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Lactate–albumin ratio improves combined predictive value of qSOFA and MEWS for 30-day mortality in ICU patients with sepsis

A retrospective cohort study

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Abstract

Evaluating disease severity and predicting adverse outcomes using various risk prediction tools in early disease stages is essential to reduce sepsis-related mortality. Unfortunately, there is still no clear consensus on the best score. The present study aimed to develop and validate a multivariable risk prediction model for 30-days mortality by combining the lactate-to-albumin (L/A) ratio, Modified Early Warning Score (MEWS), and quick Sequential Organ Failure Assessment (qSOFA) in sepsis patients admitted to the intensive care unit (ICU). This retrospective study included ICU patients with suspected sepsis. We computed L/A ratio, MEWS, and qSOFA within 24 hours of ICU admission. Patients were followed until either death/hospital discharge or 30 days, whichever came first. The predictive performance of each scoring system and their combinations was assessed using logistic regression and receiver operating characteristic curve analyses. A total of 130 patients with sepsis admitted to the ICU were included in the study. The mortality rate was 63.07% (82/130). A higher L/A ratio, MEWS, and qSOFA were found to be associated with mortality in ICU sepsis patients. A statistically significant difference in terms of predicting mortality was demonstrated in the pairwise comparison after combining the L/A ratio with both the qSOFA and MEWS (difference between areas: –0.098, $P = .011$ and difference between areas: –0.098, $P = .013$ respectively). Mortality models combining L/A ratio with selected clinical variables have improved mortality prediction performance compared with models that use MEWS and qSOFA alone. The L/A ratio at ICU admission provide valuable prognostic information for predicting 30-days mortality in sepsis patients. Combining these ratio with MEWS and qSOFA improves the accuracy of predicting mortality in patients with sepsis.

Abbreviations: AUC = area under the curve, AUROC = area under the receiver operating characteristic curve, CI = confidence interval, DBA = difference between areas, ICU = intensive care unit, L/A ratio = lactate-to-albumin ratio, MEWS = Modified Early Warning Score, NPV = negative predictive value, OR = odds ratio, qSOFA = quick Sequential Organ Failure Assessment, ROC = receiver operating characteristic, SIRS = systemic inflammatory response syndrome, SOFA = Sequential Organ Failure Assessment.

Keywords: Intensive care unit, Lactate/albümin ratio, MEWS, Sepsis

1. Introduction

Sepsis is characterized by life-threatening organ failure that occurs due to the host's unregulated response to an infection. Despite advancements in medical care, sepsis remains the leading cause of death among critically ill patients in hospitals and represents a significant public health challenge worldwide.[1] This heightened mortality rate is likely attributable to the overall poorer health status of intensive care unit (ICU) patients. The rise in morbidity and mortality can be linked to delays in diagnosis and treatment, which are often caused by low clinical suspicion and atypical, subtle manifestations of the disease.[2] Although widely accepted clinical guidelines have improved the detection rate of sepsis patients,

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the diagnosis of sepsis in critically ill patients remains challenging.[3] Considering these challenges, it is understandable that effective treatment policies depend on the early and accurate assessment of sepsis.

Rapid identification of high-risk patients continues to pose difficulty, and various efforts are underway to uncover easily accessible and cost-effective biomarkers for predicting outcomes and stratifying the risk of septic patients. In this context, various prediction models, including the Modified Early Warning Score (MEWS), National Early Warning Score (NEWS), Sequential Organ Failure Assessment (SOFA), Quick Sequential Organ Failure Assessment (qSOFA), Acute Physiological and Chronic Health Evaluation, and the lactate-to-albumin (L/A) ratio, are presented as valuable dynamic scores for predicting mortality in sepsis patients within the ICU. All of these scoring systems utilize clinical and laboratory data collected either from patients' initial days in the ICU or throughout their entire ICU stay.[4] Among these models, we chose L/R ratio, MEWS, and qSOFA scores to assess a patient's organ function and the likelihood of failure or mortality during their ICU stay.

