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Lactate dehydrogenase to albumin ratio and prognosis in patients with acute exacerbation of chronic obstructive pulmonary disease: a retrospective cohort study

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Abstract

Background Chronic obstructive pulmonary disease (COPD) is a global public health challenge and a major cause of death. The lactate dehydrogenase to albumin ratio (LAR) is a simple and practical indicator of disease prognosis, but its prognostic value in acute exacerbation of COPD (AECOPD) remains unclear. Therefore, we aimed to explore the prognostic value of LAR for the short-term all-cause mortality risk in patients with AECOPD.

Methods This retrospective cohort study included 654 patients with AECOPD from the MIMIC-IV database. LAR was analyzed after natural logarithm transformation and the patients were divided into three groups. The clinical outcome was the 1-month and 3-months all-cause mortality. The relationship between LAR and all-cause mortality was assessed using Kaplan–Meier survival analysis and a Cox regression model. Generalized additive models were employed to identify non-linear relationships, and a subgroup analysis was performed to determine the stability of the results.

Results The study showed that LAR levels significantly and positively correlated with short-term all-cause mortality in patients with AECOPD. Compared to the low LAR group, patients in the medium LAR group had a significantly increased 1-month all-cause mortality risk, with a hazard ratio (HR) of 1.74 (95% [Confidence Interval, CI] 1.16–2.63, $P=0.008$). Patients in the high LAR group had an even higher 1-month all-cause mortality risk, with an HR of 2.58 (95% CI 1.75–3.80, $P<0.001$). For 3-month all-cause mortality, patients in the medium LAR group had an HR of 1.54 (95% CI 1.10–2.16, $P=0.012$), while those in the high LAR group had an HR of 2.18 (95% CI 1.58–3.01, $P<0.001$). The results remained stable in all three adjusted models and in the subgroup analyses. The relationship between LAR and

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all-cause mortality due to AECOPD was non-linear, with inflection points at 8.13 and 6.05 for 1-month and 3-month all-cause mortality, respectively.

Conclusions Elevated LAR is an independent predictive indicator of short-term all-cause mortality risk in patients with AECOPD and can be used to improve decision-making for the clinical management of these patients.

Clinical trial number Not applicable.

Keywords Albumin, Lactate dehydrogenase to albumin, Mortality, Chronic obstructive pulmonary disease, MIMIC IV

Introduction

Chronic obstructive pulmonary disease (COPD) is a public health concern. There were approximately 400 million COPD patients worldwide in 2019, with 3.23 million deaths, 90% of which occurred in low- and middle-income countries [1, 2]. Moreover, with the acceleration in population aging and extension of life expectancy, the prevalence and mortality of COPD are expected to increase by 2030 [3]. Independent factors related to poor prognosis in patients with COPD include advanced age, low body mass index, comorbidities, history of hospitalization due to acute exacerbation, clinical severity of acute exacerbation indicators, the need for long-term oxygen therapy after discharge, and adherence to medication maintenance treatment [4]. Acute exacerbation of COPD (AECOPD) is an important event in the clinical course of COPD that affects quality of life and is closely related to patient prognosis [5]. Currently, the prognosis of AECOPD mainly relies on clinical parameters and pulmonary function tests; however, these methods have limitations in predicting short-term mortality risk, such as the lack of recent pulmonary function data from the stable period when patients are admitted for acute exacerbation. A systematic review included 9–12 prognostic factors as prognostic tools, which are restricted in clinical applications [6]. Therefore, identifying simple and practical biomarkers is of great significance to improve the prognosis of Intensive Care Unit (ICU) patients with AECOPD and reduce mortality.

Lactate dehydrogenase (LDH) is an enzyme widely distributed in human tissues that is involved in the interconversion of lactic acid and pyruvic acid and is closely related to cellular metabolic activities [7]. Some studies have indicated that LDH levels are correlated with the prognosis of many diseases, including sepsis [8], tumors [9], and stroke [10]. Albumin (Alb), the main protein in plasma, is often used as an indicator to assess the nutritional status and inflammatory response of patients [11]. The LDH-to-Alb ratio (LAR) combines the characteristics of both indicators and may reflect the comprehensive impact of the body's metabolism and inflammatory state, which has a certain predictive value for short-term adverse outcomes in various diseases such as sepsis [12], pulmonary embolism [13], and acute kidney injury [14]. Although LDH and Alb have not traditionally been recognized as key indicators of COPD, their importance in reflecting systemic inflammation and metabolic status has been increasingly highlighted in recent years. For example, elevated LDH levels may indicate tissue hypoxia, inflammation, and oxidative stress, which are common pathological processes in AECOPD [15, 16]. Similarly, hypoalbuminemia is often associated with poor nutritional status and increased inflammatory burden, both of which are detrimental to the prognosis of COPD patients [17]. Therefore, the LDH-to-Alb ratio (LAR) may serve as a potential prognostic marker that integrates these metabolic and inflammatory aspects. However, its role in the prognosis of AECOPD patients has not been evaluated.

Therefore, this study aimed to explore the relationship between LAR and the prognosis of patients with AECOPD and to provide new prognostic assessment indicators for clinical practice.

