Interventions for Necrotizing Pancreatitis

Summary of a Multidisciplinary Consensus Conference

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Abstract: Pancreatic and peripancreatic necrosis may result in significant morbidity and mortality in patients with acute pancreatitis. Many recommendations have been made for management of necrotizing pancreatitis, but no published guidelines have incorporated the many recent developments in minimally invasive techniques for necrosectomy. Hence, a multidisciplinary conference was convened to develop a consensus on interventions for necrotizing pancreatitis. Participants included most international experts from multiple disciplines. The evidence for efficacy of interventions was reviewed, presentations were given by experts, and a consensus was reached on each topic. In summary, intervention is primarily indicated for infected necrosis, less often for symptomatic sterile necrosis, and should ideally be delayed as long as possible, preferably 4 weeks or longer after the onset of disease, for better demarcation and liquefaction of the necrosis. Both the step-up approach using percutaneous drainage followed by minimally invasive video-assisted retroperitoneal debridement and per-oral endoscopic necrosectomy have been shown to have superior outcomes to traditional open necrosectomy with respect to short-term and long-term morbidity and are emerging as treatments of choice. Applicability of these techniques depends on the availability of specialized expertise and a multidisciplinary team dedicated to the management of severe acute pancreatitis and its complications.

Key Words: necrotizing pancreatitis, infected necrosis, endoscopic necrosectomy, percutaneous catheter drainage, open necrosectomy, video-assisted retroperitoneal debridement

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Pancreatic parenchymal and/or peripancreatic tissue necrosis (ie, necrotizing pancreatitis) occurs in approximately 15% of patients with acute pancreatitis (AP) and confers substantial additional morbidity and mortality. Persistent (>48 hours) organ failure, including pulmonary, renal, circulatory, or other organ dysfunction, occurs in approximately half of patients with necrosis and in up to two thirds of those with infected necrosis.[1] Mortality is approximately 15% in patients with necrotizing pancreatitis and up to 30% in those with infected necrosis, which occurs at some point in the clinical course in about a third of patients with necrosis.[1–4]

Intervention is generally required for patients with infected pancreatic necrosis and, less commonly, in patients with sterile necrosis who are symptomatic, especially those with gastric outlet or biliary obstruction. Although open surgical debridement has been the traditional treatment, it has been long suspected that the physiologic stress of open surgical debridement increases morbidity and mortality.

Over the last decade, there have been substantial developments in at least 3 areas in the treatment of necrotizing pancreatitis. First, the terminology of severe AP and its complications has been redefined based on the enhanced understanding of pathophysiology and natural history of the condition and improved imaging techniques. Second, there has been a proliferation of minimally invasive treatment approaches to drainage and evacuation of pancreatic and peripancreatic necrosis, including image-guided radiological, peroral flexible endoscopic, laparoscopic, and retroperitoneal rigid endoscopic techniques (Tables 1 and 2). The third development has been publication of studies to provide evidence related to the efficacy of different treatments and techniques.

There is wide variation in conceptual and technical approaches to interventions for necrotizing pancreatitis. The minimally invasive or open surgical approach taken is often determined by institutional preferences, availability of equipment, expertise, and subspecialty background and interest of involved physicians. Care of patients with necrotizing pancreatitis should ideally include a team of specialists in intensive care medicine, gastroenterological medical management (gastroenterology, medical pancreatology), interventional radiology, interventional endoscopy, and surgery. However, there is such wide variation in clinical practice that a few physicians with variable expertise often are responsible for managing these patients.

Because of the rapid developments within this field and the variations in approaches to the treatment of necrotizing pancreatitis, the leadership of the American Pancreatic Association felt it timely to organize an international consensus conference to summarize available evidence, develop a consensus on treatment, and where possible provide direction for clinical care and research.

A 1-day meeting was held in conjunction with the annual meeting of the American Pancreatic Association in Chicago, Ill, in November 2010. Leading international experts in various aspects of pancreatology, diagnostic and interventional radiology, open and minimally invasive surgery, and interventional endoscopy were identified by the principal course directors based on publications and peer recognition and were invited to participate as moderators and/or speakers. Care was taken to represent as many major centers and countries as possible. The participants are listed in the Appendix. The focus of this meeting was on interventions for necrotizing pancreatitis. Because of time constraints, it was not possible to address medical and nutritional approaches to severe pancreatitis. These topics will

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TABLE 1. Classification of Interventions for Pancreatic Necrosis by Visualization, Route, and Purpose

Visualization
V1 Radiological
Using only radiological modalities (e.g. fluoroscopy, CT, ultrasound, MR) to visualize and assist entering the target lesion
V2 Endoscopic
Using any white light endoscopic instrument (e.g. flexible, or rigid endoscope, urological endoscope) to visualize the target lesion
V3 Hybrid
Using an endoscopic technique as the primary mode of visualization, assisted by a real time radiological modality (e.g. EUS)
V4 Open
Using any method where skin and any other body layers are cut to expose the site of the procedure
Vx Insufficient information
Vz Other visualization technique
Route
R1 Per-os transpapillary
External orifice entry point, internal route traversing duodenal papilla to enter pancreatic duct
R2 Per-os transmural
External orifice entry point, internal route traversing gastrointestinal wall
R3 Percutaneous retroperitoneal
Skin external entry point, internal route traversing retroperitoneum
R4 Percutaneous transperitoneal
Skin external entry point, internal route traversing peritoneum
R5 Percutaneous transmural
Skin-external entry point, internal route traversing gastrointestinal wall
Rx Insufficient information
Rz Other route
Purpose
P1 Drainage
Letting out fluid and/or solid material, externally out of the body or internally into the gastrointestinal tract
P2 Lavage
Flushing away solid matter with fluid to facilitate external or internal drainage
P3 Fragmentation
Breaking down solid matter by instrumental or mechanical disruption to facilitate external or internal drainage
P4 Debridement
Taking or cutting out solid matter with either sharp or blunt dissection
P5 Excision
Cutting out all or part of the pancreas, with the intention to fully remove all necrotic tissue
Px Insufficient information
Pz Other purpose

From Loveday et al[5] (reproduced with permission, with minor changes).

be reviewed in the update of the International Association of Pancreatology and APA Guidelines on the treatment of AP, which is currently in progress.

A series of lectures was prepared, each focusing on a specific question assigned by the meeting codirectors. After each session, a panel of experts reviewed the presentations, and questions and comments were taken from the audience. Where applicable, levels of evidence were graded according to the Oxford Center for Evidence-Based Medicine.[6] Drafts of the manuscript were circulated to all participants for comments and editing on a repeated basis before publication. Any important evidence that became available after the conference was incorporated into revisions of the manuscript, and then conclusions were updated accordingly and approved by the coauthors. Participants in the consensus process who contributed substantially to preparation or editing of the manuscript are listed as principle coauthors, whereas all participants are listed in the Appendix. The unedited video of the entire conference has since been uploaded to YouTube, LLC, for public viewing (http://tinyurl.com/pancreaticnecrosis).

Consensus questions (CQs) 1 to 19 (some of the questions were combined and reorganized after the original conference) were as follows:

CQ 1 and 2: What are the main points in the revision of the Atlanta classification with regard to pancreatic and peripancreatic necrosis?

CQ 3 and 4: What is the diagnostic role of computed tomography, magnetic resonance cholangiopancreatography, and endoscopic ultrasound in management of necrotizing pancreatitis?

CQ 5: How is infected necrosis diagnosed, and is fine needle aspiration still required?

CQ 6: When is intervention indicated for sterile and infected necrosis, and is there a role for medical management alone?

TABLE 2. Taxonomy of Minimally Invasive Approaches for Pancreatic Necrosis

Technique Name	Visualization	Route	Purpose
PCD	Radiological	Perc retroperitoneal Perc transperitoneal Perc transmural	Drainage
Minimally invasive radiological-assisted necrosectomy	Radiological	Perc retroperitoneal	Debridement
Laparoscopic cystogastrostomy	Endoscopic	Per-os transmural	Drainage
VARD	Hybrid	Perc retroperitoneal	Debridement
Endoscopic transpapillary drainage	Hybrid	Per-os transpapillary	Drainage
EUS-guided endoscopic transmural drainage	Hybrid	Per-os transmural	Drainage
EUS-guided drainage	Hybrid	Per-os transmural	Lavage
Aggressive endoscopic therapy	Hybrid	Per-os transmural	Debridement
Minimally invasive retroperitoneal pancreatic necrosectomy	Endoscopic	Perc retroperitoneal	Debridement
Retroperitoneal laparotomy	Open	Perc retroperitoneal	Debridement
Subtotal resection	Open	Perc transperitoneal	Excision
Open necrosectomy and continuous local lavage	Open	Perc transperitoneal	Debridement
Open cystogastrostomy	Open	Perc transmural	Drainage

From Loveday et al[5] (reproduced with permission, with minor changes).

CQ 7: What are the available methods for intervention in pancreatic and peripancreatic necrosis?

CQ 8: When is open surgical debridement indicated for treatment of necrotizing pancreatitis and which technique has the best results?

CQ 9: What are the currently available minimally invasive approaches to necrosectomy?

CQ 10 and 11: What are the results with a laparoscopic approach to necrosectomy?

CQ 12: What are the results with a minimally invasive retroperitoneal approach to necrosectomy, including video-assisted retroperitoneal debridement?

