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The blood lactate/serum albumin ratio might represent a good prognostic indicator of 28-day mortality in patients with acute respiratory distress syndrome: a retrospective observational study

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Abstract

Background: Acute respiratory distress syndrome (ARDS) is an acute inflammatory lung injury with a high mortality rate. However, previous ARDS prognostic scoring systems or predictors have been limited by complex formulas that are relatively expensive and inconvenient to obtain. Thus, this study aimed to explore the clinical significance of the blood lactate/serum albumin ratio (LAR) in assessing the prognosis of ARDS patients and compare it with other indicators related to 28-day mortality in ARDS patients.

Methods: We conducted a single-center retrospective study involving patients who fulfilled the Berlin definition of ARDS between 2016 and 2021. Clinical data were collected from medical records within 24 hours after ARDS diagnosis. The LAR, neutrophil-to-lymphocyte ratio, and monocyte-to-lymphocyte ratio (MLR) were calculated. The primary clinical outcome was 28-day mortality. The risk factors for 28-day mortality were determined using conditional logistic regression analysis. The receiver operating characteristic curve was used to evaluate the area under the curve (AUC).

Results: A total of 276 ARDS patients met the inclusion criteria and were divided into surviving and nonsurviving groups according to 28-day mortality. There were significant differences in the Acute Physiologic Assessment and Chronic Health Evaluation II scores, Sequential Organ Failure Assessment scores, MLRs, and LARs between the surviving and nonsurviving groups. The AUC for the LAR was 0.790 ($P < 0.001$), whereas the AUCs for the Acute Physiologic Assessment and Chronic Health Evaluation II score, Sequential Organ Failure Assessment score, neutrophil-to-lymphocyte ratio, and MLR were 0.584, 0.599, 0.524, and 0.587, respectively. After grouping according to an LAR optimal cutoff value of 0.07, 28-day mortality was significantly higher in the high-LAR group than in the low-LAR group (47.18 vs. 12.69, $P < 0.001$).

Conclusion: The LAR is an independent risk factor for 28-day mortality in ARDS patients and can be used to assess the severity of ARDS to a certain extent, making it superior to other commonly used indicators.

Keywords: Acute respiratory distress syndrome, Albumin, Lactate, Mortality, Predictor

Acute respiratory distress syndrome (ARDS), an acute inflammatory lung injury, is associated with high mortality.[1] Even if patients survive, they experience the risk of sequelae such as cognitive decline and persistent skeletal muscle weakness.[2,3] Over the last decade, numerous studies have improved our understanding of the pathophysiology and treatment options for ARDS; however, the incidence and mortality of ARDS remain high.[4,5] Given the limited number of effective treatments, early identification and intervention may constitute an important approach to reducing the case fatality rate.[6] In previous studies, Acute Physiologic Assessment and Chronic Health Evaluation II (APACHE II) scores, Sequential Organ Failure Assessment (SOFA) scores, red blood cell distribution width values, procalcitonin/albumin (ALB) levels, lactate (Lac) clearance data, pleural fluid content levels, oxygenation index scores, and other measures have been used to judge prognosis.[7,8] However, these scoring systems or predictors have limitations due to their complex calculation formulas, as well as their relatively expensive and inconvenient nature of obtaining them. At the same time, the subjectivity of these predictors poses challenges for accurate clinical prognosis assessment. Therefore, the selection and use of reliable and easily accessible predictors are crucial.

Many studies have implicated that acid-base balance disorders are common in critical illnesses, including ARDS. Furthermore, these disorders may serve as one of the main factors in the progression of the disease.[9–12] Lactate is an important indicator of the acid-base balance of the body, which can be easily and quickly detected by blood gas analysis. Elevated Lac levels are associated with hypoxia, insufficient circulatory perfusion, and disruptions in the acid-base balance. The accumulation of Lac can lead to acidosis, posing a significant threat to the lives of patients.[13] However, Lac levels may also increase because of other conditions, such as liver and kidney dysfunction.[14,15] Therefore, the use of Lac alone as a prognostic indicator may have limitations in reflecting the adverse development and outcomes of diseases.

The data sets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Decreased serum albumin levels are frequently observed in critically ill patients. Specifically, hypoproteinemia (serum albumin <35 g/L) is strongly associated with poor prognosis and increased mortality.[16] Recent research on sepsis has shown that the blood Lac/serum albumin ratio (LAR) is an independent risk factor for death in patients with sepsis.[17] Importantly, unlike Lac or albumin alone, the LAR remains unaffected by initial Lac levels or liver and kidney dysfunction.[18]

Based on the aforementioned observations, we propose that the LAR may be related to the severity and mortality of ARDS. In this study, we sought to investigate the relationship between LARs and 28-day mortality in ARDS patients and explore whether the LAR has a significant advantage over other indicators.

