

Acute Necrotizing Pancreatitis-Current Concepts and Latest Treatment Strategies: A Surgeon's Perspective

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Abbreviations:

ANP: Acute Necrotizing Pancreatitis; NP: Necrotizing Pancreatitis; AP: Acute Pancreatitis; WOPN: Walled off Pancreatic Necrosis; TPN: Total Parenteral Nutrition; VARD: Video Assisted Retroperitoneal Debridement; ANC: Acute Necrotic Collections

1. Abstract

Acute Necrotizing Pancreatitis is a difficult clinical condition with a high death rate. Because of the severe inflammatory reaction, it is a difficult condition to treat. Treatment for this illness now includes less invasive options such percutaneous drainage and endoscopic drainage in addition to less invasive endoscopic and video-assisted or laparoscopic debridement. The timing and technique of treatment have also changed. This research reviews the literature on various interventions for acute necrotizing pancreatitis with the goal of shedding light on the "step-up approach" to acute necrotizing pancreatitis care.

2. Introduction

The severity of acute pancreatitis varies extensively, from a clinically self-limiting course to a rapid fatal course [1]. The most terrible evolution, Necrotising Pancreatitis (NP), carries a poor prognosis; mortality ranges from 15% to 30-39% in cases of infected necrosis, which is the main cause of death [2]. Infected pancreatic necrosis typically requires intervention, as do patients with sterile necrosis who have symptoms such a biliary blockage or a gastric or duodenal outlet obstruction [2]. Open necrosectomy has historically been the most common treatment for infected necrosis, but it is also linked with significant rates of morbidity (34-95%) clincicsofsurgery.com

and mortality (11-39%) [2, 3]. Treatment for NP has substantially changed during the past few decades, moving from open surgery to minimally invasive procedures including laparoscopy and rigid retroperitoneal videoscapy [2, 3].

AP can be mild, moderate or severe, while mild pancreatitis is commonly self-limited, severe pancreatitis can be associated with development of complications such as parenchymal / peri pancreatic fluid collection and necrosis [1-4]. Severe AP is defined by single or multiple organ failure lasting more than 48 hours and is associated with a mortality rate of as high as 25%. Acute necrotizing Pancreatitis is diagnosed when more than 30% of the gland is affected by necrosis & accounts for accounts for 5-10 % of pancreatitis cases [1-6].

The revised Atlanta classification is used to classify pancreatic fluid collection that develops following AP [1,2]. When fluid collection develops within 4 weeks of the diagnosis of pancreatitis and are without any solid or liquefied components they are referred to as Acute Pancreatic Fluid Collection (APFCs) [4, 5]. Fluid collections arise from necrotising pancreatitis and contain both fluid and necrotic material they are referred to as Acute Necrotic Collections (ANC) [4-6]. After 4 weeks of diagnosis, an APFC may develop into a Pancreatic Pseudocyst (PP) with a well defining enhancing

wall [1-4].

Walled off Pancreatic Necrosis (WOPN) results when the ANC matures and develops a wall after 4 weeks [3]. These collections may be sterile or infectious and may be present alongside the pancreatic parenchyma, next to it, or both [3]. While sterile necrosis is linked to a mortality rate of 5–10%, this rises to 20–30% when the necrosis contracts an infection [1-3, 5]. Early detection and the implementation of suitable therapy are essential [5]. The pancreatic parenchyma and peripancreatic adipose tissue are necrosed in necrotising pancreatitis most frequently (70–80%) [5]. Necrosis may occasionally be restricted to the pancreas (5%) or the peripancreatic adipose tissue (20%) [1-4, 7, 8]. Compared to pancreatic parenchymal necrosis, isolated peripancreatic necrosis had a better prognosis [7]. Within the first few days, a contrast-enhanced CT may not detect necrosis; however, after the first week, a CECT may detect non-enhancing pancreatic parenchymal, which is regarded as pancreatic necrosis [2, 3, 9]. A WOPN can be sterile or infected, asymptomatic or symptomatic; the diagnosis of the latter is essential for prompt administration of antibiotics and any other intervention that may be required [4, 10]. Extra luminal gas is one of the CT findings is indicative of an infection [5]. The most prevalent etiology of necrotising pancreatitis is gallstones (40-48%) followed by alcohol usage (24-27%), however no predisposing variables have been proven to enhance the chance of developing pancreatic necrosis [5, 10]. Based on fresh conceptual understandings and data from clinical studies, the treatment of NP has undergone substantial alterations over the past 20 years [1, 2]. Sterile necrosis, which is present in the majority of NP patients is treatable [1, 2]. The focus of conservative treatment is on supportive measures, infection control, necrosis prevention, and other complications prevention [1, 2, 10, 11].

