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The Predictive Value of Hemoglobin-to-Red Blood Cell Distribution Width Ratio for the Prognosis of Patients with Aortic Dissection: Based on the Medical Information Mart for Intensive Care-IV Database

ABSTRACT

Background: The hemoglobin-to-red blood cell distribution width ratio (HRR) is a new inflammatory marker in evaluating tumor prognosis. However, its application in cardiovascular diseases (CVDs) is relatively limited. This research was designed to illuminate the relationship between HRR and mortality in patients with aortic dissection (AD).

Methods: The Medical Information Mart for Intensive Care-IV (MIMIC-IV) database was applied in this retrospective cohort study. The primary outcome was the 30-day mortality rate. The Cox proportional hazards model was utilized to explore the relationship between HRR and mortality in AD patients. Through restricted cubic splines (RCS), the relationship between mortality and HRR levels was analyzed. The ROC curves were graphed to evaluate the prognostic value of HRR.

Results: This retrospective cohort study included 292 patients. A significant negative linkage between HRR quartiles and 30-day mortality was identified ($P < .05$). Kaplan-Meier analysis demonstrated that participants in the low-HRR group exhibited worse survival rates than those in the high-HRR group (Q1 vs. Q2, log-rank $P = .005$; Q1 vs. Q3, log-rank $P < .001$; Q1 vs. Q4, log-rank $P = .014$). No great difference was observed between other groups. In RCS analysis, a non-linear linkage between HRR and 30-day mortality rate was observed ($P < .05$). Through analyzing ROC curves, HRR was found to perform well in predicting AD mortality, with AUC values of 0.628, 0.662, and 0.669 at 7, 14, and 30 days, respectively.

Conclusion: Low levels of HRR may elevate the risk of death in AD patients. The research pinpointed the potential of HRR as a prognostic biomarker for AD patients, which can provide reliable auxiliary indicators for clinical routine and interventional treatment.

Keywords: Aortic dissection, hemoglobin-to-red blood cell distribution width ratio, Medical Information Mart for Intensive Care-IV, survival analysis

INTRODUCTION

Aortic dissection (AD) is a life-threatening, serious cardiovascular disease (CVD) characterized by the tearing of the intimal layer of the aorta or hemorrhage within the aortic wall, leading to the separation of the aortic layers and the formation of a false lumen, which in severe cases can result in aortic rupture or other fatal complications.[1,2] This disease usually has a rapid onset, manifested as sudden and severe chest pain, which often catches patients off guard and makes it difficult to identify the cause in time. In addition, the mortality rate of acute AD is high. It causes half of the AD patients to die before arriving at specialized centers, seriously threatening their life and health.[3-5] Although achievements in surgery and the application of intravascular stents have greatly elevated the survival rate of AD patients in recent years,[6,7] the treatment effectiveness of some patients is still disappointing due to the insidious onset and invasive prognosis of AD, as well as its complex and variable condition.[8] Therefore, innovating a fast, non-invasive, accurate, and timely diagnosis is instrumental for the prognosis of AD patients.

ORIGINAL INVESTIGATION

Jianqiang Wu[1]
Zhengli Zou[2]

[1]*Department of Cardiovascular Surgery, Deyang People's Hospital, Deyang City, China*
[2]*Department of Clinical Nutrition, Deyang People's Hospital, Deyang City, China*

Corresponding author:
Zhengli Zou
✉ zzzhenglizou@163.com

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Hematological parameters are now widely applied in diagnosing and predicting the prognosis of diseases, garnering growing attention in clinical practice.[9-11] Red blood cell distribution width (RDW) is a readily available parameter representing the volume of red blood cells, primarily used for the differentiation and diagnosis of anemia.[12] For AD patients, higher RDW is considered a strong risk factor affecting mortality and prognosis.[13,14] Similar to RDW, hemoglobin (Hb) is also an essential component of hematological parameters. It reflects, to some extent, the decline of the host immune response and malnutrition, which is linked to the patient's resistance to external invasion.[15] Preoperative Hb levels are prognostic markers for long-term adverse outcomes in patients with acute type B AD after thoracic aortic endovascular repair.[16]

The Hb-to-RDW ratio (HRR) is a simple yet powerful composite indicator, initially used to predict the prognosis of cancer.[17] With the deepening of research, it has become a new independent prognostic marker for many CVDs, such as stroke, cerebral hemorrhage, coronary atherosclerotic heart disease, and other patients.[18-21] It performed well in prediction. However, there seems to be no current data linking HRR to the prognosis of AD patients. Therefore, this research was intended to analyze the linkage between HRR and the prognosis of AD patients.

