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

Li-ya Pan<sup>1</sup> and Jing Song<sup>1\*</sup>

# Abstract

**Background** Atrial fibrillation (AF) is a common cardiac arrhythmia. The ratio of red cell distribution width (RDW) to albumin has been recognized as a reliable prognostic marker for poor outcomes in a variety of diseases. However, the evidence regarding the association between RDW to albumin ratio (RAR) and in hospital mortality in patients with AF admitted to the Intensive Care Unit (ICU) currently was unclear. The purpose of this study was to explore the association between RAR and in hospital mortality in patients with AF in the ICU.

**Methods** This retrospective cohort study used data from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database for the identification of patients with atrial fibrillation (AF). The primary endpoint investigated was in-hospital mortality. Multivariable-adjusted Cox regression analysis and forest plots were utilized to evaluate the correlation between the RAR and in-hospital mortality among patients with AF admitted to ICU. Additionally, receiver operating characteristic (ROC) curves were conducted to assess and compare the predictive efficacy of RDW and the RAR.

**Results** Our study included 4,584 patients with AF with a mean age of  $75.1 \pm 12.3$  years, 57% of whom were male. The in-hospital mortality was 20.3%. The relationship between RAR and in-hospital mortality was linear. The Cox proportional hazard model, adjusted for potential confounders, found a high RAR independently associated with in hospital mortality. For each increase of 1 unit in RAR, there is a 12% rise in the in-hospital mortality rate (95% Cl 1.06–1.19). The ROC curves revealed that the discriminatory ability of the RAR was better than that of RDW. The area under the ROC curves (AUCs) for RAR and RDW were 0.651 (95%Cl: 0.631–0.671) and 0.599 (95% Cl: 0.579–0.620).

**Conclusions** RAR is independently correlated with in hospital mortality and in AF. High level of RAR is associated with increased in-hospital mortality rates.

Keywords Atrial fibrillation, Mortality, Inflammation, Red cell distribution width, Albumin

\*Correspondence: Jing Song jing\_song1983@hotmail.com



<sup>1</sup>Department of Cardiology, The Second Affiliated Hospital, Yuying Children's Hospital of Wenzhou Medical University, Wenzhou 325000, China



**Open Access** 

24:174

## Introduction

Atrial fibrillation (AF) is the most prevalent cardiac arrhythmia, characterized by irregular and rapid atrial contractions [1, 2]. Its prevalence increases with age, and it is associated with various cardiovascular and cerebrovascular complications [3, 4]. AF significantly heightens the risk of stroke, heart failure, and mortality [4–7]. Although many risk factors for atrial fibrillation have already been identified, including age, hypertension, diabetes, obesity, left atrial volume and smoking [8–10], the potential modifiable risk factors still need to be investigated.

RDW is a relatively easily obtainable indicator, representing the heterogeneity in the size of circulating red blood cells [11]. It is commonly used for the differentiation of anemia [11]. Research has revealed associations between RDW and various diseases, including diabetes, pulmonary embolism, chronic obstructive pulmonary disease, heart failure, and cerebrovascular diseases [12– 14]. Current studies indicate that an elevated RDW is linked to adverse cardiovascular outcomes, serving as a marker of inflammation and oxidative stress [14–16].

Albumin, the most abundant circulating protein in the blood, plays a crucial role in binding and transporting various drugs and substances. It contributes to maintaining blood osmolality and influencing the physiological functions of the circulatory system [17]. Extensive evidence indicates that albumin serves as a robust predictor of cardiovascular risk across diverse patient populations [18].

RDW/ALB has emerged as a composite marker, integrating inflammatory status (RDW) and nutritional status (albumin) .To date, there have been few studies on the prognostic value of the RDW/ALB ratio in AF [19]. Although RAR is a reliable indicator of mortality based on systemic inflammation in many diseases [20–22], there is insufficient evidence that RAR has predictive value for prognosis in AF patients. In this study, we sought to explore the association of RDW/ALB ratio on hospital mortality in a relatively large cohort of patients with atrial fibrillation.

# **Materials and methods**

## Data source

This retrospective study was based on the Medical Information Mart for Intensive Care IV database (MIMIC-IV, Version 2.2). The database comprises data from over 70,000 patients admitted to Beth Israel Deaconess Medical Center's ICUs in Boston, MA, from 2008 to 2019.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) [23]. To safeguard the privacy of patients included in the study, all personal information has been systematically removed. Individuals who have successfully completed the Collaborative Institutional Training Initiative exam are granted access to this database. Considering the retrospective nature of this study and the extraction of patient data from a public database, the requirement for informed consent has been waived.

