Severe acute pancreatitis: advances and insights in assessment of severity and management

Giuseppe Brisinda, Serafino Vanella, Anna Crocco, Andrea Mazzari, Pasquina Tomaiuolo, Francesco Santullo, Ugo Grossi and Antonio Crucitti

The patients with acute pancreatitis are at risk to develop different complications from ongoing pancreatic inflammation. Often, there is no correlation between the degree of structural damage to pancreas and clinical manifestation of the disease. The effectiveness of any treatment is related to the ability to predict severity accurately, but there is no ideal predictive system or biochemical marker. Severity assessment is indispensable to the selection of proper initial treatment in the management of acute pancreatitis. The use of multiparametric criteria and the evaluation of severity index permit us to select high-risk patients. Furthermore, contrast-enhanced computed tomographic scanning and contrast-enhanced MRI play an important role in severity assessment. The adoption of multiparametric criteria proposed together with morphological evaluation consents the formulation of a discreetly reliable prognosis on the evolution of the disease a few days from onset. *Eur J Gastroenterol Hepatol* 23:541–551 © 2011 Wolters Kluwer Health | Lippincott Williams & Wilkins.

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Department of Surgery, Catholic School of Medicine, University Hospital Agostino Gemelli, Rome, Italy

Correspondence to Giuseppe Brisinda, MD, Department of Surgery, University Hospital Agostino Gemelli, Largo Agostino Gemelli 8, Rome 00168, Italy
Tel: +39 06 3015 4199; fax: +39 06 3015 6086;
e-mail: gbrisin@tin.it

All authors contributed equally to the writing of this article

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Introduction

Acute pancreatitis (AP) is the third most common diagnosis at discharge for gastrointestinal diseases [1–3]. AP is predominantly caused by symptomatic gallstone disease and excessive alcohol intake [4,5]. As a result of improvements in the management including better diagnostics and treatment modalities, disease-related mortality has declined during the past two decades despite an increase in the overall incidence of AP in many countries [4]. Most AP episodes do not require a particular intervention, as they are mild and self-limiting. In contrast, about one-fifth of patients develop a severe AP (SAP), which is still associated with a mortality rate exceeding 30%; SAP is usually accompanied by necrosis of the pancreas and the surrounding tissues [6,7]. Such necrosis formation is best assessed by contrast-enhanced computed tomography (ce-CT), and the Balthazar score is most commonly used to define the extent of necrosis [8,9]. According to the Atlanta system of Classification, SAP is associated with multiple organ failure (MOF) and may additionally include local complications such as necrosis, abscess, or pseudocyst formation [10]. Antibiotic treatment with agents penetrating well into the pancreas has been shown to prevent infection in SAP and to lower the death rate [11–13]. However, the general treatment principles in necrotic pancreatitis (NP) and particularly the role of surgery are controversial issues. During 1980s, 60–70% of patients with NP were treated surgically. Furthermore, the concept of nonsurgical management of sterile necrosis has been introduced, applying early antibiotic treatment [6,14–16]. Patients with SAP should be nursed in a critical care setting, as this facilitates optimization of fluid status and cardiorespiratory parameters. Identifying the cohort of patients who require critical care support is vital to rationalize healthcare resources, as it would not be feasible or appropriate to manage all patients with AP in such an environment. For this reason, scoring systems and other variables can be used, in conjunction with regular clinical review, to ensure prompt and timely intervention.

Moreover, several challenges and controversies remain in the management of this disease, including how best to predict organ failure, the use and timing of diagnostic tests, and the type and timing of surgical intervention [17]. Furthermore, we still do not know why AP remains mild in some patients, whereas other patients suffer multiple complications.

This study addresses recent trends in the diagnosis and management of SAP. Important clinical guidelines, randomized controlled trials, meta-analyses, large case series from centers of excellence, and consensus conference reports form the basis of this study.

Classification and definitions

The widely used Atlanta Classification categorizes AP as mild or severe. AP without parenchymal necrosis is referred to as interstitial or edematous pancreatitis and is

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usually mild. Patients with AP are classified as having SAP if they meet any of the criteria reported in Table 1.