METHODS

AI statement: This article was not written using AI.

Database

The Medical Information Mart for Intensive Care-IV (MIMIC-IV) database provides an extensive collection of intensive care data.[22] It is essential for supporting in-depth studies in epidemiology, machine learning, and clinical informatics. This database is an updated version of MIMIC-III that incorporates new data and improves upon many features of the original dataset. As stated in the ethical declaration, since all protected health information was de-identified and the study had no effect on clinical care, the need for individual patient agreement was waived.[23]

Inclusion and Exclusion Criteria

This research screened 455 patients with a diagnosis code of 4410 (ICD9) or I710 (ICD10)[24,25] where AD was the primary diagnosis. Patients who met the following exclusion criteria were excluded: (1) multiple hospitalizations; (2) individuals under 18 years of age; and (3) individuals with Marfan syndrome (75982, Q874), Ehlers-Danlos syndrome (75683, Q796), and congenital aortic valve abnormalities (7464, Q231). A total of 292 patients were ultimately enrolled in this research. The selection process of participants is shown in Figure 1.

Data Collection

Based on existing literature and clinical judgment, the authors gathered the intensive care unit (ICU) variables, including demographic data, laboratory measurements, severity scores, and medical history, which were considered confounding factors for AD outcomes. Vital signs, severity scores, and laboratory measurements conducted multiple times during the ICU stay were all determined by the values corresponding to the most severe level collected within the first 24 hours following ICU admission.

Statistical Analysis

Continuous variables are represented by mean ± SD or median (interquartile range). The normal distribution was determined through the Kolmogorov–Smirnov test and combined with a histogram and Q-Q chart for comprehensive judgment. According to the distribution characteristics of the data, the *t*-test was used for inter-group comparisons that satisfy normal distribution and homogeneity of variance; otherwise, the Mann–Whitney *U*-test was used. To compare categorical variables, the chi-squared test was undertaken, and differences were expressed in percentages (%). Multiple and univariate Cox regression analyses were undertaken to assess the hazard ratio of HRR on the 30-day mortality of patients with AD. Multiple Cox prognostic models were created by comprising statistically significant variables determined by multiple regression analysis. Kaplan–Meier (K-M) survival curves were applied to assess the mortality outcomes between groups, and the log-rank test was employed for evaluation. By utilizing restricted cubic splines (RCS), the linkage between HRR and the 30-day mortality of AD patients was dissected, with 4 knots placed at the 5th, 35th, 65th, and 95th percentiles of HRR.[26] To further demonstrate the predictive efficacy of HRR for AD mortality at various follow-up time points, the receiver operating characteristic (ROC) curves of HRR were plotted.

The database lacked certain biological parameters. Variables with missing values that made up less than 5% of the entire sample were filled using the Random Forest (RF) approach throughout the parameter extraction procedure. The proportion of missing variables is displayed in Supplementary Table 1.

Data in this research were collected from the MIMIC-IV (Version 2.2) database with SQL (Structured Query Language) and analyzed by utilizing the R (Version 4.2.3) software, including R packages *rms*, *timeROC*, *mice*, *jskm*, and *tableone* (2-sided *P*-value < .05: statistically significant).

HIGHLIGHTS

- There is a negative correlation between HRR width ratio and 30-day mortality risk in AD patients.
- The relationship between HRR width ratio and the 30-day mortality rate in AD patients is non-linear.
- The HRR width ratio has a good predictive value for mortality in AD patients.

RESULTS

Baseline Characteristics

The median age of the enrolled 292 patients was 67.35 ± 13.47 years. A total of 168 were men (57.5%). Based on the 30-day survival status of the patients, 2 groups of participants were formed: the survival group (n = 261) and the death

