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Acute necrotizing pancreatitis: challenges and interventions—a narrative review

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Abstract

Acute pancreatitis (AP) is a complicated disease with rising incidence over the years. Twenty percent of AP will develop into acute necrotizing pancreatitis (ANP). Interventions for ANP have evolved from traditional open surgery to minimally invasive step-up approaches. Infected pancreatic necrosis (IPN) is the most serious event of ANP and associated with extremely poor prognosis. The contrast-enhanced computed tomography(CECT)-based classification of IPN describes various types of IPN and will help to carry out surgical interventions for each subtype. Nevertheless, many challenges are still remaining during the treatment of ANP. Including the balance between endoscopic and surgical approaches, and the selection of optimal timing of surgical intervention for infected necrosis. In nowadays treatment scenario of ANP, the necessity for open surgery remains to be debated. Despite of the development of advanced interventional techniques, postoperative residual infection (PRI) remains thorny, and effective prevention and treatment of PRI is of significance.

Keywords: Acute necrotizing pancreatitis, Acute pancreatitis, Infected pancreatic necrosis, Postoperative residual infection, Step-up approach

Introduction

The incidence of acute pancreatitis (AP) has been highly mounted over the years.[1] According to the revised Atlanta classification, AP is distinguished by 3 types. Mild acute pancreatitis (MAP) is classified by pancreatitis without organ failure or local and systemic complications; moderately severe acute pancreatitis (MSAP) is defined by pancreatitis with organ failure lasting <48 hours, and/or the presence of local and systemic complications; severe acute pancreatitis (SAP) is characterized by pancreatitis with single organ failure lasting >48 hours or multiple organ failure.[2] The mortality rate of MAP is relatively low, and patients with MAP can be typically discharged from hospital at early stage. Compared with SAP, the mortality rate of MSAP is much lower, and 20% of patients with AP could develop into SAP, which high mortality rate of 36% to 50%.[1,2]

AP is morphologically subtyped into interstitial edematous pancreatitis and acute necrotizing pancreatitis (ANP).[2,3] The revised Atlanta classification divides ANP into 3 morphological types, including parenchymal necrosis, peripancreatic necrosis, and combined necrosis.[4] The parenchymal necrosis and peripancreatic necrosis represent the nonviability of pancreatic tissue and peripancreatic fat, respectively.[5–7] The combined necrosis is the most common type, accounting for approximately 75% to 80% among patients with ANP.[8] Surgical interventions for ANP has substantially transformed from traditional open surgery to minimally invasive strategy (MIS). The current article aims to focus on the equivocal topics in ANP treatment and present the current challenges and interventions in treating ANP.

Database search strategy

We conducted a systematic literature search through the PubMed and Google Scholar for English articles, China national knowledge infrastructure and Wanfang database for Chinese articles. The database search of papers published in English and Chinese between January 1990 and June 2022 was performed by selecting following key words: severe acute pancreatitis, necrotizing pancreatitis, infected necrotizing pancreatitis, therapeutic strategy, surgical intervention, step-up approach, minimally invasive strategy, open pancreatic debridement. All relevant guidelines, original articles, reviews, case reports, and meta-analysis were included.

Contrast-enhanced computed tomography-based classification of infected pancreatic necrosis

Infected pancreatic necrosis (IPN) is characterized as a late event during the course of AP and is associated with extremely high morbidity and mortality.[9,10] IPN may occur in pancreatic or peripancreatic tissues, and areas of peripancreatic necrosis include the peripancreatic regions and poorly defined areas, such as the lesser sac and retroperitoneum.[8] Surgical interventions for IPN depends on the areas of necrotic tissues.[7] Loveday et al proposed a systematic taxonomy to classify various minimally invasive strategies by the method of route (peroral, transpapillary or transmural, percutaneous retroperitoneal/transperitoneal, with/without transmural puncture) and visualization (open, radiologic, endoscopic, hybrid, or other).[11,12] Trikudanathan et al[13] suggested percutaneous approach/endoscopic approach with or without minimal access retroperitoneal pancreatic necrosectomy and endoscopic approach should be performed for walled-off necrosis (WON) in perigastric or duodenal areas when necrosis is formed with and without deep extension respectively.

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

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Based on the classification system introduced by Loveday et al and computed tomography(CT) presentation, as well as our years of experience in treating ANP, we have classified 4 types of IPN regarding the dynamic change of necrotic fluid distribution in CT findings (Figs. 1 and 2, Table 1).[14] In type I IPN (central type), the peripancreatic fluid collection locates inside the lesser omental sac and its peripheral spaces. As for type II (peripheral type), the necrotic fluid tends to be spread into abdominal peripheral areas. Three subtypes are then branched in this type by the infected site, including type IIa, IIb, and IIc. For type IIa and IIb, the infections are localized into the left kidney-colon and right kidney-colon spaces, respectively. For type IIc, infection locates in the pelvic-rectum zone. Type III is a mixed type of type I and type II with extensive infected necrosis in the peritoneal cavities. The infections are internally connected inducing a widespread infected intraperitoneal fluid or cellulitis. Patients of this type present more deteriorated physical status with an extremely poor prognosis. IPN in type IV (isolated type) typically diffuses into deep tissues with poor liquidity. It usually presents in central part of anterior pararenal space, and medium vessels-included retroperitoneal spaces (abdominal aorta and its