Methods

Study design and patient population

This study included 276 adult inpatients who were diagnosed with ARDS, admitted to the First Affiliated Hospital of Soochow University from December 2016 to November 2021, and who met the inclusion criteria (Fig. 1). All eligible patients met the Berlin definition criteria for ARDS.[19] The study inclusion criteria were as follows: (1) arterial O_2 pressure over inspiratory O_2 fraction (PaO_2/FIO_2) ≤300 mmHg; (2) bilateral opacities on chest radiography; and (3) blood Lac and serum albumin collected within 24 hours after an ARDS diagnosis. We excluded patients (1) who were immunosuppressed or had cancer; (2) who received an albumin infusion within 24 hours; (3) who died or were discharged within 24 hours; or (4) who had missing data. This study was approved, and written informed consent was waived by the Clinical Research Ethics Committee of the First Affiliated Hospital of Soochow University (Jiangsu, China; ethical number: 2019050; registration date: July 29, 2019) owing to the anonymized retrospective nature of the analysis.

Data collection

The clinical data of all eligible patients were collected through the medical record system of our hospital, including baseline demographic information (sex, age) and medical history (smoking, alcohol abuse, hypertension, diabetes, and coronary heart disease). Clinical data and chest radiographs were independently reviewed by 2 physicians to determine diagnostic accuracy. Laboratory test results included the following: PaO_2/FIO_2, hemoglobin, hematocrit (HCT), red cell distribution width, platelets (PLT), neutrophil counts, lymphocyte counts, monocyte counts, Lac, albumin, high-density lipoprotein cholesterol, aspartate aminotransferase (AST), alanine aminotransferase, creatinine (Cr), and blood urea nitrogen (BUN). The APACHE II and SOFA scores were calculated based on component variables during the first 24 hours after admission.[20,21] All patients were followed up for 28 days. The primary clinical outcome was 28-day mortality, and the secondary outcome was mechanical ventilation. Data on the duration of mechanical ventilation, length of intensive care unit (ICU) stay, and length of hospital stay were recorded when the primary clinical outcome was present. Next, a check was performed to ensure that the numerator and denominator of the same ratio were measured at the same point in time. In cases where multiple ratios were measured after blood sampling from the same patient, the average value was used in the analysis.

Definition

According to the Berlin definition, ARDS is a type of acute diffuse inflammatory lung injury presenting with chest imaging scans that reveal bilateral opacities that cannot be fully explained by effusions, lobar/lung collapse, or nodules.[19] Therefore, in this study, the physicians and researchers reviewed whether the lung imaging assessment was consistent with a diagnosis of ARDS. Based on the degree of hypoxemia, ARDS was categorized into 3 groups: mild (200 mmHg < PaO_2/FIO_2 ≤ 300 mmHg), moderate (100 mmHg < PaO_2/FIO_2 ≤ 200 mmHg), and severe (PaO_2/FIO_2 ≤ 100 mmHg).[19] Circulatory failure was defined when patients had systolic blood pressure of less than 100 mmHg and required the use of vasoactive drugs. Liver failure was defined as a total bilirubin of greater than 15 μmol/L or elevated liver enzymes more than 10 times the normal values. Renal failure was defined as a Cr level of greater than 50% of the baseline level or the use of hemodialysis or continuous renal replacement therapy. After finding the best cutoff LAR according to the receiver operating characteristic (ROC) curve, all enrolled patients were divided into high-LAR and low-LAR groups.

Statistical analysis

Stata/SE 15.1 (StataCorp LLC, College Station, TX) was used for statistical analysis of the data. Comparisons between continuous variables were analyzed using the *t* test or the Mann-Whitney *U* test, depending on the variable distribution. For normally distributed samples, the results were presented as mean ± SD, whereas for non–normally distributed samples, medians (quartiles) were reported. Categorical variables were compared using the χ^2 or Fisher exact test,

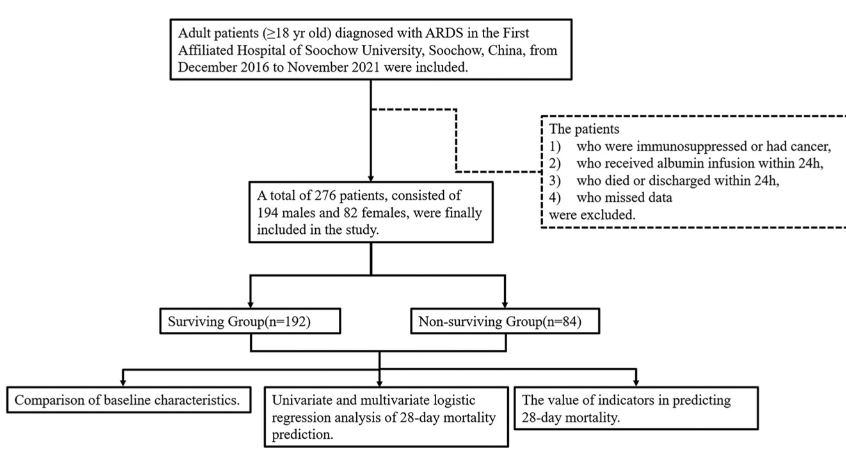

Figure 1. Research flowchart. ARDS, acute respiratory distress syndrome.

