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Comparative Analysis of Crp/Albumin Ratio, Procalcitonin/Albumin Ratio, and Lactate/Albumin Ratio for Predicting 28-Day Mortality in Icu Patients with Sepsis

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KEYWORDS

Sepsis; SOFA score; CRP/albumin ratio; Procalcitonin/albumin ratio; Lactate/albumin ratio; Mortality;

ABSTRACT:

Introduction: Sepsis, a life-threatening condition caused by the body's overreaction to infection, remains a leading cause of death in ICUs. Despite better care, septic patient mortality is hard to predict. The SOFA score has been used for this purpose in the past. But other markers like CRP, procalcitonin, and lactate, when combined in ratios with albumin, have been useful as prognostic markers.

Objective: The aim of this study is to evaluate the CRP/albumin ratio (CAR), procalcitonin/albumin ratio (PAR), and lactate/albumin ratio (LAR) as independent predictors of 28-day mortality in patients with sepsis in the ICU, and contrast them with the predictive ability of the SOFA score.

Methods: A prospective observational study of 105 ICU patients with sepsis was analyzed. The measurements made were CRP, procalcitonin, lactate, and albumin. Differences in CAR, PAR, and LAR values were compared against the SOFA score to predict a prognosis that categorized in which group the patient would be at 28 days. Test results for significance were evaluated using the Mann-Whitney U test and the ROC curve.

Results: Non-survivors exhibited significantly higher CAR, PAR, LAR, and SOFA scores compared to survivors. ROC curve analysis revealed PAR to be the best predictor of 28-day mortality (AUC = 0.978) followed by CAR and LAR. While CAR and LAR were less powerful predictors of mortality, they also provided good information regarding patient outcome and the severity of the disease in the management of sepsis.

Conclusion: PAR is a superior 28-day mortality predictor among sepsis patients compared with SOFA, CAR, and LAR. While CAR and LAR are still beneficial, PAR is more predictive, and therefore it is a useful risk stratification and management tool in the critical care setting.

INTRODUCTION

Sepsis is a serious and potentially fatal disease characterized by the overwhelming and uncontrolled reaction of the body to infection. It can lead to widespread inflammation, tissue destruction, organ failure, and, in most cases, mortality [1]. Despite significant advances in the treatment of medicine, including the development of new antibiotics and organ-supporting technologies, sepsis remains one of the leading causes of death in critically ill patients admitted to intensive care units (ICUs). The acute and unpredictable nature of sepsis necessitates early detection and management at an optimal time for improving patient outcomes [2]. Early aggressive management has been proven to greatly enhance survival. Therefore, mortality prediction among septic patients is very important for prioritization of care and efficient use of resources. Stable and sensitive biomarkers together with well-established clinical scoring systems are essential in this regard [3].

Sequential Organ Failure Assessment (SOFA) score has also been extensively employed as a universal scoring

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system in measuring the severity of organ dysfunction in sepsis. SOFA score was initially intended to evaluate the time-dependent evolution of organ function but was identified as a good marker of mortality among septic patients [4]. The SOFA score is given for six organ systems' function: respiratory, cardiovascular, hepatic, coagulation, renal, and neurological. The more elevated the SOFA score, the more pronounced the organ dysfunction, and various studies have reported that there exists a linear association between high SOFA scores and high mortality among septic patients. SOFA is thus an important clinical tool in sepsis management, used to inform treatment and prognosticate [5].

Yet, although SOFA score is a good predictor of organ dysfunction, it does not reflect the dynamic and multifactorial pathophysiology of sepsis, especially the patient's inflammatory response, severity of infection, and metabolic disturbances [6]. Sepsis is an extremely interactive set of factors, such as the immune response to infection, inflammation, tissue hypoxia, and metabolic disturbances. These biomarkers have thus been studied to complement or augment the predictive utility of the SOFA score, potentially providing more sensitive determinations of septic patients [7]. C-reactive protein (CRP), procalcitonin (PCT), and lactate are some of the most well-established biomarkers in sepsis management, offering essential information regarding the patient's inflammatory and metabolic condition [8].