Early warning scores (EWSs) and qSOFA were created for bedside assessment as track-and-trigger systems to facilitate the early detection of patient deterioration. MEWS is one of the most widely used EWSs for adult patients. It has been validated in various critically ill patients and has demonstrated its ability to predict hospital admissions and mortality outcomes, especially in ICU settings.[5,6] qSOFA is another important scoring system that assists in monitoring a patient's health status during their ICU stay. It is utilized to evaluate organ function and the likelihood of failure. It serves as a quick and simplified version of the SOFA score, designed to help identify critically ill patients with sepsis who are at high risk and require a higher level of care. Originally developed for assessing septic patients, recent studies have highlighted its effectiveness in predicting mortality across various diseases.[7–9]

Elevated blood lactate levels and reduced serum albumin concentrations are well-established indicators of increased morbidity and mortality among ICU patients. Due to the limitations of lactate as a single predictive marker and the necessity for a surrogate indicator of disease severity, the L/A ratio has recently been proposed as a predictive tool for patients with sepsis.[10] Studies have demonstrated that the L/A ratio is likely to be a better discriminator than lactate or albumin alone and correlates with poorer outcomes in cases of sepsis. Recent publications have validated this association across various conditions, including traumatic brain injury, cardiac arrest, cirrhosis, and pancreatitis.[11–16] However, there is still scarce evidence demonstrating the importance of L/A ratio as a prognostication tool in sepsis patients admitted to the ICU. Therefore, the main objective of the present study was to evaluate whether the combination of the L/A ratio with MEWS and qSOFA improves the prediction of 30-day mortality in ICU sepsis patients. We hypothesized that such a combination would provide better prognostic accuracy than any score used alone. To test this hypothesis, we developed and validated a multivariable risk stratification model integrating the L/A ratio, MEWS, and qSOFA in our patient group.

2. Materials and methods

2.1. Study design and patient recruitment

This retrospective cohort study was conducted at the Training and Research Hospital of Canakkale Onsekiz Mart University following approval from the local ethics committee (Approval number 2023/17-26). We retrospectively analyzed clinical and laboratory variables of consecutive sepsis patients admitted into our ICU during the period of September 2021 to December 2023. Our ICU has 8 beds and is staffed by 2 full-time, board-certified intensivists.

Data on the clinical, laboratory, and demographic features of sepsis patients were collected through the Canakkale Onsekiz Mart University Hospital Information and Management System. These patient data, sourced from the hospital's electronic health records, allowed us to analyze various variables including age, gender, vital parameters at ICU admission, hospital length of stay, source of ICU admission, comorbidities, type and sites of infection, interventions administered including antibiotics and mechanical ventilation, complete blood cell counts, biochemical parameters including glucose, blood urea nitrogen, creatinine, initial serum lactate, albumin, total protein, total bilirubin, and liver transaminase activity. Variables associated with mortality, treatments used by patients, chronic medical histories, and discharge status, were also recorded. Clinical examinations and initial laboratory tests were performed within 12 hours of ICU admission. All patients were monitored from the time of admission until their discharge from the hospital or death. Sepsis was defined in accordance with the Third International Consensus Definitions for Sepsis and Septic Shock (Sepsis-3) guidelines as the presence of an infection along with indications of organ dysfunction, which is indicated by a SOFA score of 2 or more points.[17]

The inclusion criteria for study participation were being over 18 years of age, having a confirmed diagnosis of sepsis or septic shock upon ICU admission, and undergoing measurement of both serum lactate and serum albumin within 6 hours of admission, along with having a complete set of descriptive data. Patients were excluded if they did not meet all of the inclusion criteria or if they met one or more of the following exclusion criteria: (1) identified as septic patients but did not meet sepsis-3 criteria; (2) pregnant patients; (3) patients with a malignant tumor; (4) patients with missing data; (5) patients with a "do-not-resuscitate" status. The flow chart of the study selection process is summarized in Figure 1.

2.2. Screening tools and outcome measures

Clinical severity of patients were measured by 3 scoring systems; L/A ratio, MEWS, and qSOFA. Initial lactate and albumin measurements were the earliest values obtained within 6 hours following ICU admission. The primary factor of interest, L/A ratio, was calculated by dividing the initial serum lactate by the initial serum albumin. The MEWS score was calculated according to the method described by Subbe et al.[18] In brief, 4 physiological variables (systolic blood pressure, pulse rate, temperature, and respiratory rate) along with an assessment of the level of consciousness, were assigned a numerical weighting ranging from 0 to 3. The total MEWS score was then derived by summing the 5 sub-scores (0–14; higher = greater hemodynamic instability). The qSOFA was calculated according to the Third International Consensus Definitions for Sepsis and Septic Shock.[17] The qSOFA score was assessed for all ICU patients using 3 clinical criteria (respiratory rate ≥ 22/min, altered mental status (Glasgow Coma Scale < 15), and systolic blood pressure ≤ 100 mm Hg) with each criterion assigned 1 point. The qSOFA score was calculated using the most critical values of these 3 clinical variables recorded during the first 24 hours of ICU admission.

