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REVIEW

Application and Value of Percutaneous Catheter Drainage in Contemporary Surgical Treatment of Pancreatic Necrosis

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Abstract

Acute necrotizing pancreatitis (ANP) is a relatively severe disease in clinical practice, and the selection of treatment strategies has a significant impact on the prognosis of patients. Percutaneous catheter drainage (PCD) serves as an effective treatment method and holds an important position in the treatment of ANP. With the in-depth development of medical research, the intervention strategies and management methods for ANP are constantly evolving. However, there is still controversy regarding when to adopt the step-up approach. This review aims to elaborate on the role of percutaneous catheter drainage, different drainage timings, and the evaluation of various drainage techniques, explore the current status and deficiencies of the research, with the expectation of providing more scientific and reasonable treatment decision-making basis for clinicians in dealing with ANP.

Introduction

Acute pancreatitis (AP) is one of the most common gastrointestinal diseases. Pancreatic fluid collection (PFC) is a well-known complication, which is caused by the entry of proteolytic fluid into the adjacent peritoneal cavity due to pancreatic injury. It is an abnormal accumulation of fluid and/or debris inside and around the pancreas. According to the revised Atlanta classification [1], PFC can be divided into: acute peripancreatic fluid (APF), pancreatic pseudocyst (PP), acute necrotic collections (ANC), and walled-off necrosis (WON).

Although AP is mild and self-limited in most patients, approximately 20% of patients will develop ANP, and 40 to 63% of them require intervention [2]. About one third of patients with NP develop infected pancreatic necrosis (IPN), which leads to an increased mortality rate and a prolonged hospital stay [3], and the mortality rate can increase to 35% [4]. For patients with infected necrosis or symptomatic pancreatic fluid collection, the American Gastroenterological Association recommends drainage and/or debridement of pancreatic necrosis [5]. The step-up approach consisting of percutaneous catheter drainage or endoscopic drainage is usually the first line treatment. If the drainage does not lead to clinical improvement, then minimally invasive or open pancreatic necrosectomy (OPN) is performed.

Overview of PCD Treatment

Before the twentieth century, the treatment of IPN was mainly conservative [6]. With the deepening of understanding of the disease, the concept of OPN gradually reached a consensus about 10 years ago [7]. Entering the twenty-first century, more and more evidence has shown that minimally invasive treatment is superior to open surgery [8, 9]. The landmark Dutch multicenter randomized trial of step-up minimally invasive approach versus necrosectomy for patients with necrotizing pancreatitis (PANTER) demonstrated that the step-up approach from PCD to minimally invasive surgery is as effective as open surgery, with better short- and long-term clinical outcomes and fewer complications [8].

As an alternative to open surgery, the step-up approach aiming to control the source rather than completely resect the pancreatic necrotic tissue has been advocated as the standard treatment for NP [5]. For PCD, the Seldinger and tandem trocar techniques are used, and most radiological interventions are guided by ultrasound or CT. The size of the drainage tubes used ranges from 8 to 28 Fr (2.7 to 9.3 mm)

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[10]. The guidelines recommend drainage for infected or symptomatic pancreatic necrosis, including patients with compressive symptoms (resulting in gastric outlet obstruction or biliary obstruction), unrelieved organ failure, persistent systemic inflammatory response syndrome, and intra-abdominal hypertension [11]. The rationale for this treatment is to improve the clinical condition of these severely ill patients by draining the infected fluid under pressure, thereby delaying surgical intervention and even avoiding the need for surgical resection of necrosis. In addition, PCD can be used as an adjunct to endoscopic drainage (as part of bimodal drainage) or as a route for necrosectomy (endoscopic or minimally invasive surgery).

It remains inconclusive which patients can benefit from PCD. Moreover, repeated minimally invasive treatments and relatively insufficient surgical interventions may also lead to the delay and subsequent deterioration of the patient's condition [12, 13] For patients with IPN who have poor treatment results, it is very necessary to resolutely choose the next stage debridement treatment. OPN as the ultimate means of the step-up treatment concept, still needs to be rationally considered.

Timing of PCD

Regarding the optimal timing of PCD, different studies hold varying opinions. International guidelines recommend waiting at least 4 weeks after the onset of AP before any invasive treatment. This waiting period allows the fluid collection time to form an adequate encapsulation [14]. Such encapsulation can clearly distinguish the necrotic tissue from the normal tissue, thereby leading to better prognosis. However, the recommendation for delayed intervention is mainly based on studies of open surgical intervention. For minimally invasive treatment, early drainage may prevent the escalating inflammatory response or cytokine storm [15], and whether to delay treatment remains to be clarified.

