



THE NECESSITY OF RE - EVALUATION OF SCORING SYSTEMS ACCORDING TO THE NEW CLASSIFICATION OF ACUTE PANCREATITIS *LITERATURE REVIEW*

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ABSTRACT

Background and Aims - This study examined and analyzed the clinical significance of scores systems used in the evaluation of acute pancreatitis according to the new classification. The scope of study covered the period from 1974 to 2013. Committed is gathering and analyzing information published in PUBMED, COHRANE and BIOMED systems for the period .

Conclusions - The Organ Failure Based Scoring Systems look as better choice according new classification. Although using different components with strong predictive capabilities, no scale is characterized by a high enough sensitivity and specificity to ensure complex evaluation of patients with acute pancreatitis

Key Words: acute pancreatitis, severity assessment, organ failure, mortality prediction, local complications

INTRODUCTION

The clinical assessment of acute pancreatitis (AP) is in the background of the proper approach to this condition, with primary importance of the classification. The 1992 Atlanta Symposium has classified AP into two large groups: mild (MAP) and severe (SAP). The differentiation is made on the basis of presence of local and systemic complications [1].

Ultimately, the accuracy of prognostic indicators is related to the measures that are used during the hospitalization to classify the severity of AP. A drawback of many studies thus far has been the use of a variety of measures of severity and in particular, reliance on the outdated initial Atlanta classification [2, 3, 4]. In this regard, the 2012 revision of the Atlanta classification stratifies severity into three levels: MAP - absence of organ failure and absence of local complications. Moderately severe acute (ModAP) pancreatitis -

presence of transient organ failure and/or local complications (transient organ failure is defined as organ failure that persists for 48, or less hours). SAP - presence of persistent organ failure (for more than 48 hours). [3, 4, 5].

For several years, considerable effort has been targeted to the early evaluation of patients with AP, with the goal of identifying the most - appropriate scoring system [6]. The useful scoring system should correspond with follow condition: easy calculation, good predictive values about severity and outcome, permit dynamic calculation, absent of time frame for calculation, appropriate assessment of organ failure (OF) (differentiation of transient and persistent OF). Despite the numerous scientific reports, there is still not a specific clinical and laboratory marker, sensitive enough to be used independently for assessment of AP. In our review we analyze the scoring systems and differentiate their benefits and weaknesses in everyday clinical practice.

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differentiation between mild, moderate and severe AP [3].

Ranson and Imrie

The attempts to assess the severity and to predict outcome in such patients dates back to 1974 when Ranson criteria were introduced [7]. It had enduring popularity but neither originally being subjected to any rigorous statistical validation, nor proved superior to any other quantification scheme. In 1980 a similar system was proposed by Imrie et al. [8]. Despite its predictive capabilities proven by clinical studies in recent years Imrie doesn't allow dynamic monitoring of the clinical condition and therapeutic results [9]. A meta-analysis published in 1999 has evidence a similar evaluation utility of both scoring systems and at the same time has shown that none of them could provide clinicians with a complex assessment of AP. [10] The role of systemic complications in mortality and morbidity decrease the usefulness of pathology-specific scoring systems such as Ranson and Imrie scores. According revision of Atlanta's criteria from 2012 we can conclude these systems as Ranson and Imrie aren't allowed

APACHE scoring systems

The APACHE score was introduced in 1985 by Knaus [11]. It was created to evaluate patients in intensive care units and then was used to evaluate patients with AP. It is more precise than aforementioned two systems and could be calculated at any time during the disease course. Numerous studies reported sensitivity from 60 to 95 % and specificity from 70 to 90 %, PPV about 60 %, NPV about 80 % [12, 13, 14]. **(Table 1)** The daily determination of APACHE II is at the background of the proper monitoring of critically ill patients. Calculated by the 48th hour, the sensitivity to detect organ failure (OF) ($P = 0.007$), necrosis ($P = 0.001$) and mortality attains 93 %. Markedly higher scores by the 48th hour are observed in patients with SAP who developed necrosis, as well as in those with fatal outcome.