The primary outcome of this study was defined as overall mortality at day 30 days after admission in ICU.

2.3. Statistical analysis

Descriptive statistics were expressed as mean (standard deviation) for variables with normal distribution and as frequencies and percentages (%) for categorical variables. Differences in mean values between groups were assessed using the Student *t* test. Categorical data were analyzed using Pearson chi-square test or Fisher exact test, as appropriate. The predictive

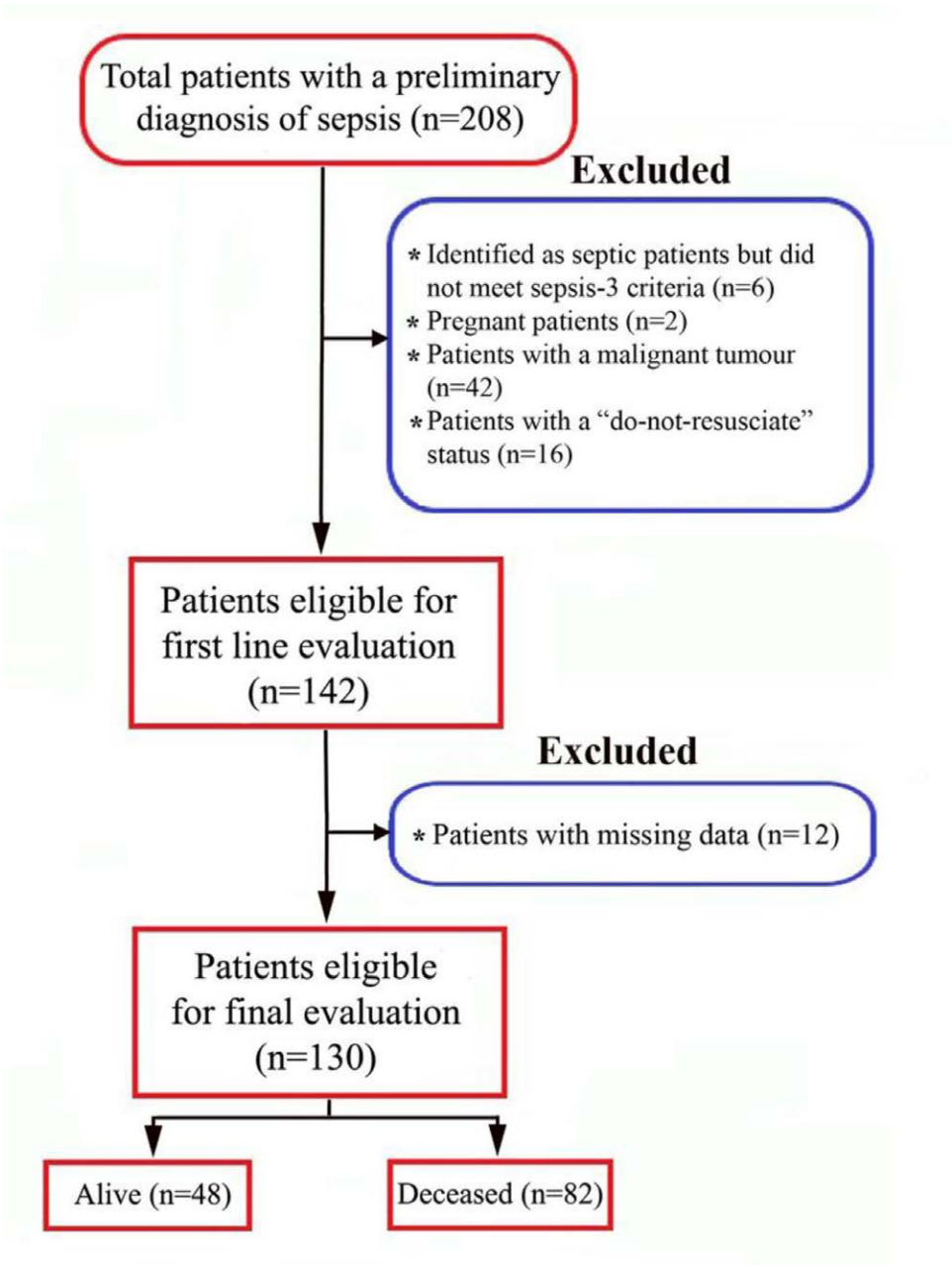

Figure 1. The study flowchart of patient selection.

