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Comparison between APACHE II score and lactate/albumin ratio in predicting mortality in septic patients

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Abstract

***Objective*: To compare the Acute Physiological And Chronic Health Evaluation II (APACHE II) scores and lactate/albumin ratio (LAR) in relation to mortality rates among septic patients in intensive care units (ICU).**

***Design*: Retrospective case-control study.**

***Setting*: Research from medical record data at the ICU of Dr. Wahidin Sudirohusodo Hospital in January-December 2023.**

***Patients and participants*: 147 septic patients were collected using the total sampling technique.**

***Measurements and results*: Patients were identified based on 28-day mortality and APACHE II and LAR measurements. APACHE II and LAR were significantly greater in deceased patients than survivors within 28 days of sepsis diagnosis ($p<0.05$). The area under the receiver operating characteristic (ROC) curve (AUC) of the APACHE II was 0.784 (95% CI=0.704-0.864, $p<0.001$) with a cut-off of 21.5, sensitivity of 71.6%, and specificity of 75.6%. The AUC of LAR was 0.733 (95% CI=0.651-0.815, $p<0.001$) with a cut-off of 0.955, sensitivity of 67.6%, and specificity of 68.9%.**

***Conclusions*: The APACHE II and LAR were good predictors of 28-day sepsis mortality, whereas the APACHE II obtained better diagnostic accuracy, sensitivity, and specificity than the LAR.**

Keywords: Lactate/albumin ratio, APACHE II, mortality, sepsis.

Introduction

Sepsis is a medical emergency as a systemic immune response of the body to infection that results in end-stage organ dysfunction and death. (1) The prevalence of mortality in sepsis globally is 26%. (2) The high mortality of sepsis occurs due to delays in identifying patients with sepsis and inadequate resuscitation. Early identification of the risk of mortality due to sepsis is a strategy that can reduce mortality in patients with sepsis. However, prediction of mortality due to sepsis is still a challenge until now. (3)

Lactic acidosis occurs as a consequence of tissue hypoxia in sepsis and septic shock. (4) When there is low oxygen saturation and oxygen supply is inadequate to tissue demand, anaerobic metabolism will occur and increase lactate production. (5) One of the biomarkers of sepsis prognosis is albumin. (4) Albumin may serve as an additional parameter as a predictor of mortality and prognosis in septic patients. (6) Decreased serum albumin levels are correlated with a higher risk of death in sepsis. (7) Lactate and albumin levels have limitations in predicting mortality due to the various factors that influence them. (4) Serum lactate/albumin ratio

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(LAR) is a better predictor of sepsis mortality than albumin and lactate levels. (5)

So far, to predict patient mortality in the intensive care unit (ICU), we use the Acute Physiology and Chronic Health Evaluation II (APACHE II) scoring system, a physiologically based classification system used to measure the severity of critical illness. The appropriate measurement tools in identifying sepsis mortality can be useful as a guide for doctors in developing individualized care strategies according to the patient's specific risk level, allowing for timely and appropriate intervention. (8) LAR is a simpler parameter and assessment instrument in predicting sepsis mortality, which has been reported separately in previous studies. Still, no study has compared the accuracy between APACHE II and LAR in predicting mortality in sepsis. Therefore, this study was interested in comparing APACHE II and LAR in predicting mortality in septic patients in the ICU.

Methods

This was a retrospective case-control design in the ICU of Dr. Wahidin Sudirohusodo Hospital in January-December 2023, with a total sampling technique collected from medical records. Inclusion criteria included patients with sepsis, over 18 years old, and had complete medical records. Patients with incomplete data, chronic liver or kidney disease, immunosuppressive diseases, uncontrolled type II diabetes mellitus, and patients who had received albumin therapy were excluded. Data collected included patient demographic and clinical characteristics, APACHE II score, LAR, and 28-day mortality. This study obtained ethical approval from the Hasanuddin University Ethics Committee on November 8, 2024, with protocol number UH24100867, and a research permit from Dr. Wahidin Sudirohusodo Hospital on November 25, 2024, with letter number DP.04.03/D.XIX.2.3.1/440/2024. Data were analyzed using SPSS 27, the chi-square test, and the receiver operating characteristic (ROC) curve to determine the area under the ROC curve (AUC) cut-off value, sensitivity, and specificity.

