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Red cell distribution width as a predictor of mortality after hip fracture: a systematic review and meta-analysis

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Abstract. – OBJECTIVE: This review examined the association between red cell distribution width (RDW) and mortality after hip fracture.

MATERIALS AND METHODS: PubMed, CENTRAL, Scopus, Web of Science, and Embase were searched up to 10th January 2023 for studies comparing mortality after hip fracture based on RDW. All cut-offs of RDW were accepted. Crude and adjusted mortality ratios were pooled separately.

RESULTS: Nine studies with 5,274 patients were eligible. Meta-analysis of eight studies reporting crude mortality rates showed that patients with high RDW had a significantly higher risk of mortality than those with low RDW (RR: 2.81 95% CI: 2.05, 3.86 I^2=82%). The results did not change in significance on subgroup analyses based on study location, sample size, the cut-off of RDW, and follow-up. Four studies reported adjusted mortality rates. Analysis of the same showed that high RDW was an independent predictor of mortality in hip fracture patients (HR: 3.14 95% CI: 1.38, 7.14 I^2=95%).

CONCLUSIONS: Within the limitations of the review, RDW was found to be an indicator of mortality in hip fracture patients. High RDW was significantly associated with increased mortality despite different cut-offs among studies. Further research is needed to generate more rigorous evidence.

Key Words:
Hip fracture, Trauma, Elderly, Red cell.

Introduction

Hip fracture is one of the commonest injuries and the reason for hospitalization in the geriatric population across the world[1]. With approximately 300,000 admissions for hip fractures in the USA alone, the incidence of this debilitating condition is on the rise due to the aging population[2]. Indeed, it is estimated that the incidence of hip fractures shall continue to increase and reach up to around 4.5 million patients worldwide by 2050[2]. High mortality rates have been a major problem with hip fractures, with 1-year mortality rates ranging from 20 to 40%[3] and 8-year mortality rates ranging up to 80%[4]. Furthermore, a large proportion of patients are unable to return to their initial ambulatory status post-injury[5]. Given the high morbidity and mortality associated with hip fractures, it is necessary that suitable and easy-to-use biomarkers are identified to predict mortality and prioritize the management of those at risk of adverse outcomes.

Red blood cell distribution width (RDW) is a commonly used tool to examine red blood cell volume heterogeneity and is a standard component of complete blood cell counts. It provides an indication of red blood cell size variation within the sample and is based on the distribution curve width and the mean cell size[6]. Recent evidence shows that RDW can be a prognostic indicator in various diseases like sepsis, pulmonary embolism, coronary artery disease, heart failure, atrial fibrillation, kidney disease, liver disease, stroke, and several types of cancer[7-13]. The accumulating evidence has shown that RDW is a strong and independent predictor for death, even in the general population[7]. The utility of this inexpensive and readily available clinical marker is being increasingly recognized owing to the shortage of healthcare resources across the globe, as RDW could be valuable for primary and cost-effective risk stratification of patients[14].

While there have been studies[15-17] examining the prognostic ability of RDW for hip fractures, many of them have been of small sample size and no review has attempted to consolidate available evidence. Hence, the current study was undertaken to systematically analyze and pool data from the literature on the ability of RDW to predict mortality after hip fractures.

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Materials and Methods

Search and Eligibility

The protocol registration was done on PROSPERO before commencing the literature search (CRD42023390455). The PRISMA statement reporting guidelines were followed[18]. An intensive literature search was conducted by two independent reviewers and supervised by the medical librarian for PubMed, CENTRAL, Scopus, Web of Science, and Embase databases. It encompassed all articles published between 1st January 1980 to 10th January 2023. All studies were considered without any limitation on the date of publication and language.

The inclusion criteria were defined beforehand and consisted of all types of studies conducted on hip fracture patients (population). The exposure variable was high RDW *vs.* low RDW (comparison). The Outcome of interest was the mortality rate. The cut-off for high RDW was not predefined, and all cut-offs were acceptable.

Exclusion criteria were: 1. studies not reporting separate data on hip fractures; 2. studies not reporting separately on RDW; 3. studies with duplicate/overlapping data. If two or more articles used the same dataset from the same period, the study with the highest number of patients was included. Abstracts, review articles, and editorials were not considered for inclusion.