accuracy of 30-days mortality in ICU sepsis patients was evaluated using receiver operating characteristic (ROC) curves and the area under the curve (AUC). Odds ratios (ORs) with 95% confidence intervals (CIs) for independent clinical parameters were calculated through univariate and multivariate logistic regression analyses to predict 30-days mortality. A multivariate logistic regression model was constructed via stepwise variable selection for variables with a univariate *P*-value < .25. Model fit was assessed using the Hosmer–Lemeshow test, with a non-significant *P*-value indicating adequate model calibration. Covariate-adjusted ROC curve analyses were conducted using multivariate logistic regression to determine diagnostic accuracy and compute the areas under the ROC curves (AUROCs). Pairwise comparisons of AUROCs were performed using the DeLong test. All statistical analyses were carried out using SPSS version 26.0 for Windows (IBM Corp., Armonk, NY) and R software version 3.6.2. Statistical significance was defined as a *P*-value < .05.

3. Results

A total of 130 septic patients were included in the final analysis (Fig. 1). The mean age was 73.6 ± 12.1 years; 56.9% were male. Baseline demographic and clinical characteristics are summarized in Table 1. The overall 30-day mortality in hospital rate was 63.1%, and the overall mean age of deceased patients was 75.2 ± 12.0. Of the deceased patients, 44 (59.5%) were male. As anticipated, the patients who succumbed were older and exhibited a greater number of comorbidities and complications. The mean prognostic scores, namely MEWS, QSOFA, and L/A ratio, were found to be higher in deceased patients, as seen in Table 2. Serum lactate levels at admission were significantly higher ($P < .001$) in deceased ICU patients. As demonstrated in Table 3, we performed univariable and multivariable logistic regression analyses along with L/A ratio, MEWS, and qSOFA to assess the impact of various demographic and clinical factors on 30-day mortality. Univariable analysis revealed that each year of age increased the 30-day mortality rate by 3% (95%

Table 1

Demographic and clinical characteristics of study patients.

Variables	All patients (n = 130)
Age (yr)	73.6 ± 12.1
Male, n (%)	74 (56.9)
Vital signs at ICU admission	
Heart rate (/min)	104.4 ± 22.3
Respiratory rate (/min)	22.4 ± 4.6
SBP (mm/Hg)	102.2 ± 24.5
MAP (mm/Hg)	76.5 ± 17.3
Temperature (°C)	36.8 ± 0.8
Complete blood count	
WBC ($\times 10^3$/μL)	14.6 ± 9.1
Hemoglobin (g/dL)	10.3 ± 2.1
Platelet ($\times 10^3$/uL)	216.6 ± 150.4
Biochemical measurements	
Blood glucose (mg/dL)	155.0 ± 104.9
Urea (mg/dL)	112.4 ± 63.7
Creatinine (mg/dL)	2.3 ± 1.7
ALT (U/L)	91.5 ± 336.3
AST (U/L)	149.5 ± 506.2
LDH (U/L)	414.5 ± 477.7
Albümin (g/dL)	2.63 ± 0.52
CRP (mg/L)	201.4 ± 100.8
Sedimentation (mm/h)	55.8 ± 35.7
Procalcitonin (ng/mL)	19.4 ± 29.8
Blood gas analysis	
pH	7.34 ± 0.13
HCO_3 (mmol/L)	20.5 ± 6.6
Lactate (mmol/L)	3.3 ± 3.7
Illness acuity assessment tools	
MEWS	4.8 ± 2.2
qSOFA	2.25 ± 0.44
L/A ratio	1.34 ± 1.63

CRP = C-reactive protein, L/A ratio = the lactate-to-albumin ratio, LDH = lactate dehydrogenase, MAP = mean arterial pressure, MEWS = Modified Early Warning Score, qSOFA = quick Sequential Organ Failure Assessment, SBP = systolic blood pressure, WBC = white blood cell.

Table 2

Comparison of baseline characteristics of sepsis patients according to survival status.