CQ 13: What are the results of an image-guided percutaneous-only approach to debridement of necrosis, and when is it indicated?

CQ 14 and 15: What are the various techniques of endoscopic necrosectomy, including the endoscopic ultrasound–guided technique?

CQ 16: What are the outcomes of multicenter studies on endoscopic necrosectomy?

CQ 17: What are the results of a combined endoscopic and percutaneous approach?

CQ 18: What are the results with the "step-up" approach?

CQ 19: What are the outcomes of endoscopic, percutaneous image-guided, and surgical management of disconnected pancreatic duct and recurrent fistula?

CONSENSUS QUESTIONS 1 TO 19

CQ 1 and 2: What are the main points in the revision of the Atlanta classification with regard to pancreatic and peripancreatic necrosis?

The Atlanta symposium in 1992 was a landmark consensus conference that attempted to provide a universally applicable classification system for AP.[7] Because of many developments since that time, a multidisciplinary consensus panel has recently recommended a revision of the classification and definitions.[8] Accurate and unambiguous definitions are essential in selecting interventions for different complications of AP, for communication between clinicians, and for studies.

The proposed terms for AP and its complications in the revision of the Atlanta classification by the International working group (Gut, in press) are as follows:

Acute pancreatitis (AP) is defined as either interstitial or necrotizing. The former is usually clinically mild and the latter clinically severe. Necrotizing pancreatitis is defined by lack of enhancement of pancreatic parenchyma on cross-sectional imaging after intravenous contrast administration and can involve either pancreatic parenchyma alone (uncommon), pancreatic parenchyma and peripancreatic tissues (most common), or peripancreatic tissues alone (least common). From a clinical standpoint, pancreatic and peripancreatic necrosis behave similarly, although isolated peripancreatic necrosis may be associated with improved outcomes compared with pancreatic necrosis.[4]

A number of local complications can occur with AP and can be either sterile or infected. The recognition and diagnosis of these complications are important for selecting the best treatment approach. The proposed terms for these in the revision of the Atlanta classification are as follows:

1. Acute peripancreatic fluid collections, which arise in the setting of interstitial pancreatitis, are adjacent to the pancreas, homogeneous, fluid filled, and without full encapsulation. They occur fewer than 4 weeks after the onset of AP.
2. Acute necrotic collections, which occur in necrotizing pancreatitis, can be intrapancreatic or extrapancreatic, heterogeneous, contain nonliquid material with varying amounts of fluid, and are without full encapsulation. They occur less than 4 weeks after the onset of AP.
3. Pseudocysts comprise only a minority of collections in pancreatitis, develop adjacent to the pancreas, are homogeneous, fluid filled, with a defined wall, lack significant nonliquid debris, and occur at least 4 or more weeks after the onset of AP.
4. Walled-off necrosis (WON), which occurs only in the context of acute necrotizing pancreatitis, can be intrapancreatic or extrapancreatic, is heterogeneous, contains nonliquid material with varying amounts of fluid, and has an encapsulating wall. This process occurs 4 or more weeks after the onset of AP.

CQ 3 and 4: What is the diagnostic role of computed tomography, magnetic resonance cholangiopancreatography, and endoscopic ultrasound in management of necrotizing pancreatitis?

Contrast-enhanced CT (CECT) remains the standard imaging modality in the setting of severe AP (Figs. 2–9). It is rarely required to diagnose AP. It is not routinely required for the prediction of the severity of pancreatitis because the CT severity index does not perform better than other commonly used systems based on clinical and biochemical parameters.[8] The most important roles for CECT are the diagnosis of pancreatic parenchymal necrosis, determining the extent of necrosis, and diagnosing other local complications, including venous thrombosis and pseudoaneurysms. It is important to keep in mind that complete development of pancreatic necrosis may not occur in some patients until up to 5 days after presentation. Thus, imaging cannot be used to reliably determine presence or full extent of necrosis before that time.[2] Disadvantages of CECT include radiation exposure, especially with repeated imaging, and potential nephrotoxicity associated with intravenous contrast media particularly in patients with impaired renal function. Contrast-enhanced CT cannot reliably detect underlying necrotic debris in an acute necrotic collection or WON, especially fluid-predominant collections.[8]

Magnetic resonance imaging (MRI) and magnetic resonance cholangiopancreatography (MRCP) may be equivalent to CT for detection of parenchymal necrosis; in patients with renal insufficiency, MRI can suggest the presence of pancreatic necrosis, even without intravenous gadolinium, based on fat-suppressed T1-weighted images.[8–14] Advantages of MRI include lack of radiation, superior detection of nonliquid material in pancreatic and peripancreatic collections, ability of MRCP to detect bile duct stones, and ability to demonstrate the presence of disconnected pancreatic duct in the subacute phase, particularly when secretin stimulation is used. Disadvantages of MRI/MRCP include variability in availability and quality of scanners, longer acquisition times, difficult patient tolerance in the setting of a critical illness, toxicity of gadolinium in patients with renal insufficiency, and contraindication of MRI in pacemakers and other metallic objects.[9–14] Both fat-saturated T2-weighted MRI and endoscopic ultrasound (EUS) seem to be superior to CT for detecting nonliquid necrosis and debris within pancreatic and peripancreatic collections, which is important when determining the type of intervention. Although MRI/MRCP are solely diagnostic, EUS allows the combination of imaging with image-guided intervention. EUS has the added advantage of providing the highest available sensitivity in detecting bile duct stones without the risk associated with endoscopic retrograde cholangiopancreatography (ERCP) and can be done at the bedside in severely ill patients. Limitations of EUS are the inconsistent availability of skilled endosonographers, a small potential for adverse events in critically ill patients, and tendency to overestimate the necrotic debris content of pancreatic fluid collections.

CQ 5: How is infected necrosis diagnosed, and is fine needle aspiration still required?

Infection of pancreatic or peripancreatic necrosis increases morbidity and mortality, and usually mandates intervention. Peak occurrence is between 2 and 4 weeks after presentation but may occur at any time during the clinical course of necrotizing pancreatitis. Infection may be proven by culture or Gram stain of tissue or fluid, strongly suspected when there is gas in the necrotic area documented by abdominal imaging in the correct clinical setting (gas may occur because of gas-forming organisms or, alternatively, as a result of fistula to the stomach, small bowel, or colon). Infected necrosis is probable if the patient develops sepsis, systemic inflammatory response syndrome (SIRS) or organ failure later in the course of disease (typically >7 days after the onset of AP), especially in a patient who was previously clinically stable or improving as indicated by parameters such as hemodynamics, white blood cell count, and fever curve.[2,15,16]

Image-guided fine needle aspiration (FNA) to obtain culture and Gram stain was introduced more than 20 years ago, and in the past, a positive aspirate was thought to mandate immediate surgical intervention.[17] However, trends in therapy have altered this approach such that the clinical relevance of FNA has been substantially diminished. These include avoidance of early interventions, and the acceptance of minimally invasive percutaneous or endoscopic interventions early in the course of the disease either to avoid or postpone more invasive surgical interventions (Table 3). At the time of intervention, cultures for bacteria and fungi may be obtained, such that simple diagnostic FNA is not necessary. Moreover, there is potential for the treatment of infected necrosis with antibiotics alone when there are no signs of sepsis. Increasingly, even proven infected necrosis can be managed with antibiotics and supportive care until the necrotic collections can partially liquefy, wall-off, and thus allow safer, more organ-preserving and more effective interventions.[2] In summary, at the present time, there are relatively few indications for purely diagnostic FNA to diagnose infected necrosis; possible indications include suspicion of fungal superinfection when combination antibiotic therapy does not normalize temperature curves and/or resolve leukocytosis in patients with presumed infected necrosis.

CQ 6: When is intervention indicated for sterile and infected necrosis, and is there a role for medical management alone?

A central question for management of sterile and infected pancreatic and peripancreatic necrosis is determining if and when intervention is required for drainage and/or debridement. Several points have been established:

1. Sterile acute necrotic collections almost never require intervention early in the course of disease, and in the later phase (ie, after several weeks), only in the presence of disabling symptoms such as abdominal pain and/or significant mechanical obstruction (eg, gastric outlet or biliary).
2. Infected acute necrotic collections may occasionally require early intervention, but since early open surgery is associated with high morbidity and mortality, it should be avoided whenever possible. Instead, radiological or endoscopic drainage should be used before surgery in the treatment of infection and to postpone or obviate the need for surgical debridement.[4,8,40]
3. Intervention by any method is optimal when infected necrosis is walled-off and demarcated with at least partial liquefaction, and discrete encapsulation. This typically requires a delay of 4 to 6 weeks.
4. Asymptomatic WON does not mandate intervention regardless of the size and extension of the collection, and may resolve spontaneously over time, even in rare cases of infected necrosis.
5. Symptomatic WON generally requires intervention late in the course (ie, >4 weeks) if there is intractable pain, obstruction of a viscus such as the stomach or bile duct, or in the presence of infection.