A mix of free-text and medical subject headings (MeSH) search terms with Boolean operators (AND/OR) were used in the literature search. The search terms included "hip fracture", "proximal femoral fracture", "red cell distribution", "red blood cell", "RDW", and "mortality". The PubMed search strategy is presented in detail in **Supplementary Table I**. Identical search strings were used for the remaining databases. The search results were deduplicated and scrutinized based on the eligibility criteria by two reviewers separately, first at the title/abstract level and then at the full-text level. Articles completing all eligibility criteria were finally included. Any disagreements were solved by consensus. The references list of eligible articles was hand searched for additional articles.

Data Management and Study Quality

Data on the author's last name, year of publication, study database, location, study type, included patients, sample size, age, gender, treatment for hip fracture, the timing of measurement of RDW, cut-off used, follow-up, and outcome data were extracted by two reviewers independent of each other.

Two authors judged the study's quality based on Newcastle Ottawa Scale (NOS)[19]. The NOS has three domains: representativeness of the study cohort, comparability, and measurement of outcomes. Points are given based on the preformatted questions. The final score of a study can range from 0-9.

Statistical Analysis

Statistical analysis was done using Review Manager (RevMan), version 5.3 [Nordic Cochrane Centre (Cochrane Collaboration), Copenhagen, Denmark, 2014]. Crude mortality data was sourced from studies and combined to generate risk ratios (RR) with 95% confidence intervals (CI) in a random-effects model. Adjusted mortality data were pooled to calculate the Hazard ratio (HR). Publication bias was examined using funnel plots. The I^2 statistic was the tool to determine inter-study heterogeneity. I^2 <50% meant low, and >50% meant substantial heterogeneity. A sensitivity analysis was performed to check if the results changed on the exclusion of any study. Subgroup analysis was done based on study location, sample size, the cut-off of RDW, and follow-up. p-values <0.05 were considered statistically significant.

Results

Figure 1 shows the number of articles encountered at different review steps. Initially, 390 studies were obtained. These underwent deduplication to generate 232 search results. The reviewers examined these articles for primary eligibility, and 218 were unrelated to the review. The 14 studies which were elected for full-text analysis underwent detailed examination by both reviewers. Five were excluded, and nine[15-17,20-25] were found to be appropriate based on the inclusion criteria.

The baseline details of included studies are shown in Table I. The included studies were either prospective or retrospective cohort studies published between 2012 and 2022. Four studies[6,15,17,23] included only elderly (≥50/60/65-year-old) patients with hip fractures, while the remaining included all patients irrespective of age. Nevertheless, the mean age of patients in all studies was >70 years, with a predominance of females in most studies. The total sample size of the studies was 5,274 patients. All studies included patients undergoing surgical intervention for hip fracture, except for one which

Table I. Details of included studies.

Study	Location	Country	Study type	Included patients	Sample size	Mean age	Male Gender (%)	Treatment	Timing of measurement	Cut-off of RDW (%)	Follow-up	NOS score
Marom et al[16] 2022	Meir Medical Center	Israel	R	≥65-year-old with hip fracture	1,574	90.7	31.3	THA, CRIF, & HA	Admission	14.5	1 year	7
Karadeniz et al[15] 2022	Amasya University	Turkey	R	≥65-year-old with hip fracture	190	82.8	33.2	HA	Admission	14.5	1 year	7
Wei-Hsiang et al[17] 2021	Shanghai Xuhui Central Hospital, Zhongshan Hospital	China	P	≥60-year-old with hip fracture	203	71.7	33	Internal fixation or THA	Before treatment	13.35	30 days	9
Hamdan et al[25] 2021	University of Jordan	Jordan	R	≥50-year-old with hip fracture	549	76.4	50.1	HA, DHC, IMF	Admission	15	6 months	7
Cruz-Vargas et al[24] 2019	Hospital Central de la Fuerza Aérea	Peru	R	All patients with hip fracture	99	83	35	Surgery	NR	14	6 months	6
Temiz et al[23] 2018	Edremit State Hospital	Turkey	R	≥65-year-old with first time hip fracture	166	79,2	41.6	Surgery	Admission	14.5	1 year	8
Lv et al[22] 2016	PLA General hospital	China	R	All patients with hip fracture with >2 years of follow-up	1,479	73	41.3	IMF, DHC, external fixation, non-surgery	Admission	13.8	4 years	6
Zehir et al[21] 2014	Hitit University	Turkey	R	All patients with hip fracture undergoing HA	316	77.5	42	HA	Admission	14.5	1 year	6
Garbharran et al[20] 2012	St Thomas' Hospital	UK	R	All patients with hip fracture	698	78	33	Surgery	Admission	14.2	1 year	8

R, retrospective; P, prospective; THA, Total hip arthroplasty; CRIF, Closed reduction internal fixation; HA, Hemiarthroplasty; DHC, dynamic hip screw; IMF, intramedullary fixation.

