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# Diagnostic importance of lactate-albumin ratio in terms of mortality in patients with postoperative Sepsis

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**Abstract**
We designed our study to investigate the relationship between lactate-albumin ratio and mortality in inpatients in the intensive care department due to postoperative sepsis. Inpatients in the intensive care department due to postoperative sepsis were included in our study. Clinical and demographic data of the inpatients were obtained from hospital information management system. The blood gas lactate and albumin values of all inpatients in the intensive care department due to sepsis were measured. The lactate albumin ratios, some biochemical and hematological parameters of patients with and without mortality were compared. ROC curve statistical analyzes were performed to found the predictive diagnostic value of lactate-albumin ratio in predicting mortality. The lactate-albumin ratio and lymphocyte levels of the not-survival patients were higher than the lactate-albumin ratio and lymphocyte levels of the patients who survived. The area under the ROC curve for lactate-albumin ratio in predicting mortality between survival and non-survival by ROC analysis was 0.695 (95% CI: 0.522-0.756) (p=0.025). As a result of the analysis, it was determined that lactate-albumin ratio was positively related with lactate, neutrophil and monocyte values, and negatively correlated with albumin and $pO_2$ values.
The lactate-albumin ratio is an important determinant of mortality in inpatients with postoperative sepsis. Due to the hospitalization of the patient, close monitoring of the lactate-albumin ratio may change the treatment management and clinical results.

**Keywords:** Mortality, lactate albumin ratio, sepsis, postoperative, intensive care department

## Introduction
Sepsis is a medical condition in which the body's immune system reacts to an infection with a systemic inflammatory response, leading to severe organ dysfunction and potentially life-threatening complications. Despite advances in medical technology and our understanding of the disease, sepsis resulting from disruptions in circulation and cellular metabolism remains a significant factor causing to death in severely inpatients [1]. Sepsis accounts for approximately 50% of intensive care department admissions and approximately 10% of readmissions. It is a severe illness with a high death rate, with a mortality rate of 18-56% [2]. While the timely administration of appropriate antibiotics, adequate blood flow, and timely elimination of the source of infection may reduce mortality, this rate is still alarmingly high [3]. Therefore, early diagnosis and prompt treatment remain critical factors in determining the outcome of sepsis. Early identification of infection and pathogenic site and aggressive fluid resuscitation, as well as monitoring of various clinical indicators to evaluate the efficacy of treatment is also important. Sepsis is a condition that results from inflammation and leads to platelet-mediated destruction of endothelial cells. Toll-like receptors play an significant role in the development of sepsis as they are activated by microbial agents. This activation can result in multiple organ failure, shock, and eventually death. Recent research shows that both endogenous chemicals and microorganisms have the ability to activate Toll-like receptors [4]. Although clinical indicators such as infection site, pathogen and intense fluid resuscitation are taken into account in risk stratification in sepsis, more rapid laboratory findings are needed.
In shock situations, adenosine triphosphate (ATP) is produced through the anaerobic breakdown of glucose, leading to the production of lactate. Under normal conditions, the

blood lactate value is about 2 mmol/L. However, lactate formation is an indicator of insufficient tissue perfusion in individuals with sepsis. Blood lactate is a critical parameter used in clinical medicine to evaluate tissue perfusion and infection. High lactate levels may indicate cellular ischemia and hypoxia. This situation causes metabolic imbalances caused by the reduction of effective circulation in the tissues. The development of a systemic response to injury is mainly attributed to hypoxia and energy depletion. This could potentially explain the negative consequences observed in sepsis. High lactate values have been associated with increased mortality regardless of presence of shock, organ failure, or underlying critical illness. Therefore, lactate levels are a useful prognostic indicator for patients with sepsis and other critical illnesses [5].

Lactic acidosis is a condition that occurs in cases of sepsis and severe sepsis, characterized by cellular dysfunction, tissue hypoperfusion, and increased aerobic glycolysis [6]. Low albumin values in inpatients with serious condition indicate the severity of inflammation. Both blood lactate and serum albumin provide separate estimates of sepsis and mortality in critically ill individuals, while a combined assessment of serum lactate-albumin ratio provides a more precise and accurate estimate. The lactate-albumin ratio shows superior efficacy in identifying high-risk patients and preventing death. Wang *et al*. concluded that high lactate-albumin ratio is related with death in inpatients with sepsis [7].