Indications for intervention within the first few weeks of onset of AP include clearly infected acute necrotic collections associated with clinical deterioration and signs of sepsis. In contrast, clinical deterioration despite maximum medical support, including intensive care, specific organ support, and ERCP for cholangitis in patients without documented infection, does not seem to be an indication for local treatment such as radiological, endoscopic, or surgical drainage or necrosectomy.[41,42] In particular, patients within the first week of disease with fulminant AP characterized by SIRS with rapid clinical deterioration and multiorgan failure, despite intensive care treatment,

TABLE 3. Outcomes of Various Open Surgical Necrosectomy Techniques for Necrotizing Pancreatitis

First Author (Year)	No. Patients	Patients Infected, n (%)	Timing of Intervention (Days After Presentation)	Morbidity, %	Reoperations, % or n/Patient	Mortality, n (%)
Open packing						
Bradley (1993)[18]	71	53 (74)	NA	61 F: 46 B: 7	1–5/patient	11 (15)
Branum (1998)[19]	50	42 (84)	27 (mean)	46 F: 8	2–13/patient	6 (12)
Bosscha (1998)[20]	28	28 (100)	NA	F: 25 B: 50	61%	11 (39)
Nieuwenhuijs (2003)[21]	38	NA	NA	89 F: 21 B: 42	3–70/patient	18 (47)
Olakowski (2006)[22]	144	120 (83)	NA	43	3–8/patient	26 (21)
Planned relaparotomy						
Sarr (1991)[23]	23	18 (75)	NA	52 F: 78 B: 26	2 to more than 5/patient	4 (17)
Tsiotos (1998)[24]	72	57 (79)	NA	50 F: 35 B: 18	79% (1–7/ patient)	18 (25)
Howard (2007)[25]	102					
1993–2001	55	42 (76)	46	89 F: 49 B: 48	67%	10 (18)
2002–2005	47	34 (72)	44	72 F: 49 B: 24	68%	2 (4)
Closed packing						
Fernandez-del Castillo (1998)[26]	64	36 (56)	31 (median)	F: 69 B: 3	17%	4 (6)
Rodriguez (2008)[27]	167	113 (68)		F: 50 B: 4	11%	19 (11)
			17.5 (<28 d)	F: 60 B: 6	19%	20
			77.1 (>28 d)	F: 54 B: 2	8%	5
Postoperative continuous lavage						
Beger (1988)[28]	95	37 (39)	NA	41	27%	8 (8)
Farkas (1996)[29]	123	123 (100)	18.5 (mean)	F: 14 B: 2	46%	9 (7)
Büchler (2000)[30]	29	27 (93)	21.7 (10–49)	F: 29 B: 7	22%	7 (24)
Nieuwenhuijs (2003)[21]	21	NA	NA	44 F: 14 B: 10	0–3/patient	7 (33)
Rau (2005)[31]	140	140 (100)	20	78	27%	38 (27)
Reddy (2006)[32]	118	85 (72)	NA	57 F: 36 B: 16	38%	
1990–1996	60	32 (53)	17 (12–25)	NA	20%	28 (47)
1997–2002	58	45 (78)	26 (19–40)	NA	26%	17 (29)
Farkas (2006)[33]	220	220 (100)	19 (8–25)	33 F: 13 B: 2.8	22%	18 (8)

(Continued on next page)

TABLE 3. *(Continued)*

First Author (Year)	No. Patients	Patients Infected, n (%)	Timing of Intervention (Days After Presentation)	Morbidity, %	Reoperations, % or n/Patient	Mortality, n (%)
Kingham (2008)[34]	29	19 (66)	31 (6–289)	75 F: 24 B: 13	5/patient	4 (14)
van Santvoort (2010)[35]	59	55 (93)	29 (12–155)	84 F: 60 B: 22	42%	9 (16)
Babu (2010)[36]	28	23 (82)	34 (5–149)	86 F: 21 B: 3	43%	6 (22)
Wittau[37]						
1992–1997	78	44 (56)	19.5	NA	NA	32 (41)
2001–2006	32	29 (90)	30	NA	NA	6 (18)
Mixed series						
De Rai (2010) (Italy)[38]	29	8 (28)	14 (median)	48 F: 17 B: 3	21%	6 (21)
Parikh (2009) (United States)[39]	161	NA	NA	62 B: 6	20%	11 (7)

B indicates bleeding; F, fistula; NA, not available; OR, operating room.

sometimes undergo surgery as a last resort even if the process is sterile.[3] However, the prognosis for these patients is poor regardless of surgical intervention.[41] One exception may be abdominal compartment syndrome, where surgical or percutaneous radiological decompression may be life-saving.

For patients with infected necrosis, there is convincing evidence that delayed intervention is superior to early intervention. Attempts to debride pancreatic necrosis before 3 weeks increases the risk of bleeding and other adverse events. The use of less invasive techniques allows surgical debridement to be deferred or avoided altogether.[4,41,43–45] With delay in intervention, demarcation of necrotic from vital tissue occurs, so that if necrosectomy is performed later in the course, resection of vital tissue is minimized, leading to better long-term endocrine and exocrine function and a reduction in postoperative adverse events.[3]

In a randomized trial, early necrosectomy (within the first 2–3 days after onset of AP) produced a higher morbidity and mortality than delayed intervention after at least 12 days.[45] In addition to the presence of multiorgan failure and a high APACHE II score, early surgery has been shown to be an independent predictor of poor outcome of acute necrotizing pancreatitis.[4] Several case series also underscore that mortality decreases when interventions are postponed.[37,41,42,44,46] As advocated in guidelines by the International Association of Pancreatology in 2002,[3] delay in open surgery for at least 3 to 4 weeks leads to lower morbidity and mortality rates than earlier intervention. The advantage of delayed surgery is especially evident in series in which timing of intervention was changed within a single institution.[32,37,42,46] The same advantage has been demonstrated in large numbers of patients managed in different centers around the world (Table 3). When emergency interventions are needed for perforated viscus, acute bleeding, fistula to or obstruction of a viscus, and abdominal compartment syndrome, drainage or debridement of necrosis is not required at the same setting.[3]

Initial case reports and series have supported primary noninterventional medical treatment with administration of antibiotics alone for infected necrosis.[47,48] Subsequently, larger series have confirmed that selected patients with infected necrosis who are clinically stable and minimally symptomatic can be treated using antibiotic therapy alone.[46,49–52] However, such patients require intervention if clinical deterioration occurs.

CQ 7: What are the available methods for intervention in pancreatic and peripancreatic necrosis?

Interventions to drain and/or debride pancreatic and peripancreatic necrosis can be categorized into open surgical, minimally invasive surgical approaches including laparoscopy and retroperitoneoscopy, image-guided percutaneous, and endoscopic, and hybrid approaches. Access points are transperitoneal (through the abdominal wall), retroperitoneal usually through a flank approach, and/or orally via a transmural approach through the stomach or duodenum, the latter representing a true natural orifice transluminal endoscopic surgery procedure (Table 1). Minimally invasive approaches are increasingly being used.

CQ 8: When is open surgical debridement indicated for treatment of necrotizing pancreatitis and which technique has the best results?

Open surgical debridement historically has been the standard treatment for infected necrosis and for symptomatic sterile WON with the aim of complete removal of necrotic tissue. The oldest and most established approach includes open laparotomy or retroperitoneal flank incision with manual debridement. Necrosectomy is performed using an organ-preserving technique by blunt dissection; formal resections are avoided to minimize the incidence of bleeding, fistulae, and removal of vital tissue. After necrosectomy, the abdomen may be left open (the retroperitoneum is "marsupialized"), packed, and repeatedly debrided until there is no residual necrosis. The abdomen is allowed to close by secondary intention (Table 3). In contrast, 2 other surgical techniques using abdominal closure are used, namely "closed packing" and "postoperative continuous lavage." When closed packing is performed, the abdomen is closed with packing and external drains remaining. Repeated open necrosectomy is performed and the packing is removed when there is no residual necrosis. Drains are eventually withdrawn. Postoperative continuous lavage is performed after the abdomen is closed to allow continuous removal of residual necrotic material by irrigation and to decrease inflammatory mediators. Multiple catheters are placed in the lesser sac/retroperitoneum and behind the colon for postoperative irrigation; reinterventions and repeat laparotomies are avoided in most cases, with a decrease in postoperative morbidity.[53] The technique of closed packing is mainly advocated by a single group.[26] In some cases of incomplete necrosectomy, percutaneous drains can be placed if needed to provide irrigation and to further debride residual postoperative collections ("step-down" approach; Table 3).

Open necrosectomy is associated with relatively high morbidity (34%–95%) and mortality ranging from 6% to 25%, depending on the series, the severity of illness at the time of surgery and other factors.[24–28,30,35,37,39,53–56] Potential immediate postoperative adverse events include organ failure, perforation of a hollow viscus, wound infection, and hemorrhage, any of which may require reoperation. Long-term adverse events include chronic pancreaticocutaneous and enterocutaneous fistulae, diabetes mellitus, exocrine pancreatic insufficiency, and abdominal wall hernias.

Comparing the 4 principal approaches for open necrosectomy, there are consensus but limited data to support the claim that postoperative continuous irrigation and "closed packing" are superior to open packing and planned relaparotomies (Table 3). Relaparotomy increases the local intra-abdominal and systemic trauma and has negative systemic effects on hemodynamics and systemic inflammatory response. Although mortality is similar (around 15% to 20% across series), morbidity seems to be decreased by avoiding surgical reinterventions. Randomized controlled trials have demonstrated that delayed surgical necrosectomy is superior to early necrosectomy.[45] Subsequently, a step-up approach (initial percutaneous drainage followed by minimally invasive debridement) has been shown to be superior to open surgical necrosectomy with postoperative lavage with respect to short-term and long-term morbidity in patients with infected necrosis.[35]

CQ 9: What are the currently available minimally invasive approaches to necrosectomy?

