

Classification of acute pancreatitis

Classificação de gravidade na pancreatite aguda

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A B S T R A C T

The Atlanta Classification defines acute pancreatitis as mild or severe. A number of aspects have been discussed in recent years, such as, how many categories of severity should be considered; whether the patient with organ failure is similar to the patient with infected necrosis; the role of transient organ failure; and how to evaluate organ failure. The meeting "Evidence Based Telemedicine - Trauma and Acute Care Surgery" (EBT-TACS) conducted a critical review on the topic, selected three main papers that have outlined two major reviews published in recent months. These articles suggest the severity classification in three or four categories, rather than mild or severe only, and discuss what is the best score to assess organ failure. The following recommendations were proposed: (1) Acute pancreatitis should be classified into four categories: mild, moderate, severe and critical, which allows a better stratification of patients, (2) Evaluation of organ failure with a severity score that preferably evaluate directly each organ failure, such as the SOFA and MODS (Marshall). The SOFA seems to have greater accuracy, but the MODS has better applicability due to the ease of use.

Key words: Pancreatitis. Pancreatitis/classification. Pancreatitis, acute necrotizing. Acute disease. Severity of illness index.

INTRODUCTION

According to the Atlanta classification that is completing 20 years of its publication, acute pancreatitis can be classified as mild or severe¹. However, a number of aspects have been discussed in recent years, such as: how many categories of severity should be considered?; Are every severe pancreatitis according to Atlanta similarly severe? Is the patient with organ failure similar to the patient with infected necrosis?; What is the role of transient organ failure?; and how to assess organ failure?

In recent months, two papers were published regarding severity of acute pancreatitis; one being a proposed revision of the Atlanta classification^{2,3}.

The meeting "Evidence Based Telemedicine - Trauma and Acute Care Surgery" (EBT-TACS) Journal Club conducted a review of relevant papers about the severity of acute pancreatitis, particularly related to the Atlanta classification. Three articles were selected in order to answer

two questions: how many categories of severity should be used and how to evaluate organ failure⁴⁻⁶.

The first article discusses the need for inclusion of the term moderately severe acute pancreatitis⁴. The second paper discusses the need to include four categories of severity, comprising the term critical acute pancreatitis⁵. The third article discusses ways to properly assess organ failure⁶.

Based mainly on these three articles, which report on the most important available evidence on the topic, the EBT-TACS group generated recommendations on staging of acute pancreatitis.

STUDY 1

"Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus"⁴

EBT-TACS Journal Club: March 5th, 2013, with the participation of the following institutions: Emergency Division, Santa Casa Sao Paulo, Sao Paulo, SP, Brazil; Trauma Program of the Department of Surgery of Sunnybrook Health Sciences Center, University of Toronto, Toronto, Canada; Division of Trauma Surgery, Department of Surgery, Faculty of Medical Sciences, University of Campinas, Campinas, SP, Brazil; Discipline of Trauma and Emergency Surgery, Department of Surgery and Anatomy, Faculty of Medicine of Ribeirao Preto, University of São Paulo (USP), Brazil.

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Rationale

When analyzing patients with severe acute pancreatitis (SAP) without organ failure (OF), the authors note that, despite pancreatitis-related morbidity being significant, overall mortality associated with this condition is invariably low. However, in a subgroup of patients with SAP and OF, high mortality rates are documented. It is unknown whether the extent of organ failure is related to higher or lower mortality in patients with SAP. However, it is known that patients with transitory OF, which reverts 48 hours after onset of the disease, have a better prognosis. Thus, the reversible OF has been called "transient", and OF that does not revert has been called "persistent".

Therefore, the issue occurs in patients with local complications, but with no persistent OF. The authors' hypothesis was that these patients should be classified as a new subtype: moderately severe acute pancreatitis.

Question

What is the clinical course of patients with SAP, comparing with patients without OF (WFO); patients with single OF (SOF); and those with multiple OF (MOF)? And what is the role of each OF in mortality?