Table 1. Characteristics of prognostic systems in recent years

Prognostic Score	Author	Timeframe (\geq 48 hours)*	Sensitivity %	Specifity %	PPV %	NPV %	Accuracy%	Severity (AUC/p)	Mortality (AUC/p)
RANSON	Su Mi Woo et al 2011		91.67	96.15	95.65	92.59	94	0.879	$P = 0.001$
	Schutte K et al 2008	+	91.2	74.4	57.4	95.7	88	0.94	
IMRIE	Su Mi Woo et al 2011		66.67	92.31	88.89	75	80	0.805	$P = 0.001$
	Barreto et al 2007 Schutte K et al 2008	+	98 73.5	56 71.1	94 49%	80 87.7	84 78		
CTSI	Su Mi Woo et al 2011		62.5	65.38	62.5	65.38	64	0.84	$P = 0.017$
	Schutte K et al 2008 Bollen et al 2012	+	26.7 87	100.0 83	100.0 53	68.6 97	80 84	0.715 0.88	
BISAP	Su Mi Woo et al 2011 Bollen et al 2012	-	79.17 48	88.46 82	86.36 38	82.14 88	84 72	0.82 0.68	$P < 0.00$
SOFA	Mason JM, et al 2010	-	91	79	48	82	84	0.80	$P < 0.00$
MODS	Mason JM, et al 2010	-	84	78	49	85	82	0.80	$P < 0.00$
LODS	Mason JM, et al 2010	-	90	69	38	80	86	0.82	$P < 0.00$
APACHE II	Su Mi Woo et al 2011		75	76.92	75	76.92	76	0.904	$P < 0.001$
	Schutte K et al 2008 Bollen et al 2012	-	83.3 83	68.9 52	51.7 28	91.2 93	91 88	0.861 0.892	

This clinical assessment score system is associated with different threshold values assessing the development of a severe disease

and fatal outcome. The Atlanta Symposium has proposed cases with scores > 8 to be considered as severe. The Santorini Consensus Conference

in 1999 has accepted the APACHE system as the most accurate to assess AP patients, with threshold APACHE II and APACHE O scores > 6. The using of fixed cut-off value for predicting clinically severe disease and mortality is associated with increase the sensitivity and negative predictive value and concomitant decrease in specificity and positive predictive value compared with the optimal cut-off [15, 16]. Rithin Suvarna et al. 2011 [13] have reported on admission APACHE II score of more than 9 predicted more number of severe attacks (75%) but less number of mild attacks (60%). An APACHE II score of more than 10 had the best sensitivity, specificity and predictive value (P value <0.001) [17].

APACHE O is proposed by Johnson et al. [18], and has the evaluation power of the other systems used for AP scoring. Papachristou et al. 2006 [19] published a prospective study assessing the predictive value of APACHE O for SAP in patients with a BMI > 30, which showed similar results between APACHE O and APACHE II (AUC 0.895 and 0.893, respectively). Both APACHE II and APACHE O provide opportunity for daily monitoring of the time course of parameters, but the latter is inferior with regard to its evaluation and predictive value to APACHE II. Therefore, APACHE II and O have similar accuracy and efficacy in assessing the severity, systemic complications and need of intensive care in AP. The disadvantages of the systems is the difficult calculation, another flaw is the insufficient information provided with respect to local complications. So we conclude that APACHE II is the most usefull system of APACHE family and their dynamic calculation provides better information of disease course than single score value.

CT scoring systems

CT is the gold standard to distinguish and diagnosis local complications. Some CT criteria were proposed and included in Balthazar grading system [20] and CTSI [21]. CTSI score under 3 is related with lower morbidity and mortality less than 2% [22]. CTSI values > 5 detected on the 48th hour are associated with SAP and high incidence of subsequent necrosectomies [12]. CTSI score of 7-10 was able to predict a 92% morbidity and 17% mortality rate [22]. In the study of Thomas L. Bollen et al. (2012) [15] CTSI and Balthazar grade demonstrated the highest accuracy for predicting clinically SAP

(AUC 0.88; AUC 0.79 respectively). However, no statistically significant difference were observed between the two scoring systems [15]. Among the CT indices, Balthazar grade had the highest AUC for mortality (AUC 0.81) [15].

CT based scores possessed good sensitivity and specificity for local complications [22], but remains with low specificity as a parameters for starting and monitoring of intensive therapy [23]. Despite the results of Tsuji et al. 2012 [24], the calculation of CT based systems before 48 hour is less informative. In patients with peripancreatic collection without necrosis and in these with acute necrotic collection without/or transient OF the behavior is quite same. In these cases despite of characteristics of local complication all of patients will be evaluated as ModAP. In 2% of cases OF is present despite absence of serious local damage, so we'll evaluate AP as severe although the CTSI score will be low. So "Do we need CT based score in evaluation of AP?" is the main question although positives results in literature.

BISAP

The simplicity of a scoring system is one of the most important factors when deciding what system to utilize in a clinical setting. BISAP is designed to predict the mortality risk during the first 24 hours of the diseases [25]. In a cohort study, BISAP was proved to have a high specificity but also a high negative predictive value at scores > 3 [25]. Incremental increases in the BISAP score (3 or more) have been shown to correlate with an increased risk of organ failure (P < 0.0001), pancreatic necrosis and mortality [25, 26, 27]. In compare with other systems BISAP is characterized with similar capabilities in prediction severe forms and fatal outcome (BISAP - AUC 0.82; APACHE II - AUC 0.83; Ranson - AUC 0.94; CTSI - AUC 0.84) [26]. BISAP could assess the presence or lack of organ failure but could not define it as transient or persisting after the 24th hour. So this scoring system may suggest the need for intensive care or predicts severe course, but couldn't detect moderate pancreatitis and couldn't be used for dynamic tracking and monitoring of patient's started therapy.