The many different approaches to minimally invasive pancreatic necrosectomy can be classified according to the access route (peritoneal, retroperitoneal, transoral) and the method used for visualization (laparoscopic, rigid nephroscopic, flexible endoscopic).[5,57] Features missing from this classification include radiological insertion of percutaneous drains. Percutaneous catheter drainage originally played an adjuvant role in draining residual collections after open necrosectomy[53] but is increasingly used in a step-up approach to defer or obviate the need for surgery or as an adjunct to endoscopic necrosectomy.[35]

As a result of the many different modalities used for the treatment of necrotizing pancreatitis, a comprehensive classification system of minimally invasive techniques for the treatment of pancreatic and peripancreatic necrosis and associated complications was developed.[5,57] This taxonomy was based on the *method of visualization* (open, radiological, endoscopic, hybrid, or other), *route* (per oral transpapillary or transmural, percutaneous retroperitoneal, percutaneous transperitoneal, percutaneous transmural, or others), and *purpose* (drainage lavage, fragmentation, debridement, excision, or other). This taxonomy has good to excellent interobserver agreement[5] (Fig. 1 and Tables 1 and 2). Using this system may prove cumbersome for routine clinical use, but it allows for the unambiguous classification of all techniques for the purposes of audit, evaluation, publication, and comparisons of outcome.

Results using various minimally invasive methods described in this article, along with results of open surgery and medical management, are shown in Tables 3 to 6. It must be emphasized that these studies involve heterogeneous patient populations, definitions of infected necrosis, and techniques. As a result, outcomes are not directly comparable outside of randomized trials. Mortality does not seem to be consistently influenced by the adoption of minimally invasive approaches. This is underscored by the results of a randomized multicenter trial comparing the step-up approach to open surgery[35] and another study comparing endoscopic necrosectomy with surgical management.[56] Advantages of minimally invasive approaches include a reduction in systemic complications after intervention and a lower risk of developing new organ failure.[35,36] Local adverse events including bleeding and fistula seem to be slightly increased in some retrospective studies when certain minimally invasive treatment regimens are used, although this finding may reflect a difference in the definition of adverse events or represent a learning curve associated with early results.[35,54,69,70]

CQ 10 and 11: What are the results with a laparoscopic approach to necrosectomy?

Few authors advocate the use of laparoscopy for treatment of necrotizing pancreatitis. Laparoscopic-assisted pancreatic debridement is performed with laparoscopic visualization followed by hand-assisted or laparoscopic debridement through a separate port. This technique allows access to all compartments of the abdomen and successful single session debridement of acute necrotic collections or WON is feasible in most patients. Reoperation is needed in approximately 20% of cases (Table 5).[69–75] Potential advantages include less wound infections and pulmonary adverse events than open necrosectomy, but risks include dissemination of retroperitoneal infection into the peritoneum.

Laparoscopic enteric drainage involves a peritoneal approach with creation of a large anastomosis between the stomach or small bowel and the necrotic collection. A single intervention is usually adequate even for large WON.[79] This technique is best reserved for highly experienced minimally invasive surgeons and well-demarcated WON near the stomach or small bowel lumen. An advantage of this approach is that it allows simultaneous laparoscopic cholecystectomy in patients whose pancreatitis was gallstone induced.

CQ 12: What are the results with a minimally invasive retroperitoneal approach to necrosectomy, including video-assisted retroperitoneal debridement?

A variety of techniques exist whereby a percutaneous tract into the necrotic collection is established (usually under radiological image-guided percutaneous guidance). The tract is subsequently enlarged via dilation or with a limited incision to allow passage of a rigid nephroscope, laparoscope, or flexible endoscope for direct visualization, debridement, and lavage of the necrotic cavity. These techniques are all variants of retroperitoneoscopy (Table 5) and collectively have been termed *sinus*

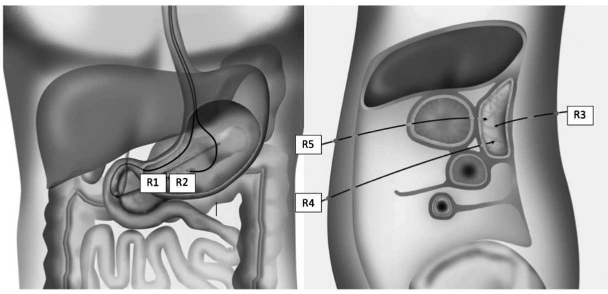

FIGURE 1. Figure showing routes of interventions for pancreatic necrosis by visualization, route, and purpose (from Loveday et al[5]; reproduced with permission).

TABLE 4. Outcomes of Percutaneous Catheter Drainage for Necrotizing Pancreatitis

First Author (Year)	No. Patients	Patients Infected, n (%)	Timing of Drainage (Days After Presentation)	Technique	Duration of Drainage, d	Catheter Exchanges, Mean (Range)	Clinical Success for PCD Alone, n (%)	Morbidity, %	Operation Required for Infected Necrosis, n (%)	Mortality, n (%)
Lee (1992)[89]	30	6 (20)	NA	Mean 1.4 drains (12–24 Fr)	35	3 (1–6)	1 (3)	NA	5 (17)	10 (33)
Rotman (1992)[90]	14	12 (86)	21	Mean 1.1 drains (14 Fr)	17 (2–24)	0.2 (0–1)	0	NA	11 (79)	3 (21)
Sunday (1994)[91]	8	0 (6 PCs, 1 hematoma)	NA	NA	NA	2.25 (1–7)	2 (25)	NA	6 (75)	1 (13)
Aultman (1997)[92]	19	10 (53)	NA	NA	NA	NA	7 (37)	NA	3 (16)	2 (11)
Freeny (1998)[82]	34	34 (100)	63 (7 to >300)	Mean 3 transperitoneal drains (10–28 Fr)	25–152	3.3	16 (47)	26	18 (53)	4 (12)
Echenique (1998)[93]	20	20 (100)	NA	Mean of 2 drains (10%–14 Fr), catheter necrosectomy	83	17 (7–32)	20 (100)	NA	0	0
Gambiez (1998)[76]	10	3 (30)	17 (10–25)	1–2 drains (15–30 Fr)	4–22 (mean, 16)	NA	0	60	3 (30)	2 (20)
Fotoohi (1999)[71]	60	44 (73)	NA	8–24 Fr drains	NA	NA	54 (90)	10	3 (5)	3 (5)
Baril (2000)[94]	25	19 (76)	NA	Mean 1.4 drains (10–12 Fr)	NA	14–56	19 (76)	4	7 (18)	2 (8)
Baron (2002)[95]	38	38 (100)	NA	10–12 Fr drains	NA	2 (1–6)	30 (79)	NA	7 (18)	2 (5)
Cheung (2005)[96]	8	8 (100)	55 (21–154)	20 Fr drains	NA	NA	3 (38)	50	5 (63)	1 (13)
Olah (2006)[46]	25	15 (60)	12	NA	NA	0.1	3 (12)	NA	12 (48)	2 (8)
Navalho (2006)[97]	30	30 (100)	18	12–14 Fr drains	24 (5–92)	2	19 (63)	NA	10 (33)	5 (17)
Lee (2007)[98]	18	18 (100)	10 (1–58)	14 Fr drains dilated to 20 Fr combined with irrigation	NA	NA	15 (83)	11	3 (17)	1 (6)
Szentkereszty (2008)[99]	61	NA	>28	NA	NA	NA	7 (11)	NA	15 (25)	10 (16)
Bruennler (2008)[100]	80	80 (100)	>15	2 catheters per patient (8–24 Fr), necrosectomy by catheter in 18 patients	37 (1–260)	2 (17–9)	42 (53)	29	24 (30)	27 (34)
Mortele (2009)[101]	35	35 (100)	Mean 11 (2–33)	14 Fr drains	42 (3–120)	3.3	17 (49)	11	13 (37)	6 (17)
Rocha (2009)[88]	28	9 (32)	NA	NA	NA	NA	5 (18)	11	17 (61)	8 (29)
Van Santvoort (2010)[35]	43	43 (100)	Median 30 (11–71)	Minimum 12 Fr	NA	0–2	15 (35)	40	26 (60)	8 (19)

Only series with more than 5 patients are shown[38,72–76,78,89–101] (excluding Aultman et al,[92] Baril et al,[94] and Cheung et al[96]).
Fr indicates French; NA, not available; PC, pseudocyst.