Methods

Study design and data source

This retrospective cohort study included 654 cases of AECOPD from the Medical Information Market for Intensive Care-IV (MIMIC-IV) database that met the inclusion criteria. MIMIC-IV is a public clinical dataset maintained by the Massachusetts Institute of Technology that was released to the public in 2020 and updated (version 3.0) in 2024 [18]. The database contains detailed medical data of more than 90,000 ICU patients collected by Beth Israel Deaconess Medical Center from 2008 to 2022, involving demographics, vital signs, treatment measures, nursing records, imaging results, and discharge summaries, etc [18]. This study was authorized to use the database (authorization number ID: 55303142, 64990539). Because the analysis used publicly available de-identified data, institutional review board review at the Beth Israel Deaconess Medical Center was waived, and informed consent procedures were not needed. Clinical trial number (Not applicable).

Inclusion and exclusion criteria

This study initially included patients diagnosed with COPD according to the International Classification of Diseases (ICD) codes, with the specific codes as follows: 49,121 and 49,122 in ICD-9 and J44, J440, J441, and J449

in ICD-10. On this basis, patients with AECOPD were further screened, with codes 49,121 and 49,122 and ICD-9 and J440, J441 in ICD-10. To avoid data duplication, this study only considered the patients' first hospitalization records. The index date for each patient was defined as the date of the first hospital admission recorded in the MIMIC-IV database. This date served as the reference point for both exposure assessment (measurement of LAR) and outcome evaluation (all-cause mortality within 1 and 3 months). Patients with a hospital stay of less than 24 h and missing LDH and Alb data were excluded. All selected patients were aged > 18 years (Fig. 1).

Data extraction

We collected the clinical information of the patients, including demographic characteristics (age, sex, race), vital signs (heart rate, blood pressure, respiration rate, oxygen saturation, body temperature) recorded within the initial 24-hour period, first hematological tests (blood count, liver and kidney function index, blood glucose, and electrolytes) taken within 24 h of admission, comorbidities (hypertension, diabetes mellitus, liver disease, and obesity), ventilator use, and sequential organ failure assessment (SOFA) score. The clinical outcome was the all-cause mortality of patients within 1 and 3 months after admission. Before data analysis, we excluded any variables with more than 20% missing data and handled the remaining missing values using multiple imputation methods.

Statistical analysis

Given that the distribution of LAR did not follow a normal distribution, we performed a natural logarithmic transformation of LAR (Log2 LAR) and treated it as a continuous variable for analysis. Subsequently, the data were divided into three groups according to the tertiles of Log2 LAR: low, medium, and high LAR groups. For continuous variables, we used the mean ± standard deviation or median (interquartile range) to represent and