and relative frequencies and percentages were reported. To compare LAR values between the 2 groups, 1:1 propensity score matching was used to minimize the influence of the baseline characteristics. Propensity scores were calculated using Cox regression with the outcome as the dependent variable and the following confounders initiation as independent variables: age, sex, medical history, laboratory tests, APACHE II scores, SOFA scores, and interventions received. The caliper value was 0.05.

Univariate and multivariate conditional logistic regression analyses were performed to identify the independent prognostic factors of 28-day mortality. All variables were analyzed using categorical and forward stepwise logistic regression models. Variables with $P < 0.05$ in the univariate logistic regression analysis were entered as independent variables in the multivariate logistic regression analysis. The efficiency of predicting 28-day mortality in patients with ARDS was evaluated using ROC analysis, and the area under the ROC curve (AUC), cutoff value, maximum sensitivity, and specificity were determined. Two-tailed $P < 0.05$ was considered to be statistically significant.

Power analysis

To calculate the sample size for the current research, a power analysis was carried out using Stata/SE 15.1. We estimated that the incidence of high LAR in the surviving group would be approximately 30%, and the odds ratio (OR) was 5. This assumption was based on pilot data. Assuming a 1:2 ratio of patients in the nonsurviving and surviving groups, 78 patients were required to show an association between high LAR and 28-day mortality in ARDS patients at a 2-tailed α of 0.05 and a power of 0.90. Considering a certain exclusion rate, we eventually included 276 ARDS patients over a period of 5 years.

Results

Baseline patient characteristics

A total of 276 ARDS patients met the inclusion criteria, including 194 male patients and 82 female patients. The patients were divided into surviving and nonsurviving groups according to their 28-day mortality. The baseline and clinical characteristics of the 2 groups are illustrated in Table 1. The average age of the surviving group was 70.5 years, and the proportion of male patients in this group was 70.83%. The average age of the nonsurviving group was 73.5 years, and the proportion of male patients in this group was 69.05%. Sex, age, smoking, drinking habits, hypertension, diabetes, and coronary heart disease were not statistically significant between the 2 groups. Compared with the surviving group, HCT, PLT, ALB, and PaO_2/FIO_2 values in the nonsurviving group were significantly reduced ($P = 0.046$, $P = 0.003$, $P = 0.003$, and $P = 0.038$, respectively). In contrast, the APACHE II scores, SOFA scores, monocyte counts, BUN, AST, Lac, monocyte-to-lymphocyte ratio (MLR), and LARs were significantly increased in this group ($P = 0.026$, $P = 0.008$, $P = 0.010$, $P = 0.012$, $P = 0.042$, $P < 0.001$, $P = 0.021$, $P < 0.001$, respectively). The 28-day mortality rate was 30.4%. After propensity score matching, there was still a statistically significant difference in the LARs between the 2 groups. In addition, the proportion of patients with circulatory dysfunction in the nonsurviving group was higher compared with the surviving group ($P < 0.001$) (Table 1).

Independent predictors for 28-day mortality in ARDS patients

As displayed in Table 2, the variables with $P < 0.05$ in the univariate logistic regression models were selected for the multivariate logistic regression model to identify the independent predictors for death. However, because of the collinearity between the Lac and LAR values, with a tolerance of 0.035 and variance inflation factor of 28.585, Lac was excluded from the multivariate logistic regression. This demonstrated that LAR (OR: 5.926; 95% confidence interval [CI]: 3.041–11.548; $P < 0.001$) and PLT (OR: 0.996; 95% CI: 0.993–0.999; $P = 0.024$) were independent risk factors for 28-day mortality in patients with ARDS.