	Patients alive (n = 48)	Patients deceased (n = 82)	*P*-value
Age (yr)	70.8 ± 11.9	75.2 ± 12.0	.043
Gender (M)	30 (40.5 %)	44 (59.5 %)	.326
Heart rate (/min)	102.3 ± 21.6	105.6 ± 22.8	.426
Respiratory rate (/min)	22.0 ± 4.6	22.6 ± 4.6	.369
SBP (mm/Hg)	102.5 ± 25.7	102.1 ± 23.9	.930
MAP (mm/Hg)	75.6 ± 17.7	77.0 ± 17.1	.660
Temperature (°C)	36.8 ± 0.9	36.8 ± 0.7	.917
Urea (mg/dL)	90.8 ± 58.9	124.9 ± 63.4	.003
AST (U/L)	48.5 ± 72.3	208.5 ± 628.8	.025
pH	7.37 ± 0.13	7.32 ± 0.13	.017
Lactate (mmol/L)	2.0 ± 1.8	4.0 ± 4.2	<.001
MEWS	4.2 ± 2.1	5.2 ± 2.2	.016
qSOFA	2.12 ± 0.48	2.32 ± 0.52	.005
L/A ratio	0.73 ± 0.53	1.70 ± 1.92	<.001

L/A ratio = the lactate-to-albumin ratio, MAP = mean arterial pressure, MEWS = Modified Early Warning Score, qSOFA = quick Sequential Organ Failure Assessment, SBP = systolic blood pressure.

CI: 1.001–1.063). Additionally, a 1-point increase in MEWS and L/A ratio was associated with ×1.247 and ×2.501 increased mortality rate, respectively. After univariable analysis, we performed a multivariable logistic regression analysis. In the final step, only MEWS and L/A ratio were kept in the multivariate model for mortality prediction in ICU sepsis patients.

Table 4 shows the diagnostic performance of several parameters for mortality prediction based on ROC analysis. The optimal cutoff for MEWS was ≥ 4 (sensitivity: 81.7%, specificity: 52.1%), for L/A ratio was ≥ 0.88 (sensitivity: 59.8%, specificity: 83.3%), and for qSOFA was > 2 (sensitivity: 32.9%, specificity: 87.5%). Similar analysis for procalcitonin, lactate, and urea was also conducted in relation to mortality rates (Table 4). The difference between AUROCs was tested for significance via pairwise comparison of ROC curve analysis. Pairwise comparisons of the ROC curves revealed significant improvement in predictive performance when L/A ratio was added to qSOFA or MEWS (difference between areas [DBA]: –0.098, $P = .011$ and 0.013, respectively; Table 5).

A combined evaluation of MEWS and L/A ratio demonstrated notable differences in 30-day mortality across subgroups. The addition of L/A ratio significantly improved risk stratification within MEWS categories. Importantly, patients with MEWS ≥ 4 and L/A ratio ≥ 0.88 had a 35-fold higher risk of mortality compared to those with MEWS < 4 and L/A ratio < 0.88 (95% CI: 8.885–137.872).

The predictive accuracy of L/A ratio, MEWS, and qSOFA was further evaluated within several mortality models (Table 6). Initially, a base model was created to identify patients at high mortality risk considering factors such as advanced age, male gender, and elevated procalcitonin levels. Pairwise analysis showed that integrating the L/A ratio into the base model produced a significantly higher accuracy in predicting in-hospital mortality (DBA – 0.130, $P = .006$). Combining the L/A ratio to base model + MEWS and base model + qSOFA also yielded a significantly higher accuracy in predicting mortality (DBA– 0.089, $P = .012$ and DBA: –0.077, $P = .028$ respectively). Thus, combining the L/A ratio with the base model + MEWS + qSOFA demonstrated significant accuracy in predicting mortality (DBA: –0.063, $P = .043$; Table 6).

4. Discussion

This study investigated the prognostic significance of the L/A ratio in conjunction with MEWS and qSOFA for predicting mortality in sepsis patients admitted to the ICU. Our findings revealed that higher L/A ratio and MEWS are significantly associated with mortality, as evidenced by crude and adjusted multivariable logistic regression analyses. Meanwhile, qSOFA demonstrated a significant predictive capability not only as a standalone marker, it also improved the prognostic ability of MEWS across various models, as indicated in Table 6. Moreover, a qSOFA score above 2 exhibited high specificity (87.5%), though with low sensitivity (32.9%) for mortality prediction. Furthermore, predictive models that included the L/A ratio proved to be more accurate than those that did not. These results emphasize the importance of integrating a validated laboratory tool with established risk stratification scores to better assess the likelihood of severe critical deterioration in sepsis patients.

As established, sepsis, characterized by a dysregulated immune response to infection, remains a significant challenge, especially in ICU settings. Despite advancements in medical treatment, sepsis continues to produce high morbidity and mortality, highlighting the need for better risk stratification and personalized management strategies.[4,19] Sepsis is a major concern in ICUs due to its rapid progression and high mortality rate, especially in vulnerable patient populations. Early identification and appropriate management of sepsis is therefore essential for improving patient outcomes, which makes risk stratification crucial.

