BMC Cardiovascular Disorders

RESEARCH

Open Access

Association of red cell distribution width/albumin ratio and 28-day mortality in chronic obstructive pulmonary disease patients with atrial fibrillation: a medical information mart for intensive care IV study

Jian-min Qu[1], Xia-hong Tang[1], Wen-juan Tang[2] and Li-ya Pan[3*]

Abstract

Background Chronic obstructive pulmonary disease (COPD) complicated by atrial fibrillation (AF) in ICU patients is associated with higher risks of adverse outcomes. The red cell distribution width to albumin ratio (RAR), may predict mortality in critical illness, yet its link to 28-day mortality in ICU patients with COPD and AF remains unclear.

Methods This retrospective cohort study analyzed 693 ICU patients with COPD and AF from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database, grouped by RAR tertiles. The primary endpoint was 28-day mortality, with secondary endpoints including 90-day, 365-day, and ICU mortality. Multivariate cox models estimated hazard ratios (HRs) for mortality, while restricted cubic spline regression assessed the linearity of the RAR-mortality relationship. Kaplan-Meier curves compared survival across tertiles, and subgroup analyses explored RAR's impact across age, gender, race, and comorbidities.

Results Our study included 693 ICU patients with both COPD and AF, with an average age of 74.9 years. The 28-day mortality was 30.7%. Patients in the highest RAR tertile had significantly worse 28-day survival ($p < 0.0001$). Higher RAR was linearly associated with increased 28-day mortality (p for non-linearity > 0.05), with each 1-unit increase in RAR linked to an 18% rise in mortality risk (95% CI: 1.08–1.29). Sensitivity analyses confirmed RAR's relevance for 90-day, 365-day, and ICU mortality.

Conclusions RAR is independently associated with 28-day mortality in COPD patients with AF. Elevated RAR levels correlate with higher 28-day mortality rates in this population.

Clinical trial number Not applicable.

Keywords Chronic obstructive pulmonary disease, Atrial fibrillation, Mortality, Red cell distribution width, Albumin

*Correspondence:
Li-ya Pan
panliya@qq.com
[1]Department of Intensive Care Unit, Tongxiang First People's Hospital, Tongxiang, Zhejiang 314500, China
[2]Department of Intensive Care Unit, The Second Affiliated Hospital, Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, Zhejiang 325000, China
[3]Department of Cardiology, The Second Affiliated Hospital, Yuying Children's Hospital of Wenzhou Medical University, Wenzhou, Zhejiang 325000, China

Introduction

Chronic obstructive pulmonary disease (COPD), as defined by the Global Initiative for Chronic Obstructive Lung Disease (GOLD) [1], is a progressive respiratory disorder characterized by persistent airflow limitation, diagnosed by a post-bronchodilator FEV1/FVC ratio of less than 0.7 [2]. According to the Global Burden of Disease (GBD) study, COPD affected 251 million people worldwide in 2016. By 2030, it is projected to become the third leading cause of death globally [3]. Atrial fibrillation (AF), the most common sustained heart arrhythmia, affects 2–4% of the global population and frequently complicates the clinical course of COPD, resulting in higher hospitalization rates, poorer quality of life, and increased mortality [4, 5]. The coexistence of these two conditions is common due to shared risk factors such as smoking, aging, and systemic inflammation [6]. COPD patients are particularly vulnerable to developing AF, as the chronic hypoxia, inflammation, and hemodynamic changes associated with COPD can trigger arrhythmogenesis, while AF can worsen COPD outcomes by impairing pulmonary function and gas exchange [5, 7].

In recent years, the red cell distribution width to albumin ratio (RAR) has emerged as a novel biomarker with potential prognostic value across various diseases. The red cell distribution width (RDW), which reflects the variability in red blood cell size [8], is a marker of systemic inflammation, oxidative stress, and nutritional deficits—all of which are prevalent in COPD [9]. Albumin, a negative acute-phase protein, is a well-established marker of both inflammation and nutritional status. Low plasma albumin levels are a significant predictor of increased mortality in COPD and are robustly associated with cardiovascular diseases [10, 11]. The combination of these two parameters into a single ratio, RAR, provides a more comprehensive assessment of both inflammatory burden and nutritional status. High RAR levels have been identified as independent risk factors for poor outcomes in non-ischemic heart failure and are significantly associated with increased in-hospital mortality in patients with atrial fibrillation. Additionally, elevated RAR is linked to worse clinical prognosis in sepsis [12–15].

However, the specific relationship between RAR and outcomes in patients with COPD complicated by AF remains underexplored. Understanding this relationship is crucial given the significant impact both diseases have on patient prognosis. In this study, we aim to investigate the association between RAR and 28-day mortality in patients with COPD and AF.

Materials and methods

Data source

This retrospective study utilized data from the Medical Information Mart for Intensive Care IV (MIMIC-IV, Version 3.0) database. MIMIC-IV includes records from over 94,000 patients admitted to the intensive care units at Beth Israel Deaconess Medical Center in Boston, MA, between 2008 and 2022. The database is approved by the Institutional Review Boards of the Massachusetts Institute of Technology (Cambridge, MA, USA) and Beth Israel Deaconess Medical Center (Boston, MA, USA) [16]. To ensure patient privacy, all personally identifiable information has been removed. Access to this database is restricted to individuals who have completed the Collaborative Institutional Training Initiative (CITI) program. Due to the retrospective study design and the use of a public database, informed consent was not required.

