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Review Article

Less Invasive Treatment Methods for Infected Pancreatic Necrosis

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Abstract

The management of infected pancreatic necrotic collections following necrotizing pancreatitis substantially evolved with continuous growing expertise and important research works. 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 appropriate treatment option to consider depends on the clinical conditions of each patient. Indeed, the optimal treatment approach should be based on a multidisciplinary discussion including gastroenterologist, surgeon, radiologist, and anesthetist. Currently, the step-up technique is the advocated treatment option for infected pancreatic collections after 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

Introduction

Acute Pancreatitis (AP) is a heterogeneous clinical condition [1]. AP is divided into mild, moderately severe, and severe, according to revised Atlanta Criteria published in 2012 [2]. Approximately, necrotizing pancreatitis accounts 20% to 30% of acute 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 remains a life-threatening complication with associated mortality varying from 15% to 20% [4,5]. Additionally, a prolonged length stay and high costs are associated with infected pancreatic necrosis management. The effectiveness and efficacy of a treatment approach for infected necrosis results in improving survival and reducing sequelae. This review provides a comprehensive insight on the less invasive methods for the current treatment of the infected pancreatic necrosis.

The Step-Up Approach

The Acute Necrotizing Pancreatitis (ANP) is associated with one or more organ failure persisting more than 48 hours [2]. It approximately occurs in 5% to 10% of cases. ANP often results in a substantial inflammatory response with a potential risk for super infection. Acute necrotic collections are formed about with 4 weeks, containing fluid and necrotic debris. These collections evolve becoming mature, encapsulated within 4 weeks and are called walled-off necrotic collection which can have multiple locations and sizes.

Despite the advantages of open surgery in treating necrosis including facility to perform complete and selective necrotic debridement, easy control of bleeding, possibility to perform internal drainage between collection and digestive organ including the stomach or the small bowel. In addition, the open surgery can be complete resulting in reduced number of surgical procedure [6]. Currently; 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 controllable using less invasive treatment methods, and peritonitis secondary to intestinal perforation [7]. Subsequently, delayed surgery was demonstrated to have the lowest mortality [8,9].

In a bite to reducing inflammatory response and complications related to open surgery, less invasive treatment have been recommended to treat infected necrotic collections. The less invasive treatment techniques include percutaneous and endoscopic drainage, laparoscopic or video-assisted, and laparoscopic internal drainage including cystgastrostomy or cystojejunostomy.

The term 'step-up' is commonly used as a reference to less invasive methods to drain infected necrotic collection following acute pancreatitis. This treatment procedure can be repeated with escalation. The benefits of the step-up approach over laparotomy have been clearly demonstrated in treating infected pancreatic necrosis. As a step-up approach, percutaneous or endoscopic transgastric drainage has been randomly compared with open surgery [4]. Death and major complications including intestinal perforation, fistula, hemorrhage and new organ failure have been assessed. The death was similar in both compared techniques, however, major complications were significantly higher in open surgery group (p=0.002). Also, endoscopic transgastric drainage was reported associated with reduced risk of major complications (p=0.03), compared to open necrosectomy [10]. Additionally, regarding the long-term results, the superiority of step-up method over open option has been clearly confirmed [11].

Furthermore, less invasive procedures including the step-up method have been retrospectively compared with open surgery during the last 5 years. A large single institution study including 394 patients has clearly showed the significant advantages of minimally invasive approach over open necrosectomy [12]. The postoperative

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complication and organ failure rates were lower in the minimally invasive group (63.9% *vs.*81.7%). In addition, the minimally invasive approach was associated with a significant reduced risk of mortality, compared to open surgery group (p≤ 0.001).

Another, large retrospective study including 220 patients has compared percutaneous and endoscopic drainage with open surgery [13]. The step-up approach was associated with lower rate of severe complications including sepsis, persistent multi organ failure and bleeding, compared to open surgery procedure (44% *vs.*73.3%). Additionally, a lower mortality rate was showed in the less invasive drainage (10.5% *vs.*33.3%). Also, some retrospective studies reported similar results following open surgical necrosectomy with trends towards favoring the step-up approach to treat necrotizing pancreatitis [14-16]. In addition, an increased in-hospital and 90-day mortality risk and hospital stay have been reported with open necrosectomy [17]. Recently, a large observational study including 1980 patients has compared minimally invasive necrosectomy and endoscopic necrosectomy with open surgery [18]. A significant lower risk of mortality in group of patients who received minimally invasive and endoscopic necrosectomy (p=0.02 and p=0.03, respectively).

