OXID COMPARATIVE ANALYSIS OF THE SIGNIFICANCE OF BISAP AND MEWS SCORE FOR AN EARLY ASSESSMENT OF ILLNESS SEVERITY AND TREATMENT OUTCOME OF ACUTE PANCREATITIS

Olivera Marinkovic[1], Slađana Trpkovic[2], Ana Sekulic[1], Aleksandra N. Ilic[3], Nataša Zdravkovc[4], Aleksandar Pavlovic[2], Barbara Loboda[1]
[1]*Department of Anesthesia and Intensive Care, CHC "Bezanijska Kosa", Belgrade, Serbia*
[2] *University of Pristina, Medical Faculty, Kosovska Mitrovica, Serbia*
[3]*University of Pristina, Medical Faculty, Department of Preventive Medicine, Kosovska Mitrovica, Serbia*
[4]*University of Kragujevac, Faculty of Medical Sciences, Department of Internal Medicine, Kragujevac, Serbia*

UPOREDNA ANALIZA ZNAČAJA BISAP I MEWS SKORA ZA RANU PROCENU TEŽINE BOLESTI I ISHODA LEČENJA AKUTNOG PANKREATITISA

Olivera Marinković[1], Slađana Trpković[2], Ana Sekulić[1], Aleksandra N. Ilić[3], Nataša Zdravković[4], Aleksandar Pavlović[2], Barbara Loboda[1]
[1] *Odeljenje anestezije sa intenzivnom negom, KBC „Bežanijska Kosa", Beograd, Srbija*
[2] *Univerzitet u Prištini, Medicinski fakultet, Kosovska Mitrovica, Srbija*
[3] *Univerzitet u Prištini, Medicinski fakultet, Odeljenje preventivne medicine, Kosovska Mitrovica, Srbija*
[4]*Univerzitet u Kragujevcu, Fakultet medicinskih nauka, Katedra za internu medicinu, Kragujevac, Srbija*

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ABSTRACT

The aim of this study was to determine the significance of the use of the BISAP score, which is specific for patients with AP, in relation to the application of the MEWS score that is important for assessing the condition of critically ill patients in intensive care units, but is not specific for patients with AP. The research was conducted as a cohort prospective study and included patients of both sexes, older than 18 and diagnosed with AP. BISAP and MEWS score were monitored at least at four time points: on admission to the hospital (zero), 48 hours, 72 hours and 7 days after admission to the hospital.

High levels of discrimination between patients with fatal outcome and cured patients are determined in both cases, with discrimination at MEWS being somewhat higher than BISAP score. The $BISAP_0$ had the best discrimination for BISAP score, AUROC (0.807) and also $MEWS_0$ for MEWS score, AUROC (0.899). In our research, the highest sensitivity was shown by $BISAP_{7d}$ (92.1%) and $MEWS_{48}$ (88.1%), and a high specificity of 87.5% had BISAP score, 48h, 72h and MEWS score at all four points of measurement.

BISAP score has a better prognostic value in relation to the form of pancreatitis, the development of complications and the outcome. However, the calculation of the MEWS score is based on monitoring the basic vital parameters so that its application is much simpler and does not require additional costs.

***Keywords**: pancreatitis acute, BISAP, MEWS.*

SAŽETAK

Cilj ovog rada bio je da se utvrdi značaj primene BISAP skora koji je specifičan za bolesnike sa AP u odnosu na primenu MEWS skora koji je važan za procenu stanja kritično obolelih bolesnika u JIM, ali nije specifičan za bolesnike sa AP.

Istraživanje je sprovedeno kao kohortna prospektivna studija u koju su uključeni bolesnici oba pola, stariji od 18 godina kod kojih je postavljena dijagnoza AP. BISAP MEWS skor su praćeni u najmanje 4 vremenske tačke: na prijemu-nultog dana, 48 i 72 sata i 7 dana nakon prijema u bolnicu.

Visoki stepen diskriminacije između pacijenata sa smrtnim ishodom i pacijenata koji su preživeli je utvrđen kod oba skora, pri čemu je diskriminacija kod MEWS-a nešto viših vrednosti u odnosu na BISAP. Za BISAP skor najbolju diskriminaciju daje $BISAP_0$, AUROC (0.807), a kod MEWS skora, $MEWS_0$, AUROC (0.899). U našem istraživanju, najveću senzitivnost su pokazali $BISAP_{7d}$ (92.1%) i $MEWS_{48}$ (88.1%), a visoku specifičnost 87,5% imali su BISAP skor, nultog dana, 48h, 72h i MEWS skor u sve četiri tačke merenja.

BISAP skor ima bolju prognostičku vrednost u odnosu na formu pankreatitisa, razvoj komplikacija i konačni ishod. Međutim, izračunavanje MEWS skora se zasniva na praćenju osnovnih vitalnih parametara tako da je njegova primena znatno jednostavnija i ne zahteva nikakve dodatne troškove.

***Ključne reči:** akutni pankreatitis, BISAP skor, MEWS skor.*

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INTRODUCTION

Acute pancreatitis (AP) is an inflammatory condition of the pancreas that can cause local injury, systemic inflammatory response syndrome, and organ failure (1).

On acute inflammatory process in the pancreas, the organism responds with an adaptive response which is marked as Systemic Inflammatory Response Syndrome – SIRS (2). In the initial phase, SIRS is characterized by increased immune function, hyperdynamic and hypermetabolic processes. The aim of these processes is to eliminate the causative agent, localize the process and provide sufficient amount of oxygen and nutritional substances necessary for tissue reparation and immune cell function. In parallel with the release of inflammatory mediators from different type of cells (monocytes, endothelial cells), they release anti-inflammatory mediators and lead to compensatory anti-inflammatory syndrome - CARS. At the same time, pro-coagulation and anti-coagulation systems are activated. Ideally, CARS and SIRS function to provide defense against an invasion of the pathogen. However, if the inflammatory response prevails, progressive endothelial damage, microcirculation vasodilatation and micro thrombi will occur. These changes occur in selected areas of all organs and lead to a progressive damage of their function and to multiple organ disfunction syndrome – MODS, which often has lethal outcome. About 30-50 % of patients who develop severe form of AP in the first 72 hours, despite the use of all available treatment options, die due to MODS development (2).The presence of SIRS during the early phase, in the first 24h, has high sensitivity for prediction of organ failure, but it does not have adequate specificity for severe forms of the disease (3). The sooner the AP is diagnosed and intensive treatment begins, there is greater chance to achieve reversal of organic insufficiency which significantly reduces the morbidity and mortality in these patients (4).

