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Development and validation of a multivariate prediction model for patients with acute pancreatitis in Intensive Care Medicine

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ABSTRACT

Background/objectives: Development and validation of a multivariate prediction model for patients with acute pancreatitis (AP) admitted in Intensive Care Units (ICU).
Methods: A prospective multicenter observational study, in 1 year period, in 46 international ICUs (EPAMI study). Patients: adults admitted to an ICU with AP and at least one organ failure. Interventions: Development of a multivariate prediction model, using the worst data of the stay in ICU, based in multivariate analysis, simple imputation in a development cohort. The model was validated in another cohort.
Results: 374 patients were included (mortality of 28.9%). Variables with statistical significance in multivariate analysis were age, no alcoholic and no biliary etiology, development of shock, development of respiratory failure, need of continuous renal replacement therapy, and intra-abdominal pressure. The model created with these variables presented an AUC of ROC curve of 0.90 (CI 95% 0.81−0.94) in the validation cohort. We developed a multivariable prediction model, and AP cases could be classified as low mortality risk (between 2 and 9.5 points, mortality of 1.35%), moderate mortality risk (between 10 and 12.5 points, 28.92% of mortality), and high mortality risk (13 points of more, mortality of 88.37%). Our model presented better AUC of ROC curve than APACHE II (0.91 vs 0.80) and SOFA in the first 24 h (0.91 vs 0.79).
Conclusions: We developed and validated a multivariate prediction model, which can be applied in any moment of the stay in ICU, with better discriminatory power than APACHE II and SOFA in the first 24 h.

Introduction

Acute pancreatitis (AP) is a clinical entity with low mortality in its mild forms. Nevertheless, the most severe forms, and consequently, patients with AP admitted in Intensive Care Units, showed high mortality. This mortality has been divided in two groups, according to the moment of development: early mortality, which appears in the first two weeks, mainly due to Systemic Inflammatory Response Syndrome; and late mortality, after 14 days of evolution, in relation to local complications, especially infected necrosis. Authors debated if mortality shared up in 50% between two groups, or late mortality was the main cause [1–4]. In recent years, there were great changes in the management of AP, and this reality could be different: need of adequate fluid resuscitation [5],

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use of early enteral nutrition [6], minimally invasive treatment of infected necrosis [7,8] …

In the same way, prediction of mortality of AP is very difficult, due to the low incidence of the most severe forms, and its fluctuating clinical course. Several prediction score systems had been developed, but all of them presented a high rate of false positive results, and are complex and cumbersome to complete [9–14]. Additionally, these score systems were not developed and validated in patients admitted in ICU. The aim of this study was the description of mortality of patients with AP admitted in ICU, and the search of factors related with mortality, to finally develop and validate a multivariable prediction model for mortality. The discriminatory power of this prediction model was compared with the discriminatory power of APACHE II and SOFA in the first 24 h.

Methods

Study design: This was a prospective, observational multicenter international study. At the Consensus Conference on the management of acute pancreatitis under the auspices of the Spanish Intensive Care Society (SEMICYUC) [15], it was decided to initiate this study, sending an invitation to all Critical Care Units who are members of the SEMICYUC. In addition, we contacted several Critical Care Departments in South America, inviting them to participate in the study. The study inclusion criteria were as follows: patients aged over 18, admitted to an ICU with a diagnosis of acute pancreatitis and at least one organ failure. There were no exclusion criteria. The study recruitment was from January 1st to December 31st, 2013.

Definitions

Acute pancreatitis. Acute pancreatitis was diagnosed by at least two of these three criteria: compatible abdominal pain, two fold increase in amylase or lipase over laboratory baseline levels, and suitable findings in imaging techniques (CT, ultrasound or MRI).

Etiology

Biliary: Presence of gallstones in the bile duct, without other causes of pancreatitis.

Alcoholic: Alcohol consumption higher than 60 gr/day, sustained for more than 5 years, without another defined cause of pancreatitis.

