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Could the Lactate-Albumin Ratio be Successful in Predicting Mortality due to COVID-19 Infection?

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Abstract

BACKGROUND/AIMS: High death rates are associated with coronavirus disease-2019 (COVID-19), particularly in severely ill hospitalized patients. Early detection of particularly severe cases will be beneficial for treatment decisions and clinical courses. Therefore, we aimed to discern the capacity of the lactate-albumin ratio (LAR) parameter in predicting the outcomes of patients admitted to the intensive care unit (ICU) to COVID-19 infection.

MATERIALS AND METHODS: The study comprised 535 COVID-19-diagnosed patients who were admitted to the ICU. The data of the patients were obtained by retrospectively scanning the patient files.

RESULTS: The study population consisted of 535 patients, 270 patients in the non-survival group and 265 patients in the survival group. In the non-survival group, the plasma lactate level was 2.3±1.4 mmol/L, whereas in the survival group, it was 1.74±0.8 mmol/L, and this difference was statistically significantly higher in the non-survival group ($p<0.001$). The plasma albumin level in the non-survival group was also 2.87±0.47 g/dL, whereas in the survival group, it was 3.36±0.55 g/dL. It was determined that this difference was statistically significant ($p<0.001$). The cut-off value of lactate in determining mortality in critically progressing COVID-19 patients was 1.725 [area under the curve (AUC): 0.637, %95 confidence interval (CI): 0.590-0.685] with 63% sensitivity and 60% specificity; albumin 3.03 (AUC: 0.763, 95% CI: 0.723-0.803) with 70% sensitivity and 66% specificity; and LAR 0.57 (AUC: 0.719, 95% CI: 0.676-0.763) with 68% sensitivity and 68% specificity.

CONCLUSION: LAR can be safely used as a sepsis-related mortality marker in the ICU. However, although LAR is a successful indicator in patients hospitalized in the ICU because of COVID-19, it has yet to be as successful as it was in patients with sepsis. Its routine use may facilitate more information about LAR and patient decision-making.

Keywords: COVID-19, albumin, lactate, mortality

INTRODUCTION

Severe acute respiratory syndrome-coronavirus-2, also known as coronavirus disease-2019 (COVID-19), was first identified in late 2019 in China. Despite strict quarantine practices, it has spread to all countries and has become a pandemic. Many scientific studies have been conducted to accelerate the diagnosis and find the treatment of COVID-19.[1] Infection with COVID-19 increases the risk of intensive care unit (ICU) admission and mortality in older persons, smokers, and patients with chronic diseases. The mortality rate in the ICU generally varies between 40% and 85%, which is higher than in the ward patients. The average cost per day or during hospitalization is higher for patients admitted to the ICU. Accurate mortality risk estimation can increase life expectancy and help more rational use of healthcare costs.[2] Numerous new molecules potentially serving as prognostic and mortality determinants for COVID-19 have been investigated. However, the cut-off values for these molecules have yet to be discovered for the newly defined COVID-19 condition, and efforts have been made to establish

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these values.[3] Alternatively, existing scoring systems employed in non-COVID-19-related cases were utilized to predict patient mortalities. These datasets may encompass demographic characteristics, laboratory parameters, and mechanical ventilator modes employed by the patients.[4]

Sepsis and septic shock are global causes of mortality in the ICU.[5] Clinical and laboratory parameters were used to determine the mortality risk of sepsis or septic shock. Hyperlactatemia is considered a strong predictor of mortality in sepsis or septic shock.[6] Albumin, which is responsible for regulating plasma colloid oncotic pressure, plays a vital role in acid-base balance.[7] Decreased serum albumin levels are strong markers of mortality in patients with sepsis or septic shock.[8] The serum lactate-albumin ratio (LAR), which evaluates high lactate levels and low albumin levels together, is a good indicator that can be used to predict mortality in sepsis and septic shock in recent years.[9] LAR has been used as a sepsis-induced mortality marker in the ICU.[9]

Hence, there persists a requirement for assessing mortality rates among individuals admitted to the ICU because of COVID-19. In response to this exigency, we sought to scrutinize the efficacy of mortality prediction predicated on LAR value under ICU care for COVID-19. Our aim encompasses an inquiry into the efficacy of the LAR metric, recognized for its pertinence in appraising mortality tendencies in patients with sepsis and septic shock characterized by elevated mortality rates. Specifically, we aimed to discern the capacity of the LAR parameter in predicting the outcomes of patients admitted to the ICU due to COVID-19 infection.