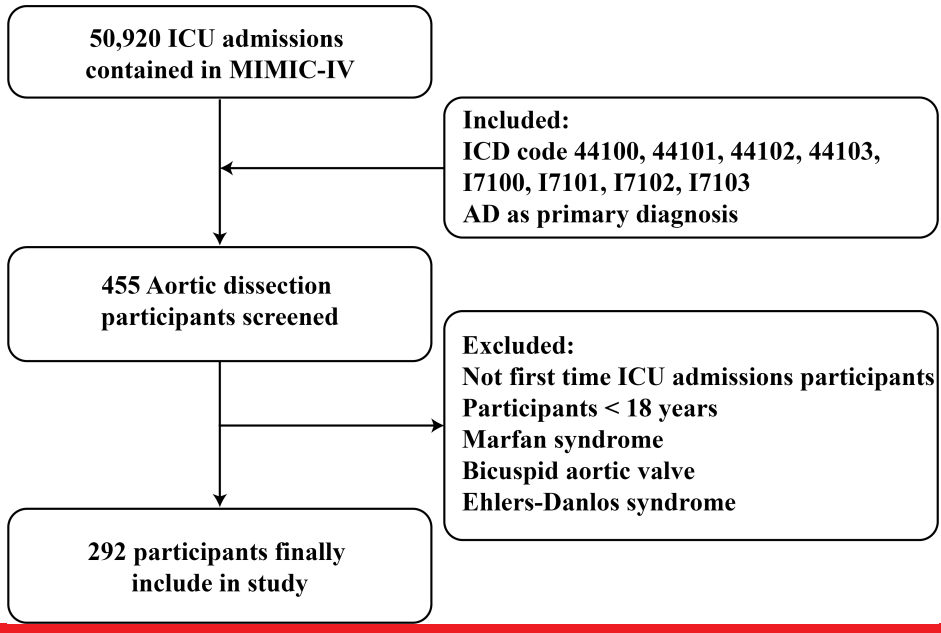

Figure 1. Flowchart of the selection process of patients.

group (n = 31). The death group had higher respiratory rates and blood glucose levels, higher SAPS II, SOFA, LODS, and SIRS scores, as well as elevated levels of anion gap, lactate, BUN, potassium ions, creatinine, ALT, AST, and pCO_2 ($P < .05$). Hemoglobin-to-RDW ratio was lower than that in the survival group (0.57 ± 0.22 vs. 0.68 ± 0.19, $P = .004$) (Table 1).

Table 1. Baseline Characteristics of Patients

Characters	Total (n = 292)	Survivor (n = 261)	Non-survivors (n = 31)	*P*
Age (years)	67.35 (13.47)	67.33 (13.12)	67.48 (16.40)	.953
Gender				.369
Female	124 (42.5)	108 (41.4)	16 (51.6)	
Male	168 (57.5)	153 (58.6)	15 (48.4)	
Race				.079
White	155 (53.1)	143 (54.8)	12 (38.7)	
Black	39 (13.4)	36 (13.8)	3 (9.7)	
Other race	98 (33.6)	82 (31.4)	16 (51.6)	
Marital status				.737
Married	126 (43.2)	114 (43.7)	12 (38.7)	
Unmarried	166 (56.8)	147 (56.3)	19 (61.3)	
LOS (days)	3.67 [2.16, 7.49]	3.62 [2.09, 7.13]	4.26 [2.44, 15.56]	.298
Height (cm)	170.59 (11.25)	170.91 (11.16)	168.04 (11.88)	.239
Weight (kg)	84.21 (22.41)	83.56 (21.78)	89.59 (26.92)	.164
Smoking status	60 (20.5)	55 (21.1)	5 (16.1)	.683
Heart rate (times/min)	77.74 (12.03)	77.75 (11.98)	77.71 (12.71)	.988
SBP (mm Hg)	114.63 (11.20)	114.68 (10.94)	114.22 (13.44)	.83
DBP (mm Hg)	59.74 (8.72)	59.59 (8.24)	61.01 (12.16)	.391
MBP (mm Hg)	76.10 (8.72)	75.97 (8.29)	77.21 (11.84)	.453
Breath rate (times/min)	18.19 (2.90)	17.98 (2.73)	19.94 (3.63)	<.001
Temperature	36.65 (0.55)	36.66 (0.54)	36.55 (0.58)	.361
SpO2	96.67 (1.92)	96.64 (1.91)	97.01 (1.99)	.319
Glucose (mg/dL)	131.15 [117.56, 143.45]	130.67 [116.85, 142.80]	137.13 [126.62, 146.07]	.049
SAPSII	38.24 (12.66)	37.39 (12.19)	45.39 (14.40)	.001

(*Continued*)

Table 1. Baseline Characteristics of Patients (*Continued*)