Patients with infected necrosis generally need to undergo an intervention which has shifted from primary open necrosectomy in an early disease to step up approach [1, 2]. In this paper we emphasize and throw light on the current concepts and treatment strategies for necrotising pancreatitis [2, 3].

3. Review of Literature

3.1. Management of Severe AP and ANP

Aggressive intravenous fluid hydration is the first step in the therapy of AP, with the goal of maintaining intravascular volume as well as pancreatic and systemic perfusion [1, 6, 11]. Antibiotics are only used in individuals with highly suspected or proven infected pancreatic necrosis because they have no preventive effect in preventing infection and did not show benefit in sterile pancreatic necrosis [2, 12]. Treatment for people with necrotizing pancreatitis must include proper nutritional support [11]. If pancreatitis is moderate and oral intake is tolerable, patients are typically kept off food and only given small amounts of liquids later [12]. Patients are usually kept nil per mouth with early feeding if pancreatitis is

mild and oral intake can be tolerated [2, 6, 13].

For fear of introducing pancreatic enzymes, which could exacerbate inflammation, patients with more severe illness have traditionally been kept off food [3]. However, we now know that severe pancreatitis enhanced catabolic state and the absence of nutritional assistance are linked to high mortality [3, 6, 14]. For patients with severe AP, total parenteral nutrition was the norm; nevertheless, enteral nutrition that went beyond the ligament of Treitz was discovered to be more advantageous [5, 6]. The results of a significant Cochrane meta-analysis showed that enteral feeding outperformed TPN [5]. Reduced infectious complications, hospital stay, and overall mortality in cases with severe AP [5]. Thus, enteral nutrition is favoured over total parenteral nutrition (TPN), with early initiation of feeding (within 48 hours) preferred over later, however the precise timing is disputed [3, 6, 10].

Historically, early laparotomy and necrosectomy were performed on individuals with necrotizing pancreatitis [4]. Within the previous 20 years, this has seen a significant transformation [4]. Early intervention has been shown to be harmful and is now only used in cases of abdominal compartment syndrome, hollow viscus perforation, and haemorrhage that is not susceptible to interventional embolization [4, 6, 14]. It was found that outcomes for patients with severe pancreatitis improved by avoiding exacerbation of the inflammatory phase with surgery [4, 5].

When surgical intervention was postponed, mortality significantly decreased, according to a 1997 prospective randomised study, which was cut short for a reason [1, 2]. Another early study evaluated mortality rates for three distinct historical periods during which various practise patterns were prevalent [2, 3]. They discovered a pattern: the most recent time period with the longest delay in intervention had the lowest mortality [2, 3]. The question of how to treat known infected necrosis was addressed after these studies with a retrospective review of 53 patients, a systematic review of 10 studies, as well as a sizable prospective study, which once more showed that delayed intervention was found to have the lowest mortality [2-6]. Today, national guidelines still reflect this opinion [1-6].

When an infected necrosis is walled and demarcated, with at least partial liquefaction with discrete encapsulation typically after 4-6 weeks from the onset of the disease, the intervention is mandatory in any procedure [5-7]. Intervention is required in any technique when an infected necrosis is walled and defined, with at least partial liquefaction and discrete encapsulation often after 4-6 weeks after the commencement of the disease [5, 14].