Risk stratification allows healthcare providers to categorize patients based on their likelihood of deterioration, guiding resource allocation and prioritizing interventions for those at the highest risk. Given the potential for rapid deterioration in septic patients, an accurate assessment of risk within the initial hours

of disease onset can significantly reduce ICU mortality rates and improve recovery outcomes.[20] Therefore, we examined the combined effectiveness of various clinical and laboratory risk stratification tools and analyzed how L/A ratio influences the discriminating accuracy of different mortality models to identify an effective risk stratification tool for sepsis patients admitted to the ICU.

EWSs serve as tracking and triggering mechanisms for physiological parameters, facilitating the early identification of patient deterioration in various healthcare settings such as pre-hospital environments, emergency departments, and inpatient wards.[21,22] Although multiple variations of EWS have been implemented in clinical practice, the most widely used versions continue to be MEWS and NEWS. In this study, we used MEWS

Table 3

Univariable and multivariable logistic regression analysis for the prediction of ICU mortality in sepsis patients.

	Death (n = 82)			
	Univariable analysis		Multivariable analysis	
	Odds ratio (95% CI)	*P*-value	Odds ratio (95% CI)	*P*-value
Age	1.031 (1.001–1.063)	0.045		
Gender M (ref)	1.439 (0.695–2.981)	0.327		
MEWS	1.247 (1.036–1.500)	0.019	1.262 (1.026–1.553)	.027
D-dimer	1.011 (0.970–1.053)	0.610		
qSOFA	1.463 (0.765–2.800)	0.250		
CRP	1.001 (0.998–1.005)	0.490		
Procalcitonin	1.001 (0.989–1.013)	0.934		
L/A ratio	2.501 (1.367–4.578)	0.003	2.160 (1.191–3.916)	.011
WBC	1.010 (0.971–1.051)	0.614		
Urea	1.010 (1.003–1.016)	0.004		
AST	1.003 (0.999–1.007)	0.101		

CRP = C-reactive protein, L/A ratio = the lactate-to-albumin ratio, MEWS = Modified Early Warning Score, qSOFA = quick Sequential Organ Failure Assessment.

Table 4

Performance of MEWS, qSOFA, L/A ratio, and procalcitonin for predicting 30-day mortality.

	Cutoff	AUROC (95% CI)	Sensitivity % (95% CI)	Specificity % (95% CI)	PPV % (95% CI)	NPV % (95% CI)	Accuracy % (95% CI)
Procalcitonin	≥11.2	0.550 (0.445–0.656)	36.6 (26.2–47.9)	66.7 (51.6–79.6)	65.2 (53.4–75.4)	38.1 (32.2–44.4)	47.7 (38.8–56.6)
MEWS	≥4	0.652 (0.549–0.754)	81.7 (71.6–89.4)	52.1 (37.2–66.7)	74.4 (68.1–79.9)	62.5 (49.5–73.9)	70.8 (62.2–78.4)
qSOFA	>2	0.602 (0.504–0.700)	32.9 (22.9–44.2)	87.5 (74.8–95.3)	81.8 (66.7–91.0)	43.3 (38.8–47.9)	53.1 (44.1–61.9)
L/A ratio	≥0.88	0.683 (0.592–0.774)	59.8 (48.3–70.4)	83.3 (69.8–92.5)	86.0 (76.1–92.2)	54.8 (47.5–61.9)	68.8 (59.7–76.3)

AUROC = area under curve receiver operating characteristics, CI = f, L/A ratio = the lactate-to-albumin ratio, MEWS = Modified Early Warning Score, NPV = negative predictive value, PCT = procalcitonin, PPV = positive predictive value, qSOFA = quick Sequential Organ Failure Assessment.

Table 5

Pairwise comparisons of receiver operating characteristic curves.

				95% CI			
	AUC	DBA	SE	Lower	Upper	Z statistics	*P*-value
qSOFA vs qSOFA + L/A ratio	0.602 vs 0.700	-0.098	0.282	-0.173	-0.022	-2.538	.011
MEWS vs MEWS + L/A ratio	0.652 vs 0.750	-0.098	0.305	-0.175	-0.021	-2.493	.013
qSOFA vs qSOFA + MEWS	0.602 vs 0.699	-0.097	0.287	-0.170	-0.024	-2.614	.009

AUC = area under the curve, CI = confidence interval, DBA = difference between areas, L/A ratio = the lactate-to-albumin ratio, MEWS = Modified Early Warning Score, qSOFA = quick Sequential Organ Failure Assessment, SE = standard error.

