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ORIGINAL RESEARCH

Red Cell Distribution Width/Albumin Ratio: A Predictor of In-Hospital All-Cause Mortality in Patients with Acute Myocardial Infarction in the ICU

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Purpose: Red cell distribution width (RDW) and albumin level are linked to adverse outcomes in patients with acute myocardial infarction (AMI). Nonetheless, it remains unknown whether the RDW/albumin ratio (RAR) is associated with the short-term prognosis of AMI. Using a large cohort, we aimed to explore the association between RAR and in-hospital all-cause mortality in intensive care unit (ICU) patients with AMI.

Patients and Methods: The patients' data analyzed in this retrospective cohort investigation were obtained from the eICU Collaborative Research Data Resource. RAR was calculated based on the serum albumin level and RDW. The primary outcome was in-hospital all-cause mortality. Receiver operating characteristic curve, multiple logistic regression model, and Kaplan–Meier survival analysis were performed to explore the prognostic value of RAR.

Results: We enrolled 2594 patients in this study. After correcting for confounding factors, the RAR was an independent predictor for in-hospital mortality in our model (odds ratio [OR] 1.27, 95% confidence interval [CI] 1.12, 1.43). A similar relationship was observed with mechanical ventilation use. RAR showed a better predictive value with an area under the curve (AUC) of 0.738 (cutoff, 4.776) for in-hospital all-cause mortality compared to RDW or albumin alone. Kaplan–Meier estimator curve analyses for RAR demonstrated that the group with RAR ≥4.776%/g/dL had poorer survival than the group with RAR <4.776%/g/dL ($p< 0.0001$). The subgroup analysis revealed no significant interaction between RAR and in-hospital all-cause mortality in all strata.

Conclusion: RAR was an independent risk factor for in-hospital all-cause mortality in ICU patients with AMI. Higher RAR values corresponded to higher mortality rates. RAR is a more accurate predictor of in-hospital all-cause mortality in patients with AMI in the ICU than albumin or RDW. Thus, RAR may be a potential biomarker of AMI.

Keywords: red blood cell distribution width, albumin, in-hospital all-cause mortality, eICU-CRD, acute myocardial infarction

Introduction

Acute myocardial infarction (AMI), an inflammatory disease,[1] remains the leading cause of cardiac death globally.[2] Inflammation plays a pivotal role in the acute phase as well as the healing process following AMI.[3] In the course of clinical practice, the vast majority of patients with AMI will be admitted to the intensive care unit (ICU)/ critical care unit (CCU). Routine ICU/CCU use for patients with AMI is recommended in Japanese and European guidelines.[4,5] Although reduced by successful early reperfusion therapy, mortality is still substantial, particularly for

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patients who do not receive reperfusion therapy. Therefore, it is feasible to identify a convenient and effective inflammatory marker to identify high-risk patients with AMI admitted to the ICU and guide anti-inflammatory therapy.

Studies have shown that inflammatory markers are associated with the prognosis of AMI,[6,7] and we speculated that complex markers may have advantages over single markers. RDW is a hematological parameter that reflects the size heterogeneity of red blood cells (RBCs) and is utilized for the differential diagnosis of anemia. As an easily available marker of systemic inflammation, a previous study also suggested that RDW is associated with poor prognosis in AMI.[8–10] Serum albumin, a major protein in the human blood circulation system, is a conventional indicator of the nutritional and inflammatory status. Serum albumin content has been shown to be a remarkable predictor of adverse outcomes in individuals with AMI.[11,12] The RDW/albumin ratio (RAR) is a newly identified novel risk marker, which is defined as the ratio of RDW to serum albumin value (%/g/dl). Studies have shown that bioindicators are important for determining the prognosis of diverse inflammatory diseases.[13–15] RAR is a relatively new index measure; however, the established prognostic scoring systems for AMI do not include inflammatory indicators. Moreover, its application in people with AMI has not yet been investigated.

Thus, in this study, our objective was to evaluate the association between RAR and in-hospital mortality in patients with AMI admitted to the ICU, using real-world data.

Materials and Methods

Data Source

The eICU Collaborative Research Database (CRD) is a large, open-access, multicenter critical care data resource created by the Massachusetts Institute of Technology (MIT) Laboratory for Computational Physiology in collaboration with Philips Healthcare between 2014 and 2015. The CRD contains data on over 200,000 admissions from over 200 hospitals across the United States. The Health Insurance Portability and Accountability Act safe harbor provisions allow data resources to be distributed without revealing the identity of any patient. As data in the eICU-CRD are de-identified, the requirement of informed consent is waived. This database was approved by the Institutional Review Board (IRB) of the MIT. This study was reviewed and approved by the Medical Ethics Committee of the First People's Hospital of Changde (No. 2022–162-01). Furthermore, this study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guidelines, and was conducted in accordance with the ethical principles of the Declaration of Helsinki and its later amendments.