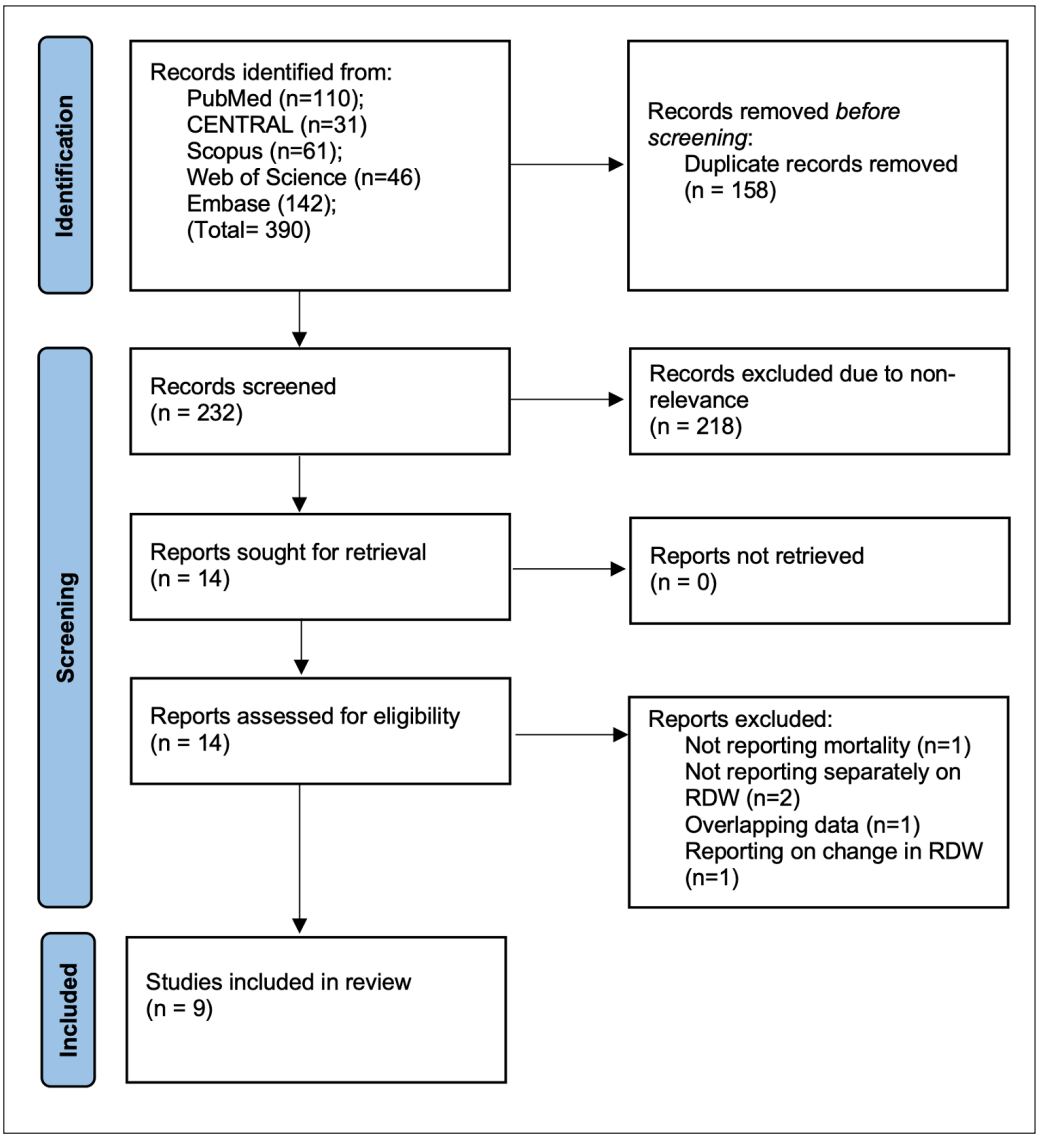

Figure 1. Study flow chart.

included a small proportion of non-surgical treatment. RDW was calculated at admission in all studies except for one[17], which was calculated just before surgery. Four studies[15,16,21,23] used an RDW cut-off of 14.5, while for the remaining studies, it ranged from 13.35 to 15. The follow-up duration was between 30 days to 4 years. The NOS score ranged from 6 to 9.