In our study, we aimed to examine the relationship between lactate-albumin ratio and mortality in patients hospitalized in the intensive care department due to postoperative sepsis.

## Materials and Methods

### Study Protocol and Patient Selection

All inpatients (>18 years old) in the intensive care department due to postoperative sepsis between January 1, 2022 and September 1, 2022 were included in our study. Our study was carried out as a result of retrospective examination of inpatient records in Samsun University Samsun Research and Training Hospital intensive care department. Permission for the study was obtained from the Clinical Research Ethics Committee of Samsun University Samsun Research and Training Hospital (SKÜAEK-2023-5/16). All researchers conducted the study in accordance with the Declaration of Helsinki's tenets. Inpatients with sepsis during postoperative hospitalization were included in the study. The lactate levels of the inpatients with sepsis after admission to the intensive care department were not evaluated. The blood culture samples taken at the time of application were evaluated as a result of reproduction. The age, gender, co-morbidities (Diabetes Mellitus, hypertension, malignancy, etc.), hospital stay, intensive care mortality data of the inpatients with sepsis according to the sepsis criteria were obtained from the medical file records. Serum lactate levels of all hospitalized patients were measured at the time of admission. All arterial blood samples were obtained from a radial/femoral/arterial catheter, if available. Lactate levels obtained at admission were studied without waiting (Radiometer ABL 90 FLEX automatic blood gas analyzer, Copenhagen, Denmark). For blood culture, approximately 10 mL of whole blood samples were taken from two different locations at the same time. Blood culture samples were analyzed at BACTEC (Becton Dickinson, Sparks, MD, USA). Demographic characteristics, clinical outcomes and lactate levels of surviving and non-surviving patients were compared.

### Statistical analysis

Statistical analyzes were performed using SPSS v22 for Windows (IBM, Chicago, USA). Continuous data were expressed as mean ± standard deviation, and categorical data were expressed as percent frequency. Group comparisons were made using the Mann-Whitney U test. Receiver operating characteristic (ROC) curve analysis was performed to evaluate the sensitivity and specificity of the lactate albumin ratio. In addition, Spearman correlation analysis was used to examine the correlations between the data.

## Results

A total of 92 inpatients aged between 24 and 91 in the intensive care department with the diagnosis of postoperative sepsis were included in the study. Descriptive information about these patients is presented in Table 1.

The patients were divided into two groups according to their prognosis status (Discharged/Ex). While the mean age of the patients with Ex was 69.88±12.21, the mean age of the discharged patients was 71.08±10.54. Eighteen (32.14%) patients with Ex were female and 38 (67.86%) were male. Of the discharged patients, 13 (36.11%) were female and 23 (63.88%) were male. In patients with Ex, the number of those with gram (-) bacteria was 20 (35.71%), and the number of those with gram (+) bacteria was 36 (64.29%). In the discharged patients, the number of gram (-) bacteria was 12 (33.33%), and the number of gram (+) bacteria was 24 (66.66%). There was no significant difference between the mean age, gender and pathogen factor rates of these patient groups. In addition, no significant difference was found between the type and comorbidity rates found in patients with ex and the type and comorbidity rates found in discharged patients. Laboratory findings of these patient groups are presented in Table 2.

The lactate-albumin ratio and lymphocyte values of the inpatients with Ex were higher than the lactate-albumin ratio and lymphocyte levels of the discharged patients (Table 2).

ROC analysis was performed to evaluate the specificity and sensitivity of lactate-albumin ratio levels in predicting prognostic status. (Figure 1).

According to the ROC analysis results, the cut-off level for lactate-albumin ratio was 0.895, Area under curve (AUC) 0.639, Sensitivity 62.50%, Specificity 61.10% among ex and discharged patients (p= 0.025) (Figure 1).

Correlation analysis was performed between the lactate-albumin ratio and other parameters. As a result of the analysis, it was determined that there was a positive correlation with the lactate albumin ratio, lactate (r=0.897, p<0.001), neutrophil (r=0.230, p=0.028), and monocyte (r=0.242, p=0.020) levels. In addition, it was found to be negatively correlated with albumin (r=-0.304, p=0.003) and $pO_2$ (r=-0.257, p=0.013) levels.