Study Population

We included adult patients with AMI based on the ICD-9 code 410, adopted in eICU-CRD. The following inclusion criteria were applied: i) age ≥18 years, ii) first ICU admission with a primary diagnosis of AMI, and iii) ICU length of stay >24 h. The exclusion criteria were as follows: i) age ≥89 years; ii) if key information (in-hospital mortality, body mass index [BMI], acute physiology and chronic health evaluation [APACHE] scores, hospital length of stay, ICU length of stay, and mechanical ventilation use) could not be obtained; iii) missing RDW and albumin measurements after ICU admission; and iv) blood transfusion received within 24 h before admission. The study population comprised 2594 patients with AMI [median age (interquartile range, IQR), 66.0, 57.0–76.0 years; female, 1634 (63.0%)]. The selection procedure for the study participants is summarized in Figure 1.

Data Extraction

One of the authors was granted permission to use the eICU-CRD data for medical research (certificate number 42039823). In this research, PostgreSQL v.11.2 (The PostgreSQL Global Development Group, https://www.postgresql.org/) was employed to extract patient data from the CRD. Clinical and laboratory findings of each patient were recorded on admission. The data, including demographic features, past medical history, type of AMI, APACHE scores, mortality, laboratory assessments, cause of admission, length of admission, and ICU stay, were obtained from the eICU-CRD following the first laboratory indicators after admission.

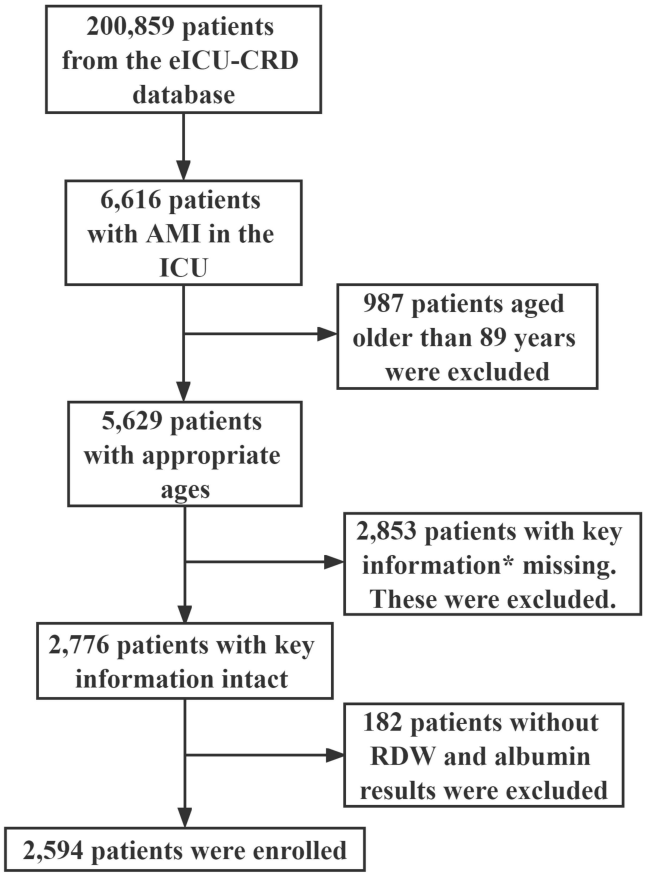

Figure 1 Flowchart of study participant selection. *Key information refers to mortality, body mass index (BMI), acute physiology and chronic health evaluation (APACHE) score, hospital length of stay, intensive care unit (ICU) length of stay, and mechanical ventilation use.

Definition of AMI

The term AMI is used when acute myocardial injury occurs, with clinical evidence of acute myocardial ischemia, and detection of a rise and/or fall of cTn values, with at least one value above the 99th percentile URL and at least one of the following:[16]

- Symptoms of myocardial ischemia
- New ischemic electrocardiographic (ECG) changes
- Development of pathological Q waves
- Imaging evidence of new loss of viable myocardium or new regional wall motion abnormality in a pattern consistent with ischemic etiology
- Identification of coronary thrombi by angiography or at autopsy

RAR Assessment and Outcomes

RDW is expressed as a percentage (%), and albumin in g/dL. The RAR was calculated as a ratio of RDW to albumin. In our study, the primary outcome was in-hospital mortality, while the secondary outcomes were mechanical ventilation use, length of ICU stay, and length of hospital stay. The observation period was from each patient's first admission to the hospital until death.

Statistical Analysis

Continuous data are presented as median and IQR, whereas categorical variables are provided in terms of frequency and percentage. The outcome variable was used to stratify the baseline characteristics of all patients. To compare the

groups, we employed the chi-square test for categorical variables and the Kruskal–Wallis test for continuous variables. Receiver operating characteristic (ROC) curve assessment was performed to test the capacity of RAR to differentiate between survivors and non-survivors and to determine the optimal RAR cutoff value. Additionally, RAR was compared with other prognostic indicators to verify its superiority. We performed a multivariate logistic regression analysis to determine whether RAR was related to in-hospital mortality in individuals with AMI, and the data were reported as odds ratios (OR) with 95% confidence interval (CI). In Model I, factors were adjusted for age, sex, and ethnicity. Age, sex, ethnicity, past medical history, AMI category, APACHE scores, white blood cell (WBC), RBC, hemoglobin (Hb), aspartate aminotransferase (AST), alanine aminotransferase (ALT), blood urea nitrogen (BUN), creatinine, total bilirubin (TB), total protein (TP), glucose, potassium, sodium, calcium, magnesium, bicarbonate, activated partial thromboplastin time (APTT), international normalized ratio (INR), troponin I, and natural log of B-type natriuretic peptide (lnBNP) were all adjusted for in Model II. Kaplan–Meier survival curves and the Log rank test were used to describe survival distributions. Stratified analysis was used to determine whether the impact of RAR was different in different subgroups. R (v3.42) and Empower Stats v2.17.8 (http://www.empowerstats.com/cn/) were used to analyze all data. All reported p values were two-sided, and two-tailed probability values of less than 5% were deemed statistically significant.