## Study subjects

Patients for this study were identified within the MIMIC-IV database from 2008 to 2019. The study population consisted of individuals diagnosed with atrial fibrillation (AF) and subsequently admitted to the intensive care unit (ICU). The diagnosis of AF was established through the International Classification of Diseases (ICD) codes (Table S1 in Supplementary Appendix). Inclusion criteria were defined as follows: patients with atrial fibrillation admitted to the ICU for the first time (N=13,366). 8,782 patients lacking Red Cell Distribution Width (RDW) and Albumin (ALB) measurements were excluded. Ultimately, a cohort of 4,584 patients with complete data on RDW and ALB, diagnosed with atrial fibrillation, were included in this study (Fig. 1).

### Demographical and laboratory variables

The MIMIC-IV database was queried for patient information using structured query language (SQL). Data extraction included information such as population statistics (age, gender, height and weight), vital signs (respiratory rate, heart rate, systolic and diastolic blood pressure), comorbidities (hypertension, diabetes, myocardial infarction, heart failure, cerebrovascular disease, and chronic pulmonary disease), and laboratory parameters (minimum hemoglobin and platelet counts, maximum white blood cell count, creatinine, blood urea nitrogen, glucose, lactate, ALT, AST, INR, albumin, RDW). In instances where an indicator had multiple records, the mean measured value was used. The Body Mass Index (BMI) was computed by dividing body weight (kg) by the square of height (m).

# **RAR** assessment and outcomes

RAR was calculated using the following formula: [RDW (%)/serum albumin (g/dL)]. The study's outcome focused on in-hospital mortality after admission to the ICU.

### Statistical analysis

Continuous variable data were described as mean±standard deviation (SD) or median and interquartile range (IQR), while categorical variable data were described as frequencies or percentages. Baseline characteristics underwent comparison using the Mann–Whitney test for continuous variables and the chi-square test for categorical variables. Multivariate logistic regression



Fig. 1 Flow chart of the study population

Abbreviations: ICU, intensive care unit; MIMIC, Medical Information Mart for Intensive Care IV; RDW, red cell distribution width; ALB, albumin

analysis was executed to evaluate the association between RAR and in-hospital mortality in individuals with AF. Results were conveyed as odds ratios (OR) with 95% confidence intervals (CI). RAR values were categorized into quartiles, with the first quartile serving as the reference group. Four models were applied in the regression analysis, adjusting for diverse factors: Model 1 adjusted for age, gender, and BMI; Model 2 for age, gender, BMI, sbp, dbp, heart rate, and respiratory rate; Model 3 for Model 2 plus hypertension, diabetes, myocardial infarction, congestive heart failure, cerebrovascular disease, and chronic pulmonary disease; and Model 4 for Model 3 plus hemoglobin and platelet counts, white blood cell count, creatinine, blood urea nitrogen, glucose, lactate, alanine aminotransferase(ALT), aspartate aminotransferase(AST), international normalized ratio(INR). The predictive performance of RDW and RDW/ALB ratio was assessed through pairwise Receiver Operating Characteristic (ROC) curve analyses. Additionally, subgroup analysis was conducted to assess whether there were differences in the impact of RAR on in-hospital mortality rates among different subgroups of patients with AF.

All analyses were per formed using R 4.2.2 (http://www.R-project.org, R Foundation) and Free

Statistics version 1.9, P < 0.05 was considered statistically significant.

# Results

# Baseline characteristics of study subjects

After screenings, the presented study included 4,584 MIMIC-IV patients with AF. The baseline characteristics were classified according to RDW/ALB quartiles (Table 1). In MIMIC-IV, there were 1,146 patients in quartile 1(Q1), 1,146 patients in quartile 2(Q2), 1,142 patients in quartile 3(Q3), and 1,150 patients in quartile 4(Q4). There were 1,969 females and 2,615 males in these patients. Patients in the high quartile group had lower systolic and diastolic blood pressure, faster heart rate, lower hemoglobin and albumin levels, higher leukocytes, blood creatinine, urea nitrogen, lactate, ALT, AST, INR, and RDW, and higher in-hospital mortality rates.