Table 6

Impact of L/A ratio, qSOFA, and MEWS on the discrimination accuracy of different mortality prediction models.

	AUROC (95% CI)	AUROC (95% CI)	Pairwise analysis					
					95% CI			
Prognostic model	Without L/A ratio	With L/A ratio	DBA	SE	Lower	Upper	Z statistic	*P*
Base model = age, gender, procalcitonin	0.603 (0.503–0.703)	0.733 (0.649–0.818)	-0.130	0.304	-0.224	-0.037	-2.740	.006
Base model + MEWS	0.662 (0.566–0.758)	0.751 (0.667–0.815)	-0.089	0.299	-0.158	-0.019	-2.506	.012
Base model + qSOFA	0.671 (0.579–0.764)	0.749 (0.666–0.832)	-0.077	0.295	-0.147	-0.008	-2.192	.028
Base model + MEWS + qSOFA	0.708 (0.617–0.799)	0.761 (0.677–0.832)	-0.053	0.294	-0.111	-0.005	-1.792	.043

AUROC = area under the receiver operating characteristic curve, DBA = difference between areas, L/A ratio = the lactate-to-albumin ratio, MEWS = Modified Early Warning Score, qSOFA = quick Sequential Organ Failure Assessment, SE = standard error.

because it is often considered more responsive compared to NEWS in detecting early signs of patient deterioration, particularly in acute settings, due to its emphasis on vital sign changes. Additionally, MEWS has been shown to better stratify patients at risk for adverse outcomes, making it a valuable tool for early intervention and improving overall patient safety in various healthcare environments.[23] Hence, we evaluated MEWS both alone and in conjunction with other scoring systems as a risk stratification tool in our hospitalized sepsis patients.

We also compared the discriminatory ability of MEWS, qSOFA, and L/A ratio for combined prediction of 30-days mortality. Our results indicated that non-survivor sepsis patients had significantly higher MEWS than survivors. Moreover, the AUROC analysis indicates that MEWS demonstrates superior predictive performance compared to qSOFA, as illustrated in Table 4. Similarly, a recent study involving a large cohort of patients with suspected infections in emergency departments or hospital wards determined that MEWS had superior discrimination for hospital mortality (AUC 0.73), followed by qSOFA (AUC 0.69) and systemic inflammatory response syndrome (SIRS) (AUC 0.65). The study highlighted that traditional track-and-trigger EWS are more effective at detecting adverse outcomes in sepsis patients than the qSOFA criteria.[24] Contrary to our findings, a meta-analysis by Hamilton et al[25] demonstrated that EWSs are not accurate in the prediction of mortality of sepsis patients, with a summary of AUC at 0.68 (sensitivity 66% and specificity 62%). Tirotta et al[26] assessed the ability of the MEWS to predict hospital mortality in septic patients admitted to medical wards. Their study revealed that MEWS had limited effectiveness in predicting hospital mortality, with an AUC of 0.596.

The qSOFA was initially designed as a bedside tool to identify adult patients with suspected infections who are at risk of poor outcomes, serving as an alternative to SIRS.[17] Therefore, qSOFA is better suited for predicting poor outcomes than for diagnosing sepsis. Most studies indicated that the AUROC for qSOFA surpasses that of SIRS in predicting in-hospital mortality.[27] However, other scoring systems, such as the NEWS and the MEWS, have demonstrated better prognostic value than both SIRS and qSOFA, with AUROC values of 0.77 for NEWS, 0.73 for MEWS, 0.69 for qSOFA, and 0.65 for SIRS.[24,28] Additionally, all 3 scores exhibited higher sensitivity at their recommended cutoff values compared to qSOFA.

In this study, the qSOFA score (cutoff: ≥ 2) was found to have a sensitivity of 32.9% and a specificity of 87.5% for predicting mortality with a positive predictive value of 81.8%, and negative predictive value of 43.3%. Although all scores performed moderately well in predicting mortality, qSOFA had the highest specificity and lowest sensitivity. MEWS (81.7% sensitivity and 52.1% specificity) and L/A ratio (59.8% sensitivity and 83.3% specificity) had a more balanced accuracy. Thus, in line with previous studies highlighting qSOFA's prognostic accuracy for predicting mortality, we found that qSOFA exhibits high specificity but low sensitivity. This discrepancy may be attributed to the absence of important variables, such as oxygenation, body temperature, and heart rate.[29,30] Basham et al[31] found that a mean qSOFA score of 3 predicted a 67% mortality rate in sepsis patients admitted to the ICU. In a univariate logistic analysis using odds ratio, Basham et al demonstrated that the mean qSOFA score was comparatively more effective in predicting mortality, followed closely by the mean SOFA score. Therefore, we maintain that given its predictive accuracy and high specificity, qSOFA is appropriate for identifying patients at risk of deterioration.[32]