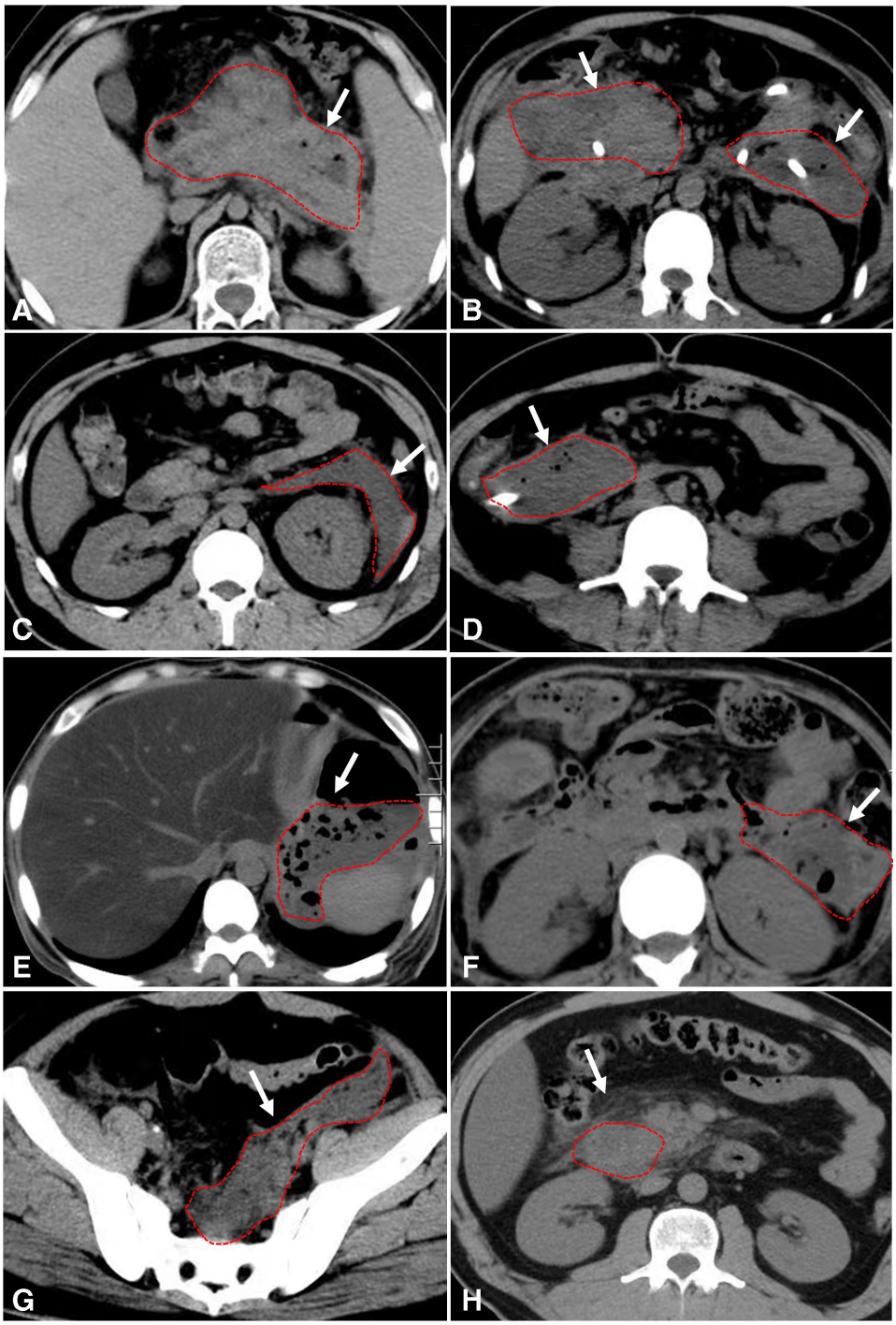

Figure 1. Four types of IPN in contrast-enhanced computed tomography(CECT) image (white arrow marks the infection). (A) Type I: infections locate in lesser omental sac and its peripheral spaces. (B) Type II: infections locate in bilateral kidney-colon spaces. (C) Type IIa: infection locates in left kidney-colon space. (D) Type IIb: infection locates in right kidney-colon space. (E–G) Type III (images are from 1 patient): infections locate in the lesser omental sac and its peripheral spaces, the left kidney-colon space and pelvic-rectum zone, respectively. (H) Type IV: infection locates in central part of right anterior pararenal space. IPN = infected pancreatic necrosis.

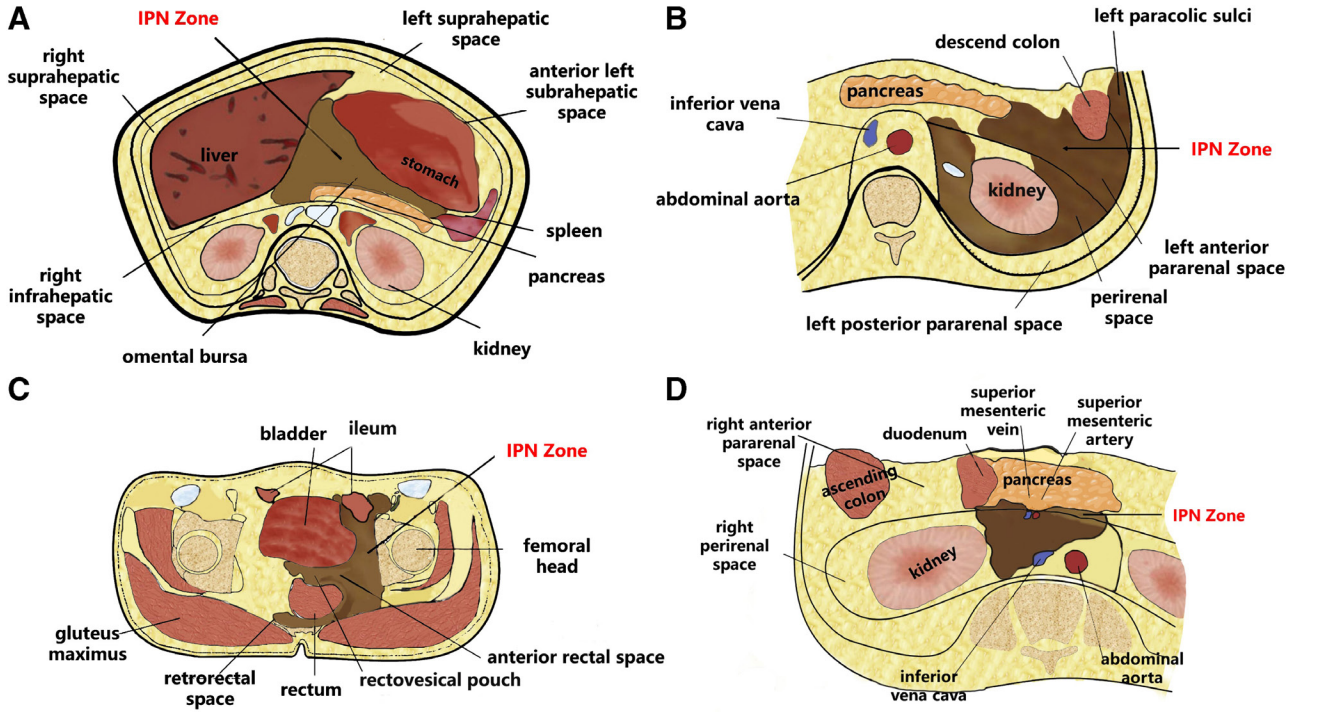

Figure 2. Illustration of 4 types of IPN. (A) Type I: infections locate in the lesser omental sac and its peripheral spaces. (B) Type II a: infection locates in the left kidney-colon. (C) Type II c: infection locates in the pelvic-rectum zone. (D) Type IV: infections locate in the retropancreatic and retroperitoneal spaces. IPN = infected pancreatic necrosis.

branches, inferior vena cava) upper mesentery root, and is adjacent to duodenum neck and head of pancreas (uncinate process), retropancreatic and introduodenal segments of common bile duct. The incredibly strong corrosive fluid spreads to the surrounding organs or vessels leading to gastrointestinal fistula or bleeding. The sealed space establishes a high-pressure environment to neighboring tissues, and drives the spread of infections. Cao et al explored the difference between multiple surgical interventions in terms of clinical outcome by dividing patients into 3 types according to the locations of IPN (n = 233).[15] This study suggested IPN was most commonly located in the peripancreatic and left retroperitoneal spaces, interventions should be selected by considering the locations and extension of necrotic areas.[15] In view of the classification and clinical characteristics of different types of IPN, we explored the value of this taxonomy and evaluated efficacy of different surgical interventions. Among 126 patients with different IPN types, no significance was found between each type in terms of mortality rate ($P > .05$). However, type IV had higher incidence of SAP ($P = .044$) and postoperative residual infection (PRI; $\chi^2 = 24.273$, $P < .001$), with increased hospital days (68.5 vs 19 days, $P < .001$; T.Q. Lu, MD, unpublished data, August 2022). Compared to the study by Cao et al, our re-classification added type IV IPN, which represents a more deadly type with necrosis in deeper extension, and normal surgical therapies can rarely reach the necrosis leading to failure of drainage or debridement of necrotic tissues, as well as lethal surgical complications (bleeding, intestinal fistula, and other serious complications). The progression of IPN is highly heterogeneous with strong variation in extent and course, the enhancement of comparison between different classified types and different minimally invasive procedures will help to perform tailored interventions, and boost communication between clinicians.

Renovation of step-up approach

"Step-up" approach has been recognized as the most standard treatment for ANP.[16,17] The first step is image-guided percutaneous catheter drainage (PCD), followed by MIS if PCD fails, and open surgery will be the final step.[18] Step-up approach was first introduced into the clinic in Netherlands by PANTER trial (PAncreatitis, Necrosectomy versus sTEp up appRoach) to yield evidence for the policy decision.[19] The upgraded PANTER trial analyzed the long-term outcomes of participants treated by step-up approach and open necrosectomy approach. Seventy-three patients were followed up for a mean of 86 months. Nineteen patients died in the step-up group compared with 33 patients in the open necrosectomy group (44% vs 73%, $P = .005$). Complications such as pancreatic exocrine insufficiency (29% vs 56%; $P = .03$), incisional hernias (23% vs 53%; $P = .004$), or endocrine insufficiency (40% vs 64%; $P = .05$) were significantly lower in step-up group.[20]

The minimally invasive step-up approach has become the standard treatment for ANP, and its efficacy has been validated by multiple studies.[21,22] Cases have been reported to emphasize the significance of dynamic surveillance during step-up strategy.[23,24] Recently, several therapeutic strategies including step-jump approach, skip-up approach and even one-step approach have been proposed.[25,26] Cao et al[26] retrospectively analyzed 94 patients (n = 45 in 1-step and n = 49 in step-up groups) and found there was no significance in terms of death (8.89 vs 8.17%; $P = .949$), long-term complications (18.37 vs 15.56%; $P = .717$), and new organ failure (14.29 vs 14.33%; $P = .832$) between 2 groups.[26] Based on the standard step-up approach protocol, these approaches designed a more tailored treatment strategy for each private by distinguishing the physical status as well as the dynamic clinical progression of each patient. The progression of ANP is highly heterogeneous, "One size fit all" does lead to the negative consequences for patients who cannot benefit from "step-by-step" approach. Patient who may benefit less from strict step-up approach may obtain unexpected satisfying prognosis from step-jump approach, skip-up approach, and one-step approach. Thus, we need to distinguish complicated conditions of each individual and set up a preferable scheme in treating ANP.

