COMPARISON OF BISAP, NLR AND HAPS IN PREDICTING SEVERITY OF ACUTE PANCREATITIS, ACCORDING TO THE 2012 REVISION OF ATLANTA CLASSIFICATION*

COMPARAÇÃO DO BISAP, NLR E HAPS NA PREVISÃO DA GRAVIDADE NA PANCREATITE AGUDA, SEGUNDO A REVISÃO DE 2012 DA CLASSIFICAÇÃO DE ATLANTA

iD FILIPE BORGES[1, 2], iD JOANA MIRANDA[2], iD SOFIA SILVA[2], iD NUNO CARVALHO[1, 2],

iD PAULO MATOS COSTA[1, 2]

[1] Serviço de Cirurgia, Hospital Garcia de Orta; Almada – Portugal
[2] Faculdade de Medicina da Universidade de Lisboa – Portugal

ABSTRACT

Backgrond. Early risk stratification is crucial in Acute Pancreatitis (AP). The *BedSide Index for Severity in Acute Pancreatitis* (BISAP) allows risk stratification at the time of hospital admission through a five-variable analysis. Several inflammatory markers have shown prognostic value in AP. Amongst them the Neutrophil to Lymphocyte Ratio has the best predictive accuracy. The *Harmless Acute Pancreatitis Score* (HAPS) is used to predict mild AP. Our objective was to compare BISAP, NLR and HAPS as predictors of severity in acute pancreatitis. **Material and Methods.** A six-year (January 2014 – December 2019) retrospective analysis of a prospective database of all the patients admitted with the diagnosis of AP. Included variables: age, sex, BISAP score, NLR, HAPS score, length of stay, severity and mortality. Severity was defined according to 2012 revision of Atlanta classification. Accuracy of prediction was measured by the area under the receiver operating characteristic curve (AUC). Positive Predictive Value (PPV), Negative Predictive Value (NPV), Sensitivity and Specificity were also calculated. **Results.** Total of 284 cases; 121 male and 163 female; median age was 71 years [21 – 95]. 216 patients presented mild AP, 34 moderate and 34 severe AP; overall mortality was 4.2%. The BISAP AUC for prediction of severity was 0,86 [0,796 – 0,936]. Sensivity was 44.1% and specificity was 93.2%. PPV was 68.2% and NPV was 92.8%. The NLR AUC was 0,7 [0,607 – 0,798]. Sensivity was 78.8% and specificity was 51.8%. PPV was 78.8% and NPV was 94.8%. Finally, HAPS AUC for prediction of mild AP was 0,706 [0,623 – 0,790]. Sensitivity was 60.6% and specificity was 72.1%. PPV was 87.3% and NPV was 36.6%. **Conclusion.** BISAP, NLR and HAPS are valuable tools for an early risk stratification and prognosis evaluation in AP. The best calculated accuracy for the prediction of severity was for BISAP.

Keywords: Acute Pancreatitis, Risk Score, Severity, BISAP, HAPS, NLR.

RESUMO

Introdução. A estratificação precoce do risco é essencial na Pancreatite Aguda (PA). O *BedSide Index for Severity in Acute Pancreatitis* (BISAP) permite estratificar o risco na admissão hospitalar através da análise de cinco variáveis. Vários marcadores inflamatórios demonstraram valor prognóstico na PA. Entre eles, a razão Neutrófilos / Leucócitos (NLR) possui a melhor

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capacidade preditiva. O *Harmless Acute Pancreatitis Score* (HAPS) é utilizado para a previsão de formas ligeiras de PA. o objectivo deste trabalho é comparar o BISAP, NLR e o HAPS na previsão da gravidade na PA. **Material e Métodos.** Análise retrospectiva de seis anos (Janeiro 2014 – Dezembro 2019) de base de dados prospectiva de todos os doentes consecutivos internados com o diagnóstico de PA. Variáveis incluídas: idade, sexo, score BISAP, NLR, score HAPS, duração de internamento, gravidade e mortalidade. A gravidade foi avaliada de acordo com critérios de Atlanta revistos em 2012. A capacidade preditiva foi avaliada pela área sob a curva (AUC) ROC, tendo sido determinados também o valor preditivo positivo (VPP) e o valor preditivo negativo (VPN), sensibilidade e especificidade. **Resultados.** Amostra de 284 doentes consecutivos; 121 homens e 163 mulheres; mediana de idade de 71 anos [21 – 95]. 216 doentes apresentaram PA Ligeira, 34 Moderada e 34 Grave; mortalidade global de 4.2%. O BISAP apresentou para a predição de gravidade uma AUC de 0,86 [0,796 – 0,936], Sensibilidade de 44.1% e Especificidade de 93.2%. O VPP foi de 68.2% e o VPN de 92.8%. O NLR apresentou uma AUC de 0,7 [0,607 – 0,798], Sensibilidade de 78.8% e Especificidade de 51.8%. O VPP foi de 78.8% e o VPN de 94.8%. Por fim, o HAPS apresentou para a predição de forma ligeira de PA uma AUC de 0,706 [0,623 – 0,790], Sensibilidade de 60.6% e Especificidade de 72.1%. O VPP foi de 87.3% e o VPN de 36.6%. **Discussão / Conclusão.** O BISAP, o NLR e o HAPS apresentaram-se como ferramentas úteis na estratificação e avaliação precoces do risco e prognóstico na PA, tendo o BISAP apresentado a maior capacidade preditiva entre três.