Results

This study collected 161 septic patients, with 147 patients meeting the inclusion criteria consisting of 102 patients dying within 28 days, while 45 patients survived in the same period (**Figure 1**).

Comparison of baseline characteristics of septic patients, including age, gender, body mass index (BMI), and comorbidities, did not differ significantly between patients who died and those who survived within 28 days (**Table 1**).

APACHE II and LAR scores were significantly correlated with 28-day mortality in sepsis with p-values<0.05 (**Table 2**). The values of both parameters were higher in patients who died compared to patients who survived within 28 days, indicating that the higher the APACHE II scores and LAR, the greater the risk of death in sepsis.

Figure 2 shows that the AUC value of the APACHE II was 0.784 (95% CI=0.704-0.864, p<0.001), and the LAR was 0.733 (95% CI=0.651-0.815, p<0.001). Both parameters had an AUC value ≥0.70, indicating that the APACHE II and LAR have good predictive ability for 28-day mortality in septic patients. Diagnostic accuracy is greater in APACHE II at 72.79% (**Table 3**).

Figure 3 shows that patients with higher APACHE II scores had a significantly lower survival rate at 28 days than patients with lower scores. Patients with a higher LAR experienced a significant decrease in survival at 28 days compared to patients with a lower one.

Discussion

These results showed that high APACHE II scores were correlated with greater mortality. This supports the study by Farhanah et al. that APACHE II was significantly associated with 28-day mortality in sepsis with severe and critical coronavirus disease 2019 (COVID-19). (9) Similar results by Mumtaz et al. showed that high APACHE II scores increased the likelihood of higher mortality. (10)

These results illustrate the high severity of the disease with the increasing APACHE II score. These results may explain that increased APACHE II scores in septic patients who died were associated with increased cytokines (interleukin [IL]-2, IL-6, and IL-10), which were related to immune dysfunction. Especially patients who died showed a high APACHE II score, impaired cytokine secretion, and lymphocyte subsets. (11) Other studies confirmed that there was a positive correlation between APACHE II score and plasma concentrations of procalcitonin, C-reactive protein (CRP), and copeptin. Patients who survived at day 28 had significantly lower APACHE II scores and procalcitonin, CRP, and copeptin levels than septic patients who died. This suggests that the APACHE II score reflects the severity of sepsis. (12)

In this study, the APACHE II score could be a good assessment tool in predicting 28-day mortality in sepsis with an AUC value of 0.784, a cut-off value of 21.50, a sensitivity of 71.6%, and a specificity of 75.6%. Wang et al. stated that the APACHE II with

a cut-off of 18.5, an AUC value of 0.763, a sensitivity of 65.8%, and a specificity of 68.4% could predict 28-day mortality in sepsis. (11) Edipoglu et al. reported that the APACHE-II had a cut-off of 23 with a sensitivity of 74.14%, specificity of 60.87%, and an AUC of 0.673 in predicting sepsis mortality. (13) The results of this study indicated that an APACHE II score ≥21.50 can predict 28-day mortality in sepsis.