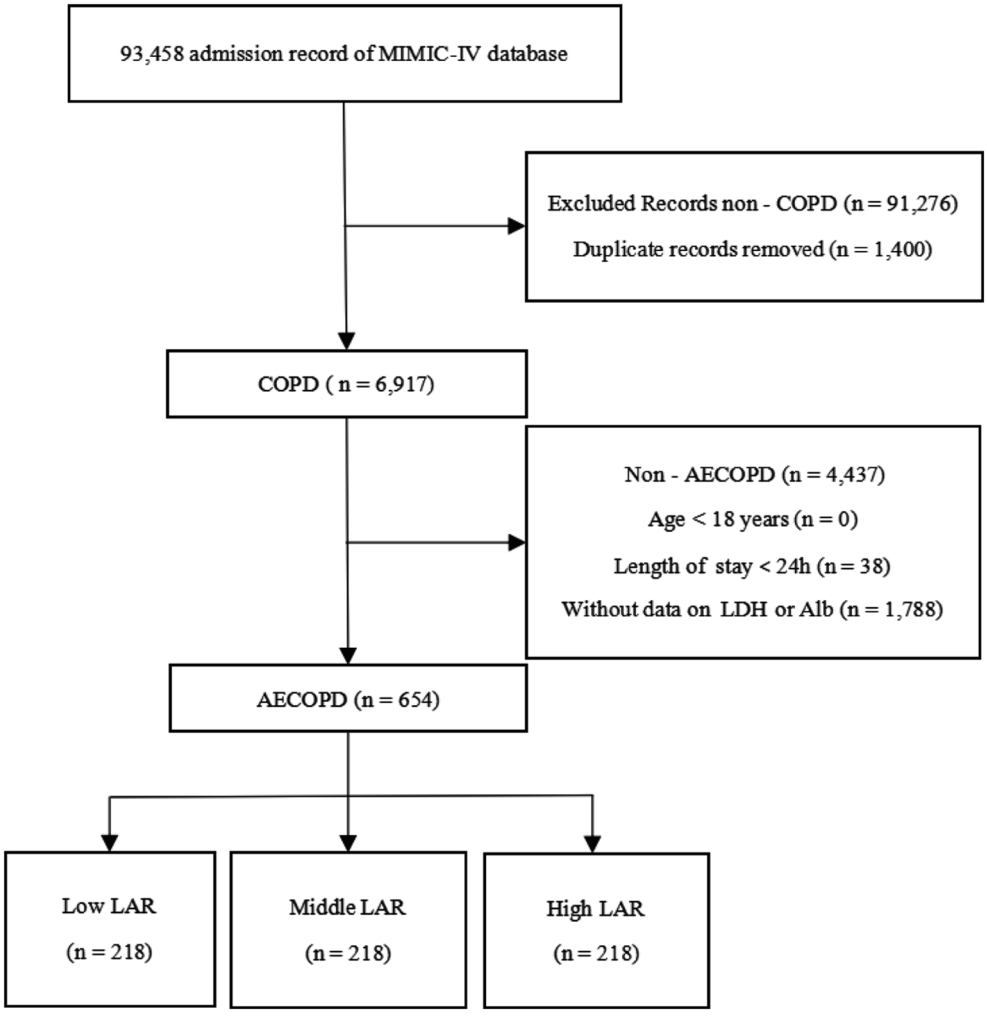

Fig. 1 The flowchart of patient selection

categorical variables were presented through frequency and percentage. To identify statistical differences in means and proportions between groups, we used a one-way analysis of variance (ANOVA), the Kruskal-Wallis H test, and the chi-square test. Kaplan-Meier (KM) survival analysis and the log-rank test were used to assess the differences in all-cause mortality among patients in the different LAR groups.

To ensure the validity of the Cox regression model, we assessed the proportional hazards assumption using Schoenfeld residuals. The weighted analysis showed that the global *P*-value for Schoenfeld residuals exceeded 0.05, indicating that the proportional hazards assumption was met (see Supplementary Figure S1).

To ensure the robustness of our Cox regression model, we calculated the variance inflation factors (VIF) for all covariates included in the model. All VIF values were less than 3, indicating that multicollinearity was within an acceptable range.

We constructed four statistical models to analyze the data: Model 0 without any adjustment; Model I adjusted for age, gender, and race; Model II further adjusted for hypertension, diabetes, coronary artery disease (CAD), heart failure, chronic kidney disease, liver disease, malignant tumors, and obesity on the basis of Model I. Model III added heart rate, respiratory rate, systolic blood pressure (SBP), blood oxygen saturation, sodium ions, potassium ions, glucose, blood urea nitrogen (BUN), creatinine (Cr), hemoglobin, white blood cell count (WBC), platelet (PLT), the use of ventilator, SOFA, and other variables on the basis of Model II.

In addition, we employed generalized additive models (GAM) to explore the non-linear relationship between LAR and AECOPD mortality; when a non-linear association was found, we used segmented linear regression models to determine the threshold effect of LAR on mortality. We also performed stratified and interaction analyses of age, sex, and the above-mentioned chronic diseases. All results were shown using hazard ratios (HRs) and 95% confidence intervals (CI), with statistical significance set at a *P*-value < 0.05. R software version 3.3.2 and EmpowerStats 4.0 were used for all statistical analyses.

Results

Baseline characteristics

A total of 654 AECOPD patients who met the criteria were included in the study, evenly distributed into three LAR level groups: low LAR group (2.68–4.71) with 218 cases; medium LAR group (4.71–6.09) with 218 cases; high LAR group (6.09–15.45) with 218 cases. The average age of the patients was 61.43 ± 16.91 years, and the proportion of females was approximately 48.62%. Within 1 and 3 months of admission, there were 178 and 242 patient deaths, respectively; the specific baseline characteristics are detailed in Table 1. There were no statistically significant differences in age, sex, race, or prevalence of hypertension, diabetes, heart failure, or other diseases among the three LAR groups. Compared with the low-LAR group, patients in the medium- and high-LAR groups had lower SBP, higher serum sodium, BUN, Cr, and WBC levels, and a higher prevalence of CAD.

Kaplan-Meier curves

We created Kaplan-Meier survival plots for the patients (Fig. 2), and the results showed that compared with the low LAR group, the mortality of patients in the medium and high LAR groups increased significantly ($P < 0.05$).

Association between LAR and all-cause mortality of AECOPD

Before conducting the Cox regression analysis, we assessed the proportional hazards assumption using Schoenfeld residuals. The weighted analysis showed that the global *P*-value for Schoenfeld residuals exceeded 0.05, indicating that the proportional hazards assumption was met (see Supplementary Figure S1). To ensure the robustness of our Cox regression model, we calculated the variance inflation factors (VIF) for all covariates included in the model. All VIF values were less than 3, indicating that multicollinearity was within an acceptable range. We then established four statistical models to analyze the data using Cox proportional risk analysis. Compared with the low LAR group, the 1-month all-cause mortality risk of patients in the medium and high LAR groups was significantly increased, with the HRs of 1.74 (95%CI 1.16–2.63, $P = 0.008$) and 2.58 (95%CI 1.75–3.80, $P < 0.001$), respectively. The 3-month all-cause mortality risk showed similar results, with the HRs of 1.54 (95%CI 1.10–2.16, $P = 0.012$) and 2.18 (95%CI 1.58–3.01, $P < 0.001$) in the medium and high LAR groups, respectively. Similar results were observed for the other three models. Detailed data are shown in Table 2. These results indicate that LAR is an effective indicator of short-term all-cause mortality risk in patients with AECOPD.