Timing of surgical interventions

Consensus on the timing of surgical interventions for IPN has not been reached.[27] Several international guidelines suggest a

Table 1

Features of each IPN type

Type	Localizations of infectious tissues	Suggested surgical interventions
Type I (central type)	Lesser omental sac and its peripheral space: 1. peripancreatic and perisplenic spaces 2. left subphrenic zone 3. anterior left subhepatic space 4. posterior left subhepatic space	PCD/ETD, ETN, LPN
Type II (peripheral type)		
Type II a	Left kidney-colon space: 1. left paracolic sulci 2. left anterior pararenal space 3. left perirenal space 4. left posterior pararenal space	PCD, MIAPN, with or without VARD, LPN
Type II b	Right kidney-colon space: 1. right paracolic sulci 2. posterior duodenal space 3. right anterior pararenal space 4. right perirenal space 5. right posterior pararenal space	
Type II c	Pelvic-rectum space: 1. left pelvis zone 2. anterior and posterior rectal spaces	
Type III (mixed type)	Mixed type of type I and type II	Diversified interventions in combination of type I and II
Type IV (isolated type)	1. central part of anterior pararenal space, and medium vessels-included retroperitoneal spaces (abdominal aorta and its branches, inferior vena cava) 2. upper mesentery root 3. adjacent to duodenum 4. neck and head of pancreas (uncinate process) 5. retropancreatic and introduodenal segments of common bile duct	OPN, LPN

ETD = endoscopic transluminal drainage, ETN = endoscopic transluminal necrosectomy, IPN = infected pancreatic necrosis, LPN = laparoscopic pancreatic necrosectomy, MIAPN = minimal incision access pancreatic necrosectomy, OPN = open pancreatic necrosectomy, PCD = percutaneous catheter drainage, VARD = video-assisted retroperitoneal debridement.

postponed PCD should be performed until the "walled-off necrosis" has been reached (typically 4 weeks).[28–30] A large randomized controlled trial showed that patients could achieve a better outcome with delayed open pancreatic necrosectomy (OPN; >4 weeks) compared to an early treatment.[31] The same cut off was suggested regarding PCD and endoscopic transluminal drainage (ETD). Lee et al proposed the principle of "3D"(delay, drainage, debridement) in treating SAP.[4] In a worldwide investigation, up to 55% pancreatologists preferred postponed catheter drainage.[32] The possible explanation for favoring delayed catheter drainage may include (1) IPN is typically diagnosed at a late stage; (2) Drainage is easier to be placed when WON has been reached and collections have been completely liquefied; (3) Antibiotic therapy rescues some patients from PCD.

Currently, the candidate selection for the delayed intervention becomes the central issue. Is 3D concept suitable for all? Latest research shows the mature WON can be formed in 3 weeks since the onset of SAP.[33] The American Gastroenterological Association recommends 2 weeks after the onset of AP as the best interventional time for patients with persistent IPN and organ failure.[34] A recent study compared the outcome in patients treated in less than 4 weeks and 4 or more weeks in an attempt of endoscopically centered step-up approach, suggesting that early treatment for patients with infection and organ failure had a lower mortality in contrast to the standard treatment after 4 weeks.[35] Oblizajek et al[36] found the early endoscopic intervention for ANP prolonged the hospitalization days and increased the mortality rate. Recently, a randomized superiority trial was conducted to compare clinical features of immediate drainage (within 24 hours once the diagnosis of IPN was confirmed, n = 55) and postponed drainage (4 weeks after the onset of SAP or the complete formation of WON, n = 49) by step-up approach, no difference was found regarding the mortality (13% vs 10%) and complication (score 57 vs 58, P = .90) rates between 2 groups. However, patients received fewer invasive interventions in the postponed drainage group, and one-third of which acquired clinical rehabilitation only with antimicrobials.[37] The traditional practice suggests to intervene over 4 weeks after the onset of disease. However, the trial by Boxhoorn et al[37] highlighted that the diagnosis of WON by a defined period of 4 weeks was arbitrary and invalid. In the immediate-drainage group, the necrosis was largely encapsulated in nearly 60% of (n = 33) patients in a mean of 24 days, compared with 70% (n = 21) in a mean of 34 days in the postponed drainage group. The results indicated that the pancreatic and peripancreatic necrosis can be walled off before or beyond 4 weeks. The drainage-related decisions should be guided according to the patient's actual condition, radiologic findings, and response to antibiotic treatment rather than a defined period of 4 weeks.[38] The "window of opportunity" for SAP is extremely narrow, and a blind emphasis of delayed principle leads to the deterioration of the disease. From our experience, early catheter drainage may not cause increased operation-related fatality rate and long-term pancreatic dysfunction. More evidence is needed regarding the optimal timing of surgical interventions.

Interventions for ANP

There are 2 distinct peaks of mortality in SAP, and the second one usually occurs at least 2 weeks after the onset of symptoms mainly due to the infection of necrosis.[27,28] Surgical interventions for ANP include percutaneous approach, endoscopic transluminal approach, laparoscopic approach, video-assisted minimal incision access approach, and open debridement.

Percutaneous approach

PCD is the first step and practicable for necrotic collections in flank or pelvic with deep extension into retroperitoneal or intraperitoneal spaces.[39] It can be performed with or without ETD and followed by endoscopic transluminal necrosectomy (ETN), laparoscopic pancreatic necrosectomy (LPN), video-assisted retroperitoneal debridement (VARD), or minimal incision access pancreatic necrosectomy (MIAPN) if collections do not resolve.[39] During the procedure of PCD, single or multiple catheters were placed through abdominal or retroperitoneal path under the guidance of ultrasonic or CT.[40] In our center, we prefer to use 12 to 14F pigtail catheter through abdominal or retroperitoneal path to drain, as size and numbers of the catheter matter in drainage, and larger-bore catheters will improve the success rate if PCD fails or has undesirable efficacy.[40] The proper route for PCD is through a flank approach retroperitoneal assess to the collections. Left retroperitoneal assess is the optimal choice since it is ideally suitable for subsequent minimally invasive strategies if PCD fails.[40] In a retrospective study, 47% of patients with IPN were cured by PCD alone, and 74% of IPN-associated sepsis was successfully controlled without catheter-related complications.[41] PCD could significantly reduce the occurrence of reoperation, infection, and death.[42] A systematic review evaluated the effectiveness of PCD and demonstrated that 55.7% of patients were avoided from subsequent surgical necrosectomy by conducting PCD with the mortality rate of 17.4%.[43] As the primary step, PCD is essential in draining

the collection fluid, and it works as "bridge to MIS," by extending endoscope, nephroscope, or laparoscope through the established percutaneous passage.[39] Studies suggested that minimally invasive retroperitoneal approach led to the proinflammatory response and was correlated with new-onset organ failure compared with open surgery, this may be attributed to accompanied complications of PCD or retroperitoneal approach, such as exterior pancreaticocutaneous and enterocutaneous fistula.[44,45]

The timing of PCD has not yet been unified, varying from 9 to 55 days.[33] In our center, we perform PCD 12 days after the onset of the disease, since early catheter drainage will limit the spread of infected necrosis and prompt the optimal physical stage for surgical intervention.[39] Early PCD is recommended for patients who have massive peripancreatic effusion with elevated intraperitoneal pressure and intermittent fever(>38.5°C) or malnutrition.[44] Babu et al[46] suggested that APACHE II score(>7.5), organ failure, and sepsis could predict the incidence for surgical debridement.[47]