### Associations between RAR and mortality

There is a significant positive linear association between RAR and in hospital mortality in patients with AF (p for non-linearity>0.05, Fig. 2). The results of the multivariate Cox regression analysis indicate a significant association between RAR and in-hospital mortality in patients with atrial fibrillation (AF). The odds ratios (OR) of RAR were significant in all models when RAR is considered as

Characteristics	Total ( <i>n</i> = 4584)	Q1(<3.93) (n=1146)	Q2 (3.93–4.73)	Q3 (4.73–5.83) (n=1142)	Q4 (>5.83)	P-value	
			( <i>n</i> = 1146)		( <i>n</i> = 1150)		
Age(years)	75.1±12.3	74.9±12.2	76.4±12.2	75.5±12.0	73.8±12.5	< 0.001	
gender, n (%)						0.469	
Female	1969 (43.0)	479 (41.8)	511 (44.6)	497 (43.5)	482 (41.9)		
Male	2615 (57.0)	667 (58.2)	635 (55.4)	645 (56.5)	668 (58.1)		
BMI (kg/m <sup>2)</sup>	29.3±8.0	29.2±6.8	$29.0 \pm 7.9$	29.2±8.3	29.7±8.6	0.493	
SBP (mmHg)	116.8±17.2	124.6±17.9	118.6±16.8	114.1±16.0	$110.0 \pm 14.3$	< 0.001	
DBP (mmHg)	62.9±11.4	67.5±12.4	63.4±11.1	$61.2 \pm 10.5$	$59.4 \pm 9.8$	< 0.001	
Heart rate, beats/min	86.8±17.9	82.2±17.1	85.9±17.4	88.3±17.9	$90.9 \pm 18.1$	< 0.001	
Respiratory rate, beats/min	$20.1 \pm 3.8$	19.5±3.3	$20.1 \pm 3.6$	$20.4 \pm 4.0$	$20.5 \pm 4.3$	< 0.001	
hypertension, n (%)						< 0.001	
No	4049 (88.7)	902 (78.8)	1010 (88.6)	1038 (91.6)	1099 (96)		
Yes	514 (11.3)	243 (21.2)	130 (11.4)	95 (8.4)	46 (4)		
Diabetes, n (%)						0.025	
No	3404 (74.3)	871 (76)	872 (76.1)	814 (71.3)	847 (73.7)		
Yes	1180 (25.7)	275 (24)	274 (23.9)	328 (28.7)	303 (26.3)		
Myocardial infarct, n (%)						0.73	
No	3525 (76.9)	888 (77.5)	877 (76.5)	867 (75.9)	893 (77.7)		
Yes	1059 (23.1)	258 (22.5)	269 (23.5)	275 (24.1)	257 (22.3)		
Congestive heart failure, n (%)						< 0.001	
No	2354 (51.4)	699 (61)	527 (46)	549 (48.1)	579 (50.3)		
Yes	2230 (48.6)	447 (39)	619 (54)	593 (51.9)	571 (49.7)		
Cerebrovascular disease, n (%)						< 0.001	
No	3629 (79.2)	767 (66.9)	895 (78.1)	974 (85.3)	993 (86.3)		
Yes	955 (20.8)	379 (33.1)	251 (21.9)	168 (14.7)	157 (13.7)		
Chronic pulmonary disease,						< 0.001	
n (%)							
No	3251 (70.9)	887 (77.4)	762 (66.5)	778 (68.1)	824 (71.7)		
Yes	1333 (29.1)	259 (22.6)	384 (33.5)	364 (31.9)	326 (28.3)		
hemoglobin/dl	10.1±2.3	11.6±2.1	$10.4 \pm 2.1$	$9.6 \pm 2.1$	$8.8 \pm 1.9$	< 0.001	
WBC,10 <sup>9</sup> /L	15.1±13.8	13.1±9.0	14.2±11.5	15.6±16.0	17.4±16.8	< 0.001	
platelets, 10 <sup>9</sup> /L	183.8±99.0	187.4±76.1	188.1±93.9	183.2±99.0	176.5±121.2	0.018	
creatinine, mg/dl	1.3 (0.9, 2.1)	1.1 (0.8, 1.5)	1.3 (0.9, 1.9)	1.5 (1.0, 2.5)	1.6 (1.0, 2.7)	< 0.001	
BUN, mg/dl	29.0 (19.0, 48.0)	22.0 (16.0, 31.0)	27.0 (19.0, 46.0)	35.0 (22.0, 55.0)	36.0 (23.0, 58.0)	< 0.001	
glucose, mg/dl	150.0 (119.0, 203.5)	146.0 (118.0, 191.8)	149.0 (119.0, 199.0)	153.0 (122.0, 208.8)	152.0 (119.0, 211.0)	0.049	
lactate, mmol/L	2.3 (1.5, 4.2)	2.2 (1.5, 3.4)	2.1 (1.4, 3.5)	2.3 (1.4, 4.4)	2.8 (1.6, 5.8)	< 0.001	
ALT, U/L	26.0 (16.0, 61.0)	23.0 (16.0, 41.0)	25.0 (16.0, 59.0)	29.0 (17.0, 75.0)	32.0 (16.0, 81.5)	< 0.001	
AST, U/L	39.0 (24.0, 90.0)	32.0 (23.0, 56.0)	37.0 (24.0, 82.0)	45.0 (25.0, 110.0)	50.0 (26.0, 133.0)	< 0.001	
INR	1.5 (1.2, 2.1)	1.3 (1.1, 1.7)	1.4 (1.2, 2.2)	1.5 (1.3, 2.2)	1.6 (1.3, 2.3)	< 0.001	
Albumin, g/dl	3.2±0.7	3.9±0.3	3.4±0.3	3.0±0.4	$2.5 \pm 0.5$	< 0.001	
RDW, %	15.5±2.3	13.7±0.9	$14.8 \pm 1.4$	15.9±1.9	17.5±2.8	< 0.001	
RAR [%/(g/dl)]	$5.1 \pm 1.6$	3.5±0.3	4.3±0.2	5.2±0.3	7.3±1.5	< 0.001	
hospital mortality, n (%)						< 0.001	
No	3652 (79.7)	1017 (88.7)	959 (83.7)	903 (79.1)	773 (67.2)		
Yes	932 (20.3)	129 (11.3)	187 (16.3)	239 (20.9)	377 (32.8)		

