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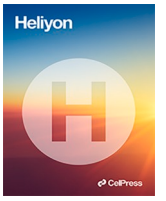

Research article

Association between red blood cell distribution width and all-cause mortality of patients after intra-aortic balloon pump in the intensive care unit

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ABSTRACT

Objectives: This study aimed to explore the relationship between red blood cell distribution width (RDW) and all-cause mortality in critically ill patients undergoing intra-aortic balloon pumping (IABP) in the intensive care unit (ICU).

Methods: This study retrospectively analyzed data from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database. The primary endpoint was the 30-day mortality rate, while the secondary endpoint was the in-hospital mortality rate. Restricted cubic splines were used to assess the dose–response relationship. The receiver operating characteristic (ROC) curve and Kaplan-Meier curve analysis were carried out to evaluate the predictive performance of RDW. Moreover, multiple logistic regression analyses and subgroup analyses were conducted to investigate the relationship between RDW and 30-day mortality. Finally, propensity score matching (PSM) was performed to adjust for the imbalance of covariates.

Results: In total, 732 patients were finally identified from the MIMIC-IV database in this study. The RDW of patients in the non-survivor group was significantly higher compared with those in the survivor group ($P < 0.01$). Multiple logistic regression analyses corroborated RDW was an independent predictor of all-cause 30-day mortality in critically ill patients post-IABP. Meanwhile, ROC analysis identified an RDW cutoff of 14.2%. High RDW patients exhibited a 131% (OR = 2.31, 95% CI: 1.49–3.61) elevated risk of 30-day mortality after adjusting for confounders in multivariable logistic regression. After PSM, 412 patients were included in the matched cohort. In the original and matched cohorts, the high RDW group had higher 30-day and in-hospital mortality rates, as well as longer ICU stays. Lastly, the area under the ROC curve for 30-day mortality was 0.686, with an optimal cutoff point of 14.2 for RDW (sensitivity: 69.09 % and specificity: 63.32%).

Conclusion: RDW could be a simple and valuable prognostic tool to predict mortality in critically ill patients after IABP.

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1. Introduction

1.1. Background

The intra-aortic balloon pump (IABP) is presently a commonly used circulatory assist device and is routinely applied in patients with severe cardiovascular conditions, encompassing cardiogenic shock, acute myocardial infarction, and coronary artery bypass grafting [1,2]. It is positioned in the descending thoracic aorta and has been proven effective for optimizing systemic hemodynamics [3–5].

In recent years, technological advances and increased usage have driven significant improvements in outcomes for patients implanted with IABP. However, attributed to the complexity and seriousness of the disease, the all-cause mortality of patients after IABP remains unacceptably high, with a real-world study reporting an in-hospital mortality rate of up to 30% in-hospital [6]. Therefore, there is an urgent need for a practical and effective indicator to predict patient mortality, which can assist clinicians in timely screening patients at elevated mortality risk and implement more aggressive measures.

Red blood cells (RBCs) are non-nucleated blood cells with a typical oval biconcave shape. Their normal volume ranges from 80 to 100 fL (fL), but their degree of heterogeneity can increase in response to different physiological and pathological conditions.

The red blood cell distribution width (RDW), which reflects the degree of heterogeneity as a routine laboratory value, is considered a core component of the standard Comprehensive Blood Count (CBC). Indeed, it has been extensively investigated and is traditionally used for the identification of anemia [7], while its effect is almost an unknown parameter in numerous diseases. Existing evidence suggests that RDW may provide valuable information for diagnosing inflammatory diseases and establishing the prognosis of patients with cardiovascular and cerebrovascular diseases [7–9].

However, studies exploring the relationship between RDW and the prognosis of patients after IABP are scarce. Hence, the objective of this study was to examine the relationship between RDW and mortality in ICU patients to provide a theoretical reference for the clinical management of critically ill patients with IABP.

2. Materials and methods

2.1. MIMIC IV database

The data for this restrictive observation study was retrieved from the Medical Information Mart for Intensive Care IV (MIMIC-IV) database (https://doi.org/10.13026/s6n6-xd98) [10]. MIMIC-IV (version 2.0) is an open-access critical care database that has been updated from MIMIC-III and contains information on 76,540 ICU admissions from 2008 to 2019 at the Beth Israel Deaconess Medical Center in Boston. Author Zhongheng Jia successfully underwent an online training course sanctioned by the National Institutes of Health and passed a related human research participant protection exam, allowing access to the database for research endeavors (No.47115389). The study was carried out in accordance with the Declaration of Helsinki (2013 Edition). Considering that the database contains randomized specific patient information, formal ethical approval was waived for this study. Our access to the database was approved by the institutional review boards of the Massachusetts Institute of Technology. As a result, the Ethics Committee of the Second Affiliated Hospital of Wenzhou Medical University waived the need for informed consent for this study.