Endoscopic transluminal approach

Endoscopic drainage of ANP has been evolved from the traditional transmural drainage through an ordinary endoscope to access the necrotic cavity with endoscopic ultrasound (EUS).[48,49] The endoscopic transluminal approach is more suitable for IPN close to stomach or duodenum, and it has been recognized by multiple studies.[50–52] In endoscopic transluminal approach, creation of multiple tracts reduced repeated intervention and improved the efficiency of necrosis debridement, providing the alternative sites for subsequent ETN.[49] Meanwhile, multiple accessories such as baskets, balloons, nets will improve the efficiency of irrigation and debridement.[50] ETN can be conducted after ETD if necessary.[39] Both ETD and ETN may cause postoperative complications such as hemorrhage and perforation.[39] The pure application of endoscopic transluminal approach without other surgical interventions is feasible when necrotic collections localize in lesser sac or central part of pancreas, but this method is only used in less than two-thirds of patients with ANP even in advanced pancreatic centers.[39]

Several hallmark trials have compared the endoscopic and surgical step-up approaches.[53–56] PENGUIN trial compared the clinical outcomes (new-onset organ failure, death, composite endpoint of major complications) between endoscopic and surgical necrosectomy, and demonstrated that the endoscopic approach had a less occurrence rate of composite clinical end point (20% vs 80%) and pancreatic fistulas (10% vs 70%). Besides, no new-onset multiple organ failure was found in the endoscopic group (0% vs 50%).[53] A larger randomized TENSION trial compared major complications of endoscopic step-up approach (ETD + ETN, n = 51) and surgical step-up approach (PCD, VARD if needed, n = 51). Among 98 patients enrolled, the primary endpoint occurred 43% in the endoscopy group compared to 45% in the surgical group (P = .88), no difference was found between 2 groups in terms of death and major complications. However, the endoscopic approach had lower rate of pancreatic fistulas (5% vs 32%; P = .001) and increased hospital days (mean 53 vs 69 days; P = .014).[54] Onnekink et al[55] compared long-term clinical outcomes of endoscopic and surgical step-up approaches in a mean follow-up period of 7 years in TENSION trial (exTENSION). The primary end point (composite of death and major complications) occurred in 53% (n = 27) and 57% (n = 27) of patients in endoscopy and surgery groups, respectively (P = .688). Patients in endoscopic group had fewer pancreaticocutaneous fistulas (8% vs 34%; risk ratio [RR], 0.23; 95% confidence interval [CI], 0.08–0.83) and reintervention rate was significantly lower (7% vs 24%; RR, 0.29; 95% CI, 0.09–0.99) than surgery group after the initial follow-up period of 6 months.[55] MISER trial compared clinical outcome of MIS (laparoscopic or VARD, n = 32) and endoscopic approaches (ETD with or without ETN, n = 34). The occurrence of primary endpoint was 11.8% in the endoscopic group, while 40.6% in the MIS group (P = .007). No significant difference was found in terms of mortality (endoscopy 8.8% vs surgery 6.3%; P = .999). Nevertheless, the incidence of enteral or pancreatic-cutaneous fistula in the endoscopic group was extremely lower compared with MIS (0 vs 28.1%, P = .001). Endoscopic group reduced hospital stay (mean 53 vs 69 days; P = .014) and lowered indirect hospital expense.[56] Besides, ETD or ETN has been suggested to shorten the length of hospitalization and decrease total medical costs compared to surgical debridement.[57]

Although endoscopic step-up approach is a promising alternative for infected collection, it has not been compared with surgical step-up approach until recently. van Brunschot et al[54] found there was no difference in mortality and major morbidity rates (43% in endoscopic vs 45% in surgical; P = .88) between endoscopic step approach and surgical step-up approach in patients with IPN. However, the endoscopic procedures reduced pancreatic fistulas (5% vs 32%; P = .0011) and length of hospital day (mean 53 vs 69 days; P = .014).[54] A single-center and randomized trial comparing ETD with minimally invasive surgery showed that ETD had reduced major complications and lowered the cost of hospitalization.[56] Regarding the unestablished and unstandardized protocols of endoscopic approach, more prospective, randomized, and multicenter studies should be conducted to verify the feasibility of endoscopic therapies.[58,59] Apart from that, the consequences of the bias in favor of the endoscopic step-up approach may lead to an unfair comparison to surgical necrosectomy.[60] A systematic review concluded that ETD was superior to PCD with decreased reintervention rate and hospitalization days, as well as higher success rate.[61] To date, the endoscopic step-up approach has received more attention accounting for more than 80% among patients with ANP overseas. In China, the rate is far below in China with the percentage less than 20%. This may due to the lacking of evidence to support the priority of this technique, as well as different concepts for dealing with IPN. Patients with IPN should be treated by multidisciplinary groups where both the endoscopic and surgical step-up approach are available. However, endoscopic approach is a highly intricated operating technique and has a long learning curve which requires highly skilled endosonographers.

Laparoscopic approach

Laparoscopic pancreatic necrosis debridement includes the laparoscopic transabdominal access (transgastric approach and retrogastric approach) and laparoscopic retroperitoneoscopic approach, which has 75% of success rate.[62] A mature WON with smaller fluid collection and retrogastric position adjacent to pancreatic and peripancreatic tissues are amenable to laparoscopic transgastric necrosectomy.[62] The posterior wall of the stomach during the procedure is incised to assess the cavity, followed by repeated irrigation and drainage.[62] Advantages of laparoscopic transgastric necrosectomy include complete debridement without use of drains, decreased hospital stays, limited long-term complications, and shorter recovery.[63] Major limitations of laparoscopic transabdominal access involve requirement of specific anatomic considerations, higher likelihood of pancreatic and enterocutaneous fistulas and contamination of peritoneal cavity.[64] In contrast, retroperitoneoscopic necrosectomy is advantageous for reduced operative injury and postoperative complications. However, a successful performance depends on the localization of necrotic collection.[65] The application of retroperitoneoscopic necrosectomy is not recommended when necrotic collections are multifocal and discontinuous, or localized in the head or uncinate of the pancreas.[66] A thick fibrosis or the presentation of edema will reduce the success rate.[67] A large fluid collection with smaller

pancreatic necrosis (<30%) in the left retroperitoneal space is apt for 3-port retroperitoneoscopic necrosectomy.[68,69]

Video-assisted MIAPN

Video-assisted MIAPN is privileged to offer a distinct visualization of necrotic collections by extending a rigid laparoscope, endoscope, or nephroscope through the primarily establishing percutaneous passage.[70] The minimal access retroperitoneal approach is often performed when infection spreads to the posterior colonic space.[70,71] While minimal access lesser omentum sac pancreatic necrosectomy is applicable for patients with necrosis limited into peripancreatic areas.[71] Retroperitoneal access involves the bilateral, multiple unilateral, and right-sided procedures, with complications such as hemorrhage, pancreatic fistula, damage to bowel and spleen, persistent infection.[71,72] Retroperitoneal access could reduce overall complication rate, and the longer hospital days compared to OPN may be caused by more severe cases and delayed interventional timing(29.5 vs 24.0 days; $P = .029$).[72]

A retrospective study compared the outcome between nephroscope-associated MIAPN approach and OPN, MIAPN reduced death rate, hospitalizations days as well as postoperative complications, with increased reinterventions rate.[66] In the contrary, the incidence of postoperative organ failure, intensive care unit (ICU) support, and postoperative complications were significantly lower compared with OPN (43% vs 77%, 31% vs 56%, 55% vs 81%, respectively; $P < .0001$).[45] However, enteric fistula was found in 10 patients (7.3%) in nephroscope-assisted MIAPN group, which may be caused by repeated colon stimulation and oppression by drainage tube.[45] Zelga et al[73] assessed the feasibility and availability of video-assisted MIAPN for patients with ANP in terms of long-term life quality, and found that MIAPN wielded a relative better life quality than open surgery. Video-assisted MIAPN is generally performed for necrosis in infected bilateral retrorenal space, however, hemorrhage is one of the most common complications of this approach. In Connor et al[66] study, 2 patients had intra-necrosis vascular bleeding, which may be attributed to instrument-induced tissue-tearing. Dong et al[74 compared therapeutic values of different techniques (transnasal gastroscopy: n = 9, conventional gastroscopy: n = 15) in treating patients with IPN through percutaneous endoscopic necrosectomy. Transnasal gastroscopy significantly reduced the operation time than the conventional gastroscopy (119.7 ± 47.4 vs 172.8 ± 56.2 minutes; $P = .018$). However, there was no difference between 2 groups in terms of the volume difference of necrotic collections before and after surgery.[75]

