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Mortality assessment in patients with severe acute pancreatitis: a comparative study of specific and general severity indices

Avaliação da mortalidade na pancreatite aguda grave: estudo comparativo entre índices de gravidade específicos e gerais

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ABSTRACT

Objective: This study compared the general and specific severity indices to assess the prognosis of severe acute pancreatitis at a polyvalent intensive care unit.

Methods: This retrospective study included 108 patients who were diagnosed with severe acute pancreatitis from July 1, 1999 to March 31, 2012. Their demographic and clinical data were collected, and the following severity indices were calculated: Ranson, Osborne, Blamey and Imrie, Balthazar, POP, APACHE II, SAPS II, and SOFA. The discriminative power of these indices with regard to mortality at the intensive care unit and hospital was assessed using the area under the ROC curve.

Results: The demographic data of the surviving and deceased patients did not significantly differ at baseline. The mortality rates were 27% and 39% at the intensive care unit and hospital, respectively. The severity indices that exhibited the greatest discriminative power with regard to mortality at the intensive care unit and hospital were the POP 0, POP 24, SOFA (at admission, 24 hours, 48 hours, and discharge), SAPS II, and APACHE II.

Conclusion: The POP performed better than the other indices (aROC>0.8) at admission and 24 hours later (as originally described). The general physiological dysfunction indices also exhibited reasonable discriminative power (aROC=0.75-0.8), which was unlike the remaining pancreatitis specific indices, whose discriminative power was lower.

Keywords: Acute pancreatitis; Hospital mortality; Mortality; Severity of illness index; Critical care; Prognosis

INTRODUCTION

The clinical presentation and severity of acute pancreatitis is widely variable.[1] Approximately 20% of patients develop severe cases, and these outcomes are associated with multiple organ dysfunction syndrome (MODS) and eventually death.[2] Although the global mortality of acute pancreatitis has significantly decreased over the last decades (from approximately 12% to approximately 2%), this rate remains high among the subgroup of patients with severe forms of the illness.[3] Although severe acute pancreatitis (SAP) represents a small fraction of the admissions to polyvalent intensive care units (ICUs), it demands considerable human and technical resources and exhibits high mortality and morbidity rates at both ICUs and hospitals because this condition is usually associated with long hospitalization periods.[4] Therefore, the early prediction of the severity of this disease

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plays an important role in the timely and appropriate management of these patients.[5]

Several tools have been suggested to classify the severity of SAP including biochemical markers, imaging methods, and complex mathematical methods.[5] An ideal marker should be fast, reproducible, inexpensive, minimally invasive, sensitive, and specific; its ability to predict complications in low-risk patients has been emphasized in particular. Unfortunately, none of the available SAP-severity stratification systems is sufficiently precise with regard to predicting patient clinical progression, particularly the early identification of patients at high risk for developing the most severe forms of the disease.[3] A majority of the studies on prognostic systems has focused on identifying patients with SAP within heterogeneous groups of patients with pancreatitis, most of whom exhibit non-severe forms. Conversely, the role of such indices in the identification of patients with the worst prognoses in pre-selected groups of patients with SAP has been less studied.[5]

Two types of specific severity indices have been applied to patients with acute pancreatitis. One type (including Ranson, Osborne, Blamey, Imrie, and Balthazar) correlates clinical, laboratory, and radiologic markers specific to pancreatitis with the severity of the illness and its subsequent outcomes. The most recent of this type is the Pancreatitis Outcome Prediction (POP) score, described in 2007, which is grounded on a retrospective data analysis prospectively collected from 2,462 individuals with SAP who required admission to an ICU by the Intensive Care National Audit and Research Center (ICNARC) of the United Kingdom. This index is based on six demographic and laboratory variables recorded 24 hours after admission to the ICU.[6]

The second type of indices corresponds to the use of general, non-SAP specific severity/dysfunction indices originally developed for non-selected populations of critically ill patients, e.g., the Acute Physiology and Chronic Health Evaluation II (APACHE II), the New Simplified Acute Physiology Score (SAPS II), and the Sequential Organ Failure Assessment (SOFA) score. These general severity and organ failure indices were initially developed to quantify (and eventually compare) the severity of heterogeneous populations of critically ill patients.[7] A previous study conducted at our ICU supports the use of the SOFA in the classification of risk in patients with acute pancreatitis in ICUs.[8] The Atlanta classification was established by consensus in 1992, which defines SAP as being associated with local complications or MODS. However, this classification uses definitions to assess organ dysfunction that are not consistent with the current criteria for assessing this pathology. Therefore, the international consensus conference sponsored by the European Society of Intensive Care (ESICM), the American Thoracic Society (ATS), the European Respiratory Society (ERS), the Society of Critical Care Medicine (SCCM), and the Société de Réanimation de Langue Française (SRLF) held in Washington, DC in April 2004 moved to consider SAP within the context of organ dysfunction independent of the presence of local complications.[9] Despite its limitations, the Atlanta classification is still widely used to define SAP in most clinical studies outside the ICU setting; thus, its use allows for appropriate comparisons.[10]