Characters	Total (n = 292)	Survivor (n = 261)	Non-survivors (n = 31)	*P*
SOFA	4.00 [2.00, 8.25]	4.00 [2.00, 8.00]	9.00 [4.00, 12.00]	<.001
GCS	13.94 (2.88)	13.95 (2.91)	13.81 (2.64)	.788
LODS	5.00 [2.00, 8.00]	4.00 [2.00, 7.00]	7.00 [4.00, 9.50]	.002
SIRS	2.17 (0.92)	2.14 (0.92)	2.48 (0.89)	.048
HRR	0.66 (0.20)	0.68 (0.19)	0.57 (0.22)	.004
Chloride (mmol/L)	107.24 (4.98)	107.16 (4.94)	107.94 (5.35)	.412
Hematocrit (μmol/L)	28.69 (6.74)	28.98 (6.56)	26.25 (7.75)	.033
Hemoglobin (g/dL)	9.60 (2.31)	9.72 (2.23)	8.52 (2.71)	.006
Potassium (K/μL)	4.61 (0.82)	4.57 (0.78)	4.88 (1.03)	.048
Anion gap (mEq/L)	15.69 (3.97)	15.29 (3.29)	19.03 (6.80)	<.001
Bicarbonate (mEq/L)	22.11 (3.13)	22.37 (2.86)	19.97 (4.33)	<.001
Sodium (mEq/L)	138.05 (3.50)	13800 (3.39)	138.48 (4.40)	.468
PTT (s)	36.50 [30.00, 52.30]	36.00 [30.02, 51.82]	45.30 [29.95, 63.65]	.199
INR	1.59 (0.73)	1.58 (0.74)	1.70 (0.70)	.386
PT (s)	15.30 [12.70, 19.20]	15.20 [12.70, 18.70]	16.70 [12.90, 20.70]	.136
Lactate (mmol/L)	4.75 [2.30, 7.23]	4.60 [2.30, 6.77]	7.10 [3.05, 9.98]	.011
Platelets (K/μL)	142.50 [92.75, 186.75]	147.00 [100.00, 190.00]	96.00 [73.50, 144.50]	.006
WBC (K/μL)	12.91 (5.01)	12.79 (4.96)	13.89 (5.40)	.249
RBC (M/μL)	3.20 (0.82)	3.24 (0.80)	2.86 (0.89)	.013
pO_2 (mm Hg)	77.66 (33.96)	79.90 (34.25)	62.35 (27.92)	.013
pCO_2 (mm Hg)	53.37 (13.62)	52.48 (12.74)	59.46 (17.67)	.014
pH	7.26 (0.12)	7.27 (0.11)	7.17 (0.13)	<.001
Base excess (mEq/L)	−5.00 [−8.00, −1.00]	−4.67 (4.67)	−9.58 (5.87)	<.001
MCH (pg)	29.74 (2.27)	29.81 (2.26)	29.15 (2.27)	.124
MCHC (g/dL)	32.75 (1.57)	32.88 (1.49)	31.62 (1.72)	<.001
MCV (fL)	89.06 (5.81)	89.05 (5.89)	89.13 (5.19)	.946
RDW	14.75 (1.77)	14.68 (1.77)	15.28 (1.73)	.076
Open chest surgery	136 (46.6)	120 (46.0)	16 (51.6)	.686
BUN (mg/dL)	20.00 [15.75, 27.00]	20.00 [15.00, 26.00]	25.00 [20.00, 32.00]	.006
Creatinine (mg/dL)	1.20 [0.90, 1.63]	1.10 [0.90, 1.60]	1.50 [1.15, 2.40]	.005
ALT (U/L)	22.00 [16.00, 42.75]	21.00 [15.00, 38.75]	42.50 [24.50, 174.75]	.007
ALP (U/L)	61.00 [45.00, 83.00]	61.00 [44.50, 81.50]	65.50 [47.25, 88.75]	.452
AST (U/L)	33.00 [21.00, 71.00]	29.50 [21.00, 59.00]	68.00 [30.00, 276.75]	.015
Bilirubin (mg/dL)	0.60 [0.40, 1.20]	0.60 [0.40, 1.20]	1.00 [0.43, 1.62]	.261
Site				.802
Abdominal	34 (11.6)	31 (11.9)	3 (9.7)	
Thoracic	192 (65.8)	170 (65.1)	22 (71.0)	
Thoracoabdominal	60 (20.5)	54 (20.7)	6 (19.4)	
Unspecified	6 (2.1)	6 (2.3)	0 (0.0)	
Myocardial infarct	18 (6.2)	17 (6.5)	1 (3.2)	.745
Diabetes	40 (13.7)	35 (13.4)	5 (16.1)	.889
Coronary artery disease	53 (18.2)	46 (17.6)	7 (22.6)	.667
Congestive heart failure	44 (15.1)	37 (14.2)	7 (22.6)	.331
Liver disease	15 (5.1)	11 (4.2)	4 (12.9)	.101