# Table 1 Baseline characteristics of the study participants

Data were presented as n (%), mean (SD) and median (IQR).

SD, standard deviation; IQR, interquartile range; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; WBC, white blood cell; BUN, blood urea nitrogen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; RDW, red cell distribution width; RAR, RDW to albumin ratio



Fig. 2 linear dose-response relationship between RAR and in hospital mortality of patients with atrial fibrillation. Adjustment factors included age, gender, BMI, sbp, dbp, Heart rate, respiratory rate, hypertension, diabetes, myocardial infarct, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, hemoglobin, WBC, platelets, creatinine, BUN, glucose, lactate, ALT, AST, INR.

a continuous variable (p<0.001). For each increase of 1 unit in RAR, there is a 12% rise in the in-hospital mortality rate (95% CI 1.06–1.19). Furthermore, when RAR is categorized into quartiles and adjusting for various factors including age, gender, body mass index (BMI), heart rate, respiratory rate, systolic and diastolic blood pressure, hypertension, diabetes, congestive heart failure, myocardial infarction, cerebrovascular disease, chronic pulmonary disease, and laboratory indicators, a notable trend is observed. As RAR quartiles increase,

the in-hospital mortality rate exhibits a corresponding increase. (p for trend < 0.05) (Table 2).

## **Subgroup Analysis**

We analyzed several subgroups, including age, gender, hypertension, diabetes, and heart failure. The impact of RAR on in-hospital mortality rates was found to be consistent across these subgroups. Additionally, no interaction effects were observed among the different subgroups (Fig. 3).

													<i>c</i> .					• •
Inh	0.0	Ilpac	lu ictod	200	mill	ti) /つ r	unto.	COV	roa	roccior	202	NICOC	torir	hor	nita	ma	vrt ol	1 + 1 /
140	~ ~	Uniac				пуаг	Idie	(())	1				1()		יהותו		והות	II V
		Oride			11101	ci v cai	i a c c	~~~~	100	1033101		1, 505			prea		/	109
			,															