Although the Atlanta Classification has proved useful over the years, many of the definitions proved confusing and have not been accepted or used by the pancreatic community [18]. Better understanding of the NP pathophysiology, improved diagnostic imaging of the pancreatic parenchyma and peripancreatic collections, and the development of minimally invasive radiologic, endoscopic, and operative techniques for the management of complications have made it necessary to revise the Atlanta Classification [18]. Important issues that must be incorporated into a new, state-of-art classification include assessment of clinical severity and appropriate and more objective use of terms addressing fluid collections and areas of necrosis in and around the pancreas [6,19]. In addition, AP is a dynamic, evolving process, and the recognition of two different peaks in mortality, one very early after onset (usually within the first week) and another after 2–6 weeks from onset, reflects the two distinctly different clinical phases of the evolution of this disease not recognized by the Atlanta Classification [5,20,21].

Assessment of severity

The AP severity is variable and does not always correlate with structural and functional changes in the pancreas [12,22]. Moreover, without accepted definitions, the natural history of a disease cannot be defined; without natural history information, therapy cannot be evaluated; and without stratification for severity, therapeutic options cannot be meaningfully compared. Ranson [23] proposed the first numeric system in 1974 (Table 2). It focuses on different clinical and hematochemical variables. With an increased number of positive risk factors, there is a corresponding increase in the mortality rates. In patients with less than three positive signs, there is no mortality, whereas in patients with at least six signs the mortality rate is over 50%. Individuals with a score of more than 6 usually have NP. This system is particularly useful at the two ends of the scale. Moreover, correlation with severity of disease or development of necrosis in patients with a score of 3–5 (which is a common occurrence) is deficient.

Alternative grading systems, each using different parameters, have since been constructed, with a prognostic capability generally similar to that of the Ranson system. The Glasgow (also called the Imrie) criteria were originally introduced in 1985 (Table 3). The original Glasgow, or modified system, has been used for the prediction of mortality [24]. More recently, the Acute Physiology and Chronic Health Evaluation II (APACHE-II) assessment and monitoring system has become popular, because it is considered to be more reliable [25]. The system is complex and more difficult to perform because 12 physiologic measurements are used. The higher the total score, the more severe the AP, with a corresponding increase in morbidity and mortality [26]. The major advantage of the APACHE-II numeric system compared with the other systems is that, it can be used throughout the patient's

Table 1 Predictors and definition of severe acute pancreatitis

Severity criteria	Definitions
Predictors of SAP	
Ranson score	>3
APACHE II score	>8
Systemic complications	
Respiratory	PaO_2 <60 mmHg (8 kPa)
Renal	Serum creatinine >177 μmol/l (2 mg/dl) after resuscitation
Cardiovascular	Systolic blood pressure <90 mmHg (after resuscitation)
Coagulation system	Platelet count <100 × 109/l or fibrinogen level <1 g/l
Gastrointestinal hemorrhage	>500 ml/24 h
Metabolic	Corrected serum calcium <1·85 mmol/l (7·5 mg/dl) Serum lactate levels >5 mmol/l
Local complications	
Acute fluid collections	Occur early in the natural history of acute pancreatitis and lack a fibrous capsule
Pseudocyst	Occurs at least 4 weeks after the onset of symptoms and has a fibrous capsule
Pancreatic abscess	A localized collection of pus containing little or no necrotic pancreatic material
Pancreatic necrosis	Pathological features: diffuse or focal area of nonviable pancreas that may be associated with peripancreatic fat necrosis CT features: an area of nonenhancing pancreas measuring >3 cm in diameter or 30% of pancreatic tissue

The presence of each item by itself constitutes severe acute pancreatitis.
APACHE, acute physiology and chronic health evaluation; PaO_2, arterial partial pressure of oxygen; SAP, severe acute pancreatitis.

Table 2 Ranson's criteria

At admission	During initial 48 h
Age >55 years	Hematocrit decrease >10%
White blood cell count >16000/μl	Blood urea nitrogen increase >5 mg/dl (>1.8 mmol/l)
Serum glucose level >200 mg/dl (>11.1 mmol/l)	Calcium <8 mg/dl (<2 mmol/l)
Serum lactate dehydrogenase >350 IU/l	PaO_2 <60 mmHg
Aspartate aminotransferase >250 IU/l	Base deficit >4 mEq/l
	Fluid sequestration >6 l

For a diagnosis of severe acute pancreatitis in a patient with pancreatitis, three or more above criteria must be present.
PaO_2, arterial partial pressure of oxygen.