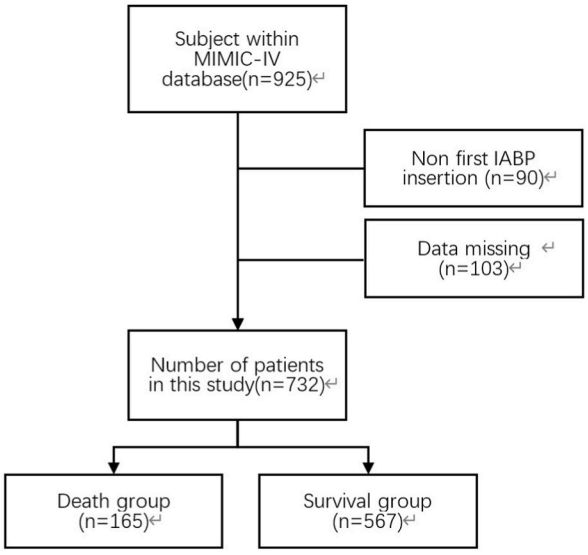

Fig. 1. Flowchart of included patients. MIMIC-IV, Multiparameter Intelligent Monitoring in Intensive Care Database IV.

2.2. Study population

The database included a total of 382,278 individuals in the hospital and 76,540 in the ICU. Patients who underwent IABP after admission to the ICU were selected for the present study. Additionally, only the first IABP procedure was assessed for patients undergoing IABP more than once. Patients with missing study variables in the original dataset were excluded from this study. Of the original 925 patients, 90 patients received IABP support multiple times, and 103 patients were excluded due to incomplete clinical data. Ultimately, 732 patients were included in this study. The selection procedure of study participants is summarized in Fig. 1.

2.3. Data extraction

The following data were extracted from the MIMIC IV database: age, gender, simplified acute physiology score II(SAPS II), weight, comorbidities, survival time, length of ICU stay (ICU LOS), vital signs, in-hospital diseases, indication for IABP, medical operations, and laboratory values. SAPS is a medical scoring system designed to assess the severity of a patient's acute physiological condition. It is utilized to calculate a severity score, which can be employed to predict the degree of illness and prognosis for the patient. Baseline information, comprising age, gender, weight, SAPSII and comorbidities, was collected upon the patient's hospital admission. Cardiac diseases, including myocardial infarction and cardiogenic shock, were identified based on the in-hospital diagnoses documented before IABP initiation. Baseline laboratory values were obtained as the most recent laboratory test results prior to the induction of IABP. Peripheral venous blood samples were collected from each patient before IABP. Of note, variables with missing data are prevalent in the MIMIC IV database. Consequently, serum laboratory values with over 40% missing data, such as left ventricular ejection fraction (LVEF), albumin and anion gap, were excluded from this analysis. The imputation method using linear regression was employed for continuous variables with less than 5% missing data. The primary endpoint of our study was the 30-day mortality rate. Secondary outcomes were ICU mortality rate and ICU LOS from the date of ICU admission. The in-hospital mortality refers to patients who experience explicit death during their hospitalization, while the 30-day mortality is based on official death records registered by the state.

Table 1
Baseline characteristics of the study population.

Characteristics	Total N = 732	Death N = 165	Survival N = 567	P-value
Age, year	71 (61–79)	74 (67–83)	70 (61–77)	<0.01
Male,%	69.67	67.88	70.19	0.57
Weight, kg	83.17 (±18.01)	82.39 (±18.58)	83.39 (±17.85)	0.53
SAPS II	38 (30–48)	48 (41–61)	36 (28–43)	<0.01
Temperature,°C	36.63 (±0.77)	36.46 (±0.98)	36.67 (±0.69)	<0.01
MAP, mmHg	80 (71–93)	76 (66–84)	82 (73–94)	<0.01
Comorbidity				
Hypertension, %	43.85	35.15	46.38	0.01
Diabetes, %	38.52	43.64	37.04	0.13
Renal insufficiency, %	26.5	39.39	22.75	<0.01
Cerebrovascular disease, %	10.38	9.09	10.76	0.54
Pulmonary disease, %	20.9	24.24	19.93	0.23
Cardiac history				
Prior myocardial infarction, %	62.98	63.03	62.96	0.99
Prior congestive heart failure, %	56.15	68.48	52.56	<0.01
Indications for IABP				
Myocardial infarction, %	54.64	51.52	55.56	0.36
Cardiogenic shock, %	36.07	34.55	36.51	0.65
Coronary bypass grafting, %	29.92	9.09	35.98	<0.01
Coronary angioplasty, %	20.77	24.24	19.75	0.21
Treatments				
Ventilation, %	78.28	84.24	76.54	0.04
CRRT, %	13.39	33.33	7.58	<0.01
Laboratory values				
Platelet, 109 cells/L	215.83 (±95.84)	207.53 (±100.92)	218.22 (±94.29)	0.22
Neutrophil, 109 cells/L	10.24 (±5.78)	11.94 (±6.49)	9.75 (±5.47)	<0.01
Lymphocytes, 109 cells/L	1.91 (±1.64)	1.88 (±1.97)	1.92 (±1.53)	0.80
Hemoglobin, g/dL	11.61 (±2.25)	10.88 (±2.25)	11.83 (±2.21)	<0.01
Glucose, mmol/L	9.67 (±5.17)	11.5 (±6.48)	9.12 (±4.57)	<0.01
RDW, %	14.49 (±1.87)	15.50 (±2.39)	14.21 (±1.57)	<0.01
Creatinine, μmoI/L	136.04 (±110.14)	196.30 (±128.28)	118.44 (±97.58)	<0.01
Urea nitrogen, mmol/L	28.86 (±18.82)	41.60 (±22.59)	25.14 (±15.76)	<0.01

