Commentary
Risk management in patients with severe acute pancreatitis
Herwig Gerlach

Professor and Director, Department of Anesthesiology, Critical Care Medicine, and Pain Management, Vivantes – Klinikum Neukoelln, Berlin, Germany

Corresponding author: Herwig Gerlach, herwig.gerlach@vivantes.de

Related to *Research* by De Waele *et al*., see page 513

Abstract

Primary or secondary infection of necrotized areas by enteral bacteria is considered a primary cause of mortality in patients with severe acute pancreatitis (SAP). Indeed, 20–30% of patients die during the course of the disease from multiple organ dysfunction after infection. This is why strategies such as antibiotic prophylaxis and early surgical intervention are appealing, but the controlled data that support these measures are insufficient. On the other hand, environmental risk factors (e.g. smoking, alcohol) and genetic predisposition have been identified; together, these led to SAP being considered a 'multifactorial' disease. However, this description does not help the intensivist to assess risk in the individual patient. A number of prognostic factors in SAP have been identified, and different scoring systems have been developed that include therapy-associated and patient-related factors. Nevertheless, at present no prognostic model is available that takes into account all of these predictors. Moreover, despite several attempts to create guideline-based strategies, SAP is still characterized by rapidly progressive multiple organ failure and high mortality, and both surgical and conservative therapies yield poor outcomes. This brief commentary highlights the most recent developments in risk management for patients with SAP.

Keywords organ failure, pancreatic necrosis, predictors, risk assessment, severe acute pancreatitis

Introduction

Severe acute pancreatitis (SAP) can progress to a critical condition within a few hours or days after the onset of symptoms. Particularly during the early course of the disease, patients are at high risk for developing infections with subsequent multiple organ dysfunction syndrome. Therefore, early surgical intervention has been favoured, although evidence-based data are lacking. In this issue of *Critical Care*, De Waele and coworkers [1] present findings from a critical review conducted over nearly a decade. In contrast to many prior recommendations, the authors could not find any significant association between the timing of surgery and patient outcomes. Moreover, they identified patient age, severity of organ dysfunction at the time of surgery, and the presence of sterile necrosis as the main risk factors, and concluded that an early surgical intervention is not justified in the absence of proven infection when necrosis is detected after computed tomography (CT) scan [1]. These important findings once again raise the issue of risk assessment in the individual patient with SAP.

Current practice

A major problem in the treatment of patients with SAP is the lack of randomized trials. Recently, King and coworkers [2] reported results from the first pan-European survey conducted among specialists in hepato-pancreato-biliary surgery of surgical strategies for management of SAP, with the aim being to highlight areas of discordance and thus provide a rational focus for future research. A questionnaire survey of 866 surgeons was undertaken, and the response rate was 38%. Severity stratification was used by 324 respondents (99%), with the Ranson score being the most popular. Antibiotic prophylaxis was utilized by 73%, and fine needle aspiration biopsy (FNAB) was undertaken by 53% of respondents. Furthermore, the results show that there were further aspects of practice that were concordant among

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CT = computed tomography; FNAB = fine needle aspiration biopsy; SAP = severe acute pancreatitis.

surgeons, such as use of early CT and agreement that infected necrosis should be treated surgically. However, there were unexpected findings that demonstrate that enclaves of heterodox practice in the treatment of SAP persist in Europe; for example, some surgeons advocated nonoperative management of FNAB-proven infected necrosis. Importantly, there was no consensus regarding the optimal timing of surgery. Chiang and coworkers [3] compared management of patients with SAP between two centres in Australia. They found that all diagnostic tests for severity stratification recommended by current practice guidelines were performed in only 38% of patients.