Study subjects

The study included a cohort of adult patients (age > 18 years) diagnosed with COPD and AF, who were admitted to the ICU using data from the MIMIC-IV database. COPD and AF diagnoses were identified using International Classification of Diseases (ICD) codes [17], with chronic obstructive pulmonary disease classified under ICD-10 codes J44, J440, J441, and atrial fibrillation under ICD-10 codes I480, I481, I482, and I4891. Detailed ICD codes are provided in the supplementary materials in Table S1. For patients with multiple ICU admissions, only data from the first admission were used. Patients were excluded if key data, such as albumin or RDW, were missing, or if survival information was incomplete. Additional exclusion criteria included an ICU stay of less than 24 h. Ultimately, 693 patients with complete RDW and albumin data, diagnosed with both COPD and AF, were included in the final cohort (Fig. 1).

Demographical and laboratory variables

Patient data from the MIMIC-IV database were extracted using structured query language (SQL). The extracted data included demographics (age, gender, race, height, weight), vital signs (heart rate, respiratory rate, mean arterial pressure (MAP)), laboratory values (hemoglobin, white blood cell count, pH, partial pressure of carbon dioxide in arterial blood ($PaCO_2$), partial pressure of oxygen in arterial blood (PaO_2), creatinine, lactate, albumin, RDW), comorbidities (hypertension, congestive heart failure), clinical severity scores (Acute Physiology Score III (APSIII), Charlson Comorbidity Index (CCI)), and information on medications or procedures such as vasoactive agents and invasive mechanical ventilation (IMV). For variables with multiple measurements, the first recorded value was utilized. Body Mass Index (BMI) was calculated by dividing weight (kg) by height squared (m^2). To handle missing data, multiple imputation was conducted, creating and analyzing five datasets.

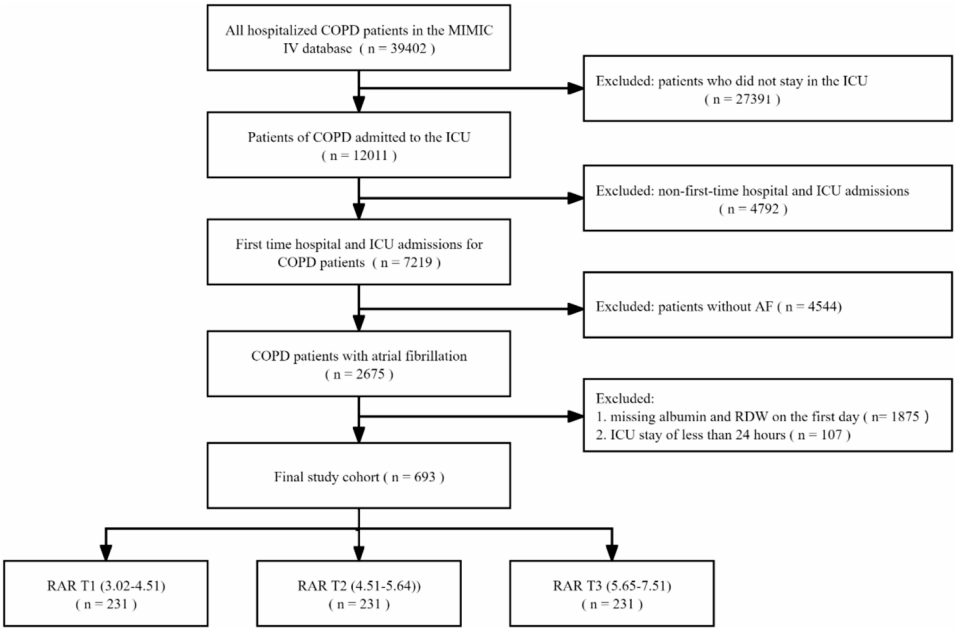

Fig. 1 Flow chart of the study population. Abbreviations: COPD, chronic obstructive pulmonary disease; MIMIC IV, Medical Information Mart for Intensive Care IV; ICU, intensive care unit; AF, atrial fibrillation; RDW, red cell distribution width; RAR, red cell distribution width to albumin ratio. T, tertile

RAR assessment and outcomes

RAR was calculated as [RDW (%)/serum albumin (g/dL)]. The primary outcome was 28-day mortality, while secondary endpoints included 90-day, 365-day, and ICU mortality.

Statistical analysis

Continuous variables were summarized as mean ± standard deviation (SD) if normally distributed, otherwise as median with interquartile range (IQR). While categorical variables were represented as counts and percentages. Continuous variables were evaluated with either ANOVA or the Kruskal-Wallis test, as appropriate, while categorical variables were compared using the chi-square test. Multivariate Cox proportional hazards models were utilized to estimate hazard ratios (HRs) and 95% confidence intervals (CIs) for the association between RAR and 28-day mortality. Three models were developed: Model 1 was unadjusted, while Model 2 was adjusted for age, gender, race, and BMI; and Model 3 included additional adjustments for heart rate, respiratory rate, MAP, WBC, hemoglobin, creatinine, lactate, pH, PaO_2, $PaCO_2$, hypertension, CHF, APACHE II, CCI, IMV, and vasoactive agent use. Restricted cubic spline (RCS) regression was employed to explore the relationship between RAR and 28-day mortality. Kaplan-Meier curves were generated to compare survival probabilities across different RAR groups, and subgroup analyses were performed based on age, gender, race, CHF, hypertension, and IMV. To assess the robustness of RAR's significance, sensitivity analyses were performed for 90-day, 365-day, and ICU mortality using the same multivariate Cox models employed in the primary analysis for 28-day mortality. We constructed receiver operating characteristic (ROC) curves and calculated the area under the curve (AUC) to compare the predictive abilities of the APACHE II, SOFA score, lactate, and RAR for 28-day mortality.

All statistical analyses were performed using R software version 4.2.2 (http://www.R-project.org, R Foundation) and Free Statistics version 2.0, with statistical significance set at $P < 0.05$.