Regardless of size or extent, an asymptomatic WON does not require treatment because it may clear on its own, even if it may sporadically become infected [3, 6]. In the event of infection, discomfort, or obstruction of a viscus or bile duct, a symptomatic WON typically necessitates intervention later in the course of the

disease, usually more than 4 weeks [3, 6, 15].

When an infected acute necrotic collection is identified, it must be treated within a few weeks after AP development and be linked to clinical worsening and sepsis symptoms [2, 3]. Otherwise, clinical deterioration despite maximal medical support including intensive care and specific organ support does not seem to be an indication for local treatment such as radiological, endoscopic or surgical drainage or necrosectomy [2, 3, 16]. These patients may undergo surgery within the first weeks of onset of AP as a last chance even if the process is sterile but the prognosis regardless of the intervention only in abdominal compartment syndrome, the early surgical or percutaneous decompression may be lifesaving [3, 16].

Delay in intervention is preferable to prompt intervention in patients with infected necrosis [5, 15]. When pancreatic necrosis is removed before three weeks, there is a higher chance of haemorrhage and other adverse effects [15, 16]. Delaying intervention enables the separation of necrotic from vital tissue, which reduces the amount of important tissue removed during necrosectomy, improving long-term endocrine and exocrine function and minimizing post-operative adverse effects [15, 16]. Additionally, the adoption of less intrusive procedures enables the surgical debridement to be delayed or avoided, enhancing the outcome [5, 15, 16].

The International Association of Pancreatology recommended in their guidelines from 2002 that delaying open surgery for at least 3 to 4 weeks would result in lower rates of morbidity and mortality than earlier intervention [4, 17]. In an RCT, Mier showed that, when compared to delayed intervention after at least 12 days, early necrosectomy within 2-3 days after the onset of AP increased morbidity and death. According to the Van Santvoort research (Dutch Pancreatitis research Group), early surgery was a reliable indicator of a worse result in patients with acute NP [5, 6, 17]. Reddy Wittau, Papachristou, and Olah's study, in which the time of intervention was altered within a single institution, confirmed the benefit of postponing surgery [1-6, 17].

In the past ten years, basic non-interventional medical care for infected necrosis has been suggested along with the prescription of antibiotics [5, 6, 19]. The research by Olah, Runzi, Sivasankar, Garg, and Wysocki proved that patients who are clinically stable and have few symptoms can be managed with antimicrobial therapy without the need for additional treatment. In the event of clinical worsening, the intervention is necessary [1-6, 19].

Traditionally, surgical necrosectomy was used to treat NP [2, 3, 19]. This invasive procedure carries a high risk of pancreatic failure along with a high percentage of complications (34–95%) and death (11–39%) [2]. The step-up strategy is currently regarded as the gold standard for managing ANP [2]. It entails a multidisciplinary evaluation and the application of procedures that are at least intrusive and progressive as possible, such as retroperitoneal necrosectomy, percutaneous drainage, endoscopic drainage, and,

in certain circumstances, surgical necrosectomy [1-6, 18]. On a video-assisted necrosectomy, the first feasible technique is percutaneous drainage, which can be followed by endoscopic drainage [2-4]. However, even if the step-up strategy is used, it may still be required to use surgical necrosectomy right away to avoid the risk of the condition getting worse [1-3, 19].

Indication of Surgical Necrosectomy [1-6]

- 1) Onset of compartment syndrome.
- 2) Bleeding which cannot be controlled with interventional radiology techniques.
- 3) Intestinal Perforation.
- 4) Intestinal or biliary obstruction resulting from extrinsic compression.
- 5) Failure of minimally invasive techniques.

It may be necessary to resort to surgical necrosectomy in spite of percutaneous drainage as drains could not discharge the necrotic material, the patients present with fever and worsening of sepsis despite of personalized antibiotic therapy [20]. With a minimally invasive strategy in mind, the procedure involved inserting a drain where the previous percutaneous one had been [5, 6]. This allowed for the debridement of the intracavitary septa as well as additional communicating drains to guarantee that the material was constantly being washed [1-6, 17].