MATERIALS AND METHODS

The population of the study consists of patients between 2020 and 2022. The study comprised 535 COVID-19-diagnosed patients who were admitted to the ICU between these periods. The data of the patients were obtained by retrospectively scanning the patient files. The lactate albumin value was checked from the blood taken during admission to the ICU. The data of the retrospective design study were conducted in accordance with the Declaration of Helsinki and after obtaining the approval of the Sakarya University Faculty of Medicine Ethics Committee (approval number: E-71522473-050.01.04-194690-334, date: 05.12.2022).

Statistical Analysis

To provide details on the general characteristics of the study population, descriptive analyses were performed. To evaluate whether they are regularly distributed or not, analytical and visual techniques (Kolmogrog-Simirlow/Shapiro-Wilk's test) were applied. For categorical data, % (percentage) values were used, whereas the mean and standard deviation were used for numerical variables. Student's t-test was used to examine whether continuous numerical variables differed between the two independent groups. Chi-square tests were used to examine whether there was a difference between the two categorical groups. The odds ratio was calculated for risk analysis, and the results were reported with confidential intervals. Receiver operating characteristic (ROC) analysis was performed to determine the cut-off value of the LAR in COVID-19 patients in the ICU. The area under the curve (AUC), sensitivity, and specificity values were determined. A p-value <0.05 was considered significant. Analysis was performed using the statistical program SPSS (IBM SPSS Statistics, version 21.0.). To determine the type II error value of the study, post-hoc analysis was performed using the G*Power application.

RESULTS

The study population consisted of 535 patients, 270 patients in the non-survival group and 265 patients in the survival group. The mean age of the non-survival group was 70.9±10.7 years, and that of the survival group was 59.7±16.3 years (Table 1). The mean age difference between

Table 1. Baseline characteristics and laboratory parameters of patients; survivors vs. non-survivors

	Non-survival, (n=270)	Survival, (n=265)	p
Age, years	70.9±10.7	59.7±16.3	**<0.001**
Gender			
Male, n (%)	174 (64.4%)	150 (56.6%)	0.064
Female, n (%)	96 (35.6%)	115 (43.4%)	
Comorbidities			
Diabetes mellitus, n (%)	100 (37.0%)	69 (26.1%)	**0.007**
Hypertension, n (%)	160 (59.3%)	123 (46.4%)	**0.003**
Coronary artery disease, n (%)	75 (27.8%)	44 (16.6%)	**0.002**
Labratory			
White blood cells, K/uL	12.1±10.1	7.5±3.9	**<0.001**
Hemoglobin, g/dL	12.1±2.1	12.5±1.9	**0.004**
Platelet, K/uL	200.6±94.2	207±86.7	0.416
Estimated glomerular filtration rate, mL/min/1.73 m^2	71.3±26.9	79.5±25.8	**0.006**
C-reactive protein, mg/L	140±97	70.5±70.46	**<0.001**
Procalcitonin, ng/mL	4.6±13.7	2.9±14.7	0.173
Erythrocyte sedimentation rate, 1 h, mmHg	63.6±27	51.2±28.7	**<0.001**
Lactate, mmol/L	2.3±1.4	1.74±0.8	**<0.001**
Albumin, g/dL	2.87±0.47	3.36±0.55	**<0.001**
Lactate-albumin ratio	0.82±0.5	0.55±0.38	**<0.001**
Intubation requirement, n (%)	230 (85.2%)	12 (4.6%)	**<0.001**

the non-survival and survival groups was statistically significant (p<0.001). There were 324 (60.6%) males and 211 (39.4%) females in the study population, and there was no statistically significant gender difference between the non-survival and survival groups (p=0.064). Comorbid conditions such as diabetes mellitus, hypertension, and coronary artery disease were investigated. These chronic conditions were more prevalent in the non-survival group (with p-values of 0.007, 0.003, and 0.002).

During ICU monitoring, 242 (45.6%) patients required intubation; among them, 230 (85.2%) patients had fatal outcomes. The number of patients who required intubation in the survival and non-survival groups differed statistically significantly (p<0.001). Odds ratios were calculated for mortality risk analysis. The mortality risk of a patient who developed the need for intubation in the ICU increased by 125 times (CI: 63-250).

The laboratory variables that significantly differed between the two groups, non-survival and survival, were as follows: white blood cell count (p<0.001), hemoglobin level (p=0.004), estimated-glomerular filtration rate (e-GFR) (p<0.001), and 1-h erythrocyte sedimentation rate (p<0.001).

In the non-survival group, the plasma lactate level was 2.3±1.4 mmol/L, whereas in the survival group, it was 1.74±0.8 mmol/L, and this difference was significantly higher in the non-survival group (p<0.001). The plasma albumin level in the non-survival group was also 2.87±0.47 g/dL, whereas in the survival group, it was 3.36±0.55 g/dL. It was determined that this difference was statistically significant (p<0.001).