Table 3 Glasgow (Imrie) severity scoring system for acute pancreatitis

Age >55 years
White cell count >15 × 10^9/l
PaO_2 <60 mmHg (8 kPa)
Serum lactate dehydrogenase >600 units/l
Serum aspartate aminotransferase >200 units/l[a]
Serum albumin <32 g/l
Serum calcium <2 mmol/l
Serum glucose >10 mmol/l
Serum urea >16 mmol/l

Each variable has a binary score of 0 or 1. The Glagow (Imrie) outcome score is derived from the sum of scores for all variables at 48 h after presentation.
PaO_2, arterial partial pressure of oxygen.
[a]Removed from the revised Glasgow outcome score.

hospital course in monitoring the response to therapy. Gocmen *et al.* [27] also calculated the Mortality Probability Model II (MPM) at 24 h, Williams and Simms [28] calculated the APACHE III (a modified version of the APACHE II including the earlier site of healthcare and additional physiologic parameters) at 96 h.

SAP is predicted when the APACHE-II score is at least 8, or when the Glasgow score and the Ranson criteria are at least 3 [29]. These scores, whether performed at admission or throughout the recovery, seem to be extremely valuable in the exclusion of mortality when the values fall below the proposed cutoffs. The development of the Sepsis-related Organ Failure Assessment (SOFA) score was an attempt to objectively and quantitatively describe the degree of organ dysfunction over time and to evaluate morbidity in septic patients intensive care unit (ICU) (Table 4) [30,31]. Later, when it was realized that it could be applied equally well in nonseptic patients, the acronym SOFA was taken to refer to Sequential Organ Failure Assessment. Since its introduction, the SOFA score has also been used for predicting mortality, although it was not developed for this purpose. Most studies evaluated prognosis based on SOFA scores in the first 24 h after ICU admission. Good-to-excellent discrimination between survivors and nonsurvivors were reported, which did not markedly differ from that of traditional models such as APACHE-II [32–34]. This relatively good performance of SOFA is remarkable, given the fact that the score is based on fewer physiological parameters and that it does not include information on reason for admission or comorbidity. In contrast, information on instituted treatments, such as vasopressors and mechanical ventilation, is included in SOFA but not in APACHE-II [35].

Recently, a new prognostic scoring system, the bedside index for severity in AP, has been proposed as an accurate method for early identification of patients at risk for mortality [36–38]. The bedside index for severity in AP uses five points: urea nitrogen more than 25 mg/dl, impaired mental status by evidence of disorientation or disturbance in mental status, presence of systemic inflammatory response syndrome (SIRS), age above 60 years, and pleural effusions.

Multiple single factors were investigated to assess the severity of AP. Blood glucose values in patients who died were significantly different from those who survived and the likelihood ratio of mortality was 2.51 when serum glucose was at least 8.3 mmol/l. The C-reactive protein (CRP) was found to be significantly higher in patients who died. In a recent study, CRP higher than 170 mg/l and albumin lower than 30 g/l increased the fatal outcome ($P < 0.05$). Moreover, the researchers noted that low albumin was a stronger predictor than CRP [39]. Age above 70 years was associated with mortality, with a 55% sensitivity and 88% specificity [4]. The prognostic utility of hemoconcentration remains controversial [40]. It has been emphasized that hemoconcentration on admission was a poor prognostic sign. In contrast, it was found that initial hematocrit levels below 30% correlated with increased mortality [26]. Ranson [23] have not found a significant relationship between initial hematocrit levels and prognosis, but the degree of fall of hematocrit during the initial 48 h period of treatment had a significant relationship with mortality and morbidity.

Procalcitonin is the inactive propeptide of the hormone calcitonin. In patients with AP, procalcitonin has been shown to predict the development of infected necrosis [41]. In addition, procalcitonin has been found to be an early predictor of severity and organ failure in patients with AP [42,43]. The accuracy of procalcitonin seems to be dependent on cut-off values and timing of assays. Several researchers performed serial daily serum procalcitonin measurements and reported that patients who subsequently developed infected pancreatic necrosis had a sustained increase in serum procalcitonin levels; the degree of procalcitonin increase reflected the SIRS severity and MOF. Interestingly, Rau *et al.* [44] observed that the most marked increase in procalcitonin occurs as a result of abdominal infections, and other sources of sepsis, such as chest and urinary tract infections had a less dramatic effect on serum procalcitonin levels.