Higher LAR was associated with an increased risk of all-cause mortality within 28 days of admission (14) and can help identify individuals with high mortality rates. (15) The LAR was an independent predictor of in-hospital mortality in adult septic patients presenting to the emergency department. (16) The meta-analysis study stated that a high LAR was associated with mortality in sepsis, so the LAR can be considered a predictive marker in predicting mortality in sepsis. (17)

A high LAR means high lactate levels and low albumin levels. Increased blood lactate levels indicate organ and tissue dysfunction and low tissue perfusion that can occur due to anaerobic metabolism. Meanwhile, albumin levels correlate with inflammation because it is a negative acute-phase protein. (15) LAR was associated with serum procalcitonin levels, a predictor of sepsis mortality. (18)

LAR is a good assessment tool for predicting 28-day mortality in septic patients with an AUC value of 0.733, a cut-off value of 0.955, a sensitivity of 67.6%, and a specificity of 68.9%. Kabra et al. reported that the albumin lactate ratio with a cut-off of 0.96 had a sensitivity of 100% and a specificity of 88% in predicting sepsis mortality. (7) In the study by Chebl et al., the LAR with a cut-off of 1.22 obtained an AUC value of 0.67 with a sensitivity of 59% and a specificity of 62%. (16) Bajaj et al. reported that the LAR was a good mortality indicator with a sensitivity of 91.1% and a specificity of 75% at a cut-off value of 0.650. (19) Thus, the LAR in this study could be a good mortality prediction tool in sepsis.

This study found the highest diagnostic accuracy in the APACHE II score. This supports Thapa et al.'s study that the APACHE II score had a slightly higher area of 0.96 under the ROC curve than the albumin lactate ratio of 0.90. The superiority of the APACHE II score compared to the LAR in predicting sepsis mortality is because the APACHE II uses the sum of acute physiology scores, age, and chronic health scores. In contrast, the LAR only uses two variables: lactate and albumin. (5) The APACHE II has the advantages of a single measurement, no need for additional investigations, and is well established in other sepsis systems. It has been validated in several countries and shown to be highly reproducible. (20)

This study's limitations included being conducted retrospectively, which limited its ability to collect additional data. It also did not measure predictive biomarkers of sepsis mortality and did not control for all factors that could affect bias, such as differences in treatment or severity of sepsis.

Conclusion

APACHE II score and LAR are good predictors of 28-day sepsis mortality. APACHE II score produces better diagnostic accuracy, sensitivity, and specificity than LAR, but LAR can be used as a simpler alternative predictive marker to predict mortality in septic patients.

APACHE II score is more recommended for a predictor of sepsis mortality than LAR. Further studies can be done using a longer observation duration, and other sepsis biomarker measurements can be performed.

Table 1. Sample characteristics

Characteristics		28-day mortality		p-value
		Yes (n=102)	No (n=45)	
Age (years), mean±SD		51.40±17.09	52.47±15.17	0.630[a]
Gender, n (%)	Male	52 (51)	30 (66.7)	0.078[b]
	Female	50 (49)	15 (33.3)	
BMI (kg/m^2), mean±SD		23.38±4.31	22.68±3.59	0.371[a]
Comorbid, n (%)	Yes	63 (61.8)	25 (55.6)	0.479[b]
	No	39 (38.2)	20 (44.4)	

Legend: SD=standard deviation; BMI=body mass index.
[a]Mann-Whitney test, [b]chi-square test.

Table 2. Relationship between APACHE II score and LAR to mortality

Parameter	28-day mortality		p-value
	Yes (n=102)	No (n=45)	
APACHE II score, mean±SD	24.26±5.83	18.53±4,91	<0.001
LAR, mean±SD	1.57±1.46	0.85±0.30	<0.001