Results

Characteristics of Patients

A total of 2594 patients with AMI were enrolled; of these, 2276 survived and 318 died during hospitalization. The baseline clinical features of the patients who died and those who survived are listed in Table 1. A remarkable

Table 1 Baseline Clinical Features of the Enrolled Participants, Survivors, and Non-Survivors

Variables	Overall (2594)	Survivor (2276)	Non-Survivor (318)	*p*
Demographics				
Age, years	66.00 (57.00–76.00)	66.00 (56.00–75.00)	72.00 (65.00–80.00)	<0.001
Female, n (%)	1634 (63.00%)	1459 (64.10%)	175 (55.03%)	0.002
BMI, (kg/m2)	28.00 (24.00–32.00)	28.00 (25.00–32.00)	27.00 (24.00–31.00)	<0.001
Ethnicity*, n (%)				0.084
African	236 (9.20%)	216 (9.60%)	20 (6.35%)	
Asian	42 (1.64%)	35 (1.56%)	7 (2.22%)	
Caucasian	2008 (78.28%)	1749 (77.73%)	259 (82.22%)	
Hispanic	96 (3.74%)	85 (3.78%)	11 (3.49%)	
Native	10 (0.39%)	7 (0.31%)	3 (0.95%)	
Other	173 (6.74%)	158 (7.02%)	15 (4.76%)	
Past medical history, n (%)				
Hypertension	1495 (57.74%)	1329 (58.49%)	166 (52.37%)	0.039
Diabetes	929 (35.88%)	812 (35.74%)	117 (36.91%)	0.684
Previous MI	512 (19.78%)	457 (20.11%)	55 (17.35%)	0.247
CHF	402 (15.53%)	332 (14.61%)	70 (22.08%)	<0.001
PCI	378 (14.60%)	338 (14.88%)	40 (12.62%)	0.286
CABG	250 (9.66%)	216 (9.51%)	34 (10.73%)	0.491
Characteristics of the hospitalization				
LOS_hosp, days	5.36 (2.83–10.05)	5.41 (2.85–9.84)	5.10 (2.40–11.06)	0.542
LOS_ICU, hours	51.00 (29.00–111.00)	48.00 (28.00–97.00)	95.00 (42.25–196.00)	<0.001
APACHE score	50.00 (36.00–69.00)	47.00 (35.00–62.25)	85.00 (66.00–113.75)	<0.001
STEMI, n (%)	1196 (46.11%)	1076 (47.28%)	120 (37.74%)	0.001
MV, n (%)	1680 (64.76%)	1400 (61.51%)	280 (88.05%)	<0.001

Note: *The discrepancy between the total number of patients and the actual number was due to missing data.

Abbreviations: BMI, body mass index; MI, myocardial infarction; CHF, chronic heart failure; PCI, percutaneous coronary intervention; CABG, coronary artery bypass grafting; LOS_hosp, hospital length of stay; LOS_ICU, ICU length of stay; APACHE, acute physiology and chronic health evaluation; STEMI, ST-segment elevation myocardial infarction; MV, mechanical ventilation.

number of patients who died had abnormal laboratory values, including greater WBC counts; higher blood glucose, RDW, creatinine, and ALT concentrations; and decreased RBC counts, total cholesterol, Hb, high-density lipoprotein (HDL), and albumin concentrations ($p<0.01$), as shown in Table 2. The average overall RAR was 4.18 (%g/dL). However, non-survivor patients had significantly higher RAR than the survivor group (5.04%/g/dL vs 4.09%/g/dL, $p <0.001$, Table 2).

Univariate analysis showed that RAR, age, chronic heart failure, APACHE score, mechanical ventilation use, WBC, RDW, creatinine, BUN, total bilirubin, potassium, calcium, bicarbonate, APTT, troponin I, and lnBNP were positively correlated with mortality. Female sex, hypertension, ST-segment elevation myocardial infarction (STEMI), RBC, Hb, albumin, TP, sodium, magnesium, glucose, and triglyceride levels were negatively correlated with mortality (Supplemexntary Table 1).

Relationship of RAR with Outcomes

We used ROC curve analysis to evaluate the RAR prediction ability and determine the optimal threshold to forecast in-hospital all-cause mortality in patients with AMI. Different ROC curves for RAR, RDW, albumin, APACHE score, and RAR combined with APACHE score were constructed. The AUCs (95% CI) for RAR, RDW, and albumin were 0.738 (0.720, 0.755); 0.624 (0.605, 0.643); and 0.696 (0.678, 0.714), respectively (Figure 2). The cutoff point for RAR was 4.776.