## Discussion

Recent global research indicates that sepsis remains a significant cause of mortality and morbidity. According to these studies, over 30 million individuals worldwide are affected by sepsis annually. Sepsis impacts approximately 1%-2% of hospitalized patients each year. Approximately 15% of sepsis patients will progress to septic shock, which

occurs in around 10% of intensive care department admissions. The fatality rate associated with septic shock is approximately 50% [8].

Recent studies reveal that sepsis, one of the top causes of death in intensive care departments for patients with serious illnesses, consistently leads to high morbidity and mortality. Global studies show that around 30 million people struggle with sepsis each year. The incidence of sepsis in hospitalized patients is estimated to be approximately 1-2%.[8] In another retrospective study, 419 sepsis inpatients treated in the intensive care department (ICU) were analyzed and it was reported that the fatality rate among these inpatients was as high as 43.9% and the most common pathogens in the ICU were Gram-negative bacteria [9, 10]. These discoveries underscore the utmost significance of accurately diagnosing and effectively managing sepsis. Our study revealed an alarmingly high in-hospital mortality rate of 60.87% among sepsis patients.

Studies have determined that a single venous lactate value is a reliable marker in inpatients admitted to the emergency unit with suspected sepsis, and that lactate can be used continuously for risk stratification. Elevated lactate levels in patients with serious illnesses are widely recognized as an excellent prognostic marker for fatality and the development of organ failure [11]. Although sepsis-induced circulatory failure and shock can result in higher lactate levels due to anaerobic glycolysis and hypoxemia, it is not clear if elevated serum lactate is a direct outcome of tissue hypoperfusion. Elevated lactate levels, on the other hand, are typically interpreted in septic shock as a syptom of tissue hypoperfusion and secondary anaerobic metabolism [2]. Lactic acid, generated through tissue anaerobic metabolism, serves as an indicator of tissue hypoperfusion and cellular sensitivity to hypoxia. Additionally, lactic acid plays an important role in aerobic glycolysis and serves as an essential marker of mitochondrial dysfunction and stress response. An elevation in the level of lactic acid indicates a higher risk of mortality in patients. In clinical practice, regular monitoring of blood lactate levels is performed to assess tissue perfusion, metabolic status, and the therapy response of the patient. In patients receiving treatment for shock, a high blood lactate level is related with an important increase in fatality rate. The findings of the present study indicate that lactate levels partially reflect the severity of the disease, as they were higher in the group of patients who did not survive sepsis compared to those who did survive [12]. Furthermore, albumin levels are critical in sustaining plasma colloid osmotic pressure. The endothelial cells, neutrophils and mononuclear phagocyte system are over-activated during an inflammatory react, resulting in the generation of high amounts of inflammatory mediators. These mediators decrease the expression of albumin mRNA in hepatocytes, resulting in hypoproteinemia. Albumin has been examined extensively in the context of sepsis and is now included in the APACHE II score, which is routinely used to predict death in patients with serious illnesses. Any hepatic malfunction can affect plasma levels, which are further regulated by the patient's nutritional state and the level of inflammation present. Due to the potential influence of various factors on lactate and albumin levels, utilizing the lactate-albumin ratio as a prognostic tool in sepsis inpatients may offer a more robust evaluation of the patient's condition. By considering the lactate-albumin ratio, which accounts for potential confounding factors, the lactate-albumin ratio provides a more reliable and comprehensive assessment of the patient's prognosis in sepsis.

Because of its capacity to reflect opposite changes generated by two separate causes, the lactate-albumin ratio has attracted increased attention as a prognostic indicator in patients with serious illnesses in recent years. A normal or lower ratio suggests a better prognosis, but a higher ratio frequently indicates a worse prognosis. Shin *et al*. conducted a multicenter retrospective study on inpatients admitted to the emergency unit with severe sepsis. The lactate-albumin ratio predicts the prognostic outcomes of sepsis patients well. The lactate-albumin ratio has a greater AUC than the lactate AUC alone. This means that lactate-albumin ratio is a better predictor of patient outcomes [13, 14]. In another study evaluating pediatric patients with severe sepsis, lactate-albumin ratio was more effective than lactate clearance ratio in predicting length of hospital stay and fatality in these patients. The findings show that the lactate-albumin ratio is a valuable prognostic biomarker in evaluating the severity and outcome of the disease [15]. In addition, several additional studies have provided further evidence supporting the use of the lactate-albumin ratio in predicting the possibility of in-hospital mortality and risk stratification in inpatients with sepsis [16].