Prognostic models

Early deaths in patients with SAP are rare, mainly as a result of modern intensive care treatment. A retrospective analysis [4] found that nine out of 10 deaths occurred more than 3 weeks after the onset of disease. This emphasizes the importance of prognostic models, especially early in the course of disease. Several risk factors for SAP have been described. Patients with android fat distribution and higher waist circumference are at greater risk for developing SAP [5]. This finding was interpreted to be related either to the amount of abdominal fat or to an overactive systemic inflammatory response that tended to be upregulated in those with android fat distribution. A meta-analysis of the same group 2 years later [6] revealed that obesity (defined as a body mass index of ≥ 30 kg/m^2) carries a significant 2.6-fold higher risk for development of SAP, and up to a 4.6-fold higher risk for complications. Pupelis and coworkers [7] found increased intra-abdominal pressure (≥ 25 cmH$_2$O), which is related to body weight, to be a risk factor for early organ dysfunction, and therefore they recommended monitoring of intra-abdominal pressure in patients with SAP.

Primary and secondary infections, however, are still considered the determining factors for fatal outcome in patients with SAP. In particular, Luiten and coworkers [8] reported that Gram-negative intestinal colonization (except that with *Escherichia coli*) carries a significantly increased risk for pancreatic infection and mortality, and De Waele and colleagues [9] found a trend toward increased risk for development of renal failure among patients with fungal infections, although no significant difference in patient outcomes was described. Halonen and coworkers [10] attempted to develop a multivariate model using new strategies involving neuronal networks. Interestingly, their optimal prediction model (logistic approach) identified four variables: age, greatest serum creatinine value within 60–72 hours from primary admission, need for mechanical ventilation, and chronic health status. In contrast, 'classic' scores (Ranson, Imrie) were inaccurate, with accuracy values of 0.65 and 0.54, respectively. However, the model was developed primarily to permit early prediction of hospital mortality and not to classify the severity of SAP over time, and so infection status was not included in the analysis.

Current trends in treatment for severe acute pancreatitis

Although the studies cited above yielded contradictory findings regarding the importance of infection status, current recommendations are clearly aimed at preventive and therapeutic measures to reduce the bacterial focus. Büchler and coworkers [11] concluded that patients with infected necrosis should be treated surgically, whereas conservative management, including early antibiotic administration, is promising in the case of sterile pancreatic necrosis. The same group formulated an algorithm including antibiotic administration as a standard in SAP [12], and repetitively stated that 'there is no doubt that pancreatic infection is the major risk factor in necrotizing pancreatitis with regard to morbidity and mortality' [13]. Recently, the validity of that statement was cast into doubt by the findings of a placebo-controlled, double-blind trial [14], which surprisingly revealed that antibiotic prophylaxis had no benefit with respect to risk for developing infected necrosis or mortality. In conclusion, antibiotic prophylaxis in SAP remains controversial. In contrast, for treatment of infected necrosis, surgical intervention with either laparotomy or ultrasound- or CT-guided drainage is widely accepted, and the International Association of Pancreatology recently reported guidelines that include recommendations for surgical techniques [15]. Altogether, in contrast to therapy-associated risk factors, the importance of patient-related variables in SAP remain undetermined and merits further attention.

Conclusion

Data from different groups of investigators lead to the following conclusion; assessment of individual risk and optimal treatment in SAP remain areas of uncertainty. A major reason for this uncertainty is misleading statistics, or at least questionable interpretation of them, which often take only single variables into consideration. However, several studies using multivariate strategies [1,10] confirmed that there is considerable coupling of variables, and that conclusions should be drawn with caution. For example, if early surgical intervention is associated with increased mortality, then this does not necessarily mean that the surgeon employed the wrong strategy. The severity of organ dysfunction at the time of surgery clearly is a major risk factor. In other words, the increased risk for death in these patients is not necessarily treatment associated, but rather it could be patient related. Hopefully, new imaging techniques [16] as well as novel approaches with which to assess genetic predisposition [17] may lead to improved risk management in patients with SAP. Future studies should focus on the identification of individual risk factors, which might permit application of specific, evidence-based guidelines rather than general recommendations.

Competing interests

The author(s) declare that they have no competing interests.

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