Table 2 Baseline Laboratory Features in Survivors and Non-Survivors

Variables	Overall (2594)	Survivor (2276)	Non-Survivor (318)	*p*
Laboratory variables of admission				
WBC, k/mcl	11.20 (8.50–14.78)	10.90 (8.40–14.20)	13.66 (10.03–18.67)	<0.001
RBC, m/mcl	4.34 (3.76–4.82)	4.39 (3.80–4.85)	4.09 (3.47–4.53)	<0.001
Hb, g/dl	13.10 (11.20–14.60)	13.20 (11.38–14.70)	12.10 (10.20–13.90)	<0.001
RDW, %	14.00 (13.30–15.10)	13.90 (13.20–15.00)	14.65 (13.60–16.00)	<0.001
Platelets, k/mcl	221.00 (176.00–274.00)	221.00 (176.00–273.00)	222.50 (163.75–284.00)	0.946
Creatinine, mg/dl	1.12 (0.86–1.60)	1.10 (0.84–1.52)	1.40 (1.05–2.18)	<0.001
BUN, mg/dl	20.00 (14.00–31.00)	19.00 (14.00–29.00)	27.00 (18.00–45.00)	<0.001
Albumin, g/dl	3.40 (2.90–3.80)	3.40 (3.00–3.80)	2.95 (2.50–3.40)	<0.001
ALT, U/L	32.00 (21.00–55.00)	31.00 (21.00–51.00)	41.00 (23.00–103.25)	<0.001
AST, U/L	46.00 (27.00–112.00)	43.00 (27.00–104.00)	77.00 (37.00–206.00)	<0.001
TB, mg/dl	0.60 (0.40–0.90)	0.60 (0.40–0.90)	0.70 (0.40–1.10)	0.003
TP, g/dl	6.60 (6.00–7.20)	6.60 (6.00–7.20)	6.20 (5.50–6.90)	<0.001
Potassium, mol/L	4.10 (3.70–4.50)	4.00 (3.70–4.40)	4.20 (3.70–4.70)	0.001
Sodium, mmol/L	138.00 (135.00–140.00)	138.00 (135.00–140.00)	138.00 (135.00–141.00)	0.828
Calcium, mg/dl	8.80 (8.30–9.30)	8.80 (8.40–9.30)	8.50 (8.00–9.10)	<0.001
Magnesium, mg/dl	1.90 (1.70–2.10)	1.90 (1.70–2.10)	2.00 (1.70–2.20)	0.031
Bicarbonate, mol/L	24.00 (21.00–26.00)	24.00 (22.00–26.00)	21.00 (18.00–25.00)	<0.001
APTT, sec	31.10 (27.10–40.40)	31.00 (27.00–39.50)	34.20 (28.13–47.00)	<0.001
INR	1.10 (1.00–1.30)	1.10 (1.00–1.22)	1.20 (1.10–1.50)	<0.001
Glucose, mg/dl	144.00 (116.00–206.00)	141.00 (114.00–199.00)	175.00 (132.00–249.00)	<0.001
TC, mg/dl	156.00 (127.00–187.00)	158.00 (129.00–190.00)	131.00 (105.00–162.00)	<0.001
Triglycerides, mg/dl	118.00 (83.00–172.00)	119.00 (84.00–172.00)	105.00 (78.50–172.00)	0.122
HDL, mg/dl	38.00 (30.00–46.00)	38.00 (31.00–46.00)	33.00 (24.00–47.00)	<0.001
LDL-C, mg/dl	88.00 (62.00–118.00)	89.00 (64.00–118.00)	72.00 (50.00–96.00)	<0.001
Troponin-I, ng/mL	1.56 (0.28–8.12)	1.51 (0.26–8.17)	1.82 (0.37–8.08)	0.249
ln-BNP	6.71 (5.56–7.88)	6.47 (5.44–7.68)	7.78 (6.69–9.27)	<0.001
RAR, %/g/dl	4.18 (3.64–5.03)	4.09 (3.59–4.87)	5.04 (4.17–6.16)	<0.001

Abbreviations: WBC, white blood cell; RBC, red blood cell; Hb, hemoglobin; RDW, red cell distribution width; BUN, blood urea nitrogen; ALT, alanine transaminase; AST, aspartate transaminase; TB, total bilirubin; TP, total protein; APTT, activated partial thromboplastin time; INR, international normalized ratio; TC, total cholesterol; HDL, high-density lipoprotein; LDL-C, low-density lipoprotein cholesterol; ln-BNP, the log-transformed brain natriuretic peptide; RAR, red cell distribution width/albumin ratio.