CRP is a nonspecific acute-phase reactant that is synthesized by the liver in response to inflammation, infection, or trauma. CRP is among the most popular biomarkers to have been applied within a clinical context because it has the potential to indicate the existence of systemic inflammation. While a distinction in CRP level is not specific for sepsis, it will yield useful information concerning the degree of the inflammatory process in sepsis [9]. Procalcitonin (PCT) is more bacterial infection-specific and has been utilized as a discriminator between bacterial sepsis and other systemic inflammatory processes. PCT increases with bacterial endotoxins and pro-inflammatory cytokines, and a number of studies have demonstrated that increased levels of PCT correlate with mortality in septic patients [10]. Lactate is another important biomarker that is a marker of tissue hypoxia and metabolic derangement. Increased lactate levels are also typically observed in septic shock and severe sepsis patients, reflecting inadequate tissue oxygenation and perfusion. Lactate has also been used as a disease severity marker and is capable of predicting mortality in septic patients, especially those with septic shock [11].

Albumin, being the most common plasma protein that is produced by the liver, has a vital function in oncotic pressure maintenance, transportation of hormones and drugs, as well as regulation of inflammation [12]. In acute disease, such as sepsis, albumin level falls as a result of decreased production, enhanced capillary permeability, and augmented breakdown, proportionate to the severity of the patient's inflammatory and metabolic disturbance. Hypoalbuminemia is also linked with poor prognosis in critically ill patients, including septic patients, and is a marker of acute phase response and malnutrition [13].

Given the differential roles of CRP, PCT, lactate, and albumin in sepsis pathophysiologic processes, recent studies have emphasized the use of these biomarkers in ratio form to enhance their predictive value [14]. The CAR, PAR, and LAR are introduced as new prognostic indicators of sepsis that provide a more complete description of the infectious, inflammatory, and metabolic status of the patient [15]. These ratios indicate the proportion between the acute phase reaction, as described by CRP, PCT, or lactate, and the patient's physiological and nutritional reserve, as described by albumin. Increased CAR, PAR, and LAR have also been associated with increased mortality among septic patients, indicating that these ratios could potentially in determining disease severity and prognosis [16].

The albumin to CRP ratio (CAR) is premised on the hypothesis that CRP indicates the severity of the inflammatory process and albumin indicates the physiological reserve of the patient. There have been several studies that have shown that high CAR has been proven to be linked with higher mortality in patients who were septic. Since procalcitonin is pathogen-specific in infection with bacteria, procalcitonin also has been matched against albumin to offer the procalcitonin/albumin ratio (PAR) [17]. PAR has been implicated in poor prognosis of sepsis, especially in patients of severe bacterial sepsis. As has the lactate/albumin ratio (LAR), which was explored as an mortality predictor for septic patients and where increasing LAR is evidence of tissue hypoxia as well as

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evidence of patient physiological reserve loss in response to the septic injury [18].

Against this backdrop, the objective of the present study is to conduct a comparative analysis of the CRP/albumin ratio, procalcitonin/albumin ratio, and lactate/albumin ratio as standalone predictors of 28-day mortality in septic ICU patients [19]. The ratios will be compared against the SOFA score, the standard method for predicting mortality in septic patients. The main aim is to establish whether such biomarker ratios provide improved or additional predictive information compared to the SOFA score and thus enhance early risk stratification and management of septic patients [20]. Since sepsis carries extremely high mortality, especially in severe forms, the identification of better prognostic markers is of immense interest to enhance patient outcomes and inform clinical decision-making [21].

The objective of this study is to compare the CRP/albumin ratio (CAR), procalcitonin/albumin ratio (PAR), and lactate/albumin ratio (LAR) in isolation as predictors of 28-day mortality among septic ICU patients compared to the SOFA score. The purpose is to identify if these biomarker ratios are more or additive to the prognostic information in predicting risk for mortality to allow for early risk stratification and clinical intervention. The objective of this study is to enhance the prognostic accuracy of sepsis and optimize patient management in critical care.

MATERIALS AND METHODS

A 12-month prospective observational study was conducted at KIMS Hospital among 105 ICU patients with diagnosis of sepsis and SOFA score of greater than 2. Baseline measurements were taken of CRP, procalcitonin, lactate, albumin, and the other biochemical and hematological parameters. The CRP/albumin (CAR), procalcitonin/albumin (PAR), and lactate/albumin (LAR) ratios were compared with the SOFA score to predict both primary and secondary study outcomes. Patients aged over 18 years with sepsis were included in the study, while those with pre-existing organ dysfunction, such as chronic kidney disease or decompensated liver disease, were excluded.

RESULTS

Table 1: Comparison of mean CAR, PAR, LAR & SOFA scores based on the survival status among study patients using Mann Whitney Test

Parameter	Survival	N	Mean	SD	Mean Diff	p-value
CAR	Non-survivor	18	11.715	6.441	7.801	<0.001*
	Survivor	87	3.914	3.964		
PAR	Non-survivor	18	15.846	10.599	14.357	<0.001*
	Survivor	87	1.489	2.043		
LAR	Non-survivor	18	1.070	0.471	0.333	0.004*
	Survivor	87	0.737	0.434		
SOFA	Non-survivor	18	14.00	2.06	7.340	<0.001*
	Survivor	87	6.66	3.34		

The table compares the mean CAR, PAR, LAR, and SOFA scores between survivors and non-survivors. Non-survivors consistently show higher values in all parameters, with significant differences (p-values <0.001 for CAR, PAR, and SOFA; 0.004 for LAR). The highest differences are observed in CAR and PAR, indicating these scores are more elevated in non-survivors.

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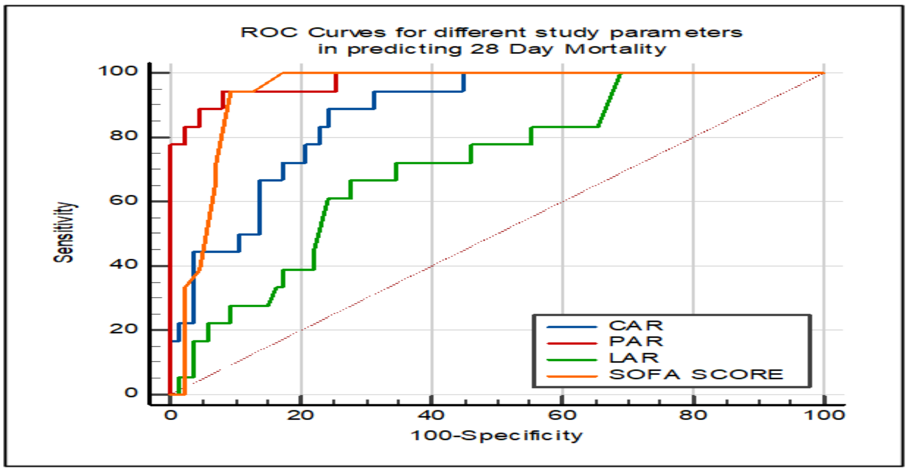

Figure 1: ROC Curve for CRP Albumin Ratio for Predicting 28-day Mortality

The ROC curve compares the performance of different parameters (CAR, PAR, LAR, SOFA Score) in predicting 28-day mortality. CAR (blue) and PAR (red) show the highest sensitivity and specificity, indicating better predictive ability. The SOFA score (orange) also performs well, while LAR (green) demonstrates a relatively lower predictive capability based on its ROC curve trajectory.

Table 2: Comparison of mean CAR values based on the treatment variables among study patients using Mann Whitney Test

Variable	Category	N	Mean	SD	Mean Diff	p-value
ICU	≤ 3 days	58	3.712	5.043	-3.439	<0.001*
	> 3 days	47	7.151	5.123		
Ionotropes	Yes	27	8.958	6.671	4.990	<0.001*
	No	78	3.968	4.121		
MV	Yes	28	8.685	6.015	4.683	<0.001*
	No	77	4.002	4.497		
RRT	Yes	28	7.373	6.657	2.894	0.08
	No	77	4.479	4.582		

The table compares mean CAR values based on treatment variables. ICU stays longer than 3 days, use of ionotropes, mechanical ventilation (MV), and renal replacement therapy (RRT) are associated with higher CAR values. Significant differences are observed for ICU stay, ionotropes, and MV, all with p-values <0.001, while RRT shows a non-significant difference (p = 0.08). Longer ICU stays and treatment intensity correlate with increased CAR.

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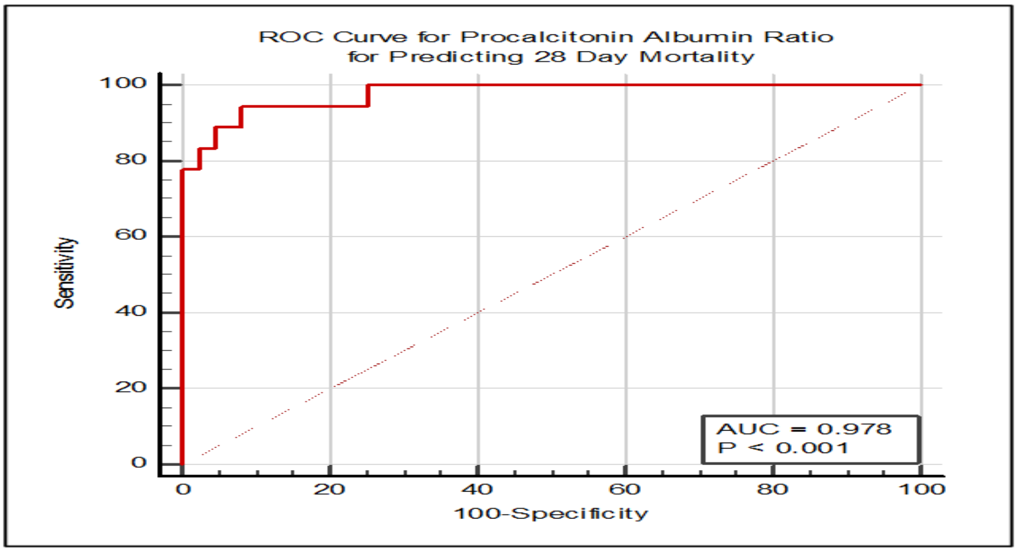

Figure 2: ROC Curve for Procalcitonin Albumin Ratio for Predicting 28 Day Mortality

The ROC curve for Procalcitonin Albumin Ratio in predicting 28-day mortality shows excellent predictive ability with an area under the curve (AUC) of 0.978, indicating high sensitivity and specificity. The p-value of <0.001 further confirms the statistical significance of the prediction. This curve demonstrates that the Procalcitonin Albumin Ratio is a strong indicator for 28-day mortality risk.

Table 3: Comparison of mean PAR values based on the treatment variables among study patients using Mann Whitney Test

Variable	Category	N	Mean	SD	Mean Diff	p-value
ICU	≤ 3 days	58	3.115	7.728	-1.865	<0.001*
	> 3 days	47	4.980	6.339		
Ionotropes	Yes	27	9.132	11.243	6.976	<0.001*
	No	78	2.156	3.745		
MV	Yes	28	10.229	10.842	8.562	<0.001*
	No	77	1.667	2.954		
RRT	Yes	28	8.556	11.729	6.281	0.01*
	No	77	2.275	3.282		

The table compares mean PAR values based on treatment variables. Higher PAR values are observed in patients with longer ICU stays, ionotrope use, mechanical ventilation (MV), and renal replacement therapy (RRT). All differences are statistically significant ($p < 0.001$), except for RRT ($p = 0.01$), with significant PAR increases in patients with more intensive treatments.