Table 4 Sequential Organ Failure Assessment score

	Score				
Organ system involved	1	2	3	4	5
Cardiovascular	No hypotension	MAP <70 mmHg	Dopamine or dobutamine (any dose)	Dopamine >5 μg/kg/min or adrenaline (epinephrine) <0.1 μg/kg/min	Dopamine >15 μg/kg/min or adrenaline >0.1 μg/kg/min or noradrenaline >0.1 μg/kg/min
Respiratory PaO_2/FiO_2 (mmHg)	>400	400–300	300–200	200–100[a]	≤ 100[a]
Renal creatinine (μmol/l)	<100	100–200	200–350	350–500	>500
Neurological Glasgow coma score	15	14–13	12–10	9–7	≤ 6
Hematological platelet count ($\times 10^9$)	>150	150–100	100–50	20–50	≤ 20
Hepatic bilirubin (μmol/l)	<20	20–60	60–120	120–240	>240

The Sequential Organ Failure Assessment score is calculated as the sum of the scores for the individual organs.
FiO_2, fraction of inspired oxygen; MAP, mean arterial pressure; PaO_2, arterial partial pressure of oxygen.
[a]These values are calculated with ventilatory support.

The concentration of serum amyloid A in the acute-phase response rises simultaneously with the increase in CRP. On the basis of the studies carried out thus far, this parameter was found to be more sensitive than CRP in the way that it reflects the changes during the inflammatory process regardless of its etiology [45]. Nevertheless, the role of serum amyloid A as a prognostic marker for AP has not been clearly established yet.

The recommended panel of biochemical tests enabling an early prognosis of AP should include the measurement of the procalcitonin level, total calcium concentration, and lactic dehydrogenase activity within 12 h from the onset of symptoms and a complementary measurement of procalcitonin concentration and blood glucose concentration within the next 24 h should the earlier tests be inconclusive.

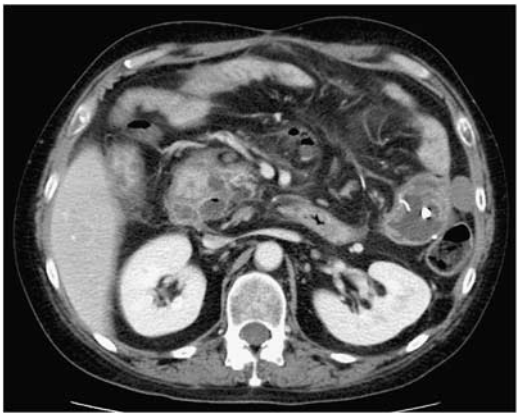
In 1985, Balthazar *et al.* [46] initially proposed a scoring system for the grading of disease severity based on CT findings (Table 5). Most patients with SAP exhibited one or several pancreatic fluid collections (grades D and E) on the initial CT study, with a mortality rate of 14% and a morbidity rate of 54%, compared with no mortality and a morbidity rate of only 4% in patients with grades A, B, or C. This CT grading was easy to perform, fast, and could be used to identify a subgroup of individuals (grade D or E) at risk of death or a high morbidity rate. A major improvement in this early grading system was achieved with the introduction of the incremental dynamic bolus CT technique (Fig. 1). An excellent correlation was demonstrated between NP and death. Furthermore, the extent of necrosis proved to be of major importance. Patients with less than 30% necrosis exhibited no mortality, whereas larger areas of necrosis (30–50% and > 50%) were associated with mortality rates of 11–25%. The combined morbidity rate in patients with more than 30% necrosis was 94%. In an attempt to improve the predictive value of the initial Balthazar score, a new simple scoring system was created combining the former with the degree of pancreatic necrosis. The new score was called CT Severity Index (CTSI) [47–50]. It showed a statistically significant correlation with mortality, with a continuous increasing incidence in patients stratified according to CTSI groups. Those with a severity index of 0, 1, or 2 exhibited no mortality, whereas those with a CTSI of 7–10 yielded a 17% mortality rate.

Table 5 Computed Tomography Severity Index[a]

	Necrosis			
CT grade	Points	Percentage	Additional points	CT severity index[b]
A	0	0	0	0
B	1	0	0	1
C	2	<30	2	4
D	3	30–50	4	7
E	4	<50	6	10

A, normal pancreas; B, enlarged pancreas; C, pancreatic and/or peripancreatic inflammation; CT, computed tomography; D, a single peripancreatic collection; E, at least two peripancreatic collections and/or retroperitoneal air.
[a]Reproduced with permission from Balthazar.
[b]Grade points are added to points assigned for percentage of necrosis.