The present study characterized the demographics of patients with acute pancreatitis at a polyvalent ICU and assessed the ability of specific and general severity indices to predict outcomes in those with SAP.

METHODS

All patients with a discharge diagnosis of acute pancreatitis admitted to the Polyvalent ICU of Hospital de Santo António dos Capuchos between July 1, 1991 and March 31, 2010 were identified using a computerized database. Most data were extracted from that database, and additional information was retrieved by reviewing patient clinical records. Readmitted patients, those hospitalized for less than 24 hours, and those who did not exhibit acute pancreatitis at admission to the ICU were excluded. The protocol was approved by the institutional ethics committee that waived the need of informed consent. The Atlanta classification severity definition was used. Basic and clinical patient demographic data, including age, gender, race, length of hospitalization, origin, etiology of pancreatitis, presence of complications, and need for surgery, were recorded. The causes of pancreatitis were classified as lithiasis related (especially when confirmed by ultrasonography), alcohol related, other (when another cause was identified), or unknown (when no cause was found). Local complications were defined as the presence of pancreatic necrosis, pancreatic hemorrhage, acute pseudocyst, pancreatic abscess, or ascites. The outcomes at ICU/hospital discharge were recorded, as were the data needed to calculate the various severity indices. The following indices were calculated: Ranson (at admission and 48 hours in the ICU), Osborne,

Blamey, Imrie (48 hours in the ICU), Balthazar (based on the first computed tomography [CT] of the abdomen performed at the ICU), POP (at admission and 24 hours in the ICU), APACHE II, SAPS II (at 24 hours in the ICU), and SOFA (at admission, 24 hours, 48 hours, and discharge from the ICU).

The data were expressed as means ± standard deviations (SDs) except when indicated otherwise. An alpha of 0.05 was considered as the statistical significance threshold. Data analysis was performed using the Statistical Package for Social Sciences, Version 18 (SPSS, SPSS Inc., Chicago, USA). The discriminative power of the various severity indices with regard to mortality at the ICU and hospital was assessed using the area under the ROC curve (aROC). These curves were compared using the non-parametric method described by Hanley and McNeil.[11,12]

RESULTS

Over this 20-year investigation, 130 patients were admitted to the ICU with a discharge diagnosis of acute pancreatitis. Only 108 patients (54 males and 54 females) met the inclusion criteria, and their average age was 59 ± 16 years (ranging from 18 to 88 years). The cause of pancreatitis was lithiasis related in most cases (43.5%), followed by unknown (30.6%), other (16.7%), and alcohol related (9.3%). Other causes included viral, ischemic, postoperative, and post-endoscopic retrograde cholangiopancreatography (ERCP) etiologies. One hundred and four patients (96.3%) exhibited SAP according to the Atlanta classification. Most patients (53.7%) were referred by clinical or surgical wards (46.2% from Hospital de Santo António dos Capuchos and 7.5% from another hospital), and 31.4% were referred by the External Emergency Service (19.4% from Centro Hospitalar de Lisboa Central and 12% from another hospital). The median length of hospitalization in the ICU was 12 days, with an interquartile range of 23 days. Sixty-four percent of patients developed local complications, and 44% required surgery during hospitalization at the ICU. Twenty-nine patients died at the ICU (27%), and the global mortality rate at the hospital was 39% (42 patients). The baseline data collected at admission to the ICU did not significantly differ between the patients who survived and those who did not. Table 1 describes the major demographic characteristics as well as the ICU and hospital outcomes.

Tables 2 and 3 display the means ± SDs and the aROC ± standard error for the severity indices by mortality rates at the ICU and the hospital, respectively. Figures 1 and 2 depict the ROC curves for the severity indices with regard to the mortality rates at the ICU and the hospital, respectively.

