“Step Up” Approach in the Management of Pancreatic Necrosis. Is it A Step in the Right Direction?

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Editorial

Acute pancreatitis is a relatively common, potentially life threatening disease that is often associated with biliary disease or alcohol consumption [1-3]. While majority of the patients with pancreatitis have a benign course and are likely to be discharged within a week to ten days of conservative management, the rest may encounter an unpredictable severe course [2,3]. Around 20% of them develop necrosis of the pancreas or peripancreatic fat tissue with or without peripancreatic collection [1-3]. These are associated with a mortality of 15-30%, in sharp contrast to 0-1% mortality seen in patients with mild pancreatitis [2]. While in the initial two weeks the mortality is related to organ failure in response to systemic inflammatory response syndrome (SIRS), in the subsequent weeks the organ failure is due to a counteractive anti-inflammatory response syndrome (CARS) [1]. The ensuing organ failure in CARS is invariably a consequence of infected pancreatic necrotic tissue. The pancreatic necrosis is at risk of developing infection in 30% of the cases, usually within [3,4] weeks after the onset of pancreatitis [2]. If left untreated, the mortality could approach 100% [3]. Should these patients be dealt by an initial aggressive surgical approach or is a graduated “step up management plan” with initial percutaneous drainage followed by minimal invasive debridement, a step in the right direction? Would this lead to a paradigm shift in the management of infected pancreatic necrosis in the future?

Off late, several studies on the step up approach in the management of infected pancreatic necrosis have been reported [4-20]. The enthusiasm in the step up management was raised by the results of the Dutch multicenter-randomized trial (PANTER) in patients with infected pancreatic necrosis who were either subjected to step up approach or open necrosectomy [4]. The step up approach consists of percutaneous drainage, followed if necessary, by drain-guided minimally invasive necrosectomy [4,5]. The outcome of this approach was associated favourably in the PANTER trial with a significant reduction in major complications and costs [4]. Importantly, in 35% of the patients no further intervention other than percutaneous drainage was required [4]. For few decades prior to the Dutch trial, percutaneous drainage has been a subject of many, mostly uncontrolled observational studies [7,8]. Success rate of percutaneous drainage alone has been observed in several studies and ranged from 25% to 55%; this was further emphasized in one of the recent systematic review [7]. Among these patients, 77% had preoperative organ failure and despite 99% technical success rate there was 17% mortality rate in them [7].

PCD is an important adjunct and is the first step of the step up approach [7]. Catheters are placed optimally in the left or right retroperitoneal space based on the location of the collection. The size of the drains used varies from 8 to 28 Fr and is occasionally dilated stepwise [7]. The catheters are flushed daily with saline, usually every 8 hour. The daily flushing in combination with the frequent need for catheter replacements makes PCD a relatively intensive and time consuming therapy. However, in majority of the cases only one replacement of catheter with a median size of 14Fr is required [4,6,7]. There may be some difference in the timing and indication for placement of PCD. While some would place PCD after confirmation of infection on FNA in the second and third week, others would treat initially such patients with antibiotics and consider PCD on further clinical deterioration [4,5,6-8]. However, the concern is that of some clinicians being overambitious in draining every necrotic tissue; this should be carried out only when there is a definite evidence of infection of the necrotic tissue as reflected by deterioration in clinical condition despite maximal conservative treatment or bacteriological evidence on FNA. Early placement of PCD in patients without definite evidence of infection may lead to the risk of infection of uninfected pancreatic necrosis with further clinical deterioration; hence may be counterproductive [4,7]. In one of the reports, culture negative collections became more frequently infected after PCD than after simple fine needle aspiration (13 of 22 versus 3 of 15 respectively; p<0.03) [21]. Successful treatment of infected pancreatic necrosis with PCD alone has been reported in 30-55% of the cases [4,6-8].

In the event PCD fails to achieve clinical improvement, the next step in the step up approach would be necrosectomy [4-8]. Necrosectomy is performed by a minimally invasive approach, usually in the fourth week [4-8]. By then, the necrotic tissue would have walled off, reducing the risk of injury to adjoining structures during necrosectomy [22,23]. Minimally invasive necrosectomy is performed by different techniques. This could involve endoscopic transluminal necrosectomy (ETN) [17-20], or percutaneous minimally invasive retroperitoneal necrosectomy using scopes (nephroscope or laparoscope) [4,6,9].

Endoscopic transluminal necrosectomy is appealing as it is the least invasive of all the minimal invasive approaches [17-20]. The infected walled off pancreatic necrotic tissue is accessed transluminally, usually puncturing the stomach wall or duodenal wall. Under direct vision or endoscopic ultrasound guidance, the gastric wall is punctured to reach the walled off necrosis [17-20]. The transluminal tract is dilated sequentially using a balloon. Short pigtail catheter drains or stents can be used to prevent closing of the access to the retroperitoneum after the initial procedure [17]. Continuous irrigation can be carried out, by placing a nasocystic catheter in the necrotic cavity [24]. In order to avoid additional interventions, multiple transluminal gateways have been suggested to improve drainage of infected material and in a small cohort of selected patients, success has been achieved in 90% of these
In case the ETN fails or is not feasible to perform for some technical reasons, then in those cases the patients undergo minimally invasive retroperitoneal approach for debridement. These approaches include sinus tract endoscopy (STN) also referred to as minimal access retroperitoneal necrosectomy, (MARPN), using scopes like nephroscope or laparoscope [8,27,28]. The other approach is Video Assisted Retroperitoneal Debridement (VARD) [6]. In both procedures, access to the necrotic pancreas is achieved by following the tract of a radiologically placed drainage catheter [6,8,27,28].

In STN, which was pioneered in the Glasgow Royal Infirmary, Glasgow, UK and then modified by Liverpool group, a nephroscope is inserted into the infected collection after dilatation of the drain tract to 30 Fr under fluoroscopic guidance [8,27,28]. Long forceps are used to carry out the debridement and the necrotic cavity is flushed using a jet irrigation and suction devices [20,29]. Some of these patients may require repeated interventions in the event they fail to recover with the possible residual infected necrotic tissue being retained. A median of three to five procedures is needed for adequate necrosectomy [8-10].

The VARD technique was developed in the university of Washington Medical centre, Seattle, Washington, USA [30]. The retroperitoneal space is approached through the left flank and occasionally through the right, using a 5 cms subcostal incision close to exit point of the percutaneous drain [6,30]. The cavity is entered using the drain to guide. The content of the cavity both fluid and loose tissues are removed with long forceps after initially entering the cavity with blunt dissection [30]. After initial debridement using finger dissection, a 10 mm, 30 degree laparoscope is inserted through the incision into the cavity to assess the completeness of necrosectomy. The cavity is then insufflated through the percutaneous drain with carbon dioxide. Under direct vision, the loose necrotic tissue is then removed [6,30]. Necrotic tissue that are adherent and cannot be easily removed are left behind to resorb. The goal of both the procedures is to remove as many loosely adherent pieces of necrotic tissues as possible and not to remove all necrosis, in order to reduce the risk of bleeding [5,6,8,11,14]. A 28 Fr catheter is placed into the cavity for drainage and postoperatively about 2 L of normal saline is used for daily irrigating the cavity through the smaller drain tube which is drained through the larger drain. Daily lavage is continued until the drainage becomes clear and the patient improves symptomatically. The patient is discharged with the larger drain in situ and this is removed during the subsequent follow up once the drain becomes nil and the absence of collection is confirmed on ultrasound [6,8,9,11,30]. While repeated interventions may be required with percutaneous techniques, VARD technique is mostly a one staged procedure [6,30]. ETN is generally considered as a preferred procedure for centromedial collections in the head and neck that abut the stomach and duodenal walls, the location most problematic for VARD [6]. But the paracolic gutter and pelvic collection, which are often seen in patients with pancreatic necrosis cannot be accessed by ETN and are more suited to be dealt by VARD [6].

Open surgical necrosectomy

If the minimally invasive approach fails in improving the condition of the patient, and the pancreatic necrosis persists, then an open necrosectomy may be warranted (Figures 1 and 2) [23,31-34].
morbidity attributed to exacerbation of stress induced by the surgery, in an already critically ill patient [28]. The minimally invasive approach was designed to reduce this risk.

Timing of intervention

A Multidisciplinary team including gastroenterologists, interventional radiologists, surgeons and intensivist, should evaluate the need and choice of intervention [1]. Postponing interventions until the intra- and/or extrapancreatic collections are encapsulated is beneficial, and this process usually takes around 4 weeks [1,5,6-8]. Such encapsulated collections called as walled off necrosis ensures debridement of necrotic tissue with minimal damage to the adjoining structures, particularly the vessels [6-11]. Those patients who develop infection at an early stage (2-3 weeks) would need to be managed with broad spectrum antibiotics and percutaneous drainage till the necrosis walls of at 4 weeks [1-3,5,8].

Impact of step up approach

Most recent series suggest a decrease in mortality, due to the use of minimally invasive approach. This reduction is significant from over 30 to 15-20% [4,6-12]. PCN is among the least invasive technique for treatment of infected necrosis and importantly has a success rate of 25-55% and these patients would not need further treatment like surgical necrosectomy [7]. In patients who did require surgical intervention, PCN allowed additional intervention to be postponed for several weeks [7,8].

Over the past two decades, PCD has been used increasingly as a primary minimally invasive treatment for necrotising pancreatitis with proven or suspected infection. The rationale for such treatment is to improve the clinical condition of these usually seriously ill patients by drainage of infected fluid (pus) under pressure [1,7,8]. This would either achieve to postpone surgical intervention or even avoid the need for surgical necrosectomy [7,8]. ETN is the next approach, and is also less invasive compared to other minimally invasive approach. In a recent systematic review of 233 patients in eight studies, success rates following ETN was noted in 80 to 93% with a low mortality ranging from 0 to 6% [18]. The mean size of the necrotic cavity in this review was reported to be 12.87 cms (10.54 to 15.20 cms) and the mean number of endoscopic procedures required to resolve the necrotic cavity was 4.09 (2.31 to 5.87) [18]. The pooled proportion of recurrence in the form of persistence of cavity or pseudocyst was 10.88% and the surgery for failure to treat with ETN was required in 12.98% of the cases [18]. Complications were noted in 21.33% (bleeding, sepsis, perforation) and the mean number of days of hospital stay was 32.85 days [18]. Unfortunately, most of the publications in this systematic review suffered from selection bias and some had unacceptably low rate of infection, raising the question of the need of necrosectomy in some of these patients in the first place.

Patients in whom the above procedures have failed to achieve a clinical improvement, will need to undergo minimally invasive approach for pancreatic debridement. Several reports indicate the benefit of these minimally invasive approach. In one of the recent reports were VARD was employed in 23 patients with infected pancreatic necrosis, a low rate of ICU stay (median of 4 days- range 2-14 days), shorter hospital stay (mean postoperative stay of 22.5 days (± 6.6 days) and low incidence of re-intervention (11.5% - 3 out of 26 patients) was reported [9]. The PANTER trial noted a significant reduction in major complications and costs. Major morbidity was noted in 40% versus 69%; P=0.006 and new onset multiple organ failure in 12% versus 40%; p=0.002, between the step up and primary necrosectomy group respectively [4]. Nearly half of these patients undergoing minimally invasive approach would require surgical necrosectomy due to failure to achieve clinical improvement [4,6,8]. The concern however is the overall mortality between the two groups is similar. A recent review (1994-2008) of 11 series with more than 100 patients undergoing open necrosectomy reported a mean mortality rate of 19% [35]. The same study also observed a mortality of 19% in a series of 137 patients undergoing minimally invasive necrosectomy [35]. In a pooled data of a recent systematic review, 21.2% of patients had one or more complications, with nine reported procedure related complications [7]. Series on surgical necrosectomy reported a considerably higher complication rate, ranging from 34 - 68% [33,36]. The risk of pancreatic fistula was noted in 15% of patients undergoing minimally invasive procedure compared to 22 to 47% in the studies on surgical necrosectomy [37-39]. Most of the studies do not report late complications. Late complications were however reported in PANTER trial and a 6 month complication rate of 30% was noted in the step up group and included incisional hernia (7%), endocrine insufficiency (16%) and the need for pancreatic enzyme supplementation (7%) [4].

So it appears that the management of infected pancreatic necrosis is demanding with the options of several modalities at hand. Over the years there is a definite trend in delaying the necrosectomy to around 4 weeks and beyond, by when the necrosis walls off. The initial approach in all these patients where the necrosis is confirmed to be infected, is a step up approach. PCN, which is the first step in this approach, while being least invasive, achieves success without the need of any further intervention in one third to half the number of cases. Those patients who fail to respond, can be managed by ETN. ETN however while being least invasive compared to other minimally invasive approach and with reported good results in outcome emerging from some specialized centers is most suited for centromedial necrosis. The minimally invasive approach including VARD has been reported (including in the recent RCT- PANTER trial) to significantly reduce the costs, hospital stay and morbidity. Those of these patients who fail to respond to the above measures may need open necrosectomy. Recent reports however suggest that while there are distinct advantages in minimally invasive approach as delineated above, the mortality between the 2 groups (minimally invasive and open) is similar. A significant number of these patients also have early and late complications, though significantly less in minimally invasive group than in the open approach one. This may reflect the severity of illness in these select group of patients who fail the lesser invasive approach (PCD or ETN) initially. Based on the present evidence it appears that the step up approach is the step in right direction in the management of these patients. However because of the gravity of the illness, certain degree of morbidity and mortality is unavoidable in some of these critically ill patients.

References