TABLE 5. Outcomes of Various Minimally Invasive Surgical Necrosectomy Techniques for Necrotizing Pancreatitis

First Author (Year)	No. Patients	Patients Infected, n (%)	Timing of Intervention (Days After Presentation)	Clinical Success of Minimally Invasive Necrosectomy, n (%)	Morbidity, %	Reoperations, % or n/Patient	Mortality, n (%)
Laparoscopic (transperitoneal)							
Gagner (1996)[72]	8	NA	NA	6 (75)	NA	38% (0.3/patient)	0
Zhu (2001)[73]	10	0	1–3	7 (70)	NA	NA	1 (10)
Cuschieri (2002)[74]	11	11 (100)	NA	10 (90)	NA	0	2 (18)
Zhou (2003)[75]	13	4 (31)	NA	12 (92)	NA	0	2 (15)
Parekh (2006)[69]	19	9 (47)	NA	16 (84)	21	11% (0.1/patient)	2 (11)
Retroperitoneoscopy (flexible or rigid endoscopic, laparoscopic, etc)							
Gambiez (1998)[76]	20	13 (65)	18 (13–26)	15 (75)	60	5 (mean)	2 (10)
Carter (2000)[77]	10	10 (100)	40 (13–187)	8 (80)	28	2.4 (1–4)	2 (20)
Castellanos (2002)[78]	15	15 (100)	NA	11 (73)	40	8–10	4 (27)
Connor (2005)[70]	47	38 (81)	28 (3–161)	35 (75)	92	3 (1–5)	9 (19)
Horvath (2010)[84]	25	25 (100)	80 (33–208)	15 (60)	NA	8%	0
Van Santvoort (2010)[35]	24	22 (92)	30 (11–71)	15 (63)	65	NA	4 (17)
Raraty (2010)[54]	137	88 (64)	32 (1–181)	115 (84)	55	33%	26 (19)
Bakker (2012)[56]	10	9 (90)	59 (29–69)	6 (60)	80	40%	4 (40)

tract endoscopy and *video-assisted retroperitoneal debridement* (VARD), with the former involving purely endoscopic debridement and lavage in serial sessions and the latter generally involving a small (5–7cm) subcostal incision and limited direct debridement followed by subsequent video-assisted debridement.[80] In several uncontrolled series using minimally invasive retroperitoneal approaches, periprocedural adverse events were less than 5%, median number of interventions was fewer than 3, morbidity ranged from 10% to 30%, and mortality ranged from 0% to 20%.[70,77,80–88] In a series of 400 patients from 3 centers in the United Kingdom, this approach has essentially replaced open surgery for sepsis control with a trend toward decreased postoperative organ failure and a reduction in need for ICU management, although with an increase in hospital stay compared with historical controls who underwent open surgery.[83] In retrospective comparisons from experienced centers, need for open necrosectomy for infected necrosis has been reduced from more than 90% to less than 10%. However, reductions in hospital stay and/or mortality have been demonstrated by relatively few studies.[54]

CQ 13: What are the results of an image-guided percutaneous-only approach to debridement of necrosis, and when is it indicated?

Percutaneous catheter drainage (PCD) of pancreatic and peripancreatic necrosis can range from placement of single, small-caliber drains to placement of multiple, large-bore catheters that are rapidly upsized, irrigated and manipulated along with direct percutaneous necrosectomy. Percutaneous catheter drainage can be used as primary therapy, as an adjunct to other techniques, and as salvage management of residual necrotic or infected collections.[35,82,85] Approaches include transperitoneal or retroperitoneal placement of 12- to 30-Fr catheters. A retroperitoneal approach is generally preferred because it avoids contamination and enteric leaks and facilitates a step-up approach.[86,87] Percutaneous catheter drainage is most useful for collections that do not resolve, to control sepsis, and the first step in the step-up approach, in combination with endoscopic transmural debridement, as a bridge to surgery , or to treat residual collections after surgery (Table 4).

Percutaneous catheter drainage is technically feasible in most cases using a retroperitoneal route. A systematic review of PCD as primary treatment for pancreatic necrosis included 11 studies involving 384 patients.[87] Seventy percent of patients had infected necrosis and an average of 2 separate catheters were placed, with an overall success rate of 56%. In 2 prospective studies, the clinical success of PCD alone was found to be 33% and 35%.[35,84] Adverse events such as external fistulae occur in up to 27% of patients.

A dedicated team of radiologists willing to closely observe patients, place multiple catheters, and exchange and flush catheters is widely thought to be required for the successful percutaneous management of pancreatic necrosis. In general, at least one separate catheter is required for each collection; in 1 study, a mean number of 3.3 catheters were placed per patient[88] with up to 100 total catheter exchanges. In contrast, in the Dutch PANTER trial, most patients only required one 14-Fr catheter irrigated 3 times daily.[35] Thus, optimal size, number of drains, and management of drains when PCD is used is unknown.

CQ 14 and 15: What are the various techniques of endoscopic necrosectomy, including the endoscopic ultrasound–guided technique?

Peroral flexible endoscopic drainage of pseudocysts performed via transpapillary or transmural techniques was first described more than 25 years ago. The addition of a nasocystic catheter through a transmural entry site alongside 10-Fr stents to provide irrigation as a method to treat WON was described in 1996.[58] Transluminal direct endoscopic necrosectomy (DEN) for debridement of WON was first reported in 2000.[59,61,68] A systematic review of endoscopic necrosectomy has been published recently.[102] Direct endoscopic necrosectomy is performed by passing a flexible endoscope transorally then transmurally into the necrotic cavity; mechanical debridement and lavage are performed using a variety of accessories and techniques. DEN requires a collection to be located within several centimeters of the gastric or duodenal lumen. After transmural puncture into the cavity, large-diameter balloon dilation of the tract, and placement of multiple large-bore double-pigtail stents (or recently, removable self-expanding metallic stents), repeated mechanical debridement is performed using baskets, balloons, forceps, nets,

TABLE 6. Outcomes of Endoscopic Management With or Without Adjunctive Techniques for Necrotizing Pancreatitis

First Author (Year)	No. Patients	Patients Infected, n (%)	Timing of Intervention (Days After Presentation), Mean (Range)	Technique	Endoscopic Reinterventions, Mean (Range)	Clinical Success of Endoscopic Management Plus Any Adjunctive PCD, n (%)	Morbidity, %	Mortality, n (%)
Baron (1996)[58]	11	3 (27)	50	Transmural stents plus nasocystic or per gastrostomy lavage ± transpapillary stenting	2.7 (2–4)	9 (82)	45	0
Seifert (2000)[59]	3	1 (33)	14–64	DEN (first report)	NA	3 (100)	0	0
Park (2002)[60]	9	9 (100)	42	Transmural stents ± nasocystic lavage	0.3	8 (89)	11	0
Seewald (2005)[61]	13	13 (100)	NA	DEN ± nasocystic lavage, ± transpapillary stenting, sealing of pancreatic duct fistula	15	10 (77)	30 (mild)	0
Charnley (2006)[62]	13	11 (85)	27	DEN	4	9 (69)	NA	2 (15)
Papachristou (2007)[42]	53	26 (49)	49 (20–300)	Transmural stenting ± DEN ± transpapillary stenting ± PCD	3 (1–12)	43 (81)	26 (49)	3 (6)
Voermans (2007)[63]	25	19 (76)	84 (21–385)	DEN plus nasocystic lavage	NA	23 (92)	40 (7 severe)	0
Hocke (2008)[64]	30	30 (100)	NA	DEN	2.7 (1–16)	27 (90)	10 (all severe)	2 (7)
Escourrou (2008)[65]	13	13 (100)	28 (21–32)	DEN ± PCD	1.8 (1–3)	13 (100)	46 (15 severe)	0
Seifert (2009)[66]	93	50 (54)	43	DEN	6	78 (84)	26	7 (8)
Ross (2010)[67]	15	9 (60)	29 (4–207)	Transmural stenting plus PCD in all	1.4	100 (100)	13	0
Gardner (2011)[68]	104	40 (39)	63	DEN	3 (1–14)	95 (91)	14 (4 severe, 2 fatal)	2 (2)
Bakker (2012)[56]	10	10 (100)	59 (29–69)	DEN ± PCD or VARD	3 (2–6)	10 (100)	20 (10 severe, fatal) occurring in treatment group, not procedure related)	1 (10)

and/or irrigation. Typically, 3 to 6 sessions are necessary to completely debride the cavity, with or without adjunctive nasocystic or percutaneous drain placement to provide irrigation (Table 6).

The site of transmural puncture for DEN can sometimes be determined visually and fluoroscopically by an observed bulge representing the extrinsic compression of the collection into the gut lumen. Approximately 50% to 60% of potentially drainable collections can be accessed via this approach. However, a bulge is often absent with smaller collections, low serum albumin, and collections in or near the tailed of the pancreas.[103–105] Therefore, to minimize the risk of puncturing adjacent structures, bleeding, and perforation, EUS is increasingly used to perform direct access and drainage. Advantages of EUS include ability to visualize the collection, to determine the optimal trajectory for puncture, to avoid intervening blood vessels, to assess the contents of the cavity, and, in some case, to exclude noninflammatory processes such as cystic neoplasms. Bleeding into the collection after puncture can also be visualized. Two randomized trials of endoscopic transmural drainage with and without EUS guidance showed a higher technical success (>95% vs 33%–66%), and a trend toward lower adverse event rates (0%–4% vs 13%–15%) using EUS.[103,104] The consensus is that EUS-visualization is preferred over conventional endoscopic techniques for initial access and drainage in most circumstances, with the possible exception of endoscopically obvious bulges.

CQ 16: What are the outcomes of multicenter studies on endoscopic necrosectomy?

Multicenter case series of endoscopic necrosectomy that included 1 German study[66] and 1 American study[68] involving a total of 93 and 104 patients, respectively (Table 6). Patients were primarily those with infected pancreatic or peripancreatic necrosis. Initial drainage was performed using EUS guidance in most cases. Primary success was achieved in 80% and 91% of patients after a median of 3 to 6 necrosectomies. Adverse events occurred in 15% to 26% of patients, including perforation, peritonitis, bleeding, and air embolism. Two procedure-related deaths occurred (air embolism and bleeding). Bleeding occasionally required angiographic or surgical intervention.