A nonlinear relationship analysis

We explored the linear relationship between LAR and all-cause mortality due to AECOPD as a continuous variable. This study found that the relationship between LAR and all-cause mortality due to AECOPD was nonlinear (Fig. 3). Through GAM analysis of the correlation and threshold effect of LAR on all-cause mortality and adjustment for all indicators in Model II, we determined the threshold values for 1-month and 3-month all-cause mortality as 8.13 and 6.05, respectively. On the left side of the threshold, the effect size was 1.76 (95%CI 1.41–2.19, $P < 0.001$) and 5.88 (95%CI 1.97–17.51, $P = 0.002$); on the

Table 1 Baseline characteristics of participants

Variables	All	Low LAR	Middle LAR	High LAR	*P*-value
Number	654	218	218	218	
LAR	89.85 (67.34-137.43)	58.93 (49.61–67.28)	89.85 (82.37-101.09)	170.31 (137.81-248.59)	< 0.001
Log2 LAR	6.68 (0.94)	5.83 (0.30)	6.51 (0.18)	7.70 (0.84)	< 0.001
Age, years	71.45 (10.97)	70.86 (12.12)	72.86 (10.21)	70.64 (10.39)	0.065
Gender, Female	318 (48.62%)	108 (49.54%)	110 (50.46%)	100 (45.87%)	0.598
Race					0.700
White	434 (66.36%)	148 (67.89%)	145 (66.51%)	141 (64.68%)	
Black	52 (7.95%)	20 (9.17%)	18 (8.26%)	14 (6.42%)	
Asian	12 (1.83%)	2 (0.92%)	5 (2.29%)	5 (2.29%)	
Other	156 (23.85%)	48 (22.02%)	50 (22.94%)	58 (26.61%)	
Heart Rate (beats/min)	93.95 (21.04)	92.55 (19.01)	93.22 (23.00)	96.07 (20.86)	0.179
Respiration rate (beats/min)	21.96 (6.14)	22.01 (6.43)	21.32 (5.17)	22.54 (6.67)	0.116
SBP (mmHg)	125.45 (25.71)	128.47 (25.05)	125.89 (25.33)	121.99 (26.43)	0.029
SpO2 (%)	95.63 (4.51)	95.79 (3.96)	95.76 (3.94)	95.33 (5.47)	0.485
Na^+ (mmol/L)	138.35 (5.92)	137.41 (6.01)	138.54 (5.88)	139.10 (5.76)	0.014
K^+ (mmol/L)	4.46 (0.84)	4.46 (0.79)	4.43 (0.83)	4.50 (0.91)	0.687
Glucose (mg/dL)	159.93 (90.58)	159.92 (85.34)	160.09 (71.39)	159.78 (110.73)	0.999
LDH (U/L)	279.00 (212.00-397.75)	198.00 (170.25–226.00)	280.50 (244.25–319.00)	493.00 (390.75-740.75)	< 0.001
ALB (g/dl)	3.13 (0.57)	3.45 (0.47)	3.08 (0.50)	2.86 (0.58)	< 0.001
BUN (mg/dl)	26.00 (17.00–41.00)	22.00 (16.00–33.00)	29.00 (18.00–42.00)	28.00 (18.00–48.00)	< 0.001
Cr (mg/dL)	1.10 (0.80–1.60)	0.90 (0.70–1.30)	1.10 (0.80–1.70)	1.20 (0.80–1.80)	0.002
WBC (K/μL)	11.20 (7.70–15.70)	10.00 (7.20–13.40)	11.00 (7.60-14.55)	13.15 (8.40-18.48)	< 0.001
HGB (g/dl)	10.73 (2.37)	10.89 (2.35)	10.45 (2.44)	10.83 (2.30)	0.130
PLT (K/μL)	204.00 (139.00-268.50)	215.00 (147.50-271.50)	202.00 (140.50-267.75)	187.00 (120.75–266.00)	0.071
Hypertension	234 (35.78%)	82 (37.61%)	77 (35.32%)	75 (34.40%)	0.771
Diabetes	218 (33.33%)	73 (33.49%)	75 (34.40%)	70 (32.11%)	0.877
CAD	275 (42.05%)	64 (29.36%)	98 (44.95%)	113 (51.83%)	< 0.001
CHF	344 (52.60%)	110 (50.46%)	121 (55.50%)	113 (51.83%)	0.552
CKD	162 (24.77%)	47 (21.56%)	58 (26.61%)	57 (26.15%)	0.402
Liver disease	83 (12.69%)	22 (10.09%)	28 (12.84%)	33 (15.14%)	0.285
Malignancy	120 (18.35%)	37 (16.97%)	37 (16.97%)	46 (21.10%)	0.437
Obesity	215 (32.87%)	64 (29.36%)	75 (34.40%)	76 (34.86%)	0.398
Use of invasive ventilation	848 (35.86%)	105 (48.17%)	120 (55.05%)	154 (70.64%)	< 0.001
Use of non-invasive ventilation	497 (20.50%)	43 (19.72%)	39 (17.89%)	23 (10.55%)	0.022
SOFA	4.21 (3.02)	3.92 (3.21)	4.26 (3.73)	5.12 (4.33)	< 0.001
OASIS	37.06 (9.01)	34.70 (8.41)	36.56 (8.48)	39.92 (9.37)	< 0.001
SAPSII	42.60 (13.81)	37.97 (11.98)	41.93 (12.00)	47.90 (15.36)	< 0.001
1-month all-cause mortality	178 (27.22%)	45 (17.51%)	98 (29.97%)	35 (50.00%)	< 0.001
3-month all-cause mortality	178 (27.22%)	178 (27.22%)	81 (37.16%)	103 (47.25%)	< 0.001