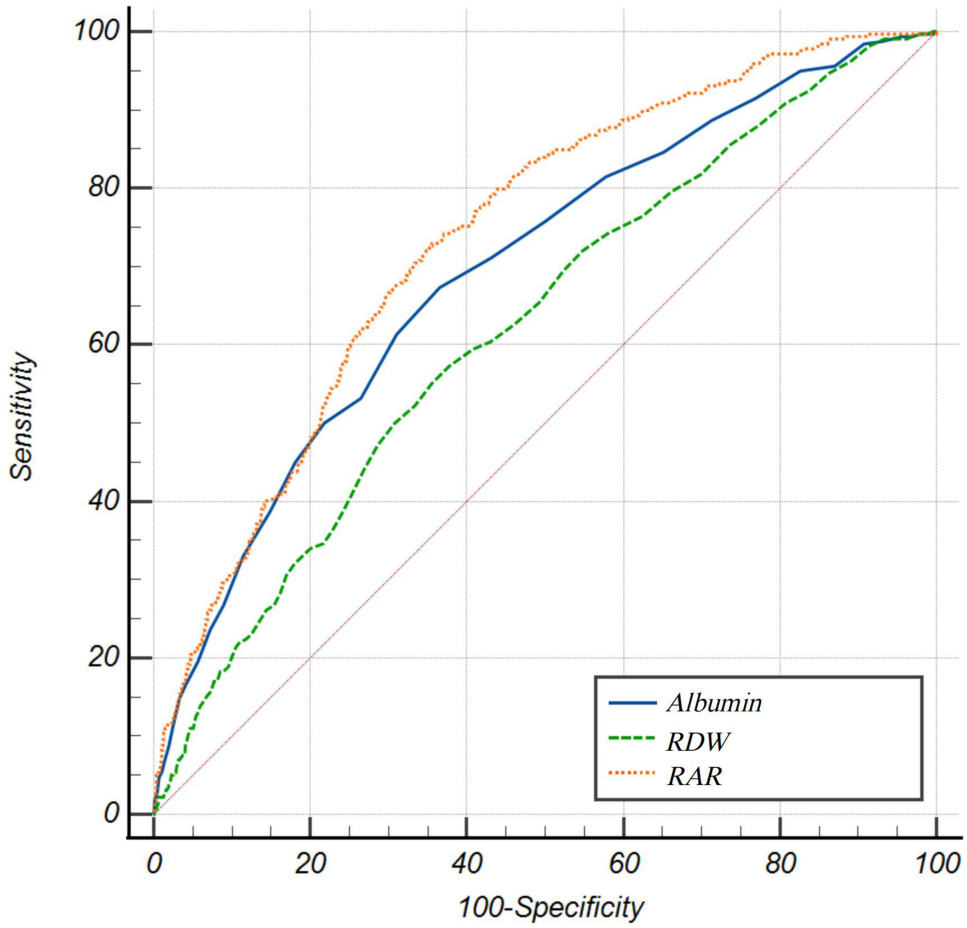

Figure 2 Receiver-operating characteristic curve of RAR, albumin, and RDW to predict in-hospital all-cause mortality of AMI.
Abbreviations: RAR, red cell distribution width/albumin ratio; RDW, red cell distribution width; AMI, acute myocardial infarction.

We observed that RAR predicted in-hospital all-cause mortality better than RDW and albumin levels (p<0.01). The AUC (95% CI) of RAR combined with APACHE score and APACHE score was 0.860 (0.845, 0.872) and 0.841 (0.833, 0.861), respectively (p<0.01) (Figure 3). These results indicate that RAR combined with the APACHE score has a better predictive power than the APACHE score alone.

The patients were divided into two sets according to the cutoff point. Greater RARs (≥4.776%/g/dL) were related to longer hospital and ICU stay, higher rates of mechanical ventilation use, and a higher in-hospital mortality (P <0.001, Table 3). We further explored these findings using multivariate logistic regression analysis, as shown in Table 4. After adjusting for the clinical confounders listed, RAR levels (per 1%/g/dL increase) were related to a 27% higher risk of in-hospital mortality (OR 1.27, 95% CI, 1.12, 1.43, p <0.001). Compared to the lower RAR group (<4.776%/g/dL), patients in the higher RAR group (≥4.776%/g/dL) showed elevated in-hospital mortality (OR 1.62, 95% CI 1.05, 2.51, p=0.03) in the adjusted Model II. A similar relationship was observed for the secondary outcomes.

Subgroup assessment was performed to explore the relationship between RAR and in-hospital mortality rate (Table 5). No remarkable interaction was observed across the strata (p =0.0800–0.7854).

Figure 4 shows the Kaplan–Meier survival curves for the RAR. We found that patients with high levels of RAR (≥4.776%/g/dL) had remarkably poorer survival than those with low levels (<4.776%/g/dL) (p <0.0001).

