up approaches were deemed possible by multidisciplinary experts. Authors defined IPN as a positive culture in fine-needle aspiration or presence of gas within necrotic collection on contrast-enhanced computed tomography. Infected necrosis was suspected in patients with pancreatic necrosis when these patients had clinical signs of persistent sepsis or persistent clinical deterioration despite maximum Intensive Care Unit support without other causes of infection. After obtaining informed consent, patients were randomly assigned in 1:1 ratio to either of the treatment arm and there was no blinding.

The treatment strategies were similar at all the participating centers. In the endoscopic group, transduodenal or transgastric drainage was done under EUS guidance and two 7F double pigtail stents and 8.5F nasocystic catheter were placed as the first step of management. If drainage did not lead to clinical improvement, transluminal endoscopic necrosectomy was performed. Patient assigned to surgical group underwent ultrasound or computed tomography-guided PCD as the first step and if drainage was clinically unsuccessful, a video-assisted retroperitoneal debridement (VARD) was done. In both the groups, additional drainage and necrosectomies were allowed.

The primary end point was either a composite of major complication and/or death within 6 months of

randomization. Major complications were defined as new onset of organ failure, bleeding, perforation in visceral organ requiring intervention, and incisional hernia. Secondary end points included individual component of primary outcome, exocrine and endocrine pancreatic insufficiency, pancreatic fistula, biliary strictures, need for necrosectomy, total number of interventions, length of hospitalization, total direct and indirect medical cost, quality of life, and a total number of crossovers.

Four hundred and eighteen patients with pancreatic necrosis were screened and 98 patients were found eligible. Following randomization, 51 patients were assigned in the endoscopic step-up group and 47 patients were assigned in surgical step-up group. In both the groups, one patient each did not undergo any intervention due to spontaneous clinical improvements after randomization. In endoscopic step-up group, two other patients could not be treated because of technical reasons and these patients were treated by surgical step-up approach. The baseline demographics were comparable between the two groups.

The primary composite end point occurred in 22 (43%) patients of the endoscopic group and 21 (45%) patients of the surgical group. Mortality was similar in both the groups, with most of the patient dying due to progressive sepsis and multiple organ failure. There was no significant difference in the incidence of new-onset single organ failure between the groups but the new-onset as well as persistent cardiovascular organ failure occurred more frequently in the surgery group. The incidence of pancreatic fistula was lower in endoscopic group than surgical group (5% vs. 32%; $P = 0.0011$). Authors found no significant differences in the frequency of exocrine and endocrine insufficiency, biliary strictures, and wound infections between the two groups. Furthermore, there was no significant difference in the incidence of major complications including bleeding, perforation, enterocutaneous fistula, and incisional hernias between the two groups.

Patients undergoing endoscopic step-up treatment had significantly lower rate of pancreatic fistulas (2 [5%] vs. 13 [32%] patients; relative risk 0.15, 95% confidence interval 0.04–0.62; $P = 0.0011$) as well as a shorter hospital stay (53 days vs. 69 days; $P = 0.014$). Forty-three percent patients in the endoscopy group and 51% patients in the surgery group were treated with catheter drainage only, and rest of the patients underwent necrosectomy, occurring sooner in the endoscopy group compared to the surgery group. More number of necrosectomy procedures were done in the endoscopy group compared with the surgery group ($P = 0.0004$). However, there was no significant difference in the median

number of interventions (drainage or necrosectomy) between the two groups. The mean total expenditure per patient from the time of randomization until 6-month follow-up were less in endoscopic group as compared to the surgical group, but the differences were not significant. The authors concluded that the major complications or death are comparable between the endoscopic step-up approach and the surgical step-up approach. However, the rate of pancreatic fistulas formation and the length of hospital stay were lower in the endoscopy group.

COMMENTARY

Management of IPN is a challenging task for both gastroenterologists and surgeons because of high morbidity and mortality. Acute necrotizing pancreatitis in the initial first 4 weeks of illness is associated with fluid collections that are termed as acute necrotic collections, and this later on gets liquefied and walled-off, leading on to the formation of WON.^[1] The patients with WON have a variable clinical course with some spontaneously resolving, some getting reduced in size and liquefied and some getting symptomatic or infected.^[15] This symptomatic WON needs intervention, and simple percutaneous catheter (PCD) drainage is not effective for these collections as they contain varying amount of solid necrotic debris that cannot be removed by PCD alone. These collections were earlier treated with open surgical necrosectomy, but over the past decade, there has been paradigm shift in their management toward minimally invasive interventional radiologic, laparoscopic, surgical, and endoscopic procedures.^[16]

Along with the advancement of endoscopic technology and techniques, there has been simultaneous advancement in the field of laparoscopic as well as minimally invasive surgery. Availability of VARD and laparoscopic necrosectomy has improved the results of surgical treatment of pancreatic necrosis, and studies have shown that minimally invasive surgical and endoscopic necrosectomy is associated with reduced death rates compared with open necrosectomy.^[17,18] However, the next obvious question is that, of these two minimally invasive approaches which approach is better? However, till date, only a few studies have compared these two modalities and most of these past studies have limitations of small sample size, nonrandomized design, lack of uniform treatment protocol, or retrospective analysis.^[19,20] These initial studies have demonstrated the superiority of endoscopic approach in both the outcomes and complications as well as the decreased pro-inflammatory response.^[19,20] However, this well-conducted, randomized study has shown that the endoscopic step-up approach is not superior to step-up surgical necrosectomy in terms

of reduction of major complications or death in IPN. However, the endoscopic approach was found to be better in terms of secondary end points such as length of hospital stay and pancreatic fistula formation.

The results of this study have shown that, although both the endoscopic as well as surgical step-up approach had similar outcomes as well as major complications, lower frequency of secondary end points in the endoscopic group should make it the procedure of choice for treatment of IPN. Importantly, in this study, no metal stents were used in the endoscopic group. Theoretically, larger diameter of the fully covered metal stents would allow the passage of solid necrotic material more easily as compared to narrower diameter of plastic stents used in the current study. As discussed earlier, fully covered metal stents and LAMS have further improved the results as well as safety profile of endoscopic drainage with recent studies using metal stents showing that their use is associated with fewer endoscopic necrosectomy sessions, lesser adverse events, shorter hospital stay, and reduced need for salvage surgery.^[12,13] It is quite possible that the use of metal stents might have tilted the outcome and complications rate in favor of endoscopic step-up approach.

Although endoscopic step-up approach seems to be superior, it is important that all necrotic collections cannot be drained endoscopically. The WON located away from gastroduodenal area and located in the root of mesentery, pelvis, and paracolic gutters cannot be drained endoscopically. Furthermore, WON with intestinal necrosis and retroperitoneal hemorrhage will be best managed surgically. In conclusion, endoscopic treatment of pancreatic necrosis leads on to internal drainage of infected collections, is incision-less approach with less procedural stress, and appears to be better than minimally invasive surgical step-up approach but surgery is still needed in some situations.

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