ALB, albumin; BUN, blood urea nitrogen; CAD, coronary atherosclerotic disease; CHF, congestive heart failure; CKD, chronic renal failure; Cr, creatinine; HGB, hemoglobin; LAR, LDH/ALB ratio; LDH, lactic dehydrogenase; OASIS, oxford acute severity of illness score; PLT, platelet; SAPS II, simplified acute physiology score II; SBP, systolic pressure; SOFA, sequential organ failure assessment; SpO2, blood oxygen saturation; WBC, white blood cells

right side of the threshold, the effect of 1-month all-cause mortality was 0.89 (95%CI 0.56–1.41, $P = 0.618$), and the effect of 3-month all-cause mortality was 1.24 (95%CI 1.07–1.44, $P = 0.003$), with specific results seen in Table 3.

Subgroup analysis

We also conducted subgroup analysis and interaction tests to assess whether the correlation between LAR and all-cause mortality in patients with AECOPD was consistent across different subgroups and adjusted for other factors in the subgroup analysis. The results showed that in most subgroups of patients with AECOPD, the medium and high LAR groups were associated with higher all-cause mortality (Table 4). It is important to note that an interaction was found in the sex subgroup analysis for 1-month all-cause mortality (interaction, $P < 0.05$), but the risk of death increased in both groups; therefore, we believe the results are still robust.

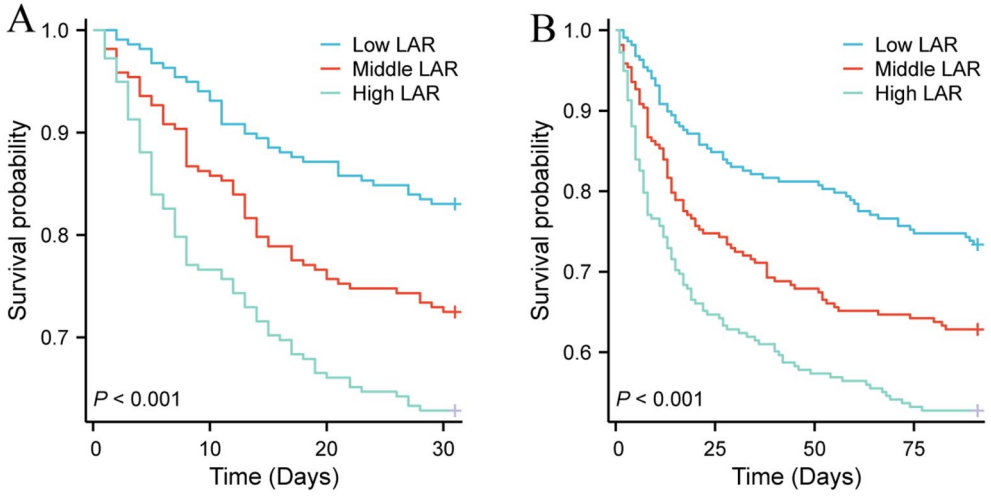

Fig. 2 Kaplan-Meier curve analysis of all-cause mortality risk for AECOPD patients. **A** 1-month all-cause mortality risk.**B** 3-month all-cause mortality risk

Table 2 Cox proportional hazard ratios (HRs) for all-cause mortality based on LAR

Log2 LAR	Unadjusted model		Model I		Model II		Model III	
	HR (95%CI)	*P*	HR (95%CI)	*P*	HR (95%CI)	*P*	HR (95%CI)	*P*
1-month mortality								
Low LAR	Ref		Ref		Ref		Ref	
Middle LAR	1.74 (1.16, 2.63)	0.008	1.65 (1.10, 2.49)	0.017	1.68 (1.11, 2.54)	0.015	1.74 (1.09, 2.77)	0.020
High LAR	2.58 (1.75, 3.80)	< 0.001	2.69 (1.82, 3.99)	< 0.001	2.67 (1.79, 3.98)	< 0.001	2.38 (1.45, 3.92)	< 0.001
3-month mortality								
Low LAR	Ref		Ref		Ref		Ref	
Middle LAR	1.54 (1.10, 2.16)	0.012	1.49 (1.06, 2.08)	0.022	1.51 (1.08, 2.13)	0.016	1.61 (1.09, 2.35)	0.015
High LAR	2.18 (1.58, 3.01)	< 0.001	2.26 (1.64, 3.12)	< 0.001	2.27 (1.63, 3.16)	< 0.001	2.20 (1.45, 3.33)	< 0.001