Post-ERCP acute pancreatitis: pancreatitis developed in the next 7 days after endoscopic retrograde cholangiopancreatography.

Other causes: This category other causes, as posttraumatic and postsurgical pancreatitis, or hypertriglyceridemia.

Idiopathic: there were not criteria for the rest of etiologies.

Organ failure. Organ failures were defined according to SEMICYUC Consensus Conference criteria (hypotension, respiratory failure, acute renal failure) [15].

- Hypotension. Systolic arterial pressure less than 90 mmHg or a reduction of 40 mmHg in basal systolic arterial pressure, with tissue hypoperfusion signs (lactate >3 mMol/L); Saturation of central venous oxygen SvcO2 < 70%.
- Respiratory failure. Basal PaO2 < 60 mmHg; or PaO2/FiO2 < 300 mmHg (with supplementary O2).
- Acute renal failure. An increase of basal creatinine by 2 (AKI-2, o RIFLE-I) and/or reduction of urinary flow (oliguria) < 0.5 ml/kg/ h × 12 h.

Each organ failure was defined as transitory if the duration was shorter than 48 h or as persistent if the duration was longer than

48 h.

The severity was evaluated with APACHE II and SOFA scores, using the worst values in the first 24 h after ICU admission.

The **measurement of intra-abdominal pressure (IAP)** was done using a urinary catheter, according to the definitions of the International Conference of Experts on Intra-abdominal Hypertension and Abdominal Compartment Syndrome [16]. The highest value measured in the stay of ICU was registered.

The use of **mechanical ventilation** was defined as the need of invasive mechanical ventilation, at any moment of the stay in ICU.

The use of **continuous renal replacement therapy (CRRT)** was defined as the use of CRRT for acute renal failure with RIFLE Failure criteria [17], at any moment of the stay in ICU.

Local complications

Sterile necrosis. Necrosis was defined by the presence of no viable tissue in pancreas or peripancreatic tissues, observed in computer tomography (CT), magnetic nuclear resonance (MNR) or surgical view. Necrosis was defined as sterile when there was no evidence of infection.

Infected necrosis was defined by the presence of gas in (peri) pancreatic tissue, a positive result in Gram staining, or samples obtained by fine needle aspiration guided by image techniques, or samples obtained in surgery or drainage samples [18].

Abdominal hemorrhage was defined by the presence of liquid collections with hematic density in image techniques (CT, MNR), especially if active extravasation was observed after contrast administration, or by the direct visualization of the hemorrhage in surgery.

Intestinal perforation was defined by direct surgical visualization, or by the presence of one of this information in image techniques: pneumoperitoneum, presence of gas bubbles grouped adjacent to the wall of the intestinal loop, wall thickening and loss of continuity defect or discontinuity of the wall of the intestinal loop.

Need of surgery was defined by the SEMICYUC Consensus conference of AP in 2012 [15]. The main indications were:

- Infected necrosis or pancreatic abscess, which can't be treated by less invasive drainage techniques (step-up approach).
- Intestinal bowel perforation.
- Abdominal hemorrhage, which can't be treated by endovascular techniques.
- The management of sterile necrosis should be conservative, unless cases of more than four weeks of evolution, and persistent patient affectation.
- Abdominal Compartmental Syndrome, which cannot be treated by conservative techniques.

Mortality was defined as early mortality if it happened in the first 14 days after symptoms initiation, and as late mortality when happened in the next days. The mortality causes definitions used were as follows:

Initial Systemic Inflammatory Response Syndrome (SIRS). Patients who died due to organ failure originated by acute pancreatitis initiated in the first 14 days of clinical development, without data of infection in the (peri)pancreatic area, or another cause of death.

(Peri)pancreatic infection. Patients who died due to organ failure originated by (peri)pancreatic infection, defined by the presence of gas in (peri)pancreatic tissue, a positive result in Gram staining, or samples obtained by fine needle aspiration