There are a several caveats to video-assisted MIAPN: (1) remaining the integrity of peritoneum to prevent infection to peritoneal cavity; (2) colon and associated vessels should be carefully noted during retroperitoneal procedure; (3) keeping attention on ureters and blood vessels of reproductive system in back-sided procedure; (4) inferior vena cava and abdominal aorta should be carefully noted in midaxillary line-sided procedure; (5) damages of pancreas head and duodenum should be avoided in right-sided retroperitoneal access; (6) left-sided retroperitoneal is more favorable to assess the peripancreatic space along left posterior colonic space, anterior pararenal space, and over inferior splenic pole.[45,70–72,76] From our experience, following events are required before performing video-assisted MIAPN: (1) making a definite diagnosis of IPN by radiology and microbiological examination; (2) the infected necrotic collection should be close to the abdominal wall, with a proper degree of liquefaction of the necrotic tissues; (3) establishing a clear boundary between the necrotic focus and normal tissue.

Open debridement

Traditional OPN is performed through midline abdominal incision or retroperitoneal flank incision, and it can easily cause causes lethal complications such as hemorrhage and gastrointestinal fistula.[77,78] The morbidity and mortality rates of OPN has been reported ranging from 60% to 90% and 25% to 60%, respectively.[79,80] van Santvoort et al compared clinical outcome of patients with IPN between minimally step-up approach and open surgery, the occurrence rate of primary end point in open necrosectomy and step-up approach were 69% and 40%, respectively ($P = .006$).[16] Step-up approach had a reduced new-onset multiple organ failure (12% vs 40%; $P = .002$) and incisional hernias (7% vs 24%; $P = .03$) compared to open surgical debridement.[14]

In step-up approach, where OPD is placed as the final step, is OPD over or out? Multiple studies have found patients treated by OPD had a higher morbidity rate, because patients underwent OPD were more critically ill and had much worse physical condition.[81] In a comparative study, among 305 patients with ANP treated by endoscopically centered step-up approach, OPD was required in 1% of patients in standard (>4 weeks) step-up approach group, while it was up to 7% in early (<4 weeks) step-up intervention.[35] Despite the encouraging clinical outcome of MIS, there is still a considerable proportion of patients in need of OPD for multiple indications. Early indications are refractory compartment syndrome, ischemic bowel, perforation of a viscus, and failure of step-up approach. In the late course of interventions, indications include bowel obstruction, pancreaticocutaneous fistula, and chronic pancreatitis due to disconnected pancreatic duct syndrome, and persistent enterocutaneous and cyst-enteric fistula.[78] In general, OPD is especially required for patients with extensive necrosis, uncontrolled sepsis, symptomatic WON not accessible via PCD or ETD/ETN, who have attained little efficacy through MIS, those with intractable complications like abdominal compartment syndrome, bowel perforation, or hemorrhage, or those in the grassroot medical institutions lacking of advanced medical techniques.

IPN usually presents as highly dynamic, what approach should be performed in terms of different types of IPN? Based on our IPN typing, the flow of IPN management adopted in our center is shown in Figure 3. For type I, PCD or ETD is recommended as priority, followed by ETN. PCD is primarily performed for type II, followed by MIAPN. VARD should be considered when necessary. Type III is mixed type of type I and type II, interventions need to be better employed in consideration of both types. Type IV will directly go to OPN.[22,76,82] Therapeutic strategies for IPN need to be selected on the principle of comprehensiveness, stage-targeted, and individualized, which requires a concentration of specialization and complexity of knowledge.[83] Therefore, the multidisciplinary team should be introduced for management of ANP. The decisions made by surgeons, gastroenterologists, radiologists, pathologists, and specialist nurses should be coordinated for the delivery of treatment to maximize clinical benefit.[84,85]

Intervention of postoperative residual infection

PRI is defined as the presentation of residual infected necrotic tissues in the abdominal or retroperitoneal spaces after active surgical treatment, and it usually occurs 2 or 3 months after SAP.[86] In PANTER trial, both minimally invasive step-up approach and open necrosectomy include several patients requiring additional drainage performance (11% vs 13%) or pancreatic surgery (11% vs 5%).[19] The occurrence of residual necrosis remains challenging and it may be caused by following reasons: (1) incomplete necrosis debridement: (2) premature timing of surgical interventions: (3) surgical interventions cannot hinder the development of SAP, pancreatic and peripancreatic tissues continue necrotizing: (4) the spread of infection from the retroperitoneal into the peritoneal space; (5) blocked drainages after surgery.[87,88] PRI is commonly suggested by signs of local and systematic inflammation, visible gas in CT scan, positive results from bacteria culture of fluid

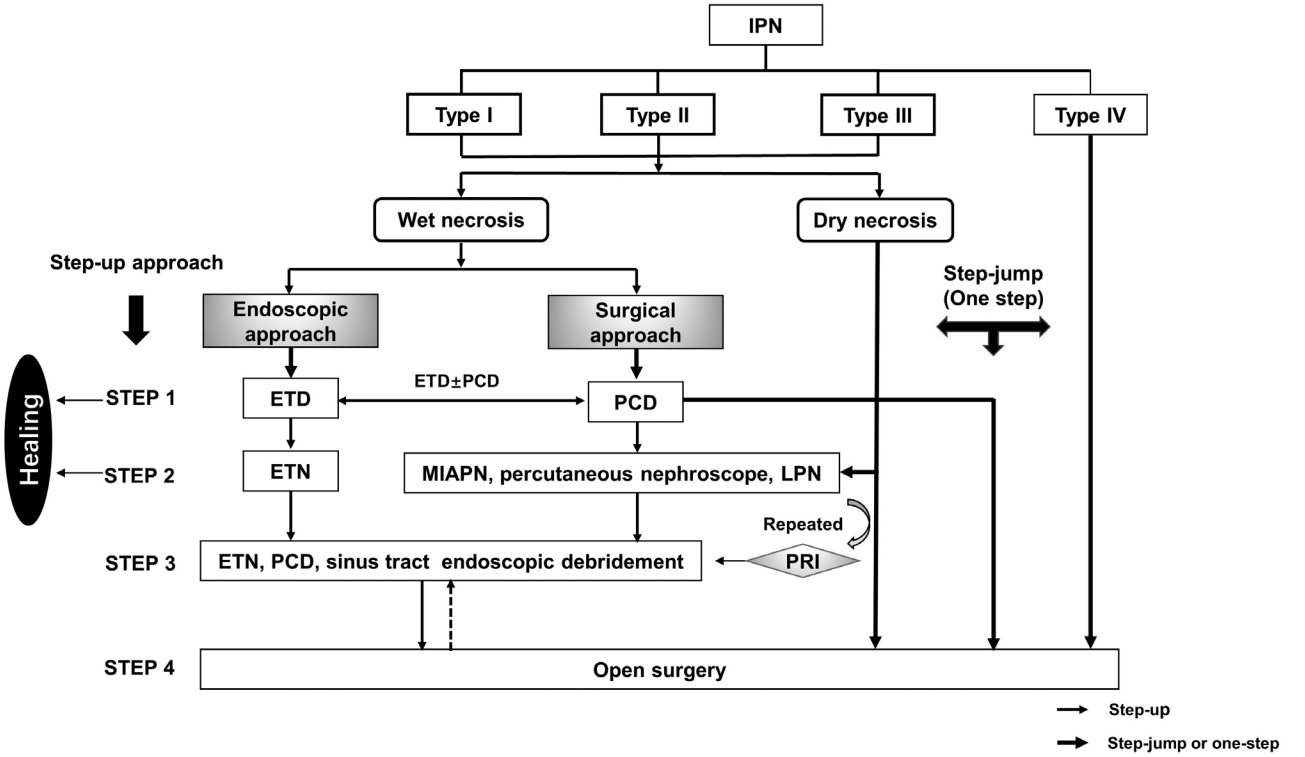

Figure 3. Treatment strategies for IPN based on CT protocol. Four steps strategy in treating IPN: PCD or ETD is performed as the first step (step 1), followed by video-assisted MIAPN, percutaneous nephroscope, LPN or ETN (step 2), after which STED, PCD and/or ETN should be performed if PRI occurs(step 3), OPN is the final step (step 4). ETD = endoscopic transluminal drainage, ETN = endoscopic transluminal necrosectomy, IPN = infected pancreatic necrosis, LPN = laparoscopic pancreatic necrosectomy, MIAPN = minimal incision access pancreatic necrosectomy, OPN = open pancreatic necrosectomy, PCD = percutaneous catheter drainage, STED = sinus tract endoscopic debridement.