Fig. 1



Abdomen computed tomographic scanning showed reacutization of pancreatitis with fluid collection of the head in a patient with annular pancreas previously underwent the Frey pancreaticojejunostomy for chronic pancreatitis.

Management

All patients with signs of SAP should be admitted to an ICU and referred to specialized centers for maximum supportive care [51–59]. The most important supportive therapy is an adequate and prompt fluid resuscitation with intravenous fluids and supplemental oxygen [60]. Cardioinotropic drugs, hemofiltration, or dialysis may also be needed to allow optimal fluid therapy despite acute renal failure or hypoperfusion [61–64]. There is some evidence that vigorous fluid resuscitation may be associated with MOF resolution. As plasma expanders are more effective and long acting, colloids should be preferred compared with crystalloids. Dextran 60 seems to be the most potent colloid available for SAP treatment, as it is characterized not only by a long intravascular persistence, but also by antithrombotic properties and inhibitory effects on leukocyte adhesion [65,66].

As infection of NP is thought to derive from the gastrointestinal tract, enteral nutrition (EN) might thereby decrease the incidence of this severe complication. In contrast to initial concerns, EN does not stimulate the exocrine pancreatic function, if the feeding tube is positioned in the jejunum [67,68]. Furthermore, the evidence is not conclusive to support EN in all patients with SAP; the enteral route may be used if that can be tolerated [69–71]. However, as newer data contravene historic concerns against EN, there is still an ongoing debate about the indication of EN in SAP. One meta-analysis on EN versus total parenteral nutrition on the trials by Kalfarentzos *et al.* [72] and McClave *et al.* [73] found a reduced relative mortality risk in patients

receiving EN, but this difference did not reach statistical significance [74]. Abou-Assi *et al.* [75] included 53 patients with mild-to-SAP and found significantly less metabolic complications and line infections as well as lower hospital cost in patients under EN. The meta-analysis of Heinrich *et al.* [76] has shown equal mortality rates but less infectious complications for EN. It seems conceivable that patients with AP should preferably receive EN. However, larger trials are necessary to confirm these results and to define the optimal content of nutrients. A recent review comparing total parenteral nutrition with EN, including eight trials with a total of 348 patients, showed that EN significantly reduced mortality, MOF, systemic infections, and the need for operative interventions compared with those who received total parental nutrition [71]. Supplementation of EN with probiotics may further decrease septic complications [77,78]. Olah *et al.* [79] performed a randomized double-blind trial on patients with mild and SAP, in which patients received either active or inactivated *Lactobacillus plantarum* in addition to fiber containing EN. The addition of active *Lactobacillus* significantly reduced the infection rate and indication for surgery. In addition, in several clinical trials probiotic prophylaxis did not reduce the risk of infectious complications. Recently, no significant trend was identified for an effect of probiotics on gut permeability or endotoxemia in SAP [80]. Larger trials are necessary to confirm these results and to define the optimal content of nutrients [81]. The supportive therapy also includes an adequate analgesia [82].

A causative therapy exists for gallstone SAP with an impacted stone, biliary sepsis, or obstructive jaundice. Endoscopic retrograde cholangiopancreatography (ERCP) and endoscopic sphincterotomy (ES) ameliorate symptoms and progression of the disease when applied early [83]. Emergency ERCP and ES should be strongly considered in patients with biliary SAP and in patients with standard indications such as cholangitis [84,85]. The decision for the management of patients with predictive biliary SAP is still a matter of debate; even if endoscopic treatment appears safe and effective and may be the definitive treatment in patients with AP with a high anesthesiological risk [86–88]. Several guidelines recommend that urgent therapeutic ERCP be performed within 72 h of admission for all patients with predicted SAP, whether or not cholangitis is present [89,90]. However, two recent meta-analyses [91,92] suggested that early ERCP, with or without ES, had no beneficial effects in patients with predicted mild or biliary SAP without cholangitis or persistent biliary obstruction; this point of view has also been supported by two recent papers [90,93]. However, what happens in clinical practice is not completely known [86].