Results

Baseline characteristics of study subjects

After screening, the study included 693 patients with COPD and AF who were admitted to the ICU (Fig. 1). The baseline characteristics were categorized according to RAR tertiles (Table 1), with 231 patients in each tertile: tertile 1 (T1), tertile 2 (T2), and tertile 3 (T3). The mean age of the participants was 74.9 years, comprising 297 females and 396 males. No significant differences were observed in age, gender, race, BMI, respiratory rate, pH, PaO_2, $PaCO_2$, creatinine, lactate, hypertension, or CHF among the three groups. However, patients in the high tertile exhibited lower MAP, higher heart rates, reduced hemoglobin and albumin levels, increased leukocyte counts and RDW, as well as elevated CCI and APACHE II scores. This group also received more vasoactive agents and IMV and had higher rates of 28-day, 90-day, 365-day, and ICU mortality.

Table 1 The clinical characteristics of critically ill patients with COPD and AF according to RAR levels

Variables	RAR	T1(3.02–4.51)	T2(4.51–5.64)	T3(5.65–7.51)	*P* value
	Total (*n* = 693) [%/(g/ dL)]	[%/(g/ dL)] (*n* = 231)	[%/(g/ dL)] (*n* = 231)	[%/(g/ dL)] (*n* = 231)	
General characteristics					
Gender, (female), n (%)	297 (42.9)	87 (37.7)	106 (45.9)	104 (45)	0.146
Age, (years)	74.9 ± 10.4	74.8 ± 10.4	75.7 ± 9.9	74.3 ± 10.8	0.336
Race, (white), n(%)	473 (68.3)	160 (69.3)	156 (67.5)	157 (68)	0.917
BMI, (kg/m^2)	29.7 ± 8.7	30.1 ± 8.7	29.5 ± 8.4	29.4 ± 9.0	0.628
Vital signs					
Heart rate, (beats/min)	111.1 ± 26.1	109.4 ± 24.8	108.2 ± 25.3	115.8 ± 27.8	0.004
Respiratory rate, (breaths/min)	29.4 ± 6.1	29.7 ± 6.0	28.9 ± 5.8	29.7 ± 6.5	0.255
MAP, (mmHg)	56.2 ± 13.2	58.9 ± 14.9	56.1 ± 13.5	53.6 ± 10.3	< 0.001
Laboratory parameters					
WBC, (10^9/L)	13.1 (9.1, 18.8)	13.3 (9.4, 18.8)	12.2 (8.7, 16.8)	14.1 (9.4, 20.0)	0.044
Hemoglobin, (g/dL)	9.9 ± 2.3	11.1 ± 2.1	9.9 ± 2.3	8.9 ± 2.0	< 0.001
pH	7.3 ± 0.1	7.3 ± 0.1	7.3 ± 0.1	7.3 ± 0.1	0.117
PaO_2, (mmHg)	73.0 (56.0, 94.0)	74.0 (61.0, 100.5)	73.0 (55.0, 93.0)	72.0 (55.0, 92.0)	0.21
$PaCO_2$, (mmHg)	50.0 ± 15.3	51.3 ± 15.9	49.2 ± 14.3	49.3 ± 15.7	0.254
Lactate, (mmol/L)	1.9 (1.4, 3.1)	2.0 (1.4, 3.2)	1.9 (1.3, 3.0)	1.9 (1.4, 3.3)	0.688
Creatinine, (mg/ dL)	1.4 (1.0, 2.2)	1.4 (1.0, 1.8)	1.4 (0.9, 2.2)	1.5 (1.0, 2.5)	0.092
Comorbidities					
Hypertension, n (%)	525 (75.8)	177 (76.6)	183 (79.2)	165 (71.4)	0.138
CHF, n (%)	441 (63.6)	147 (63.6)	155 (67.1)	139 (60.2)	0.302
Disease severity scores					
CCI, (scores)	8.1 ± 2.5	7.8 ± 2.3	8.0 ± 2.4	8.6 ± 2.7	0.003
APACHE II, (scores)	23.2 ± 7.2	21.4 ± 6.9	23.0 ± 6.9	25.3 ± 7.2	< 0.001
Medication or procedures on the first day of ICU admission					
Vasoactive agent, n (%)	275 (39.7)	67 (29)	88 (38.1)	120 (51.9)	< 0.001
IMV, n (%)	339 (48.9)	105 (45.5)	106 (45.9)	128 (55.4)	0.054
Outcomes					
Mortality of 28-day	213 (30.7)	49 (21.2)	67 (29.0)	97 (42.0)	< 0.001
Mortality of 90-day	264 (38.1)	69 (29.9)	78 (33.8)	117 (50.6)	< 0.001
Mortality of 365-day	355 (51.2)	96 (41.6)	111 (48.1)	148 (64.1)	< 0.001
Mortality of ICU	126 (18.2)	27 (11.7)	37 (16.0)	62 (26.8)	< 0.001

COPD, chronic obstructive pulmonary disease; AF, atrial fibrillation; RAR, ratio of red cell distribution width to albumin; BMI, body mass index; T, tertile; MAP, mean arterial pressure; WBC, White Blood Cell Count; pH, potential of hydrogen; PaO_2, partial pressure of oxygen in arterial blood; $PaCO_2$, partial pressure of carbon dioxide in arterial blood; CHF, congestive heart failure; APACHE II, acute physiology and chronic health evaluation II; CCI, Charlson Comorbidity Index; IMV, invasive mechanical ventilation; ICU, Intensive Care Unit

Associations between RAR and 28-day mortality

In Fig. 2, Kaplan-Meier survival curves demonstrate that patients in the highest RAR tertile (T3) had the worst survival outcomes ($p < 0.0001$). A significant positive linear relationship exists between RAR and 28-day mortality in patients with COPD and AF (p for non-linearity > 0.05, Fig. 3).