When possible, non-invasive interventional radiology procedures should be used to address the bleeding issue as well, limiting the need for surgery in the operating room [2, 3]. The erosion of the vessel adjacent to the collection or the formation of false aneurysm can arise as a late complication of ANP and even as a complication of drainage of necrotic material, bleeding also can treat with interventional radiology techniques [1-3, 11]. In the literature, percutaneous drainage by itself has been shown to have an above-average effectiveness rate of 50% [2, 3]. Like this, endoscopic procedures have an acceptable effectiveness rate of between 75 and 95 percent [3, 4]. However, according to the same studies, lengthy and inadequate non-invasive treatment followed by surgery can raise the death rate. The step-up method must be regarded as the gold standard for treating ANP [4-6, 19].

3.2. The Step-Up Approach

Open surgery in the treatment of infected pancreatic necrosis has been replaced by the minimally invasive approach [2, 3]. This method is used to treat necrotizing pancreatitis which reduces patient mortality, multi-organ failure, cost, and late surgical complications, according to the results of the multi-centre randomised clinical trial PANTER [1-6]. The current standard of care is a step-up approach that starts with minimally invasive necrosectomy only when clinically necessary, then percutaneous catheter drainage or endoscopic transluminal drainage [6].

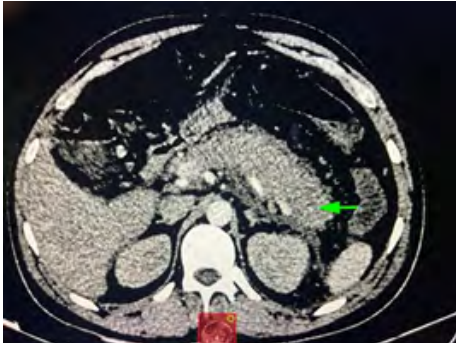


Figure 1: CT scan image depicting Necrotizing pancreatitis of the body and tail.

3.2.1. Percutaneous Catheter Drainage

Long-term use of antibiotics may increase the frequency of fungal infections and antibiotic resistance [1]. Secondary infection of pancreatic or peripancreatic necrosis might happen during the first three weeks of disease onset [1, 2]. Early drainage has been shown to be beneficial, but its use must be determined after an infection has been confirmed since otherwise, we risk contaminating a sterile collection [1, 2, 14]. The best percutaneous drainage would take the retroperitoneal route on the left side, making it easier to access the area for subsequent minimally invasive surgery, if needed [1].

According to recent research, 35% of patients treated with percutaneous drainage during this phase won't need extra surgical necrosectomy, and in 50% of cases, a drainage catheter's diameter is gradually increased [1, 4].

1. If poor evolution persists after 48 hours and the patient's conditions permit it, a new drainage with a larger diameter would be attempted.
2. If the poor clinical condition is maintained, despite the use of larger drains, surgical drainage should be carried out.

Nowadays, it's popular to avoid any unnecessary intrusion [5]. There have been several techniques mentioned that will progressively be used in our service, such as video assisted retroperitoneal access, which has much lower abdominal complication rates than the majority of traditional techniques [4, 5]. It was important to keep it as long as possible on the left side because this procedure used radiological drainage as a guide to the collection [4, 21]. Endoscopic drainage could be assessed after 4 weeks in addition to percutaneous radiological drainage in the event of infection, as described above [5]. In most cases, an inflammatory wall would have already developed and been strong enough to tolerate trans gastric endoscopic draining at this point [5].

3.2.2. Trans gastric endoscopic drainage

The step-up method can be performed endoscopically or surgically [4]. Two randomised trials have been conducted to compare the two alternative techniques [2, 3]. The first is the TENSION study, which found that the rate of pancreatic fistulas and length of hospital stay were higher in the endoscopic group [3, 4]. However, clincicsurgery.com

the endoscopic step-up method was not superior to the surgical step-up approach in preventing serious complications or death [4]. The second experiment, the MISER randomised controlled trial, demonstrated that an endoscopic transluminal method for infected necrotizing pancreatitis dramatically reduced serious complications, decreased expenses, and improved quality of life when compared to minimally invasive surgery [1-6, 23]. Recent investigations have shown that the endoscopic staggered technique is now the preferred method for treating infected necrotizing pancreatitis [3, 4].