Analysis of the predictive value of indicators for 28-day mortality in patients with ARDS

Receiver operating characteristic curve analyses were used to assess the value of the APACHE II score, SOFA score, neutrophil-to-lymphocyte ratio (NLR), MLR, LAR, NLR + MLR, MLR + LAR, and NLR + LAR to predict prognosis in patients with ARDS (Table 3, Fig. 2). The AUC for the APACHE II score was 0.584 (95% CI: 0.523–0.643; $P = 0.033$). The AUC for the SOFA score was 0.599 (95% CI: 0.539–0.657; $P = 0.005$). The AUC for the MLR was 0.587 (95% CI: 0.527–0.646; $P = 0.027$). The AUC for the LAR was 0.790 (95% CI: 0.737–0.836; $P < 0.001$), and the cutoff LAR was 0.07 (60.42% specificity and 90.48% sensitivity) (Table 3, Fig. 2).

Baseline characteristics of ARDS patients according to the cutoff LAR value

Table 4 displays the baseline characteristics of the ARDS patients included in the study, stratified by low LAR (<0.07) and high LAR (≥0.07). The 28-day mortality was significantly higher in the high-LAR group than in the low-LAR group (47.18 vs. 12.69; $P < 0.001$). In addition, compared with patients with lower LAR levels, patients with higher LAR levels had lower hemoglobin, HCT, and ALB. However, these patients also presented with higher SOFA scores, high-density lipoprotein cholesterol, Cr, BUN, alanine aminotransferase, AST, Lac, and NLRs and were more likely to develop circulatory failure and hepatic failure.

Discussion

Acute respiratory distress syndrome is the most common severe acute lung disease and one of the main causes of admission and mortality in ICUs.[1] In this study, the 28-day mortality rate was 30.4%, suggesting a poor prognosis for ARDS patients. The causes of ARDS include acute osmotic noncardiogenic pulmonary edema and progressive hypoxic respiratory failure secondary to severe extrapulmonary or intrapulmonary disease.[22] In the early exudative phase of ARDS, neutrophils and monocytes or macrophages are recruited because of proinflammatory cytokines being secreted by alveolar macrophages. Meanwhile, alveolar epithelial cells and effector T cells are activated. Together, these promote and maintain inflammation and tissue damage.[1] In current treatment, in addition to addressing the underlying primary disease, symptomatic treatment, such as mechanical ventilation, prone position ventilation, and renal replacement therapy, plays a vital role.[1]

Considering the lack of specific treatment measures, early judgment of the prognosis of ARDS patients is of great significance in early individual-based treatment to reduce mortality and alleviate the disease. Although APACHE II and SOFA scores are common outcome predictors for ICU patients, their subjective measurement methods and complicated calculations have led to certain limitations in predicting the disease severity and progression of ARDS.[23,24] Recently, some ready-made parameters extracted from the conventional complete blood count tests have shown satisfactory results as potential biomarkers. Li et al.[25] demonstrated that a high NLR was associated with a poor outcome in critically ill patients with ARDS (AUC: 0.747; specificity: 0.734; sensitivity: 0.7). Regarding severe COVID-19 (coronavirus disease 2019), the initial NLR value has also been used to

Table 1

Comparison of the Baseline Characteristics of Patients According to Survival Status

