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REVIEW ARTICLE

Prognostic Value of Lactate/Albumin Ratio and NEWS-Lactate in Predicting Sepsis-Associated Acute Kidney Injury: A Retrospective Analysis

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Abstract: **Introduction:** Sepsis-associated acute kidney injury (SA-AKI) is a frequent complication in critically ill patients and is associated with increased mortality. This study aimed to evaluate the prognostic value of the lactate/albumin ratio (LAR) and other albumin-based biomarkers in predicting SA-AKI. **Methods:** A retrospective observational study was conducted on 564 patients with sepsis, divided into two groups based on the presence (n = 298) or absence (n = 266) of AKI. Clinical characteristics, laboratory parameters, and disease severity scores (SOFA, APACHE II, NEWS, NEWS-Lactate) were compared between groups. The predictive performance of each marker in detecting SA_AKI was assessed using receiver operating characteristic (ROC) curve analysis. **Results:** Patients with SA-AKI had significantly higher levels of lactate (p = 0.001), procalcitonin (PCT) (p = 0.001), urea (p = 0.019), creatinine (p = 0.004), and lower albumin (p = 0.001) concentrations upon admission. The LAR demonstrated the highest discriminative performance among all tested markers, with an AUC of 0.800 (95% CI: 0.765–0.835), sensitivity of 70.5% (95% CI: 64.9 – 75.6), and specificity of 70.3% (95% CI: 64.4 – 75.7) at a cut-off value of 0.101. NEWS-Lactate also showed good prognostic ability (AUC = 0.772, 95% CI: 0.734–0.809), sensitivity of 71.1% (95% CI: 65.6 – 76.2), and specificity of 63.2% (95% CI: 57.1 – 69.0) at a cut-off value of 7.11. Other indices, including serum creatinine/albumin ratio (sCAR), blood urea nitrogen/albumin ratio (BAR), and procalcitonin/albumin ratio (PAR), and procalcitonin (PCT) × lactate, yielded moderate AUCs. While NEWS alone showed limited predictive value (AUC = 0.508), both SOFA and APACHE II scores were significantly higher in the SA-AKI group. **Conclusion:** It seems that, the LAR and NEWS-Lactate are promising biomarkers for early detection of SA-AKI and may outperform conventional severity scores and standalone laboratory parameters.

Keywords: Acute kidney injury; Prognosis; Biomarkers; Serum albumin; Sepsis

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1. Introduction

Sepsis remains a significant cause of morbidity and mortality worldwide, often leading to multiple organ dysfunction, among which acute kidney injury (AKI) is a common and serious complication. Sepsis-associated acute kidney injury (SA-AKI) accounts for approximately 50% of AKI cases in the intensive care unit (ICU) and is associated with higher mortality, prolonged hospital stay, and increased healthcare costs (1, 2).

The pathophysiology of SA-AKI is complex and involves hemodynamic instability, systemic inflammation, and microcirculatory dysfunction, making early detection and risk stratification essential for optimal management (3). Despite various efforts, there remains a lack of sensitive and specific biomarkers to predict AKI development in septic patients. Commonly used scores such as the Sequential Organ Failure Assessment (SOFA), Acute Physiology and Chronic Health Evaluation II (APACHE II), and National Early Warning Score (NEWS) have shown limited performance in predicting renal complications (4, 5).

Recently, interest has grown in combining traditional laboratory parameters with markers of inflammation and organ perfusion to improve prognostic accuracy. The lactate/albumin ratio (LAR) has emerged as a promising biomarker in critically ill patients, reflecting both tissue hypoperfusion and nutritional-inflammatory status. Other ratios such as the serum creatinine/albumin ratio (sCAR), blood urea nitrogen/albumin ratio (BAR), and procalcitonin/albumin ratio (PAR) have also been proposed as potential indicators of disease severity and prognosis (6-9).

The pathophysiological rationale for using albumin-indexed ratios, such as LAR, lies in the dual role of lactate and albumin in the body. Lactate is a byproduct of anaerobic metabolism, and its elevated levels in sepsis reflect tissue hypoperfusion, metabolic acidosis, and the severity of systemic inflammation. On the other hand, albumin is a critical plasma protein that decreases during inflammation and stress, thus affecting fluid balance and tissue perfusion. The combination

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of these markers in a single ratio, such as LAR, provides a more comprehensive reflection of both metabolic derangements and nutritional-inflammatory status, which are essential in the early detection of organ dysfunction, particularly AKI. The kidneys play an essential role in lactate metabolism. Under normal conditions, the renal cortex primarily absorbs and metabolizes lactate, with minimal amounts excreted in the urine. This process is part of the glucose-lactate recycling system between the renal cortex and medulla. In conditions such as acute kidney injury (AKI) and diabetic kidney disease (DKD), the kidneys' ability to metabolize lactate is impaired, leading to lactate accumulation and exacerbating kidney dysfunction (10). In clinical practice, hypoalbuminemia often occurs due to decreased albumin synthesis from liver dysfunction, redistribution of serum albumin due to capillary leak, or increased loss through the gastrointestinal tract and kidneys (11). Hypoalbuminemia is an independent risk factor that increases short- and long-term mortality and is associated with a higher incidence of AKI in patients with acute conditions such as trauma, cardiogenic shock, and sepsis (12).