Crude model: we did not adjust other covariates. Model I: we adjusted age, gender and race. Model II: we adjusted age, gender, race, hypertension, diabetes, CAD, CHF, CKD, liver disease, malignancy and obesity. Model III: we adjusted age, gender, race, HR, RR, SBP, SpO2, hypertension, diabetes, CAD, CHF, CKD, liver disease, malignancy, obesity, serum sodium, serum potassium, glucose, BUN, Cr, WBC, HGB, PLT, use of ventilator/ noninvasive ventilator, SOFA, OASIS, SAPSII. AECOPD, acute exacerbation of chronic obstructive pulmonary disease; BUN, blood urea nitrogen; CAD, coronary atherosclerotic disease; WBC, white blood cells; CHF, congestive heart failure; CI, confidence interval; CKD, chronic renal failure; Cr, creatinine; HGB, hemoglobin; LAR, Lactate dehydrogenase to albumin ratio; OASIS, oxford acute severity of illness score; PLT, platelet; SAPSII, simplified acute physiology score II; SBP, systolic pressure; SOFA, sequential organ failure assessment; SpO2, blood oxygen saturation; Ref, reference

Discussion

In this retrospective cohort study, we conducted an in-depth analysis of the relationship between LAR levels and the prognosis of patients with AECOPD. The results showed that LAR levels were significantly and positively correlated with short-term all-cause mortality in patients with AECOPD. Specifically, the medium- and high-LAR groups had significantly increased 1-month and 3-month all-cause mortality risks compared with the low-LAR group, and the results remained stable in the subgroup analysis and three adjusted models. These findings suggest that LAR may be an important prognostic predictor in patients with AECOPD and may serve as a potential biomarker for clinical practice.

In interpreting the clinical relevance of our results, we acknowledge that statistical significance (e.g., *P*-values) alone may not fully capture the practical implications of observed HRs. Recent methodological advancements propose the concept of minimal clinically important difference (MCID) for effect sizes beyond mean differences, such as HRs [19]. Horita et al. (2024) suggested that HR thresholds ≥ 1.2 could represent clinically meaningful differences in prognostic studies [20], as smaller effects may lack practical impact despite statistical significance. In our study, the adjusted HRs for medium and high LAR groups (1.74 and 2.58 for 1-month mortality; 1.54 and 2.18 for 3-month mortality) substantially exceeded this threshold. This indicates that elevated LAR may not only be statistically associated with mortality but also carry clinical significance in risk stratification for AECOPD patients. However, further validation of MCID thresholds specific to COPD populations is warranted.

The metabolic characteristics of AECOPD are related to various factors including abnormalities in energy production pathways, and an imbalance between oxidation and antioxidation. Disorders of these metabolic pathways may activate inflammatory signaling pathways, release inflammatory cytokines, activate oxidative stress,

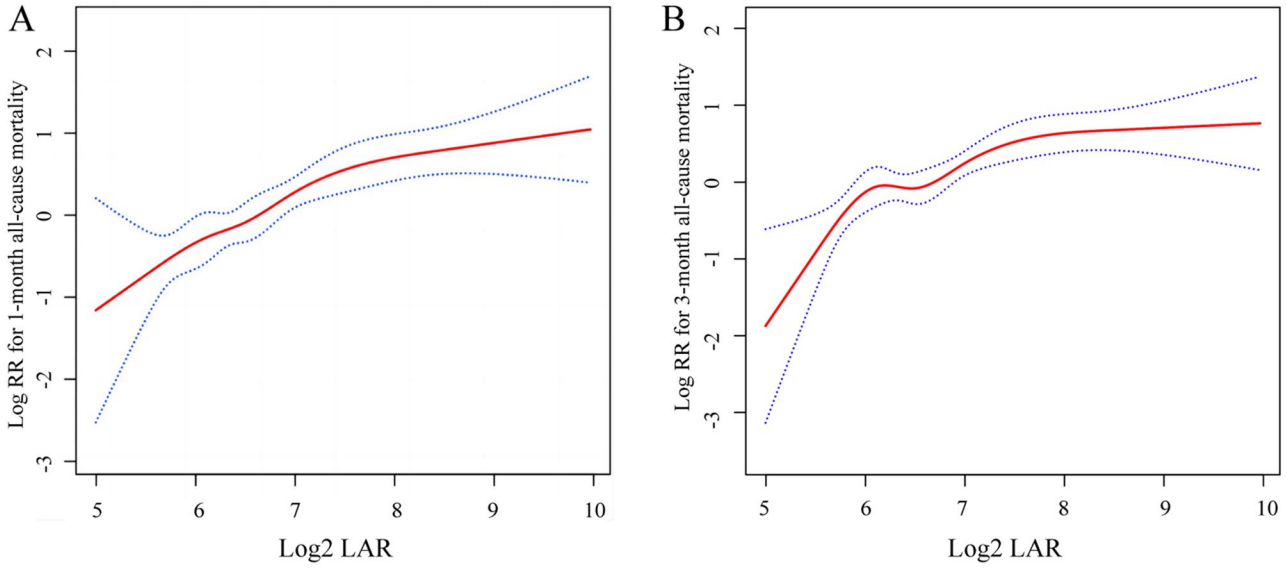

Fig. 3 A nonlinear relationship analysis between LAR and all-cause mortality due to AECOPD. **A** 1-month all-cause mortality risk. **B** 3-month all-cause mortality risk