Outcome	Non-adjusted Model		Model I		Model II		Model III		Model IV		
	OR(95%CI)	P-value	OR(95%CI) P-va		OR(95%CI)	P-value	OR(95%CI)	P-value	OR(95%CI)	P-value	
RAR [%/	1.16	< 0.001	1.15	< 0.001	1.12 (1.07,1.17)	< 0.001	1.12 (1.07,1.17)	< 0.001	1.12 (1.06,1.19)	< 0.001	
(g/L)]	(1.13,1.20)		(1.1,1.19)								
RAR quartiles											
Q1	1(Ref)		1(Ref)		1(Ref)		1(Ref)		1(Ref)		
Q2	1.23 (0.98,1.54)	0.074	1.28 (0.96,1.72)	0.091	1.2 (0.89,1.60)	0.234	1.25 (0.93,1.68)	0.136	1.57 (1.06,2.32)	0.024	
Q3	1.46 (1.18,1.81)	0.001	1.46 (1.1,1.92)	0.008	1.26 (0.95,1.68)	0.112	1.31 (0.99,1.75)	0.062	1.66 (1.13,2.43)	0.009	
Q4	1.94 (1.59,2.38)	< 0.001	1.9 (1.46,2.47)	< 0.001	1.56 (1.18,2.05)	0.002	1.6 (1.21,2.11)	0.001	1.79 (1.23,2.61)	0.002	
P for trend		< 0.001		< 0.001		0.001		0.001		0.007	

Crude model: no other covariates were adjusted

Model I: Adjust for age, gender and BMI

Model II: Adjust for age, gender, BMI. sbp, dbp, Heart rate, respiratory rate

Model III: Adjust for age, gender, BMI. sbp, dbp, Heart rate, respiratory rate, hypertension, diabetes, myocardial infarct, congestive heart failure, cerebrovascular disease, chronic pulmonary disease

Model IV: Adjust for Model III plus hemoglobin, WBC, platelets, creatinine, BUN, glucose, lactate, ALT, AST, INR

OR, odd ratio; CI, confidence interval; Ref, reference; BMI, body mx index; WBC, white blood cell; SBP, systolic blood pressure; DBP, diastolic blood pressure; BUN, blood urea nitrogen; ALT, alanine aminotransferase; AST, aspartate aminotransferase; INR, international normalized ratio; RDW, red cell distribution width; RAR, RDW to albumin ratio

Subgroup	Variable	Total	Event (%)	HR (95%CI)		P for interaction
Age,years						
age<65	RAR	928	153 (16.5)	1.19 (1.05~1.35)		0.074
age≥65	RAR	3656	779 (21.3)	1.11 (1.05~1.17)	-	
Gender						
femal	RAR	1969	409 (20.8)	1.08 (0.99~1.17)	-	0.542
male	RAR	2615	523 (20)	1.18 (1.1~1.25)	-	
Hypertension						
No	RAR	4049	847 (20.9)	1.13 (1.07~1.19)	-	0.093
Yes	RAR	514	78 (15.2)	1.18 (0.77~1.8)	•	
Diabetes						
No	RAR	3404	684 (20.1)	1.14 (1.07~1.2)	-	0.658
Yes	RAR	1180	248 (21)	1.09 (0.99~1.21)		
congestive heart failure						
No	RAR	2354	489 (20.8)	1.1 (1.03~1.18)	-	0.481
Yes	RAR	2230	443 (19.9)	1.16 (1.07~1.24)	-	
<u>e</u>					i I	
				0.71	1.0 1.41 2 Effect(95%CI)	.0

Fig. 3 Subgroup analysis of relationships between RAR and in hospital mortality among AF patients

ORs were adjusted for age, gender, BMI, sbp, dbp, Heart rate, respiratory rate, hypertension, diabetes, myocardial infarct, congestive heart failure, cerebrovascular disease, chronic pulmonary disease, hemoglobin, WBC, platelets, creatinine, BUN, glucose, lactate, ALT, AST, INR

## Predictive performance of RAR

The ROC curve comparative analysis demonstrated that the RAR exhibited a superior discriminatory capacity compared to RDW. (Fig. 4). The area under the ROC curves (AUCs) for RAR and RDW were 0.651 (95%CI: 0.631–0.671) and 0.599 (95% CI: 0.579–0.620), respectively (p < 0.001).

### Discussion

This study showed a significant positive linear association between RAR and in hospital mortality in patients with AF. With each one-unit increase in RAR, there is a 12% elevation in the in-hospital mortality rate (95% CI 1.06–1.19). Even after adjusting for potential confounding factors, RAR remains independently correlated in hospital mortality among patients with AF. ROC curves suggest that RAR exhibits superior predictive capability



# **Statistical comparison**

Fig. 4 ROC curves of RDW and RAR for in hospital mortality of patients with atrial fibrillation ROC, receiver operating characteristic; RDW, red cell distribution width; RAR, RDW to albumin ratio

for in-hospital mortality in ICU patients with AF compared to RDW. The subgroup analysis did not unveil any interaction within subgroups.