This study, which includes a large cohort, is among the most comprehensive investigations into the prognostic potential of the L/A ratio in ICU sepsis patients. With a cutoff value of 0.88, the L/A ratio demonstrated good diagnostic sensitivity of 59.8% (range: 48.3–70.4), specificity of 83.3% (range: 69.8–92.5), and AUROC (range: 0.592–0.774) for predicting mortality in sepsis patients, consistent with findings from previous studies.[33]

Lactate has been recognized as a reliable prognostic marker for predicting multiorgan dysfunction in septic patients, as well as for forecasting poor health outcomes. Albumin levels can also serve as a reliable indicator of frailty, heightened vulnerability to stress, and unstable homeostasis, and they are closely associated with prognosis following severe illness. Additionally, hypoalbuminemia signifies inflammatory status and can effectively predict health outcomes in both chronic and inflammatory diseases.[34] However, since albumin levels can be influenced by nutritional status and chronic inflammation, depending solely on these levels for predictions may have certain limitations. Additionally, measuring lactate alone has disadvantages as several disease conditions can lead to elevated lactate levels, such as post-cardiac arrest, trauma, excessive muscle activity, necrotizan soft tissue infections, liver cirrhosis, malignancy, seizure, diabetic ketoacidosis, metformin use, mitochondrial disease, and smoke inhalation.[35–37] Therefore, the ratio between the 2 may provide a more significant prediction of a patient's prognosis than either measurement alone.

Shin et al[38] revealed that the prognostic performance of the L/A ratio surpassed that of a single lactate measurement in predicting 28-day mortality among critically ill sepsis patients. The L/A ratio proved to be a valuable prognostic factor, regardless of the initial lactate level or the presence of hepatic or renal dysfunction. Shin et al study not only highlighted the value of L/A ratio in sepsis patients but also demonstrated its ability to differentiate levels of mortality risk within the MEWS and qSOFA strata. Our findings, based on both crude and adjusted models, indicate that ICU sepsis patients with a MEWS ≥ 4 have an increased mortality risk. Moreover, incorporating the L/A ratio significantly enhances the accuracy of identifying patients at higher risk for 30-day mortality. Specifically, patients with a MEWS ≥ 4 and L/A ratio ≥ 0.88 had 35 times (95% C.I.: 8.885–137.872) greater risk of mortality compared to those with MEWS < 4 and L/A ratio < 0.88.

To the best of our knowledge, this is the first study to evaluate the effectiveness of the L/A ratio in conjunction with MEWS and qSOFA for predicting mortality in sepsis patients. Our data underscores the importance of integrating the L/A ratio with other clinical and laboratory parameters to enhance decision-making processes in healthcare management.

Nevertheless, this study has several limitations. First, as a retrospective cohort study conducted in a single academic public hospital, the findings may not be generalizable to other institutions or healthcare settings, including private hospitals or community-based facilities. Second, while the L/A ratio shows promise as a prognostic marker in combination with qSOFA and MEWS, the study's reliance on electronic health records may introduce information bias due to incomplete or inaccurate data entries. Third, although we applied a commonly accepted definition for suspected infection, this approach may have resulted in the exclusion of patients who had infections but did not undergo culture testing or who had cultures taken later in their treatment. Additionally, despite the discharge diagnoses being conducted by experienced specialists, there remains a possibility of miscoding, partly because discharge records do not specify the timing or causal links between infection and organ dysfunction. Finally, L/A ratio, MEWS, and qSOFA score data were collected within the first 24 hours of ICU admission; therefore, these measurements may not precisely correspond to the exact timing of sepsis diagnosis.

5. Conclusion

In conclusion, this study demonstrates that L/A ratio, when combined with MEWS and qSOFA, enhances mortality prediction in ICU patients with sepsis. The findings indicate that a higher L/A ratio and MEWS score are associated with increased mortality risk, suggesting that combining these parameters allows for more accurate patient stratification. Although qSOFA alone had limited predictive power, it significantly improved MEWS's

predictive ability when integrated into our models. Furthermore, using the L/A ratio in combination with these scoring systems offers a more robust approach to identifying patients at greater risk of 30-day mortality.

Author contributions

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