AP can be diagnosed if at least two of the following three conditions are met: abdominal pain, triple increase in pancreatic amylase levels in relation to the upper reference limit, positive CT findings, rarely magnetic resonance findings or transabdominal ultrasonography findings (5-9). The first symptom of the disease is most commonly acute development of persistent, intense epigastric pain propagating towards the back and is often accompanied by nausea and vomiting. However, this is not sufficient to set the diagnosis because these symptoms are non-specific and may indicate to a series of other illnesses. Setting the diagnosis significantly contributes to the increase in pancreatic enzymes (amylase/lipase) to values that are at least three times higher than the upper limit of the reference values. The increase in these enzymes usually occurs in the first 24 hours after the onset of pain (2). If severe abdominal pain (with or without irradiation in the back) indicates AP, but serum amylase/lipase values are not increased at least three times in relation to the reference values, it is necessary to do computerized tomography in order to confirm the diagnosis (4, 9).

In patients already diagnosed with AP, treatment, the prediction of complications and treatment outcome depend on an early assessment of the illness severity. According to the currently valid recommendations (1), the AP can be: a mild AP in which the fatal outcome is extremely rare, moderately severe AP that is characterized with transient insufficiency of an organ system and is associated with relatively low mortality and severe AP that is characterized by persistent organ failure and high mortality which is 36-50% according to various authors (10, 11, 12).

Laboratory analysis, diagnostic imaging and scoring systems can be used to predict the severity and outcome of the disease. Most score systems primarily provide early identification of organ failure considering that this is one of the most important predictors of the treatment outcome in patients with severe forms of AP (13).

Scoring systems specific to AP are: Ranson score, Pancreas score (Glasgow - Imrie Criteria for Severity of Acute Pancreatitis), BISAP (Bedside index of severity in acute pancreatitis), HAPS (Harmless Acute Pancreatitis Score), modified CTSI (Modified Computed Tomography Severity Index), Hong Kong criteria. There are some of the score systems which are used in intensive care units (ICU) for assessment of critically ill patients, but are not specific for AP: APACHE (Acute Physiology and Chronic Health Evaluation), SOFA (Sequential Organ Failure Assessment), MEWS (Modified Early Warning Score), etc. In our research, we decided to compare the significance of calculating BISAP and MEWS score.

BISAP score was defined in 2008 by Wu and co. for the assessment of illness severity and the prognosis of the risk of intra-hospital mortality in patients with AP. Patient with a score of 0-2 have <2% chance of lethal outcome. Patients with a score of 3-4 have >15% chance of death, and a score of 5 predicts mortality of 22%.

MEWS score is derived from the EWS score which was first applied in the UK (14). EWS score initially included 5 parameters, but later the diuresis measurement was added so that the EWS score was changed to the modified EWS or MEWS. Monitoring of this score is especially important for patients in the early postoperative period, as with all critically ill patients. The maximum score is 14. The value of the score ≥4 indicates that patient condition is getting worse. The value of the score >5 indicates that the chance of fatal outcome is about 30%.

The aim of this study is to determine the significance of the use of the BISAP score, which is specific for patients with AP, in relation to the application of the MEWS score that is important for assessing the condition of critically ill patients in intensive care units, but is not specific for patients with AP.

Based on this research, it will be possible to evaluate which score system is simpler and more objective for

assessing the condition of patients with AP, and which score system at different stages of treatment of patients with AP has the highest calibration and discrimination power, best shows the relationship between the predicted and the realized mortality rate.

MATERIAL AND METHODS

The research was conducted as a cohort prospective study in the period from 01/01/2016 until 31/12/2017 at the Clinical Hospital Center (KBC) Bezanijska kosa in Belgrade. It was approved by the competent Ethics Committee and the patients or their relatives signed an information form on the study. The study included patients of both sexes, older than 18 and diagnosed with AP. The study excluded pregnant women and patients who were translated into ICU KBC Bezanijska kosa from other hospitals after more than 48 hours since the onset of the disease. The parameters that were necessary for calculating the BISAP and MEWS scores are given in Table 1 and 2. For the calculation of these scoring systems, we used the calculators that can be found online on the site: www.mdcalc.com.

Table 1. Calculating BISAP score

Parameters	**Parameter value**	**Score**
B lood urea nitrogen	BUN>25 mg/dL (8.92 mmol/L)	1
I mpaired mental status	Impaired mental status: Disorientation, lethargy, coma or stupor	1
S IRS	Systemic inflammatory response syndrome ≥ 2 SIRS criteria	1
A ge	age > 60years	1
P leural effusion	pleural effusion present	1

Table 2. Calculating MEWS score

	3	2	1	0	1	2	3
AVPU Score	Unresponsive	Confused or agitated		Alert	Reactive to voice	Reactive to pain	Unresponsive
Respiratory rate	<8			8-20	21-30	31-35	>35
Heart rate	<40		40-50	51-100	101-110	11-130	>130
Systolic BP	<70	70-80	81-100	101-200		201-220	>220
Temperature	<34	34-35	35,1-36,0	36,1-37,9	38,0-38,5	38,6-40,0	>40
Pulse oksimetry	<85%	<90%					
Urin output		<20ml/2h or anuria 4 hours after admission	20-50ml/2h or anuria 4 hours after admission	>50ml/2h			

For BISAP score calculating it was needed to determine if the patient meets SIRS criteria based on having any of the following parameters: body temperature <36°C or >38°C, heart rate > 90/min, respiratory rate >20/min or $PaCO_2$<32mm Hg, WBC < 4000/mL or > 12000/mL or >10% immature (band) forms (15). If a patient has ≥2 parameters, it can be said that the patient meets SIRS criteria and gets 1 point for SIRS variable in BISAP score.