Table 3 The results of two-piece wise linear regression model

Log2 LAR	Inflection point	HR(95%CI)	*P*-value
1-month mortality	< 8.13	1.76 (1.41, 2.19)	< 0.001
	≥ 8.13	0.89 (0.56, 1.41)	0.618
	Likelihood ratio test		0.021
3-month mortality			
	< 6.05	5.88 (1.97, 17.51)	0.002
	≥ 6.05	1.24 (1.07, 1.44)	0.003
	Likelihood ratio test		0.003

Adjusted: age, gender, race, heart rate, respiration rate, SBP, SpO_2, Temperature, hypertension, diabetes, CAD, CHF, CKD, liver disease, malignancy, obesity. CAD, coronary atherosclerotic disease; CHF, congestive heart failure; CI, confidence interval; CKD, chronic kidney disease; Ref, reference; SBP, systolic pressure; SpO2, blood oxygen saturation

and thus promote the development and exacerbation of COPD [21, 22]. Lactic acid metabolism plays an important role in AECOPD, and the accumulation of lactic acid may be related to tissue hypoxia, inflammation, and oxidative stress, which together promote the pathological process of AECOPD [23, 24]. LDH is a key enzyme in the glycolysis pathway, acting as a catalyst for the conversion of pyruvic acid to lactic acid. It is widely distributed in various tissues and cells and is a diagnostic marker of diseases and tissue damage [25]. A cohort study found that patients with a poor prognosis of AECOPD had higher serum LDH levels [26]. When a tissue is severely hypoxic or cell damage occurs, LDH is released from cells into the blood, and a significant increase in serum LDH levels can be detected [26].

Inflammation markers play a crucial role in the pathophysiology of COPD, particularly C-reactive protein (CRP) and interleukin-6 (IL-6), which not only reflect disease severity but are also closely related to smoking status [27]. Smoking, a major risk factor for COPD, induces inflammatory responses and oxidative stress, thereby exacerbating the disease process. Therefore, levels of inflammation markers may be influenced by both the severity of COPD and the patient's smoking status [28]. Notably, LAR, which combines metabolic and inflammatory characteristics, may also play a role in reflecting the inflammatory burden in COPD patients [14].

Several studies have confirmed that increased LDH levels are associated with disease severity and poor prognosis. In sepsis, one study found that high levels of LDH were associated with increased 28-day mortality [29]. Another study confirmed that LDH was related to 1-year all-cause mortality in patients with sepsis and was an important component in the model predicting 1-year all-cause mortality, which can significantly improve the accuracy of the model's prediction [8]. In a retrospective cohort study involving 8,436 patients with acute kidney injury, in-hospital mortality increased with increased LDH and was almost linearly related [30].

Alb plays a key role in maintaining colloidal osmotic pressure in the human body. In addition to reflecting nutritional status, Alb is involved in inflammatory responses and antioxidant processes. Ma et al. [31] reported a negative association between the serum albumin and in-hospital mortality rates. A clinical cohort study found that low serum Alb levels were associated with poor short-term prognosis in patients with acute pulmonary embolism [32]. A recent retrospective cohort study indicated that low serum Alb levels were significantly associated with the risk of adverse cardiac events, hospitalization frequency, and death in patients with chronic heart failure [33]. Another cohort study found

Table 4 The results of subgroup analysis and interaction tests

		1-month mortality			3-month mortality		
Variables	**Total (*n*)**	**Effect size (HR)**	***P***	***P* for interaction**	**Effect size (HR)**	***P***	***P* for interaction**
Age				0.430			0.384
<72	330	1.46 (1.20, 1.77)	0.001		1.36 (1.15, 1.61)	0.001	
≥72	324	1.57 (1.31, 1.88)	<0.001		1.48 (1.25, 1.75)	<0.001	
Gender				0.040			0.033
Male	336	1.73 (1.42, 2.10)	<0.001		1.59 (1.34, 1.88)	<0.001	
Female	318	1.32 (1.10, 1.57)	0.002		1.25 (1.07, 1.46)	0.006	
Hypertension				0.077			0.463
No	420	1.35 (1.13, 1.61)	0.001		1.35 (1.16, 1.57)	0.001	
Yes	234	1.71 (1.40, 2.09)	<0.001		1.46 (1.22, 1.75)	<0.001	
Diabetes				0.148			0.135
No	436	1.55 (1.32, 1.82)	<0.001		1.46 (1.26, 1.69)	<0.001	
Yes	218	1.34 (1.06, 1.69)	0.014		1.27 (1.05, 1.54)	0.016	-
CAD				0.772			0.944
No	379	1.47 (1.20, 1.79)	0.002		1.40 (1.18, 1.66)	0.001	
Yes	275	1.49 (1.24, 1.78)	<0.001		1.39 (1.18, 1.64)	<0.001	
CHF				0.980			0.968
No	310	1.50 (1.25, 1.80)	<0.001		1.40 (1.20, 1.64)	<0.001	
Yes	344	1.47 (1.22, 1.78)	<0.001		1.38 (1.16, 1.64)	0.002	
CKD				0.421			0.824
No	492	1.51 (1.30, 1.75)	<0.001		1.38 (1.21, 1.58)	<0.001	
Yes	162	1.40 (1.04, 1.88)	0.027		1.42 (1.10, 1.83)	0.006	
Liver disease				0.789			0.855
No	517	1.47 (1.27, 1.70)	<0.001		1.39 (1.22, 1.58)	<0.001	
Yes	83	1.53 (1.12, 2.09)	0.007		1.39 (1.06, 1.83)	0.017	
Malignancy				0.392			0.454
No	534	1.56 (1.33, 1.82)	<0.001		1.46 (1.27, 1.67)	<0.001	
Yes	120	1.24 (0.99, 1.56)	0.066		1.17 (0.95, 1.44)	0.144	
Obesity				0.578			0.582
No	439	1.49 (1.26, 1.76)	<0.001		1.40 (1.21, 1.62)	<0.001	
Yes	215	1.51 (1.22, 1.86)	0.002		1.40 (1.15, 1.69)	0.001	