Main findings

The comparison between the groups showed a significant difference ($p < 0.05$) with respect to length of stay (WOF +3 = 28 days; SOF +5 = 36 days; MOF = 55 +4 days), need of intensive care (WOF = 50%; SOF = 65%; MOF = 90%), mean length of stay in intensive care (WOF = 5 days; SOF = 9 days; MOF = 34 days) and hospital mortality (WOF = 2%; SOF = 18%; MOF = 46%). Analyzing the various organ failures individually, it was noted that the risk of death was higher in patients who developed renal failure (odds ratio, OR = 56), followed by cardiovascular failure (OR = 22), respiratory failure (OR = 12) and gastrointestinal failure (OR = 10). In multivariate analysis, the risk of in-hospital death was higher for patients with MOF and SOF. There was no increase in mortality for the presence of pancreatic necrosis, peripancreatic fluid collections or systemic infection. In the group of patients with only one organ failure ($n = 91$), there were 51 patients with pancreatic necrosis and 83 with pseudocysts or

abscesses. Forty-nine patients required any surgical procedure, including surgical drainage (43%) open necrosectomy (29%) and percutaneous necrosectomy (4%). The specific analysis of this subgroup demonstrated that there was no impact of necrosis on mortality, length of stay and need for ICU. The conclusion of the study suggests the need for revision of the Atlanta classification to include the term "moderately severe acute pancreatitis", which includes patients with PAG but without organ failure (Table 1).

Strengths

* The research question is extremely relevant to medical practice for physicians managing similar patients with acute pancreatitis.

* * The hypothesis and objectives are clearly stated, and the study is well-designed to address its question.

* The cohort included 207 patients with SAP, which is a significant sample size for this condition.

* Groups (WOF, SOF, MOF) are apparently comparable and, when analyzed variables of interest (eg, in-hospital mortality), the difference between them was significant.

Limitations

* Despite the characterization of SAP be clear by Atlanta criteria, details that led to patients being classified as having PAG were not exposed. For example, an elderly patient with jaundice (for biliary disease and not organ failure) and hypertension has APACHE II score greater than 8, even without major problems related to the pancreas.

* There was no comparison between groups regarding the presence and percentage of IPN, as well as the percentage of necrotic infection.

* There was no comparison between the groups regarding the surgical procedures performed and their evolution.

* The study was conducted in nine years; allowing for changes over time in treatment protocols and monitoring of acute pancreatitis and organ failure.

* There was no comparison of severity scores, such as SOFA, APACHE II, MARSHAL and between groups. These scores are directly linked to mortality and could give the reader a better assessment of the severity of each group.

Table 1 - Severity categories following the Revision of Atlanta Classification³.

Acute pancreatitis severity	Organ failure and local or systemic complications
Mild acute pancreatitis	- No organ failure - No local or systemic complications
Moderately severe acute pancreatitis	- Transient organ failure (resolves in 48 hours)
	Local or systemic complications without persistent organ failure
Severe acute pancreatitis	- Persistent organ failure (single or multiple)

STUDY 2

“Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis”⁵

Rationale

In Atlanta classification, local complications and extra-pancreatic organ failure are determinants of severity in acute pancreatitis. Recently, the concept that organ failure is the key factor to determine severity has been expressed, independent of local complications. Studies that assess infected necrosis and mortality are not unanimous in their conclusions due to heterogeneous population of patients with and without organ failure, beyond the small number of patients analyzed.

Question

To determine through a meta-analysis of published clinical studies the influence of organ failure and infected pancreatic necrosis, alone or together, in the mortality of patients with acute pancreatitis.

Main findings

Fourteen studies published between 1997 and 2009 were selected, seven from Europe, three from North America, two from Asia and two from Latin America. Eleven studies were written in English, one in Russian, one Turkish and one in Spanish. In these 14 studies were considered in 1,478 patients with acute pancreatitis, and 876 with necrosis confirmed. Considering the total patients, 600 (40%) had organ failure and 314 (21%) had infected necrosis. The mortality rate was 13% (191 patients), of which 30% (179 of 600) were patients with organ failure independent of infected necrosis, and 32% (102 of 314 patients) were patients with infected necrosis, regardless of the presence organ failure. However, mortality was 43% (92 of 213) in patients with organ failure and infected necrosis confirmed, versus 22% (87 of 387) in those with infected necrosis without organ failure. The presence of infected necrosis was associated with a significantly increased risk of death in patients with organ failure (RR = 1.94, p = 0.0007).

Infected necrosis when compared with sterile was associated with a significantly increased risk of death (RR = 1.84 p <0.0001). The mortality rate was 11% (10 of 93) in patients with infected necrosis but without organ failure.

Strengths

- * First meta-analysis of determinants of mortality in acute pancreatitis.
- * Includes papers from around the world regardless of language or location.
- * Strict criteria for evaluating articles.
- * Significant number of patients for conclusion.
- * Proposal for a new category of severity, “critical acute pancreatitis”, based on the data obtained (Table 2).

Limitations

- * Includes retrospective and prospective studies.
- * Difficulty in studies on severe acute pancreatitis due to the limited number of cases in each institution.
- * Definition of organ failure variable between articles.
- * Management variable between services.

STUDY 3

“The performance of organ dysfunction scores for the early prediction and management of severity in acute pancreatitis: an exploratory phase diagnostic study”⁶

Rationale

The Atlanta classification defines two categories of severity: mild and severe. Severe acute pancreatitis is defined by the presence of organ failure and / or local complications. However, two major limitations are present in the Atlanta classification: this classification does not consider the term transient organ failure, treating these patients, who have a better prognosis, as seriously ill, as well as promoting a classification after episode without objective of promoting information related to prognosis at the time of admission. However, it is necessary to differentiate patients at high risk from those at low risk of mortality and morbidity. This test should be sensitive and

Table 2 - Severity categories following determinants of severity².

Determinants of severity	Classification of severity in acute pancreatitis			
	Mild	Moderate	Severe	Critical
(Peri)pancreatic necrosis	No	Sterile	Infected	Infected
	AND	AND/OR	OR	AND
Organ failure	No	Transient	Persistent	Persistent

predictive. The predictive tests are used to identify patients for study.

The early identification of patients with severe acute pancreatitis is difficult, despite a large number of prognostic factors described. Organ failure scores used in ICU gain relevance across the importance of organ failure in AP (LODS / Marshall), but are poorly evaluated in acute pancreatitis. The organ dysfunction scores have several attractions: the score is calculated with a relevant and comprehensive set of biological data; indicate patients requiring intensive care, and indicate patients with higher risk of adverse events.

Question

What is the best score considering organ dysfunction to predict severity in acute pancreatitis?

Main findings

The authors analyzed 181 patients with acute pancreatitis, 29 (16%) classified as severe. The main cause was the biliary (53%), followed by alcohol (23%) and idiopathic (15%), post-ERCP (6%), and others (3%). Four patients died in the group of severe acute pancreatitis. The time between the onset of symptoms to admission was 18.7 ± 17 hours. Patients with APACHE II > 11 at admission classified as mild PA did not require ICU nor organ failure support, and were released within 10 days. The area under the curve (AUC) for the admission APACHE II score was 0.78. Using a APACHE II score of 7, the sensitivity was 74% and specificity of 67%, which was not adequate to predict the need for ICU. Considering this value, 26% of severe cases were lost. The positive predictive value of 32% means that 1 in 3 patients selected for ICU subsequently was classified as serious.

Considering the need for a test with high specificity ($> 90\%$), then the MODS, SOFA and APACHE II scores were similar at 24 hours. The balance between sensitivity and specificity were best achieved by LODS. The AUC was similar for the four tests. The LODS score with a cutoff of 1 achieved 90% of sensitivity and 69% of specificity, corresponding to a predictive value of 38%.

The LODS, MODS and SOFA seem to be better than the APACHE II and the C-reactive protein within 48 hours. The AUC was similar for the five tests. The SOFA score with a cutoff of 1 achieved 80% sensitivity and 84% specificity, corresponding to a predictive value of 50%. The sensitivity of a test plays an important role in the identification of seriously ill patients, and positive predictive value becomes a measure of the uniformity selection (proportion of selected patients who become severe). LODS with the score equal to or greater than 1, 90% of severe cases are included, but only 38% of all recruited were considered severe.

SOFA score of 3 or more will identify half of the severe cases, and the selection will cover almost three

quarters of severe cases. This can be considered an adequate performance.

This approach can also be considered for mild cases, where the specificity becomes important and the negative predictive value has an accuracy in selection. Selecting APACHE II scores less than or equal to 9, it was obtained 90% of homogeneity and efficient recruitment of 92%. Similarly, on admission, APACHE II is inadequate to predict severe cases. However, it detects mild cases. With a score of 9 (selecting scores less than or equal to 8) we obtain homogeneity of 91% and 79% of efficiency.

In 24 hours, APACHE II, LODS, MODS and SOFA were all moderately or highly correlated. A similar pattern occurs in 48 hours (APACHE II, PCR, LODS, MODS and SOFA). Consequently, with these tests, combinations probably will not help in the identification of patients mild and severe pancreatitis.

The performance tests were similar, so it is adequate to choose one of them. Due to the high correlation between them, it seems to have no advantages in combining them. SOFA score of 3 rated at 24 hours has an accuracy of 70% for identifying severe cases (which could also be identified with clinical parameters). APACHE II score less than 9 classified 91% of patients as mild acute pancreatitis.

Strengths

- * Significant number of patients in a single center.
- * The analysis considered the main scores commonly used in the ICU, and in this paper in acute pancreatitis.
- * Useful conclusions to select and exclude severity.