Scoring was conducted at several time points: on admission to the hospital (zero), 48 hours, 72 hours and 7 days after admission to the hospital. In all patients, after receiving hospitalization, a X- ray image of the lungs was performed and in the course of further treatment at the request of the physician. All obtained data were included in the forms specially prepared for this research. For all patients, the number of days spent in the hospital was recorded and for the patients who were accommodated in the ICU, the number of days spent in the ICU was recorded, and for those who needed respiratory support, the number of days spent on mechanical ventilation was recorded. Treatment complications (pleural effusion, sepsis, septic shock) and final outcome were also reported: hospital release or death.

All data obtained were statistically processed on a personal computer using standard statistical procedures and

purpose-built programs. The following methods of statistical processing were used: tabular and graphical representation of results, statistical testing using Student's t-test, χ^2 (hi-square), Mann-Whitney, Kruskal Wallis test, ANOVA procedure in variance analysis and Spearman coefficient of correlation of rank. Significance testing was carried out at $p < 0.05$, which is necessary and sufficient in the medical scientific and research work to make relevant conclusions. The IBM SPSS Statistics 22 statistical software package was used in statistical analysis.

RESULTS

Demographic and general characteristics of patients are shown in Table 3. The study included 50 patients, of whom 8 (16%) did not survive. The frequency of the full structure of subjects, the etiology, the frequency of patients being treated, and the incidence of necrosis did not significantly differ in survival according to statistics.

Table 3. Demographic and clinical characteristics of the respondents towards the final outcome (survivors/non-survivors)

	Total	Survivors	Non-survivors	p
Total number n (%)	50 (100.0)	42 (84%)	8 (16%)	
Sex				
Male, n(%)	26 (52.0)	22 (52.4)	4 (50.0)	0.902
Female, n(%)	24 (48.0)	20 (47.6)	4 (50.0)	
Age Group				
36-45, n(%)	6 (12.0)	6 (14.3)	0 (0)	
46-55, n(%)	7 (14.0)	5 (11.9)	2 (25.0)	
56-65, n(%)	8 (16.0)	8 (19.0)	0 (0)	
66-75, n(%)	21 (42.0)	17 (40.5)	4 (50.0)	
> 76, n(%)	8 (16.0)	6 (14.3)	2 (25.0)	
Etiology				
Gallstone	30 (60.0)	26 (61.9)	4 (50.0)	
Hyperlipidemia	8 (16.0)	6 (14.3)	2 (25.0)	
Alcohol	4 (8.0)	4 (9.5)	0 (0)	
Idiopathic	8 (16.0)	6 (14.3)	2 (25.0)	
Necrosis				
Yes, n(%)	24 (48.0)	20 (47.6)	4 (50.0)	0.902
No, n(%)	26 (52.0)	22 (52.4)	4 (50.0)	
Complications				
Without complication, n(%)	22 (44.0)	22 (52.4)	0 (0)	
Pleural effusion, n(%)	18 (36.0)	16 (38.1)	2 (25.0)	
Sepsis, Septic shock, n(%)	10 (20.0)	4 (9.5)	6 (75.0)	
Duration of MV, median (range)	0 (0-20)	0 (0-2)	4.5 (0-20)	<0.001*
Length of stay in ICU, median (range)	2 (0-20)	1.0 (0-7)	7.0 (0-20)	0.018*
Length of stay in hospital,median (range)	15 (6-62)	12.5 (6-62)	17.5 (9-27)	0.183
Severyt of AP				
Mild, n(%)	20 (40.0)	18 (42.9)	2 (25.0)	
Moderate, n(%)	20 (40.0)	19 (45.2)	1 (12.5)	
Severe, n(%)	10 (20.0)	5 (11.9)	5 (62.5)	

The incidence of sepsis and septic shock among the deceased is 75% and in the survivors 9.5%. Sepsis and septic shock are statistically more common in the group of non-surviving patients compared to a group of surviving patients (hi-square = 18.006, $p < 0.001$). The severe form of pancreatitis is statistically more common in patients with fatal outcome (hi-square = 10.752, $p = 0.001$).

The duration of MV as well as the length of stay in the ICU were statistically significantly higher in patients who died ($U = 45.0$, $p < 0.001$), ($U = 80.0$, $p = 0.018$). However, the length of stay in the hospital did not differ statistically between these two groups of subjects ($U = 118.0$, $p = 0.183$).

Subjects with a fatal outcome are significantly more common in severe forms of pancreatitis (hi-square = 10.752, p = 0.001).

In patients with fatal outcome, the values of the applied score systems were higher.

BISAP-5 and MEWS score > 5 with a predicted mortality rate of 22% and 30% monitored at all 4 time points are statistically more common in patients who did not survive (Table 4).

Table 4. The ratio of BISAP and MEWS scores in relation to the final outcome (survivors/non-survivors)

	Outcome		
	Total	Survivor	Non-survivors
Total number (predicted mortality rate %)	50 (100.0)	42 (84%)	8 (16%)
BISAP $_0$			
0-2 (<2%), n(%)	29 (58.0)	29 (69.0)	0 (0)
3-4 (>15%), n(%)	17 (34.0)	11 (26.2)	6 (75.0)
5 (22%), n(%)	4 (8.0)	2 (4.8)	2 (25.0)
BISAP $_{48}$			
0-2 (<2%), n(%)	29 (58.0)	29 (69.0)	0 (0)
3-4 (>15%), n(%)	11 (22.0)	9 (21.4)	2 (25.0)
5 (22%), n(%)	10 (20.0)	4 (9.5)	6 (75.0)
BISAP $_{72}$			
0-2 (<2%), n(%)	34 (68.0)	34 (81.0)	0 (0)
3-4 (>15%), n(%)	8 (16.0)	4 (9.5)	4 (50.0)
5 (22%), n(%)	8 (16.0)	4 (9.5)	4 (50.0)
BISAP $_{7d}$			
0-2 (<2%), n(%)	32 (69.9)	30 (78.9)	2 (25.0)
3-4 (>15%), n(%)	8 (17.4)	6 (15.8)	2 (25.0)
5 (22%), n(%)	6 (13.0)	2 (5.3)	4 (50.0)
MEWS $_0$			
0-2 (<7.9%), n(%)	30 (60.0)	30 (71.4)	0 (0)
3-4 (>12.7%), n(%)	12 (24.0)	10(23.8)	2 (25.0)
>5 (30%), n(%)	8 (16.0)	2 (4.8)	6 (75.0)
MEWS $_{48}$			
0-2 (<7.9%), n(%)	36 (72.0)	36 (85.7)	0 (0)
3-4 (>12.7%), n(%)	2 (4.0)	2 (4.8)	0 (0)
>5 (30%), n(%)	12 (24.0)	4 (9.5)	8 (100.0)
MEWS $_{72}$			
0-2 (<7.9%), n(%)	30 (60.0)	30 (71.4)	0 (0)
3-4 (>12.7%), n(%)	10 (20.0)	8 (19.0)	2 (25.0)
>5 (30%), n(%)	10 (20.0)	4 (9.5)	6 (75.0)
MEWS $_{7d}$			
0-2 (<7.9%), n(%)	30 (65.2)	30 (78.9)	0 (0)
3-4 (>12.7%), n(%)	10 (21.7)	6 (15.8)	4 (50.0)
>5 (30%), n(%)	6 (13.0)	2 (5.3)	4 (50.0)

