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Red blood cell distribution width is a short-term mortality predictor in middle-aged and older adults with hip fracture

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Abstract

Objective To study the relationship between red blood cell distribution width (RDW) and short-term mortality of hip fracture in middle-aged and older adults.

Methods A retrospective cohort of electronic medical records at a single hospital over a 2-year period between 2020 and 2021. We received the records of 233 patients aged > 50 years who suffered from hip fracture. the clinical data including patients demographics, comorbidities at the time of admission, type of surgery, blood examination, 3-months mortality, 6-months mortality and 1-year mortality. the relationship between RDW and short-term mortality of hip fracture were analyzed. the cohort was then divided into two groups based on their RDW levels at the time of admission: low (RDW < 13.6%) and high (RDW ≥ 13.6%).

Results Results the mean age was 78.03 ± 12.09 years; 64.81% were woman. At admission, 80 patients (34.33%) had high RDW levels and 153 patients (65.67%) had low RDW levels. there were no statistically significant differences between the groups with regard to sex, type of operation, duration of surgery and hospitalization length. Patients with high RDW had more comorbidities when compared to patients with low RDW levels ($p < 0.05$). All-cause mortality was higher for patients with high RDW levels, at 3 months ($p < 0.05$), 6 months ($p < 0.05$), and 12 months ($p < 0.05$).

Conclusion RDW is significantly related with short-term mortality in hip fracture. The higher RDW, the higher risk of mortality.

Keywords Hip fracture, Red blood cell distribution width, Middle-aged and older adults, Short-term mortality

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Introduction

Osteoporosis is a systemic metabolic disease characterized by low bone mass and microstructural deterioration of bone tissue, leading to increased bone fragility and susceptibility to fractures [1]. Hip fracture is one of the most serious consequences of osteoporosis [2, 3]. With the increasing aging population in China, the incidence of hip fracture is on the rise [4]. Due to the fact that elderly patients often have multiple comorbidities before injury, patients with hip fracture have a high rate of disability and mortality [5, 6]. It has been reported that the 6-month mortality rate for hip fractures is 6.7-13.2% [7–9], and the one-year mortality rate is 10.0-22.8% [10–13]. Age, gender, comorbidities, type of fracture, ability of daily living before injury, cardiovascular disease or chronic respiratory disease before injury, surgical treatment, time from injury to hospitalization, time from surgery to operation, and pulmonary infection during hospitalization have been considered as the risk factors for death of hip fracture. However, using these models is untimely and imprecise. Therefore, it is important to identify biomarkers related to the mortality risk of hip fractures in clinical practice.

RDW is a parameter that reflects the heterogeneity of red blood cell volume in peripheral blood and can objectively reflect the degree of inequality in red blood cell size [14]. RDW is timely and inexpensive. RDW, calculated as a percentage, is derived from the standard deviation of red blood cell (RBC) sizes divided by the mean corpuscular volume (MCV). It is a simple process to acquire RDW values from a complete blood count (CBC) analysis [15, 16]. Typically, the average volume of RBCs in humans falls between 80 and 100 femtoliters (fL), with RDW values typically ranging from 12 to 15%; however, these ranges can differ based on the specific testing laboratory and the demographic being tested [17, 18].

Recent studies have shown that RDW is a predictor of mortality risk in various internal diseases, such as coronary heart disease, heart failure, and pulmonary infections [14, 19, 20]. Most patients with hip fractures have complicating diseases, which can result in an increased RDW value. Therefore, can RDW be used as a predictor of mortality risk in patients with hip fractures? This article aims to explore the relationship between RDW and the short-term mortality rate of hip fractures.

Materials and methods

Study population

The study was approved by the Ethics Committee of the Jinjiang Municipal Hospital, Fujian, China. This study was conducted in accordance with the Declaration of Helsinki. Informed consent was obtained from all patients. A total of 287 patients were recruited from the Department of Orthopaedics, Jinjiang Municipal Hospital, between January 2020 and December 2021.