Continuous variables are presented as mean (SD) or median [interquartile range]; categorical variables are presented as n (%).
BUN, blood urea nitrogen; DBP, diastolic blood pressure; GCS, Glasgow Coma Score; HRR, hemoglobin-to-red blood cell distribution width ratio; INR, International Normalized Ratio; LODS, Logistic Organ Dysfunction System scoring; LOS, length of stay; MBP, mean blood pressure; PT, prothrombin time; PTT, partial thromboplastin time; RBC, red blood cell; RDW, red cell volume distribution width; SAPSII, Simplified Acute Physiology Score II; SBP, systolic blood pressure; SIRS, systemic inflammatory response syndrome; SOFA, Sequential Organ Failure Assessment; SpO2, percutaneous oxygen saturation; WBC, white blood cell; Po2, Partial pressure of oxygen; Pco2, Partial pressure of carbon dioxide; MCH, Mean corpuscular hemoglobin; MCHC, Mean corpuscular hemoglobin concentration; MCV, Mean corpuscular volume; ALT, Alanine aminotransferase; ALP, Alkaline phosphatase; AST, Aspartate aminotransferase.

The Linkage between Hemoglobin-to-Red Blood Cell Distribution and 30-Day Mortality in Aortic Dissection Patients

By constructing Cox regression models adjusted and unadjusted for confounding factors, the authors dissected the impact of HRR on the mortality of AD patients (Table 2). The constructed Crude (OR: 0.55, *P* = .005, 95% CI: 0.36-0.83) and Adjusted (OR: 0.55, *P* = .028, 95% CI: 0.32-0.94) models indicated a great negative linkage between HRR and the mortality risk of AD patients.

Subsequently, the authors grouped HRR into quartiles and treated it as a categorical variable in the multiple Cox analysis, using the lowest quartile as the reference. When HRR was considered as a categorical variable, Q2 (OR: 0.25, *P* = .014, 95% CI: 0.08-0.75) and Q3 (OR: 0.15, *P* = .005, 95% CI: 0.04-0.56) after adjustments for confounding factors demonstrated a lower mortality compared to the lowest quartile Q1.

The K-M survival curve manifested that with prolonged follow-up time, the survival rate of the Q1 group was considerably lower than that of the other groups (Q1 vs. Q2, log-rank *P* = .005; Q1 vs. Q3, log-rank *P* < .001; Q1 vs. Q4, log-rank *P* = .014) (Figure 2). Survival differences among the Q2, Q3, and Q4 groups were not significant (all *P* > .05).

The Nonlinear Linkage between Hemoglobin-to-Red Blood Cell Distribution and 30-Day Mortality Risk in Aortic Dissection Patients

The above data suggested that there may be a non-linear linkage between HRR and AD mortality risk. The authors therefore conducted an RCS analysis to evaluate the relation between the two. The RCS curves indicated a significant overall trend between HRR and AD mortality risk (*P* = .0092), with a non-linear association (*P*-non-linear = 0.0214) in the model adjusted for all confounding factors, and two inflection points at 0.63 and 0.93, respectively (Figure 3).

Table 2. Multivariate Cox Regression Models Evaluating the Association between Hemoglobin-to-Red Blood Cell Distribution Width Ratio and Hazard Ratios (95% Confidence Intervals) for 30-Day Mortality

Outcomes	HR (95% CI)	*P*
HRR (Per 1 SD increment)		
Crude	0.55 (0.36-0.83)	.005
Adjust[a]	0.55 (0.32-0.94)	.028
Quartiles[a]		
Q1 <0.509 (n = 73)	Ref.	
Q2 0.509-0.631 (n = 73)	0.25 (0.08-0.75)	.014
Q3 0.631-0.818 (n = 73)	0.15 (0.04-0.56)	.005
Q4 ≥ 0.818 (n = 73)	0.36 (0.11-1.24)	.105
P_{trend}		.018

[a]Adjusted model: adjust for age, gender, race, smoking status, heart rate, weight, mean blood pressure, percutaneous oxygen saturation, platelets, partial thromboplastin time, prothrombin time, mean corpuscular volume, white blood cell, sodium, systemic inflammatory response syndrome, coronary artery disease, diabetes, and site. HRR, hemoglobin-to-red blood cell distribution width ratio.