However, the BISAP score determined at admission to the hospital - $BISAP_0$ even with lower values of 3-4 (with a predicted mortality rate of> 15%) was statistically more common in patients who did not survive, which is not the case with the MEWS score, likewise determined at the admission to the hospital - MEWS0. $BISAP_{72}$ value of 0-2 (<2%) was statistically more common in patients who survived (hi-square = 16.689, p <0.001)

The value of $BISAP_0$ and $MEWS_0$ has no relevance in relation to the form of pancreatitis. BISAP and MEWS value >5 determined for 48, 72 hours and 7 days after admission >5 (22% and 30%) is significantly more common in severe AP form (Table 5).

Table 5. Relation of BISAP and MEWS in relation to form of AP

	Severity of AP		
	Mild	Moderate	Severe
Total number n (predicted mortality rate %)	20 (40.0)	20 (40.0)	10 (20.0)
BISAP $_0$			
0-2 (<2%), n(%)	13 (65.0)	12 (60.0)	4 (40.0)
3-4 (>15%), n(%)	6 (30.0)	7 (35.0)	4 (40.0)
5 (22%), n(%)	1 (5.0)	1 (5.0)	2 (20.0)
BISAP $_{48}$			
0-2 (<2%), n(%)	13 (65.0)	14 (70.0)	2 (20.0)
3-4 (>15%), n(%)	5 (25.0)	3 (15.0)	3 (30.0)
5 (22%), n(%)	2 (10.0)	3 (15.0)	5 (50.0)
BISAP $_{72}$			
0-2 (<2%), n(%)	14 (70.0)	17 (85.0)	3 (30.0)
3-4 (>15%), n(%)	5 (25.0)	0 (0)	3 (30.0)
5 (22%), n(%)	1 (5.0)	3 (15.0)	4 (40.0)
BISAP $_{7d}$			
0-2 (<2%), n(%)	13 (72.2)	15 (83.3)	4 (40.0)
3-4 (>15%), n(%)	5 (27.8)	1 (5.6)	2 (20.0)
5 (22%), n(%)	0 (0)	2 (11.1)	4 (40.0)
MEWS $_0$			
0-2 (<7.9%), n(%)	14 (70.0)	12 (60.0)	4 (40.0)
3-4 (>12.7%), n(%)	4 (20.0)	6 (30.0)	2 (20.0)
>5 (30%), n(%)	2 (10.0)	2 (10.0)	4 (40.0)
MEWS $_{48}$			
0-2 (<7.9%), n(%)	16 (80.0)	16 (80.0)	4 (40.0)
3-4 (>12.7%), n(%)	1 (5.0)	1 (5.0)	0 (0)
>5 (30%), n(%)	3 (15.0)	3 (15.0)	6 (60.0)
MEWS $_{72}$			
0-2 (<7.9%), n(%)	12 (60.0)	15 (75.0)	3 (30.0)
3-4 (>12.7%), n(%)	6 (30.0)	2 (10.0)	2 (20.0)
>5 (30%), n(%)	2 (10.0)	3 (15.0)	5 (50.0)
MEWS $_{7d}$			
0-2 (<7.9%), n(%)	13 (72.2)	14 (77.8)	3 (30.0)
3-4 (>12.7%), n(%)	5 (27.8)	2 (11.1)	3 (30.0)
>5 (30%), n(%)	0 (0)	2 (11.1)	4 (40.0)

The BISAP-5 and MEWS score of >5 (22% and 30%), determined per day, was most common in sepsis and septic shock. On the other hand, the BISAP and MEWS 0-2 values (with a predicted mortality rate <2% and <7.9%) are more frequent in patients who did not have complications (Table 6).

Table 6. BISAP and MEWS ratio in relation to complications.

	Complications		
	Without complica-tions	Pleural effusion	Sepsis, septic shock
Total number n (%) (predicted mortality rate %)	20 (40.0)	20 (40.0)	10 (20.0)
BISAP $_0$			
0-2 (<2%), n(%)	19 (86.4)	10 (55.6)	0 (0)
3-4 (>15%), n(%)	3 (13.6)	8 (44.4)	6 (60.0)
5 (22%), n(%)	0 (0)	0 (0)	4 (40.)