In a systematic review of 10 series on endoscopic necrosectomy, overall morbidity was 27% and mortality was 5%, which seems lower than in most surgical series. However, it should be noted that, in the German series, in which mortality was 7.5%, only 20% of patients initially required admission to the ICU and 4% showed signs of sepsis; and proven infected necrosis was present in 54%, suggesting a less severely ill group of patients. These observations reinforce the concept that it is necessary to consider patient characteristics when comparing different reports and techniques.

A recently published multicenter randomized controlled trial conducted by the Dutch Pancreatitis Study Group compared endoscopic necrosectomy with surgical necrosectomy (VARD or, if not feasible, open necrosectomy).[56] Twenty patients completed randomization with 10 in each group. The study showed superiority of endoscopic necrosectomy over surgical necrosectomy with regard to inflammatory markers and a composite end point of major complications. New-onset organ failure occurred significantly less frequently with endoscopic necrosectomy (0% vs 50%, $P = 0.03$), as did pancreatic fistulas (10% vs 70%, $P = 0.02$). There was also a nonsignificant trend toward lower mortality with endoscopic necrosectomy compared with surgery (10% vs 40%). This landmark study suggests a superiority of endoscopic necrosectomy over surgical necrosectomy for infected necrosis. Replication of these results in other centers and studies is awaited.

Major challenges to peroral transluminal DEN include quantifying necrotic burden and how best to manage a large burden of necrotic tissue, especially with deep retroperitoneal extension. Further studies to determine predictors of poor outcome such as immobilization and poor nutritional status because of long hospitalization and assessment of the role of comorbid conditions on outcome are needed. Technical challenges include the limited instruments available for debridement that are mostly borrowed from other endoscopic applications, limited ability to fix the bowel lumen to the cavity wall with staples or sutures, and avoidance of vessels and other vital structures within the necrotic cavity.

Endoscopic necrosectomy is a complex and potentially risky procedure that requires advanced endoscopic expertise in both ERCP and interventional EUS and a multidisciplinary team for support. Carbon dioxide insufflation is now widely used to reduce the risk of air embolism, but its efficacy in preventing this adverse event is unproven. The reliability of transpapillary stenting to resolve ductal disconnection in patients with a disrupted pancreatic duct is unknown. Combinations of endoscopic necrosectomy with other techniques have not been extensively explored but may improve outcome.

Consensus is that endoscopic transmural drainage and necrosectomy of WON is a viable technique with established safety, efficacy, and mortality when performed at specialized expert centers. Major questions are whether complete necrosectomy is necessary, or whether the "step-up" approach with endoscopic transmural drainage followed by further endoscopic necrosectomy only as clinically indicated is superior to complete necrosectomy, and whether combination of endoscopic and percutaneous approaches are superior to either alone. One of the limitations of the transgastric endoscopic approach is the location of the target collection. Central collections are almost always accessible, but not left-sided and flank collections. As a result, VARD procedure and the other percutaneous retroperitoneal approaches are likely to continue to have a significant role to play when there is no close abutment of the collection to the stomach or duodenum.

CQ 17: What are the results of a combined endoscopic and percutaneous approach?

Advantages of PCD include widespread availability, access by transperitoneal and retroperitoneal approaches to the left and right sides of the abdomen and pelvis, ability to place multiple catheters, and the ability to flush catheters between procedures. However, a major limitation is the development in at least 20% of patients of pancreaticocutaneous fistulae, some of which do not close because of communication of the drain with an upstream disconnected duct.[89–100] Advantages of endoscopic necrosectomy include internal drainage and avoidance of external fistulae, but limitations include the need for multiple repeated procedures under sedation or anesthesia. Combining a percutaneous approach with endoscopic transmural drainage can prevent external fistulae and avoid repetitive and laborious endoscopic interventions to perform direct necrosectomy.[67] Irrigation through the percutaneous approach with egress through the transmural fistula results in a form of debridement. After resolution of the WON, the percutaneous drains are removed; the transmural stents can remain in place indefinitely in patients with a disconnected duct. In case-control series from a single center, the combined percutaneous-endoscopic approach has been shown to increase the rate of nonsurgical resolution and result in a decrease in hospitalization, time to drain removal, number of CT scans, and number of drains compared to percutaneous drainage alone.[67,106] As for all endoscopic transmural drainage techniques, this approach is limited to selected patients with WON located within 2 cm of the gastric or duodenal wall. Further studies are awaited to evaluate the efficacy of various combinations of techniques, including endoscopic transmural, PCD, and retroperitoneoscopic techniques.

CQ 18: What are the results with the "step-up" approach?

An alternative to immediate open or other methods of complete initial necrosectomy is the "step-up" approach, using minimally invasive techniques to control infected necrosis, with definitive necrosectomy deferred or sometimes avoided altogether based on the clinical course of the patient. The first step is usually PCD, preferably into the retroperitoneum via the left flank. Alternative routes are percutaneous transabdominal or endoscopic transluminal. The objective is to postpone or obviate the need for surgery. If drainage fails to control sepsis, the next step is taken, and debridement accomplished via VARD, sinus tract endoscopy, or peroral DEN. These approaches are thought to induce less stress than open surgery in already critically ill patients.[70,77,80,82]

The step-up approach is currently supported with phase 1 feasibility and phase 2 prospective safety and efficacy data.[80,84,107] To test whether the step-up approach is superior to open necrosectomy as first-line treatment, a randomized controlled trial (PANTER trial) was performed, which included 7 university hospitals and 12 major teaching hospitals in the Netherlands.[35] All patients had pancreatic or peripancreatic necrosis and in whom either percutaneous or endoscopic drainage was judged to be feasible. Intervention was undertaken for proven or suspected infected necrosis. Patients with a perforated viscus or other intra-abdominal catastrophe or prior laparotomy were excluded. Patients were randomized to primary open necrosectomy and continuous postoperative lavage or to the step-up approach with percutaneous (or endoscopic) drainage, and if no clinical improvement was seen after 72 hours, a second drainage performed, followed by VARD. If this failed, then open necrosectomy was performed. If possible, any intervention was delayed until at least 30 days after onset of pancreatitis. Primary end points were death or major morbidity. Forty-five patients were randomized to immediate open necrosectomy, and 43 patients were randomized to the step-up approach. Baseline patient characteristics were similar in both groups. Approximately half of the patients were in an ICU, half had organ failure, a third had multiorgan failure, and all had SIRS. Outcomes were significantly better in the step-up group compared to the open surgery group. Death or major morbidity occurred in 40% of the step-up group compared with 69% of the open necrosectomy group; mortality was similar in both groups (19% vs 16%). Twelve percent of patients in the step-up group experienced new onset multiorgan failure compared to 42% in the open necrosectomy group. Long-term morbidity including incisional hernia (7% vs 24%), new-onset diabetes mellitus (16% vs 38%), pancreatic enzyme use (7% vs 33%), and cost of care were all significantly lower in the step-up group. Notably, 35% of patients in the step-up group did not require necrosectomy.

The Dutch PANTER trial is a landmark study that provides the strongest evidence available that incorporates a minimally invasive and step-up approach to infected necrosis to avoid the need for open surgical necrosectomy. The subsequent PENGUIN trial provides initial evidence to suggest that endoscopic necrosectomy is superior to VARD or open surgery.[56] Whether a step-up approach applied to purely endoscopic necrosectomy is preferrable is unknown and is the subject of an ongoing randomized trial.

CQ 19: What are the outcomes of endoscopic, percutaneous image-guided, and surgical management of disconnected pancreatic duct and recurrent fistula?

Disconnected pancreatic duct syndrome occurs in up to 40% of patients with pancreatic necrosis. This syndrome results from destruction of a central portion of the neck or body of the pancreas that includes the main pancreatic duct and/or from intervention that disrupts or disconnects the main pancreatic duct, causing persistent drainage of pancreatic juice from the upstream portion of the gland through an external fistula or catheter. In the absence of a catheter or fistula, disconnected pancreatic duct syndrome may lead to persistent or recurrent fluid collections proximal to the site of the disconnection, acute recurrent pancreatitis in the excluded tail, and duct leaks resulting in pancreatic ascites or pancreaticopleural fistula. Such pancreatic fistulas can be detected by persistent drainage of pancreatic juice through an external catheter or drain, by aspiration of pleural or peritoneal fluid to assay for amylase, or by imaging of the pancreatic duct including direct pancreatography, CT, or MRCP.[14,108] Endoscopic or surgical transmural drainage results in an internal fistula, but recurrent pancreatic fluid collections occur in up to 40% of patients after stent removal since the transmural fistula tract inevitably closes. Methods to prevent external fistula primarily consist of internal endoscopic drainage leaving stents in place indefinitely. A randomized trial showed a significant reduction in recurrence of pancreatic fluid collections when transmural stents were left in place indefinitely compared to routine stent removal.[109] Other endoscopic alternatives to treat disconnected duct syndrome include placement of a transpapillary stent through duct disruptions into a collection, with later "reconnection" of the duct with the tail once the cavity has resolved; there are limited data on this approach. Additional options to treat established disconnected pancreatic duct syndrome include catheter clamping and removal after prolonged drainage, fistula embolization with sclerosing agents, or EUS-guided transmural drainage of the pancreatic duct. There is another preliminary report of using a percutaneous-endoscopic approach, where the percutaneous tract is used to puncture directly into the stomach or duodenum to internalize the fistula.[110] There is limited experience with these techniques.