SAPS II, simplified acute physiology score II; MAP, mean arterial pressure; CRRT, continuous renal replacement therapy; RDW, red blood cell distribution width.

2.4. Statistical analysis

Continuous data were presented as mean ± SD or median with IQR and compared using the *t*-test or Mann-Whitney test. Categorical data were expressed as frequencies or percentages and compared using the Fisher exact test. The receiver operating characteristic (ROC) curve was plotted to evaluate the predictive value of indicators before IABP for the mortality rate. The optimal cutoff value derived from the ROC curve was used to stratify patients into the high and low RDW groups. Kaplan-Meier curve analysis was conducted to analyze differences between groups and 30-day mortality rates. Univariate and multiple logistic regression were employed to identify correlations between RDW and 30-day mortality rates after IABP, with variables showing a univariate analysis p-value <0.1 included in the multivariate regression analysis. PSM was adopted to limit the influence of confounding factors using the nearest neighbor matching algorithm with a caliper width of 0.01. Subgroup analysis was utilized using the *t*-test to identify potential interactions between RDW and 30-day mortality. In order to conduct subgroup analysis, we employed RCS analysis, revealing a significant non-linear relationship between age and 30-day mortality. Accordingly, we selected 70 years as the cut-off value to facilitate more effective subgroup analysis and explore potential differences in 30-day mortality across distinct age groups. Stratification was performed according to age (<70, ≥70), gender (male, female), diabetes (Yes, No), hypertension (Yes, No), cerebrovascular disease (Yes, No), chronic pulmonary disease (Yes, No), renal insufficiency (Yes, No), prior myocardial infarction (Yes, No), prior congestive heart failure (Yes, No), myocardial infarction (Yes, No), cardiogenic shock (Yes, No), Coronary bypass grafting (Yes, No), coronary angioplasty (Yes, No), ventilation (Yes, No) and continuous renal replacement therapy (CRRT; Yes, No). All statistical analyses were performed using R (http://www.R-project.org, version R.4.2.3) and Stata 15.0.

3. Results

3.1. Study population and baseline characteristics

A total of 732 patients who underwent IABP were enrolled in this study. The median age was 71 (61–79) years, with 510 patients (69.67%) male patients. The most prevalent admission diagnosis among IABP patients was myocardial infarction (54.64%), followed by cardiogenic Shock (36.07%). Coronary bypass grafting (29.92%) and Coronary angioplasty (20.77%) were also performed during the hospitalization period. Table 1 presents the baseline clinical information of patients with IABP. As detailed in Table 1, there were several differences in baseline characteristics between the two groups in this cohort. For instance, the prevalence of hypertension, congestive heart failure, and renal insufficiency was different among the two groups. Besides, advanced age was positively correlated with the 30-day mortality rate. Baseline glucose level, neutrophil count, creatinine level, urea nitrogen level, and RDW were substantially higher in the mortality group.

3.2. Association between RDW and 30-day mortality

The RCS analysis revealed a significant nonlinear correlation between RDW and the 30-day mortality rate of patients (Fig. 2A, p for non-linearity = 0.0054). The mortality odds ratio (OR) remained under 1 when RDW was below 14.2%, showing minimal variation. However, beyond this threshold, the risk of mortality increased linearly with increasing RDW. To determine the predictability of RDW, ROC curve plots were analyzed. The area under the curve for the RDW was 0.686 (Fig. 3). Similarly, the optimal cut-off point of the