	Complications		
	Without complications	Pleural effusion	Sepsis, septic shock
BISAP $_{48}$			
0-2 (<2%), n(%)	17 (77.3)	12 (66.7)	0 (0)
3-4 (>15%), n(%)	5 (22.7)	6 (33.3)	0 (0)
5 (22%), n(%)	0 (0)	0 (0)	10 (100.0)
BISAP $_{72}$			
0-2 (<2%), n(%)	18 (81.8)	16 (88.9)	0 (0)
3-4 (>15%), n(%)	4 (18.2)	2 (11.1)	2 (20.0)
5 (22%), n(%)	0 (0)	0 (0)	8 (80.0)
BISAP $_{7d}$			
0-2 (<2%), n(%)	15 (78.9)	17 (100.0)	0 (0)
3-4 (>15%), n(%)	4 (21.1)	0 (0)	4 (40.0)
5 (22%), n(%)	0 (0)	0 (0)	6 (60.0)
MEWS $_{0}$			
0-2 (<7.9%), n(%)	19 (86.4)	11 (61.1)	0 (0)
3-4 (>12.7%), n(%)	3 (13.6)	5 (27.8)	4 (40.0)
>5 (30%), n(%)	0 (0)	2 (11.1)	6 (60.0)
MEWS $_{48}$			
0-2 (<7.9%), n(%)	22 (100.0)	14 (77.8)	0 (0)
3-4 (>12.7%), n(%)	0 (0)	2 (11.1)	0 (0)
>5 (30%), n(%)	0 (0)	2 (11.1)	100 (100.0)
MEWS $_{72}$			
0-2 (<7.9%), n(%)	16 (72.7)	14 (77.8)	0 (0)
3-4 (>12.7%), n(%)	6 (27.3)	2 (11.1)	2 (20.0)
>5 (30%), n(%)	0 (0)	2 (11.1)	8 (80.0)
MEWS $_{7d}$			
0-2 (<7.9%), n(%)	17 (89.5)	13 (76.5)	0 (0)
3-4 (>12.7%), n(%)	2 (10.5)	4 (23.5)	4 (40.0)
>5 (30%), n(%)	0 (0)	0 (0)	6 (60.0)

There is a statistically significant positive correlation between CRP_0 and $BISAP_0$ ($r = 0.386$, $p = 0.006$). Between PCT_0 and both scoring systems there is statistically significant positive correlation - PCT_0 and BISAP $_0$ ($r = 0.537$, $p < 0.001$) and PCT_0 and MEWS $_0$ ($r = 0.490$, $p < 0.001$).

Between CRP_{48} and $BISAP_{48}$, there is statistically significant positive correlation ($r = 0.368$, $p = 0.008$). Between PCT_{48} and both scoring systems there is statistically significant positive correlation - PCT_{48} and BISAP $_{48}$ ($r = 0.682$, $p < 0.001$) and PCT_{48} and $MEWS_{48}$ ($r = 0.734$, $p < 0.001$).

Between CRP_{72} and $BISAP_{72}$ there is statistically significant association ($r = 0.291$, $p = 0.040$), while values of CRP_{72} and $MEWS_{72}$ are not statistically significantly related ($r = 0.241$, $p = 0.092$).

PCT_{72} values have a statistically significant association with $BISAP_{72}$ ($r = 0.572$, $p < 0.001$) as well as with $MEWS_{72}$ ($r = 0.474$, $p = 0.001$).

There is a statistically significant relationship between CRP_{7d} and $BISAP_{7d}$ values ($r = 0.406$, $p = 0.005$), while the values of CRP_{7d} and $MEWS_{7d}$ are not statistically significantly related ($r = 0.289$, $p = 0.051$), although this is close to statistical significance $p = 0.051$.

PCT_{7d} values have a statistically significant association with $BISAP_{7d}$ ($r = 0.830$, $p < 0.001$) as well as with $MEWS_{7d}$ ($r = 0.778$, $p < 0.001$).

Values of PCT determined by days have a statistically significant positive association with both BISAP and MEWS. However, the CRP determined by days is statistically significantly related to BISAP but not with the MEWS score (Table 7).

Between the severity of pancreatitis and duration of MV there is a statistically significant positive correlation ($r = 0.318$, $p = 0.024$) same as between the severity of pancreatitis and the length of stay in ICU ($r = 0.285$, $p = 0.044$) (Table 8). Conclusion: patient with more severe form of AP spent more days on MV and treatment lasted longer.

High levels of discrimination between patients with fatal outcome and cured patients are determined in both cases, with discrimination at MEWS being somewhat higher than BISAP score. For the BISAP score, $BISAP_0$, AUROC (0.807) is best discriminated, and at MEWS, $MEWS_0$, AUROC (0.899) (Table 9).

Table 7. Correlation between CRP, PCT, MEWS and BISAP per days.

Parameters	Scoring system	Number	r	p
CRP_0	$MEWS_0$	50	0.207	0.149
	$BISAP_0$	50	0.386	0.006*
PCT_0	$MEWS_0$	50	0.490	<0.001*
	$BISAP_0$	50	0.537	<0.001*
CRP_{48}	$MEWS_{48}$	50	0.190	0.187
	$BISAP_{48}$	50	0.368	0.008*
PCT_{48}	$MEWS_{48}$	50	0.734	<0.001*
	$BISAP_{48}$	50	0.682	<0.001*
CRP_{72}	$MEWS_{72}$	50	0.241	0.092
	$BISAP_{72}$	50	0.291	0.040*
PCT_{72}	$MEWS_{72}$	50	0.474	0.001*
	$BISAP_{72}$	50	0.572	<0.001*
CRP_{7d}	$MEWS_{7d}$	50	0.289	0.051
	$BISAP_{7d}$	50	0.406	0.005*
PCT_{7d}	$MEWS_{7d}$	50	0.778	<0.001*
	$BISAP_{7d}$	50	0.830	<0.001*

Table 8. Correlation between forms of pancreatitis and MV duration and duration of treatment in ICU.

Parameters	Correlation	Form of pancreatitis
Duration of MV	r	0.318
	p	0.024*
	n	50
Length of stay in the ICU	r	0.285
	p	0.044*
	n	50

Spearman's correlation coefficient (r) was calculated, and significant relationships were marked (*).