Surgical approaches to persistent pancreatic duct disconnection with external fistula include distal pancreatectomy (usually involving splenectomy) or internal Roux-en-Y drainage of the excluded pancreatic duct (pancreatico-jejunostomy) or pseudocyst (cyst-jejunostomy). Available data suggest similar outcomes with less operative blood loss with Roux-en-Y drainage. Distal resection with islet cell autotransplantation is a relatively new approach to treatment of refractory disconnected duct syndrome.[111]

CONCLUSIONS

Many different interventions in varying states of evolution and with varying evidence to support their use are available for the treatment of pancreatic and peripancreatic necrosis. It is well accepted that these interventions should be offered in the context of optimal intensive care and medical management and that a multidisciplinary approach is required in a center with specialized expertise in interventional radiology, interventional endoscopy, intensive care, nutritional support, and surgery.

Intervention is required primarily in patients with infected pancreatic or peripancreatic necrosis, for those with clinical deterioration despite maximum medical support (ie, suspected infection), for symptomatic patients and especially those with obstruction of a viscus, and possibly for patients with septic syndrome in the absence of another explanation. Specific scenarios such as abdominal compartment syndrome or perforated viscus require urgent intervention but not necrosectomy. Interventions within the first few weeks for pancreatic or peripancreatic

FIGURE 2. A CT scan showing a large, heterogeneous acute necrotic collection replacing normal pancreas and containing gas bubbles. Intravenous contrast was not given because of acute renal failure. See text regarding case 1 for clinical presentation and consensus management.

necrosis are generally associated with poor outcomes and should be reserved for infected necrosis in a severely deteriorating patient. Poorly organized necrosis is more difficult to manage by any method than partially liquefied and walled off necrosis.

Traditionally, the most widely used approach to infected necrosis has been open surgical necrosectomy. Most cases can now be managed using minimally invasive techniques in specialized centers with the appropriate expertise. Percutaneous catheter drainage, endoscopic, laparoscopic and rigid videoscopic methods are all feasible approaches for treating infected necrosis. Combination approaches may be useful in selected patients with extensive peripancreatic necrosis. Laparoscopic approaches are technically demanding but allow for simultaneous cholecystectomy when indicated.

Current evidences favors endoscopic necrosectomy or percutaneous catheter drainage followed by minimally invasive necrosectomy as the preferred routes for intervention for infected necrosis. The step-up approach involves percutaneous or endoscopic transmural drainage for sepsis control followed by minimally invasive or open necrosectomy as indicated. In a multicenter randomized controlled trial, short-term and long-term outcomes using the step-up approach have been shown to be superior to immediate open surgery for patients with infected necrosis.[35] Further, a multicenter randomized controlled trial from the same group showed that endoscopic necrosectomy is superior to VARD.[56]

The overriding principle of interventions for necrosis is that no single approach is optimal for all patients. The best approach is multimodal and adaptable to the individual patient. Multidisciplinary management of these patients by specialists with specific expertise in management of necrotizing pancreatitis is essential to achieve the best outcomes. Patients with severe necrotizing pancreatitis are best served at specialized centers with teams dedicated to management of this disorder. Further research, preferably randomized trials or prospective collaborative studies are required to improve current techniques and to define optimal approaches to intervention for necrotizing pancreatitis.

Representative Cases to Illustrate Various Aspects of Interventions for Necrotizing Pancreatitis

The following cases are as presented to speakers, moderators and attendees. The entire group was given a multiple choice of available management strategies and answered by a show of hands.

Case 1

A 53-year-old previously healthy patient was transferred from an outside facility 2 weeks after onset of severe AP and 2 days after a transperitoneal percutaneous drain was placed into an acute necrotic collection. He has developed sepsis, multiorgan failure,and rapid deterioration during the last 24 hours with progressive respiratory and renal failure. By CT, a large, heterogeneous acute necrotic collection is replacing normal pancreas and contains gas bubbles. The percutaneous drain is in position with the pigtail in the center of the collection (Fig. 2).

Most participants recommended upsizing and adding multiple large-bore percutaneous drains to stabilize the patient (with additional catheter via a left flank retroperitoneal approach) followed by VARD, and a minority opted for either endoscopic transgastric necrosectomy or laparoscopic debridement. One participant opted for open surgery. The actual management in this patient was immediate laparotomy with open debridement and drainage. Infected pancreatic necrosis with minimal liquefaction was found. After serial debridements, the patient recovered but with resultant disconnected pancreatic duct and high-output pancreaticocutaneous fistula.

Case 2

A 78-year-old patient is now 4 weeks after onset of severe gallstone pancreatitis. Seven weeks prior, he underwent open hemicolectomy. He has heart disease and is chronically malnourished with a serum albumin of 2.6 g/dL. A computed tomographic scan reveals walled off necrosis indenting the posterior wall of the stomach. It is heterogeneous, has a well-defined wall, and contains gas bubbles (Fig. 3).

Most of the audience at the consensus conference voted for endoscopic transgastric drainage and DEN. A few suggested percutaneous drainage and none recommended laparoscopic or open surgical necrosectomy. The actual management was endoscopic transgastric EUS-guided drainage followed by DEN combined with transpapillary pancreatic stent placement into the necrotic cavity, with eventual resolution of the cavity and the disconnected duct.

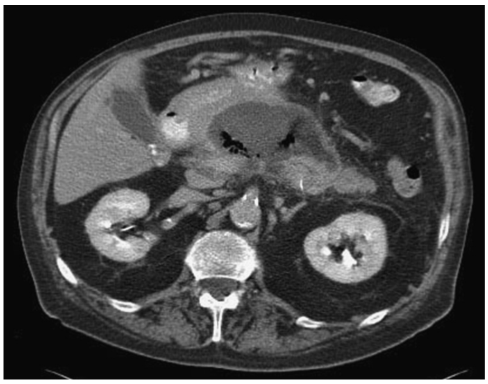

FIGURE 3. A CT scan revealing walled off necrosis indenting the posterior wall of the stomach. It is heterogeneous, has a well-defined wall and contains gas bubbles. See text regarding case 2 for clinical presentation and consensus management.

Case 3

A 53-year-old woman is now 4 weeks from the onset of severe AP. Immediately on admission at an outside hospital, she underwent exploratory laparotomy and cholecystectomy for "acute abdomen" with findings of acute necrotizing pancreatitis. She subsequently developed severe acute respiratory distress syndrome requiring tracheostomy and now has marginal oxygenation despite a fraction of inspired oxygen (Fio_2) of 100%. She is now febrile with gram-negative bacteremia and clinical deterioration. The CT scan shows a large heterogeneous walled-off necrotic collection extending from the lesser sac to the left pelvis; a nasojejunal feeding tube can be seen in the gastric lumen (Fig. 4).

Most participants voted for percutaneous drainage via a left flank retroperitoneal approach. A minority voted for endoscopic necrosectomy or a combined endoscopic-percutaneous approach and none for open or laparoscopic surgery. The actual management was combined endoscopic transgastric drainage and percutaneous left flank retroperitoneal catheter placement for drainage and irrigation, followed by DEN. The patient made a complete recovery with near-full recovery of pulmonary function and no external fistula.

Case 4

A 39-year-old morbidly obese male is now 2 weeks after presentation to an outside hospital with severe acute biliary pancreatitis accompanied by multiorgan failure and pancreatic necrosis. Shortly after admission he had undergone ERCP with biliary sphincterotomy as well as placement of biliary and pancreatic stents for multiple bile duct stones. He was discharged from the admitting hospital but readmitted to a tertiary center hospital with malaise, anasarca, and a serum albumin of 2.0 g/dL. The CT scan demonstrates that the entire pancreas was replaced by an acute necrotic collection which contains a large amount of gas (Fig. 5).

Most participants opted for percutaneous drainage via a left flank approach followed by VARD or sinus tract endoscopy. A few voted for endoscopic transgastric necrosectomy or a combination of endoscopic transgastric and percutaneous left flank catheter drainage. None opted for open or laparoscopic surgery. The actual management was endoscopic transgastric and transduodenal necrosectomy. Near-complete resolution of necrosis was achieved, but the patient had a fatal air embolus during the last endoscopic procedure. CO_2 had not been used for endoscopic insufflation.

FIGURE 4. A CT scan showing a large heterogeneous walled-off necrotic collection extending from the lesser sac to the left pelvis; a nasojejunal feeding tube can be seen in the gastric lumen. See text regarding case 3 for clinical presentation and consensus management.

FIGURE 5. A CT scan demonstrating that the entire pancreas is replaced by an acute necrotic collection which contains a large amount of gas. See text regarding case 4 for clinical presentation and consensus management.