Unlike the use of antibiotics in the treatment of proven infection, the rationale for the use of prophylactic antibiotics in SAP is to prevent infection from affecting areas of pancreatic necrosis and consequently reduce the need for surgery and mortality [65,94,95]. The use of prophylactic antibiotics in SAP to prevent infection from areas of sterile necrosis is still an open question; it seems conceivable that further multicenter studies are needed [96,97]. Several randomized controlled trials have demonstrated the effectiveness of prophylactic antibiotics in the reduction of septic complications and mortality of NP [98–101]. A meta-analysis of eight previously published trials about prophylactic antibiotics in AP has shown a positive benefit for antibiotics in reducing mortality [95]. However, the advantage was limited to patients with SAP who received broad-spectrum antibiotics that achieved therapeutic pancreatic tissue levels [98,102]. Buchler *et al.* [103] have identified imipenem as the antibiotic agent of first choice because it reached higher pancreatic tissue levels and provided higher bactericidal activity against most of the bacteria present in pancreatic infection compared with other types of antibiotics. Overall, antibiotic prophylaxis significantly reduced sepsis and mortality but did not prevent infection of necrosis [104,105]. However, a subgroup analysis demonstrates a significant reduction in infected necrosis for patients receiving prophylactic imipenem (36.4 vs. 10.6%, $P = 0.002$) in contrast with those under quinolones with metronidazole [106]. Antibiotic prophylaxis is superior to antibiotic treatment in NP, and it does not result in an increased incidence of fungal infections [107–109].

When NP has developed, the differentiation between sterile and infected necrosis is essential for the management of patients [110]. In multivariate analysis by Ocampo *et al.* [111], the extent of the pancreatic necrosis was related to the development of infected pancreatic necrosis. In the study by Kemppainen *et al.* [112], necrosis in the head of the pancreas or the entire gland was associated with higher morbidity and mortality rates. In patients with necrosis involving the entire pancreas, most deaths (80%) resulted from late septic complications, whereas in patients with necrosis in the head, most deaths (60%) resulted from early MOF. As the head of the pancreas has a rich collateral blood supply, necrosis development in this area may elicit a more severe inflammatory response that may account for their higher incidence of organ failure.

The high incidence of pseudocyst formation, amylase-rich peripancreatic fluid collections, and pancreatic fistulas after an episode of SAP suggests that main pancreatic duct disruption is a common event in this disease. Neoptolemos [113] and Lau *et al.* [114] have assessed the main pancreatic duct integrity, using ERCP, and found a relationship between the presence of pancreatic necrosis, main pancreatic duct disruption, and the need for surgical intervention.

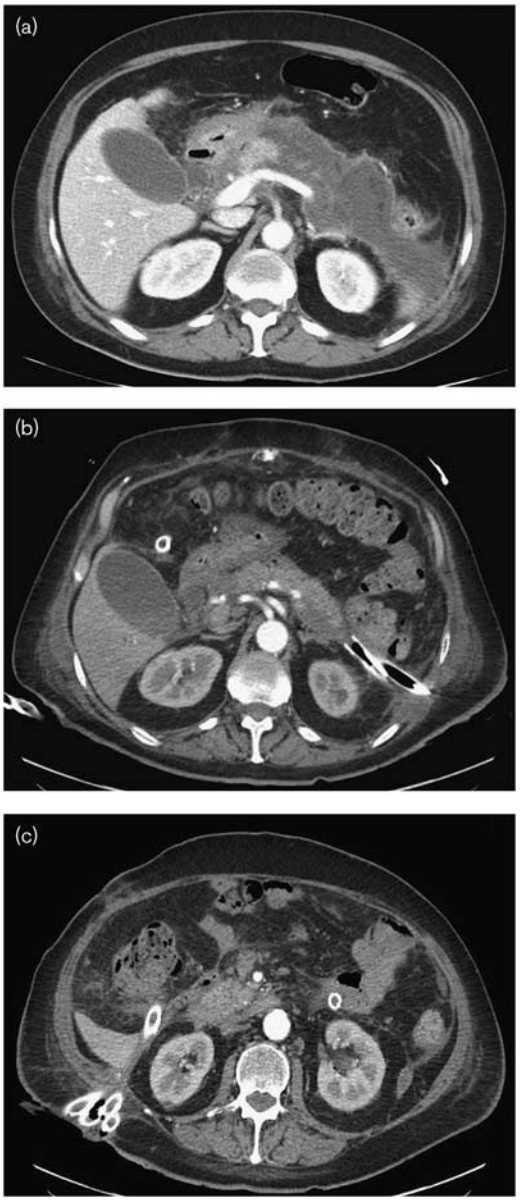
Infection of necrotic pancreatic tissue is usually suspected in patients who develop clinical signs of sepsis.