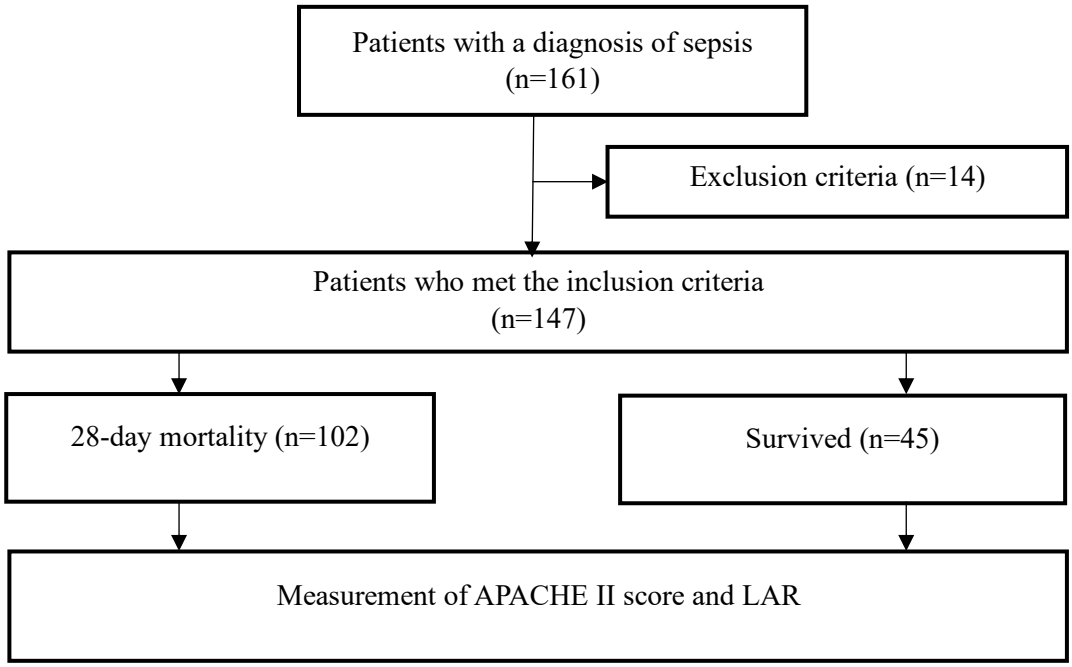
Legend: APACHE II=Acute Physiology and Chronic Health Evaluation II; LAR=lactate/albumin ratio; SD=standard deviation.

Table 3. Summary of comparison of diagnostic test results between APACHE II score and LAR

Parameter	APACHE II	LAR
AUC	0.784	0.733
Cut-off	21.500	0.955
Sensitivity	71.6%	67.6%
Specificity	75.6%	68.9%
Accuracy	72.79%	68.71%

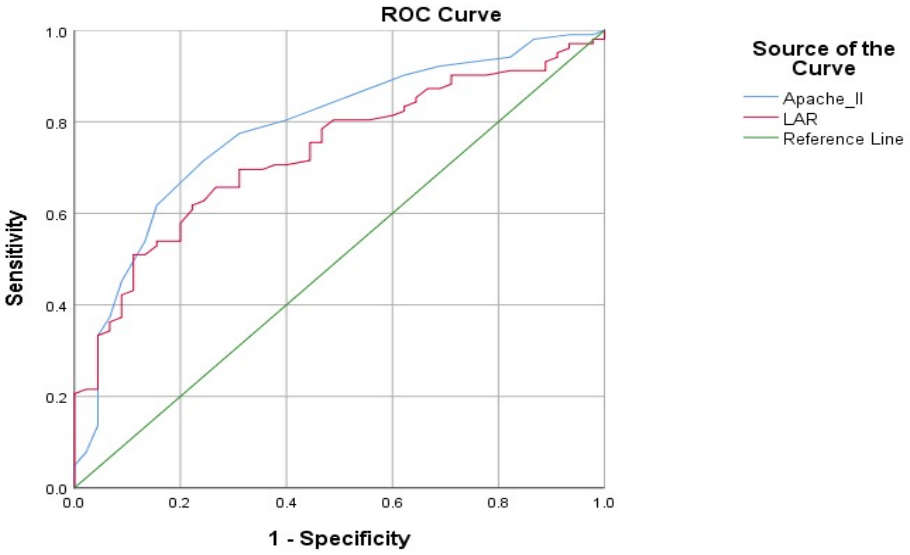
Legend: APACHE II=Acute Physiology and Chronic Health Evaluation II; LAR=lactate/albumin ratio; AUC=area under the receiver operating characteristic curve.