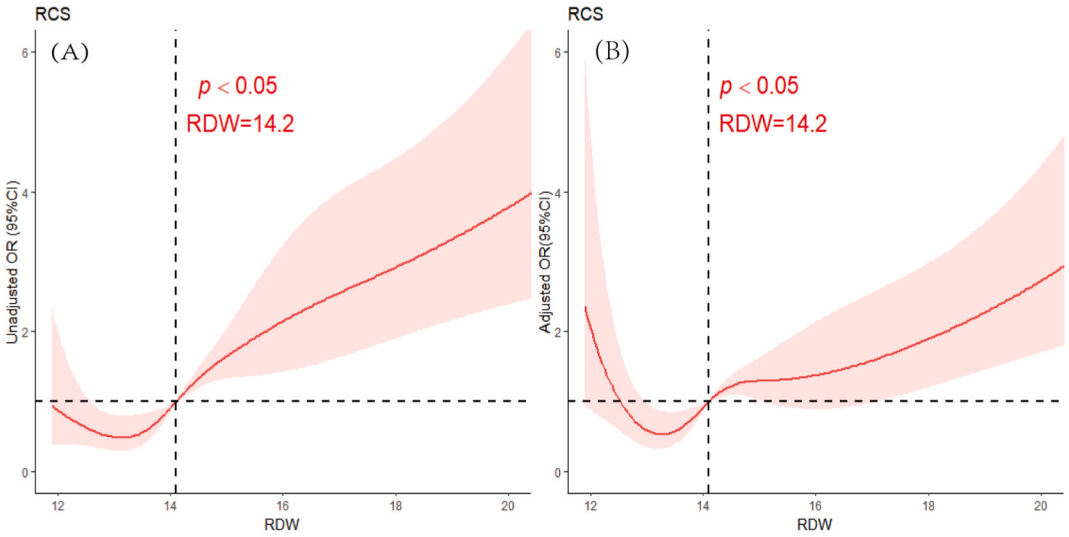

Fig. 2. Restricted cubic spline regression models of the relationship between RDW and the risk of 30-day mortality. (A): Unadjusted; (B): Adjusted for the confounding variables in multivariable logistic regression (Age、SAPSII、CRRT、Glucose、Urea nitrogen).

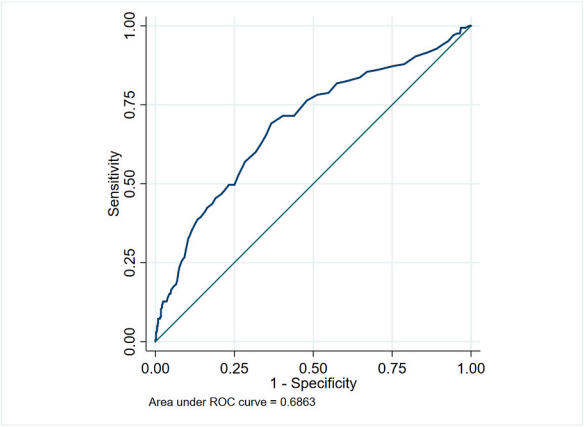

Fig. 3. Receiver-operating characteristic curve of the RDW to predict 30-day mortality of IABP patients.

ROC curve for the RDW was 14.2% (sensitivity: 69.09 % and specificity: 63.32). Based on the optimal cut-off value of 14.2%, patients were stratified into the high RDW group and the low RDW group based on their RDW. As anticipated, unadjusted Kaplan-Meier analysis with the log-rank comparison revealed a significantly higher 30-day mortality rate in the high RDW group compared to the low RDW group (Fig. 4). At the same time, the stepwise multiple logistic regression analysis revealed that age, SAPS II score, CRRT, glucose level, RDW, and urea nitrogen level were independent factors associated with 30-day mortality (Table 2). The results collectively signaled that RDW could be used to predict the risk of 30-day death following IABP ($p < 0.01$), with an adjusted odds ratio (OR) of 1.35 (95% CI 1.19–1.53). Interestingly, adjusted restricted cubic splines also illustrated a non-linear relationship (Fig. 2B, non-linear adjusted $P = 0.0127$). Compared to patients with normal RDW, high RDW patients had a 131% (OR = 2.31, 95% CI: 1.49–3.61; $P < 0.01$) increased risk for 30-day mortality after adjusting for confounding variables in multivariable logistic regression. Taken together, these results suggested that a high level of RDW is an independent risk factor for 30-day mortality in patients after IABP. In addition, We used a multimodel-adjusted logistic regression approach to assess the independent association between RDW and 30-day mortality, taking into account various potential confounders (Table S1). The results showed that RDW showed significant predictive ability for patients' 30-day mortality in different models. The models were fully adjusted to include a variety of demographic information, comorbidities, and baseline clinical characteristics to ensure the reliability of the results. These findings highlight the importance of RDW as a potential independent biomarker in patients treated with IABP. RDW remained significantly predictive of 30-day mortality even after accounting for other potential factors.