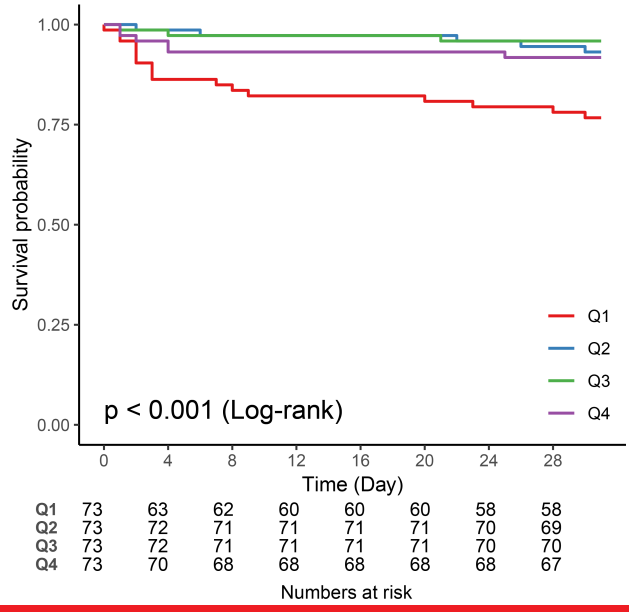

Figure 2. Kaplan-Meier survival curve of hemoglobin-to-red blood cell distribution.

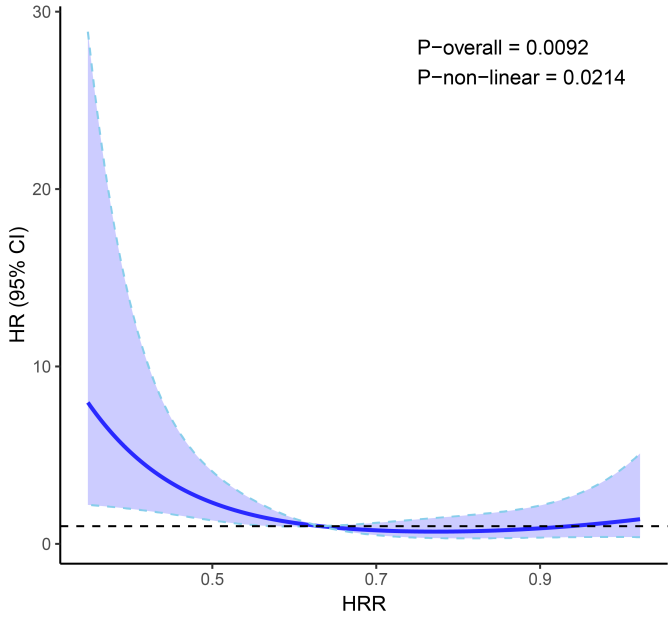

Figure 3. Association between hemoglobin-to-red blood cell distribution and 30-day mortality of participants. The Cox regression model[a] had an restricted cubic splines showing a linear relationship between HRR and the risk of 30-day mortality in the patients. The solid and shadow represented the estimated values and their corresponding 95% CIs, respectively. Model[a]: the adjusted model with adjustments for age, gender, race, smoking status, heart rate, weight, mean blood pressure, percutaneous oxygen saturation, platelets, partial thromboplastin time, prothrombin time, MCV, white blood cell, sodium, systemic inflammatory response syndrome, coronary artery disease, diabetes, and site.

Receiver Operating Characteristic Curve Analysis of Hemoglobin-to-Red Blood Cell Distribution's Predictive Value in 30-Day Mortality of Aortic Dissection Patients

The time-dependent ROC analysis was undertaken to probe into the predictive effect of HRR on the 30-day survival status of AD patients. The AUC values of HRR for 7 days, 14 days, and 30 days were 0.628, 0.662, and 0.669, respectively. In sum, HRR has good predictive value for AD mortality and can function as a promising predictor of AD patient mortality (Figure 4).