CAD, coronary atherosclerotic disease; CHF, congestive heart failure; CKD, chronic renal failure

that low serum Alb levels were closely related to persistent organ failure and risk of mortality in patients with acute pancreatitis [34]. These findings emphasize the importance of monitoring and maintaining appropriate serum albumin levels during clinical treatment.

LAR is an easily detectable biomarker that has recently received increasing attention in the field of medicine. Studies have shown that LAR can independently predict poor prognosis in patients with various diseases including stroke [35], pulmonary embolism [13], cardiac arrest [36], and other vascular diseases. In addition, in infectious or pulmonary diseases, LAR has been associated with a poor prognosis. Lee et al. pointed out that LAR can effectively predict in-hospital mortality risk in patients with lower respiratory tract infections [37]. In patients with sepsis, an increase in LAR has been confirmed as an important predictor of all-cause death risk in the ICU [12]. In COVID-19 infected patients, a high LAR is related to increased COVID-19 mortality, ICU admission rate, and hospital stay, with an optimal critical value of 136 [38]. These studies suggest that LAR is a common and reliable prognostic indicator, which supports our results. Our data analysis showed that even after adjusting for all other influencing factors, medium and high LAR levels were still independently associated with all-cause death risk in AECOPD patients. These findings may help medical workers more accurately identify patients with severe AECOPD and take targeted intervention measures in a timely manner.

Although this study was based on a large-scale intensive care database, it provides preliminary evidence for the potential application of LAR in predicting the all-cause death risk of patients with AECOPD. However, there are several limitations to the study results that should be considered. First, owing to the retrospective design of this study, there may be challenges of selection bias and incomplete data. Second, the study lacked detailed information about the severity grading of patients with COPD, the drugs used daily to control the symptoms of COPD, pulmonary function test

results, the St. George's Respiratory Questionnaire (SGRQ), the COPD Assessment Test (CAT), and quality of life (QOL) scores. These indicators are significant for evaluating the overall health status and prognosis of COPD patients. Third, the MIMIC-IV database lacks data on key inflammatory markers, such as procalcitonin, C-reactive protein, and interleukin-6, which limits the accurate assessment of the patient's inflammatory status. Additionally, the specific identification rate of severe exacerbations within the COPD cohort was not available in the database, which may affect the comprehensive evaluation of AECOPD events. Lastly, the reliance solely on the MIMIC-IV ICU dataset may limit the generalizability of the results to broader populations, particularly those outside of intensive care settings. Therefore, more studies need to be conducted in a broader population, at multiple centers, and with long-term follow-up to further validate the prognostic value of LAR.

In summary, LAR is an effective indicator for predicting short-term death risk of patients with AECOPD and is associated with poor prognosis. Future studies should further verify the prognostic value of LAR and explore its combined application with other biomarkers to improve the prediction accuracy, thereby providing a more accurate prognostic assessment and treatment for patients with AECOPD.

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12890-025-03622-z.

Supplementary Material 1

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Author contributions
CWD and SSH conceived and drafted the manuscript. YHX, XC, and LW collected, analyzed, and visualized the data. YMM and YDY provided funding. YDY and JYQ were responsible for the design and supervision of the study. All the authors contributed to the review and editing of the manuscript. All the authors agreed to be accountable for all aspects of the work, ensuring that questions related to the accuracy or integrity of any part of the work were appropriately investigated and resolved.

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Data availability
The data from this study are publicly available in the MIMIC-IV Database (https://mimic.mit.edu).

Declarations

Ethics approval and consent to participate
This study was based on the latest MIMIC-IV version 3.0 database. Because the analysis used publicly available de-identified data, institutional review board review at the Beth Israel Deaconess Medical Center was waived, and informed consent procedures were not needed.

Consent for publication
Not applicable.

Competing interests
The authors declare no competing interests.

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