

The Step-up Approach in Treating Infected Pancreatic Necrosis

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Abstract

The management of infected necrotizing pancreatitis has dramatically evolved with continuous growing expertise and ongoing research efforts. More aggressive treatment procedures can exacerbate the important inflammatory response associated with infected necrotizing pancreatitis. Therefore, the use of conservative and less invasive interventional strategy results in a clear improvement of outcomes. The optimal treatment strategy to consider may be different for each patient because of heterogenous condition. Indeed, The optimal treatment approach should be based on a multidisciplinary discussion including gastroenterologist, surgeon, radiologist, and anesthesiologist. The step-up approach is currently the preferred treatment strategy to treat infected necrotizing pancreatitis. However, optimal timing of intervention remains unclear with lack of consensus. This review provides an overview on the use of the step-up approach to treat infected necrotizing pancreatitis, in the light of the recent published reports.

Keywords: Necrotizing pancreatitis; Infected necrosis; Treatment; Step-up approach; Minimally invasive strategies

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Introduction

Acute Pancreatitis (AP) is a heterogeneous clinical conditions associated with a potential of life-threatening and related -mortality rate of 35% [1]. AP is divided into mild, moderately severe, and severe, according to revised Atlanta Criteria published in 2012 [2]. Around 20-30% of patients with acute pancreatitis develop necrotizing pancreatitis [3]. Infection of necrotizing pancreatitis occurs in 30% of patients, and infected pancreatic necrosis was associated with multiple organ failure can leading to death [3]. Furthermore, infected necrosis is a potentially lethal complication with associated mortality varying from 15 to 20% [4,5]. Additionally, the treatment of infected necrotizing pancreatitis is associated with lengthy hospital stay and high costs. As it is an arduous condition to treat, the effectiveness of various treatment strategies are being analyzed to improve survival and reducing anatomic and physiological sequelae of the infected necrotizing pancreatitis. This review provides an overview on the use of less invasive treatment approaches for infected necrotizing pancreatitis, in the light of the recent published reports.

The step-up approach

The Acute Necrotizing Pancreatitis (ANP) is characterized by the presence of one organ failure or more, and persisting more than 48 hours [2]. It approximately occurs in 5% to 10% of cases.

ANP often results in a significant inflammatory response with a potential risk for super infection.

Acute necrotic collection is formed within 4 weeks and contains fluid and necrotic pancreatic or peripancreatic debris [2]. After 4 weeks of evolution, this collection become mature, encapsulated and so named walled-off pancreatic necrosis with multiple locations, and various patterns and sizes.

Despite the advantages of open surgical necrosectomy including better visualization of tissue facilitating more selective debridement and bleeding control , performing ostomy between walled-off necrosis and either stomach or small bowel, and ability to reduce interventions to one procedure [6], it is proven that early surgery for necrotizing pancreatitis is detrimental for outcomes, and results in exacerbated inflammatory state. Indeed, early surgery is often indicated in emergency conditions including bleeding not amenable to embolization, abdominal compartment syndrome or hollow viscus perforation [7]. Subsequently, delayed surgery was demonstrated to have the lowest mortality [8-10].

In a bite to reducing inflammatory response secondary to open surgery and related complications, minimally invasive approaches have been employed to treat infected pancreatic necrosis. These less invasive techniques include percutaneous retroperitoneal or transperitoneal drainage, endoscopic transmural or transpapillary drainage, endoscopic necrosectomy,

video-assisted retroperitoneal necrosectomy, and laparoscopic cystgastrostomy or cystojejunostomy.