Meta-analysis of crude mortality rates showed that patients with high RDW had a significantly increased risk of mortality compared to those with low RDW (RR: 2.81 95% CI: 2.05, 3.86 I^2=82%) (Figure 2). The significance of the results did not change on the exclusion of any study. The funnel plot did not show any publication bias (Figure 3).

The results of the subgroup analysis are shown in Table II. High RDW was predictive of mortality for studies from Asian as well as non-Asian countries. On dividing studies based on sample size (>250 or <250), there was no change in the significance of the results. We classified the studies into three RDW cut-off groups, namely 13.35-13.8, 14-14.5, and 15. Increased risk of mortality was noted with high RDW in all three groups. Furthermore, there was no change in the results' significance based on the follow-up duration (≥1 year or < 1 year).

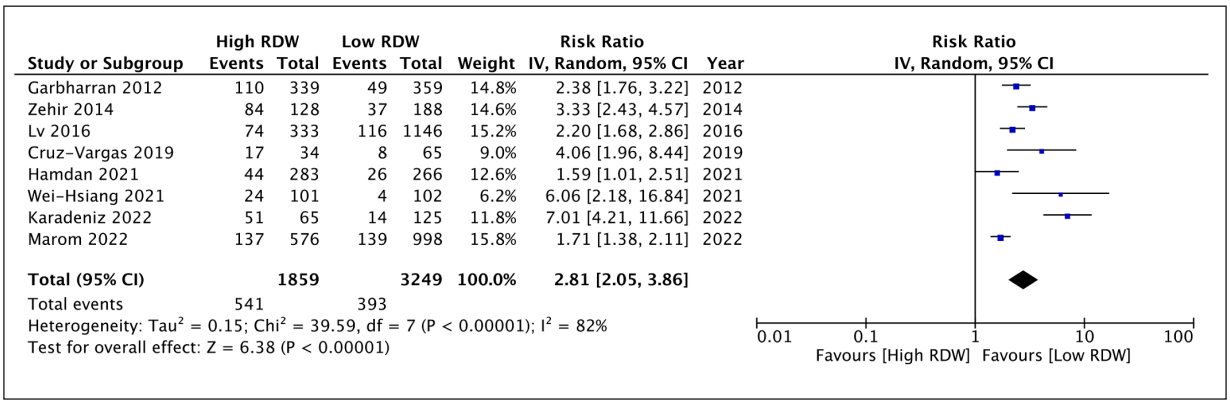

Figure 2. Meta-analysis of crude mortality rates between patients with high *vs.* low RDW.

Four studies[15,17,20,23] reported adjusted mortality rates. This meta-analysis showed that high RDW was an independent predictor of mortality in hip fracture patients (HR: 3.14 95% CI: 1.38, 7.14 I^2=95%) (Figure 4). The results turned non-significant on the exclusion of the studies of Wei-Hsiang et al[17] (HR: 3.93 95% CI: 0.69, 22.52) and Karadeniz and Yurtbay15 (HR: 2.06 95% CI: 0.94, 4.51).

Discussion

Given the high mortality burden after hip fractures, there has been intense research[26,28-30] in the past decade to identify risk factors for predicting adverse outcomes. On one end of the spectrum are relatively simple biomarkers like albumin, serum sodium, neutrophil-lymphocyte ratio, etc., which have been found to predict mortality, although with some variability in results[26-28]. On the other hand, uncommon and complex markers like alanine aminotransferase/gamma-glutamyl transferase ratio, growth differentiation factor-15, carbohydrate antigen 125, adiponectin, leptin, beta-isomerized C-terminal telopeptide of collagen type I, and parathyroid hormone have also been identified as predictors of post-hip fracture mortality[26,28-30]. It cannot be understated that a biomarker for routine clinical use should be easily available, inexpensive, easy to calculate, and have a strong association with the outcome of interest. Complete blood counts are routinely carried out across the world for all admitted patients, and RDW is a standard component of such investigation. Given its easy availability, RDW has been used to predict adverse outcomes in several diseases. In this review, we aimed to examine if RDW can be a predictor of mortality in patients with hip fractures.

Examining evidence from nine studies published in the past decade, encompassing a large cohort of 5,274 patients, this review noted that patients with high RDW had 2.8 times increased risk of mortality after hip fracture. The 95% CI was also high, demonstrating a 2 to 3.8 times increased risk of mortality with higher RDW. Importantly, the forest plot demonstrated a consistent direction of the effect size in all studies,

Table II. Subgroup analysis.