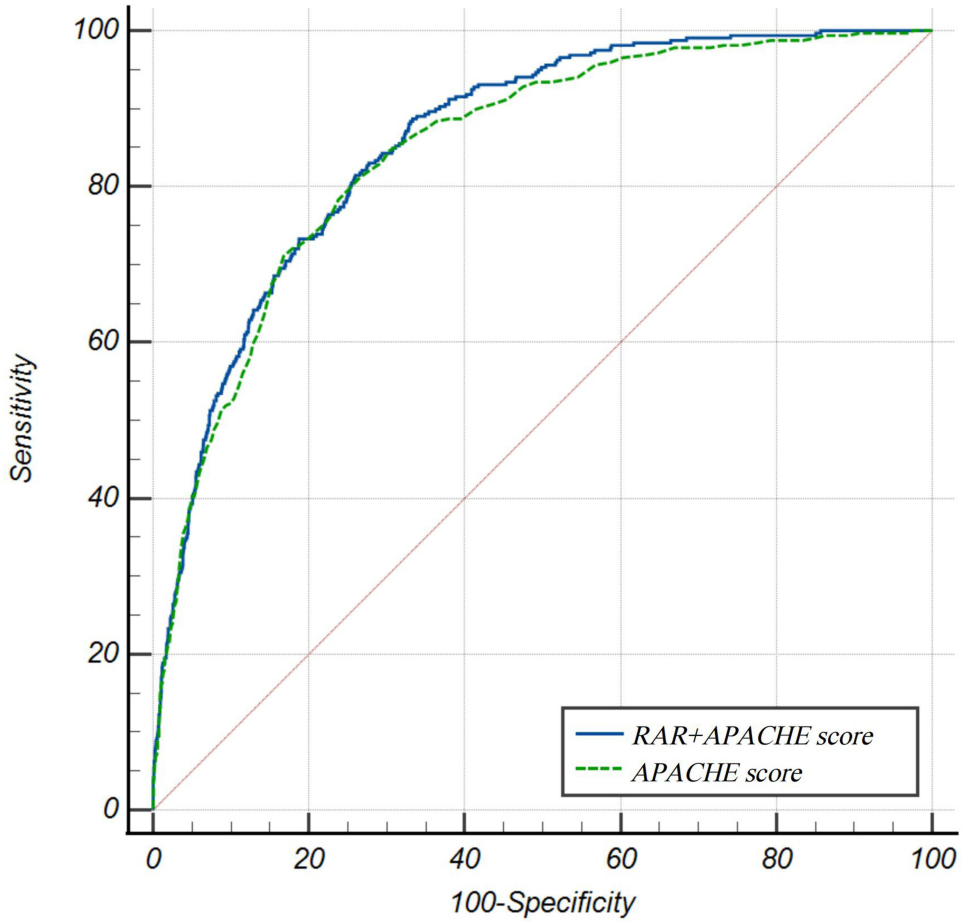

Figure 3 Receiver-operating characteristic curve of RAR and RAR combined with APACHE score to predict in-hospital all-cause mortality.
Abbreviations: RAR, red cell distribution width/albumin ratio; APACHE, Acute Physiology and Chronic Health Evaluation.

Discussion

This study illustrated that the RAR is an independent predictor of the mortality of AMI patients in the ICU and is positively associated with in-hospital all-cause mortality. We confirmed that the composite indicator has a higher predictive power for in-hospital mortality compared to albumin or RDW.

RDW is a parameter exhibiting the heterogeneity of RBC volume, which represents the variability in the size of circulating RBCs, and is an easily obtainable and inexpensive blood marker.[17,18] Previous investigations have shown that RDW is linked to acute coronary syndrome (ACS);[9,10,17,19,20] however, the mechanisms underlying this association are not completely understood. RDW is considered an inflammatory marker that can worsen arteriosclerosis and is associated

Table 3 Outcomes of the Patients with AMI Across Cutoff Points of the RAR

Variables	All Patients	RAR		p
		<4.776	≥4.776	
n	2594	1782	812	
LOS_hosp, days	5.36 (2.83–10.05)	4.27 (2.56–8.14)	8.06 (4.48–14.73)	<0.001
LOS_ICU, hours	51.00 (29.00–111.00)	45.00 (26.00–85.00)	81.00 (41.00–160.00)	<0.001
MV, n (%)	1680 (64.76%)	1071 (60.10%)	609 (75.00%)	<0.001
In-hospital mortality, n (%)	318 (12.26%)	130 (7.30%)	188 (23.15%)	<0.001

Abbreviations: RAR, red cell distribution width/albumin ratio; LOS_hosp, hospital length of stay; LOS_ICU, ICU length of stay; MV, mechanical ventilation.

Table 4 Results of Multivariable Logistic Regression of RAR and In-Hospital All-Cause Mortality

Exposure	Non-Adjusted		Model I		Model II	
	OR/β	95% CI	OR/β	95% CI	OR/β	95% CI
Primary outcomes						
Continuous variable						
In-hospital mortality	1.48	(1.38, 1.58)	1.48	(1.38, 1.58)	1.27	(1.12, 1.43)
RAR cutoff point						
In-hospital mortality						
<4.776	1.0		1.0		1.0	
≥4.776	3.83	(3.01, 4.88)	3.55	(2.77, 4.56)	1.62	(1.05, 2.51)
Secondary outcomes						
Continuous variable						
MV	1.31	(1.22, 1.40)	1.29	(1.21, 1.39)	1.31	(1.14, 1.50)
RAR cutoff point						
MV						
<4.776	1.0		1.0		1.0	
≥4.776	1.99	(1.66, 2.40)	1.93	(1.60, 2.34)	1.83	(1.32, 2.54)
Length of ICU stay[a]	17.15	(14.24, 20.06)	17.08	(14.11, 20.06)	8.28	(3.02, 13.53)
Length of hospital stay[a]	1.65	(1.47, 1.84)	1.63	(1.43, 1.82)	0.92	(0.58, 1.25)