The multivariate cox regression analysis demonstrates a notable correlation between RAR and 28-day mortality. The hazard ratio (HR) for RAR was significant in all models when treated as a continuous variable ($p < 0.001$). Each 1-unit increase in RAR corresponds to an 18% increase in the 28-day mortality rate (95% CI 1.08–1.29). Additionally, when RAR is categorized into tertiles in Model 1, the adjusted HRs for T2 (4.51–5.64) and T3 (5.65–7.51) compared to T1 (3.02–4.51) were 1.42 (95% CI: 0.98–2.05, $p = 0.065$) and 2.31 (95% CI: 1.64–3.26, $p < 0.001$), respectively. Even after adjusting for various factors—including age, gender, race, BMI, heart rate, respiratory rate, MAP, WBC, hemoglobin, creatinine, lactate, pH, PaO2, PaCO2, hypertension, CHF, APACHE II, CCI, IMV, and vasoactive agents—a consistent trend was observed. Specifically, as RAR tertiles increased, the 28-day mortality rate correspondingly increased (p for trend < 0.05) (Table 2).

Subgroup analysis

The subgroup analyses shown in Fig. 4 conducted stratified assessments to examine potential modifiers of the

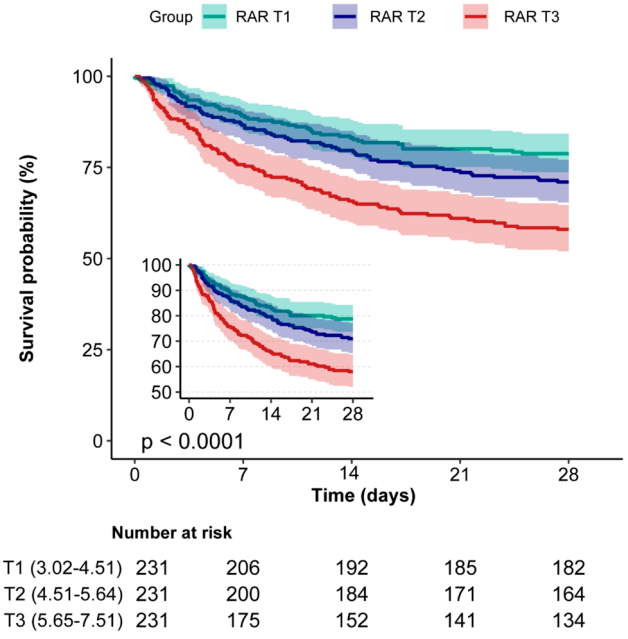

Fig. 2 Kaplan–Meier survival analysis for 28-day mortality with RAR in three groups

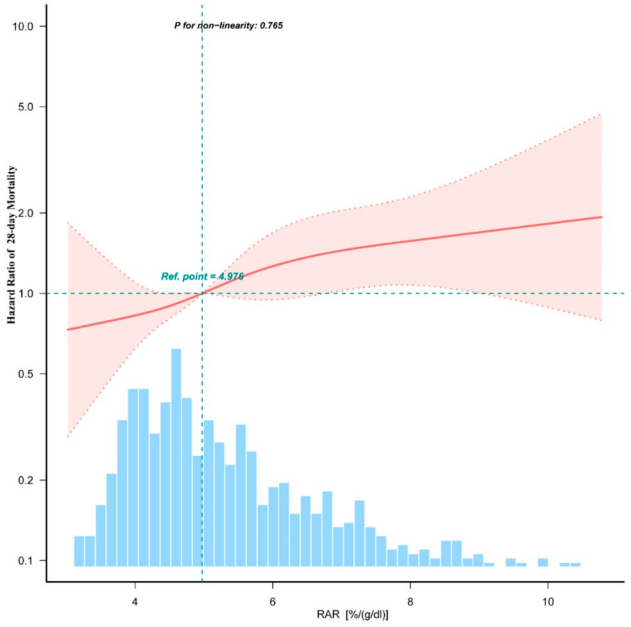

Fig. 3 Linear dose-response relationship between RAR and 28-day mortality of ICU patients with both COPD and AF. Note: This figure demonstrates multivariable adjusted HRs for all-cause mortality of 28 days in ICU according to levels of RAR on a continuous scale [%/(g/dL)]. Solid deep red lines are multivariable-adjusted HRs. Light red areas are the 95% confidence intervals derived from restricted cubic spline regressions with 4 knots. Dashed black lines are reference lines for no association at a hazard ratio of 1.0. All-cause mortality of 28 days is increased as RAR increased. Only 99.5% of the data is shown. All-cause mortality of 28 days analysis is adjusted for gender, age, race, BMI, heart rate, respiratory rate, MAP, WBC, hemoglobin, creatinine, lactate, pH, PaO2, PaCO2, hypertension, CHF, APACHE II, CCI, IMV, vasoactive agent. ICU, intensive care unit; COPD, chronic obstructive pulmonary disease; AF, atrial fibrillation; RAR, ratio of red cell distribution width to albumin; HR, hazard ratio; BMI, body mass index; T, tertile; MAP, mean arterial pressure; WBC, white blood cell count; pH, potential of hydrogen; PaO2, partial pressure of oxygen in arterial blood; PaCO2, partial pressure of carbon dioxide in arterial blood; CHF, congestive heart failure; APACHE II, acute physiology and chronic health evaluation II; CCI, charlson comorbidity index; IMV, invasive mechanical ventilation

relationship between RAR and 28-day mortality. Various subgroups were analyzed, including age, gender, race, hypertension, heart failure, and IMV. The impact of RAR on 28-day mortality was consistent across these subgroups, with no significant interaction effects detected (p for interaction > 0.05).

ROC curve analysis

In our ROC curve analysis (Fig. S1) for predicting 28-day mortality in COPD patients with atrial fibrillation, the RAR demonstrated a moderate predictive ability with an AUC of 62.26% (95% CI: 57.71–66.81%). The APACHE II score outperformed with a higher AUC of 69.00% (95% CI: 64.77–73.23%). Meanwhile, the SOFA score and lactate levels had lower AUCs of 60.75% (95%

Table 2 Associations between RAR and 28-day all-cause mortality in the multiple cox regression model

Variable	Total (*n*)	28-day mortality *n* (%)	Model I HR (95%CI)	*P*-value	Model II HR (95%CI)	*P*-value	Model III HR (95%CI)	*P*-value
RAR [%/(g/dL)]	693	213 (30.7)	1.30 (1.20 ~ 1.40)	< 0.001	1.32 (1.22 ~ 1.43)	< 0.001	1.18 (1.08 ~ 1.29)	< 0.001
RAR (tertiles)								
T1 (3.02–4.51)	231	49 (21.2)	1(Ref)		1(Ref)		1(Ref)	
T2 (4.51–5.64)	231	67 (29.0)	1.42 (0.98 ~ 2.05)	0.065	1.37 (0.94 ~ 1.98)	0.098	1.30 (0.89 ~ 1.91)	0.173
T3 (5.65–7.51)	231	97 (42.0)	2.31 (1.64 ~ 3.26)	< 0.001	2.31 (1.63 ~ 3.25)	< 0.001	1.73 (1.18 ~ 2.53)	0.005
P for trend				< 0.001		< 0.001		0.004

Model I: Unadjusted

Model II: Adjusted for gender, age, race, and BMI

Model III: Model II plus heart rate, respiratory rate, MAP, WBC, hemoglobin, creatinine, lactate, pH, PaO2, PaCO2, hypertension, CHF, APACHE II, CCI, IMV, and vasoactive agent

HR: hazard ratio, CI: confidence interval, Ref: reference, RAR; ratio of red cell distribution width to albumin; BMI, body mass index; T, tertile; MAP, mean arterial pressure; WBC, White Blood Cell Count; pH, potential of hydrogen; PaO_2, partial pressure of oxygen in arterial blood; $PaCO_2$, partial pressure of carbon dioxide in arterial blood; CHF, congestive heart failure; APACHE II, acute physiology and chronic health evaluation II; CCI, Charlson Comorbidity Index; IMV, invasive mechanical ventilation; ICU, Intensive Care Unit

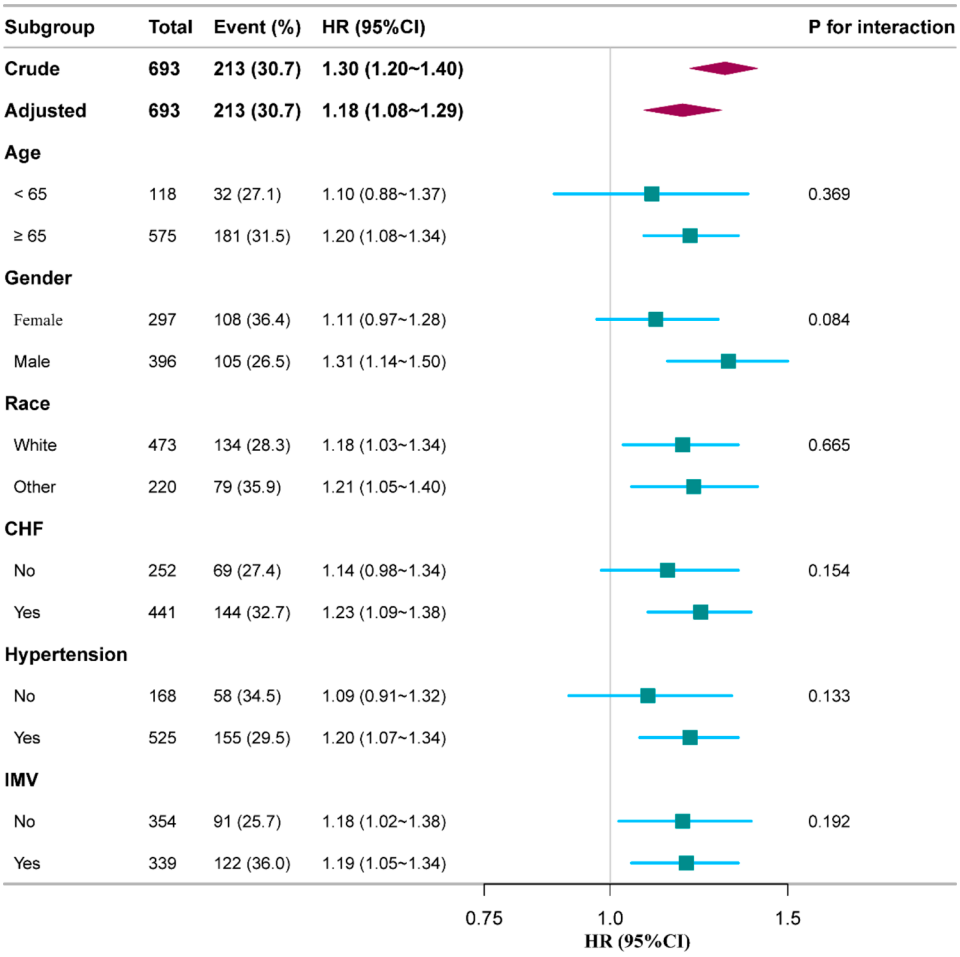

Fig. 4 Subgroup analyses of the association between RAR and 28-day all-cause mortality with different characteristics. HR: hazard ratio, CI: confidence interval, CHF, congestive heart failure; IMV, invasive mechanical ventilation; RAR, red cell distribution width to albumin ratio

CI: 56.34–65.15%) and 57.16% (95% CI: 52.49–61.83%), respectively. These findings suggest that RAR has notable predictive potential, even though APACHE II remains the most accurate measure.

Sensitivity analysis

Elevated RAR levels were significantly linked to higher 90-day, 365-day, and ICU mortality across all models. For 90-day mortality, the adjusted HRs for the highest RAR tertile remained elevated (Model 3 HR: 1.67, 95% CI: 1.19–2.32, $p = 0.003$). Similar trends were observed for 365-day mortality (Model 3 HR: 1.64, 95% CI: 1.23–2.19, $p = 0.001$) and ICU mortality (Model 3 HR: 1.69, 95% CI: 1.02–2.81, $p = 0.043$) (Table S2).

Discussion

This study demonstrated a significant positive linear relationship between the RAR and 28-day mortality in patients with COPD combined with AF. For each unit increase in RAR, the 28-day mortality rate increases by 18% (95% CI 1.08–1.29). Even after considering potential confounders, RAR continues to show an independent association with 28-day mortality among these patients. The subgroup analysis showed no significant interactions within the subgroups, and sensitivity analyses further supported its relevance for 90-day, 365-day, and ICU mortality.

COPD and AF frequently coexist, leading to worsened clinical outcomes. AF can exacerbate COPD by worsening gas exchange and inflammation, which complicates management and increases mortality risk [18, 19]. Studies have shown that COPD patients are more susceptible to AF due to chronic hypoxia, systemic inflammation, and elevated pulmonary pressures [6, 18]. The presence of AF further exacerbates gas exchange issues and inflammation in COPD, complicating management and increasing the risk of cardiovascular events and thromboembolic complications [5, 20]. Despite these risks, effective prognostic tools for identifying high-risk patients with both conditions are still lacking.

Previous studies have identified RDW as a significant prognostic marker in various diseases, including

cardiovascular disorders and chronic inflammatory conditions [8, 9, 21, 22]. For instance, Zinellu and Mangoni highlighted RDW's predictive capacity in COPD [23], while Qin demonstrated its association with all-cause mortality in ischemic stroke patients with AF [24]. In contrast to these studies, our research extends the current literature by exploring the relationship between RAR and 28-day mortality in COPD patients with AF, highlighting the potential of RAR as an important marker in this specific population.

While RDW alone is recognized as a marker of poor prognosis, integrating albumin into RAR provides a comprehensive view of a patient's inflammatory and nutritional status. This combination enhances predictive accuracy, particularly in complex comorbid conditions like COPD and AF, where both systemic inflammation and malnutrition are critical to disease progression [21, 25, 26].

The RAR has emerged as a novel biomarker for adverse outcomes in clinical settings, with studies indicating its prognostic value in heart failure, sepsis, COPD and chronic kidney disease [12, 14, 27–29]. RDW, reflecting erythrocyte size variability, is linked to inflammation and oxidative stress, while albumin serves as a negative acute-phase protein, reflecting nutritional and inflammatory status. Elevated RAR has been associated with increased mortality in critically ill patients, such as those with ischemic stroke and myocardial infarction [15, 24, 30]. However, the specific role of RAR in COPD patients with AF remains underexplored. Our study contributes to this gap by establishing that RAR is significantly associated with mortality in COPD patients with AF, further supporting the role of this biomarker in cardiovascular and respiratory comorbidities.

The connection between elevated RAR and 28-day mortality in COPD patients with AF may involve several biological mechanisms. Increased RDW suggests impaired erythropoiesis and abnormal red blood cell survival influenced by chronic inflammation and oxidative stress. In COPD, persistent inflammation inhibits erythroid maturation, leading to higher RDW levels due to the release of immature red blood cells from the bone marrow [31]. This process is intensified by pro-inflammatory cytokines that suppress erythroid cell development. In patients with both COPD and AF, inflammation is amplified, increasing oxidative stress and impairing cellular function [4–6, 19]. Conversely, serum albumin reflects nutritional status and systemic inflammation, with decreased levels commonly observed in COPD patients due to chronic inflammation and potential liver dysfunction, both linked to poor outcomes [32, 33]. Inflammatory processes reduce albumin synthesis, worsening the inflammatory state. Therefore, the RAR serves as a comprehensive marker, integrating these physiological disturbances and helping identify high-risk patients. In COPD patients with AF, an elevated RAR likely reflects a synergistic effect, with the combination of chronic respiratory inflammation and cardiovascular stress resulting in worse prognoses.

Our ROC curve analysis demonstrated that the RAR was a stronger predictor of 28-day mortality in COPD patients with AF than both the SOFA score and lactate levels. Although the predictive power of RAR was slightly lower than that of the APACHE II score, its clinical utility lies in its accessibility and ease of use. Unlike the APACHE II score, which requires complex calculations and extensive clinical data, RAR can be derived from routine blood tests, making it much more feasible for clinical practice.

Our study has several strengths. First, it introduces the RAR as a novel and comprehensive marker for assessing short-term mortality risk in COPD patients with AF. By incorporating both inflammatory and nutritional markers, the RAR provides a more holistic view of the patient's physiological status compared to traditional biomarkers. Additionally, the use of data from the MIMIC-IV database ensures a large, diverse patient population and allows for robust statistical analysis.

However, several limitations should be acknowledged. First, the retrospective design of the study limits our ability to establish causality between RAR and mortality. Although we adjusted for numerous potential confounders, the observational nature of the study cannot fully eliminate the possibility of residual confounding or bias, such as the duration and severity of COPD and AF. Second, the data originates from a single center, which may limit the generalizability of the findings. Multicenter studies with diverse patient populations are necessary to validate the prognostic value of RAR across different healthcare settings and ethnic groups.

Conclusions

In this study, we found that the RAR is a significant independent indicator of 28-day mortality in ICU patients with COPD and AF. Higher RAR levels were consistently associated with increased short-term mortality, and sensitivity analyses further supported its relevance for 90-day, 365-day, and ICU mortality. These findings suggest that RAR could serve as a valuable biomarker for risk stratification in critically ill COPD patients with AF, aiding in the early identification of high-risk individuals and potentially guiding targeted interventions.

Abbreviations

MIMIC	Medical Information Mart for Intensive Care
COPD	Chronic obstructive pulmonary disease
AF	Atrial fibrillation
ICU	Intensive care unit
RAR	Red cell distribution width to albumin ratio
HRs	Hazard ratios

ICD	International Classification of Diseases
CITI	Collaborative Institutional Training Initiative
SQL	Structured query language
MAP	Mean arterial pressure
BMI	Body Mass Index
pH	Potential of Hydrogen
PaO2	Partial Pressure of Oxygen in Arterial Blood
PaCO2	Partial Pressure of Carbon Dioxide in Arterial Blood
CHF	Congestive Heart Failure
APACHE II	Acute Physiology and Chronic Health Evaluation II
APSIII	Acute Physiology Score III
CCI	Charlson Comorbidity Index
IMV	Invasive mechanical ventilation
RCS	Restricted cubic spline
T	Tertile
LCP	MIT-Laboratory for Computational Physiology at the Massachusetts Institute of Technology
NIH	National Institutes of Health

Supplementary Information

The online version contains supplementary material available at https://doi.org/10.1186/s12872-025-04537-7.

Supplementary Material 1

Supplementary Material 2

Acknowledgements
The authors extend their sincere appreciation to the Laboratory for Computational Physiology at the Massachusetts Institute of Technology (LCP-MIT) for maintaining access to the MIMIC-IV database. We also express our gratitude to Dr. Qilin Yang (The Second Affiliated Hospital of Guangzhou Medical University, Guangzhou, China) and Dr. Jie Liu (Department of Vascular and Endovascular Surgery, Chinese PLA General Hospital) for their valuable assistance in the preparation of this manuscript.

Author contributions
All authors contributed to the study conception and design. Methodology was developed by PLY and QJM. Software support was provided by TXH and TWJ. Formal analysis and data management were handled by QJM and TXH. The first draft of the manuscript was written by PLY, QJM and TXH, and all authors contributed to writing, review, and editing. Visualization was prepared by TWJ, and supervision was provided by PLY. All authors contributed significantly to and agree with the content of the manuscript.

Funding
This study was not funded by any external source.

Data availability
All data supporting the findings of this study are available from the MIMIC-IV database (https://mimic.physionet.org/). Access to the data is subject to registration and approval for use under the appropriate data access terms. To facilitate the reproduction of our results, we provide the list of anonymous patient identifiers for the database in Supplementary table S1.

Declarations

Ethics approval
In this study, patient data was exclusively collected retrospectively for analysis, with no intervention or treatment involved. Furthermore, patients' information was anonymized during the construction of the MIMIC-IV database. The database has received approval from the Institutional Review Boards of the Massachusetts Institute of Technology (Cambridge, MA, USA) and Beth Israel Deaconess Medical Center (Boston, MA, USA) and the requirement for informed consent has been waived. Access to the database was obtained by Author Liya Pan following online training, which included an ethics examination at the National Institutes of Health (NIH).

Consent for publication
Not applicable.

Data sharing
The corresponding author will provide the datasets used and analyzed during the current work upon reasonable request.

Competing interests
The authors declare no competing interests.

Received: 14 December 2024 / Accepted: 29 January 2025
Published online: 03 March 2025

References

1. Vestbo J, Hurd SS, Agustí AG, Jones PW, Vogelmeier C, Anzueto A, et al. Global strategy for the diagnosis, management, and prevention of chronic obstructive pulmonary disease: GOLD executive summary. Am J Respir Crit Care Med. 2013;187:347–65.
2. Christenson SA, Smith BM, Bafadhel M, Putcha N. Chronic obstructive pulmonary disease. Lancet (Lond Engl). 2022;399:2227–42.
3. Al Wachami N, Guennouni M, Iderdar Y, Boumendil K, Arraji M, Mourajid Y, et al. Estimating the global prevalence of chronic obstructive pulmonary disease (COPD): a systematic review and meta-analysis. BMC Public Health. 2024;24:297.
4. Simons SO, Elliott A, Sastry M, Hendriks JM, Arzt M, Rienstra M, et al. Chronic obstructive pulmonary disease and atrial fibrillation: an interdisciplinary perspective. Eur Heart J. 2021;42:532–40.
5. Grymonprez M, Vakaet V, Kavousi M, Stricker BH, Ikram MA, Heeringa J, et al. Chronic obstructive pulmonary disease and the development of atrial fibrillation. Int J Cardiol. 2019;276:118–24.
6. Goudis CA. Chronic obstructive pulmonary disease and atrial fibrillation: an unknown relationship. J Cardiol. 2017;69:699–705.
7. Chen C-Y, Liao K-M. The impact of atrial fibrillation in patients with COPD during hospitalization. Int J Chronic Obstr Pulm Dis. 2018;13:2105–12.
8. Salvagno GL, Sanchis-Gomar F, Picanza A, Lippi G. Red blood cell distribution width: a simple parameter with multiple clinical applications. Crit Rev Clin Lab Sci. 2015;52:86–105.
9. Marvisi M, Mancini C, Balzarini L, Ramponi S. Red cell distribution width: a new parameter for predicting the risk of exacerbation in COPD patients. Int J Clin Pract. 2021;75:e14468.
10. Ronit A, Kirkegaard-Klitbo DM, Dohlmann TL, Lundgren J, Sabin CA, Phillips AN, et al. Plasma albumin and incident cardiovascular disease: results from the CGPS and an updated meta-analysis. Arterioscler, Thromb. Vasc Biol. 2020;40:473–82.
11. Gunen H, Hacievliyagil SS, Kosar F, Mutlu LC, Gulbas G, Pehlivan E, et al. Factors affecting survival of hospitalised patients with COPD. Eur Respir J. 2005;26:234–41.
12. Zhou P, Tian P-C, Zhai M, Huang Y, Zhou Q, Zhuang X-F, et al. Association between red blood cell distribution width-to-albumin ratio and prognosis in non-ischaemic heart failure. ESC Heart Fail. 2024;11:1110–20.
13. Pan L-Y, Song J. Association of Red Cell distribution width/albumin ratio and in hospital mortality in patients with atrial fibrillation base on medical information mart for intensive care IV database. BMC Cardiovasc Disord. 2024;24:174.
14. Xu W, Huo J, Chen G, Yang K, Huang Z, Peng L, et al. Association between red blood cell distribution width to albumin ratio and prognosis of patients with sepsis: a retrospective cohort study. Front Nutr. 2022;9:1019502.
15. Li D, Ruan Z, Wu B. Association of red blood cell distribution width-albumin ratio for acute myocardial infarction patients with mortality: a retrospective cohort study. Clin Appl Thromb/Hemost: off J Int Acad Clin Appl Thromb/Hemost. 2022;28:10760296221121286.
16. Johnson AEW, Bulgarelli L, Shen L, Gayles A, Shammout A, Horng S, et al. MIMIC-IV, a freely accessible electronic health record dataset. Sci Data. 2023;10:1.
17. Quan H, Sundararajan V, Halfon P, Fong A, Burnand B, Luthi J-C, et al. Coding algorithms for defining comorbidities in ICD-9-CM and ICD-10 administrative data. Med Care. 2005;43:1130–9.
18. Shin SY, Manuel ARG, Lip GYH. Atrial fibrillation and end-stage COPD: a Close Association Revisited. Chest. 2019;155:888–9.

19. Warming PE, Garcia R, Hansen CJ, Simons SO, Torp-Pedersen C, Linz D, et al. Atrial fibrillation and chronic obstructive pulmonary disease: diagnostic sequence and mortality risk. Eur Heart J Qual Care Clin Outcomes. 2023;9:128–34.
20. Liao K-M, Chen C-Y. Incidence and risk factors of atrial fibrillation in Asian COPD patients. Int J Chronic Obstr Pulm Dis. 2017;12:2523–30.
21. Guan Y-Z, Yin R-X, Zheng P-F, Liu C-X, Wei B-L, Deng G-X. Association of RDW, NLR, and PLR with atrial fibrillation in critical care patients: a retrospective study based on propensity score matching. Dis Markers. 2022;2022:2694499.
22. Wang J, Wan Z, Liu Q, Wang B, Wang L, Yang D, et al. Predictive value of red blood cell distribution width in chronic obstructive pulmonary disease patients with pulmonary embolism. Anal Cell Pathol (Amst). 2020;2020:1935742.
23. Zinellu A, Mangoni AA. The emerging clinical significance of the red cell distribution width as a biomarker in chronic obstructive pulmonary disease: a systematic review. J Clin Med. 2022;11:5642.
24. Qin Z, Liao N, Lu X, Duan X, Zhou Q, Ge L. Relationship between the hemoglobin-to-red cell distribution width ratio and all-cause mortality in ischemic stroke patients with Atrial Fibrillation: an analysis from the MIMIC-IV Database. Neuropsychiatr Dis Treat. 2022;18:341–54.
25. Günay E, Sarınç Ulaşlı S, Akar O, Ahsen A, Günay S, Koyuncu T, et al. Neutrophil-to-lymphocyte ratio in chronic obstructive pulmonary disease: a retrospective study. Inflammation. 2014;37:374–80.
26. Long J, Xu P, Chen J, Liao J, Sun D, Xiang Z, et al. Inflammation and comorbidities of chronic obstructive pulmonary disease: the cytokines put on a mask! Cytokine. 2023;172:156404.
27. Gu Y-L, Yang D, Huang Z-B, Chen Y, Dai Z-S. Relationship between red blood cell distribution width-to-albumin ratio and outcome of septic patients with atrial fibrillation: a retrospective cohort study. BMC Cardiovasc Disord. 2022;22:538.
28. Kimura H, Tanaka K, Saito H, Iwasaki T, Kazama S, Shimabukuro M, et al. Impact of red blood cell distribution width-albumin ratio on prognosis of patients with CKD. Sci Rep. 2023;13:15774.
29. Qiu Y, Wang Y, Shen N, Wang Q, Chai L, Liu J, et al. Association between Red Blood cell distribution width-albumin ratio and Hospital Mortality in Chronic Obstructive Pulmonary Disease patients admitted to the Intensive Care Unit: a retrospective study. Int J Chronic Obstr Pulm Dis. 2022;17:1797–809.
30. Chen S, Guan S, Yan Z, Ouyang F, Li S, Liu L, et al. Prognostic value of red blood cell distribution width-to-albumin ratio in ICU patients with coronary heart disease and diabetes mellitus. Front Endocrinol (Lausanne). 2024;15:1359345.
31. Canny SP, Orozco SL, Thulin NK, Hamerman JA. Immune mechanisms in Inflammatory Anemia. Annu Rev Immunol. 2023;41:405–29.
32. Nicholson JP, Wolmarans MR, Park GR. The role of albumin in critical illness. Br J Anaesth. 2000;85:599–610.
33. Eckart A, Struja T, Kutz A, Baumgartner A, Baumgartner T, Zurfluh S, et al. Relationship of nutritional status, inflammation, and serum albumin levels during acute illness: a prospective study. Am J Med. 2020;133:713–e7227.

Publisher's note