It might not be practical for all patients, though. It is dependent on the anatomical location of the infected pancreatic necrotic collections, the technology that is available, the expertise of the centre, and the trained staff [19]. In patients with bigger collections extending into the paracolic gutters or the pelvic area, dual-modality drainage, commonly known as combined endoscopic transluminal and percutaneous catheter drainage, should be considered [1, 22]. Currently, metallic stents are used to connect the stomach and infected collections [20]. They were made in 2011 and have since been superseded by plastic stents [19]. These stents offer a broader field of vision, which improves drainage and makes transluminal necrosectomy easier [20]. The study found no differences in the median number of procedures, readmissions, or length of hospital stay, making it the best available data [22]. The study examined the efficacy of plastic & metal stents in the drainage of infected pancreatic necrosis [1-6, 20].

The metallic stents' drawbacks include greater procedure costs and stent migration that have been reported [1]. To reduce the risk of problems, the most recent consensus guidelines advise using metal stents or double pigtail plastic stents for endoscopic transluminal drainage and removal after 4 weeks [1-4].

3.2.3. Surgical Necrosectomy

23-47% of patients will improve with percutaneous or endoscopic drainage [3]. Only with percutaneous or endoscopic drainage can patients' conditions improve in 23-47% of cases [4]. Surgery is the next course of action for people with chronic illness [4]. The goals of surgical debridement are to minimise the pro-inflammatory effects of the procedure on the compromised patient while controlling the infection's cause and lessening the burden of neurosis [5]. The current trend is to avoid any unnecessary intrusion [3-5, 24]. If the video assisted retroperitoneal approach is insufficient, an open approach is used to execute necrosectomy [20].

3.2.4. Video assisted retroperitoneal debridement (VARD) in infected necrotizing pancreatitis.

Several methods have been described, including VARD, which has much lower incidence of abdominal problems than the majority of traditional methods [24]. The collection is guided by radiological drainage in this method, thus keeping it as long on the left side as possible is crucial [25]. For intra cavitory video aided necrosectomy, the tract created by the anterior drainage is used to enter the

retroperitoneal area [25]. Under direct vision, traditional laparoscopic devices are employed [3, 24, 25].

We can leave strategically placed drains so that washing is possible [2]. To get rid of the infected pancreatic necrosis, the procedure might be repeated if necessary [3, 4]. It should be highlighted that the VARD technique is more successful in treating pancreatic necrosis caused by central to left paracolic infection [26]. It should be highlighted that the VARD technique is more successful in treating pancreatic necrosis caused by central to left paracolic infection [2-5, 26]. Accessing the necrosis close to the mesenteric arteries will be more challenging [26].

3.2.5. Surgical Trans Gastric Debridement

Endoscopic trans gastric drainage is similar in concept [1]. It may be carried out openly or laparoscopically [2]. To access the rear face of the stomach and the contaminated cavity, an anterior gastrotomy is necessary [2, 3]. It is especially helpful because they have no effect on the flanks in central collections [3]. It is advisable to leave a washing-related drain inside the hollow [3]. There are small-scale studies that show the technique's effectiveness with little morbidity [1-3, 29].

3.2.6. Open Surgical Necrosectomy

If these treatments fail to control the infectious illness, the patient's worsening health despite satisfactory drainage from minimally invasive surgery would point to the need for an open surgical procedure [2-4]. The patient will benefit more from delaying surgery as much as feasible in terms of mortality and morbidity since the mortality of patients with infected necrosis is greater than 30% [2-4]. A considerable rise in mortality is caused by early debridement, particularly sterile necrosis [2-4, 27]. These methods are therefore saved for situations where all other options have failed [27]. We have extensively covered open necrosectomy methods [27].