Previous studies have indicated the high prevalence of AF in critical care patients, establishing it as a prognostic marker associated with increased mortality [24, 25]. Inflammation plays an important role in the development and progression of atrial fibrillation [26]. Traditionally, inflammation has been attributed to cytokines production by infiltrating white cells in response to tissue injury and/or immune cell reactions. However, emerging evidence suggests that other cell types, including cardiomyocytes, fibroblasts, and adipocytes, may contribute to the inflammatory signaling pathways associated with atrial fibrillation. Several inflammatory markers, such as C-reactive protein (CRP), tumor necrosis factor (TNF)- $\alpha$ , interleukin (IL)-2, IL-6, and IL-8, have demonstrated associate with the presence or outcome of AF and can impact AF through mechanisms like endothelial damage and platelet activation [26-28]. Although the precise mechanisms through which inflammation affects the clinical presentation and outcomes of AF patients remain incompletely understood, it is recognized that inflammation contributes to atrial remodeling, -structural and functional changes associated with AF development, raising the risk of adverse outcomes, including stroke and mortality.

Red Cell Distribution Width (RDW) is a hematological parameter that is often elevated in the setting of inflammation and oxidative stress. RDW is currently associated with several diseases, including cardiovascular diseases such as stable angina [29], acute coronary syndrome [30], coronary bypass surgery [31], heart failure [32], and stroke [33]. Furthermore, albumin, with its antiinflammatory, antioxidant, and anti-thrombotic properties, plays a crucial role in cardiovascular health [34]. While RDW and albumin have been shown to be associated with an increased risk of atrial fibrillation [16, 35], RAR, serving as a composite marker, exhibits a superior predictive effect. In recent years, it has been discovered that RAR is associated with type 2 diabetes and foot ulcers [36], chronic kidney disease [20], chronic obstructive pulmonary disease [21], acute myocardial infarction [22] and heart failure [37]. In AF, where inflammatory processes are known contributors, an elevated RDW/ ALB ratio may signify a pro-inflammatory state. This could be indicative of a more extensive systemic impact of AF, potentially involving endothelial dysfunction, oxidative stress, and inflammatory pathways. The mechanistic underpinnings of how RDW and serum albumin levels influence in-hospital mortality in AF patients warrant further exploration. Gaining insight into these potential mechanisms has the potential to pave the way for targeted interventions focused on modulating the inflammatory environment and enhancing outcomes in patients with atrial fibrillation.

Our study has certain advantages. Firstly, it stands out as the largest retrospective cohort study examining the connection between the RAR and in-hospital mortality in patients with atrial fibrillation. Additionally, our comparative analysis of the predictive capabilities of RDW and RAR for mortality revealed that RAR outperforms RDW in prognostic accuracy for atrial fibrillation. This finding contributes valuable insights to the clinical diagnosis and prognostication of patients with atrial fibrillation.

The present study has several limitations. Firstly, its exclusive focus on AF patients, limiting generalizability to other populations. Secondly, our findings, derived solely from a single-center evaluation using the MIMIC-IV database, may face limitations in generalizability, the retrospective nature of the study introduces the potential for selection bias. Future research should involve multiple centers and a larger datasets. Thirdly, the measurement of the RAR was performed only once, neglecting the potential impact of varied processes and dynamic changes in AF over time. Future studies should explore the fluctuations in these markers to provide a more comprehensive understanding. Fourthly, we attempted to incorporate a variety of diseases into our exclusion criteria; however, certain conditions such as hematological diseases, infectious conditions, malignancies, were not excluded. And the study may not have considered confounding factors, such as smoking status and atrial volume. Despite these limitations, the prognostic efficacy of RAR for AF patients remains evident.

## Conclusions

This study reveals an independent association between RAR and in-hospital mortality in patients with atrial fibrillation in the MIMIC-IV database. Furthermore, in comparison to RDW, RAR demonstrates superior predictive capabilities. As an inflammatory biomarker, RAR aids clinicians in early and effective prognosis assessment for patients with atrial fibrillation, facilitating prompt intervention and treatment. In conclusion, recognizing the potential role of RDW/ALB in assessing patient conditions can enhance risk stratification, monitoring, and management of individuals with atrial fibrillation.