collection, or no clinical alleviation after persistent irrigation and drainage.[86] Thus, "four-steps" surgical strategies were put forward to prevent and treat PRI based on step-up approach (Fig. 3).[89,90]

Interventions for long-term complications of ANP

Major long-term complications of ANP include pancreatic fistula, pancreatic duct disruption and stricture formation, exocrine and endocrine pancreatic insufficiency, splanchnic vein thrombosis, and pseudoaneurysm.[91–95] Over the years, the rate of long-term complications has decreased as the development of various surgical interventions.[1,2] Pancreatic fistula may close spontaneously after a period of time (with median interval period of 70 days).[91] The success rate of transpapillary stent to bridge leakage site is only 27%.[91] The disruption of pancreatic duct leads to pancreatic or peripancreatic fluid collection, pancreatic fistula, or pancreatic ascites.[92] Non-surgical strategies are recommended for pancreatic duct disruption in most cases.[92] Surgery should be considered when the non-operative management fails. Interventions for exocrine and endocrine pancreatic function are determined in terms of cure and improvement of pancreatic functions.[93] Venous thrombosis and pseudoaneurysm are commonly involved with splenic vein, while the efficacy of anticoagulation therapy for splenic venous thrombosis is unclear.[94] CT, magnetic resonance imaging (MRI), or angiography will help for diagnosis of pseudoaneurysm.[95]

Limitations of the article

There are some limitations to the study. Compared to systematic reviews and meta-analyses, the retrieval of identified papers in our article is relatively rough. In our narrative review, we did not conduct data collection and re-analysis. Most of the literatures we reviewed are retrospective studies with small sample sizes, thus, more high-quality prospective controlled researches are needed.

Conclusions and future perspectives

Step-up approach is recognized as a landmark toward the evolvement of ANP treatment. In the past, pancreatic necrosectomy was the mainstay for the treatment of ANP. Recently, MIS is preferred and the step-up approach is regarded as the first-line therapeutic strategy. Among the treatment process of ANP, surgical interventions have shown great advance and brought more prospects and challenges. Surgical interventions should be employed in the context of a multidisciplinary step-up approach. Anatomy, physiology, psychology, expertise, experience, preference, and practical conditions (such as medical equipment) should be taken into consideration to decide the best mode of intervention and achieve the optimal results.

Simultaneously, under current treatment scenario, the following controvertible aspects need to be addressed further: (1) following step-up principle, how to identify patients requiring further approaches? (2) how to evaluate the effects of minimally invasive treatment and distinguish patients for open surgery conversion? (3) how to effectively prevent PRI? (4) how to select properly the size of catheter tube? the bigger, the better? Thus, there is still a long way to go in treating patients with ANP in a more acknowledged scheme. Based on national medical landscape, we drew some perspectives in futural ANP treatment: (1) prompting the coordinated development in clinical practice by a mutual complementarity in the interest of a standardized endoscopic and surgical approaches: (2) setting up an effective multidisciplinary treatment platform

for collaborative interactions between multiple departments in advancing diagnosis and treatment strategies for SAP: (3) constructing a sound referral management system to improve qualities of primary and secondary care in treating SAP: (4) establishing a proactive and continuous multidisciplinary network consultation system in treating this disease for 24 hours: (5) improving the coordination system on the basis of individual, medical institution, and government by constructing integrated health care system, medical alliance, or clinical medical research center, to boost the ability to prevent and control the occurrence of SAP.

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Data Availability Statement

Data sharing is not applicable to this article as no datasets were generated or analyzed during the current study.

Author contributions

BS initiated the conception and designed the manuscript. YL and LL collected the data and wrote the manuscript. YS and YL designed and drew the illustration. LL, RK, and BS critically revised the manuscript. All authors have approved the final version of the manuscript.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethics approval

Not applicable.

References

[1] Michael AM, Howard AR, Mark DG. Acute pancreatitis: a review. JAMA. 2021;325:382–390.
[2] Banks PA, Bollen TL, Dervenis C, et al. Classification of acute pancreatitis – 2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62:102–111.
[3] Portelli MM, Jones CD. Severe acute pancreatitis: pathogenesis, diagnosis and surgical management. Hepatobiliary Pancreat Dis Int. 2017;16:155–159.
[4] Lee PJ, Papachristou GI. New insights into acute pancreatitis. Nat Rev Gastroenterol Hepatol. 2019;16:479–496.
[5] Spanier BW, Nio Y, van der Hulst RW, et al. Practice and yield of early CT scan in acute pancreatitis: a Dutch observational multicenter study. Pancreatology. 2010;10:222–228.
[6] Isenmann R, Büchler M, Uhl W, et al. Pancreatic necrosis: an early finding in severe acute pancreatitis. Pancreas. 1993;8:358–361.
[7] Sakorafas GH, Tsiotos GG, Sarr MG. Extrapancreatic necrotizing pancreatitis with viable pancreas: a previously under-appreciated entity. J Am Coll Surg. 1999;188:643–648.
[8] Thoeni RF. The revised Atlanta classification of acute pancreatitis: its importance for the radiologist and its effect on treatment. Radiology. 2012;262:751–764.
[9] Rana SS, Chaudhary V, Sharma R, et al. Comparison of abdominal ultrasound, endoscopic ultrasound and magnetic resonance imaging in detection of necrotic debris in walled-off pancreatic necrosis. Gastroenterol Rep (Oxf). 2016;4:50–53.
[10] Yadav D, Lowenfels AB. The epidemiology of pancreatitis and pancreatic cancer. Gastroenterology. 2013;144:1252–1261.
[11] Loveday BPT, Petrov MS, Connor S, et al. A comprehensive classification of invasive procedures for treating the local complications of acute pancreatitis based on visualization, route, and purpose. Pancreatology. 2011;11:406–413.
[12] Arvanitakis M, Dumonceau J-M, Albert J, et al. Endoscopic management of acute necrotizing pancreatitis: European Society of Gastrointestinal Endoscopy (ESGE) evidence-based multidisciplinary guidelines. Endoscopy. 2018;50:524–546.
[13] Trikudanathan G, Wolbrink DRG, van Santvoort HC, et al. Current concepts in severe acute and necrotizing pancreatitis: an evidence-based approach. Gastroenterology. 2019;156:1994–2007.e3.
[14] Sui YH, Sun B. Preliminary exploration of the typing of infected pancreatic necrosis and rethinking of the surgical interventions. Zhong Hua Wai Ke Za Zhi. 2021;59:601–607.
[15] Cao F, Li A, Gao CC, et al. Clinical study on distribution characteristics of infected pancreatic necrosis and therapeutic approach of la paroscopic surgery. Chinese J Practical Surg.2020;40:457–460.
[16] van Santvoort HC, Besselink MG, Bakker OJ, et al. A step-up approach or open necrosectomy for necrotizing pancreatitis. N Engl J Med. 2010;362:1491–1502.
[17] Petrov MS, Shanbhag S, Chakraborty M, et al. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. Gastroenterology. 2010;139:813–820.
[18] Warshaw AL. Improving the treatment of necrotizing pancreatitis--a step up. N Engl J Med. 2010;362:1535–1537.
[19] Besselink MG, van Santvoort HC, Nieuwenhuijs VB, et al. Minimally invasive "step-up approach" versus maximal necrosectomy in patients with acute necrotising pancreatitis (PANTER trial): design and rationale of a randomised controlled multicenter trial. BMC Surg. 2006;6:6.
[20] Hollemans RA, Bakker OJ, Boermeester MA, et al. Superiority of step-up approach vs open necrosectomy in long-term follow-up of patients with necrotizing pancreatitis. Gastroenterology. 2019;156:1016–1026.
[21] Luckhurst CM, Hechi ME, Elsharkawy AE, et al. Improved mortality in necrotizing pancreatitis with a multidisciplinary minimally invasive step-up approach: comparison with a Modern Open Necrosectomy Cohort. J Am Coll Surg. 2020;230:873–883.
[22] Sun B, Xu DS, Jiang HC, et al. Study on combined therapy of hyperlipidemic severe acute pancreatitis. Zhonghua Wai Ke Za Zhi. 2007;45:733–735.
[23] Burek J, Jaworska K, Witkowski G, et al. A case of acute pancreatitis - does step-up protocol always indicated? Pol Merkur Lekarski. 2020;48:100–102.
[24] Maatman TK, Flick KF, Roch AM, et al. Operative pancreatic debridement: contemporary outcomes in changing times. Pancreatology. 2020;20:968–975.
[25] Huang DY, Li Q, Lu ZP, et al. From "step-up" to "step-jump": a leap-forward intervention for infected necrotizing pancreatitis. Chin Med J (Engl). 2021;135:285–287.
[26] Cao F, Duan N, Gao CC, et al. One-step verse step-up laparoscopic-assisted necrosectomy for infected pancreatic necrosis. Dig Surg 2020;37:211–219.
[27] Freeman ML, Werner J, Santvoort HC, et al. International multidisciplinary panel of speakers and moderators. Interventions for necrotizing pancreatitis: summary of a multidisciplinary consensus conference. Pancreas. 2012;41:1176–1194.
[28] Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology. 2013;13:e1–e15.
[29] Tenner S, Baillie J, DeWitt J, et al. American College of Gastroenterology guideline: management of acute pancreatitis. Am J Gastroenterol. 2013;108:1400–1415.
[30] The Italian Association for the Study of the Pancreas (AISP). Consensus guidelines on severe acute pancreatitis. Dig Liver Dis. 2015;47:532–543.
[31] Meier J, Leon EL, Castillo A, et al. Early versus late necrosectomy in severe necrotizing pancreatitis. Am J Surg. 1997;173:71–75.
[32] van Grinsven J, van Brunschot S, Bakker OJ, et al. Diagnostic strategy and timing of intervention in infected necrotizing pancreatitis: an international expert survey and case vignette study. HPB (Oxford). 2016;18:49–56.
[33] van Grinsven J, van Santvoort HC, Boermeester MA, et al. Timing of catheter drainage in infected necrotizing pancreatitis. Nat Rev Gastroenterol Hepatol. 2016;13:306–312.
[34] Baron TH, Christopher JD, Andrew YW, et al. American gastroenterological association clinical practice update: management of pancreatic necrosis. Gastroenterology. 2020;158:67–75.