Based on the above-mentioned points, this study aimed to assess the prognostic value of the lactate/albumin ratio (LAR) and other albumin-based ratios in predicting SA-AKI in septic patients. Additionally, we compared the predictive performance of these markers with established clinical scores and biomarkers, including lactate, procalcitonin (PCT), and the composite NEWS-Lactate score.

2. Methods

2.1. Study design and Setting

This retrospective cross-sectional study was conducted on patients diagnosed with sepsis who were admitted to the Emergency Department of 108 Military central hospital, Hanoi, Vietnam from January 2020 to December 2024. Adult patients (≥18 years) with sepsis were categorized into two groups based on the presence or absence of AKI. Then the predictive performance of LAR (lactate/albumin), sCAR (serum creatinine/albumin), BAR (BUN/albumin), PAR (procalcitonin/albumin), and PCT × lactate (procalcitonin × lactate), as well as NEWS, NEWS + Lactate, SOFA, and APACHE II scores in predicting the SA-AKI were accessed and compared using area under the receiver operating curve (ROC) analysis. This study was conducted in accordance with the principles outlined in the Declaration of Helsinki. Ethical approval was obtained from the Ethics Committee in Biomedical Research of 108 Military Central Hospital under decision number 310/QĐ-BV. All patients or their legal representatives provided informed consent prior to enrollment. Patient data were anonymized and handled confidentially to ensure privacy and data protection.

2.2. Participants and Eligibility Criteria

Patients aged ≥18 years who were admitted to the Emergency Department of 108 Military Central Hospital with a diagnosis of sepsis based on Sepsis-3 criteria between January 2020 and December 2024 were screened for inclusion.

2.3. Inclusion criteria

- Age ≥18 years - Diagnosis of sepsis according to Sepsis-3 definition (suspected or confirmed infection with ≥2 points increase in SOFA score) - Availability of complete clinical and laboratory data within the first 6 hours of admission

2.4. Exclusion criteria

- Chronic kidney disease (CKD) stage 4 or 5 (estimated GFR <30 mL/min/1.73 m²)
- End-stage renal disease requiring maintenance dialysis
- Pre-existing acute kidney injury prior to sepsis onset
- Terminal illness with expected survival <24 hours
- Incomplete or missing critical clinical or laboratory data
- Declined or unavailable informed consent

2.5. Data gathering and Definitions

Demographic and clinical data, including age, Glasgow Coma Scale (GCS), heart rate, temperature, systolic blood pressure, respiratory rate, and mechanical ventilation status were recorded. Laboratory parameters collected at admission included serum lactate, albumin, blood urea nitrogen (BUN), creatinine, procalcitonin (PCT), bilirubin, and white blood cell (WBC) count. Data were collected using a standardized case report form (CRF) and a predefined checklist by trained clinical research staff under the supervision of the study investigators. All data were reviewed for completeness and accuracy prior to analysis.

In this study, we utilized serum creatinine levels as the primary criterion for diagnosing AKI, following the KDIGO 2012 guidelines. Although the ADQI-2023 guidelines recommend using higher sensitivity and specificity biomarkers for diagnosing SA-AKI, such as NGAL, L-FABP, and cystatin C, they often require expensive testing and may not be readily available. Furthermore, continuous urine output monitoring, a key component of the KDIGO criteria, may not always be feasible in critically ill patients due to challenges such as the need for catheter insertion or the high patient load in emergency settings. Therefore, we opted to use serum creatinine as a surrogate marker, which remains a standard and widely accessible parameter for AKI diagnosis in various clinical settings. This approach ensures that the study's findings are applicable to routine clinical practice, especially in environments with limited resources.

Sepsis was defined according to the Sepsis-3 criteria, characterized by life-threatening organ dysfunction caused by a dysregulated host response to infection, and identified by an increase of ≥2 points in the SOFA score (13).

SA-AKI was diagnosed according to the ADQI 2023 criteria, defined as acute kidney injury (based on KDIGO 2012 guide-

lines) that developed within seven days of sepsis diagnosis (14, 15).

2.6. Statistical Analysis

The required sample size for evaluating the diagnostic performance of the studied biomarkers was estimated based on expected sensitivity and specificity. Assuming a sensitivity or specificity of 70%, with a 95% confidence level and a precision (margin of error) of ± 5%, the minimum sample size was calculated to be 323 patients using the formula: $n = Z^2 \times p(1 - p) / d^2$. With a total of 564 septic patients included in the study, the sample size was sufficient to provide reliable estimates of diagnostic accuracy.