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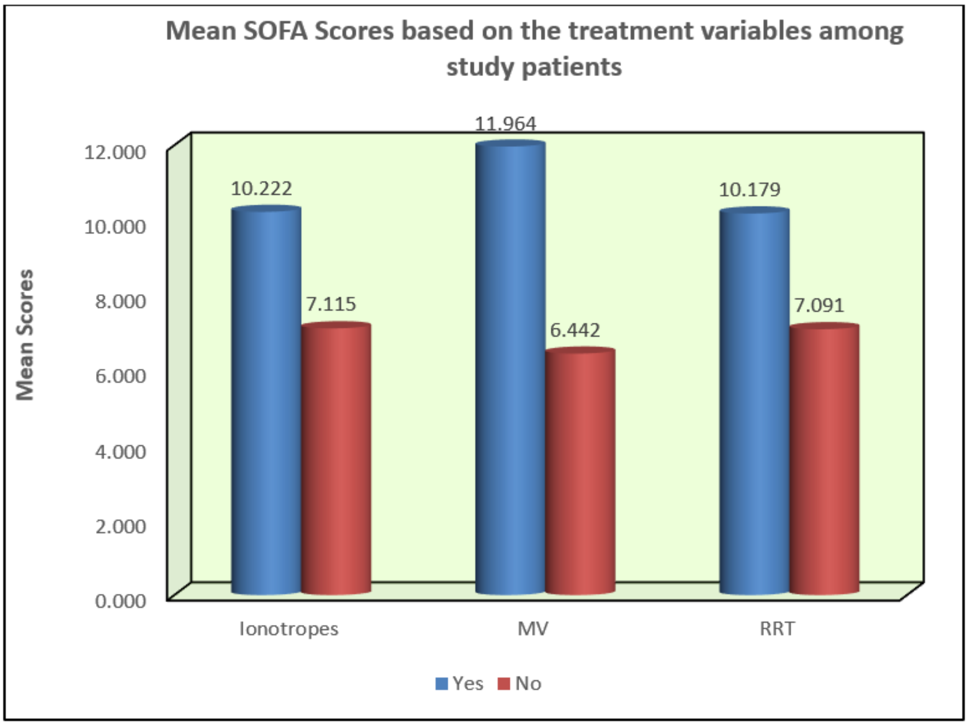

Figure 3: Mean SOFA Scores based on the treatment variables among study patients

The bar chart compares mean SOFA scores based on the use of ionotropes, mechanical ventilation (MV), and renal replacement therapy (RRT). Patients who received these treatments had higher SOFA scores (10.222, 11.964, and 10.179 respectively) compared to those who did not (7.115, 6.442, and 7.091), indicating more severe clinical conditions in treated patients.

Table 4: Comparison of mean LAR values based on the treatment variables among study patients using Mann Whitney Test

Variable	Category	N	Mean	SD	Mean Diff	p-value
ICU	≤ 3 days	58	0.662	0.402	-0.294	<0.001*
	> 3 days	47	0.956	0.470		
Ionotropes	Yes	27	1.156	0.467	0.488	<0.001*
	No	78	0.668	0.381		
MV	Yes	28	1.000	0.441	0.281	0.002*
	No	77	0.719	0.440		
RRT	Yes	28	0.939	0.466	0.198	0.04*
	No	77	0.741	0.443		

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The table compares mean LAR values based on treatment variables. Longer ICU stays, use of ionotropes, mechanical ventilation (MV), and renal replacement therapy (RRT) are associated with higher LAR values. Statistically significant differences are observed for ICU stay, ionotropes, MV (p-values < 0.001), and RRT (p = 0.04), indicating greater LAR levels with more intensive treatments.

DISCUSSION

Sepsis is an organism-killing disease because of the body's overreaction to infection, causing inflammation and organ failure. Early diagnosis and treatment are of concern, for which Sequential Organ Failure Assessment (SOFA) score is used in predicting mortality. SOFA has its limitations as a potential surrogate of sepsis, paving the way for research of other markers like C-reactive protein (CRP), procalcitonin (PCT), and lactate. This study examines the CRP/albumin ratio (CAR), procalcitonin/albumin ratio (PAR), and lactate/albumin ratio (LAR) as 28-day predictors of mortality among ICU patients and compares their ability to SOFA [22].

Our findings reveal that non-survivors exhibited significantly higher CAR, PAR, LAR, and SOFA scores compared to survivors, as per Atik et al. (2020) and Sipahioglu et al. (2022). The Mann-Whitney U test proved that non-survivors had greater SOFA (4.12 ± 1.77 vs. 3.31 ± 1.08, p < 0.001) and LAR (0.57 vs. 0.07, p < 0.001) scores. SOFA scores correlated positively with procalcitonin and lactate, but inversely with albumin. These significant differences in biomarkers between survivors and non-survivors demonstrate the prognostic importance of such scores in ARDS patients complicated by COVID-19, exemplifying how the markers are significant predictors of critically ill patients' survival outcomes [23, 24].