Firstly employed by the Dutch Acute Pancreatitis Study Group (2010), the term 'step-up' is commonly used as a reference to minimally invasive procedures to drain infected pancreatic necrosis with the potential of re-use and escalation [11]. Several studies have showed the benefits of the step-up approach over laparotomy in treating infected pancreatic necrosis. A randomized trial PANTER including 88 patients and comparing the step-up approach (percutaneous or endoscopic transgastric drainage) with open surgery [11]. Minimally invasive retroperitoneal necrosectomy was performed following the step-up approach if needed. Major complications including new-onset organ failure, perforation, fistula or bleeding were 12% and 40% ($p=0.002$) in the step-up group and the open surgery group, respectively. However, the mortality rate was similar in both groups (19% & 16%, $p=0.70$), revealing that the step-up group patients were not undertreated. Once again, these benefits were confirmed by a long-term follow-up (86 months) of 73 patients, highlighting the superiority of step-up method over open option regarding the long-term results [12].

Another randomized trial (PENGUIN) published in 2012, included a small sample (20 patients) and compared endoscopic trans gastric drainage with open necrosectomy [13]. Video-assisted retroperitoneal necrosectomy was performed in both groups when needed. The inflammatory response as well as secondary outcomes including major complications or death was assessed. Conclusively, trans gastric endoscopic necrosectomy was associated with reduced risk of major complications or death (20% vs. 80%; $p=0.03$) [13].

Furthermore, multiple retrospective studies have compared the step-up and less invasive procedures with open surgery (laparotomy) during the last 5 years. A single institution study from the Liverpool Pancreas Cener and published in 2016, has clearly showed the significant advantages of minimally invasive approach over open necrosectomy [14]. This large study included 394 patients who underwent either a minimally invasive retroperitoneal pancreatic necrosectomy or open necrosectomy. The total postoperative complications and organ failure were less frequently occurred in the minimally invasive procedure (63.9% vs. 81.7%). In addition, a significant reduction of mortality risk of 73% was associated with minimally invasive necrosectomy ($p \leq 0.001$).

The German Pancreatitis Study Group published a multicenter study (2016) including 220 patients [15]. Percutaneous and endoscopic drainage, with or without minimally invasive necrosectomy was compared with open surgery. Severe complications such as sepsis, persistent multi organ dysfunction, and bleeding were occurred in 44% and 73.3% of patients in the step-up approach group and open group, respectively. A lower mortality rate was observed in the step-up group, compared to a rate (10.5% vs 33.3%).

In addition, an increased risk of in-hospital and 90-day mortality with increased stay length, periprocedural bleeding and incisional hernia development, have been reported with open surgical

necrosectomy [16]. Also, some retrospective studies reported similar results following open surgical necrosectomy with trends towards favouring the step-up approach to treat necrotizing pancreatitis [17-19].

Recently, a large observational study comparing minimally invasive approaches with each other and with an open surgical procedure [20]. This study included 1980 patients, comparing minimally invasive surgical necrosectomy and endoscopic necrosectomy with open surgical necrosectomy. The death was assessed as a primary endpoint. A lower risk of death was observed in patients who received minimally invasive surgical procedure and endoscopic necrosectomy, compared with open surgery ($p=0.02$ and $p=0.03$, respectively). This study was unique in data collection with including an important sample of patients allowing to eliminating the confounding factors related to the retrospective of the study.

Instead of multiple published studies comparing minimally invasive techniques as a group to open surgery; studies comparing minimally invasive techniques with each other are sparse.

The Dutch Acute Pancreatitis Study Group published a randomized trial (The TENSION), comparing endoscopic drainage with percutaneous drainage [21]. The study included 98 patients presenting infected pancreatic necrosis and death or major complications were assessed as a primary endpoint [21]. In term of major complications or death, the results were comparable for both procedures (43% vs. 45%, $p=0.88$). However, differences between groups were found in secondary endpoints including new-onset cardiovascular failure and persistent cardiovascular failure in the percutaneous group ($p=0.045$). In addition, pancreatic fistula was lower in the endoscopy group (5% vs. 32%, $p=0.0011$) as well as a shorter hospital stay (53 days vs. 69 days, $p=0.014$).

Recently (2018), a randomized trial named 'the MISER' has compared endoscopic step-up strategy with minimally invasive surgery defined as a laparoscopic necrosectomy or video-assisted retroperitoneal debridement [22]. Death or major complications have been assessed as a primary outcome of the study. Major complications were significantly occurred in surgical groups (40.6% vs 11.8%, $p=0.007$) compared to endoscopic group. In addition, pancreatic fistula occurred in 28% of open surgery group ($p=0.001$), however, it did not occurred in the endoscopic group. The death rate was similar in both groups. So; this trial demonstrated the fundamental benefits of an endoscopic, natural orifice approach. Furthermore, endoscopic drainage alone has been recently shown to be a successful technique to treat 40% of patients [23]. Endoscopic drainage induces less stress and does not necessarily require general anaesthesia [21]. In addition, this endoscopic technique has been developed using stents with a larger diameter and flanges to prevent migration, may increase the rates of successful endoscopic drainage without necrosectomy during the last 10 years [24]. However, location of collections near the stomach and duodenum sweep is required limiting its application. Overall, the endoscopy as a primary treatment option for infected pancreatic collections is relatively a new strategy. Endoscopic drainage of infected pancreatic collections is largely adopted by many practitioners and, so, it is a

promising treatment option [24]. Furthermore, studies assessing safety and determining precise protocols for usage are needed in the bite to optimizing endoscopic use in clinical practice for the treatment of infected necrotizing pancreatic collections.

Approach and timing of treatment

The infected necrotizing pancreatitis can be managed using various treatment strategies. The appropriate decision for optimal treatment is based on multiple criteria including the location of infected collections, extent of disease, availability of equipment and experience skills and expertise in the different techniques. So, the appropriate decision to choose the right treatment option should be based on a multidisciplinary discussion including gastroenterologist, surgeon, radiologist and anaesthetist.

The primary goal is to rapidly reduce the SIRS response and assuage organ failure. Antibiotic therapy is used to delay interventional procedures until reaching the maturity of collections, and sometimes, may completely avert the need for intervention [10].

The recent published guidelines recommended either percutaneous catheter drainage or endoscopic drainage as a first procedure to treat patients, ideally 4 weeks after the onset of disease [25,26]. Currently, the step-up approach is now the preferred treatment strategy for infected necrotizing pancreatitis. Percutaneous drainage alone can be used to treat many patients and is useful to reach nearly the entire abdominal cavity. Also, it can be repeated with upsizing drainage preventing necrosectomy [27]. However, percutaneous drainage is less useful to treat very extensive collections, and can enabling extravation of pancreatic enzymes leading to the development of pancreatic fistula [10,11,22,28,29]. However, Consensus is lacking regarding the timing of catheter drainage.

Despite the clear benefits of minimally invasive procedures

over open surgery, laparotomy may be necessary only as rescue measure in decompensating patients.

Postponing all interventions including the step-up approach for infected necrosis until the stage of walled-off necrosis has been a standard practice for many years. Notably suggested by observational studies, encapsulation of infected necrosis is not mandatory for safe and successful catheter drainage [4,30-34]. Furthermore, international expert pancreatologists demonstrated “equipoise” between immediate and postponed catheter drainage of infected necrosis [35]. The aim of immediate catheter drainage is to prevent further clinical deterioration.

Overall, there is no uniformity regarding the timing of intervention in the first 2-3 weeks of infected necrotizing pancreatitis [36]. Further preferably randomized controlled studies are highly needed and should address these issues and especially determine early catheter drainage compared to postpone catheter drainage could improve outcomes in patients with infected necrotizing pancreatitis.

Conclusion

During the last 20 years, infected necrotizing pancreatitis management has dramatically evolved and continues to evolve with growing expertise, new techniques and ongoing efforts of research. Conservative and less invasive interventional strategy leads to clear improvement of outcomes. The optimal treatment approach should be based on a multidisciplinary discussion including gastroenterologist, surgeon, radiologist, and anesthetist. Currently, the step-up approach is the preferred treatment option for infected necrotizing pancreatitis. However, optimal timing of intervention remains unclear with lack of consensus. Therefore, further randomized controlled studies are highly needed to determine whether early or delayed step-up approach strategy could improve outcomes in infected necrotizing pancreatitis.

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