	Prematched			Postmatched		
	Surviving (n = 192)	Nonsurviving (n = 84)	*P*	Surviving (n = 64)	Nonsurviving (n = 64)	*P*
Variables						
Sex (male)	136.00 (70.83)	58.00 (69.05)	0.765	41.00 (64.10)	44.00 (68.80)	0.575
Age, y	70.50 (61.00–79.00)	73.50 (64.50–80.00)	0.197	74.00 (64.00–80.00)	73.50 (64.00–80.00)	0.937
Smoking	56.00 (29.17)	25.00 (29.76)	0.920	21.00 (32.80)	19.00 (29.70)	0.703
Alcohol abuse	41.00 (21.35)	18.00 (21.43)	0.989	14.00 (21.90)	13.00 (20.30)	0.828
Hypertension	37.00 (19.30)	11.00 (13.10)	0.213	8.00 (12.50)	6.00 (9.40)	0.571
Diabetes	40.00 (20.80)	11.00 (13.10)	0.127	12.00 (18.80)	10.00 (15.60)	0.639
Coronary heart disease	20.00 (10.40)	9.00 (10.70)	0.941	4.00 (6.30)	5.00 (7.80)	0.730
APACHE II score	11.50 (9.00–15.00)	13.00 (9.00–17.50)	0.026	12.00 (10.00–17.00)	12.00 (9.00–17.00)	0.945
SOFA score	7.00 (5.00–8.00)	8.00 (6.00–9.00)	0.008	7.00 (6.00–9.00)	8.00 (6.00–8.00)	0.753
Laboratory tests						
RDW, %	13.70 (12.90–14.90)	13.60 (13.00–14.50)	0.245	13.95 (13.05–14.88)	13.60 (12.80–14.60)	0.336
HGB, g/L	113.73 ± 24.25	110.62 ± 20.69	0.154	108.95 ± 23.686	110.77 ± 20.18	0.642
HCT, %	34.51 ± 7.20	32.88 ± 7.53	0.046	32.93 ± 6.43	33.27 ± 7.68	0.788
PLT, $\times 10^9$/L	191.50 (138.00–276.00)	148.00 (111.50–212.50)	0.003	159.00 (127.75–226.75)	153.00 (121.75–263.75)	0.825
LY, $\times 10^9$/L	0.71 (0.43–1.22)	0.67 (0.42–1.11)	0.751	0.56 (0.39–1.18)	0.67 (0.46–1.01)	0.464
MO, $\times 10^9$/L	0.41 (0.25–0.69)	0.60 (0.29–0.86)	0.010	0.40 (0.22–0.67)	0.57 (0.25–0.76)	0.151
NE, $\times 10^9$/L	8.69 (5.48–12.36)	8.59 (5.68–13.91)	0.533	8.31 (5.70–11.99)	7.98 (5.77–13.70)	0.755
HDL-C, mmol/L	0.82 (0.59–1.13)	0.97 (0.69–1.32)	0.054	0.90 (0.59–1.18)	0.98 (0.67–1.30)	0.418
ALB, g/L	32.83 ± 6.15	30.72 ± 5.24	0.003	32.49 ± 6.76	30.54 ± 5.39	0.083
Cr, μmol/L	102.60 (60.50–175.15)	132.80 (58.45–214.85)	0.142	127.60 (65.65–196.25)	138.60 (56.98–219.30)	0.834
BUN, mmol/L	11.05 (6.00–16.10)	13.70 (9.75–19.25)	0.012	12.95 (7.85–18.08)	13.70 (9.58–18.80)	0.580
ALT, U/L	49.20 (18.50–112.75)	38.05 (22.40–136.60)	0.843	56.35 (19.25–107.98)	39.95 (22.35–138.70)	0.911
AST, U/L	41.55 (20.10–127.50)	65.10 (28.70–138.05)	0.042	100.95 (20.70–183.08)	73.35 (28.70–136.10)	0.642
Lac, mmol/L	1.80 (1.20–2.85)	3.00 (2.30–4.65)	<0.001	2.15 (1.15–2.90)	3.00 (2.25–4.58)	<0.001
Pao_2/Fio_2, mmHg	142.00 (105.00–196.55)	126.00 (85.50–175.53)	0.038	124.50 (95.25–163.00)	129.00 (88.21–184.61)	0.717
NLR	13.09 (6.92–21.05)	12.90 (6.66–25.04)	0.521	14.77 (7.21–25.61)	12.90 (6.63–22.48)	0.564
MLR	0.56 (0.32–0.83)	0.69 (0.38–1.38)	0.021	0.58 (0.31–1.03)	0.67 (0.38–1.24)	0.563
LAR	0.06 (0.04–0.09)	0.10 (0.07–0.16)	<0.001	0.07 (0.04–0.09)	0.10 (0.07–0.16)	<0.001
Outcomes, n (%)						
Circulatory failure	51.00 (26.56)	42.00 (50.00)	<0.001	30.00 (46.90)	28.00 (43.58)	0.723
Hepatic failure	27.00 (14.06)	19.00 (22.62)	0.079	10.00 (15.60)	12.00 (18.80)	0.639
Renal failure	49.00 (25.52)	26.00 (30.95)	0.351	20.00 (31.30)	19.00 (29.70)	0.848
Length of ICU stay	5.00 (1.00–11.00)	4.00 (0–6.50)	0.010	3.00 (0–8.00)	4.00 (0–7.00)	0.990
Length of stay	19.00 (12.00–26.00)	16.50 (10.50–22.00)	0.015	17.00 (12.00–23.00)	16.50 (10.00–23.00)	0.486
Mechanical ventilation	102.00 (53.10)	52.00 (61.90)	0.177	35.00 (54.70)	38.00 (59.40)	0.592
Duration of ventilation	5.50 (0–13.00)	7.00 (3.00–12.50)	0.085	6.00 (1.00–13.00)	6.50 (3.00–11.00)	0.626

Data are n (%), mean ± SD, or median (interquartile range).

ALB, albumin; ALT, alanine aminotransferase; APACHE II, Acute Physiology and Chronic Health Evaluation II; ARDS, acute respiratory distress syndrome; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Cr, creatinine; HCT, hematocrit; HDL-C, high-density lipoprotein cholesterol; HGB, hemoglobin; ICU, intensive care unit; Lac, lactate; LAR, lactate-to-albumin ratio; LY, lymphocyte count; MLR, monocyte-to-lymphocyte ratio; MO, monocyte count; NE, neutrophil count; NLR, neutrophil-to-lymphocyte ratio; Pao_2/Fio_2, arterial O_2 pressure over inspiratory O_2 fraction; PLT, platelet; RDW, red blood cell distribution width; SOFA, Sequential Organ Failure Assessment.

identify high-risk patients with moderate to severe ARDS.[26,27] Although the MLR is associated with the prognosis of many pulmonary diseases,[28–31] there is limited research specifically focusing on its association with ARDS. Recently, Yang et al.[32] demonstrated that higher MLR values were associated with 28-day mortality in patients with ARDS, whereas its low sensitivity prevented it from being a good predictor of 28-day mortality in patients with ARDS.