Notes: Model I was adjusted for age, sex, and ethnicity. Model II was adjusted for age; sex; ethnicity; past medical history: chronic heart failure, hypertension, diabetes; PCI, and CABG; AMI category; APACHE scores; white blood cell; red blood cell; hemoglobin; aspartate transaminase; alanine transaminase; blood urea nitrogen; creatinine; total bilirubin; total protein; glucose; potassium; sodium; calcium; magnesium; bicarbonate; activated partial thromboplastin time; international normalized ratio; troponin-I; and lnBNP. [a]Linear regression was used to evaluate the association between RAR and length of stay. The results are expressed as β (95% CIs).
Abbreviations: OR, odds ratio; CI, confidence interval; RAR, red cell distribution width/albumin ratio; MV, mechanical ventilation.

with several inflammatory markers.[20,21] In atherosclerosis, RBCs are influenced by inflammatory factors, which trigger the generation of numerous immature RBCs from the bone marrow, resulting in higher RDW levels and elevated ineffective hematopoiesis in the bone marrow.[22–24] The rupture of the unstable fibrous cap causes thrombosis, and the deformability of RBCs trapped within a fibrin clot decreases, resulting in an increased RDW.[18] The study by Uyarel et al[19] demonstrated that higher RDW values at baseline were more remarkably linked to a higher cardiovascular mortality among patients with STEMI undergoing primary percutaneous coronary intervention (pPCI) both in-hospital and (1.8±1.3 years) after AMI. In a median follow-up time of 27 months, a recent study illustrated that an RDW increase during hospitalization was likewise related to eventual death (adjusted hazard ratio [HR] 1.13 for 1-standard deviation [SD] increase in RDW, 95% CI 1.02–1.25) in 1709 patients with AMI.[10] In individuals with and without anemia, there was a link between a greater RDW and worse outcomes. Similarly, in our study, the non-survivor group had higher RDW levels than the survivor group.

Serum albumin levels were routinely measured in patients with AMI, and albumin also plays a role in the acute early inflammatory response.[25–28] Nutritional intake and systemic inflammation influence albumin production rates.[29] Inflammatory cytokines such as interleukin (IL)-6 and tumor necrosis alpha (TNF-α) restrict albumin production by inhibiting albumin gene transcription, resulting in decreased albumin synthesis. Previous investigations[11,30,31] revealed that hypoalbuminemia is linked to adverse events in individuals with ACS. Moreover, one of these studies indicated that albumin content ≤3.50 g/dL is an independent prognostic factor for new-onset heart failure and in-hospital mortality in individuals with ACS. Plakht et al[32] reported that decreased albumin level on admission, consisting of levels within "normal" clinical range, is remarkably linked to long-term all-cause mortality in hospital survivors of AMI with a "dose-response" type association. Comparable results were obtained in our study, showing that the albumin contents were lower in patients who died.

Several studies exist on composite indicators for AMI. In most studies, composite indicators are better than single-characteristic indicators. According to Tong et al,[33] RDW-to-platelet ratio is an independent predictor of in-hospital mortality in AMI patients. In our study, the RAR predicted in-hospital mortality in AMI patients in the ICU better

Table 5 Subgroup Assessments of the Associations of In-Hospital All-Cause Mortality with RAR

	n	RAR		P for Interaction
		<4.776	≥4.776	
Age				0.4472
<65	1136	1.91 (0.92, 3.99)	1.01 (0.88, 1.15)	
≥65	1458	1.13 (0.75, 1.71)	1.16 (1.06, 1.27)	
Gender				0.1468
Male	960	1.42 (0.81, 2.49)	1.06 (0.96, 1.18)	
Female	1634	1.33 (0.82, 2.14)	1.08 (0.97, 1.19)	
AMI category				0.2031
NSTEMI	1398	1.00 (0.63, 1.59)	1.04 (0.95, 1.14)	
STEMI	1196	2.56 (1.44, 4.52)	1.19 (1.04, 1.37)	
MV				0.3938
No	914	0.37 (0.12, 1.13)	0.96 (0.73, 1.26)	
Yes	1680	1.59 (1.08, 2.33)	1.08 (1.00, 1.16)	
CHF				0.3597
No	2187	1.60 (1.09, 2.35)	1.08 (0.99, 1.17)	
Yes	402	0.77 (0.28, 2.11)	1.05 (0.90, 1.22)	
Diabetes				0.1363
No	1660	1.53 (0.99, 2.36)	1.04 (0.94, 1.15)	
Yes	929	1.25 (0.66, 2.37)	1.11 (1.00, 1.24)	
Hypertension				0.7854
No	1094	1.49 (0.89, 2.50)	1.07 (0.98, 1.17)	
Yes	1495	1.39 (0.84, 2.30)	1.06 (0.94, 1.19)	
Previous MI				0.7238
No	2077	1.46 (0.99, 2.15)	1.05 (0.97, 1.14)	
Yes	512	1.23 (0.47, 3.24)	1.16 (1.00, 1.35)	
APACHE score*				0.0800
T1	849	5.52 (0.61, 49.91)	1.20 (0.65, 2.21)	
T2	851	0.85 (0.36, 2.01)	0.86 (0.63, 1.17)	
T3	894	0.88 (0.58, 1.33)	1.06 (0.98, 1.14)	

Note: *APACHE scores are grouped based on tertiles.