Case 5

A 14-year-old obese female developed severe acute gallstone pancreatitis with transient organ failure, and necrosis. Organ failure resolved. She is now 4 weeks after presentation and has worsening symptoms of abdominal pain. Ultrasound shows numerous gallstones, no ductal dilation, and mildly abnormal liver chemistries. The CT scan shows WON involving more than 50% of the pancreas and also involving peripancreatic tissues (Fig. 6)

Responses were evenly divided between laparoscopic transgastric drainage and debridement combined with laparoscopic cholecystectomy, open transgastric drainage and debridement combined with open cholecystectomy, and waiting several more weeks for further organization and endoscopic drainage/necrosectomy. The actual management was laparoscopic cholecystectomy followed by attempted laparoscopic cystgastrostomy by a surgeon with minimal experience with complex laparoscopic techniques. Unfortunately, perforation occurred and resulted in conversion to open surgery with external drainage of WON. A

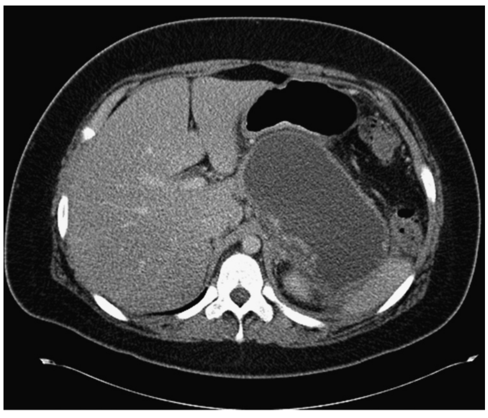

FIGURE 6. A CT scan showing more than 50% necrosis of the pancreas, with WON involving pancreas and peripancreatic tissues. See text regarding case 5 for clinical presentation and consensus management.

FIGURE 7. A CT scan demonstrating a walled-off necrotic collection containing gas and extending into the right side of the pelvis. See text regarding case 6 for clinical presentation and consensus management.

retained common bile duct stone required subsequent ERCP for removal.

Case 6

A 75-year-old woman is 6 weeks from onset of idiopathic necrotizing pancreatitis. She now has abdominal pain, fever, leukocytosis, and CT scan demonstrating a walled-off necrotic collection containing gas and extending into the right side of the pelvis. Percutaneous catheter drainage was performed at outside hospital (Fig. 7).

Most participants opted for VARD or sinus tract endoscopy through the percutaneous tract, a few for open surgery or for laparoscopic surgery, a few for upsizing percutaneous drain, and one for endoscopic transgastric necrosectomy. Actual management was repeated sessions of endoscopic necrosectomy performed through the sinus tract via a large-diameter covered self-expandable metal stent placed through the right percutaneous drain site, with resolution of the necrosis but difficulty removing the stent.

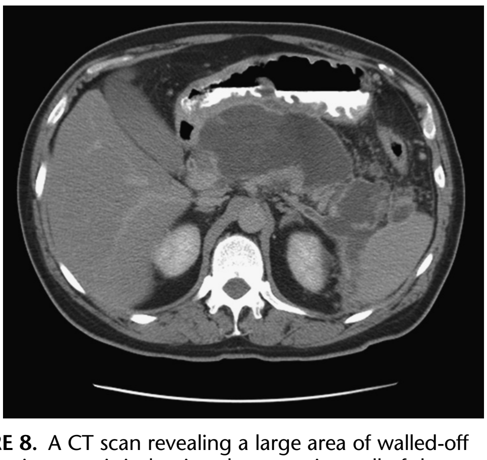

FIGURE 8. A CT scan revealing a large area of walled-off pancreatic necrosis indenting the posterior wall of the stomach and extending into the left retroperitoneum. See text regarding case 7 for clinical presentation and consensus management.

FIGURE 9. A CT scan showing a viable, enhancing tail of the pancreas consistent with disconnected duct syndrome. Peripancreatic drains are in place. See text regarding case 8 for clinical presentation and consensus management

Case 7

A 56-year-old man is now 6 weeks after presentation with acute necrotizing pancreatitis and is being seen in the outpatient clinic. He is doing well, with mild early satiety, and has minimal abdominal and back pain. The CT scan reveals a large area of walled-off pancreatic necrosis indenting the posterior wall of the stomach and peripancreatic necrosis extending into the left pelvis (Fig. 8).

The participants were unanimous for no intervention. The actual outcome was no intervention, with eventual spontaneous resolution of the WON.

Case 8

A 48-year-old man is 6 months after open necrosectomy for idiopathic necrotizing pancreatitis with infected necrosis. He has a high-output fistula from a drain near the residual tail 6 months later. He has no evidence of diabetes. The CT scan shows a viable, enhancing tail of the pancreas consistent with disconnected duct syndrome. Peripancreatic drains are in place (Fig. 9).

There were multiple opinions and varied responses: Some suggested withdrawing the drain slowly and waiting for atrophy of the tail; a few voted for simply removing the catheter and following the patient's course; 1 voted for removing the catheter to intentionally allow a true pseudocyst to form, followed by internal endoscopic drainage; a few suggested Roux-en-Y-drainage, a few suggested distal pancreatectomy; and 2 suggested distal pancreatectomy with a islet autotransplantation. Actual management was distal pancreatectomy with islet autotransplantation. The patient did well without development of diabetes.

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APPENDIX. Conference Participants

Name	Primary Expertise	Affiliation
Peter A. Banks, MD	Internal medicine/gastroenterology	Brigham & Women's Hospital, Boston, MA
Todd H. Baron, MD	Interventional endoscopy	Mayo Clinic, Rochester, MN
Hans G. Beger, MD	Surgery	University of Ulm, Ulm, Germany
Greg J. Beilman, MD	Surgery	University of Minnesota, Minneapolis, MN
Marc G. Besselink, MD, PhD	Surgery	Academic Medical Center, Amsterdam, Netherlands
Thomas L. Bollen, MD	Radiology	St Antonius Hospital, Nieuwegein, the Netherlands
Pascal Bucher, MD	Surgery	Geneva University Hospital, Geneva, Switzerland
David Carr-Locke, MD	Interventional endoscopy	Beth Israel Medical Center, New York, NY
C. Ross Carter, MD	Surgery	Glasgow Royal Infirmary, Glasgow, United Kingdom
Suresh T. Chari, MD	Internal medicine/gastroenterology	Mayo Clinic, Rochester, MN
Darwin L. Conwell, MD	Internal medicine/gastroenterology	Brigham & Women's Hospital, Boston, MA
Carlos Fernandez del Castillo, MD	Surgery	Massachusetts General Hospital, Boston, MA
Martin L. Freeman, MD	Interventional endoscopy	University of Minnesota, Minneapolis, MN
Patrick C. Freeny, MD	Interventional radiology	University of Washington, Seattle, WA
Christopher E. Forsmark, MD	Internal medicine/gastroenterology	University of Florida, Gainesville, FL
Timothy B. Gardner, MD	Interventional endoscopy	Dartmouth-Hitchcock Medical Center, Lebanon, NH
Andres Gelrud, MD	Interventional endoscopy	University of Chicago, Chicago, IL
Karen D. Horvath, MD	Surgery	University of Washington, Seattle, WA
Colin D. Johnson, FRCS	Surgery	University of Southampton, Southampton, United Kingdom
Peter Layer, MD, PhD	Internal medicine/gastroenterology	Israelitic Hospital, Hamburg, Germany
Olivier Le Moine, MD, PhD	Interventional endoscopy	Erasme University Hospital, Brussels, Belgium
Jeffrey B. Matthews, MD	Surgery	University of Chicago Medical Center, Chicago, IL
Desiree E. Morgan, MD	Radiology	University of Alabama at Birmingham, Birmingham, AL
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William H. Nealon, MD	Surgery	Vanderbilt University, Nashville, TN
Georgios I. Papachristou, MD	Interventional endoscopy	University of Pittsburgh Medical Center, Pittsburgh, PA
Dilip Parekh, MD	Surgery	University of Southern California, Los Angeles, CA
Bettina M. Rau, MD	Surgery	University of Rostock, Rostock, Germany
D. Nageshwar Reddy, MD	Interventional endoscopy	Asian Institute of Gastroenterology, Hyderabad, India
Andrew Ross, MD	Interventional endoscopy	Virginia Mason Medical Center, Seattle, WA
Micheal G. Sarr, MD	Surgery	Mayo Clinic, Rochester, MN
Stefan Seewald, MD	Interventional endoscopy	Hirslanden Clinic Zurich, Zurich, Switzerland
Hans Seifert, MD	Interventional endoscopy	Klinikum Oldenburg, Oldenburg, Germany
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Ajith K. Siriwardena MD	Surgery	Manchester Royal Infirmary, Manchester, United Kingdom
Scott Tenner, MD, MPH	Internal medicine/gastroenterology	Maimonides Medical Center, Brooklyn, NY
Hjalmar C. van Santvoort, MD, PhD	Surgery	University Medical Center, Utrecht, Netherlands
Eric vanSonnenberg, MD	Interventional radiology	Kern/UCLA Medical Center, Bakersfield, CA
Shyam Varadarajulu, MD	Interventional endoscopy	University of Alabama at Birmingham, Birmingham, AL
Santhi Swaroop Vege, MD	Internal medicine/gastroenterology	Mayo Clinic, Rochester, MN
Andrew L. Warshaw, MD	Surgery	Massachusetts General Hospital, Boston, MA
Jens Werner, MD	Surgery	University of Heidelberg, Heidelberg, Germany
John A. Windsor, MD	Surgery	University of Auckland, Auckland, New Zealand