To investigate if RDW is a risk factor for 30-day mortality in specific subgroups, an exploratory subgroup analysis was undertaken (Fig. 5). The forest plot displayed that in different subgroups the relationship between baseline RDW and the risk of 30-day mortality stably existed except for Coronary bypass grafting (OR 2.38, 95% CI 0.83–6.86, $P = 0.199$) and CRRT (OR 1.27, 95% CI 0.99–1.61, $P = 0.050$).

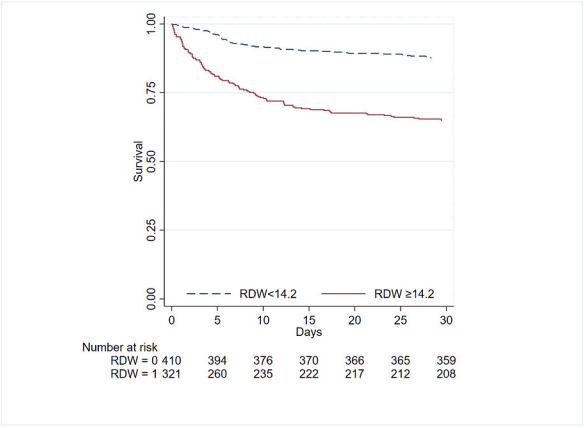

Fig. 4. Kaplan–Meier method estimated 30-day mortality in patients with IABP stratified by RDW. RDW = 0 indicates that RDW<14.2; RDW = 0 indicates that RDW≥14.2.

Table 2
Multivariable logistic regression analysis of RDW for predicting 30-day mortality in patients with IABP.

Variables	Unadjusted OR (95% CI)	P-value	Adjusted OR (95% CI)	P-value
Age	1.04 (1.02–1.05)	<0.01	1.03 (1.01–1.05)	<0.01
Male	0.89 (0.61–1.30)	0.57		
Weight	0.99 (0.98–1.01)	0.53		
SAPSII	1.07 (1.06–1.09)	<0.01	1.05 (1.04–1.07)	<0.01
Temperature	0.71 (0.57–0.91)	<0.01		
MAP	0.98 (0.97–0.99)	<0.01		
Hypertension	0.62 (0.43–0.89)	0.01		
Diabetes	1.31 (0.93–1.87)	0.13		
Renal insufficiency	2.21 (1.52–3.19)	<0.01		
Cerebrovascular disease	0.89 (0.45–1.50)	0.54		
Pulmonary disease	1.28 (0.85–1.94)	0.23		
Prior myocardial infarction	1.00 (0.70–1.43)	0.99		
Prior congestive heart failure	1.96 (1.35–2.83)	<0.01		
Myocardial infarction	0.85 (0.60–1.20)	0.36		
Cardiogenic shock	0.92 (0.64–1.32)	0.64		
Coronary bypass grafting	0.18 (0.10–0.31)	<0.01		
Coronary angioplasty	1.30 (0.86–1.96)	0.21		
Ventilation	1.63 (1.03–2.59)	0.04		
CRRT	6.09 (3.88–9.54)	<0.01	3.51 (1.96–6.30)	<0.01
Platelet	0.99 (0.99–1.00)	0.22		
Neutrophil	1.06 (1.03–1.09)	<0.01		
Lymphocytes	0.98 (0.88–1.11)	0.80		
Hemoglobin	0.82 (0.75–0.89)	<0.01		
Glucose	1.08 (1.05–1.12)	<0.01	1.05 (1.01–1.10)	0.02
RDW	1.41 (1.28–1.55)	<0.01	1.35 (1.19–1.53)	<0.01
Creatinine	1.01 (1.00–1.01)	<0.01		
Urea nitrogen	1.04 (1.03–1.05)	<0.01	1.02 (1.00–1.03)	<0.01

SAPS II, simplified acute physiology score II; MAP, mean arterial pressure; CRRT, continuous renal replacement therapy; RDW, red blood cell distribution width.