Statistical analyses were conducted using IBM SPSS Statistics for Windows, version 23 (IBM Corp., Armonk, NY, USA), MedCalc Statistical Software version 22.1.3 (MedCalc Software Ltd, Ostend, Belgium), and Stata version 15 (StataCorp, College Station, TX, USA). Categorical variables were expressed as counts and percentages, while continuous variables were reported as mean ± standard deviation or median with interquartile range depending on the distribution. The Shapiro–Wilk test was used to assess normality. Group comparisons were performed using the Chi-square or Fisher's exact test for categorical variables and the Student's t-test or Mann–Whitney U test for continuous variables, as appropriate.

ROC curves were constructed to evaluate the discriminative performance of lactate, albumin, and derived indices (LAR, sCAR, NEWS-Lactate). The area under the ROC curve (AUC) with 95% confidence intervals (CIs) was reported. Optimal cut-off values were determined using Youden's index, and corresponding sensitivity, specificity, and predictive values were calculated. DeLong's test was used to statistically compare AUCs between models, and was performed using MedCalc software.

To determine independent predictors of sepsis-associated acute kidney injury (SA-AKI), a multivariable logistic regression analysis was conducted. Variables with $p < 0.10$ in univariate analysis and those with clinical significance were included in the model. Collinearity among variables was assessed using the variance inflation factor (VIF), and predictors with VIF > 5 were excluded to minimize multicollinearity. Linearity of continuous variables with the logit of the outcome was tested using the Box-Tidwell method. The final model was evaluated using the Hosmer–Lemeshow goodness-of-fit test, and adjusted odds ratios (ORs) with 95% CIs were reported. Missing data were minimal (<5%) and handled by complete-case analysis. A two-tailed p-value < 0.05 was considered statistically significant.

3. Results

3.1. Baseline Characteristics of the Study Population

A total of 564 septic patients were included in the study, among whom 298 (52.8%) developed SA-AKI and 266 (47.2%) did not (figure 1). Table 1 compares the baseline characteristics of studied patients between two groups. The mean age was similar between groups (67.19 ± 14.69 vs. 67.33 ± 17.56 years, p = 0.445). Patients who developed SA-AKI had significantly lower GCS scores (12.70 ± 3.01 vs. 13.36 ± 2.68, p = 0.002) and higher heart rates (113.12 ± 23.79 vs. 107.30 ± 24.56 bpm, p = 0.004). The systolic blood pressure at the time of emergency department admission, before receiving any fluid resuscitation or vasopressor treatment, was significantly lower in the SA-AKI group compared to the non-SA-AKI group (85 [74–96] vs. 100 [79–123], p < 0.001). No significant differences were noted in temperature (p = 0.474), respiratory rate (p = 0.115), or total leukocyte count (p = 0.908) between the two groups.

Significant differences were observed in acid-base status, with the SA-AKI group having lower arterial pH (7.36 [7.25–7.43] vs. 7.42 [7.33–7.47], p < 0.001) and bicarbonate levels (18.50 [14.40–22.60] vs. 21.40 [18.40–24.70] mmol/L, p < 0.001), suggesting greater metabolic acidosis.

Severity scores, including SOFA (10 [8–13] vs. 9 [6–11], p < 0.001) and APACHE II (19 [15–26] vs. 15 [12–20], p < 0.001), were significantly higher in patients with SA-AKI. The modified NEWS-Lactate score (NEWS-L) was markedly elevated in the SA-AKI group (11.5 [6.92–16] vs. 6.05 [4.48–8.43], p < 0.001). However, the difference in standard NEWS scores was not statistically significant (p = 0.745).

Patients with SA-AKI demonstrated significantly higher lactate concentrations (5.01 [1.82–8.05] vs. 2.51 [1.32–3.56] mmol/L, p < 0.001), urea (12.0 [7.71–16.1] vs. 10.0 [6.0–14.7] mmol/L, p = 0.019), creatinine (155.0 [99.0–252.0] vs. 124.5 [80.0–186.0] μmol/L, p = 0.004), and PCT levels (33.33 [7.25–94.15] vs. 16.12 [4.16–48.95] ng/mL, p = 0.001). Bilirubin was also slightly higher among patients with SA-AKI (20.0 [12.0–32.0] vs. 15.0 [10.0–31.0] μmol/L, p = 0.040). Conversely, albumin concentrations were significantly lower in the SA-AKI group (29.16 [25.51–32.21] vs. 31.25 [29.01–35.78] g/L, p < 0.001).

3.2. Albumin-based biomarkers

Table 2 compare the albumin-based biomarkers between groups. All four albumin-based biomarker ratios including LAR, sCAR, BAR, and PAR were significantly elevated in patients who developed SA-AKI. The median LAR in the SA-AKI group was 0.178 [0.087–0.294], compared to 0.064 [0.041–0.102] in the non-AKI group (p < 0.001). Similarly, sCAR (5.09 [3.42–8.71] vs. 4.11 [2.58–6.00], p < 0.001), BAR (0.404 [0.267–0.651] vs. 0.313 [0.206–0.473], p < 0.001), and PAR (1.196 [0.241–3.310] vs. 0.496 [0.116–1.657], p < 0.001) were all significantly higher in the SA-AKI group. The product

of PCT and lactate (PCT × Lactate) was also notably greater in the SA-AKI group (168.2 [30–488.4] vs. 34.9 [6.6–141.7], $p < 0.001$), highlighting the interaction between infection severity and tissue hypoperfusion.

3.3. Discriminative Ability of Biomarkers and Clinical Scores

To further evaluate the diagnostic performance of the biomarkers and scoring systems in predicting SA-AKI, receiver operating characteristic (ROC) curve analysis (figure 2, table 3) demonstrated that the LAR had the highest discriminative ability for predicting SA-AKI, with an AUC of 0.800 (95% CI: 0.765–0.835, $p < 0.001$). The NEWS-L score also showed strong predictive performance (AUC = 0.772, 95% CI: 0.734–0.809, $p < 0.001$). Standard lactate measurement alone yielded a moderate AUC of 0.696, while the PCT × Lactate index had an AUC of 0.677. Traditional scores such as SOFA and APACHE II showed moderate discriminative abilities, with AUCs of 0.637 and 0.634, respectively. Among the albumin-based ratios, sCAR, BAR, and PAR showed modest predictive performance, with AUCs of 0.599, 0.590, and 0.596, respectively. Albumin alone was a poor predictor of SA-AKI (AUC = 0.368), suggesting that its clinical relevance increases when integrated into composite indices. The NEWS score, without the inclusion of lactate, had limited discriminative value (AUC = 0.508, $p = 0.747$).

Using the optimal cutoff value of 0.101 for LAR yielded a sensitivity of 70.5% and specificity of 70.3%, whereas a NEWS-L cutoff of 7.11 provided a sensitivity of 71.1% and specificity of 63.2%, reinforcing their usefulness in early identification of SA-AKI (table 4).

A multivariable logistic regression was conducted to evaluate the association between biomarker-based indices and the development of sepsis-associated acute kidney injury (SA-AKI), adjusting for clinically relevant and statistically significant variables from the univariate analysis. As shown in table 5, the LAR remained a strong independent predictor of SA-AKI (OR: 5.65, 95% CI: 3.93 – 8.11, $p = 0.001$). Similarly, the NEWS-Lactate score was significantly associated with SA-AKI with OR of 3.62 (95% CI: 1.52–8.63, $p = 0.004$). In contrast, other variables including APACHE II, SOFA, sCAR, PAR, and the interaction term PCT × Lactate were not statistically significant in the final model ($p > 0.05$ for all).

4. Discussion

This study investigated the prognostic value of several laboratory-based ratios and clinical severity scores in predicting SA-AKI, a common and serious complication in septic patients. Our findings demonstrate that among the evaluated markers, LAR exhibited the highest AUC (0.800, 95% CI: 0.765–0.835), indicating good predictive performance for SA-AKI. While numerically higher than NEWS-Lactate (AUC = 0.772, 95% CI: 0.734–0.809), the overlap in their confidence intervals suggests that their predictive abilities might not be statistically significantly different. Both LAR and NEWS-Lactate outperformed traditional biomarkers and established severity scoring systems.

The incidence of SA-AKI in our cohort was 52.8%, consistent with prior literature reporting rates ranging from 40% to 60% among critically ill septic patients (16, 17). As shown in Table 1, patients who developed SA-AKI presented with significantly higher illness severity at baseline, characterized by lower Glasgow Coma Scale scores, higher heart rates, elevated systolic blood pressure, lower pH and bicarbonate levels, and increased levels of lactate, urea, creatinine, and PCT (all $p < 0.05$). Although albumin levels were significantly lower in the AKI group ($p < 0.001$), the prevalence of hypoalbuminemia in both groups highlights the importance of considering ratios like LAR (18). The elevated lactate levels in the AKI group underscore the role of hypoperfusion and metabolic stress in SA-AKI pathogenesis. However, in this study, we only assessed the lactate levels at the time of patient admission to the emergency department and did not monitor the changes in lactate concentrations related to resuscitation. Among the studied biomarkers, the lactate/albumin ratio stood out with the highest area under the ROC curve (AUC = 0.800), indicating good discriminatory ability. LAR is an emerging marker that reflects both tissue hypoperfusion (via lactate) and nutritional/inflammatory status (via albumin). In the multivariable logistic regression analysis, we found that LAR was an independent predictor of sepsis-associated acute kidney injury (SA-AKI). With an odds ratio of 5.65 (95% CI: 3.93 – 8.11), each unit increase in LAR was associated with a nearly six-fold increase in the odds of developing SA-AKI. This finding is consistent with previous studies highlighting the prognostic value of LAR in critically ill patients, where elevated lactate reflects tissue hypoperfusion and metabolic stress, while hypoalbuminemia indicates inflammation and poor nutritional status. LAR's superior performance compared to individual measurements of lactate or albumin supports the value of using composite biomarkers that reflect multiple pathophysiologic mechanisms in sepsis (19).

In addition to LAR, the NEWS-Lactate score also demonstrated good predictive accuracy (AUC = 0.772), reinforcing the benefit of incorporating biochemical markers into bedside clinical assessments. The original NEWS was designed for early detection of clinical deterioration, but its predictive value for SA-AKI alone was limited in our study (AUC = 0.508). In the multivariable logistic regression analysis, the NEWS-Lactate score also remained significantly associated with SA-AKI (OR 3.62; 95% CI: 1.52–8.63). This suggests that combining clinical observations with metabolic parameters may enhance early risk stratification. The modification by including lactate significantly improved its prognostic utility, aligning with recent literature emphasizing the role of hyperlactatemia in sepsis risk stratification (20).

The other albumin-based ratios (sCAR, BAR, and PAR) also showed statistically significant differences between SA-AKI and non-AKI groups, though their AUCs were modest (approximately 0.59–0.60). These ratios reflect the interplay

between renal function, inflammation, and nutritional status, and their inclusion may enhance composite risk models. However, they did not perform as well as LAR or NEWS-Lactate in this study. Traditional severity scores such as SOFA and APACHE II exhibited only moderate predictive capacity (AUCs around 0.61), suggesting limitations in their ability to capture early renal involvement in sepsis. These scores, while widely used for mortality risk stratification(21), may not sufficiently reflect the dynamic and multifactorial nature of kidney injury in septic patients.

At a cutoff point of 0.101, LAR demonstrated a sensitivity of 70.5% and a specificity of 70.3% for predicting SA-AKI. NEWS-Lactate, at a cutoff of 7.11, showed a sensitivity of 71.1% and a specificity of 63.2%. This suggests that while both markers have comparable ability to identify patients who will develop SA-AKI, LAR at this specific threshold may offer a better balance between identifying true negatives and reducing false positives. Our findings suggest that simple, accessible markers such as LAR and NEWS-Lactate can offer valuable prognostic insights for early identification of SA-AKI in septic patients. Given their ease of calculation and reliance on commonly available laboratory tests, these indices could be readily incorporated into routine emergency and critical care workflows. Early recognition of patients at high risk for SA-AKI may facilitate timely interventions, including optimization of hemodynamic support, avoidance of nephrotoxic agents, and closer monitoring of renal function.

In this study, we demonstrated the superior prognostic value of the lactate/albumin ratio (LAR) and NEWS-Lactate score in predicting sepsis-associated acute kidney injury (SA-AKI) compared to traditional biomarkers and severity scores. The findings suggest that these simple, readily available indices could provide important insights for early identification and risk stratification of septic patients at high risk of developing AKI. Given the moderate to high accuracy of LAR and NEWS-Lactate, integrating these markers into routine clinical practice may enhance early recognition of patients who require closer monitoring and prompt intervention. Future prospective studies are needed to validate these findings and determine whether early interventions based on these scores can improve patient outcomes.

Prospective multicenter studies are warranted to validate the prognostic performance of LAR and NEWS-Lactate across diverse patient populations and clinical settings. Future research should also explore whether early interventions guided by these markers can improve renal outcomes and overall survival in patients with sepsis.

5. Limitations

This study has several limitations that should be acknowledged. First, the retrospective design and single-center setting in a military hospital may limit the generalizability of the findings to broader populations. Second, the inherent nature of a retrospective study introduces the potential for selection bias. Third, a major limitation is that data were collected at the time of initial emergency department admission, prior to the administration of specific treatments or resuscitation interventions. As a result, we were unable to assess the dynamic changes in lactate and albumin levels over time, which could have provided further insights into their prognostic value for SA-AK). This single time-point assessment limits our ability to evaluate the temporal relationship between these biomarkers and AKI development. Fourth, the diagnosis of AKI in this study was based solely on serum creatinine levels without consideration of urine output criteria, which may have led to underdiagnosis of some AKI cases, particularly those without significant increases in creatinine. Finally, the absence of external validation in an independent cohort requires caution when generalizing our results to other settings.

6. Conclusions

It seems that, the LAR and NEWS-Lactate are promising biomarkers for early detection of SA-AKI and may outperform conventional severity scores and standalone laboratory parameters.

7. Declarations

7.1. Acknowledgments

None.

7.2. Authors' Contributions

All authors listed have significantly contributed to the investigation, development, and writing of this article.