We performed ROC analysis to determine the optimal cut-off values for albumin, lactate, and LAR to predict mortality. The cut-off value for lactate in predicting mortality in COVID-19 patients who were critically ill was 1.725 (AUC: 0.637, %95 CI: 0.590-0.685) with 63% sensitivity and 60% specificity; for albumin, it was 3.03 (AUC: 0.763, %95 CI: 0.723-0.803) with 70% sensitivity and 66% specificity; and for LAR, it was 0.57 (AUC: 0.719, 95% CI: 0.676-0.763) with 68% sensitivity and 68% specificity (Figure 1, Table 2). A post-hoc power analysis was performed to determine the type II error in the mortality prediction once the LAR cut-off value of 0.57 was approved. It was determined that the study had 99% power.

DISCUSSION

COVID-19 is a newly identified viral infection associated with high mortality rates, particularly in critically hospitalized patients. One of the main goals in managing these patients is to determine the prognosis and estimate the severity of the disease as soon as possible. It is known that early detection of particularly severe cases will be beneficial for treatment decisions and clinical courses. Although studies have been conducted on many laboratory parameters and scoring systems to predict the course of the disease, an ideal marker has yet to be determined. In this study, we aimed to determine the use of the LAR parameter in predicting the prognosis of patients admitted to the ICU due to COVID-19 infection.

Advanced age, male gender, concomitant diseases, and organ failure have been associated with poor prognosis in studies on COVID-19.[10,11] Similar to previous studies, patients who did not survival in our study were older and had more comorbidities (p<0.05). When the two groups were compared in terms of gender, the ratio of females to males was similar (p=0.064). In addition, increased C-reactive protein (CRP), procalcitonin, interleukin-6, creatinine, leukocyte, sedimentation levels, APACHE-II score, and low lymphocyte and albumin levels were found to be associated with severe disease and increased mortality in COVID-19 patients.[10-12] Similar to these results, in our study, significantly higher leukocyte, CRP, sedimentation, and lower hemoglobin, e-GFR, albumin, and lactate levels were obtained in those who did not survival (p<0.05). Contrary to expectations, there was no difference between the two groups in terms of procalcitonin levels (p=0.173).

Endothelial damage and increased permeability occur in patients with COVID-19 because of increased inflammation, causing albumin to accumulate in the interstitium and often causing hypoalbuminemia.[13] Low albumin levels were found to be an independent risk factor for mortality in studies conducted on these patients.[14] In a study of COVID-19 patients with sepsis and septic shock, low albumin levels were also associated with a higher risk of intubation.[15] In our study, albumin levels were lower in patients who did not survival, and the cut-off value in determining mortality was 3.03 (AUC: 0.763, 95% CI: 0.723-0.803) with 70% sensitivity and 66% specificity.

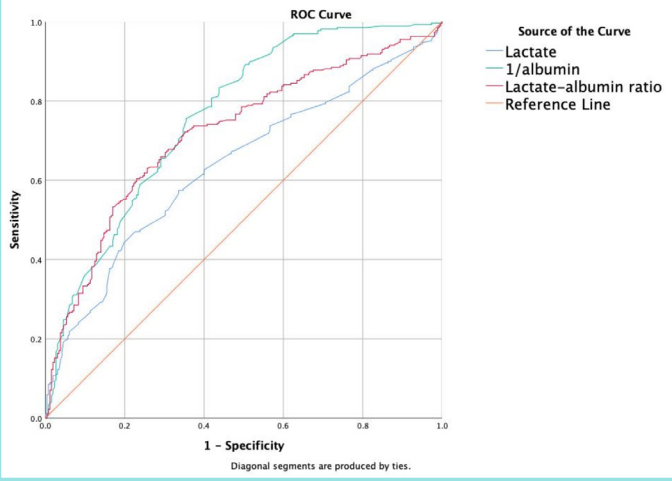

Figure 1. ROC curve of lactate, 1/albumin, and lactate-albumin ratio values for mortality.

ROC: Receiver operating characteristic.

Table 2. Values of AUC, sensitivity, and specificity of serum lactate level, serum albumin level, and lactate albumin ratio for predicting mortality

Risk factor	AUC	95% CI	Cut-off value	Sensitivity	Specificity	p
Lactate	0.637	0.590-0.685	1.725	63%	60%	**<0.001**
Albumin	0.763	0.723-0.803	3.03	70%	66%	**<0.001**
LAR	0.719	0.676-0.763	0.57	68%	68%	**<0.001**

AUC: Area under the curve, CI: Confidence interval, LAR: Lactate-albumin ratio.