Blood Lac, an important intermediate product of sugar metabolism, is mainly produced by red blood cells, striated muscles, and brain tissue.[33] Tissue hypoxia caused by pathological conditions, such as respiratory failure or circulatory failure, can lead to increased blood Lac levels.[13,34] Previous studies have established that Lac levels are useful for predicting the severity of sepsis and septic shock.[35,36] In patients with ARDS, there is impaired oxygenation followed by an increase in anaerobic metabolism due to protein-rich edema formation in the alveoli. Furthermore, pneumonia and sepsis are the main causes of ARDS.[37,38] Therefore, the Lac level is commonly

Table 2

Univariate and Multivariate Conditional Logistic Regression Analysis of 28-Day Mortality Prediction in Patients with ARDS

	Univariate Analysis		Multivariate Analysis	
Variables	OR (95% CI)	*P*	OR (95% CI)	*P*
LAR	7.056 (3.763–13.229)	<0.001	5.926 (3.041–11.548)	<0.001
APACHE II score	1.073 (1.023–1.125)	0.004		
SOFA score	1.186 (1.066–1.320)	0.002		
ALB	0.940 (0.898–0.983)	0.007		
PLT	0.996 (0.993–0.999)	0.006	0.996 (0.993–0.999)	0.024
Pao_2/Fio_2	0.995 (0.991–0.999)	0.028		

ALB, albumin; APACHE II, Acute Physiology and Chronic Health Evaluation II; ARDS, acute respiratory distress syndrome; CI, confidence interval; LAR, lactate-to-albumin ratio; OR, odds ratio; Pao_2/Fio_2, arterial O_2 pressure over inspiratory O_2 fraction; PLT, platelet; SOFA, Sequential Organ Failure Assessment.

Table 3

The Value of Indicators in Predicting 28-Day Mortality in Patients with ARDS

	AUC	95% CI	*P*	Optimal Cutoff Value	Specificity, %	Sensitivity, %
APACHE II score	0.584	0.523–0.643	0.033	14	72.92	45.24
SOFA score	0.599	0.539–0.657	0.005	7	58.33	57.14
NLR	0.524	0.464–0.584	0.528	7.85	28.65	63.10
MLR	0.587	0.527–0.646	0.027	1.29	90.10	28.57
LAR	0.790	0.737–0.836	<0.001	0.07	60.42	90.48
MLR + LAR	0.781	0.727–0.828	<0.001	0.19	57.29	92.86
NLR + LAR	0.784	0.730–0.831	<0.001	0.21	57.81	90.48
NLR + MLR	0.528	0.467–0.588	0.465	0.28	28.12	63.10

APACHE II, Acute Physiology and Chronic Health Evaluation II; ARDS, acute respiratory distress syndrome; AUC, area under the curve; CI, confidence interval; LAR, lactate-to-albumin ratio; MLR, monocyte-to-lymphocyte ratio; NLR, neutrophil-to-lymphocyte ratio; SOFA, Sequential Organ Failure Assessment.

elevated in ARDS patients, which is consistent with our research. In patients with ARDS, inflammation increases the permeability of the alveolar-capillary barrier, thereby reducing blood albumin levels when protein-rich fluid penetrates the alveoli. In addition, inflammatory mediators act on liver cells, reducing the expression of albumin mRNA and further aggravating hypoalbuminemia.[39] Hypoproteinemia has been reported to be associated with the development of acute lung injury and ARDS and the subsequent deterioration of the clinical prognosis.[40,41] Moreover, the present study found that the ALB levels in the nonsurviving group were significantly lower than those in the surviving group.

Considering that predictions that rely solely on Lac or albumin levels may have limitations, many critical care physicians have begun to pay attention to LARs recently. Gharipour et al.[42] conducted a retrospective study on data from the MIMIC-III (Multiparameter Intelligent Monitoring Intensive Care III) database that were collected from 2001 to 2012 to evaluate the predictive effect of Lac and LARs on ICU mortality prognostic performance, reporting that the LAR was a better indicator for predicting ICU mortality. Moreover, Shin et al.[18] confirmed that the LAR, as a prognostic factor for predicting the 28-day mortality of critically ill patients with sepsis, had the advantage of not being influenced by the initial Lac level, nor by liver and kidney dysfunction.