DISCUSSION

The objectives of this research were to figure out the linkage between HRR, a novel indicator, and the prognosis of AD patients and to make several important discoveries. First, the authors demonstrated that after adjustments for possible confounding factors, HRR was adversely linked with 30-day mortality. Secondly, the RCS results indicated a nonlinear linkage between HRR and AD. Thirdly, the authors applied ROC to evaluate the predictive results of HRR for AD and discovered that HRR had good predictive value for AD mortality, indicating HRR's potential as an inexpensive and easily accessible prognostic factor for AD patients.

To our knowledge, the linkage between inflammation levels and mortality has long been a concern for AD patients.[27,28] Previous studies have also shown the essential function of inflammatory cell infiltration in AD occurrence and development.[29-31] The destruction of aortic tissue triggered by dissection and thrombus in the false lumen may induce inflammatory reactions. Activated circulating white blood cells will adhere to the endothelium and be destroyed by toxic oxygen compounds and proteolytic enzymes. This change can lead to further necrosis and apoptosis of smooth muscle cells and degeneration of elastic tissue, resulting in aortic rupture.[32,33] As an indicator that combines Hb and RDW, HRR is closely related to inflammatory response levels and is readily obtainable from standard laboratory databases without the need for any additional equipment or expense. Compared with Hb and RDW alone, HRR has higher specificity and sensitivity and can better predict early inflammation levels in patients. It has become a new biomarker associated with mortality in many CVDs.[34,35] An investigation based on the MIMIC-IV database revealed that lower HRR in patients with non-traumatic subarachnoid hemorrhage is linked with an elevated risk of death.[19] In ischemic stroke patients, a study focusing on the relationship between HRR and all-cause mortality also discovered that lower HRR is linked to higher mortality in these patients.[36] These results are similar to the authors' findings, where the authors also discovered the linkage between lower levels of HRR and elevated 30-day mortality in AD patients.

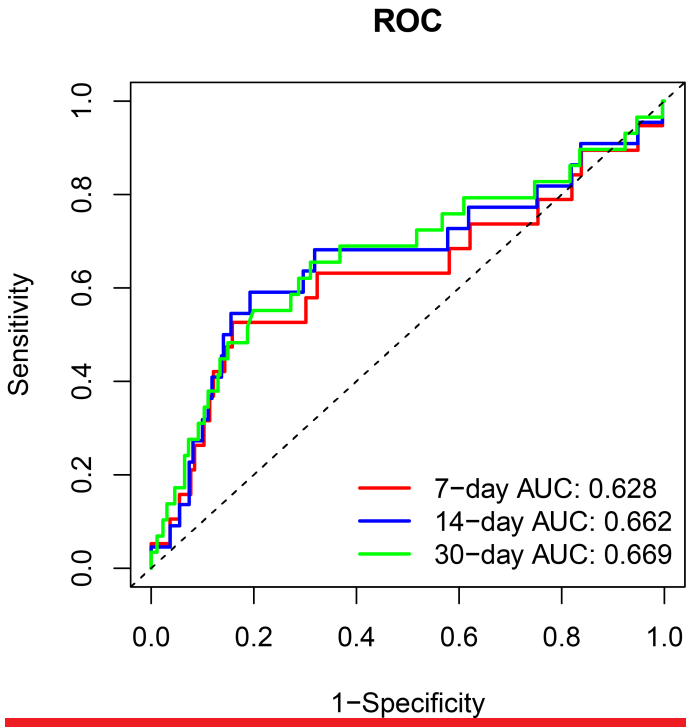

Figure 4. Time-dependent receiver operating characteristic curves of hemoglobin-to-red blood cell distribution width ratio.