These patients should undergo CT or ultrasonography-guided fine-needle aspiration of pancreatic or peripancreatic necrosis. Fine-needle aspiration is an accurate, safe, and reliable approach to differentiate between sterile and infected necrosis [115,116]. When sterile necrosis is associated with MOF, the role of surgery remains controversial [117,118]. It is still unclear why some patients with sterile necrosis can be treated nonsurgically whereas other patients die without timely intervention. MOF manifestation in AP is associated with mortality rates of 23–75% [119]. Therefore, some researchers favored early surgical therapy in extended NP, as in theory necrosectomy that eliminates the risk of necrosis getting infected. Furthermore, removal of necrosis is thought to prevent or reduce the risk of inflammatory mediators and toxic substances being released into the systemic circulation, thereby ameliorating the systemic inflammatory response. However, as proinflammatory mediators are released very early in the course of the disease, surgery is not the tool to interfere with the SIRS. Another drawback of early surgery is the risk of secondary infection of preoperative sterile necrosis, which has been shown in approximately 30% of patients [120]. Thus, surgical intervention in sterile necrosis even seems harmful with worsening the prognosis of patients [6]. ICU therapy including prophylactic antibiotic treatment has been shown to generate better survival [121–123]. Therefore, persistent or progressive organ complications, despite maximal ICU treatment, are an indication for surgery in patients with sterile necrosis. However, there is no established uniform definition of when a patient should be considered a nonresponder to ICU therapy [123]. Nevertheless, given the poor outcome with both surgical and conservative therapy and the lack of published data, the optimal therapy for this subset of patients remains unclear. As defined at the 2002 IAP Consensus Conference, indications for surgical treatment of acute NP comprise infected NP and sterile necrosis in case of fulminant AP or persistent SAP [124]. At present, there is general agreement that surgery in SAP should be performed as late as possible. The rationale for late surgery is the ease of identifying well-demarcated necrotic tissue from the viable parenchyma, with the effect of limiting the extent of surgery to pure debridement [125]. This approach decreases the risk of bleeding and minimizes the surgery-related loss of vital tissues, which leads to surgery-induced endocrine and exocrine pancreatic insufficiency [126,127].

The preferred surgical procedure for SAP is necrosectomy/debridement with the placement of wide-bore drains for continuous postoperative irrigation [128–131]. Abdominal zipper or open packing of the wound allows repeated abdominal access for subsequent debridement. In the open packing technique, the abdominal cavity is filled with nonadherent packing [76]. Successive laparotomies are performed every 48 h for further debridement, which can be carried out in ICU under sedation. This abdomen is closed with drains when granulation tissue appears. In specialized centers, open surgical management of infected necrosis can reduce the mortality from 80 to 10–20% [21] (Fig. 2).

For patients who are poor surgical candidates or who have well-contained infection, minimal-access pancreatic necrosectomy by either percutaneous or endoscopic routes

Fig. 2



(a) Preoperative abdomen computed tomographic (CT) scanning showed pancreatic necrosis with peripancreatic fluid collections. Fine-needle aspiration demonstrated infected pancreatic necrosis. (b,c) The patient underwent necrosis debridement and drainage. Postoperative abdomen CT did not show evidence residual necrosis and showed decisive reduction of peripancreatic fluid collections.

has shown encouraging results [58,132–136]. The minimal invasive techniques can be classified into two groups: video-assisted retroperitoneal debridement and laparoscopic transperitoneal debridement [137–139]. The indications for minimal-access pancreatic necrosectomy are the same as those for open intervention. Ideally the area of necrosis is approached from a retroperitoneal access route [140–142]. Most commonly this is through a window between the upper pole of the left kidney and lower pole of the spleen. A minimal access approach can offer significant benefits to the patient in terms of a reduction in systemic insult associated with intervention, which in turn translates into a reduction in mortality. Retroperitoneal debridement needed to be repeated on several occasions to achieve clearance and the technique is used mainly in patients with left-flank collections of necrotic material [143].