Table 9. Area under curve (AUROC) for evaluating the discrimination of the BISAP and MEWS

	AUROC	95%CI	Cut-off	Sensitivity (%)	Specificity (%)
$BISAP_0$	0.807	0.670-0.905	≤2.0	69.0	87.5
$BISAP_{48}$	0.789	0.650-0.891	≤2.0	69.0	87.5
$BISAP_{72}$	0.780	0.640-0.885	≤2.0	78.6	87.5
$BISAP_{7d}$	0.783	0.637-0.891	≤3.0	92.1	62.5
$MEWS_0$	0.899	0.780-0.966	≤3.0	83.3	87.5
$MEWS_{48}$	0.872	0.747-0.950	≤3.0	88.1	87.5
$MEWS_{72}$	0.854	0.726-0.938	≤3.0	83.3	87.5
$MEWS_{7d}$	0.867	0.734-0.949	≤3.0	86.8	87.5

DISSCUSION

Acute pancreatitis is an acute inflammatory process that can clinically be manifested from a mild form with localized inflammation to a severe form of the disease that affects distant organ systems (16). In the United States, AP is a leading cause of inpatient care among gastrointestinal conditions: >275,000 patients are hospitalized for AP annually, at an aggregate cost of >$2.6 billion per year. The incidence of AP ranges from 5 to 30 cases per 100,000, and there is evidence that the incidence has been rising in recent years (1) and fatal outcome occurs in 2 to 10% of patients with AP, depending on the severity of AP (17). In our study, mortality was 16%. Respondents with a fatal outcome are statistically more common in severe forms of pancreatitis. The incidence of severe form of pancreatitis in survivor patients is 12%, and in non-surviving patients is 62.5%. Of the total number of subjects with severe AP, the death rate was recorded in 50% (10/5).

As for the gender and age structure of our patients, it does not significantly affect the survival. Men were slightly more affected (52/48%) and most often belonged to a group of over 65 years of age. According to data from the literature men more frequently suffer from AP. In the prospect study of Toh and associates, the ratio was 1.3 and in Kumar 1.4 (18, 19). In the mentioned study of Kumar and associates from 2017, the respondents belonged to the younger age group, between 40 and 50 years old, while in the study of Toouli and associates the subjects were slightly older (40-60 years), which is similar to our data (20).

Early identification of patients who develop a severe form of pancreatitis would allow early onset of intensive treatment of such patients and a better outcome prognosis outcome (16). A large number of numerical scoring systems were designed back for several decades in order to anticipate the severity of AP and monitor this disease. The oldest - Ranson score was released in 1974 (21). After that, APACHE II score, BISAP and Pancreas score (Glasgow-Imrie Criteria for Severity of Acute Pancreatitis) were designed. Although none of these scores applied alone can predict with certainty the development of organic insufficiency in the AP, their importance is significant for the early identification of potentially severe forms of AP and early onset of intensive treatment. In our study, we compared the importance of the application of the BISAP score that is specific for patients with AP in relation to the application of the MEWS score that is important for assessing the condition of critically ill patients in ICU but not specific for patients with AP. In patients who did not survive, higher values of both score systems (BISAP-5 and MEWS> 5) were obtained, followed by hospital admission, followed by 48 h, 72 h and after 7 days after admission. The higher values of scoring systems predict a worse outcome. The MEWS ≥3 values on admission to hospital and in the next 2 days indicate the development of SIRS and poorer prognosis, which is the development of a severe form of AP (22).

However, the $BISAP_0$3-4 value (with a predicted mortality rate of> 15%) was statistically more common in patients who died, which is not the case with the MEWS values also determined at the admission. The significance of the scoring system for assessing the severity of AP and predicting the outcome of treatment for these patients is growing. The study of 2015 APACHE II is more important than other scoring systems or CRPs, although the differences are not statistically significant (23). In the paper of Joon Hyun in 2015, the values of AUROC for Ranson, BISAP, APACHE-II score and CRP_{24} were: 0.69 (95% CI: 0.62-0.76), 0.74 (95% CI: 0.66-0.80), 0.78 (95% CI: 0.70-0.84) and 0.68 (95% CI: 0.57-0.78). The AUROCA values in our study showed a high degree of discrimination between patients who did not survive and those who survived, with discrimination at MEWS slightly higher than BISAP score. The best disinfection for the BISAP score is $BISAP_0$ with AUROC 0.807 (95% CI: 0.670-0.905) and at MEWS of the peak $MEWS_0$ with AUROC 0.899 (95% CI: 0.780-0.966). The significance of BISAP score in relation to other scoring systems has been proven in earlier studies. Singh et al. have showed that BISAP is equivalent to APACHE II scoring in predicting mortality of patients with AP (24).

$BISAP_0$ and $MEWS_0$ have no relevance to AP weight. The BISAP-5 and MEWS score of 48, 72 hours, and 7 days after admission> 5 (22% and 30%) is significantly more common in severe pancreatitis. A recent study by Chinese authors who have been able to create an AP-based prediction model based on BISAP, MEWS and routine test indices is interesting. Multivariable logistic regression analysis showed that BISAP and serum Ca2 + are independent severity prediction factors for AP, and MEWS is not. However, the model that represents the combination of BISAP and serum Ca2 + is significantly better than their individual application in the assessment of the severity of AP. This model is simple and convenient for clinical use (25).

A group of English authors published a study in 2017 that included 629 patients with diagnosed AP (26). They compared EWS with other multifactorial scoring systems specific for pancreatitis and laboratory analysis in the first three days of hospitalization. Early Warning Score (EWS) has been shown to be highly statistically significant over all three days, compared to the form of pancreatitis and survival. It was also the best predictor of negative outcomes among all clinical and laboratory variables with AUROC values of 0.81, 0.84 and 0.83 for days 1, 2 and 3, respectively. It showed slightly more inferior in predicting the severity of pancreatitis compared to APACHE II. The multivariable logistic regression analysis showed that EWS and low lymphocytes are the dominant factors that are independently related both to the severity of pancreatitis and to the outcome. EWS ≥2 in all three days showed dominance. Univariate logistic regression analysis of all scoring systems determined in the first three days showed high significance both with the severity of pancreatitis and with an outcome, but without any dominance. In our research, only MEWS >5 proved to be statistically significant in relation to the form of pancreatitis and survival.

The incidence of sepsis and septic shock in our study with the deceased is 75% and 9.5% in survivors. Sepsis and septic shock are statistically more common in the group of non-surviving patients compared with a group of surviving patients. The severe form of pancreatitis is statistically more common in patients who did not survive.

Early onset of SIRS and MOF (multi-organ failure) during AP indicate a potentially serious illness and a bad prognosis (27). In fact, this means that morbidity and mortality at an early stage of AP are associated with systemic inflammatory response and persistent organic disorder, and not with local complications (23).

EWS, as we have said, represents an acute inflammatory response, and as such recognizes the severity of SIRS in AP. This is directly related to an increased risk of adverse outcome (28).