In our study, when the lactate-albumin ratio and lymphocyte levels were examined, we observed that these values were higher in ex patients than in patients who were discharged. To evaluate the prognostic level of the lactate-albumin ratio, we performed ROC analysis. The analysis yielded a cut-off level of 0.895 for the lactate albumin ratio, with an AUC of 0.639, sensitivity of 62.50%, and specificity of 61.10% in distinguishing between Ex and discharged patients ($p=0.025$). Our study aligns with the findings reported in the existing literature. Previous studies have consistently demonstrated that the lactate-albumin ratio is a reliable prognostic indicator for mortality in inpatients with sepsis. The largest retrospective study on the role of the lactate-albumin ratio in inpatients with sepsis was conducted by Gharipour *et al*., involving a cohort of 6,000 individuals. This study demonstrated that the lactate-albumin ratio had superior predictive ability for 28-day mortality compared to lactate alone. These findings further support the value of the lactate-albumin ratio as a prognostic biomarker in sepsis inpatients and highlight its potential as a valuable tool in clinical practice [17]. Our study yielded intriguing results, demonstrating that the lactate-albumin ratio in postoperative sepsis inpatients was a more effective prognostic indicator for mortality compared to lactate alone. This finding aligns with previous retrospective study, further reinforcing the significance of the lactate-albumin ratio as a valuable prognostic tool in sepsis. The consistent results from both studies provide robust evidence supporting the use of the lactate-albumin ratio in assessing the severity and predicting the outcome of sepsis cases [18, 19].

One possible explanation for our findings is the higher prevalence of infections among elderly patients, who generally have a higher fatality rate. In this specific inpatient population, the lactate-albumin ratio may exhibit improved performance compared to lactate alone as a prognostic indicator. Furthermore, we conducted correlation analysis between the lactate-albumin ratio and other parameters to explore their associations and potential impact on patient outcomes. The lactate-albumin ratio was shown to be favorably linked with lactate, neutrophil, and monocyte

levels. Furthermore, it was inversely associated to albumin and $pO_2$ levels. According to our detailed correlation analysis, a high lactate-albumin ratio in postoperative sepsis inpatients is related with a sustained increase in death rates and a consequent decrease in survival rates. Because lactate and albumin levels move in opposite directions during sepsis, the lactate-albumin ratio can efficiently combine both indices to provide an accurate assessment of the patient's status. Therefore, the lactate-albumin ratio emerges as a valuable independent risk factor with robust predictive potential for adverse outcomes in sepsis patients. Various studies have explored the accuracy of lactate levels in predicting fatality among sepsis patients, encompassing different ranges of lactate values. Trzeciak *et al*. conducted a study revealing that a lactate value of 4 mmol/L or higher exhibited a specificity of 95% and sensitivity of 35% in predicting early mortality within 3 days. Furthermore, it demonstrated a sensitivity of 19% and specificity of 93% in predicting in-hospital fatality [20]. Another study reported that a lactate level of 4 mmol/L or higher had a specificity of 92% and sensitivity of 36% for predicting in-hospital fatality [21].

In summary, lactate-albumin ratio levels play a critical role in assessing the severity and prognosis of postoperative sepsis inpatients, particularly in those with higher mortality rates. Monitoring lactate-albumin ratio levels can serve as an important parameter for predicting mortality in postoperative sepsis patients. The rate of decline in lactate-albumin ratio levels over time can also provide valuable information regarding treatment response and management, ultimately influencing patient outcomes and mortality.