Limitations

- * Diagnosis of pancreatitis was not clearly defined (two out of three factors: clinical, elevated amylase / lipase 3 times the normal value, and TC demonstrating pancreas enlargement).
- * The calculation of the scores was not repeated in 48 hours (except APACHE II) that prevented the determination of transient organ failure.
- * The tests were not evaluated together.
- * The referral of patients to the ICU may have been influenced by the availability of beds.
- * The study discourages the combination of scores, but suggests that the APACHE II is good to exclude severe AP and the SOFA has good accuracy to select the seriously ill patient.

Conclusions EBT-TACS

The conclusions presented are based on recent discussions on the subject, demonstrated by these articles culminating in two recent reviews published on the topic.

1. The Atlanta classification needs to be updated, especially in defining the most appropriate group of seriously ill patients.

2. More categories should be described for patients with acute pancreatitis, and not only mild or severe. A larger number of categories can determine better the characteristics of each patient.

3. The assessment of organ dysfunction plays a key role in the stratification of patients, and handling initial management including intensive care. Numerous severity scores are available and can be used.

Recommendations of EBT-TACS on "Classification of acute pancreatitis":

1. Classification of acute pancreatitis in four categories: mild, moderate, severe and critical, which allows a better determination of the characteristics of patients, as proposed in table 2.

2. Evaluation of the presence of organ failure in all patients by using a severity score, preferably some that directly evaluates each organ failure, such as LODS, SOFA and MODS (Marshall). The SOFA seems to have greater accuracy, but the MODS has better applicability due to the ease of use. APACHE II has a role in the exclusion of severity.

R E S U M O

De acordo com a Classificação de Atlanta a pancreatite aguda pode ser dividida, baseado em sua severidade, em uma forma leve ou grave. Uma série de aspectos têm sido discutidos nos últimos anos, tais como, quantas categorias de gravidade devem ser consideradas; se o doente com falência orgânica é igual ao doente com necrose infectada; qual o papel da falência orgânica transitória; e como avaliar a falência orgânica. A reunião de revista "Telemedicina Baseada em Evidência - Cirurgia do Trauma e Emergência" (TBE-CiTE) realizou uma avaliação crítica de artigos relacionados a este tema, considerando três artigos recentes que delinearam duas grandes revisões publicadas nos últimos meses. Estes artigos sugerem a classificação de gravidade em três ou quatro categorias, ao invés de pancreatite aguda leve ou grave, além de discutir qual o melhor escore para avaliar a falência orgânica. As seguintes recomendações foram propostas: (1) A pancreatite aguda deve ser classificada em quatro categorias: leve, moderada, grave e crítica, o que permite uma melhor determinação das características dos doentes; (2) Avaliação de falência orgânica com um escore de gravidade, preferencialmente algum que avalie diretamente cada falência orgânica, tais como o SOFA e o MODS (Marshall). O SOFA parece ter maior acurácia, mas o MODS tem melhor aplicabilidade devido à facilidade de uso.

Descritores: Pancreatite. Pancreatite/classificação. Pancreatite necrosante aguda. Doença aguda. Índice de gravidade de doença.

REFERENCES

- Bradley EL 3rd. A clinically based classification system for acute pancreatitis. Summary of the International Symposium on Acute Pancreatitis, Atlanta, Ga, September 11 through 13, 1992. Arch Surg. 1993;128(5):586-90.
- Dellinger EP, Forsmark CE, Luyer P, Lévy P, Maraví-Poma E, Petrov MS, Shimosegawa T, Siriwardena AK, Uomo G, Whitcomb DC, Windsor JA; Pancreatitis Across Nations Clinical Research and Education Alliance (PANCREA). Determinant-based classification of acute pancreatitis severity: an international multidisciplinary consultation. Ann Surg. 2012;256(6):875-80.
- Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, Tsiotos GG, Vege SS; Acute Pancreatitis Classification Working Group. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. Gut. 2013;62(1):102-11.
- Vege SS, Gardner TB, Chari ST, Munukuti P, Pearson RK, Clain JE, Petersen BT, Baron TH, Farnell MB, Sarr MG. Low mortality and high morbidity in severe acute pancreatitis without organ failure: a case for revising the Atlanta classification to include "moderately severe acute pancreatitis". Am J Gastroenterol. 2009;104(3):710-5.
- Petrov MS, Shanbhag S, Chakraborty M, Phillips AR, Windsor JA. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. Gastroenterology. 2010;139(3):813-20.
- Mason JM, Babu BI, Bagul A, Siriwardena AK. The performance of organ dysfunction scores for the early prediction and management of severity in acute pancreatitis: an exploratory phase diagnostic study. Pancreas. 2010;39(7):1104-8.

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