Inclusion criteria

A total of 287 patients with hip fractures who visited the Department of Orthopaedics, Jinjiang Municipal Hospital were enrolled. Of these, 54 patients were excluded, resulting in a final sample of 233 patients. Figure 1 presents a flow diagram of the study cohort.

The previously described inclusion criteria were as follows: (a) patients with hip fractures proven via imaging examination, (b) all patients suffered from minor injuries, (c) the minimum age of the patients was 50 years, (d) blood tests were collected after admission, (e) all patients had complete hospitalization data, including laboratory, imaging and follow-up data; (f) the patients were selected from inpatients.

Biochemical assays and data collected

Upon admission of the patients, venous blood samples were obtained to assess specific laboratory values. The RDW was determined using an automated hematology analyzer (SYSMEX XE-5000, Japan), with a reference interval of 11–16%.

Medical examinations were performed for all patients at the Jinjiang Municipal Hospital. Clinical and demographic information was obtained from the medical data platform of the hospital. These data included information on age, sex, comorbidities, blood pressure, type of operation, duration of surgery and hospitalization length, blood examination, date of diagnosis and date of death. Comorbidities included cardiovascular disease, chronic respiratory disease, diabetes mellitus, cerebrovascular disease and other medical diseases. Cardiovascular disease included coronary heart disease, heart failure, myocardial infarction. Cerebrovascular disease included cerebral infarction, sequelae of stroke, Parkinson's syndrome. Chronic respiratory disease included pneumonia, chronic bronchitis, COPD. Other medical diseases included anemia, and renal insufficiency. During the follow-up period, the patients were interviewed through telephone every three months until death events occurred. Survival status, disease progression and date of death were recorded. The last follow-up was conducted on June 8, 2023.

Statistical analysis

Data were analysed using IBM SPSS 26.0. The results are presented as the mean ± standard deviation. Chi-square tests were performed to compare categorical variables between groups. Independent sample t-tests were used to compared continuous variables between groups. Receiver operator characteristic (ROC) curve analysis was performed to evaluate the predictive value of RDW

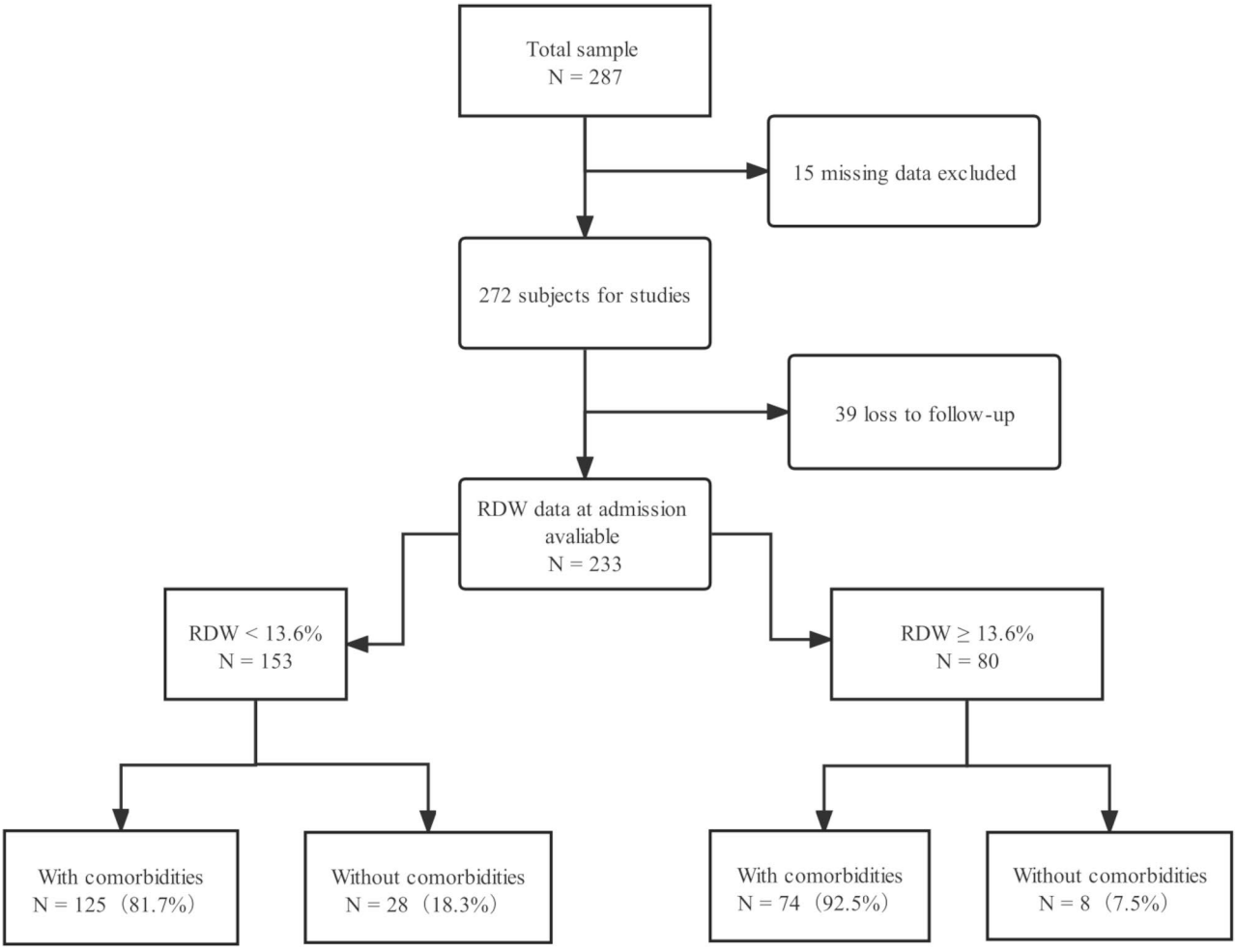

Fig. 1 Study cohort flow diagram

for 12-month mortality after surgery. In addition, the optimal cut-off values were calculated. The optimal cut-off values for the ROC curves were established using the Youden index. Cox proportional hazard models were used to obtain hazard ratios (HRs). Patient clinical endpoints were calculated using the Kaplan-Meier method and compared using the log-rank test. A two-sided $p < 0.05$ was considered statistically significant difference.

Results

During the study period, 287 patients were treated at our hospital, of these, 54 patients did not meet the study's inclusion criteria. Of the 233 patients included in this analysis, 19 (7.51%), 30 (11.86%) and 40 (15.81%) died within 3 months, 6 months and 12 months, respectively.

Baseline demographics and characteristics of patients by survival at 12 months

Of all the 233 patients, we divided them into two groups: died at 12 months and survived at 12 months. Age, RDW, hypertension and comobidities of subjects were significant difference between the groups. The distribution of the types of treatment did not differ between the groups ($p = 0.148$). There were no significant difference between the groups as regards duration of surgery, hospitalization length, pneumonia, type 2 diabetic mellitus (DM2), sex, systolic blood pressure (SBP), diastolic blood pressure (DBP), white blood cell (WBC), hemoglobin, alkaline phosphatase (ALP), glutalanine transferase (ALT), uric acid, blood calcium, serum phosphorus, total cholesterol (TC), triglyceride (TG), high-density lipoprotein (HDL) and low-density lipoprotein (LDL) ($p > 0.05$). Patient characteristics are presented in Table 1.

The ROC curve for RDW in predicting mortality

Data from 233 patients were included in the final analysis. An ROC curve analysis was conducted to determine the predictive value of RDW in predicting mortality at 12 months after surgery. The optimal cut-off value was 13.6%, with relatively high sensitivity and specificity (AUC = 0.653, 95% CI, 0.561–0.744, $p = 0$Fig. Fig. 2).

Table 1 Baseline demographics and characteristics of patients by survival at 12 months

	Died at 12 months (*N* = 40)	Survived at 12 months (*N* = 193)	t/χ^2 value	*p* value
Age	82.15 ± 7.74	77.18 ± 12.66	2.392	0.018
Male/female	19/21	63/130	3.207	0.073
RDW	13.84 ± 1.78	13.23 ± 1.53	2.235	0.026
Type of operation			1.452	0.148
Closed reduction internal fixation	18 (45.00%)	97 (50.26%)		
Total hip arthroplasty	6 (15.00%)	60 (31.09%)		
Hemiarthroplasty	13 (32.50%)	33 (17.10%)		
No operation	3 (7.50%)	3 (1.55%)		
Duration of surgery (minutes)	84.91 ± 55.51	87.24 ± 40.44	-0.289	0.773
Hospitalization length (days)	12.73 ± 7.88	11.90 ± 6.18	0.734	0.463
Comorbidities	40 (100.0%)	159 (82.4%)	8.251	0.004
DM2	10 (25.0%)	31 (16.1%)	1.825	0.177
Hypertension	27 (67.5%)	85 (44.0%)	7.304	0.007
Pneumonia	8 (20.0%)	53 (27.5%)	0.954	0.329
SBP (mmHg)	150.45 ± 28.44	152.43 ± 25.51	-0.438	0.662
DBP (mmHg)	75.85 ± 11.76	78.29 ± 12.54	-1.179	0.243
WBC (10^9 /l)	9.17 ± 2.51	10.12 ± 3.08	-1.824	0.069
Hemoglobin (g/l)	110.90 ± 22.59	117.18 ± 22.60	-1.600	0.111
Albumin (g/l)	36.73 ± 4.85	37.73 ± 5.74	-0.983	0.327
ALP (u/l)	99.98 ± 64.91	89.37 ± 55.72	1.063	0.289
ALT (g/l)	19.40 ± 14.91	19.57 ± 17.90	-0.055	0.957
Uric acid (umol/l)	308.40 ± 129.64	314.44 ± 103.27	-0.321	0.748
Blood calcium (mmol/l)	2.23 ± 0.15	2.25 ± 0.16	-1.003	0.317
Serum phosphorus (mmol/l)	1.02 ± 0.18	1.01 ± 0.19	0.254	0.800
TC (mmol/l)	4.10 ± 1.12	4.45 ± 1.11	-1.800	0.073
TG (mmol/l)	0.97 ± 0.37	1.03 ± 0.49	-0.656	0.512
HDL (mmol/l)	1.30 ± 0.38	1.33 ± 0.41	-0.330	0.742
LDL (mmol/l)	2.50 ± 0.94	2.81 ± 0.91	-1.898	0.059

Data are presented as mean ± SD or as number (%). RDW, red blood cell distribution width. DM2, type 2 diabetic mellitus. SBP, systolic blood pressure. DBP, diastolic blood pressure. WBC, white blood cell. ALP, alkaline phosphatase. ALT, glutalanine transferase. TC, total cholesterol. TG, triglyceride. HDL, high-density lipoprotein. LDL, low-density lipoprotein

Patient characteristics and demographics by low RDW (< 13.6%) and high RDW (≥ 13.6%)

Based on the ROC curve, the cut-off value of the RDW is 13.6%. The patients were divided into the RDW < 13.6% and RDW ≥ 13.6% groups. Of the 233 patients included in this analysis, 80 patients (34.33%) had high RDW levels and 153 patients (65.67%) had low RDW levels. The mortality of RDW ≥ 13.6% groups was significant higher than the RDW < 13.6% groups ($p < 0.05$). The cohort's mean ages 78.03 ± 12.09 years, with no significant difference between two groups ($p > 0.05$). The RDW ≥ 13.6% groups had more comorbidities than the RDW < 13.6% groups ($p < 0.05$). The rate of subjects underlying hypertension, pneumonia and DM2 were higher in the RDW ≥ 13.6% groups. The albumin of RDW ≥ 13.6% groups was higher. There were not significant difference between the groups regarding sex, SBP, DBP, WBC, hemoglobin, ALP, ALT, uric acid, blood calcium, serum phosphorus, TC, TG, HDL, LDL ($p > 0.05$). Patient characteristics are presented in Table 2.

RDW and mortality

Of the 233 patients included in this analysis, 19 (7.51%), 30 (11.86%) and 40 (15.81%) died within 3 months, 6 months and 12 months, respectively. The RDW were higher in the death group than in the survival group. The mortality of RDW ≥ 13.6% groups was significant higher than the RDW<13.6% groups($p < 0.05$). Among 233 patients, the association remained significant for 3-month [RR 2.889, 95% CI: (1.112–7.507), $p = 0.024$], 6-month [RR 2.906, 95% CI: (1.331–6.345), $p = 0.006$] and 12-month [RR 2.217, 95% CI: (1.111–4.422), $p = 0.022$] mortality, respectively. Mortality rates for two groups are presented in Table 2; Fig. 3.

Kaplan-Meier survival analysis

Based on the RDW, the patients divided into the RDW<13.6% and RDW ≥ 13.6% groups. Kaplan-Meier survival curves shows that the RDW ≥ 13.6% groups have a higher mortality than the RDW < 13.6% groups ($p = 0.017$) (Fig. 4).

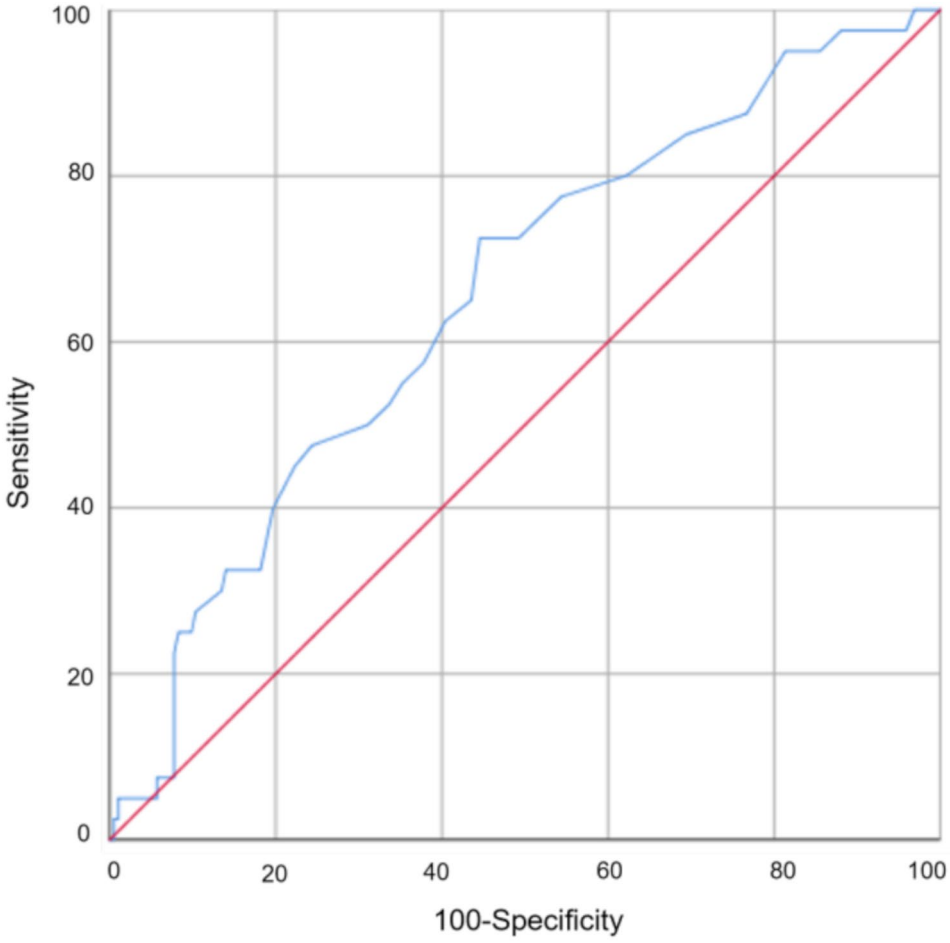

Fig. 2 The ROC curves for RDW in predicting mortality

Discussion

Hip fractures are a common injury among elderly individuals, and they are often associated with high mortality rates. Some scholars have reported that the 6-month mortality rate of elderly patients with hip fracture is 6.7-13.2% [7–9]. The 1-year mortality rate is 10.0-22.8% [10–13]. This is similar to the results of our study, where the 3-month mortality was 7.51%, 6-month mortality was 11.86% and the 1-year mortality was 15.81%. Risk factors associated with hip fractures death include: age, sex, number of complicating diseases, fracture type, cognitive status, self-care ability before injury, cardiovascular disease or chronic respiratory disease before injury and pulmonary infection during hospitalization [21].

As a result, researchers are exploring new ways to predict mortality risk in these patients. One promising predictive marker is RDW, an inexpensive and simple blood test that measures the range of sizes of red blood cells in the circulation.

In this study, we found that higher RDW values were associated with increased mortality risk in middle-aged and older patients with hip fractures. Specifically, patients with an RDW greater than 13.6% had 2.889 times higher 3-month mortality risk, 2.906 times higher 6-month mortality and 2.217 times higher 12-month mortality risk than those with an RDW less than 13.6%.

These findings suggest that RDW has predictive value for short-term mortality risk in middle-aged and older patients with hip fractures. This is consistent with previous studies that have found RDW to be a marker of mortality risk in a variety of disease states, including chronic heart failure, community-acquired pneumonia, hypertension, and stroke [19, 22–24].

To date, there are some studies examined the relationship between RDW and mortality of the middle-aged and older adults. In Cauthen's study on the relationship between RDW and mortality rate in chronic heart failure, 6159 chronic heart failure patients were divided into three groups based on their RDW levels: ≤ 13.5%, 13.5-14.9%, and RDW > 14.9%. The results confirmed that with every 1% increase in RDW, the mortality risk increased by 17% [25]. In Braun's study on the relationship between RDW and prognosis of community-acquired pneumonia, 3815 cases were grouped into RDW ≤ 15.0% and

Table 2 Patient characteristics and demographics by low RDW (< 13.6%) and high RDW (≥ 13.6%)

	RDW < 13.6% (*N* = 153)	RDW ≥ 13.6% (*N* = 80)	Total (*N* = 233)	*p*-value
Mortality (overall):			40(17.2%)	
Mortality at 3 months	8 (5.2%)	11 (13.6%)		0.024
Mortality at 6 months	13 (8.5%)	17 (21.2%)		0.006
Mortality at 12 months	20 (13.1%)	20 (25.0%)		0.022
Age	76.53 ± 12.87	90.90 ± 9.89	78.03 ± 12.09	0.009
Male/Female	54/99	28/52	82/151	0.965
Comorbidities	125 (81.70%)	74 (92.50%)	199 (85.41%)	0.027
DM2	20 (13.07%)	21 (26.25%)	41 (17.60%)	0.012
Hypertension	64 (41.83%)	48 (60.00%)	112 (48.07%)	0.008
Pneumonia	32 (20.92%)	29 (36.25%)	61 (26.18%)	0.011
SBP(mmHg)	151.61 ± 26,58	153.01 ± 24.95	152.09 ± 25.99	0.696
DBP(mmHg)	76.75 ± 11.74	79.99 ± 13.44	77.87 ± 12.42	0.059
Baseline laboratory values				
WBC (10^9 /l)	9.83 ± 3.16	10.26 ± 2.67	9.98 ± 3.00	0.308
Hemoglobin (g/l)	115.09 ± 22.37	117.75 ± 23.23	116.01 ± 22.65	0.397
Albumin (g/l)	36.87 ± 5.17	38.88 ± 6.14	37.56 ± 5.59	0.009
ALP (u/l)	91.69 ± 62.24	90.29 ± 47.30	91.20 ± 57.40	0.860
ALT (g/l)	19.39 ± 15.86	19.81 ± 20.07	19.54 ± 17.39	0.864
Uric acid (umol/l)	319.99 ± 103.95	300.93 ± 114.90	313.39 ± 108.00	0.203
Blood calcium (mmol/l)	2.24 ± 0.16	2.27 ± 0.15	2.25 ± 0.16	0.250
Serum phosphorus (mmol/l)	1.01 ± 0.20	1.01 ± 0.17	1.01 ± 0.19	0.931
TC (mmol/l)	4.34 ± 1.04	4.50 ± 1.24	4.39 ± 1.11	0.285
TG (mmol/l)	1.03 ± 0.48	0.99 ± 0.46	1.02 ± 0.47	0.480
HDL (mmol/l)	1.30 ± 0.40	1.36 ± 0.42	1.32 ± 0.41	0.288
LDL (mmol/l)	2.71 ± 0.85	2.84 ± 1.06	2.76 ± 0.92	0.333

Data are presented as mean ± SD or as number (%). RDW, red blood cell distribution width. DM2, type 2 diabetic mellitus. SBP, systolic blood pressure. DBP, diastolic blood pressure. WBC, white blood cell. ALP, alkaline phosphatase. ALT, glutalanine transferase. TC, total cholesterol. TG, triglyceride. HDL, high-density lipoprotein. LDL, low-density lipoprotein

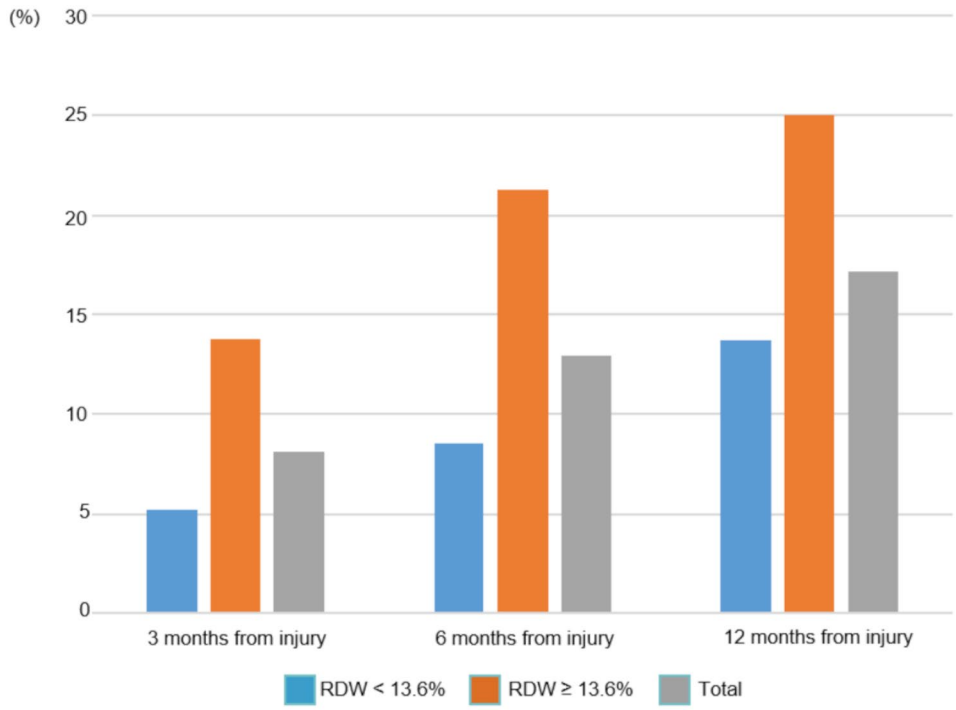

Fig. 3 Primary outcome (all-cause mortality) at 3 months, 6 months, and 12 months according to RDW (%)