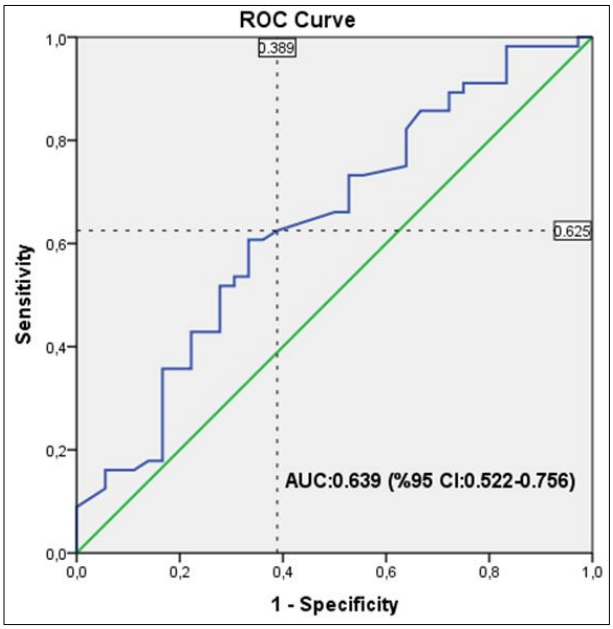


**Fig 1:** Graph of lactate-albumin ratio ROC curve

**Table 1:** Descriptive information of the patients included in the study

| Parameters | | Patients (N: 92) |
|---|---|---|
| Gender n (%) | Male | 61 (66.30) |
| | Woman | 31 (33.70) |
| **Mean age (X±SD)** | | 70.35±11.54 |
| Bacteria n (%) | Gram negative | 32 (34.78) |
| | Gram positive | 60 (65.22) |
| Type n (%) | Acinetobacter baumannii | 7 (07.61) |
| | Escherichia coli | 7 (07.61) |
| | Klebsiella pneumonia | 13 (14.13) |
| | Other Gram negative | 5 (05.43) |
| | Enterococcus faecalis | 6 (06.52) |
| | Staphylococcus aureus | 10 (10.87) |
| | Staphylococcus epidermis | 21 (22.83) |
| | Staphylococcus haemolyticus | 5 (05.43) |
| | Staphylococcus hominis | 11 (11.96) |
| | Other Staphylococcus | 7 (07.61) |
| Comorbid n (%) | Anemia | 7 (07.61) |
| | Diabetes | 9 (09.78) |
| | Hypertension | 18 (19.57) |
| | Chronic renal failure | 39 (42.39) |
| | Chronic obstructive pulmonary disease | 3 (03.26) |
| | Cardiovascular diseases | 8 (08.70) |
| | Pneumonia | 3 (03.26) |
| | Cerebral vascular diseases | 5 (05.43) |
| Prognosis n (%) | Discharged | 36 (39.13) |
| | Ex | 56 (60.87) |

**Table 2:** Laboratory findings of the groups formed according to prognosis status

| Parameter | Ex n=56 | Discharged n = 36 | p |
|---|---|---|---|
| Neutrophils (*$10^9$ /L) | 13.57±12.88 | 11.15±5.90 | >0.05 |
| Lymphocytes (*$10^9$ /L) | 1.16±1.72 | 1.10±0.61 | 0.029 |
| Monocyte (*$10^9$ /L) | 0.85±0.80 | 0.82±1.06 | >0.05 |
| Platelets (*$10^9$ /L) | 181.14±145.19 | 227.81±136.33 | >0.05 |
| Lactate (mmol/L) | 3.41±3.01 | 2.43±1.44 | >0.05 |
| Albumin (g/L) | 2.40±0.54 | 2.52±0.43 | >0.05 |

| | | | |
|---|---|---|---|
| Lactate /Albumin | 1.45±1.27 | 0.99±0.58 | 0.025 |
| CRP (mg/L) | 183.79±119.31 | 162.64±110.99 | >0.05 |
| AST (U/L) | 57.00±64.57 | 64.94±99.97 | >0.05 |
| ALT (U/L) | 49.11±137.53 | 49.00±59.45 | >0.05 |
| pH | 7.37±0.13 | 7.35±0.11 | >0.05 |
| Base deficit | -1.61±6.40 | -2.57±5.61 | >0.05 |
| sO2 | 67.94±15.60 | 63.44±17.70 | >0.05 |
| pO2 | 45.28±14.76 | 42.98±17.15 | >0.05 |

CRP: C - reactive protein, AST: Aspartate Aminotransferase ALT: Alanine Aminotransferase, $sO_2$: Oxygen saturation, $pO_2$: Partial Arterial Oxygen Pressure

## Conclusion

In conclusion, it was determined that the lactate-albumin ratio was beneficial as an independent risk factor for mortality in inpatients with postoperative sepsis. It can provide valuable information about the severity of the condition. Although a comprehensive analysis including multiple indices provides a more comprehensive assessment of sepsis prognosis, the lactate-albumin ratio and age score provide a convenient and accurate method of assessment. These findings show that the lactate-albumin ratio and related scoring systems hold promise for wider clinical applications in the future.

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