### Supplementary Information

The online version contains supplementary material available at https://doi. org/10.1186/s12872-024-03839-6.

Supplementary Material 1

### Acknowledgements

We thank the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University for supporting our work.

### Author contributions

L.Y.P designed the study,conducted the data collection and analysis ,wrote the manuscript and reviewed the manuscript. J.S conducted data analysis and reviewed the manuscript. All authors read and approved the final manuscript.

### Funding

This study was not funded by any external source.

### Data availability

All data in the article can be obtained from MIMIC-IV database (https://mimic. physionet.org/). To facilitate the reproduction of our results, we provide the list of anonymous patient identifiers for databases in Supplementary data 1.

## Declarations

### Competing interests

The authors declare no competing interests.

### Ethics approval and consent to participate

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 Statement**

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

Received: 6 December 2023 / Accepted: 12 March 2024 Published online: 21 March 2024

### References

- Fang MC, Chen J, Rich MW. Atrial fibrillation in the elderly. Am J Med. 2007;120:481–7.
- Hindricks G, Potpara T, Dagres N, Arbelo E, Bax JJ, Blomström-Lundqvist C, et al. 2020 ESC guidelines for the diagnosis and management of atrial fibrillation developed in collaboration with the European Association for Cardio-Thoracic Surgery (EACTS): the task force for the diagnosis and management of atrial fibrillation of the European Society of Cardiology (ESC) developed with the special contribution of the European Heart Rhythm Association (EHRA) of the ESC. Eur Heart J. 2021;42:373–498.
- Oldgren J, Healey JS, Ezekowitz M, Commerford P, Avezum A, Pais P, et al. Variations in cause and management of atrial fibrillation in a prospective registry of 15,400 emergency department patients in 46 countries: the RE-LY atrial fibrillation registry. Circulation. 2014;129:1568–76.
- Joglar JA, Chung MK, Armbruster AL, Benjamin EJ, Chyou JY, Cronin EM, et al. 2023 ACC/AHA/ACCP/HRS Guideline for the diagnosis and management of atrial fibrillation: a report of the American College of Cardiology/American Heart Association Joint Committee on Clinical Practice guidelines. Circulation. 2024;149:e1–156.
- Wolf PA, Abbott RD, Kannel WB. Atrial fibrillation as an independent risk factor for stroke: the Framingham Study. Stroke. 1991;22:983–8.
- Carlisle MA, Fudim M, DeVore AD, Piccini JP. Heart failure and atrial fibrillation, like fire and fury. JACC Heart Fail. 2019;7:447–56.
- Ruddox V, Sandven I, Munkhaugen J, Skattebu J, Edvardsen T, Otterstad JE. Atrial fibrillation and the risk for myocardial infarction, all-cause mortality and heart failure: a systematic review and meta-analysis. Eur J Prev Cardiol. 2017;24:1555–66.
- Benjamin EJ, Levy D, Vaziri SM, D'Agostino RB, Belanger AJ, Wolf PA. Independent risk factors for atrial fibrillation in a population-based cohort. Framingham Heart Study JAMA. 1994;271:840–4.