- Conceptualization: Duong Le Xuan, Hoa Do Thanh, Ghi Nguyen Hai, Duc Vu Anh.
- Data curation: Duong Le Xuan, Hoa Do Thanh, Ghi Nguyen Hai.
- Formal analysis: Duong Le Xuan, Hoa Do Thanh, Ghi Nguyen Hai.
- Supervision: Duong Le Xuan.
- Writing – original draft: Duc Vu Anh, Ghi Nguyen Hai.
- Writing – review & editing: Duong Le Xuan, Hoa Do Thanh, Ghi Nguyen Hai.
- All authors read and approved the final version of manuscript.

7.3. Ethics approval

The study was approved by 108 Military Center Hospital ethics committee in biomedical research, N0 310/QĐ-BV.

7.4. Funding statement

None

7.5. Data availability statement

Data will be made available on request.

7.6. Declaration of competing interest

The authors declare no conflict of interest.

7.7. Using artificial intelligence chatbots

Used artificial intelligence chatbots in language editing.

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Table 1: Comparing the baseline characteristics of studied patients between cases with and without sepsis associated acute kidney injury (SA-AKI)

Variable	SA-AKI		P value
	No (n=266)	Yes (n=298)	
Age (years)			
Mean ± SD	67.33 ± 17.56	67.19 ± 14.69	0.445
Glasgow coma Score			
Mean ± SD	13.36 ± 2.68	12.70 ± 3.01	0.002
Vital signs			
Heart rate (bpm)	107.30 ± 24.56	113.12 ± 23.79	0.004
Temperature (°C)	37.49 ± 0.98	37.43 ± 0.91	0.474
Systolic blood pressure (mmHg)	100 [79–123]	85 [74–96]	0.000
Respiratory rate (breaths/min)	20 [18–23]	20 [18–24]	0.115
Blood gas analysis			
pH	7.42 [7.33–7.47]	7.36 [7.25–7.43]	0.000
HCO (mmol/L)	21.40 [18.40–24.70]	18.50 [14.40–22.60]	0.000
Lactate (mmol/L)	2.51 [1.32–3.56]	5.01 [1.82–8.05]	0.000
Laboratory parameters			
Urea (mmol/L)	10.0 [6.0–14.7]	12.0 [7.71–16.1]	0.019
Creatinine (μmol/L)	124.50 [80.0–186.0]	155.0 [99.0–252.0]	0.004
Procalcitonin (ng/mL)	16.12 [4.16–48.95]	33.33 [7.25–94.15]	0.001
Bilirubin (μmol/L)	15.0 [10.0–31.0]	20.0 [12.0–32.0]	0.040
Albumin (g/L)	31.25 [29.01–35.78]	29.16 [25.51–32.21]	0.000
White blood cell ($\times 10^9$/L)	13.21 [9.87–17.99]	13.87 [8.33–19.42]	0.908
Severity scores			
SOFA Score	9 [6–11]	10 [8–13]	0.000
APACHE II	15 [12–20]	19 [15–26]	0.000
NEWS Score	4 [3–6]	5 [3–9]	0.745
NEWS-L Score	6.05 [4.48–8.43]	11.5 [6.92–16]	0.000

Data are presented as mean ± standard deviation (SD) or median [interquartile range (IQR)].
SOFA: Sequential Organ Failure Assessment. APACHE II: Acute Physiology and Chronic Health Evaluation II.
NEWS: National Early Warning Score. NEWSL: National Early Warning Score combined with Lactate.

Table 2: Comparing the albumin-based biomarkers between cases with and without sepsis associated acute kidney injury (SA-AKI)

Variable	SA-AKI		P value
	No (n=266)	Yes (n=298)	
LAR (mmol/L per g/L)	0.064 [0.041–0.102]	0.178 [0.087–0.294]	0.000
sCAR (μmol/L per g/L)	4.11 [2.58–6.00]	5.09 [3.42–8.71]	0.000
BAR (mmol/L per g/L)	0.313 [0.206–0.473]	0.404 [0.267–0.651]	0.000
PCT×Lactate (ng/mL × mmol/L)	34.9 [6.6–141.7]	168.2 [30–488.4]	0.000
PAR (ng/mL per g/L)	0.496 [0.116–1.657]	1.196 [0.241–3.310]	0.000

Data are presented as median [interquartile range (IQR)]. LAR = Lactate/ Albumin; sCAR = Serum Creatinine/ Albumin;
BAR = Blood Urea Nitrogen/ Albumin; PAR = Procalcitonin/ Albumin; PCT × Lactate = Procalcitonin × Lactate.