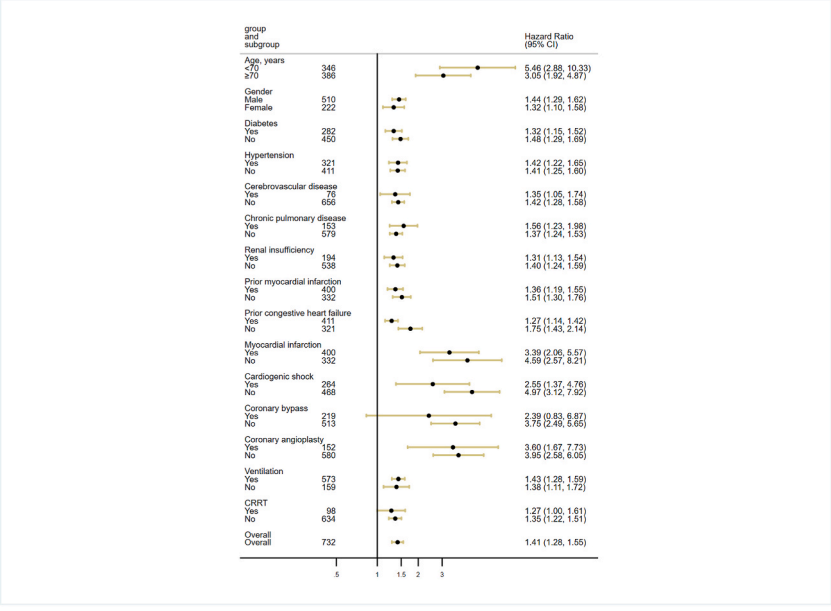

Fig. 5. Subgroup analysis of RDW for predicting 30-day mortality.
The OR values of RDW for predicting 30-day mortality in each subgroup were greater than 1 ($P < 0.05$), indicating that RDW was an independent factor for predicting 30-day mortality, except in the Coronary bypass subgroup (OR 2.38, 95% CI 0.83–6.86, $P = 0.199$) and CRRT subgroup (OR 1.27, 95% CI 0.99–1.61, $P = 0.050$).

Table 3
Baseline characteristics before and after propensity score matching.

Variables	Entire cohort (n = 732)			Matched cohort (n = 412)		
	RDW ≥ 14.2 (410)	RDW < 14.2 (322)	P-value	RDW ≥ 14.2 (267)	RDW < 14.2 (145)	P-value
Age	72 (62–81)	70 (61–77)	0.22	72 (62–81)	73 (64–81)	0.51
Male	66.46	72.2	0.10	64.79	66.9	0.67
Weight	83.39 (±19.11)	82.99 (±17.11)	0.76	83.09 (±19.44)	80.84 (±15.56)	0.23
SAPSII	41 (34–51)	36 (28–44)	<0.01	40 (33–51)	39 (31–51)	0.45
Temperature	36.61 (±0.83)	36.64 (±0.72)	0.61	36.64 (±0.79)	36.68 (±0.62)	0.61
MAP	81.66 (±27.03)	83.81 (±18.44)	0.21	83.10 (±27.87)	81.24 (±17.32)	0.47
Hypertension	41.3	45.85	0.22	42.7	46.21	0.49
Diabetes	43.79	34.39	0.01	41.95	38.62	0.51
Renal insufficiency	39.44	16.34	<0.01	31.84	23.45	0.07
cerebrovascular disease	10.25	10.49	0.92	11.24	11.72	0.88
Pulmonary disease	23.91	18.54	0.08	22.1	19.31	0.51
Prior myocardial infarction	68.78	55.59	<0.01	58.05	60	0.70
Prior congestive heart failure	63.98	50	<0.01	61.8	55.86	0.24
Myocardial infarction	47.2	60.49	<0.01	48.69	57.93	0.07
Cardiogenic shock	41.61	31.71	<0.01	40.82	36.55	0.40
Coronary bypass	22.98	35.37	<0.01	25.47	26.9	0.75
Coronary angioplasty	21.12	20.49	0.84	21.72	23.45	0.69
Ventilation	76.71	79.51	0.36	77.15	78.62	0.73
CRRT	22.67	6.1	<0.01	14.98	11.03	0.27
Platelet	211.82 (±114.86)	219.05 (±77.36)	0.33	220.20 (±118.90)	219.93 (±73.38)	0.98
Neutrophil	10.52 (±6.47)	10.02 (±5.16)	0.26	10.76 (±6.69)	10.13 (±5.23)	0.34
Lymphocytes	1.88 (±1.89)	1.94 (±1.39)	0.62	1.87 (±1.68)	1.73 (±1.32)	0.39
Hemoglobin	10.81 (±2.27)	12.25±(2.02)	<0.01	11.09 (±2.26)	11.52 (±2.06)	0.05
Glucose	9.74 (±5.21)	9.61 (±5.14)	0.75	9.66 (±4.77)	9.69 (±4.89)	0.94
Creatinine	180.35 (±140.46)	101.26 (±58.69)	<0.01	147.93 (±106.18)	119.43 (±84.43)	<0.01
Urea nitrogen	36.77 (±21.84)	22.65 (±13.08)	<0.01	32.19 (±18.83)	26.49 (±16.59)	<0.01

SAPS II, simplified acute physiology score II; MAP, mean arterial pressure; CRRT, continuous renal replacement therapy; RDW, red blood cell distribution width.