Lactate has been reported to be a reliable biomarker for predicting the development of multiorgan dysfunction in septic patients.[16] Similarly, increased lactate levels were found to be associated with severe disease and mortality in COVID-19 studies.[17] The study by Velavan et al.[18] found that blood lactate levels were higher in COVID-19 pneumonia patients than in non-COVID-19 pneumonia patients. Contrary to the literature, although high lactate levels were found to be associated with a short survival time in the study of Gök et al.[13] in critically ill COVID-19 patients, they could not be identified as a risk factor for 30-day mortality. In our study, however, lactate levels were found to be higher in patients who did not survival, and the cut-off value in determining mortality in these patients was 1.725 (AUC: 0.637, 95% CI: 0.590-0.685) with 63% sensitivity and 60% specificity.

Although LAR is a well-known marker, especially in septic and critically ill patients, there have been few studies of LAR in COVID-19 patients.[1,9,13] When only albumin levels are evaluated, such as nutritionand chronic inflammation, and when only lactate levels are evaluated, such as cardiac arrest, trauma, burns, and thiamine deficiency could affect the measurements, and many studies focused on LAR. Patients with sepsis and septic shock who had higher LAR had multiorgan failure and died more frequently, and LAR's performance in predicting mortality was higher than that of albumin and lactate alone.[19,20] In a study of COVID-19 patients with sepsis and septic shock, serum lactate levels and LAR were shown to have the best diagnostic accuracy in predicting the need for mechanical ventilation and mortality.[15] In critically ill COVID-19 patients, Gök et al.[13] discovered that LAR is an independent risk factor for 30-day mortality. ROC analysis showed that LAR was superior to albumin (AUC: 0.644, $p<0.001$) and lactate levels (AUC: 0.795, $p<0.001$) in estimating 30-day mortality, with a cut-off value of 0.60 (AUC: 0.824, $p<0.001$).[13] Contrary to these studies, Özdemir and Altunok.[21] found that LAR is not a good predictor of mortality in COVID-19 patients. In our study, LAR levels were found to be higher in patients who did not survival, and the cut-off value in determining mortality in these patients was 0.57 (AUC: 0.719, 95% CI: 0.676-0.763) with 68% sensitivity and 68% specificity. In the meta-analysis of Yoon et al.[9] covering 4,723 patients with sepsis or septic shock, the LAR cut-off value for predicting mortality was calculated as 0.71 (95% CI: 0.54-0.84). If we accepted the mortality-determining cut-off LAR value of 0.71, we could accurately predict the mortality probability of our ICU with a sensitivity of 47% and specificity of 84%. The LAR value of 0.57 in our study was similar to the result in the meta-analysis. In our study, it was determined that the cut-off values of 3.03 (AUC: 0.763, 95% CI: 0.723-0.803) for albumin and 0.57 (AUC: 0.719, 95% CI: 0.676-0.763) for LAR were superior to lactate (AUC: 0.637, %95 CI: 0.590-0.685) in predicting mortality in critical COVID-19 patients.

Study Limitations

The most important limitations of our study were that it was a single-center, retrospective study that included patients with additional comorbidities that would affect the LAR level, patients with sepsis/septic shock were not identified, and a subgroup analysis was not performed. On the other hand, the high number of patients and the inclusion of only patients in the ICU, in terms of patient specificity, were the advantages of our study.

CONCLUSION

LAR is safely used as a sepsis-related mortality marker in the ICU. However, although LAR is a successful indicator in patients hospitalized in the ICU because of COVID-19, it has yet to be as successful as it was in patients with sepsis. Its routine use may facilitate more information about LAR and patient decision-making.

MAIN POINTS

- LAR is a successful indicator in patients hospitalized in the ICU due to COVID-19; however, it has yet to be as successful as it was in patients with sepsis.
- LAR and albumin values are superior to lactate in predicting mortality in critical COVID-19 patients.
- The cut-off value of LAR in predicting mortality in critical COVID-19 patients was 0.57 (AUC: 0.719, 95% CI: 0.676-0.763) with 68% sensitivity and 68% specificity.

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ETHICS

Ethics Committee Approval: The data of the retrospective design study were conducted in accordance with the Declaration of Helsinki and after obtaining the approval of the Sakarya University Faculty of Medicine Ethics Committee (E-71522473-050.01.04-194690-334, date: 05.12.2022).

Informed Consent: Retrospective study.

Peer-review: Externally peer-reviewed.

Authorship Contributions

Surgical and Medical Practices: A.C.G., A.G.T., Concept: A.C.G., Design: A.C.G., A.G.T., Data Collection and/or Processing: A.C.G., A.G.T., Analysis and/or Interpretation: A.C.G., Literature Search: A.C.G., A.G.T., Writing: A.C.G.

DISCLOSURES

Conflict of Interest: No conflict of interest was declared by the authors.

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