The great link between lower HRR and the severity of AD suggested complex underlying mechanisms, which can be elucidated by analyzing the effects of increased RDW and decreased Hb associated with AD. The value of RDW in CVDs is implicated in multiple mechanisms in the pathophysiological process. Firstly, an increase in RDW implies impaired red blood cell maturation and a potential inflammatory state in the patient's body, which has a bearing on adverse outcomes.[37-39] By altering erythrocyte homeostasis, compromising iron metabolism, and suppressing erythropoietin synthesis, these inflammatory substances can interfere with erythrocyte maturation and cause hemolytic anemia.[12,40] Secondly, oxidative stress and microcirculation damage play essential roles.[41] Red blood cell survival and homeostasis are strongly influenced by oxidative stress, and when exposed to high inflammatory and oxidative stress environments, changes in red blood cell size may transform into pro-oxidants, further exacerbating oxidative load and reinforcing damage to AD.[42,43] The rise of RDW may lead to the loss of red blood cell deformability and changes in the half-life of red blood cells in circulation, causing high heterogeneity of red blood cell size,[41] which may hinder blood flow through the microcirculation, exacerbate ischemia, affect tissue oxygen transport, and affect the "antioxidant" function of blood vessels.[44] At present, higher RDW levels are proven to influence death and prognosis in AD patients,[13,14] which are considered strong risk factors for predicting survival. Finally, another element that could contribute to increased RDW and unfavorable prognosis is shear stress. A previous study showed that high shear stress can trigger intimal tearing, which can develop into AD.[45] Shear stress can also damage red blood cell deformation and facilitate hemolysis, leading to an elevation in RDW.[46]

The primary determinant of oxygen-carrying capacity is Hb levels, and the majority of CVDs are thought to be caused by alterations in blood flow patterns or viscosity linked to Hb,

as well as decreased oxygen-carrying ability.[47,48] A decline in Hb indicates a great reduction in oxygen delivery to the aorta, and limited tissue oxygenation may contribute to multiple organ dysfunction, influencing increased short-term mortality.[49] A relatively small retrospective study suggested that a drop in Hb in hospitalized patients with acute stroke may be linked with dismal outcomes,[50] while another study on atrial fibrillation confirmed the presence of anemia; even mild anemia (males: 10 ≤ Hb<13g/dL and females: 10 ≤ Hb < 12 g/dL) can be an independent risk factor for hospitalization.[51] An existing study in AD indicated that preoperative Hb levels are tightly linked with all-cause mortality and adverse cardiovascular events, and patients with low Hb levels seem to have a lower likelihood of survival compared to those with higher Hb levels.[16] Furthermore, changes in Hb levels can be influenced by inflammatory reactions in various ways,[52] which can affect the body's red blood cell production, shorten red blood cell survival, and reduce the production of erythropoietin.

The authors' findings are consistent with the increasing evidence of blood biochemical markers in CVD, indicating that HRR is a significant and independent predictor of mortality in AD patients. Its routine availability and low cost can become a practical tool for early risk stratification and prognosis judgment in clinical practice. However, there are certain limitations in the authors' research. Firstly, as a retrospective single-center study, the study failed to illuminate causal linkage or extend the results to participants in other regions. Moreover, acute stress and medications are two examples of missing data that could have an impact on the model but were not analyzed because of MIMIC database restrictions. Notably, the potential outcomes of these variables tend to be biased towards zero, leading to an underestimation of the linkage between HRR and mortality. Finally, since the authors only investigated short-term results and the MIMIC-IV database did not include long-term follow-up events, more studies are necessary to evaluate long-term effects.

CONCLUSION

The authors' results confirmed that HRR is an easily obtainable and cost-effective biomarker that can independently correlate with AD patients' grim prognosis. Integrating HRR into clinical risk models can improve early prognosis and guide management decisions. To clarify the underlying molecular mechanisms and validate the clinical usefulness of HRR, further investigation is necessary.

Ethics Committee Approval: Ethical approval and consent were not required as this study was based on publicly available data.

Peer-review: Externally peer reviewed.

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Supplementary Table 1. Proportion of missing values

Variables	Proportion
Height	26%
Weight	4.80%
Heart Rate	0.30%
SBP	0.30%
DBP	0.30%
MBP	0.30%
Breath rate	0.30%
Temperature	27.70%
Spo2	0.70%
Anion gap	0.30%
Lactate	35.60%
Potassium	0.30%
PTT	1%
INR	1%
PT	1%
Sodium	0.30%
Po2	30.50%
Pco2	30.50%
pH	30.50%
Base excess	30.50%
ALT	44.50%
ALP	43.50%
AST	43.80%
Bilirubin	44.90%
GCS	0.30%

SBP, systolic blood pressure; DBP, diastolic blood pressure; MBP, mean blood pressure; SpO2, percutaneous oxygen saturation; PT, prothrombin time; PTT, partial thromboplastin time; INR, International Normalized Ratio; GCS, Glasgow Coma Score.