In this retrospective study, the LAR within 24 hours after ARDS diagnosis was significantly higher in the nonsurviving group than in the surviving group. In addition, the LAR was significantly correlated with 28-day mortality in ARDS patients and was found to be an independent risk factor of 28-day mortality after multivariate conditional logistic regression analysis. A good AUC value of 0.790 was obtained for the LAR, whereas its specificity and sensitivity were 60.42% and 90.48%, respectively. However, considering its high sensitivity and low specificity, whether the LAR value can be used as a good predictor of 28-day mortality in patients with ARDS remains unclear. In addition, our study also found that the combination of MLR and LAR, the combination of NLR and LAR, and LAR alone were equivalent in predicting 28-day mortality in patients with ARDS.

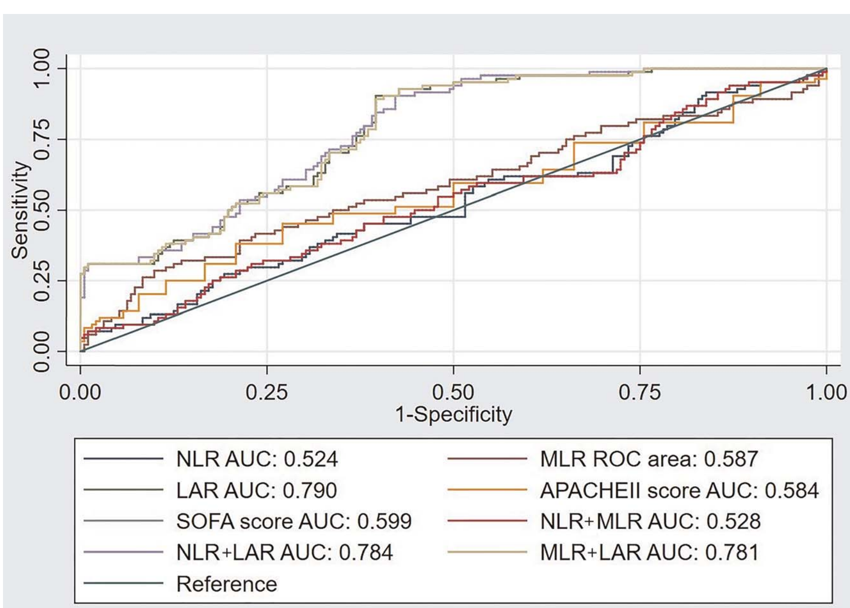

Figure 2. ROC curves for the APACHE II score, SOFA score, LAR, MLR, NLR, MLR + NLR, MLR + LAR, and NLR + LAR for predicting 28-day mortality in patients with ARDS. APACHE II, Acute Physiology and Chronic Health Evaluation II; ARDS, acute respiratory distress syndrome; LAR, lactate-to-albumin ratio; MLR, monocyte-to-lymphocyte ratio; MLR + LAR, combination of MLR and LAR; MLR + NLR, combination of MLR and NLR; NLR, neutrophil-to-lymphocyte ratio; NLR + LAR, combination of NLR and LAR; ROC, receiver operating characteristic; SOFA, Sequential Organ Failure Assessment.