Palavras-chave: Pancreatite aguda, Pontuação de risco, Gravidade, BISAP, HAPS, NLR.

BACKGROUND

Acute Pancreatitis (AP) is the most common gastrointestinal cause of hospitalization and its prevalence has been rising[1, 2]. The prognosis of AP depends on its severity, which was classified as mild, moderate or severe by the latest revised Atlanta classification[3]. Most patients present with mild or moderate AP and only 15–20% of patients have severe forms of the disease. Although the overall mortality is low (2 – 5 %), it can reach 20 – 30% among those with severe course[4].

Early risk stratification is crucial in AP. Several scoring systems have been proposed and accepted to assess and stratify the severity of AP. The *BedSide Index for Severity in Acute Pancreatitis* (BISAP) allows risk stratification at the time of hospital admission through a five-variable analysis: blood urea nitrogen level > 25 mg/dl, impaired mental status, development of systemic inflammatory response syndrome (SIRS), age > 60 years, and presence of pleural effusion[5].

Severity in AP is related to the development of a systemic inflammatory response. Therefore, several inflammatory markers have been tested and shown prognostic value. Amongst them the Neutrophil to Lymphocyte Ratio (NLR) has demonstrated the best predictive accuracy[6, 7, 8].

The *Harmless Acute Pancreatitis Score* (HAPS) is used to predict mild AP. The algorithm includes three parameters: signs of peritonitis, serum creatinine and haematocrit. The disease course is very likely to be mild if all these three parameters are normal at the time of admission[9, 10].

The objective of this study is to assess and compare BISAP, NLR and HAPS as predictors of severity in AP at the time of admission.

MATERIAL AND METHODS

A retrospective analysis of a prospective database was performed including all consecutive patients admitted in with de diagnosis of AP between January 2014 and December 2019. Variables assessed include the following: age, sex, BISAP score, NLR, HAPS score, length of stay, severity and mortality.

The diagnosis of AP was made according to 2012 of Atlanta classification. This means that it was based on the presence of at least two of the following three features: (1) acute abdominal pain, (2) at least 3-fold elevated levels of serum amylase or lipase,

and (3) characteristic findings on radiological study.

Severity was defined according to 2012 revision of Atlanta classification. Mild cases have no organ failure, moderate cases have transient organ failure (< 48h) and severe cases present persistent organ failure (>48h). A modified Marshal score of 2 or higher defines organ failure.

A cutoff of ≥ 3 was used for BISAP score for the prediction of severe cases. When all three variables in HAPS were present, we considered it as positive.

Statistical analysis was done by the *IBM® SPSS® statistics software* (v24). Continuous variables were presented as median [min – max]. Categorical variables were presented as absolute number and percentages. Accuracy of prediction was measured by the area under the receiver operating characteristic curve (AUC) with a Confidence Interval (CI) of 95%. Sensitivity, Specificity, Positive Predictive Value (PPV) and Negative Predictive Value (NPV) were also calculated.

RESULTS

A total of 284 patients were admitted with the diagnosis of AP in the mentioned period. Demographic characteristics and outcomes are summarized in Table 1.

The median age of the 284 patients was 71 [21 – 95]; 163 (57.2%) were female and 121 (42.8%) were male. 34 patients (12%) presented persistent organ failure, therefore having severe disease. The median length of stay was 6 days [1 – 73]. 12 patients died resulting in an overall mortality of 4.2%.

Comparison between severity scores

For the prediction of severe AP, a BISAP score ≥ 3 showed an AUC of 0,86 [0,796 – 0,936] (Figure 1). The sensivity was calculated as 44.1% and specificity as 93.2%. The PPV and NPV were 68.2% and 92.8%, respectively.

TABLE 1 – **Demographic characteristics and outcomes.**

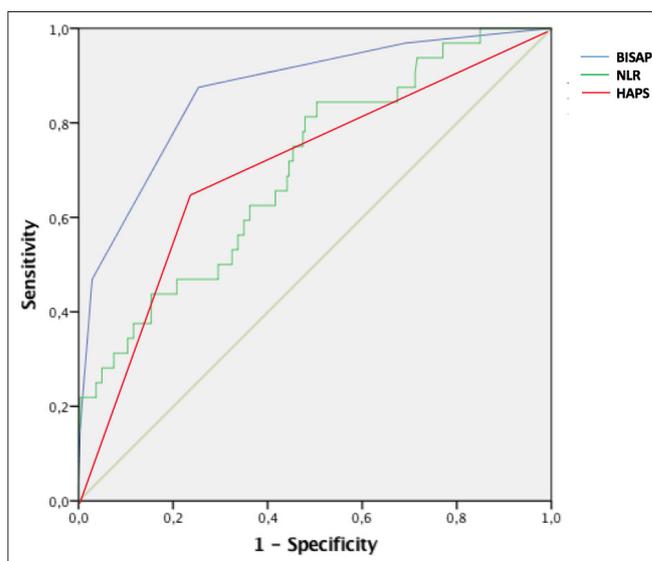| Age (years)	71 [21 – 95]
Gender [N (%)]	
Female	163 (57,2)
Male	121 (42,8)
Severity [N (%)]	
Mild	216 (76)
Moderate	34 (12)
Severe	34 (12)
Length of Stay (days)	6 [1 – 73]
Mortality [N (%)]	12 (4,2)
BISAP [N (%)]	
0	79 (27,8)
1	113 (39,8)
2	69 (24,2)
3	17 (6,0)
4	5 (1,8)
5	1 (0,4)
NLR	9,56 [0,76 – 80]
HAPS [N (%)]	
Positive	150 (53)
Negative	134 (47)