Organ Failure (OF) Based Scoring Systems

According to modern concepts of AP the great determinant of severity is OF. There are still number of controversies about correlation of local damage and presence of systemic

complications [28]. Hence, only 50% of patients with necrotizing AP develop OF and are with SAP, whereas those with oedematous AP manifested OF in 15% of cases [29]. A study from the United Kingdom [30] found a correlation between duration and resolution of OF and severity and disease outcome. Based on the 2012 global survey of pancreatologists [31] the consensus is that three organ systems (respiratory, cardiovascular and renal) fail most frequently in patients with AP. First meta-analysis of determinants of mortality in AP which includes papers from around the world with significant number of patients (1,478 patients) for conclusion is from Petrov et al. 2010 [4]. The authors have concluded that infect necrosis with persistent OF are two main determinant of fatal outcome so the correct evaluation of OF and right decision making for restoration of impaired organ function is the cornerstone of evaluation and determination of behavior in AP.

Several organ dysfunction scores have been developed for use in critically ill patients [32] as MODS, LODS, SOFA and Marshall [33, 34, 35]. Marshall et al. in 1995 developed MODS [33]. High MODS scores are related to severe multiorgan dysfunction and failure and therefore, with severe course of AP.

In 1996 Le Gall et al [35] created LODS to assess the probability of death during the hospital stay, but not to evaluate the severity of every system dysfunction, which makes it hardly applicable for monitoring of intensive care patients.

Marshall scoring systems for organ failure are the most sensitive for evaluation of AP patients. A Marshall score > 3 is associated with severe course, systemic complications and significant correlation with fatal outcome ($P = 0, 007$) [36]. Modified Marshall score is recommended by Banks et al. in the revision of Atlanta classification in 2012 as the most accurate in severity evaluation [3].

The European Society of Intensive Care Medicine since advocated a score that includes six major organ systems to describe as quantitatively and objectively as possible the degree of organ dysfunction over time in critically ill patients - Sepsis-related Organ Failure Assessment (SOFA) [34, 37].

Mason et al. [16] have found that MODS (AUC 0.80) performed similarly to SOFA (AUC 0.80), APACHE II (AUC 0.82), and LOD (AUC 0.82) in severity assessment, when are calculated at 24 hrs of admission. The AUC values for predicting mortality among patients with SAP were found to be similar amongst SOFA, MODS and LOD scores on days one (0.750, 0.775, 0.776) and three (0.738, 0.726, 0.736) of ICU stay [38]. Juneja D et al. [39] (2010) have concluded that all scoring systems had comparable accuracy in predicting 30-day mortality, but SOFA had greater efficacy with its area under curve (0.93 (95% CI, 0.85-0.99)). These systems are less informative in detection of local complication (SOFA $p=0.687$; Marshall $p=0.775$; APACHE II $p=0.789$) [36].

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. Because of better association with severity and outcome, SOFA and Modified Marshall score are now recommended by the Pancreas Club in the revised Atlanta Classification scheme to assess the severity and the need of intensive therapy in AP patients [40]. (**Table 1**)

Peter A Banks et al. (2013) (3) and Dellinger et al. (2013) [5] have been introduced, such as the idea that the evolving pancreatitis process does not allow complete severity assessment during the first hours of onset (**Table 2**) The detection of local complication is not sufficient criteria to classify AP. Thus the assessment and monitoring of dynamic OF is the main factor for accurate severity evaluation and outcome prediction. The question remains: "Which system has to use in daily practice?" The role of APACHE II system is undoubtedly confirmed with high specificity and sensitivity over the years but the difficult calculation and review of the determinants of severity leave its application in the background. SOFA and Modified Marshall score have main role in severity assessment. Modified Marshall System is easier for calculation, but SOFA seem to be more informative [4, 6]. The two main determinants in mortality prediction are persistent OF and the presence of infected necrosis [4]. SOFA and APACHE II are the most useful systems in predicting outcome with similar predictive values [40, 41]. Combining markers from scoring systems providing

detection / differentiation of OF and criteria for differentiation of local complications will

determine a system with high efficiency in the evaluation of severity and outcome prediction.

Table 2. Positives and negatives of the most used scoring systems

Scoring system	easy calculation	time frame for calculation	dynamic calculation	appropriate assessment of organ failure		appropriate assessment of local complication	appropriate prediction of severity	appropriate prediction of outcome	appropriate assessment of severity
				Detection of OF	Differentiation of persistent and transient OF				
RANSON	+	+	-	+	-	-	+	+	-
IMRIE	+	+	-	+	-	-	+	-	-
APACHE II	-	-	+	+	+	-	+	+	+
CTSI	+	+	-	-	-	+	+/-	+/-	-
BISAP	+	-	-	+	-	-	+	+	-
SOFA	-	-	+	+	+	-	+	+	+
MODIFIED MARSHALL SCORE	+	-	+	+	+	-	+	+	+

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