- Güzel T, Kış M, Şenöz O. The correlation between the left atrial volume index and atrial fibrillation development in heart failure with mildly reduced ejection fraction and long-term follow-up results. Acta Cardiol. 2022;77:647–54.
- Kılıç R, Güzel T, Aktan A, Demir M, Arslan B, Ertaş F. The effect of treatment strategy on long-term follow-up results in patients with nonvalvular atrial fibrillation in Turkey: AFTER-2 subgroup analysis. Aging Clin Exp Res. 2023;35:1695–704.
- 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.
- 12. Engström G, Smith JG, Persson M, Nilsson PM, Melander O, Hedblad B. Red cell distribution width, haemoglobin A1c and incidence of diabetes mellitus. J Intern Med. 2014;276:174–83.
- Hammons L, Filopei J, Steiger D, Bondarsky E. A narrative review of red blood cell distribution width as a marker for pulmonary embolism. J Thromb Thrombolysis. 2019;48:638–47.
- Arkew M, Gemechu K, Haile K, Asmerom H. Red blood cell distribution width as novel biomarker in cardiovascular diseases: a literature review. J Blood Med. 2022;13:413–24.
- Felker GM, Allen LA, Pocock SJ, Shaw LK, McMurray JJV, Pfeffer MA, et al. Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM program and the Duke Databank. J Am Coll Cardiol. 2007;50:40–7.
- Adamsson Eryd S, Borné Y, Melander O, Persson M, Smith JG, Hedblad B, et al. Red blood cell distribution width is associated with incidence of atrial fibrillation. J Intern Med. 2014;275:84–92.
- 17. Arques S. Human serum albumin in cardiovascular diseases. Eur J Intern Med. 2018;52:8–12.
- 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.
- Chen C, Cai J, Song B, Zhang L, Wang W, Luo R, et al. Relationship between the ratio of red cell distribution width to albumin and 28-day mortality among Chinese patients over 80 years with atrial fibrillation. Gerontology. 2023. https://doi.org/10.1159/000534259.
- 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.
- 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 Chron Obstruct Pulmon Dis. 2022;17:1797–809.
- Jian L, Zhang Z, Zhou Q, Duan X, Ge L. Red cell distribution width/albumin ratio: a predictor of in-hospital all-cause mortality in patients with acute myocardial infarction in the ICU. Int J Gen Med. 2023;16:745–56.
- 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.
- 24. Bosch NA, Cimini J, Walkey AJ. Atrial fibrillation in the ICU. Chest. 2018;154:1424–34.
- 25. Gupta S, Tiruvoipati R, Green C. Atrial fibrillation and mortality in critically ill patients: a retrospective study. Am J Crit Care. 2015;24:336–41.
- 26. Friedrichs K, Klinke A, Baldus S. Inflammatory pathways underlying atrial fibrillation. Trends Mol Med. 2011;17:556–63.
- Dobrev D, Heijman J, Hiram R, Li N, Nattel S. Inflammatory signalling in atrial cardiomyocytes: a novel unifying principle in atrial fibrillation pathophysiology. Nat Rev Cardiol. 2023;20:145–67.
- 28. Wijesurendra RS, Casadei B. Mechanisms of atrial fibrillation. Heart. 2019;105:1860–7.
- 29. Ren H, Hua Q, Quan M, Chen H, Hou H, Wang L, et al. Relationship between the red cell distribution width and the one-year outcomes in Chinese patients with stable angina pectoris. Intern Med. 2013;52:1769–74.
- Turcato G, Serafini V, Dilda A, Bovo C, Caruso B, Ricci G, et al. Red blood cell distribution width independently predicts medium-term mortality and major adverse cardiac events after an acute coronary syndrome. Ann Transl Med. 2016;4:254.
- Tatlisuluoglu D, Tezcan B, Mungan İ, Çakirli YA, Tümer NB, Taşoğlu İ. Predicting postoperative ischemic stroke problems in patients following coronary bypass surgery using neutrophil-lymphocyte ratio, platelet-lymphocyte ratio, and red blood cell distribution width values. Kardiochir Torakochirurgia Pol. 2022;19:90–5.

- Muhlestein JB, Lappe DL, Anderson JL, Muhlestein JB, Budge D, May HT, et al. Both initial red cell distribution width (RDW) and change in RDW during heart failure hospitalization are associated with length of hospital stay and 30-day outcomes. Int J Lab Hematol. 2016;38:328–37.
- Feng G-H, Li H-P, Li Q-L, Fu Y, Huang R-B. Red blood cell distribution width and ischaemic stroke. Stroke Vasc Neurol. 2017;2:172–5.
- Manolis AA, Manolis TA, Melita H, Mikhailidis DP, Manolis AS. Low serum albumin: a neglected predictor in patients with cardiovascular disease. Eur J Intern Med. 2022;102:24–39.
- Wang Y, Du P, Xiao Q, Li J, Liu X, Tan J, et al. Relationship between serum albumin and risk of atrial fibrillation: a dose-response Meta-analysis. Front Nutr. 2021;8:728353.
- Hong J, Hu X, Liu W, Qian X, Jiang F, Xu Z, et al. Impact of red cell distribution width and r on all-cause mortality in patients with type 2 diabetes and foot ulcers: a retrospective cohort study. Cardiovasc Diabetol. 2022;21:91.
- Ni Q, Wang X, Wang J, Chen P. The red blood cell distribution width-albumin ratio: a promising predictor of mortality in heart failure patients - a cohort study. Clin Chim Acta. 2022;527:38–46.

## **Publisher's Note**

Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations.