CLINICAL ARTICLE

Elevated Red Blood Cell Distribution Width Is Associated with Poor Prognosis in Fractured Patients Admitted to Intensive Care Units

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Objectives: Red blood cell distribution width (RDW) with prognosis in various infectious diseases. For fractured patients admitted to the intensive care units (ICU), an accurate and fast appraisal is essential. To investigate the association between RDW and prognosis in fractured patients admitted to the ICU utilizing the MIMIC-III database.

Methods: A retrospective cohort from the MIMIC III database from 2001 and 2012 was constructed. RDW and other information were collected with in-hospital mortality as the primary outcome and 90-day mortality and hospital and intensive care unit (ICU) length of stay (LOS) as secondary outcomes. Univariate and multivariate logistic regression models with propensity score inverse probability of treatment weighting (IPTW) were used to investigate the prognostic value of RDW. A nomogram was built with significant prognostic factors to predict in-hospital mortality, and the performance of the nomogram was evaluated and compared with other severity assessment scores. Subgroup analysis was also conducted.

Results: A total of 2721 fracture patients admitted to the ICU were identified. After IPTW, the group with higher RDW was significantly associated with elevated in-hospital mortality (odds ratio [OR]: 1.68, 95% confidence interval [CI]: 1.19–2.37), 90-day mortality (OR: 1.39, 95% CI: 1.04–1.86), prolonged hospital LOS (OR: 1.25, 95% CI: 1.03–1.50), and ICU LOS significantly (OR: 1.26, 95% CI: 1.05–1.53) in the multivariate logistics model. The nomogram showed optimal discriminative ability and predictive accuracy with an area under the receiver operating characteristic curve of 0.77.

Conclusion: RDW independently predicted in-hospital mortality, 90-day mortality, and hospital and ICU LOS in fractured patients admitted to ICU. The nomogram including RDW could also be a promising tool with potential clinical benefits.

Key words: Fracture Patients; Mortality; Prognosis; Red Blood Cell Distribution Width

Introduction

Bone fracture is a common physical injury resulting from many factors, such as trauma, osteoporosis, and cancer. It could be a great burden for patients both economically and mentally.[1–3] The incidences of osteoporosis fracture and hip fracture are estimated to reach almost 175,000 and 2.6 million by 2050, respectively.[4,5] Patients with hip fractures are more likely to experience surgical complications, disability, and high 1-year mortality estimated at 30%.[6] Severe fracture patients usually require surgery to help with bone healing and body recovery, while the healing process is complex, both biologically[7] and biomechanically.[8,9]

Accurate and timely judgment of patients' conditions is crucial in fractured patients admitted to ICU for better clinical treatment decisions. C-creative protein, white blood cells, and hematocrit are widely used indicators at present.[10]

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In one retrospective single-center cohort analysis, we found that the serum anion gap (AG) can be used as a risk stratification tool for hip fracture.[11] However, they generally lack accuracy and specificity.[12,13] For individuals with isolated hip fractures, the severity of illness (SOI) score may be a better indicator of outcomes.[14] Other scores, the Nottingham Hip Fracture Score and the orthopaedic version of the Physiologic and Operative Severity Score for the Enumeration of Mortality and Morbidity, and previously published risk prediction models could be time-consuming and inconvenient.[15–17]

The red blood cell distribution width (RDW), which is the indication of size diversity among circulating red blood cells, has been as a biomarker reflecting systemic inflammation and malnutrition among elderly people.[18] Nevertheless, its association with prognosis in various infectious diseases[19,20] and cancers[21–26] has been recently noted. Recent studies have investigated the potential relationship between vertebral body fracture, hip fracture, and RDW.[27,28] However, to our knowledge, few studies have investigated the significance of RDW and RDW in fractured patients admitted to ICU.

Hence, the goal of this study was to determine whether RDW had predictive value in fractured patients admitted to ICU and develop a nomogram to predict the probability of in-hospital mortality with performance evaluation.

Methods

Study Design and Data Source

The study used data from the Medical Information Mart for Intensive Care-III (MIMIC-III) database and is a retrospective cohort study.[29] The MIMIC-III is a publicly available critical care database that includes 50,000 hospital admissions comprising 38,645 adults as well as 7875 neonates admitted to surgical, trauma surgery, coronary, and cardiac surgery recovery intensive care units (ICUs) of Beth Israel Deaconess Medical Center in Boston from 2001 to 2012. The institutional review boards of both Beth Israel Deaconess Medical Center and Massachusetts Institute of Technology Affiliates allowed access to the database (authorization code: 40043439). We acquired anonymized data from a database; thus, informed permission was not needed. Ethical approval and consent were not required for the present study. This research is reported in compliance with the Strengthening the Reporting of Observational Studies in Epidemiology statement.

Study Population

The patients with fractures were identified by the International Classification of Diseases-9 term associated with fracture. Patients from 18 to 89 years old were enrolled in the study. If patients were hospitalized many times, only the first hospital admission with ICU stay was examined. Patients who spent fewer than 24 h in the ICU were also excluded considering that the patient's condition would be either too mild or too severe.

Data Collection and Definitions

The data were extracted from the database using structure query language (SQL) with PostgreSQL (version 9.4.6, www.postgresql.org). The variables in this study included: (1) demographics; (2) hospitalization and prognosis: in-hospital mortality, 90-day mortality, ICU and hospital length of stay (LOS); (3) mean value of severity scores containing simplified acute physiology score (SAPS II), sequential organ failure assessment (SOFA), Glasgow coma scale (GCS), and Elixhauser scores in the first 24 h after ICU admission; (4) comorbidities; (5) mean laboratory results in the first 24 h after ICU admission; and (6) mean vital signs value in the first 24 h after ICU admission. The RDW was examined both as a continuous variable and as quartiles. The ICU and hospital length of stay were dichotomized into two groups for the following analysis.

To avoid potential bias, variables with more than 30% missing values were omitted from the following analysis. Using the multiple imputation method, we completed variables with fewer than 30% missing data.[30]

In-hospital mortality was chosen as the primary outcome because we were interested in the prognosis of fracture patients. Secondary outcomes included 90-day mortality and hospital and ICU length of stay (LOS).

Statistical Analysis

The median and standard deviation (SD) for continuous variables and proportions for categorical variables were used to report demographics and clinical features. To determine normality, the Kolmogorov–Smirnov test was performed on each continuous variable. T-tests or the Mann–Whitney U test were used for continuous variables, while for categorical variables, chi-square or Fisher's exact tests were used.

A logistic linear regression model was implemented to identify the associations between the covariates and prognosis. First, we assessed the covariates with significant associations with outcomes using univariate logistic linear regression. The statistically significant covariates (p value <0.05) and a change in the effect estimate exceeding 10% in the univariate logistic analysis regarding the four outcomes were identified. We excluded the severity scores from the covariates for the multivariate analysis to avoid potential interference with the results. The multivariate analysis was conducted with the remaining covariates. An inverse probability of treatment weighting (IPTW) analysis was applied in the logistic models after adjusting the following covariates: age, fracture position, gender, ethnicity, admission type, congestive heart failure, hypertension, chronic pulmonary, renal failure, liver disease, rheumatoid arthritis, obesity, diabetes, and anemia. The IPTW analysis was derived to reduce selection bias by statistically adjusting for background factors using propensity scores on all observations before matching.[31] Based on the significant covariates in the

multivariate analysis, a dynamic nomogram for in-hospital mortality was constructed. The performance of the nomogram was assessed by discrimination and accuracy by the area under the receiver operating characteristic curve (AUC), calibration plot, and the Hosmer-Lemeshow test (H-L test). For the calibration plot, the nomogram was subjected to 1000 bootstrap resamples for internal validation. Additionally, we performed subgroup analyses for the unmatched cohort using the nomogram to further evaluate the prognostic value of RDW regarding age, anemia, diabetes, and ICU length of stay. All data cleaning, statistical analyses, and part of the illustrations were performed in R software (version 4.0.3) with "tableone,"[32] "ggplot2,"[33] "tidyverse,"[34] "lubridate,"[35] "pROC,"[36] "surve,"[37] "DynNom,"[38] "rsconnect,"[39] "rms,"[40] and "ResourceSelection."[41] A p value <0.05 was considered statistically significant.

Results

Baseline Characteristics

A total of 2721 fracture patients were eventually enrolled in this study, as shown in Figure 1. Patients were stratified by the median RDW value: 13.85, and the basic characteristics are shown in Table 1. The majority of fracture patients were identified as having a skull fracture (67.4%) and lower limb fracture (16.2%). The other types of fracture were the upper limb fracture (8.4%) and pathologic or stress fracture (8.0%). The proportions of anemia among the lower and higher RDW groups were 7.3% and 16.1%, respectively.

Primary and Secondary Outcomes

As shown in Figure 2, in the univariable logistic regression model, the higher RDW group was significantly associated with elevated in-hospital mortality (odds ratio [OR]: 2.97, 95% confidence interval [CI]: 2.24–3.95), 90-day mortality (OR: 3.49, 95% CI: 2.77–4.39), hospital LOS (OR: 1.57, 95% CI: 1.35–1.83), and ICU LOS (OR: 1.61, 95% CI: 1.39–1.88). The balance pre- and post-IPTW were shown in Table S1. After IPTW matching, the higher RDW group remained significantly associated with in-hospital mortality (OR: 2.08, 95% CI: 1.44–3.00), 90-day mortality (OR: 1.64, 95% CI: 1.22–2.22), hospital LOS (OR: 1.43, 95% CI: 1.20–1.71), and ICU LOS (OR: 1.56, 95% CI: 1.30–1.86). The mean RDW showed a similar significant association with these four outcomes (Table S2). In the IPTW matched cohort of multivariable logistic regression results (Figure 2), the higher RDW group was significantly associated with elevated in-hospital mortality (OR: 1.68, 95% CI: 1.19–2.37), 90-day mortality (OR: 1.39, 95% CI: 1.04–1.86), prolonged hospital LOS (OR: 1.25, 95% CI: 1.03–1.50), and ICU LOS (OR: 1.26, 95% CI: 1.05–1.53). The detailed results of univariate and multivariate results are provided in Tables S2 and S3.

With the aforementioned method, the prognostic nomogram was established based on fracture position, congestive heart failure, bicarbonate, anion gap, sodium, and RDW group. As the respiration rate and temperature could be extreme in certain circumstances, we excluded these significant covariates for the generalization of the model and nomogram. This final multivariable regression model demonstrated optimal predictive discrimination for in-hospital mortality with an AUC of 0.77 (95% CI: 0.74–0.79) (Figure 3A). To validate the accuracy, the model was performed using bootstrap analyses with 1000 resamples before plotting the calibration plot (Figure 3B), which indicates good agreement between the predicted and observed values. Moreover, the H-L test result showed a p value = 0.48, suggesting the goodness of the model fitting.

The probabilities of in-hospital mortality can be estimated for fractured patients admitted to ICU. The dynamic nomogram was created allowing automated estimation of probabilities with 95% confidence intervals based on the inputs (https://ly-scu-wch.shinyapps.io/DynNomapp/, Figure 4). With the aid of a nomogram, it was possible to effectively predict prognosis according to patient information. The discrimination ability of the nomogram was compared with the other severity scores, as illustrated in Table 2. Interestingly, SOFA, Elixhauser scores, and GCS showed a significant decrease in AUC compared with the nomogram, while SPAS II showed an insignificant AUC increase.

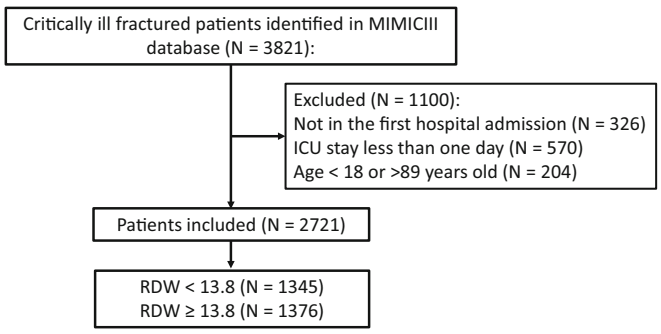

FIGURE 1 Flowchart of included patients. ICU: intensive care unit; RDW: red blood cell distribution width, N: number of patients

Subgroup Analysis

According to the results of the subgroup analysis (Table 3), the higher RDW group was linked to higher in-hospital death rates in elderly and younger patients (OR: 1.91, 95% CI: 1.31–2.77; and OR: 2.12, 95% CI: 1.20–3.73, respectively), patients without anemia (OR: 2.85, 95% CI: 2.05–3.94), patients with diabetes (OR: 3.40, 95% CI: 1.13–10.2), patients without diabetes (OR: 2.47, 95% CI: 1.74–3.41), patients with a longer ICU LOS (OR: 2.13, 95% CI: 1.46–3.09), and patients with a shorter ICU LOS (OR: 3.30, 95% CI: 1.92–5.68). Notably, in the nonanemic patients, the higher RDW group did not show a significant association with in-hospital mortality (OR: 0.73, 95% CI: 0.29–1.82).

TABLE 1 Baseline patient characteristics

	Lower RDW group	Higher RDW group	*p* value
Number of patients	1345	1376	
Age, mean (SD)	47.5 (21.3)	61.0 (19.2)	<0.01
Gender: male, n (%)	933 (69.4)	795 (57.8)	<0.01
Admission type, n (%)			<0.01
Elective	11 (0.8)	44 (3.2)	
Emergency	1326 (98.6)	1319 (95.9)	
Urgent	8 (0.6)	13 (0.9)	
Ethnicity, n (%)			0.14
White	980 (72.9)	1016 (73.8)	
Not specified	249 (18.5)	231 (16.8)	
Black	42 (3.1)	63 (4.6)	
Hispanic	57 (4.2)	45 (3.3)	
Asian	17 (1.3)	21 (1.5)	
Severity score, mean (SD)			
GCS	13.9 (2.3)	13.6 (2.5)	0.01
SOFA	2.5 (2.1)	4.1 (2.9)	<0.01
SPAS II	25.6 (12.3)	35.1 (13.7)	<0.01
Elixhauser scores	0.1 (1.1)	0.4 (2.1)	<0.01
Fracture position, n (%)			<0.01
Lower limb fracture	152 (11.3)	288 (20.9)	
Pathologic or stress fracture	38 (2.8)	181 (13.2)	
Skull fracture	1037 (77.1)	796 (57.8)	
Upper limb fracture	118 (8.8)	111 (8.1)	
Comorbidities, n (%)			
Congestive heart failure	69 (5.1)	212 (15.4)	<0.01
Hypertension	17 (1.3)	100 (7.3)	<0.01
Chronic pulmonary disease	105 (7.8)	211 (15.3)	<0.01
Renal failure	15 (1.1)	123 (8.9)	<0.01
Liver disease	24 (1.8)	87 (6.3)	<0.01
Rheumatoid arthritis	15 (1.1)	55 (4.0)	<0.01
Obesity	20 (1.5)	68 (4.9)	<0.01
Diabetes	109 (8.1)	268 (19.5)	<0.01
Anemia	98 (7.3)	221 (16.1)	<0.01
Vital signs, mean (SD)			
Heart rate	86.2 (15.6)	89.5 (15.9)	<0.01
SBP	124.7 (14.5)	121.6 (16.0)	<0.01
DBP	64.1 (9.9)	62.0 (10.8)	<0.01
MBP	82.1 (10.1)	80.0 (10.9)	<0.01
RR	17.7 (3.4)	18.6 (3.8)	<0.01
T	37.1 (0.6)	37.0 (0.6)	<0.01
SpO_2	97.9 (1.7)	97.6 (2.0)	<0.01
Laboratory results, mean (SD)			
Hematocrit, %	33.8 (4.8)	30.8 (4.9)	<0.01
Hemoglobin, g/dL	11.7 (1.7)	10.5 (1.7)	<0.01
Platelet count, 10^9/L	212.9 (68.5)	195.6 (101.8)	<0.01
WBC, 10^9/L	12.1 (4.2)	11.6 (6.1)	0.01
RBC, m/μL	3.8 (0.6)	3.5 (0.6)	<0.01
MCV, fL	89.7 (4.9)	88.9 (6.4)	<0.01
RDW, %	13.1 (0.5)	15.4 (1.6)	<0.01
Glucose, mg/dL	134.6 (35.8)	142.6 (37.8)	<0.01
Anion gap, mEq/L	13.4 (2.7)	13.5 (3.0)	0.29
Bicarbonate, mEq/L	24.1 (3.0)	23.5 (4.0)	<0.01
Creatinine, mg/dL	0.8 (0.4)	1.1 (1.0)	<0.01
Chloride, mEq/L	105.7 (4.6)	106.6 (5.5)	<0.01
Potassium, mEq/L	4.0 (0.4)	4.1 (0.5)	<0.01
PTT, s	29.0 (11.9)	33.1 (15.3)	<0.01
INR	1.2 (0.3)	1.3 (0.5)	<0.01
PT, s	13.8 (3.2)	14.8 (4.1)	<0.01
Sodium, mEq/L	139.0 (3.6)	139.2 (4.2)	0.17
BUN, mg/dL	14.5 (8.4)	20.8 (15.5)	<0.01
Calcium, mg/dL	8.3 (0.6)	8.1 (0.7)	<0.01
Hospitalization, mean (SD)			
ICU interval, day	5.3 (6.8)	6.3 (7.6)	<0.01
Hospital interval, day	11.5 (11.9)	13.9 (12.4)	<0.01

TABLE 1 Continued

	Lower RDW group	Higher RDW group	*p* value
Prognosis, n (%)			
In-hospital mortality	70 (5.2)	193 (14.0)	<0.01
90-day mortality	112 (8.3)	331 (24.1)	<0.01

Abbreviations: BUN, Blood urea nitrogen; DBP, Diastolic blood pressure; GCS, Glasgow coma scale; ICU, Intensive care unit; INR, International normalized ratio; MBP, Mean blood pressure; MCV, Mean corpuscular volume; PT, Prothrombin time; PTT, Partial thromboplastin time; RBC, Red blood cell; RDW, Red blood cell distribution width; RDW, Red blood cell distribution width; RR, Respire rate; SBP, Systolic blood pressure; SD, Standard deviation; SOFA, Sequential organ failure assessment score; SPAS II, Simplified acute physiology score II; SpO_2, Oxygen saturation; T, Temperature; WBC, White blood cell.

	Outcomes	Univariate analysis OR (95% CI)	*P* value	Multivariate analysis OR (95% CI)	*P* value
Pre IPTW	In-hospital mortality	2.97 (2.24-3.95)	**<0.01**	2.29 (1.65-3.18)	**<0.01**
	90-day mortality	3.49 (2.77-4.39)	**<0.01**	2.21 (1.69-2.89)	**<0.01**
	Hospital LOS	1.57 (1.35-1.83)	**<0.01**	1.16 (0.97-1.38)	0.1
	ICU LOS	1.61 (1.39-1.88)	**<0.01**	1.35 (1.13-1.61)	**<0.01**
Post IPTW	In-hospital mortality	2.08 (1.44-3)	**<0.01**	1.68 (1.19-2.37)	**<0.01**
	90-day mortality	1.64 (1.22-2.22)	**<0.01**	1.39 (1.04-1.86)	**0.03**
	Hospital LOS	1.43 (1.2-1.71)	**<0.01**	1.25 (1.03-1.5)	**0.02**
	ICU LOS	1.56 (1.3-1.86)	**<0.01**	1.26 (1.05-1.53)	**0.02**

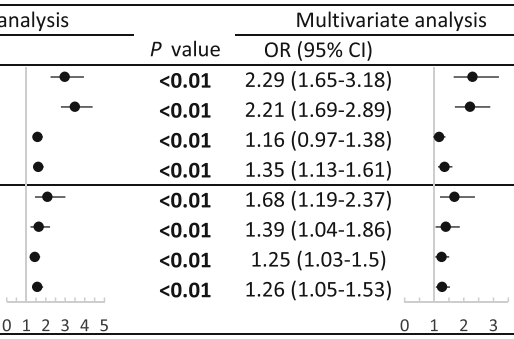

FIGURE 2 The univariate and multivariate results of the RDW groups and clinical outcomes in fractured patients admitted to ICU before and post IPTW matching. The forest plot shows the odds ratio (black circle), lower and upper levels (two ends of the line) of the 95% odds ratio. RDW: red blood cell distribution width; ICU intensive care unit; LOS: length of stay; N: number of patients; OR: odds ratio; CI: confidence interval; IPTW: inverse probability of treatment weighting. All *p* values <0.05 are bolded

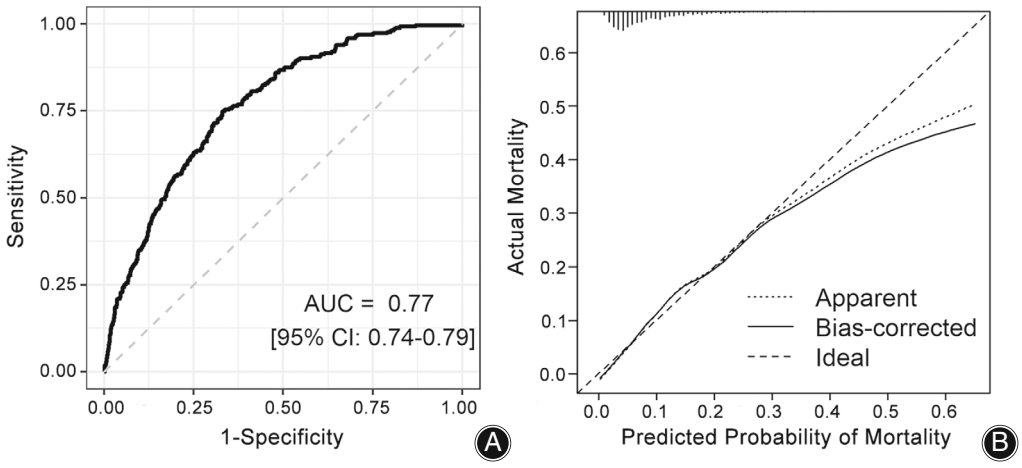

FIGURE 3 (A) The receiver operating characteristic plot demonstrated optimal predictive discrimination (AUC: 0.77, 95% CI: 0.74–0.79) for the multivariate logistic model. (B) Model accuracy is visualized by comparing predicted vs. actual probabilities, demonstrating apparent and bias-corrected predictive ability. The vertical lines at the top of the plot showed the relative prevalence of probability levels

Discussion

Summarize Results and Previous Studies

In our study, elevated RDW was independently associated with an increased risk of in-hospital mortality and 90-day mortality and prolonged ICU and hospital LOS in fracture patients. Additionally, a multivariate logistic model including RDW together with a dynamic nomogram was established to predict in-hospital mortality, and its discrimination and calibration ability was proven to be optimal.

RDW has been studied as a valid short-term and long-term prognostic factor in hip fracture and osteoporotic vertebral fracture patients.[28,42,43] In osteoporotic vertebral fracture patients, Sakai et al. demonstrated that elevated RDW (>15.0) was an independent factor associated with abasia (OR: 1.227, 95% CI: 1.003–1.500) for a 1-year follow-up

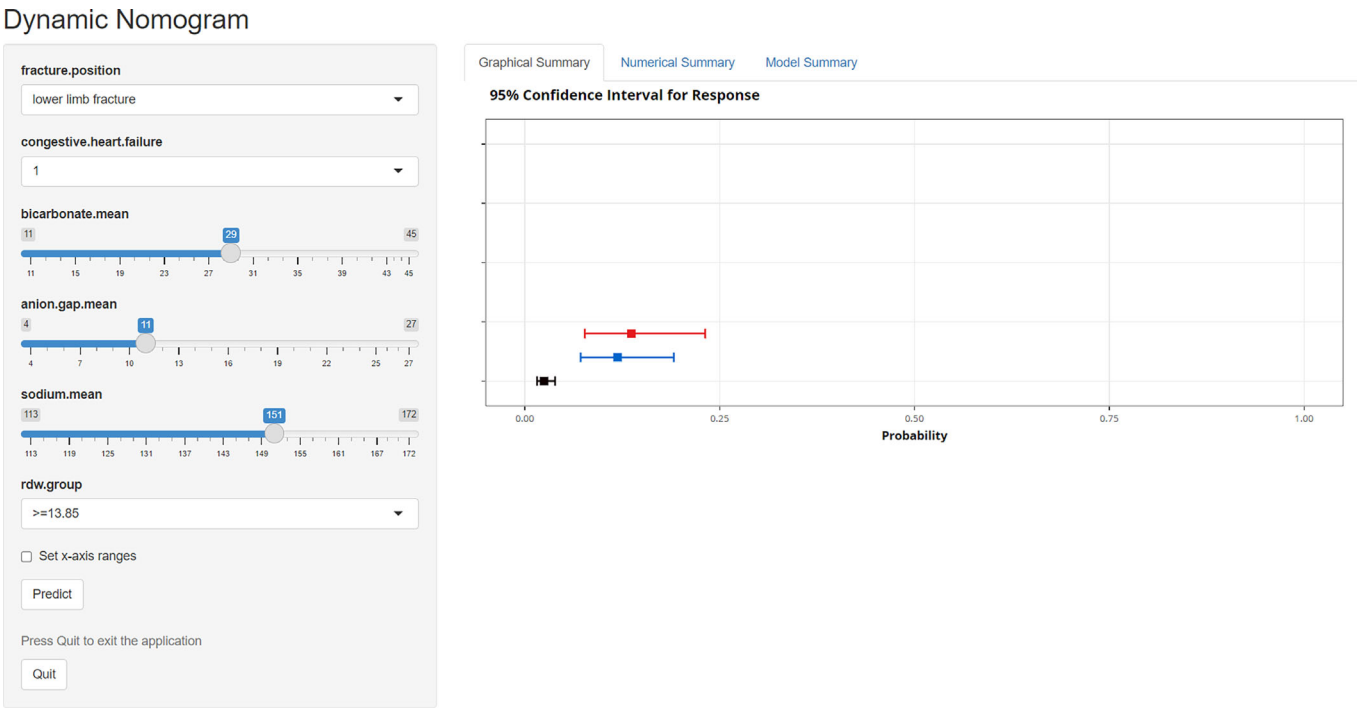

FIGURE 4 Dynamic nomogram (https://ly-scu-wch.shinyapps.io/DynNomapp/) for in-hospital mortality risk estimation of fractured patients admitted to ICU

TABLE 2 Odds ratio, discrimination ability, and H-L test for the in-hospital mortality prognostic model comprised of different severity scores and compared with the dynamic nomogram containing red blood cell distribution width

Severity scores	OR (95% CI)[a]	*p* value[b]	AUC	Compared with dynamic nomogram[c]	*p* value[d]	H-L test
SOFA	1.34 (1.28–1.41)	<0.01	0.73 (0.69, 0.76)	−1.97 (−0.08, 0)	0.05	0.36
SPAS II	1.08 (1.07–1.09)	<0.01	0.79 (0.76, 0.82)	1.22 (−0.01, 0.06)	0.22	0.55
Elixhauser scores	1.1 (1.03–1.17)	<0.01	0.52 (0.48, 0.56)	−10.78 (−0.29, −0.2)	<0.01	0.06
GCS	0.88 (0.83–0.93)	<0.01	0.53 (0.51, 0.54)	−14.78 (−0.27, −0.21)	<0.01	1

Note: a,b, the OR, 95% CI, and the *p* value of univariates logistic analysis for in-hospital mortality.; *Note*: c,d, the Z value, 95% CI, and *p* value for the comparison of AUROC value between the severity scores with the dynamic nomogram containing red blood cell distribution width.; Abbreviations: AUC, Area under the receiver operating characteristic curve; CI, confidential interval; GCS, Glasgow coma scale; H-L, Hosmer–Lemeshow; OR, odds ratio; SOFA, sequential organ failure assessment score; SPAS II, simplified acute physiology score II.

period with 460 patients.[27] In another study,[28] with 203 patients divided by RDW less or greater than 13.35, elevated RDW was the key predictor of 30-day mortality in older patients undergoing hip fracture surgery (hazard ratio (HR): 2.73, 95% CI: 2.06–3.62). Lv et al.[43] investigated the prognostic value of RDW over a 2-year follow-up period with 1479 patients. RDW showed a significant association with both 2-year mortality (HR: 1.183, 95% CI: 1.017 to 1.376) and 4-year mortality independently (HR: 1.244, 95% CI, 1.052 to 1.471).[43] To our knowledge, this is the first study to use a publicly available database to investigate the prognostic value of RDW in critically fractured patients admitted to ICU. Systemic inflammation might be a pivotal mediator in the association between RDW and the mortality of fractured patients admitted to ICU. The potential mechanism may be that the inflammatory responses could suppress renal erythropoietin (EPO) production, impair red cell survival, and cause the release of premature red cells into the circulation, resulting in an elevation of RDW.[44,45] This is more likely the case in fracture patients admitted to ICU whose injury might be complicated by prevalent inflammation.

New Insights of Study

Notably, in this study, the authors found a significant association between elevated RDW values and increased odds of all-cause mortality in nonanemic patients but not in anemic

TABLE 3 Subgroup analysis results

Subgroups	RDW group N	OR (95% CI)	*p* value
Age ≥ 55	894	1.91 (1.31–2.77)	**<0.01**
Age < 55	482	2.12 (1.2–3.73)	**0.01**
With anemia	221	0.73 (0.29–1.82)	0.5
Without anemia	1155	2.85 (2.05–3.94)	**<0.01**
With diabetes	268	3.4 (1.13–10.2)	**0.03**
Without diabetes	1108	2.47 (1.79–3.41)	**<0.01**
ICU LOS longer	771	2.13 (1.46–3.09)	**<0.01**
ICU LOS shorter	605	3.3 (1.92–5.68)	**<0.01**

Note: All *p* values <0.05 are bolded.; Abbreviations: CI, confidential interval; ICU, intensive care unit; LOS, length of stay; N, number of patients; OR, odds ratio; RDW, red blood cell distribution width.

patients,[43] which was persistent in the present study. Although the validity of this result in our study can be undermined by the small number of patients, special attention should be paid, especially to anemic patients, as RDW might be affected by hematogenesis leading to a decrease in prognostic value.[42,43,46] Therefore, for anemic fracture patients, the value of RDW in the differential diagnosis of anemia may outweigh the prognostic value of mortality.[43,47]

On the other hand, the predictive value of elevated RDW for prognosis has been investigated in various studies and groups of patients, e.g., cardiovascular disorders,[46] pulmonary hypertension,[48] sepsis,[24,49] and COVID-19.[50] For heart failure patients, RDW was predictive of mortality[46] (hazard ratio (HR): 1.18; 95% CI: 1.12, 1.24). Hampole et al. demonstrated that the highest of the three tertiles of RDW was associated with the mortality of pulmonary patients in a multivariate model (HR: 2.4, 95% CI: 1.02, 5.84) with a mean follow-up duration of 2.1 years.[48] In a recently published article, the authors found that RDW was independently associated with mortality and that 24-h RDW and admission RDW, when added to the severity scores, could improve the discrimination ability of SOFA, Logistic Organ Dysfunction System, Acute Physiology and Chronic Health Evaluation-II, and SAPS-II.[49] However, the underlying mechanism linking RDW with poor prognosis remains unclear. Researchers have revealed that the association of RDW and RPR with oxidative stress and inflammatory cytokines such as tumor necrosis factor (TNF)-alpha, interleukin (IL)-1, and IL-6 could contribute to its predictive potential.[51–53]

Strengths and Limitations

There are some strengths to our study. First, the included patients were admitted to ICU of multiple institutions and the number of included patients was more than that of previous retrospective observational studies. Also, we performed the subgroup analysis according to the causes of bone fracture and the conditions of patients to investigate the association between the RDW and the prognosis in different groups of patients.

This study also has several limitations. First, the establishment of the nomogram and prognostic model was based on a single retrospective cohort from the MIMIC dataset, which might influence the results by possible selection bias and its inherent retrospective nature. Second, although we addressed the association between RDW and the prognosis of fracture patients, the causation remains unknown. Third, some clinical information was excluded during the patient selection and data cleaning process. Moreover, the results of our study still need more external validation.

Conclusion

In summary, in fracture patients admitted to ICU, RDW appears to be a simple-to-use independent predictive indicator. For the first time, we constructed a prognostic nomogram for fractured patients admitted to ICU, which could be an easily accessible clinical tool facilitating counseling. These findings, however, need further verification and external validation.

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Competing Interest

The authors declare no competing interests.

Author's Contributions

Kaibo Sun and Bin Shen contributed to the conception and design. Yuangang Wu , Yi Zeng, and Jiawen Xu contributed to the acquisition, analysis, and visualization of the data. Kaibo Sun and Yannan Zhou wrote the main manuscript text. Bin Shen contributed to the supervision and review. All authors have approved the submission version.

Ethical Statement

This study was in accordance with ethical approvals and all methods were in compliance with relevant guidelines and regulations.

Availability of Data and Materials

The datasets used or analyzed during the current study are available from the corresponding author on reasonable request.

Authorship Declaration

All authors listed meet the authorship criteria according to the latest guidelines of the International Committee of Medical Journal Editors. All authors are in agreement with the manuscript.

Disclosure Statement

All authors declared no financial support or relationships that may pose a conflict of interest.

Supporting Information

Additional Supporting Information may be found in the online version of this article on the publisher's web-site:

Table S1. The covariates balancing in pre-IPTW and post-IPTW matching

Table S2. The univariate logistic regression models with pre-IPTW and post-IPTW matching in each outcome

Table S3. The multivariate logistic regression models with pre-IPTW and post-IPTW matching in each outcome

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