3.3. Propensity score matching of clinical outcomes

Following PSM, 267 high RDW group patients and 145 low RDW group patients were matched (Table 3). The standardized difference of means and ratio of variances between the pairs was compared, and propensity scores (Fig. S1) and Kernel Density Plot (Fig. S2) were constructed to assess PSM quality. Covariate imbalance between groups was significantly minimized. Akin to the pre-matched model results, high RDW was associated with a higher risk of 30-day mortality (OR 2.06; 95% CI 1.25–3.39; P < 0.01) and higher in-hospital survival rates (OR 2.08; 95% CI 1.28–3.39; P < 0.01) and ICU LOS (OR 1.05; 95% CI 1.01–1.44). These results showcased that RDW is an independent predictor of patient mortality after IABP. Furthermore, the association between RDW and both in-hospital mortality and length of stay was explored. The findings exposed that, following propensity analysis, RDW emerged as an independent prognostic indicator for inpatient mortality. Notably, higher RDW values were correlated with prolonged length of stay, as listed in Table 4.

4. Discussion

This study included 732 critically ill IABP-treated patients from the MIMIC-IV database and evaluated the relationship between RDW and all-cause mortality in IABP patients for the first time. Multivariate analysis determined that pre-IABP RDW is an independent risk factor for post-IABP patients, with high RDW levels being associated with higher 30-day mortality rates (OR 2.31; 95% CI 1.49–3.61; P < 0.01). PSM and subgroup analyses further corroborated the stable relationship between RDW and all-cause mortality.

RDW is a readily available, fast, and inexpensive biomarker compared with other biochemical parameters and reflects the variability in volumes of red blood cells. In other words, higher levels of RDW signify greater variation in volumes.

Table 4
Clinical outcomes of patients with IABP in the original and matched cohorts.

Variables	Entire cohort (n = 732)				Matched cohort (n = 412)			
	RDW ≥ 14.2 (410)	RDW < 14.2 (322)	RR	P-value	RDW ≥ 14.2 (267)	RDW < 14.2 (145)	RR	P-value
30-day mortality	35.4	12.44	1.35	<0.01	31.09	17.93	1.38	<0.01
in-hospital mortality	38.82	13.66	1.38	<0.01	33.33	19.31	1.36	<0.01
ICU LOS	5.01 (2.92–9.51)	3.19 (2.02–5.92)	9.96	<0.01	4.85 (2.87–8.66)	3.84 (2.09–6.72)	1.45	0.03

Continuous variables are represented as median [IQR]; Categorical variables are represented as percentage. ICU LOS, length of intensive care unit stay (day).

Recent studies have documented that elevated RDW was related to worse prognosis in various diseases such as stroke [11], myocardial infarction [12], heart failure [13], and atrial fibrillation [14]. A study undertaken by Cemin et al., enrolling 1971 patients, showed that increased RDW values were associated with adverse myocardial infarction outcomes [15]. A recent meta-analysis carried out by Huang et al. also evinced that each 1% increase in baseline RDW was associated with a 10% increased risk of future mortality events in heart failure patients [13].

While the mechanisms underlying the relationship between high RDW and poor prognosis remain elusive, the findings of existing studies are consistent with our findings. Red blood cells transport oxygen and carbon dioxide between blood and tissues. Their ability to deform and flow through the vascular system is crucial. An earlier study reported that RDW values above 14.0% significantly limited red blood cell deformability, compromising microcirculation blood flow [16]. Hematologically, RDW can be used to assess red blood cell deformability. Of note, hypoxic conditions promote red blood cell production. A large number of studies have concluded that acute hypoxia can stimulate erythropoiesis, which, in turn, induces the generation of enlarged red blood cells, resulting in an increase in RDW [17]. Recently, RDW has been found to exacerbate outcomes in multiple respiratory diseases that share the common feature of arterial hypoxemia, further demonstrating the association between RDW and circulatory hypoxia [18,19]. It can be deduced that there is an intimate correlation between RDW and microcirculatory hypoxia, especially in patients suffering from the latter. In addition, RDW can partially reflect the degree of inflammation and is associated with severe systemic inflammatory response [20].

Prior research claimed that high RDW impacts the physical characteristics of blood flow, such as turbulence and the level of interaction between blood cellular components and the vascular endothelium, which in turn facilitates inflammation, thereby triggering cytokine synthesis and thrombosis [21]. These mechanisms partly account for the fact that patients with high RDW tend to exhibit higher inflammatory responses and poorer outcomes.