FIGURE 1 – **ROC curves of the accuracy of BISAP (blue line), NLR (green line) and HAPS (red line) for the prediction of severity in AP.**

The NLR value with best sensitivity and specificity for the prediction of severity was calculated as 8,86, thus becoming the cut-off value in our sample. The accuracy of this score for the prediction of severe AP has showed an AUC of 0,70 [0,607 – 0,798]. Sensibility was 78.8% and specificity was 51.8%. Also, PPV and NPV were calculated as 78.8% and 94.8%, respectively.

For the prediction of mild AP, HAPS demonstrated an AUC of 0,706 [0,623 – 0,790] with a sensitivity of 60.6% and a specificity of 72.1%. This resulted in a PPV of 87.3% and a NPV of 36.6%.

The comparison of different accuracies for the prediction of AP severity is summarized in Table 2.

Table 2 – Comparison of the accuracy of BISAP, NLR and HAPS for the prediction of severity in AP.

	Sensitivity	Specificity	PPV	NPV	AUC
BISAP	44.1%	93.2%	68.2%	92.8%	0,86
NLR	78.8%	51.8%	78.8%	94.8%	0,7
HAPS	60.6%	72.1%	87.3%	36.6%	0,706

DISCUSSION

Severity is the main prognostic factor in AP. Support measures are the mainstay of the approach in AP since there's no specific treatment available. Recognition at admission of the patients most likely to develop severe forms would allow clinicians to consider more aggressive monitoring and treatment. Some studies have shown that early (< 24h) institution of therapeutical measures such as fluid resuscitation have a positive impact on outcomes[11,12]. The importance of early risk stratification has also been recognized in recent international guidelines regarding AP[13].

Several scoring systems have been proposed and accepted to assess and stratify the severity of AP, such as Acute Physiology and Chronic Health Evaluation II (APACHE) or Ranson scores. However, these are very cumbersome, evolving multiple complex variables and patient's history data that may not be available. Also, Ranson's score only allows risk stratification 48h after the admission, missing the potential benefits of timely treatment institution[14,15]. All the scores evaluated in this study are easy to calculate, only requiring readily available variables. They also can be obtained at admission maximizing therapeutic benefits.

For the prediction of severe AP, a BISAP score of ≥ 3 demonstrated to be a very useful tool with an AUC of 0,86. This cut-off has been shown in the literature as the most useful in predicting severity, thus being used in our sample as well[2]. Several studies including a recent systematic review and meta-analysis[1] showed similar accuracy for the prediction of severe forms of the disease (AUC 0,87).

Severity in AP is associated with the development of systemic inflammatory response syndrome and consequent multiple organ failure. Several inflammatory markers may reflect the degree of such inflammatory response and have prognostic value. Amongst them, NLR has shown to have the best predictive accuracy for severe AP[6,7,8]. In our analysis, NLR demonstrated comparable predictive accuracy, with an AUC of 0,7.

HAPS was also a valuable tool for the prediction of mild forms of AP, with a calculated AUC of 0,706. Interestingly, it´s high PPV of 87.3% shows a good predictive capacity for those patients likely to actually develop non severe AP. This may be useful for choosing suitable individuals for home hospitalization or ambulatory treatment programmes. In a pandemic era, facing significant restrictions and reduced availability in hospitals, this stratification returns special importance.

Although all scores analysed in this study were found to be useful in the early risk stratification, the highest calculated AUC was for BISAP score reflecting the best predictive accuracy in our sample.

The present study has some limitations. The retrospective setting has inherent constraints in data recording and availability. A larger number of

patients and a longer analysis period would enhance the statistic and clinical impact of the results.

CONCLUSION

BISAP, NLR and HAPS are valuable tools for an early risk stratification and prognosis evaluation in AP. The best calculated accuracy for the prediction of severity was for BISAP, making it the most adequate score to use at admission. HAPS may also be useful for identifying patients most likely to experience mild forms of AP and suitable for home hospitalization or ambulatory treatment.

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Correspondência:

FILIPE BORGES

e-mail: fcastroeborges@gmail.com

Filipe Borges, Joana Miranda, Sofia Silva, Nuno Carvalho, Paulo Matos Costa