Our results indicate that CAR (blue) and PAR (red) are the most predictive for 28-day mortality, with excellent sensitivity and specificity, and SOFA (orange) is also highly predictive, and LAR (green) is less predictive. This is concordant with ROC analysis of CRP, albumin, and other laboratory markers where the CRP level of 39 mg/L yielded an AUC of 0.648 and albumin with a threshold level of 2.06 g/dL having an AUC of 0.829. Atik D et al. (2020) presented a CRP/albumin ratio AUC of 0.536, reflecting the absence of its statistical significance for predicting mortality, as observed with Sipahioglu H et al. (2022), in which the CRP/albumin ratio was similarly not significant among severe ARDS patients [23,24].

Our findings reveal that higher CAR values are associated with longer ICU stays, use of ionotropes, MV, and RRT, with significant differences observed for ICU stay, ionotropes, and MV (p < 0.001), while RRT shows a non-significant difference (p = 0.08). This aligns with the results from Atik D et al. (2020), where the Mann-Whitney U test showed no statistically significant difference in CAR values between treatment groups (p = 0.699). Similarly, Abdou K et al. (2024) found no significant difference in CAR values between mortality and survival groups, with a median CAR value of 8.21 for the mortality group and 7.188 for the survival group (p = 0.807), indicating consistency across both studies [23,25].

Our findings show the ROC curve for the Procalcitonin Albumin Ratio demonstrates excellent predictive ability for 28-day mortality, with an AUC of 0.978 and a p-value <0.001, indicating strong statistical significance. In contrast, Atik D et al. (2020) reported a Procalcitonin/Albumin ratio AUC of 0.645, which, while relevant, is not as sensitive or specific for predicting mortality, with a threshold of 18.5. Abdou K et al. (2024) found no statistically significant difference in CAR values between mortality and survival groups (p = 0.807), suggesting that although the CAR ratio differs between studies, our study aligns with the overall relevance of these markers in predicting 28-day mortality [23,25].

Our findings show higher PAR values in patients with longer ICU stays, ionotrope use, MV, and RRT, with significant differences (p < 0.001), except for RRT (p = 0.01). This aligns with studies by Atik D et al. (2020) and Sipahioglu H et al. (2022), where a weak positive correlation was found between PAR and both APACHE-II (r=0.288, p=0.025) and SOFA (r=0.362, p=0.004) scores. This suggests that PAR correlates with illness severity, indicating a relationship between elevated PAR values and more intensive treatments in critically ill patients across studies [23, 24].

Our findings show higher SOFA scores in patients receiving ionotropes, MV, and RRT (10.222, 11.964, and 10.179), indicating more severe clinical conditions. This aligns with Atik et al. (2020), who found SOFA

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positively correlated with markers like procalcitonin (r=0.331, p=0.009), lactate (r=0.353, p=0.005), and PAR (r=0.362, p=0.004), suggesting a link between SOFA and infection severity. Similarly, Sipahioglu et al. (2022) reported significantly higher SOFA scores in nonsurvivors (4.12 ± 1.77) compared to survivors (3.31 ± 1.08) with a p-value < 0.001, further indicating that higher SOFA scores correlate with worse outcomes [23,24].

Our findings show higher LAR values with longer ICU stays, ionotrope use, MV, and RRT, with significant differences (p < 0.001) for ICU stay, ionotropes, MV, and RRT (p = 0.04). This correlates with Sipahioglu H et al. (2022), who reported significantly higher LAR in nonsurvivors (0.07) compared to survivors (0.656), with p < 0.001. Similarly, Abdou K et al. (2024) found significantly higher LAR values in the mortality group compared to the survival group, with a median LAR of 0.869 (IQR: 0.494–1.75) versus 0.57 (IQR: 0.368–0.999), and a p-value of 0.044, indicating greater LAR in nonsurvivors [24,25].

CONCLUSION

Our study highlights the potential of CAR (C-reactive protein/albumin ratio), PAR (procalcitonin/albumin ratio), and LAR (lactate/albumin ratio) as prognostic markers for predicting mortality in patients with sepsis. Among these, PAR demonstrated superior predictive accuracy compared to the SOFA (Sequential Organ Failure Assessment) score, suggesting it may be a more reliable indicator of patient outcomes. However, CAR and LAR, while still useful, were found to be less effective than SOFA in predicting mortality. These findings suggest that PAR, in particular, could serve as a valuable tool in clinical assessments of sepsis severity and patient prognosis.

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