An elevated RDW is typically the result of increased or ineffective erythropoiesis and excessive fragmentation or destruction of RBCs [22]. The IABP procedure inevitably destroys red blood cells and alters hemodynamics through mechanical factors. Consequently, high preoperative RDW may further drive body inflammatory response and hypoxia. Although related studies have explored the predictive role of various blood parameters prior to IABP on the prognosis of patients, no study has focused on RDW [6]. To the best of our knowledge, this is the first study to demonstrate the predictive value of RDW on all-cause mortality in patients undergoing IABP. RDW, as an effective biomarker, can be rapidly and easily obtained through preoperative laboratory tests performed before IABP. Ascribed to its cost-effectiveness, wide availability, and high prognostic value, RDW holds crucial implications for clinicians to swiftly assess patients after IABP.

This study presents several strengths. Firstly, it included a large sample size of 732 patients from the MIMIC-IV database (version 2.0), enhancing the credibility and persuasiveness of the results. Secondly, Propensity Score Matching (PSM) analysis was conducted to adjust for confounding factors. After PSM, the two groups were well-matched, and RDW retained its predictive significance. In the subgroup analysis, high Red Cell Distribution Width (RDW) was not found to be a significant risk factor for 30-day mortality in patients undergoing coronary artery bypass grafting or CRRT. However, in other subgroups, elevated RDW remained a significant predictor of increased 30-day mortality. This observation may reflect diverse responses of RDW to different therapeutic interventions or disease subtypes. For patients undergoing coronary artery bypass grafting or CRRT, the potential impact of other treatment interventions or disease-related factors may have masked the independent effect of RDW on mortality. Surgical procedures such as coronary artery bypass grafting and the use of CRRT can influence inflammatory states and erythropoiesis, complicating the association between RDW and mortality in these specific patient populations. Moreover, variations in sample sizes, baseline characteristics heterogeneity, and statistical power limitations across different subgroups may have contributed to our observed differences. To comprehensively understand the relationship between RDW and 30-day mortality, future studies may necessitate larger sample sizes, more detailed clinical data, and sophisticated statistical models. Although our findings indicate subgroup-specific differences, they do not dismiss the potential impact of CABG or CRRT on the relationship between RDW and mortality. Further investigation is warranted to elucidate the underlying mechanisms through which these therapeutic interventions may modulate the association of RDW with mortality in distinct subgroups, providing more precise information for individualized treatment strategies.

Nonetheless, this study has some limitations that cannot be overlooked. Firstly, it is a retrospective study, and as such, it cannot eliminate all potential confounding variables. Secondly, the data is derived from an existing database, leading to some critical information gaps. Caution should be exercised in interpreting the results, avoiding causal inferences, and recognizing the possibility of selection bias affecting the study. Additionally, as a single-center study, the possibility of selection bias cannot be excluded, warranting further validation of our results. Moreover, our analysis exclusively focused on the initial RDW value before IABP and did not consider the impact of dynamic fluctuations in RDW. Finally, our study did not involve mechanistic investigations, highlighting the need for more in-depth studies.

5. Conclusion

In summary, the current study indicated that RDW could be an independent risk factor for all-cause mortality in patients after IABP. Meanwhile, prospective multicenter studies are necessitated to verify our findings.

Ethics approval and consent to participate

Since the database contains randomized specific patient information, formal ethical approval was not necessary for this study. Our access to the database was approved by the institutional review boards of the Massachusetts Institute of Technology. The study adheres to medical ethics standards and complies with all clinical research ethical regulations related to the use of research data. Ethical review

committees at the Massachusetts Institute of Technology (MIT) (Number: 0403,000,206) and Beth Israel Deaconess Medical Center (2001-P-001699/14) have both approved the use of this database for research purposes. The study protocol was approved by the Institutional Human Research Ethics Committees of the Second Affiliated Hospital and Yuying Children's Hospital of Wenzhou Medical University, and informed consent was not applicable given the nature of the retrospective study and the use of deidentified patient data extracted from public databases and no additional ethical review is required.

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Availability of data and materials

The data incorporated in this study were obtained from the Medical Information Mart for Intensive Care IV (MIMIC-IV) Database (version 2.0), which was an open-access database and could be visited on the website after application: https://physionet.org/content/mimiciv/2.0/. The data underlying this article will be shared on reasonable request to the corresponding author.

Additional information

No additional information is available for this paper.

CRediT authorship contribution statement

Zhongheng Jia: Writing – original draft. **Can Jin:** Investigation, Data curation. **Da Pan:** Investigation, Formal analysis, Data curation. **Daqing Chen:** Writing – review & editing, Validation, Supervision, Funding acquisition.

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

Abbreviations

RDW	Red blood cell distribution width
IABP	Intra-aortic balloon pumping
ICU	Intensive care unit
ROC	Receiver operating characteristic
PSM	Propensity score matching
RBCs	Red blood cells
MIMIC-IV	The Medical Information Mart for Intensive Care IV database
SD	Standard deviation
IQR	Interquartile range
OR	Odds ratio
RCS	Restricted cubic spline

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.heliyon.2024.e27498.

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