Table 3: Discriminative ability of clinical and laboratory variables in predicting the sepsis associated acute kidney injury (SA-AKI)

Variable	AUC	95% CI	p-value
Lactate (mmol/L)	0.696	0.652–0.740	0.000
Albumin (g/L)	0.368	0.322–0.413	0.000
PCT (ng/mL)	0.582	0.535–0.629	0.001
Urea (mmol/L)	0.557	0.510–0.605	0.019
Creatinine (μmol/L)	0.569	0.522–0.616	0.004
SOFA score	0.637	0.591–0.682	0.000
APACHE II score	0.634	0.589–0.680	0.000
LAR (mmol/L per g/L)	0.800	0.765–0.835	0.000
NEWS-Lactate	0.772	0.734–0.809	0.000
NEWS Score	0.508	0.460–0.556	0.747
sCAR (μmol/L per g/L)	0.599	0.553–0.646	0.000
BAR (mmol/L per g/L)	0.590	0.543–0.637	0.000
PAR (ng/mL per g/L)	0.596	0.550–0.643	0.000
PCT × Lactate (ng/mL × mmol/L)	0.677	0.633–0.721	0.000

The DeLong test was applied to statistically compare the area under the ROC curve (AUC) of LAR with several indicators, including lactate, SOFA score, APACHE II score, and NEWS-L score. The resulting p-values were 0.04, 0.005, 0.009, and 0.3, respectively. LAR = Lactate/ Albumin; sCAR = Serum Creatinine/ Albumin; BAR = Blood Urea Nitrogen/ Albumin; PAR = Procalcitonin/ Albumin; PCT × Lactate = Procalcitonin × Lactate. SOFA: Sequential Organ Failure Assessment.; APACHE II: Acute Physiology and Chronic Health Evaluation, II; NEWS: National Early Warning Score; NEWS-Lactate: National Early Warning Score combined with Lactate; CI: confidence interval.

Table 4: Screening performance characteristics of Lactate/ Albumin (LAR) and National Early Warning Score combined with Lactate (NEWS-L) in predicting the sepsis associated acute kidney injury (SA-AKI)

Characteristics	LAR (cut-off = 0.101)		NEWS-L (cut-off = 7.11)	
	Value	95% CI	Value	95% CI
Sensitivity	70.47	64.94 – 75.59	71.14	65.64 – 76.22
Specificity	70.30	64.42 – 75.73	63.16	57.05 – 68.97
Positive Predictive Value	72.66	68.54 – 76.43	68.39	64.53 – 72.01
Negative Predictive Value	68.00	63.69 – 72.03	66.14	61.52 – 70.48
Positive Likelihood Ratio	2.37	1.94 – 2.90	1.93	1.62 – 2.30
Negative Likelihood Ratio	0.42	0.35 – 0.51	0.46	0.37 – 0.56
Accuracy	70.39	66.43 – 74.13	67.38	63.33 – 71.23

CI: confidence interval.

Table 5: Multivariate logistic regression analysis of sepsis associated acute kidney injury (SA-AKI) independent predictors

Variable	Odds ratio	95% CI	p-value
LAR	5.65	3.93 – 8.11	0.001
sCAR	0.962	0.847 – 1.092	0.550
PAR	0.699	0.390 – 1.252	0.228
APACHE II Score	0.983	0.928 – 1.041	0.551
SOFA Score	1.050	0.964 – 1.143	0.261
NEWS-Lactate	3.62	1.52 – 8.63	0.004

LAR = Lactate/ Albumin; sCAR = Serum Creatinine/ Albumin; PAR = Procalcitonin/ Albumin. SOFA: Sequential Organ Failure Assessment.; APACHE II: Acute Physiology and Chronic Health Evaluation II; NEWS-Lactate: National Early Warning Score combined with Lactate; CI: confidence interval.