[35] Trikudanathan G, Tawfik P, Amateau SK, et al. Early (<4 weeks) versus standard (≥ 4 weeks) endoscopically centered step-up interventions for necrotizing pancreatitis. Am J Gastroenterol. 2018;113:1550–1558.
[36] Oblizajek N, Takahashi N, Agayeva S, et al. Outcomes of early endoscopic intervention for pancreatic necrotic collections: a matched case-control study. Gastrointest Endosc. 2020;91:1303–1309.
[37] Boxhoorn L, van Dijk SM, van Grinsven J, et al. Immediate versus postponed intervention for infected necrotizing pancreatitis. N Engl J Med. 2021;385:1372–1381.
[38] Samanta J, Dhar J, Kochhar R. Immediate or postponed intervention for infected necrotizing pancreatitis. N Engl J Med. 2022;386:402.
[39] Trikudanathan G, Attam R, Arain MA, et al. Endoscopic interventions for necrotizing pancreatitis. Am J Gastroenterol. 2014;109:969–981; quiz 982.
[40] Wronski M, Cebulski W, Karkocha D, et al. Ultrasound-guided percutaneous drainage of infected pancreatic necrosis. Surg Endosc. 2013;27:2841–2848.
[41] Freeny PC, Hauptmann E, Althaus SJ, et al. Percutaneous CT-guided catheter drainage of infected acute necrotizing pancreatitis: techniques and results. AJR Am J Roentgenol. 1998;170:969–975.
[42] Zhang Y, Yu WQ, Zhang J, et al. Efficacy of early percutaneous catheter drainage in acute pancreatitis of varying severity associated with sterile acute inflammatory pancreatic fluid collection. Pancreas. 2020;49:1246–1254.
[43] van Baal MC, van Santvoort HC, Bollen TL, et al. Systematic review of percutaneus catheter drainage as primary treatment for necrotizing pancreatitis. Br J Surg. 2011;98:18–27.
[44] Carter CR, McKay CJ, Imrie CW. Percutaneous necrosectomy and sinus tract endoscopy in the management of infected pancreatic necrosis: an initial experience. Ann Surg. 2000;232:175–180.
[45] Raraty MGT, Halloran CM, Dodd S, et al. Minimal access retroperitoneal pancreatic necrosectomy: improvement in morbidity and mortality with a less invasive approach. Ann Surg. 2010;251:787–793.
[46] Babu RY, Gupta R, Kang M, et al. Predictors of surgery in patients with severe acute pancreatitis managed by the step-up approach. Ann Surg. 2013;257:737–750.
[47] Hollemans RA, Bollen TL, van Brunschot S, et al. Predicting success of catheter drainage in infected necrotizing pancreatitis. Ann Surg. 2016;263:787–792.
[48] Park DH, Lee SS, Moon S-H, et al. Endoscopic ultrasound-guided versus conventional transmural drainage for pancreatic pseudocysts: a prospective randomized trial. Endoscopy. 2009;41:842–848.
[49] Varadarajulu S, Christein JD, Tamhane A, et al. Prospective randomized trial comparing EUS and EGD for transmural drainage of pancreatic pseudocysts (with videos). Gastrointest Endosc. 2008;68:1102–1111.
[50] Anderloni A, Fabbri C, Nieto J, et al. The safety and efficacy of a new 20-mm lumen apposing metal stent (lams) for the endoscopic treatment of pancreatic and peripancreatic fluid collections: a large international, multicenter study. Surg Endosc. 2020;35:1741–1748.
[51] Ramouz A, Shafiei S, Ali-Hasan-Al-Saegh S, et al. Systematic review and meta-analysis of endoscopic ultrasound drainage for the management of fluid collections after pancreas surgery. Surg Endosc. 2022;36:3708–3720.
[52] Nemoto Y, Attam R, Arain MA, et al. Interventions for walled off necrosis using an algorithm based endoscopic step-up approach: outcomes in a large cohort of patients. Pancreatology. 2017;17:663–668.
[53] Bakker OJ, van Santvoort HC, van Brunschot S, et al. Endoscopic transgastric vs surgical necrosectomy for infected necrotizing pancreatitis: a randomized trial. JAMA. 2012;307:1053–1061.
[54] van Brunschot S, van Grinsven J, van Santvoort HC, et al. Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multi-centre randomised trial. Lancet. 2018;391:51–58.
[55] Onnekink AM, Boxhoorn L, Timmerhuis HC, et al. Endoscopic Versus Surgical Step-Up Approach for Infected Necrotizing Pancreatitis (ExTENSION): long-term follow-up of a randomized trial. Gastroenterology. 2022;163:712–722.e14.
[56] Bang JY, Arnoletti JP, Holt BA, et al. An endoscopic transluminal approach, compared with minimally invasive surgery, reduces complications and costs for patients with necrotizing pancreatitis. Gastroenterology. 2019;156:1027–1040.e3.
[57] Varadarajulu S, Bang JY, Sutton BS, et al. Equal efficacy of endoscopic and surgical cystogastrostomy for pancreatic pseudocyst drainage in a randomized trial. Gastroenterology. 2013;145:583–90.e1.
[58] Rizzatti G, Rimbas M, Larghi A. Endoscopic ultrasound-guided drainage for infected necrotizing pancreatitis: better than surgery but still lacking treatment protocol standardization. Gastroenterology. 2019;157:582–583.
[59] Singh AD, Mian A. Role of early endoscopically centered step-up interventions in acute necrotizing pancreatitis. Am J Gastroenterol. 2019;114:687–688.
[60] Boxhoorn L, Besselink MG, Voermans BP, et al. Surgery versus endoscopy for infected necrotizing pancreatitis: a fair comparison? Gastroenterology. 2019;157:583–584.
[61] Khan MA, Hammad T, Khan Z, et al. Endoscopic versus percutaneous management for symptomatic pancreatic fluid collections: a systematic review and meta-analysis. Endosc Int Open. 2018;6:E474–E483.
[62] Gagner M. Laparoscopic treatment of acute necrotizing pancreatitis. . Semin Laparosc Surg. 1996;3:21–28.
[63] Mangiavillano B, Arcidiacono PG, Masci E, et al. Single-step versus two-step endo-ultrasonography-guided drainage of pancreatic pseudocyst. J Dig Dis. 2012;13:47–53.
[64] Worhunsky DJ, Qadan M, Dua MM, et al. Laparoscopic transgastric necrosectomy for the management of pancreatic necrosis. J Am Coll Surg. 2014;219:735–743.
[65] Shelat VG, Diddapur RK. Minimally invasive retroperitoneal pancreatic necrosectomy in necrotizing pancreatitis. Singapore Med J. 2007;48:e220.
[66] Connor S, Ghaneh P, Raraty M, et al. Minimally invasive retroperitoneal pancreatic necrosectomy. Dig Surg. 2003;20:270–277.
[67] Risse O, Auguste T, Delannoy P, et al. Percutaneous video-assisted necrosectomy for infected pancreatic necrosis. Gastroenterol Clin Biol. 2004;28:868–871.
[68] Sileikis A, Beisa V, Simutis G, et al. Three-port retroperitoneoscopic necrosectomy in management of acute necrotic pancreatitis. Medicina (Kaunas). 2010;46:176–179.
[69] Shen B, Duan L, Yu H, et al. Retroperitoneal laparoscopic debridement therapy for infected severe acute pancreatitis. Zhonghua Yi Xue Za Zhi. 2017;97:3010–3012.
[70] Rego FR, Paredes GR, De Ardenas JDV, et al. Infected necrotizing pancreatitis. Video-assisted retroperitoneal debridement. Medicina (B Aires). 2021;81:115–118.
[71] Horvath KD, Kao LS, Wherry KL, et al. A technique for laparoscopic-assisted percutaneous drainage of infected pancreatic necrosis and pancreatic abscess. Surg Endosc. 2001;15:1221–1225.
[72] Gomatos IP, Halloran CM, Ghaneh P, et al. Outcomes from minimal access retroperitoneal and open pancreatic necrosectomy in 394 patients with necrotizing pancreatitis. Ann Surg. 2016;263:992–1001.
[73] Zelga P, Jees J, Iaculli E, et al. Patient-reported outcomes after minimally invasive retroperitoneal pancreatic necrosectomy to treat acute pancreatitis: an exploratory study. J Dig Dis. 2021;22:604–614.
[74] Dong Y, Jiang C, Guo W, et al. A comparative study on transnasal gastroscopy and conventional gastroscopy for percutaneous endoscopic pancreatic necrosectomy. Chin J Dig Endosc. 2019;36:815–820.
[75] Huang H, Wang D, Xie J, et al. A preliminary efficacy evaluation for percutaneous endoscopic necrosectomy in treating infectious pancreatic necrosis. Chin J Pancreatol. 2017;17:77–81.
[76] Lyu XJ, Sun B, Li L, et al. Clinical analysis of small incision minimally invasive approach in treatment of infected pancreatic necrosis. Zhong hua Wai Ke Za Zhi. 2018;56:687–692.
[77] van Brunschot S, Hollemans RA, Bakker OJ, et al. Minimally invasive and endoscopic versus open necrosectomy for necrotising pancreatitis: a pooled analysis of individual data for 1980 patients. Gut. 2018;67:697–706.
[78] Werner J, Hartwig W, Hackert T, et al. Surgery in the treatment of acute pancreatitis-open pancreatic necrosectomy. Scand J Surg. 2005;94:130–134.
[79] Connor S, Raraty MG, Howes N, et al. Surgery in the treatment of acute pancreatitis-minimal access pancreatic necrosectomy. Scand J Surg. 2005;94:135–142.
[80] van Dijk SM, Hallensleben NDL, van Santvoort HC, et al. Acute pancreatitis: recent advances through randomised trials. Gut. 2017;66:2024–2032.
[81] Trikudanathan G, Arain M, Attam R, et al. Interventions for necrotizing pancreatitis: an overview of current approaches. Expert Rev Gastroenterol Hepatol. 2013;7:463–475.
[82] Sun B, Ji L. The clinical practice and related reflections of staged step-up approach in the treatment of patients with severe acute pancreatitis. Zhonghua Wai Ke Za Zhi. 2015;53:653–656.
[83] Butturini G, Salvia R, Bettini R, et al. Infection prevention in necrotizing pancreatitis: an old challenge with new perspectives. J Hosp Infect. 2001;49:4–8.
[84] Alsfasser G, Schwandner F, Pertschy A, et al. Treatment of necrotizing pancreatitis: redefining the role of surgery. World J Surg. 2012;36:1142–1147.