In our study, the value of BISAP-5 and MEWS> 5 (with a predicted mortality rate of 22% and 30%) determined by days was most common in sepsis and septic shock. While the values of the scoring system of 0-2 (with a predicted mortality rate <2% and <7.9%) were more frequent in patients who did not have complications.

Multi-organ insufficiency (MODS) is the most severe complication in the study of Suppiah and associates from St James's University Hospital (The Pancreatic Unit) with the highest rate of mortality. Other causes of death include cholangitis, pneumonia, pancreatic necrosis with cardiac failure and abscesses in psoas muscle. Interesting is the fact that MEWS in patients with abscess was the first 3 days of hospitalization was low, but then there was a development of pneumonia and rapid deterioration. In patients with MODS, the $MEWS_0$ value was 2 and then the condition worsened, the third day there was a development of respiratory distress syndrome (ARDS) that was pre-graded in MODS. The mortality was 4.2% (22) while in our study it was significantly higher and amounted to 16%.

EWS is used by many medical centers. In many countries, it is working to define specific, national scores (NEWS). In the UK, the use of NEWS enabled the prediction of cardiac arrest, admission to ICU and mortality (29).

In our study, patients who died on the MV spent an average of 4.5 days and in ICU an average of 7 days, which is a statistically significant difference compared to survivors. However, the length of stay in hospital does not differ statistically between these two groups of subjects. Between the severity of pancreatitis and duration of MV and length of stay in ICU, there is statistically significant positive correlation in the following way: the greater the severity of pancreatitis, the longer the MV and the treatment in ICU were.

PCT values determined per day have a statistically significant positive correlation with BISAP and MEWS scores. However, the CRP determined by days is statistically significantly related to BISAP scores, but not with MEWS. A large number of studies assessed the role of PCT, and compared it with other inflammatory markers, in assessing the severity of AP, the final outcome, and the development of infectious necrosis (30, 31, 32, 33).

A recent study by Kim et al. from 2013 concluded that the PCT of 0.5ng/ml has a sensitivity and a specificity of only 87% and 24%. BISAP score ≥ 2 has high sensitivity and specificity (79% and 89%). This means that the PCT value at the reception in patients with AP does not predict a precise progression of the disease as opposed to BISAP score that show a significantly better correlation. The modified Glasgow score ≥ 3 and APACHE II ≥ 7 show lower sensitivity and specificity, similar to PCT (34).

In our research, the highest sensitivity was shown by $BISAP_{7d}$ (92.1%) and $MEWS_{48}$ (88.1%), and a high specificity of 87.5% had BISAP score, 48h, 72h and MEWS score at all four points of measurement.

However, some studies have shown that PCT has a better statistical significance in assessing the severity of AP and the final outcome compared to clinical scoring systems. A two-year study of Nepalese authors published in 2017, made on 135 subjects diagnosed with AP, proves that the increased value of PCT serves as a promising simple biomarker predicting the severity of AP with better accuracy compared to other scoring systems (19). The PCT serum value showed a slightly higher accuracy (AUC: 0.887, CI: 0.825-0.948) compared to CRP (AUC: 0.717, CI: 0.628-0.8.7) in predicting the severity of AP. However, both parameters showed statistical significance in the assessment of the severity of AP ($p < 0.001$).

The role of CRP in severity assessment and the course of the disease has been investigated many times. C-reactive protein is one of the most important indication of inflammation. In patients with AP elevated CRP levels may indicate the existence of pancreatic necrosis. Plasma CRP values greater than 150 mg/L in the first 72 hours of the onset of the disease are correlated with the presence of necrosis with sensitivity and specificity greater than 80%. However, given that the peak rise of CRP is registered 36-72 h after admission, this test is not helpful in assessing the severity of the disease at the reception (5). This also explains our results according to which CRP is statistically related to BISAP, but not to MEWS score.

CONCLUSION

For the positive outcome of the treatment of patients with AP, it is crucial to early assess the severity of the condition of the patients and timely apply adequate therapy. For this purpose, a number of different scoring systems have been designed, some of which are specific for AP patients such as the BISAP score and some that are applicable to all critical illnesses such as, for example, MEWS score. In our study, we have shown that in both of these scoring systems, they are

simple to calculate and do not require the carrying out of expensive hematological, biochemical, radiological or other tests, so that their calculation does not increase the cost of treatment. The application of these scores is feasible in our conditions, but requires staff to be trained and, first and foremost, to keep the medical records properly.

BISAP score has a better prognostic value in relation to the form of pancreatitis, the development of complications and the final outcome. However, the calculation of the MEWS score is based on monitoring the basic vital parameters so that its application is much simpler and does not require additional costs.