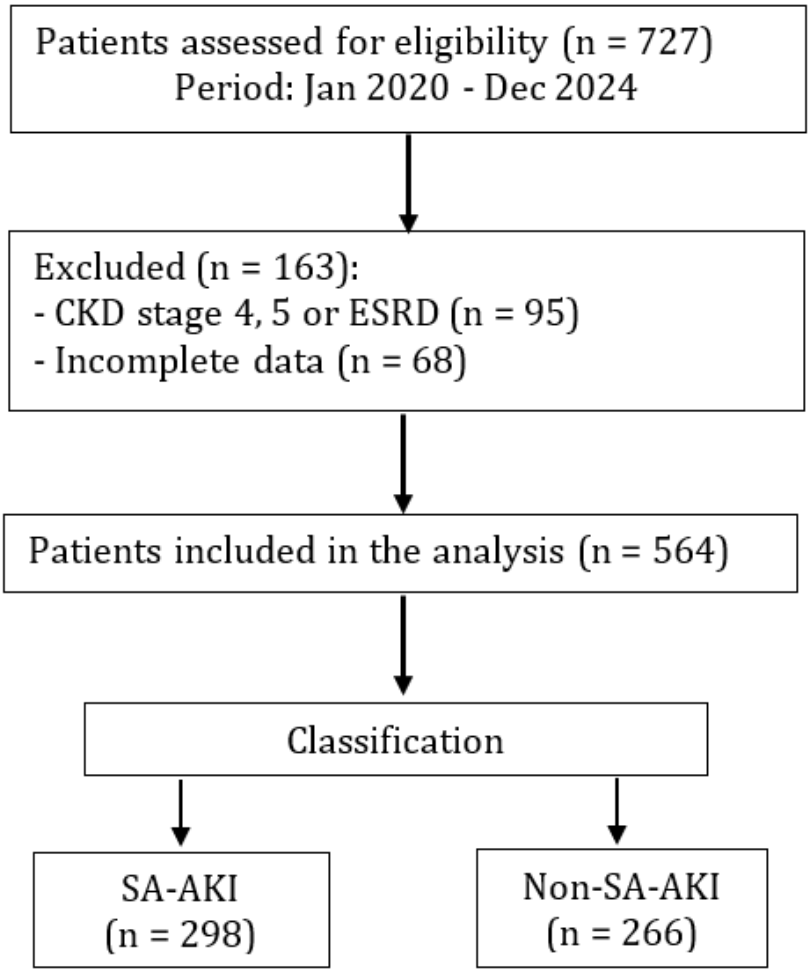

Figure 1: Flow diagram of patient selection. CKD: chronic kidney disease; ESRD: end stage renal disease; SA-AKI: sepsis associated acute kidney injury.

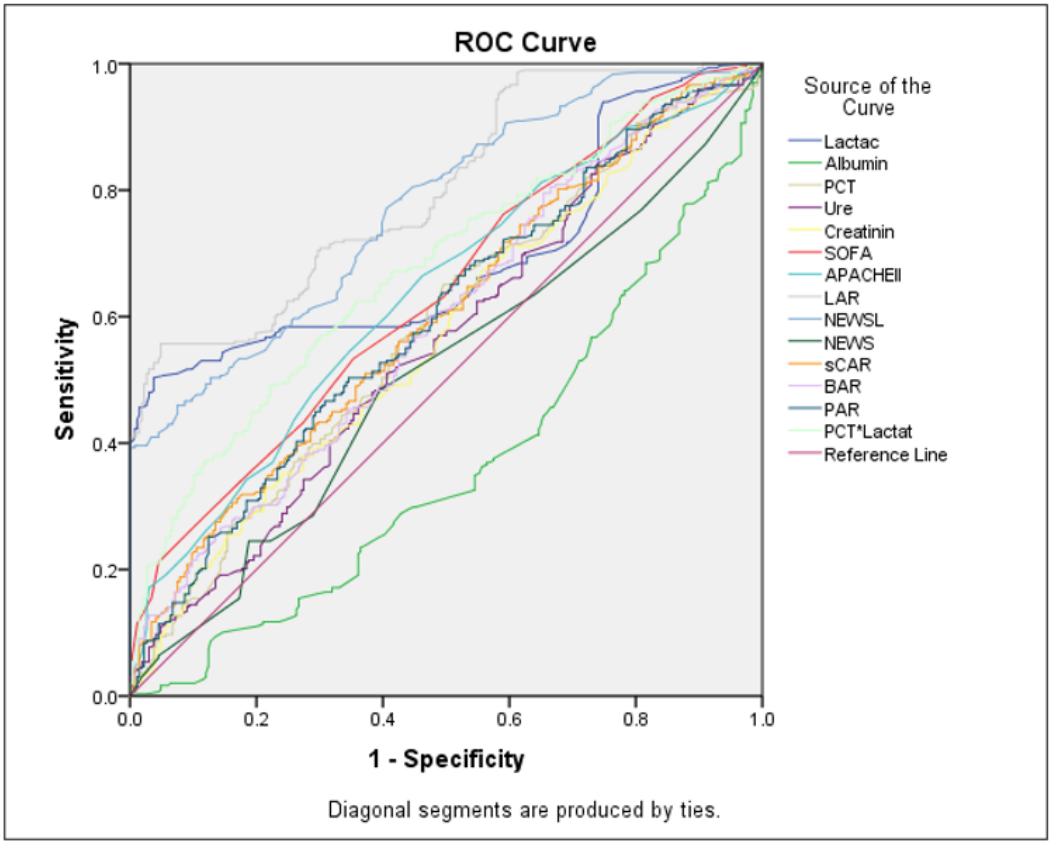

Figure 2: The area under the receiver operating characteristics (ROC) curve of different biomarkers in predicting the sepsis associated acute kidney injury (SA-AKI). LAR = Lactate/ Albumin; sCAR = Serum Creatinine/ Albumin; BAR = Blood Urea Nitrogen/ Albumin; PAR = Procalcitonin/ Albumin; PCT × Lactate = Procalcitonin × Lactate. SOFA: Sequential Organ Failure Assessment.; APACHE II: Acute Physiology and Chronic Health Evaluation II; NEWS: National Early Warning Score; NEWSL: National Early Warning Score combined with Lactate; Ure: urea.