Furthermore, minimally invasive techniques have been compared with each other; however, the studies are sparse. A randomized trial (The TENSION) included 98 patients with infected pancreatic necrosis [19]. Endoscopic drainage has been compared with percutaneous drainage, and death or major complications were assessed as a primary endpoint. In term of major complications or death, the results were comparable for both procedures (43% *vs.* 45%, p=0.88). However, significant rate of a new-onset or persistent cardiovascular failure as a secondary endpoints in the percutaneous group (p=0.045). In addition, a significant lower rate of pancreatic fistula (5% *vs.*32%, p=0.0011) and a significant shorter hospital stay (53 days *vs.*69 days, p=0.014) in the endoscopy group [20].

Another recently randomized trial 'The MISER' has compared endoscopic step-up strategy with laparoscopic necrosectomy or video-assisted retroperitoneal debridement [21]. Major complications were significantly occurred in surgical groups (40.6% *vs.*11.8%, p=0.007) compared with endoscopic group. However, mortality rate was similar in both groups.

In addition, pancreatic fistula occurred in 28% of open surgery group (p=0.001) and none in endoscopic group. Furthermore, endoscopic drainage alone has been recently shown to be a successful technique to treat 40% of patients [22]. Endoscopic drainage is associated with less stress without need to anesthesia [19]. In addition, the use of large stents with flanges to reduce the risk of migration resulted in increased successful endoscopic drainage without need to complementary necrosectomy [23]. However, location of collections near the stomach and duodenum is required limiting its application.

Overall, endoscopic drainage of infected pancreatic collections is largely adopted in clinical practice and it is a promising treatment option [25]. However, further well designed studies are needed to assess the safety and define precise protocols in the bite to optimizing the endoscopic use in clinical practice for infected pancreatic collections.

Approach and Timing of Treatment

Various treatment options can be employed to manage infected pancreatic necrotic collections. The appropriate decision for optimal treatment is based on multiple criteria including the collection location, disease extent and experience skills with different techniques. Indeed, the appropriate decision to choose the right treatment option should be based on a multidisciplinary discussion including gastroenterologist, surgeon, radiologist and anesthetist. Reducing SIRS response and avoiding organ dysfunction or failure is the main goal the treatment strategy. Antibiotic therapy is used to delay interventional procedures until reaching the maturity of collections, and sometimes, may completely avoid intervention [5]. Despite the clear benefits of minimally invasive procedures over open surgery, laparotomy may be necessary only as rescue measure in decompensating patients.

Both percutaneous drainage and endoscopic drainage have been recommended by the recent published guidelines as a first procedure to treat patients [24,25]. Currently, the step-up method or percutaneous drainage is the preferred treatment option to treat the infected pancreatic collections. The 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 [26]. 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 [4,5,21,27]. Delaying treatment of infected necrotic collections until the walled-off necrosis stage has been advocated as a standard treatment option in clinical practice. Regarding the timing of intervention, this treatment strategy is not consensual. Furthermore, the encapsulation of the infected collection is not mandatory for safety and success of drainage [4,28-32]. Furthermore, international expert pancreatologists demonstrated that there was no difference between early and delayed catheter drainage of infected collections [33]. Early catheter drainage aims to avoid further clinical deterioration.

Overall, there is no uniformity regarding the timing of intervention for infected pancreatic collections in the first 2 weeks to 3 weeks following necrotizing pancreatitis. Further randomized controlled studies are highly needed to determine the optimal timing of intervention including catheter drainage for infected pancreatic collections after necrotizing pancreatitis.

Conclusion

During the last two decades, infected pancreatic necrotic collections management has substantially evolved with continuous acquired expertise, new treatment methods and ongoing 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 method or catheter drainage is the treatment option of choice for infected necrotic collections following necrotizing pancreatitis. However, ideal timing of intervention remains unclear with lack of consensus. Therefore, further randomized controlled studies are highly recommended to clearly determine the appropriate timing and addressing the controversy regarding whether early or delayed step-up approach strategy could lead to improved outcomes in infected pancreatic collections.

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