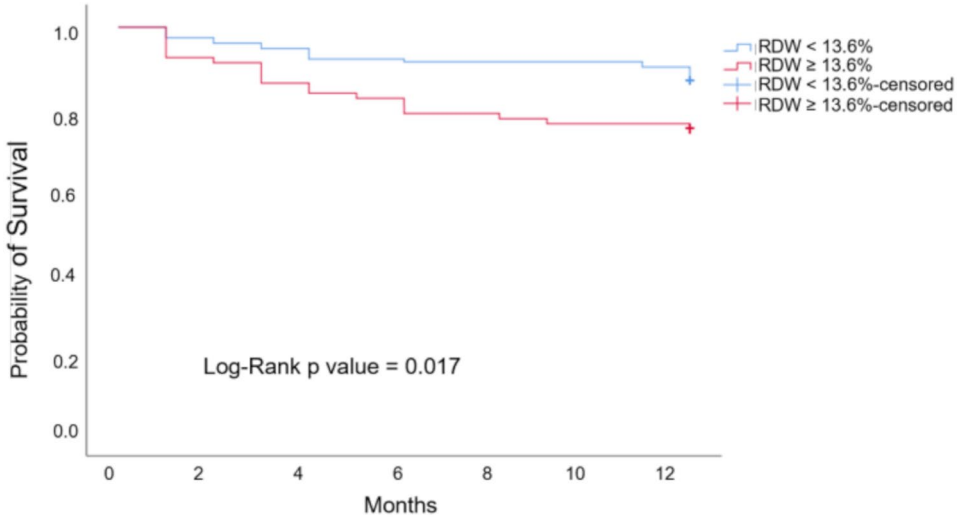

Fig. 4 Kaplan-Meier survival curves stratified by the value in terms of RDW. Pairwise log-rank tests were performed

RDW > 15.0%, with a 3-month mortality rate of 16.83% and 38.07% [14], respectively. The difference was statistically significant [14]. In the study on the relationship between RDW and 5-year mortality risk among hospitalized elderly patients, 122 elderly individuals aged over 75 were divided into four groups based on their RDW levels: < 13.75%, 13.75-14.65%, 14.65-16.32%, and > 16.32% [26]. The results showed that the mortality risk in the group with RDW > 16.32% was 2.24 times higher than that in the group with RDW < 13.75% [26]. In Patel's meta-analysis on the relationship between RDW and mortality risk in middle-aged and elderly individuals, the RDW values of 8178 individuals over 45 years old were divided into five groups: < 12.6%, 12.6-13.0%, 12.3-13.4%, 13.4-14.0%, and > 14.0% [27]. The results confirmed that the mortality rate increased sequentially in each group, and found that with every 1% increase in RDW, the mortality risk increased by 22% [27]. Garbharran's study on predicting risk factors for mortality in hip fracture patients using the Charlson comorbidity index confirmed that the higher the index, the higher the RDW values, and the greater the risk of death [13]. They found that with every 1% increase in RDW, the 1-year mortality risk increased by 13% [13].

While these findings are promising, there are several limitations to our study. First, the sample size was relatively small, and larger studies are needed to confirm our findings. Second, we did not have information on some potentially important factors that may influence mortality risk, such as preoperative and post-operative functional status and other comorbidities. Third, we did not have information on the cause of death, which could provide important insights into the underlying mechanisms by which RDW predicts mortality risk.

Conclusions

In conclusion, RDW contributes to the prognosis of short-term mortality in hip fractures, and the greater the width of red blood cell distribution, the higher the risk of death. RDW is a simple and inexpensive blood test that could potentially be used to identify high-risk patients and guide clinical decision-making. However, further research is needed to confirm our findings and to better understand the underlying mechanisms by which RDW predicts mortality risk.

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Author contributions

X.L., and J.Z., drafted and conceived the initial manuscript. Y.Z., L.L., and Z.L. provided the essential assistant for our final manuscript. X.L., and J.Z. drew the figures and arranged the tables. H.Z., X.H., and Z.W. revised the manuscript. All authors have read and approved the article.

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Declaration.

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Data availability

The datasets generated and/or analysed during the current study are not publicly available due [REASON WHY DATA ARE NOT PUBLIC] but are available from the corresponding author on reasonable request.

Declarations

Ethics approval and consent to participate

This study was approved by the Clinical Research Ethics Committee of Jinjiang Municipal Hospital (jjsyyyxll-2022110). This study was conducted in accordance with the principles of the Declaration of Helsinki.

Competing interests
The authors declare no competing interests.

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