[85] Rahnemai-Azar AA, Sutter C, Hayat U, et al. Multidisciplinary management of complicated pancreatitis: what every interventional radiologist should know. AJR Am J Roentgenol. 2021;217:921–932.
[86] Sun B, Li GQ. Reconsideration of staged step-up approach in treatment of patients with infected pancreatic necrosis. Zhong Hua Shi Yong Wai Ke Za Zhi. 2021;41:374–378.
[87] Rana SS. An overview of walled-off pancreatic necrosis for clinicians. Expert Rev Gastroenterol Hepatol. 2019;13:331–343.
[88] Globke B, Timmermann L, Klein F, et al. Postoperative acute necrotizing pancreatitis of the pancreatic remnant (POANP): a new definition of severe pancreatitis following pancreaticoduodenectomy. HPB (Oxford). 2020;22:445–451.
[89] Zhang Q, Li L, Lyu XJ, et al. Four-steps surgery for infected pancreatic necrosis based on "Step-up" strategy: a retrospective study. Zhonghua Wai Ke Za Zhi. 2020;58:858–863.
[90] Sun B, Song ZF, Jiang HC, et al. The clinical analysis of a step-up approach for severe acute pancreatitis. Zhonghua Wai Ke Za Zhi. 2013;51:493–498.
[91] Bakker OJ, van Baal MC, van Santvoort HC, et al. Endoscopic transpapillary stenting or conservative treatment for pancreatic fistulas in necrotizing pancreatitis: multicenter series and literature review. Ann Surg. 2011;253:961–967.
[92] Abdo A, Jani N, Cunningham SC. Pancreatic duct disruption and nonoperative management: the SEALANTS approach. Hepatobiliary Pancreat Dis Int. 2013;12:239–243.
[93] Kahl S, Schütte K, Glasbrenner B, et al. The effect of oral pancreatic enzyme supplementation on the course and outcome of acute pancreatitis: a randomized, doubleblind parallel-group study. JOP. 2014;15:165–174.
[94] Nadkarni NA, Khanna S, Vege SS. Splanchnic venous thrombosis and pancreatitis. Pancreas. 2013;42:924–931.
[95] Holt BA, Varadarajulu S. Perforation risk associated with percutaneous endoscopic gastrostomy-jejunal tube feeding in pancreatic walled off necrosis. Clin Gastroenterol Hepatol. 2016;14:A25–A26.

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