None of them has been shown clearly superior to the other due to lack of randomized studies, but the ones that offer the best results are: [1-6]

- Open surgical necrosectomy with closed packing; described by A.L. Warshaw with lower mortality rates than the other techniques (10%) and that would be indicated in limited necrosis.
- Open surgical necrosectomy with closed post-operative lavage; in case of more extensive necrosis. The recommended wash would be 12-24 litres every 24 hours with potassium free dialysis fluid.
- Open surgical necrosectomy with open packing: it is the technique with the highest mortality-morbidity, but it would be indicated in cases with more extensive necrosis that exceed the colon.

When abdominal closure is not attainable or when abdominal compartment syndrome is present, vacuum assisted closure therapy will be employed as a temporary closure [1-3].

Given the severity of the condition, which is frequently higher in individuals with a high necrosis load that is diffusely spread

throughout the abdomen and who do not respond to staggered management, current comparative research, except for randomised trials, should be regarded with caution [1-3].

4. Discussion

ANP was traditionally treated with surgical necrosectomy [2, 25]. This invasive procedure carries a very high risk of pancreatic failure along with a significant percentage of complications (34–95%) and mortality (11-39%) [25]. In the management ANP, the “step-up approach” is currently regarded as the benchmark [20]. It entails a multi-disciplinary examination and the use of methods that are least invasive and as progressive as possible, such as retroperitoneal necrosectomy and percutaneous endoscopic drainage [1-6]. The first method is percutaneous drainage, which may be followed by endoscopic drainage or video-assisted necrosectomy [6].

However, even when the step-up approach is adopted, it may still be necessary to resort to surgical necrosectomy without any delay to risk deteriorating the clinical outcome.

Open surgery has precise indications [1-6, 25].

- 1) Onset of compartment syndrome
- 2) Bleeding which cannot be controlled with interventional radiology techniques.
- 3) Intestinal perforation
- 4) Intestinal or biliary obstruction resulting from extrinsic compression.
- 5) Failure of minimally invasive techniques employed previously with persistence of sepsis.

Percutaneous drainage alone has been reported to have a success rate of more than 50% in the literature [2]. Similarly, other studies have shown that endoscopic procedures have an acceptable effectiveness rate between 75% and 95% [2, 3]. However, lengthy and unsuccessful non-surgical treatment followed by conversion to surgical treatment can raise fatality rates [2, 5, 26]. It is challenging to predict in advance which patients will benefit poorly from non-invasive treatments and who would fare better if they underwent surgical necrosectomy as a first step [27]. To date, it has not been possible to identify prognostic factors that can predict the success of noninvasive techniques [26]. Undoubtedly, the collection's substance as well as the quantity and location of the collections can indicate if a percutaneous approach is best [27]. The choice of the initial intervention therefore depends on several variables, including the length of time from the onset of symptoms and the location, size, and kind of necrotic collections [20]. The standard treatment for ANP must be the step-up strategy [1-6, 28-30]. Even in the case of a bleeding issue, it is advised to use interventional radiology and minimally invasive surgery procedures wherever possible [27]. This procedure necessitates a lengthy hospital stay, but it lowers the morbidity and mortality risks and guarantees greater pancreatic function in the residual organ [20].

5. Conclusion

Acute necrotizing pancreatitis patients should be treated by skilled pancreatic surgeons, endoscopists, and radiologists in centres with a high level of experience. A group of anaesthesiologists or intensive care specialists is necessary, especially in the early weeks of evolution. The morbidity and mortality rates for these individuals are remain high despite these interventions, therefore we must work to lower them through proper management and the “step-up approach”. The sequential treatment, which also includes percutaneous drainage, endoscopic (trans gastric) drainage, and minimally invasive retroperitoneal necrosectomy, is an alternative to open necrosectomy. With this method, it is possible to cure up to 35% of patients just with drainage, avoiding necrosectomy and lowering the incidence of sequelae.

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