Abbreviations: RAR, red cell distribution width/albumin ratio; MV, mechanical ventilation; NSTEMI, Non ST-segment elevation myocardial infarction; STEMI, ST-segment elevation myocardial infarction; CHF, chronic heart failure; APACHE, acute physiology and chronic health evaluation.

than the RDW or albumin alone. RAR combined with the APACHE score had better predictive power than the APACHE score alone. This study also found that the optimal cutoff value of RAR for predicting in-hospital mortality was 4.776, which is similar to that in another report (4.59 in patients with acute respiratory distress syndrome[14]). Our study demonstrates, for the first time, that RAR ≥4.776 is associated with increased in-hospital mortality in patients with AMI in the ICU. We also found that RAR is associated with a higher proportion of patients requiring mechanical ventilation use and longer ICU stay. Therefore, it is essential to carry out routine blood and albumin tests at admission. Recently, RAR was found to be a strong predictor of mortality in individuals with acute respiratory distress syndrome and diabetic ketoacidosis.[14,15] Increased RDW and low serum albumin levels are closely associated with the inflammatory response. RAR can be performed easily and rapidly in laboratories. As a biomarker, it reflects inflammatory processes in AMI and can be used to evaluate the short-term outcome of AMI. In conclusion, our data illustrate that RAR is a predictor of in-hospital mortality among ICU patients with AMI.

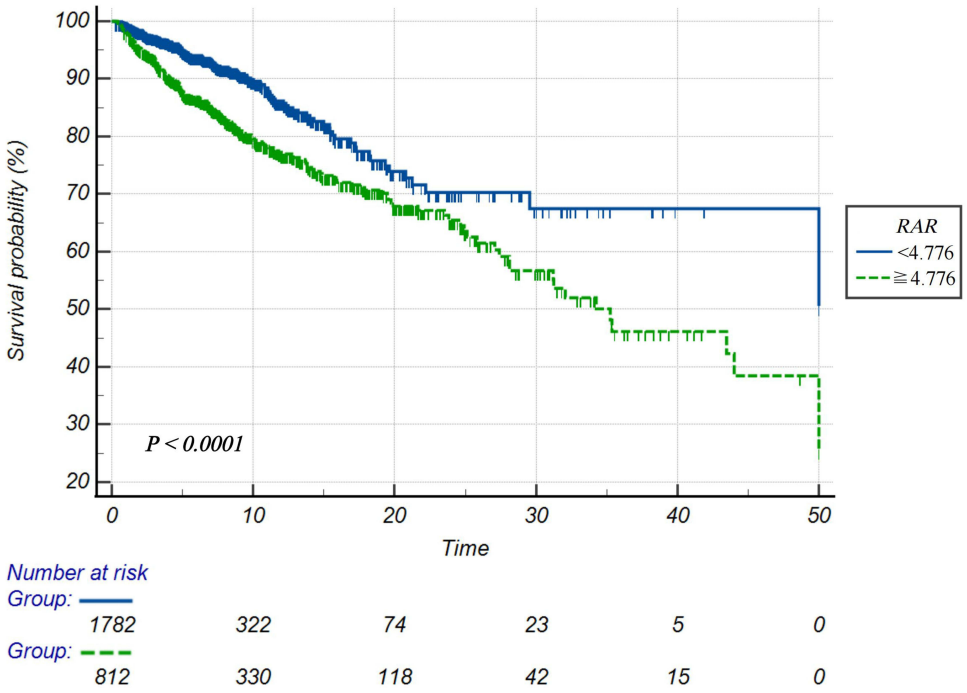

Figure 4 Kaplan–Meier curve of RAR for estimating in-hospital all-cause mortality of AMI.
Abbreviations: RAR, red cell distribution width/albumin ratio; AMI, acute myocardial infarction.

Limitations

This study has some limitations. First, due to the retrospective status of the work, selection bias cannot be totally excluded. Second, this study was limited by the fact that RAR levels were assessed only once and were not evaluated for their dynamics changes. Third, other unstudied confounders may have interfered with our results. Owing to the limitations of the eICU database, we could not obtain comprehensive hospitalization data of the patients, such as cardiac function classification, echocardiogram results, specific location of myocardial infarction, thrombolysis in myocardial infarction (TIMI) risk score, Global Registry of Acute Coronary Events (GRCAE) risk score, and other data that may affect the prognosis of patients. Further studies are required to verify the results of this study. Despite these shortcomings, our study is meaningful in exploring the relationship between RAR and AMI.

Conclusions

We concluded that the RAR is a potential biomarker of AMI, and elevated RAR is linked to increased in-hospital mortality in individuals with AMI in the ICU. RAR is a more accurate predictor of in-hospital all-cause mortality in patients with AMI in the ICU than albumin or RDW.

Data Sharing Statement

The eICU data resource (version 2.0) is freely accessible at https://physionet.org/content/eicu-crd/. Access to the data resource is granted to any researcher who follows the data usage guidelines.

Ethics Approval and Consent to Participate

This database was approved by the Institutional Review Board of the Massachusetts Institute of Technology. The Medical Ethics Committee of The First People's Hospital of Changde has approved the research (No. 2022-162-01). It was a retrospective analysis of data from a third-party anonymized and publicly accessible data resource; informed consent from the patients was not required.

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Disclosure

The authors declared that they have no conflicts of interest to this work.

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