The study by Sugimoto et al. indicates that if PCD is actively performed in the early stage of necrotizing pancreatitis, before the development of severe sepsis, better outcomes can be achieved [16]. For patients with symptomatic pancreatic necrotic fluid collection [17, 18], early intervention does not increase the mortality rate or the incidence of complications. In addition, some experts believe that patients with pancreatic necrosis and early persistent organ failure (POF) have a higher mortality rate, and delaying the intervention for up to 4 weeks may affect the risk of death [19]. For patients with non-encapsulated early infection and failed conservative treatment, the clinical guidelines of the American Gastroenterological Association recommend catheter drainage [5]. A randomized study found that [20] there were no differences in overall complications, mortality, average length of hospital stay, and costs between standard treatment (including delayed catheter drainage until the pancreatic necrosis was encapsulated) and immediate catheter drainage (within 24 h), but the latter had a higher total number of interventions. In the delayed drainage group, approximately 40% of the patients did not require surgical or non-surgical treatment for necrosis. In the POINTER trial [21], as long as the patient's clinical condition is appropriate, delaying drainage should be the preferred option and will not lead to long-term adverse outcomes in patients with IPN. Gao et al. conducted a meta-analysis [22], which showed that compared with delayed intervention, early intervention in patients with IPN did not increase the mortality rate but led to a longer hospital stay and a higher incidence of gastrointestinal fistula or perforation. Another study reached a similar conclusion. Nakai et al. believed that the step-up approach after delayed intervention is reasonable in terms of safety and effectiveness [23].

Even sterile ANC may contain inflammatory mediators and pancreatic enzymes, which can lead to systemic inflammation and long-term organ failure [24]. For patients with sterile pancreatic necrosis who have persistent discomfort or associated complications, drainage and/or debridement is required [5, 14]. A small-scale randomized trial evaluated the safety and feasibility of early PCD versus standard treatment in patients with acute pancreatitis complicated by ANC and early POF [25]. It was found that early PCD reduced mortality/major complications and shortened the duration of organ failure, but the results were not statistically significant. Inserting a drainage tube into sterile peripancreatic fluid collections may introduce bacteria, leading to secondary infections. Not all such infections are classified as iatrogenic infections because in the early stage of the systemic inflammatory response, the intestinal barrier is often damaged, and sterile necrosis may become infected due to bacterial translocation through the intestinal wall or systemic infection [26]. A retrospective analysis of cases of sterile PFC and AP of different severities showed that the mortality rate of patients with severe acute pancreatitis (SAP) who developed infections after early PCD was significantly lower than that of patients with spontaneous infections [26]. Other studies also showed that there was no evidence that early PCD increased infectious complications [25]. However, for patients with moderately severe acute pancreatitis (MSAP), early PCD may not provide any clinical benefits and may even induce more iatrogenic infections and require more debridement [26].

We believe that PCD treatment for clinically stable patients is best delayed until the appearance of walled-off necrosis. In patients with ANP, although early intervention is more beneficial than delayed intervention in reducing and improving the inflammatory response, early intervention is more suitable for ANP patients with POF. Existing studies

have not clearly confirmed the relationship between early PCD treatment and infectious complications, and there are still relatively limited systematic studies on sterile pancreatic necrosis.

Indications and Timing for Step-up Therapy

In 1998, Freeny and colleagues first described the use of PCD for the treatment of IPN [27]. In their retrospective cohort study, PCD successfully postponed surgical intervention for a median of four weeks and even obviated the need for surgical necrosectomy in nearly half of the patients. Similarly, other studies have shown that 35% of patients survived after percutaneous or endoscopic drainage alone, without the need for necrosectomy [8]. Currently, it is unclear which subgroups of patients can be successfully treated with catheter drainage alone and which patients require additional necrosectomy. Identifying the factors predicting the success of PCD is crucial to determine the subgroups of patients who need aggressive treatment from the outset. The clinical course of ANP is variable, and the timing of intervention depends on the patient's clinical condition and the extent of necrotic collections. Table 1 describes the influencing factors of the step-up approach.

Clinical Conditions and Intervention Timing

Previous studies have shown that body mass index and diabetes are associated with the need for surgical intervention after initial drainage treatment [28, 29]. As the initial intervention in the step-up approach, PCD changes the natural course of the disease by reversing sepsis and organ failure. Some studies have reported the utility of inflammatory markers in predicting the response to PCD [30]. The percentage reduction of interleukin-6 (IL-6) on the third day and C-reactive protein (CRP) on the seventh day is associated with the outcomes of patients treated with PCD. Higher CRP levels can predict the failure of catheter drainage and the need for subsequent surgery [31, 32]. Babu et al. described that an Acute Physiology and Chronic Health Evaluation II (APACHE II) score exceeding 7.5 at the time of the first intervention can predict the need for surgery [32]. Other studies have also shown that PCD can avoid surgical intervention in patients with an APACHE II score of less than 15 and is associated with improved outcomes [33].

Persistent organ failure and multiple organ failure as factors predicting the failure of catheter drainage have been confirmed in multiple studies [31]. Organ failure may increase the likelihood of surgical intervention [32]. Both single organ failure and multiple organ failure are risk factors for PCD failure [34]. Garrett et al. found that the occurrence of respiratory failure within 24 h before the first PCD can predict the failure of catheter drainage [28]. However, Hollemans et al. believed that only multiple organ failure is a risk factor for PCD failure [35]. This may be because patients with multiple organ failure often have more severe conditions, higher mortality rates, and a poorer response to catheter drainage.

Necrotic Accumulation and Intervention Timing

A retrospective analysis showed that the extension of WON to the paracolic sulcus was associated with the need for surgical intervention after initial endoscopic treatment [29]. Compared with patients with right or middle retroperitoneal drainage tubes, patients with left retroperitoneal drainage tubes were less likely to require open

Table 1 Predictors of step-up therapy after PCD treatment

Factors	Study results	Source
Biomarkers	Higher CRP levels can predict catheter drainage failure	Shenvi et al., [31]、Mallick et al., [30]
Scoring Systems	APACHE II score and BISAP score are associated with surgical intervention	Mukund et al., [33]、Venkatesan et al., [49]
Organ Failure	Single or multi-organ failure is a significant risk factor for step-up therapy	Huang et al., [34]、Garret et al., [28]
Fluid Distribution	The location of fluid accumulation is associated with step-up therapy	Papachristou et al., [29]、Zhang et al., [26]
Extent of Pancreatic Necrosis	Pancreatic necrosis > 50% significantly increases the need for step-up therapy	Shenvi et al., [31]、Hollemans et al., [35]
Characteristics of Necrotic Fluid	Higher CT density is associated with step-up therapy; Changes in fluid can predict the success rate of PCD treatment	Huang et al., [34]、Ji et al., [45]、Bellam et al., [37]
Infection	Concurrent infection increases the frequency of surgical debridement	Jiang et al., [48]
Baseline Characteristics	Diabetes and high BMI may increase the risk of step-up therapy	Garret et al., [28]、Papachristou et al., [29]

necrosectomy [36], possibly because there are more organs on the right side of the abdominal cavity than on the left, making right retroperitoneal drainage more likely to fail. In contrast, some studies have shown that the collection location does not affect the outcome [37].

Acute necrotizing pancreatitis is a dynamic disease, and radiological changes after the initial placement of PCD play an important role in determining the outcome of PCD. Some studies have reported that the volume of fluid collection does not affect the success rate of PCD drainage [38]. Bellam et al. also supported the view that the initial volume of fluid collection cannot predict the outcome, but a reduction in the volume of fluid collection one week after PCD was an independent predictor of a successful PCD outcome [37]. Cao et al. reported that > 50% reduction in the volume of fluid collection on the third day was a predictor of PCD success [38]. Horvath et al. found that a 75% reduction in the collection volume 10–14 days after PCD could predict PCD success with 100% accuracy [39].

It is generally believed that well encapsulated, homogeneous, or predominantly liquid pancreatic necrotic tissue is more suitable for PCD [40]. PCD treatment often fails due to the severe condition of the patient. The degree of pancreatic necrosis and the amount of solid debris are associated with the need for more aggressive treatment [41]. Liu et al. pointed out that a maximum degree of pancreatic necrosis exceeding 30% was associated with an increased likelihood of necrosectomy [42]. Other studies have shown that patients with more than 50% pancreatic necrosis have a negative impact on the success rate of catheter drainage [31, 32, 35]. A prospective study showed that patients with only peripancreatic necrosis had a lower need for intervention than those with parenchymal necrosis with or without peripancreatic necrosis [43]. Cao et al. [38] and Bellam et al. [37]found that the volume of extrapancreatic necrosis was not an independent risk factor for PCD failure. Recent studies have shown a positive correlation between the volume of extrapancreatic necrosis and PCD failure [34, 44], possibly because it contains more solid or semi-solid components.

After the establishment of PCD, the volume of pancreatic necrosis collection (PNC) decreases, and necrotic debris may aggregate and be difficult to drain. Therefore, the average CT density was introduced to quantify the heterogeneity of necrotic tissue [45]. In some studies, the heterogeneity of peripancreatic necrotic tissue was a risk factor for PCD failure [35, 46, 47]. A study by Huang et al. found that an average CT density value of necrotic fluid collection greater than 25 HU was an independent risk factor for PCD failure [34]. Ji et al. believed that when the average CT density exceeded 20 HU, the sensitivity for predicting the need for necrosectomy was 68.2% [45].

Infectious Pancreatic Necrosis

The frequencies of PCD treatment and surgical debridement were significantly increased in the pancreatic infection group and the group with pancreatic infection combined with extrapancreatic infection [48]. Reviewing the medical records of patients with IPN who underwent catheter drainage, a body mass index (BMI) > 25, multiple organ failure, and a Bedside Index for Severity in Acute Pancreatitis (BISAP) score ≥ 4 were independent negative predictors of successful catheter drainage [49]. The Dutch Pancreatitis Study Group found that male gender, multiple organ failure, an increased percentage of pancreatic necrosis, and heterogeneity of pancreatic fluid collections were predictors of failed catheter drainage in patients with IPN [35].

Timing of Open Surgery

In the past decade or so, the step-up approach has become the mainstream mode of surgical intervention for SAP. However, in large specialized pancreatitis centers, the proportion of OPN still remains around 25%-60% [50]. OPN allows for faster and more thorough debridement in a single operation, which may be more beneficial for patients with mature necrosis. Over emphasizing the use of the step-up approach may lead to missing the optimal timing for surgical treatment, resulting in irreversible sepsis [12]. Huang et al. proposed that for appropriately selected patients with IPN, a leap frog intervention from "step-up" to "step-jump" (mainly OPN) could be considered [40]. A retrospective study by Ning et al. on early OPN for IPN confirmed that compared with minimally invasive step-up surgery [51], early OPN had a similar incidence and mortality rate but required fewer surgical interventions. The adverse reactions of salvage OPN were significantly higher than those of direct OPN.

The exploration of which factors may be associated with a high risk of failure of the minimally invasive step-up approach and may benefit from alternative approaches remains unresolved. Babu et al. found that renal failure, the APACHE II score at the time of the first intervention, and the number of bacteria isolated from each patient were independent predictors of OPN [32]. Li et al.'s study suggested that a computed tomography severity index (CTSI) > 8 points, the APACHE II score ≥ 16 points, early spontaneous bleeding within 30 days after the onset of acute pancreatitis, fungal infection, granulocytopenia and thrombocytopenia, and extrapancreatic necrosis aggregates in the small intestinal mesentery were independent risk factors for the failure of the minimally invasive step-up approach for IPN [52]. However, Gupta et al. found that the location and size of extensive pancreatic necrosis (EPN) were not associated with the need for ON [53], which may be related to the bias caused by the small

number of patients included in certain locations. The lack of improvement in clinical symptoms should always be an indication for open necrosectomy. In cases of acute pancreatitis complicated by abdominal compartment syndrome, colonic ischemia, and intestinal perforation, open necrosectomy remains the first choice [54].

Other Drainage Techniques and Approaches

Minimally invasive upgraded interventions (Minimally Invasive Surgery, MIS) include PCD, video-assisted retroperitoneal debridement (VARD), sinus tract endoscopic necrosectomy (STE), endoscopic transgastric necrosectomy (EN), or a combination of multiple techniques, with optional use of OPN [55]. PCD is increasingly used to stabilize critically ill patients as a "bridge to minimally invasive interventions". Once a percutaneous tract is established via the retroperitoneal approach, minimally invasive necrosectomy can be performed through STE or VARD. Table 2 compares different drainage techniques.

Traditional Minimally Invasive Techniques

The sinus tract necrosectomy was first described by Carter et al. in 2000 [56]. This technique involves pre-placement of a retroperitoneal drainage tube, intraoperative dilation of the percutaneous drainage tract, followed by irrigation, lavage, and aspiration using a surgical nephroscope with a large-caliber surgical channel. A continuous irrigation system is installed postoperatively until the necrotic tissue is cleared or until the next necrosectomy [56]. However, the working channel of the endoscope limits the scope and effectiveness of debridement, and each patient needs to undergo an average of 3 to 4 operations [57, 58]. Fistula formation and bleeding are the most prominent surgery related complications [58], and 14–26% of patients need to be converted to open surgery for further necrosectomy or treatment of complications [57].

More aggressive debridement can be performed using VARD, which was first described by Horvath and his colleagues in 2001 [59]. A 5 cm incision is made near the drainage orifice, and superficial necrotic tissue is removed under direct vision. Then, carbon dioxide is injected through the initial drainage tube to expand the cavity and improve

Table 2 Comparison of different drainage techniques

Technique	Benefits	Risks and downsides	Source
PCD	-Simple operation, minimal trauma, high safety -Suitable for early intervention and stable patients	-Limited efficacy in removing solid necrotic tissue -May require multiple interventions to maintain drainage -May lead to external pancreatic fistula formation	Rana et al., [41]
ETD	-Low risk of infection and no risk of pancreatic skin fistula	-Only applicable to fluid collections near the stomach or duodenum -High technical requirements, and may require multiple procedures	Santvoort et al., [66] Woo et al., [67]
DMD	-Combines the advantages of endoscopy and percutaneous drainage, reducing the risk of pancreatic fistula	-High technical requirements and requires multidisciplinary collaboration	Ross et al., [79]
STE	-Relatively simple operation	-Requires prior percutaneous drainage -Limited working channel restricts debridement range and effectiveness -Fistula formation and hemorrhage are the most prominent complications	Raraty et al., [57] Connor et al., [58]
VARD	-Visualization allows complete necrotic tissue resection in a single procedure	-Requires prior percutaneous drainage -High risk of pancreatic leakage	Brunschot et al., [60]
one-step laparoscopic-assisted necrosectomy	-Eliminates the need for percutaneous drainage; direct necrotic tissue resection for patients without a safe PCD approach	-Requires advanced minimally invasive techniques and highly skilled doctors -Risks concentrated in a single procedure	Cao et al., [61]
EN	-Enters the digestive tract via endoscopy, minimizing damage to surrounding tissues -Significant reduction in the risk of pancreatic fistula formation	-Typically applicable to necrotic tissue near the posterior wall of the stomach or duodenum -Multiple procedures may be needed for complete necrotic tissue removal -Requires professional endoscopic skills and experience	Onnekink et al., [87]

visibility. Further debridement is carried out using laparoscopic forceps or long grasping forceps. Usually, sufficient necrosectomy can be completed in a single operation [59, 60], followed by post-operative irrigation. It has been well established that the minimally invasive retroperitoneal approach induces a less pro-inflammatory response and is associated with a lower incidence of new onset organ failure compared with open necrosectomy [57]. Regardless of the technique used, both percutaneous catheter and retroperitoneal surgical approaches are associated with a high risk of pancreatic fistula.

One-Step Minimally Invasive Debridement of Pancreatic Necrotic Tissue

In 2015, Cao et al. developed a one-step minimally invasive debridement of pancreatic necrotic tissue [61]. This method omits percutaneous drainage and directly performs laparoscopic-assisted necrosectomy on patients with relatively good general conditions or those lacking a safe PCD puncture path. Studies have shown that this surgical approach reduces the risk of overuse in PCD treatment. Compared with the step-up approach, it does not increase the incidence of complications and mortality, requires fewer surgical procedures, and shortens the total length of hospital stay.

Endoscopic Transmural Drainage (ETD)

Drainage treatment of pancreatic fluid collections through endoscopic stent placement has become increasingly popular worldwide [62]. Usually, puncture is performed under direct vision or under the guidance of Endoscopic Ultrasonography (EUS). Transmural drainage tubes such as double pigtail or metal stents are placed into the cavity through one or more entries. The latter technique is called the multiple transmural technique [63].

PCD and EUS guided endoscopic drainage are more commonly used and have comparable efficacy. There are comparisons between the two methods, but such studies are few and heterogeneous [64, 65]. The advantages of endoscopic drainage over surgical drainage are a lower risk of infection and no risk of pancreatic cutaneous fistula [8, 66]. The initial drainage tube of PCD can reach 14/16 Fr, while endoscopic drainage can use at least 36 Fr during the first use, enabling drainage with a larger diameter [65]. The narrow diameter of PCD and the blockage of the channel by necrotic substances lead to poor efficacy. Therefore, PCD should be avoided in cases of WON with a solid debris content > 40% [41]. However, endoscopic drainage has practical limitations in terms of the location of necrotic tissue accumulation. Although most of the tissue accumulations in small cysts can be accessed endoscopically through the stomach or duodenum, endoscopic treatment is not advisable when the distance between the encapsulation and the gastric wall > 1 cm, as there is a risk of fistula formation [67].

Endoscopic Necrosectomy

For patients in whom EUS guided drainage is ineffective, EN is often required directly [41, 68]. There is still controversy about how long the interval should be between the initial stent placement and the first necrotic tissue resection. In order to remove necrotic tissue debris as early as possible, more and more endoscopists tend to perform EN with the initial stent placement. A study by Timothy et al. found that compared with EN alone, direct endoscopic necrosectomy during the initial endoscopic drainage can achieve a higher treatment rate and a lower recurrence rate [69]. Similarly, Linda et al. also found that simultaneous EN can minimize the need for additional necrosectomy [70]. On the contrary, some experts prefer to perform EN one week after the initial stent placement, which can reduce the risk of stent related adverse events and prevent unnecessary interventions [71]. A retrospective study of patients with infected WON compared the necrotic tissue resection within one week and one week after the initial stent placement [72]. The patients in the deferred group received fewer additional interventions, and there were no significant differences in clinical success rate, surgery related complications, and prognosis between the two groups. A study by Pawa et al. also showed that compared with patients who received immediate EN, delaying EN for one week after stent drainage can reduce the rate of additional re- interventions [73]. It is possible that as the disease progresses and the amount of necrotic tissue increases, more subsequent necrotic tissue resections are needed in the early stage. Patients who undergo deferred necrotic tissue resection have enough time to drain the necrotic tissue, and the necrotic cavity is more mature.

Dual Modality Drainage

Endoscopic drainage is limited to the necrotic sites adjacent to the stomach or duodenum. Although endoscopic drainage can reduce the risk of pancreaticocutaneous fistula compared with PCD [74, 75], it is difficult to perform endoscopic drainage if the fluid collection involves the pelvis, paracolic gutters and other sites. In addition, a large amount of fluid collection may be separated during the treatment process, resulting in the formation of isolated parts of WON, which can no longer be reached through the intraluminal approach. Endoscopic drainage can be combined with percutaneous drainage techniques [76], which is called dual modality drainage (DMD) [77, 78]. The basis of this technique is to take advantage of percutaneous drainage for irrigation and removal, and combine it with internal drainage to reduce the risk of pancreaticocutaneous fistula, thereby improving

the prognosis. Ross et al. reported that the dual modality approach allows the redirection of pancreatic juice back to the gastrointestinal tract, thus reducing the risk of chronic pancreaticocutaneous fistula formation in patients with disconnected pancreatic duct syndrome (DPDS) due to severe pancreatic inflammation [79].

Compared with the use of PCD alone, DMD is significantly associated with a reduction in the length of hospital stay and the duration of external drainage. The overall mortality and the need for surgery are similar in both groups [80]. However, some retrospective studies have shown that the clinical success rate of the endoscopic step-up approach is higher than that of the combined drainage approach (86% and 58%, respectively) [81]. In a retrospective study of symptomatic WON [82], both the endoscopic step-up approach and the DMD approach achieved a high clinical resolution rate. However, the clinical success rate and the length of hospital stay in the endoscopic group are often better than those in the DMD approach, which may be related to the amount of fluid collection in the left and right paracolic gutters.

Surgical Step-up Versus Endoscopic Step-up

In recent years, there have been numerous comparative studies on surgical step-up and endoscopic step-up approaches. If technically feasible, the endoscopic step-up method is a potentially less invasive alternative therapy and is preferred over the surgical step-up method. It offers multiple advantages in reducing complications [83–86], which may be related to the relatively lower physiological stress generated by EN using natural orifices as the route to access the retroperitoneal cavity. A long-term follow-up study of endoscopic and surgical step-by-step treatments found that the outcomes of the two methods were comparable. The endoscopic step-up procedure had a lower incidence of pancreatic fistula, but it was not superior to the surgical step- up procedure in reducing death or major complications [87]. For patients with IPN, the endoscopic step-up treatment is not superior to the surgical step-up treatment in reducing major complications or mortality [88, 89]. The differences among different studies may be due to fundamental selection biases. Some patients are only given an initial surgical intervention if they have indications for emergency surgery or if the necrosis is difficult to access, while endoscopic treatment is mainly used for other cases.

Currently, it is still unclear which minimally invasive method is more suitable for treating necrotizing pancreatitis. The optimal approach should be tailored to the individual patient's condition. EN is a high level intervention that requires the expertise of interventional endoscopists, as well as the joint participation of interventional radiologists and pancreatic surgeons to handle potential complex situations. For these reasons, at present, the surgical step-up approach remains the preferred treatment for IPN in most centers. PCD and minimally invasive retroperitoneal necrosectomy are still important adjuncts or alternatives to endoscopic treatment for WON in many cases.

PCD Management and New Technologies

In the early stage of pancreatitis, a large amount of inflammatory exudate accumulates in the abdominal cavity, leading to a sharp increase in intra-abdominal pressure, causing a series of symptoms such as abdominal pain and distension, and may further aggravate organ dysfunction. Abdominal paracentesis drainage (APD) can create favorable conditions for subsequent PCD treatment. The drainage tube should be removed early (< 72 h) to reduce secondary infection. A study by Lu et al. showed that early application of APD in patients with AP was associated with a reduction in mortality, in-hospital costs, and length of hospital stay, without significantly increasing the risk of infectious complications [90]. The mortality rate in the APD combined with PCD group was significantly lower than that in patients who only received PCD treatment, and the average interval from the onset of the disease to further intervention was also shortened in the former group [91]. For patients with IPN, the clinical outcomes of those who received or did not receive abdominal paracentesis were similar [36].

The efficacy of PCD can be improved by actively using drainage tubes. Specific measures include using multiple drainage tubes, increasing the size of the drainage tube, performing large—volume saline irrigation, and using necrolytic agents. A recent study compared an active PCD strategy (including frequent catheter replacement and increasing the catheter size to effectively drain the fluid collection) with a standard PCD strategy [92]. The results showed that the former had a lower incidence of new organ failure, a lower incidence of sepsis, and a lower need for necrosectomy. Conversely, some studies have shown that there were no significant differences between the two groups in terms of mortality and the need for surgical intervention [93]. The size and number of drainage catheters seem to be reasonable factors determining the outcome of percutaneous drainage. Larger inner diameter catheters are considered more effective in draining solid necrotic debris. A study by Gupta et al. found that large size catheters were associated with better clinical outcomes [94]. However, most studies have shown that the number and size of drainage tubes do not seem to affect the success of PCD [33, 35, 37, 49]. This may be because the solid necrotic tissue debris will gradually liquefy, which facilitates the drainage of the contents and is independent of the catheter itself.

The main reason for the failure of PCD is the predominance of solid necrosis. To improve the patency of PCD and accelerate the dissolution of solid necrotic tissue, various methods have been used. The most commonly used method is to flush with a large amount of saline [32]. Usually, the drainage tube is flushed with normal saline every 8 h, and the tube is replaced when it is blocked [10], with a success rate ranging from 48 to 66% [32, 95]. Bhargava conducted a randomized trial on patients with necrotizing pancreatitis who showed no significant improvement in symptoms after 72 h of saline irrigation following PCD [96]. The results showed that compared with continued saline flushing, streptokinase flushing led to a significant reversal of sepsis, a significant reduction in the APACHE II score and the modified CTSI score, a significantly lower need for surgery, and a reduced risk of bleeding. This may be because streptokinase has fibrinolytic effects, which fragment the surrounding necrotic tissue and completely digest the supportive collagen framework in the fragmented necrotic tissue, transforming it into an unstructured mass [85], thereby reducing the possibility of PCD blockage [97]. Although its fibrinolytic effect may increase the risk of bleeding, streptokinase itself has no effect on the adventitia, media, or intima [98]. Necrotic material and pancreatic secretions may erode the blood vessel wall and cause bleeding, while streptokinase reduces the incidence of bleeding by effectively increasing the drainage of necrotic material [96].

Recently, multiple studies have reported the use of hydrogen peroxide (H_2O_2) flushing for the treatment of WON. The results of a large scale multicenter retrospective study indicated that the use of H_2O_2 was associated with a higher clinical success rate, with no difference in adverse events [99]. Similarly, a meta-analysis by Babu et al. on hydrogen peroxide assisted minimally invasive necrosectomy showed a clinical success rate of 91.6% [100]. H_2O_2 is a strong oxidant. When it comes into contact with tissue, it rapidly decomposes into water and oxygen, releasing local heat. It mechanically removes adherent necrotic tissue [100, 101] and closes the necrotic cavity by stimulating the formation of granulation tissue and fibrosis [102]. Usually, 3% H_2O_2 solution is diluted in a 1:1, 2:1, or 3:1 saline solution, and an amount ranging from 100 to 300 mL is delivered to the necrotic cavity. The release of nascent oxygen and heat may cause abdominal discomfort and bloating [103], and can lead to the overflow of infected fluid from the effusion into the peritoneal cavity under pressure, resulting in peritonitis [104], which may cause a temporary halt in fluid flushing. Another important issue with the use of H_2O_2 is that venous embolism can occur when the amount of released oxygen exceeds its maximum blood solubility [105]. The meta-analysis by Babu et al. did not report adverse events such as gas embolism [100]. Messallam et al. [99] and Gunay et al. [106]reported that the incidence of adverse events in patients who received H_2O_2 assisted surgery was similar to that in patients who did not, and none of these events were related to the use of H_2O_2. To determine the role of H_2O_2 in pancreatic necrosis debridement, well designed randomized controlled studies are needed in the future, and the optimal concentration and success predictors should be investigated.

Complications of PCD Treatment

An external pancreatic fistula (EPF) is a significant consequence of percutaneous drainage of pancreatic juice in ANP. They are commonly caused by DPDS, where the disconnected pancreatic segment continues to secrete protein-rich pancreatic juice [107]. Current research indicates that most low-output EPFs in the DPDS setting spontaneously close within 3 months without intervention [107], possibly due to severe necrosis of the disconnected pancreatic segment leading to the gradual atrophy of acinar cells and spontaneous closure [108, 109]. If a high-output pancreatic fistula persists after three months, patients undergo Endoscopic Retrograde Cholangio-Pancreatography (ERCP) and pancreatic duct stenting [107].

Another common complication of PCD in the treatment of necrotizing pancreatitis is enteric fistula, with an incidence rate of 17% to 23% [85, 110]. In the context of acute pancreatitis, an enteric fistula may be a complication of pancreatitis itself or a result of interventional or endoscopic treatments [111]. Enteric fistulae may arise due to weakened bowel walls from inflammation, direct perforation of the adherent bowel by the drainage tube, or due to the tube becoming hardened over time from prolonged placement [110], or even by erosion of the tube [32]. All these drainage tube-related enteric fistulae are treated through a staged removal of the drainage tube [39].

Mallick et al. [112]reported that approximately 30% of pseudoaneurysms in acute pancreatitis form after percutaneous drainage. On one hand, this could be due to direct vascular trauma during PCD insertion or long-term drainage leading to erosion of surrounding vessels. On the other hand, encapsulated necrosis may develop over time from acute necrotic collections, with the cavity wall possibly containing major vessels. After successful PCD drainage, the sudden decompression of a large necrotic collection can cause injury to the cavity wall by the PCD tip, forming a pseudoaneurysm and potentially leading to bleeding. This type of bleeding is usually self-limiting and stops when the PCD is withdrawn by a few centimeters [32, 110].

Complications of PCD also include insertion site pain, obstruction, and catheter displacement. Percutaneous catheter drainage is prone to obstruction due to necrosis, and necrolytic agents have been used to enhance the efficacy of PCD.

Discussion

Acute pancreatitis is a highly challenging disease that can lead to severe complications. It requires a multidisciplinary approach in centers with expertise in interventional endoscopy, laparoscopy, and open surgery, as well as intensive care. PCD in the first stage is a commonly used surgical technique in clinical practice. Due to its rapidity, simplicity of operation, and high safety, it can not only improve the clinical symptoms of patients but also provide a good transitional plan for endoscopic and surgical interventions.

The clinical course of ANP is variable, and objective indicators need to be established to measure the timing of enhanced treatment. In existing studies, most of the analyses of predictive factors for step-up treatment are retrospective studies. Although some key factors (such as clinical scores and imaging features) have been mentioned in multiple studies, there are still significant inconsistencies and research gaps. There may be subjective differences in the imaging evaluation of pancreatic necrosis among different studies. In addition, the results of some studies show that the volume of extrapancreatic necrosis has no direct association with the need for step-up treatment, while recent studies have found that it may increase the possibility of step-up treatment due to the heterogeneity of necrotic components. This contradiction further highlights the limitations of existing studies. More high quality prospective and randomized controlled trials (RCTs) are needed to confirm the findings in this field to guide clinicians on when to adopt a more aggressive and open approach to treat necrotizing pancreatitis. Patients who are destined to require surgical intervention should be provided with a step-skipping treatment strategy to replace the traditional step-by-step treatment procedure.

Although the dynamic changes of inflammatory factors (such as IL-6 and CRP) have been proven to be related to clinical outcomes, they have not been widely used in clinical practice, and there is a lack of unified evaluation criteria. Future research needs to integrate multiple indicators from clinical, imaging, and laboratory aspects to develop more accurate evaluation tools and prediction models to help clinicians more accurately judge the timing of step-up treatment. In addition, long-term follow-up studies are also necessary to evaluate the long-term effects of different treatment strategies and the quality of life of patients.

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Declarations

Conflict of interests The authors declare no competing interests.

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