Table 1 - Demographic and clinical data of patients admitted due to acute pancreatitis: comparisons between survivors and deceased at the hospital

Demographic data	Total	Survivors	Deceased
Age	58.7±15.8	55.2±16.8	64.1±12.3
Female	54 (50)	32 (59.3)	22 (40.7)
SAP	104 (96.3)	62 (96.9)	42 (100)
Etiology			
Lithiasis	47 (43.5)	29 (43.9)	18 (42.9)
Alcohol	10 (9.3)	10 (15.1)	0
Other	18 (16.7)	13 (19.8)	5 (11.9)
Unknown	33 (30.6)	14 (21.2)	19 (45.2)
Local complications	69 (63.9)	40 (60.6)	29 (69)
Subjected to surgery	48 (44.4)	27 (40.9)	21 (50)
Origin			
Ward	58 (53.7)	38 (57.6)	20 (47.6)
Surgical room	10 (9.3)	6 (9.1)	4 (9.5)
Recovery room	4 (3.7)	3 (4.5)	1 (2.4)
External emergency service	34 (31.5)	18 (27.3)	16 (38.1)
Other hospital ICU	2 (1.9)	1(1.5)	1(2.4)
Pleural effusion	86 (79.6)	53 (80.3)	33 (78.6)

SAP - severe acute pancreatitis; ICU - intensive care unit. The results are expressed as the mean ± SD or number (%).

Table 2 - Severity indices by mortality rate at the intensive care unit

Index	Total	Survivors	Dead	p value	aROC±SE
SOFA ADM	5.6±3.7	4.5±2.9	8.5±4.1	<0.001	0.777±0.054
SOFA 24	6.3±3.8	5.2±3.0	9.2±4.3	<0.001	0.780±0.052
SOFA 48	5.6±4.1	4.3±3.0	9.1±4.4	<0.001	0.813±0.050
SOFA 48-0	1.3±3	1±2.8	2.3±3.5	NS	0.611±0.062
SOFA MAX	7.9±4.3	6.2±3.2	12.6±3.6	<0.001	0.899±0.032
RANSON ADM	2.3±1.1	2.1±1.0	2.7±1.3	0.03	0.625±0.063
RANSON 48	2.2±1.3	1.9±1.1	2.8±1.6	0.01	0.673±0.068
IMRIE 48	5.1±1.7	4.7±1.7	6.0±1.5	<0.001	0.714±0.056
OSBORNE 48	4.4±1.5	4.1±1.5	5.2±1.4	<0.001	0.692±0.056
BLAMEY 48	4.8±1.6	4.5±1.6	5.6±1.4	<0.001	0.707±0.056
BALTHAZAR	4±2.1	3.9±2.0	4.1±2.5	NS	0.517±0.069
APACHE II	18.5±9.2	15.7±6.7	26.1±10.9	<0.001	0.784±0.049
SAPS II	39.6±20.4	32.8±15.2	58.3±21.3	<0.001	0.835±0.041
POP 0	14.9±6.4	12.6±5.5	21.2±4.2	<0.001	0.899±0.031
POP 24	15.6±6.5	13.2±5.2	22.2±4.9	<0.001	0.888±0.033

SOFA - Sequential Organ Failure Assessment Score; APACHE II - Acute Physiology and Chronic Health Evaluation II; SAPS II - New Simplified Acute Physiology Score; POP - Pancreatitis Outcome Prediction Score; MA - maximum; aROC - area under the Receiver Operating Characteristics Curve; SE - standard error; ADM - indices calculated at admission; 24 - indices calculated 24 hours after admission; 48 - indices calculated 48 hours after admission; SOFA 48-0 - change in SOFA between 48 hours and admission; BALTHAZAR - Balthazar's index based on the first abdominal CT performed at the ICU. The results are expressed as the mean ± SD except for aROC, which is expressed as the standard error.

Table 3 - Severity indices by mortality rate at the hospital

Index	Total	Survivors	Dead	p value	aROC±SE
SOFA ADM	5.6±3.7	4.2±2.8	7.9±3.8	<0.001	0.782±0.046
SOFA 24	6.3±3.8	4.8±2.8	8.6± 4	<0.001	0.786±0.046
SOFA 48	5.6±4.1	4.1±2.9	8±4.5	<0.001	0.766±0.051
SOFA 48-0	1.3±3	0.8±2.3	2.2± 3.7	0.023	0.600±0.057
SOFA MAX	7.9±4.3	5.8±3.1	11.2±4	<0.001	0.850±0.039
RANSON 0	2.3±1.1	2.1±1	2.5±1.3	NS	0.584±0.058
RANSON 48	2.2±1.3	1.9±1.1	2.5±1.5	0.018	0.629±0.058
IMRIE	5.1±1.7	4.7±1.7	5.7±1.5	0.002	0.670±0.052
OSBORNE	4.4±1.5	4.1±1.5	5±1.4	0.002	0.663±0.052
BLAMEY	4.8±1.6	4.4±1.7	5.3±1.3	0.003	0.663±0.053
BALTHAZAR	4±2.1	3.9±2	4.1±2.3	NS	0.512±0.060
APACHE II	18.5±9.2	15.4±6.6	23.4±10.6	<0.0001	0.721±0.050
SAPS II	39.6±20.4	31±14.2	53.3± 21.2	<0.001	0.814±0.043
POP 0 H	14.9±6.4	12.3±5.5	18.9±5.7	<0.001	0.812±0.044
POP 24H	15.6±6.5	12.7±5.1	20.2±5.9	<0.001	0.833±0.040

SOFA - Sequential Organ Failure Assessment Score; APACHE II - Acute Physiology and Chronic Health Evaluation II; SAPS II - New Simplified Acute Physiology Score; POP - Pancreatitis Outcome Prediction Score; MAX - maximum; aROC - area under the Receiver Operating Characteristics Curve; SE - standard error; ADM - indices calculated at admission; 24 - indices calculated 24 hours after admission; 48 - indices calculated 48 hours after admission; SOFA 48-0 - change in SOFA between 48 hours and admission; BALTHAZAR - Balthazar's index based on the first abdominal CT performed at the ICU. The results are expressed as the mean ± SD except for aROC, which is expressed as the standard error.

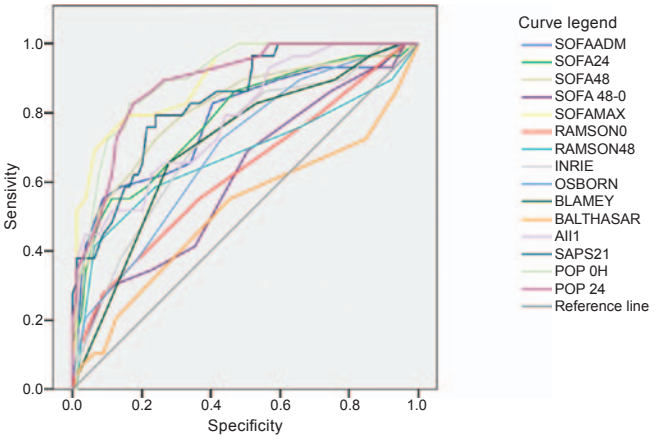

Figure 1 - ROC curves of mortality rates at the intensive care unit.

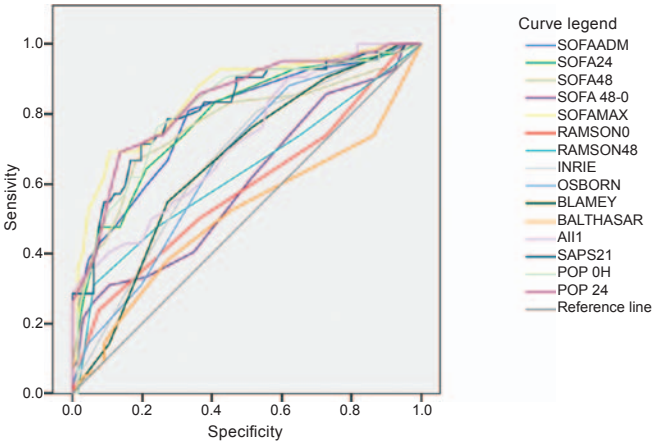

Figure 2 - ROC curves for mortality rates at the hospital.

DISCUSSION

The analysis described in tables 2 and 3 revealed that POP was the most successful predictor of mortality rates at the ICU and the hospital (aROC>0.8). The remaining severity indices regarding pancreatitis exhibited a weak discriminative power. The general severity and multiple organ failure indices exhibited reasonable discriminative power with regard to SAP (aROC>0.75).

No current system distinguishes patients who develop severe pancreatitis from those who do not without error. Thus, several severity indices have been and will continue to be developed.[3]

Ranson et al. created the most widely used acute pancreatitis specific severity index. This index was developed and gained popularity when intensive care was less sophisticated than it is today; however, it had not been subjected to rigorous statistical validation. Several clinicians still use the Ranson to determine whether patients require admission to the ICU as well as predict the need for early enteral nutrition, preemptive antibiotic therapy, prophylaxis, or other interventions. Because of the advances in areas such as cardiorespiratory resuscitation and MODS support, patient mortality associated with pancreatitis is currently decreasing,[13] and patients often survive even when they meet six or more of Ranson's criteria.[14] Many different severity indices have been developed since Ranson's initial contribution in 1974; however, these studies have several problems. For instance, some studies examined different outcomes or provided vague or inconsistent definitions of severity. In addition, the number of patients with severe pancreatitis was generally small, and most patients exhibited non-severe pancreatitis.[5] The largest such study included 1,005 patients, of whom only 25% met the criteria for severe pancreatitis.[6] Another disadvantage of specific indices (including Ranson's) is the required 48-hour interval before the total scores are calculated.

The present study calculated the specific indices 48 hours after admission to the ICU. This timeframe does not necessarily correspond to 48 hours of disease progression. Under these conditions, the indices exhibited a poor ability to discriminate between survivors and the deceased.

Imaging criteria such as Balthazar's index have predicted acute pancreatitis outcomes, and several studies argue that it is superior compared with other specific and general severity indices. However, the interval between

patient admission and the abdominal CT scan varied considerably among these studies.[15,16] In the present study, the first CT scan performed at the ICU was considered for analysis. This protocol might correspond with the highly variable stages of disease progression.

The POP index was designed to measure critically ill patients admitted to ICUs in the United Kingdom. This feature might at least partially explain its performance with regard to the population assessed in the present study. As an additional advantage, the POP index exhibited the same degree of reliability in the present study when calculated at admission and 24 hours after admission as originally described.

Previous studies have compared specific and general pancreatitis severity indices; however, most of these patients exhibited non-severe forms of pancreatitis, and only a few of them were admitted to the ICU. For instance, one study, which sought to correlate Ranson's index with the APACHE II in a population of 273 patients, found that only 12 individuals were admitted to the ICU.[14] The general severity indices were significantly correlated with patient mortality at the ICU and the hospital in the present study, which included 108 patients.

The primary limitations of the present study include are that it was conducted at one ICU, its investigation period was long, and the data collection was partially retrospective.

CONCLUSION

The present study, which included 108 patients diagnosed with acute pancreatitis at a clinical/surgical ICU, found that the POP index had a clearly superior discriminative power compared with other severity indices concerning patient mortality at the ICU and hospital. The POP index exhibited the same discriminative power when calculated at admission and 24 hours later.

The general severity and MODS indices exhibited reasonable discriminative performance, with aROC values approximately ranging from 0.75 to 0.8. These findings support the use of these indices to predict the severity of acute pancreatitis at ICUs.

RESUMO

Objetivo: Comparar os índices de gravidade gerais e os específicos de pancreatite aguda grave na avaliação do prognóstico numa unidade de terapia intensiva polivalente.

Métodos: Estudo retrospectivo de 108 pacientes com diagnóstico de saída de pancreatite aguda grave, no período de 1º de julho de 1991 a 31 de março de 2010. Foram colhidos dados demográficos, clínicos e calculados os seguintes índices de gravidade: Ranson, Osborn, Blamey e Imrie, Balthasar, POP, APACHE II, SAPS II e SOFA. O poder discriminativo dos diferentes índices foi avaliado com base na área sob a curva ROC (aROC), em relação à mortalidade, na unidade de terapia intensiva e no hospital.

Resultados: Não existiram diferenças significativas entre os dados demográficos basais dos doentes sobreviventes e dos falecidos. A mortalidade na unidade de terapia intensiva foi de 27%, com uma mortalidade hospitalar de 39%. Os índices de gravidade com maior capacidade discriminativa para a mortalidade na unidade de terapia intensiva e hospitalar foram o POP 0, POP 24, o SOFA (na admissão, 24, 48 horas e máximo), o SAPS II e o APACHE II.

Conclusão: O índice POP mostrou ser superior a todos os outros índices (aROC>0,8), quer às 24 horas (como foi originalmente descrito), quer à admissão. Os índices de disfunção fisiológica gerais apresentaram também uma capacidade discriminativa razoável (aROC na ordem dos 0,75-0,8) por oposição aos outros índices específicos de pancreatite, cujo valor discriminativo foi francamente mais baixo.

Descritores: Pancreatite aguda; Mortalidade hospitalar; Mortalidade; Índice de gravidade de doença; Unidades de terapia intensiva; Prognóstico

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