Figure 1. Flowchart for the study procedure



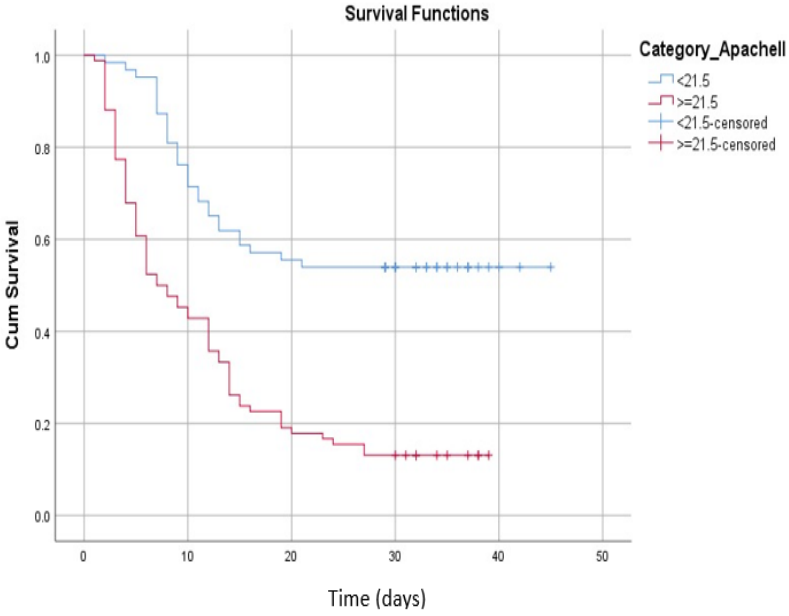
Legend: APACHE II=Acute Physiology and Chronic Health Evaluation II; LAR=lactate/albumin ratio.

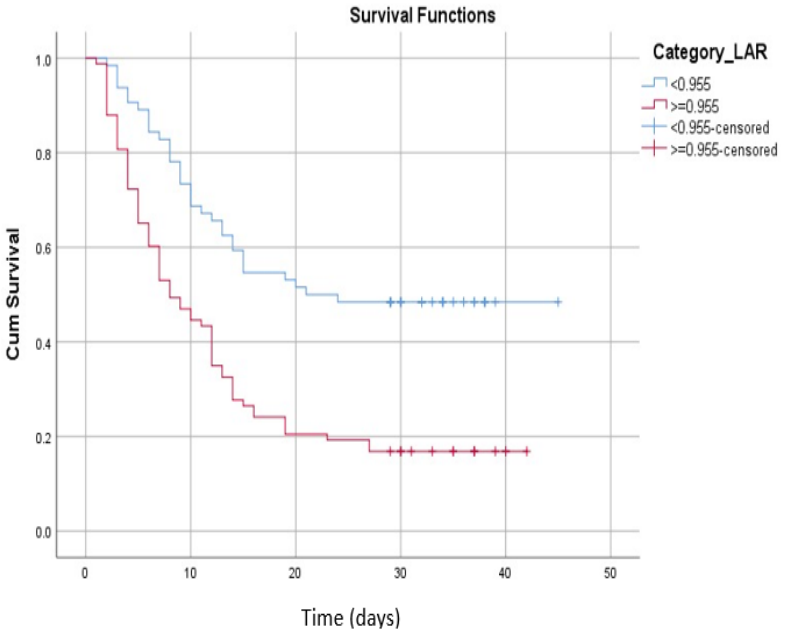
Figure 2. AUC between APACHE II score and LAR on mortality of septic patients



Legend: AUC=area under the receiver operating characteristic curve; APACHE II=Acute Physiology and Chronic Health Evaluation II; LAR=lactate/albumin ratio.

Figure 3. Kaplan-Meier graph of mortality rate on sepsis in various groups of APACHE II score and LAR





Legend: APACHE II=Acute Physiology and Chronic Health Evaluation II; LAR=lactate/albumin ratio.

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