Table 4

Comparison of Baseline Characteristics of Patients in Different LAR Levels

	Low-LAR (LAR<0.07, n = 134)	High-LAR (LAR≥0.07, n = 142)	*P*
Variables			
Sex (male)	90.00 (67.16)	104.00 (73.24)	0.270
Age, y	69.00 (56.00–79.00)	73.00 (66.00–80.00)	0.065
Smoking	35.00 (26.12)	46.00 (32.39)	0.253
Alcohol abuse	24.00 (17.91)	35.00 (24.65)	0.172
Hypertension	31.00 (23.10)	17.00 (12.00)	0.014
Diabetes	31.00 (23.10)	20.00 (14.10)	0.053
Coronary heart disease	15.00 (11.20)	14.00 (9.90)	0.718
APACHE II score	11.00 (8.00–14.00)	12.00 (9.00–17.00)	0.052
SOFA score	7.00 (5.00–8.00)	8.00 (7.00–9.00)	<0.001
Laboratory tests			
RDW, %	13.60 (12.80–14.90)	13.70 (13.10–14.60)	0.798
HGB, g/L	116.53 ± 24.68	109.25 ± 21.27	0.004
HCT, %	35.26 ± 7.32	32.83 ± 7.25	0.003
PLT, $\times 10^9$/L	185.50 (135.00–260.00)	171.50 (126.00–273.00)	0.306
LY, $\times 10^9$/L	0.74 (0.50–1.19)	0.65 (0.38–1.14)	0.057
MO, $\times 10^9$/L	0.44 (0.27–0.70)	0.40 (0.20–0.78)	0.762
NE, $\times 10^9$/L	8.71 (5.27–12.98)	8.61 (5.93–12.81)	0.763
HDL-C, mmol/L	0.76 (0.53–1.09)	0.97 (0.66–1.19)	0.004
ALB, g/L	32.97 ± 5.83	31.45 ± 6.01	0.017
Cr (μmol/L)	79.75 (55.50–153.50)	139.40 (75.00–205.10)	<0.001
BUN, mmol/L	10.11 (5.70–14.70)	13.70 (8.60–19.40)	<0.001
ALT, U/L	33.45 (17.80–67.80)	64.25 (24.80–155.90)	0.001
AST, U/L	29.70 (18.40–79.10)	90.40 (28.70–164.90)	<0.001
Lac, mmol/L	1.40 (0.90–1.80)	3.30 (2.60–4.50)	<0.001
Pao_2/Fio_2, mmHg	143.25 (108.00–199.09)	132.50 (88.00–177.58)	0.032
NLR	10.76 (5.77–20.53)	14.57 (7.19–23.78)	0.036
MLR	0.55 (0.33–0.84)	0.63 (0.32–1.08)	0.223
LAR	0.04 (0.03–0.06)	0.10 (0.08–0.14)	<0.001
Outcomes			
Circulatory failure	30.00 (22.39)	63.00 (44.37)	<0.001
Hepatic failure	16.00 (11.94)	30.00 (21.13)	0.041
Renal failure	32.00 (23.88)	43.00 (30.28)	0.232
Length of ICU stay	5.00 (0–11.00)	4.00 (1.00–8.00)	0.240
Length of stay	18.50 (12.0–26.0)	17.00 (11.00–23.00)	0.070
Mechanical ventilation	73.00 (54.48)	81.00 (57.04)	0.668
Duration of ventilation	5.50 (0–12.00)	6.00 (3.00–13.00)	0.116
28-d Mortality	17.00 (12.69)	67.00 (47.18)	<0.001

Data are n (%), mean ± SD, or median (interquartile range).

ALB, albumin; ALT, alanine aminotransferase; APACHE II, Acute Physiology and Chronic Health Evaluation II; ARDS, acute respiratory distress syndrome; AST, aspartate aminotransferase; BUN, blood urea nitrogen; Cr, creatinine; HCT, hematocrit; HDL-C, high-density lipoprotein cholesterol; HGB, hemoglobin; ICU, intensive care unit; Lac, lactate; LAR, lactate-to-albumin ratio; LY, lymphocyte count; MLR, monocyte-to-lymphocyte ratio; MO, monocyte count; NE, neutrophil count; NLR, neutrophil-to-lymphocyte ratio; Pao_2/Fio_2, arterial O_2 pressure over inspiratory O_2 fraction; PLT, platelet; RDW, red blood cell distribution width; SOFA, Sequential Organ Failure Assessment.

Limitations

This study had some limitations. First, this study was a single-center retrospective study with a small sample size; therefore, large-scale prospective studies are required to validate our results. Second, the presence of selection bias could affect the generalizability of the findings to all patients with ARDS. Finally, because of differences in the diagnosis and treatment of patients by different clinicians, inconsistencies and imperfections in the measured indicators may exist.

Conclusion

In summary, LAR is an independent risk factor for 28-day mortality in ARDS patients and can be used to assess the severity of ARDS to a certain extent. The higher the LAR, the worse the prognosis, and the higher the incidence of organ dysfunction. Compared with the commonly used prognostic indicators, the LAR demonstrated a higher diagnostic performance. Moreover, information on both Lac and albumin is easy to obtain and can be reviewed over time as the condition changes. In the future, more studies, especially prospective multicenter large-sample studies, are needed to confirm these findings.

Conflict of interest statement

The authors declare no conflict of interest.

Author contributions

Chen J, Gao C, and Yang Ling contributed equally to this article. Chen J and Guo Q contributed to study design. Chen J, He Y, and Yang L participated in literature search. Guo S, Sun Y, and He S participated in data collection. Chen J, Guo Q, and Yang L participated in analysis of data. Chen J prepared the manuscript, and Guo Q reviewed the manuscript.

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Ethical approval of studies and informed consent

The study followed the principles of the Declaration of Helsinki as revised in 2013. This study was approved, and written informed consent was waived by the Clinical Research Ethics Committee of the First Affiliated Hospital of Soochow University (Jiangsu, China; ethical number 2019050; registration date July 29, 2019) owing to the anonymous data and anonymized retrospective nature of the analysis.

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