Natural orifice translumenal endoscopic surgery is becoming the procedure of choice, replacing open surgical debridement, which is associated with a significant morbidity and mortality in patients who are often already critically ill or significantly debilitated [138]. Endoscopic debridement of pancreatic necrosis can be performed with conscious sedation or general anesthesia – the choice depends on the American Society of Anesthesiologists Classification of the patient. After necrosectomy, it is essential to maintain drainage of the cavity by placement of stents. For this purpose, two or three double pigtail stents (10 French diameter) are typically placed. A nasocystic catheter can be used in cases in which thick organized necrosis were found and irrigated with 50–100 cc/h saline solution for at least 1 or 2 days to continue the debridement process. The procedure can be repeated one or more times if there is suspicion of incomplete debridement. Patients are maintained on intravenous antibiotics throughout the debridement period. The majority of reports use postoperative irrigation and, as with retroperitoneal necrosectomy, multiple procedures are required [144]. Of the minimally invasive techniques, the retroperitoneal approach may be selected in patients with left-sided, predominantly retroperitoneal necrosis with a predominantly semisolid collection. Endoscopic necrosectomy appears most effective in addressing a unilocular collection located in a principally retrogastric position. Laparoscopic necrosectomy seems to be most effective in addressing unilocular, retrogastric fluid collections.

Mini-invasive techniques, including percutaneous drainage, endoscopic (transgastric) drainage, and minimally invasive retroperitoneal necrosectomy, are increasingly being used. In a recent multicenter study, the researchers randomly assigned 88 patients with pancreatic necrosis and suspected or confirmed infected necrotic tissue to undergo primary open necrosectomy or a step-up approach to treatment. The first step is percutaneous or endoscopic drainage of the collection of infected fluid to mitigate sepsis. If drainage does not lead to clinical improvement, the next step is minimally invasive retroperitoneal necrosectomy. This step-up approach might reduce the rates of complications and death by minimizing surgical trauma in already critically ill patients [139].

Conclusion

An ideal or desirable detection system should have high sensitivity and positive predictive value, be able to predict necrosis early (< 48 h), be performed rapidly (< 4 h), be available in most hospitals, be relatively inexpensive, and be objective and not observer-dependent. Most of the clinical prognostic scores that aim to predict the severity and mortality of AP focus on the systemic response to the disease. Current practice guidelines state that 'the two tests that are most helpful at admission in distinguishing mild from SAP are APACHE-II score and serum hematocrit' [51]. The prognostic utility of hemoconcentration remains controversial [40]. It has been emphasized that hemoconcentration on admission was a poor prognostic sign. In contrast, it was found that initial hematocrit levels below 30% correlated with increased mortality [26]. Ranson *et al.* have not found a significant relationship between initial hematocrit levels and prognosis, but the degree of fall of hematocrit during the initial 48 h period of treatment had a significant relationship with mortality and morbidity [26]. Unlike clinical scores, radiological scores are based on local anatomical changes in the pancreatic and peripancreatic tissues. ce-CT scans can be used to assess pancreatic necrosis, as loss of perfusion consequent on necrosis results in a reduced enhancement. Furthermore, it has been documented that the CTSI can predict not only death but also length of hospital stay and need for necrosectomy [47,48,145].

Limitations of CTSI scoring system regarding the evaluation of extrapancreatic necrosis or other organ complications must be taken into account when using CT imaging in the assessment of patient prognosis. De Sanctis *et al.* [146] estimated that ce-CT criteria are superior to the APACHE-II score as predictors of local complications, although APACHE-II score is superior to all ce-CT criteria as an indicator of systemic disease severity. Triantopoulou *et al.* [147] were not able to demonstrate a statistically significant association between CT scores and patient stay in the ICU, thus reflecting the limitation of imaging methods to predict organ dysfunction. With regard to necrotizing disease, the absence of statistically significant differences in CT scores among survivors and nonsurvivors suggest the limited role of CT in this patient group. Furthermore, APACHE-II score demonstrated a strong statistically significant correlation with the length of stay in the ICU and with the development of local complications. Three studies found a significant association of APACHE-II with mortality, but

conflicting results were found when the multivariate analysis was conducted: in the study by Kong *et al.* [148], independent prognostic factors for mortality were respiratory failure, cardiovascular failure, and renal failure but not the APACHE-II, whereas in the study by Bourgaux *et al.* [149] the score was highly correlated with death ($P < 0.001$), and in the study by Mofidi *et al.* [110] the APACHE-II score on admission was an independent preoperative predictor of mortality.

In conclusions, despite the proliferation of scoring systems for grading AP, there is still no one single system, which is completely reliable in the prediction of complications and mortality. The adoption of multiparametric criteria proposed together with morphological evaluation consents the formulation of a discreetly reliable prognosis on the evolution of the disease a few days from onset. Moreover, management of patients with high-risk AP is complex and is optimally provided by a multidisciplinary team at a center with expertise in all specialties dealing with pancreatic disease.

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