REFERENCES

1. Crockett SD, Sachin Wani S, Gardner TB, Falck-Ytter Y, Alan N. Barkun AN. American Gastroenterological Association Institute Guideline on Initial Management of Acute Pancreatitis 2018. 154 (4); 1096–1101. DOI: https://doi.org/10.1053/j.gastro.2018.01.032
2. Bumbasirević V i sar. Prevencija i lečenje organskih oštecenja u toku akutnog pankreatitisa ACI 2003. 1; 115-122. UDK616.37-002-089-084.
3. Zdravković N. Akutni pancreatitis, Kragujevac Fakultet medicinskih nauka Univerziteta u Kragujevcu 2018. ISBN broj978-86-7760-127-0.
4. Morgan DE. Imaging of acute pancreatitis and its complications. ClinGastroenterolHepatol 2008;6:1077–85. DOI:10.1016/j.cgh.2008.07.012
5. Banks PA, Freeman ML. Practice guidelines in acute pancreatitis. Am J Gastroenterol 2006;101:2379–400. DOI:10.1111/j.1572-0241.2006.00856.x
6. UK Working Party on Acute Pancreatitis. UK guidelines for the management of acute pancreatitis. Gut 2005;54:iii1–9. DOI:10.1136/gut.2004.057026
7. Uhl W, Warshaw A, Imrie C, et al. IAP Guidelines for the surgical management of acute pancreatitis. Pancreatology 2002;2:565–73. DOI:10.1159/000071269
8. Arvanitakis M, Delhaye M, De MV, et al. Computed tomography and magnetic resonance imaging in the assessment of acute pancreatitis. Gastroenterology 2004;126:715–23.
9. Bollen TL, van Santvoort HC, Besselink MG, et al. Update on acute pancreatitis: ultrasound, computed tomography, and magnetic resonance imaging features. Semin Ultrasound CT MRI 2007;28:371–83.
10. Buter A, Imrie CW, Carter CR, et al.Dynamic nature of early organ dysfunction determines outcome in acute pancreatitis. Br J Surg 2002;89:298–30. DOI:10.1046/j.0007-1323.2001.02025.x
11. Johnson CD, Abu-Hilal M. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. Gut 2004;53:1340–4. DOI:10.1136/gut.2004.039883
12. Muckart DJ, Bhagwanjee S. American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference definitions of the systemic inflammatory response syndrome and allied disorders in relation to critically injured patients. Crit Care Med 1997;25:1789–95.
13. Mutinga M, Rosenbluth A, Tenner SM et al. Does mortality occur early or late in acute pancreatitis? Int J Pancreatol 2000;28:91–95. DOI:10.1385/IJGC:28:2:091
14. Goldhill DR, McNarry AF. Physiological abnormalities in early warning scores are related to mortality in adult inpatients. British Journal of Anaesthesia 2004; 92: 882-4. DOI:10.1093/bja/aeh113
15. Singh, V., Wu, B. U., Bollen, T. L., Repas, K., Maurer, R., Mortele, K. J., & Banks, P. A. Early Systemic Inflammatory Response Syndrome Is Associated With Severe Acute
16. Pancreatitis. Clinical Gastroenterology and Hepatology2009; *7*(11)1247-1251
17. doi.org/10.1016/j.cgh.2009.08.012
18. Madhu1 CP, Reddy DV. A Comparison of the Ranson Score and Serum Procalcitonin for Predicting the Severity of Acute Pancreatitis. GSJ 2018; 6 (2):303-309.
19. Balthazar EJ. Acute Pancreatitis: Assessment of Severity with Clinical and CT Evaluation. Radiology 2002;223(3):603-13 DOI: 10.1148/radiol.2233010680
20. Toh SK, Phillips S, Johnson CD. A prospective audit against national standards of the presentation and management of acute pancreatitis in the South of England.Gut2000;46(2):239-43.
21. Kumar S, Jalan A, Patowary BN, Bhandari U.To Access the Role of Serum Procalcitonin in Predicting the Severity of Acute Pancreatitis. Kathmandu Univ Med J 2017; 15(57):19-24.
22. Toouli J, Brooke-Smith M, Bassi C, Carr-Locke D, Telford J, Freeny P, et al. Guidelines for the management of acute pancreatitis. J Gastroenterol Hepatol 2002;17 Suppl:S15-39.
23. Ranson JH, Rifkind KM, Roses DF, Fink SD, Eng K, Localio SA. Objective early identification of severe acute pancreatitis. Am J Gastroenterol 1974;61:443–451.
24. Suppiah A, Malde D, Arab T, Hamed M, Allgar V, Morris-Stiff G, Smith A. The Modified Early Warning Score (MEWS): An Instant Physiological Prognostic Indicator of Poor Outcome in Acute Pancreatitis. JOP. J Pancreas (Online) 2014 Nov 28; 15(6):569-576.
25. Cho JH, Kim TN, Chun HH, and Kim KH. Comparison of scoring systems in predicting the severity of acute

pancreatitis. World J Gastroenterol 2015; 21(8): 2387–2394. doi: [10.3748/wjg.v21.i8.2387].
26. Singh VK, Wu BU, Bollen TL, Repas K, Maurer R, Johannes RS, Mortele KJ, Conwell DL, Banks PA. A prospective evaluation of the bedside index for severity in acute pancreatitis score in assessing mortality and intermediate markers of severity in acute pancreatitis. Am J Gastroenterol 2009;104(4):966-71. doi: 10.1038/ajg.2009.28.
27. Ye JF, Zhao YX, Ju J, Wang W. Building and verifying a severity prediction model of acute pancreatitis (AP) based on BISAP, MEWS and routine test indexes. Clin Res Hepatol Gastroenterol 2017;41(5):585-591. doi: 10.1016/j.clinre.2016.11.013.
28. Jones JM, Nea PN, Ngu SW, Dennison RA, Garcea G. Early warning score independently predicts adverse outcome and mortality in patients with acute pancreatitis. Langenbecks Arch Surg. 2017; 402(5): 811–819. doi: 10.1007/s00423-017-1581-x.
29. Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, Tsiotos GG, Vege SS. Classification of acute pancreatitis--2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102–111.
30. Garcea G, Jackson B, Pattenden CJ, et al. Early warning scores predict outcome in acute pancreatitis. J Gastrointest Surg 2006;10:1008–1015. doi: 10.1016/j.gassur.2006.03.008.
31. Smith GB, Prytherch DR, Meredith P, et al. The ability of the national early warning score (NEWS) to discriminate patients at risk of early cardiac arrest, unanticipated intensive care unit admission, and death. Resuscitation. 2013;84:465–470. doi: 10.1016/j.resuscitation.2012.12.016.
32. Modrau IS, Floyd AK, Thorlacius-Ussing O. The clinical value of procalcitonin in early assessment of acute pancreatitis. Am J Gastroenterol 2005;100(7):1593–1597.
33. Mofidi R, Suttie SA, Patil PV, Ogston S, Parks RW. The value of procalcitonin at predicting the severity of acute pancreatitis and development of infected pancreatic necrosis: systematic review. Surgery 2009;146(1):72–81.
34. Muller C, Uhl W, Printzen G et al. Role of procalcitonin and granulocyte colony stimulating factor in the early prediction of in-fected necrosis in severe acute pancreatitis. Gut 2000;46(2):233–238.
35. Riché FC, Cholley BP, Laisné M-JC et al. Inflammatory cytokines, C reactive protein, and procalcitonin as early predictors of necrosis infection in acute necrotizing pancreatitis. Surgery 2003; 133(3):257–262.
36. Kim BG, Noh MH, Ryu CH, et al.A comparison of the BISAP score and serum procalcitonin for predicting the severity of acute pancreatitis. Korean J Intern Med 2013;28:322-329.doi: 10.3904/kjim.2013.28.3.322.