Variable	Groups	Studies	Risk Ratio
Region	Asian	6	2.82 95% CI: 1.88, 4.24 I^2=87%
	Non-Asian	2	2.79 95% CI: 1.73, 4.51 I^2=43%
Sample size	>250	5	2.18 95% CI: 1.70, 2.79 I^2=72%
	<250	3	5.89 95% CI: 4.00, 8.67 I^2=0%
Cut-off	13.35-13.8	2	3.22 95% CI: 1.23, 8.44 I^2=72%
	14-14.5	4	3.14 95% CI: 1.99, 4.94 I^2=88%
	15	1	1.59 95% CI: 1.01, 2.51
Follow-up	≥ 1 year	5	2.78 95% CI: 1.91, 4.04 I^2=87%
	<1 year	3	3.12 95% CI: 1.35, 7.20 I^2=76%

CI, confidence intervals.

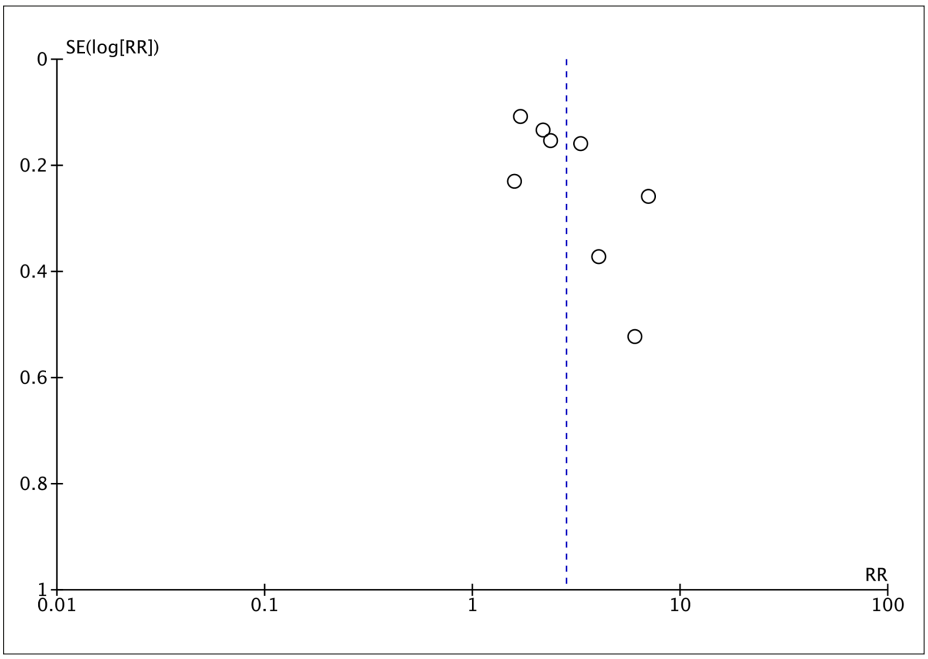

Figure 3. Funnel plot to assess publication bias of crude mortality rates.

i.e., increased risk of mortality with higher RDW. The lack of publication bias on funnel plot and no change of the results during leave-one-out analysis add to the plausibility of RDW being an important predictor of mortality in hip fracture patients. Nevertheless, cautiousness is necessary for broad interpretations, given the high heterogeneity of the meta-analysis. This could have been due to variations in the patient populations, baseline comorbidities, treatment protocols, follow-up duration, and differences in RDW cut-off used by the included studies. We attempted to explore the source of heterogeneity and generate more homogenous evidence via multiple subgroup analyses. It was found that RDW remained a predictor of mortality in Asian and non-Asian populations with hip fractures. Also, there was no "small sample size effect"[31] in the results, with both larger and smaller sample size studies demonstrating equivalent results, albeit with an arbitrary cut-off of 250. Furthermore, the results were also similar for studies with ≥ 1 year of follow-up and those with shorter follow-up. Importantly, the most significant difference among the studies was the cut-off used for RDW. While most studies in the literature have used a cut-off of 14.5% to define high RDW, other cut-offs ranging from 13 to 15% have also been used based on median values or receiver operating curve (ROC) analysis of individual cohorts[13]. We attempted to segregate the cut-offs into closely related subgroups of 13.35-13.8, 14-14.5, and 15 only to find significantly increased mortality with high RDW in all subgroups, nevertheless with a small number of studies. Further research on using coherent RDW cut-offs is needed to strengthen the current results.

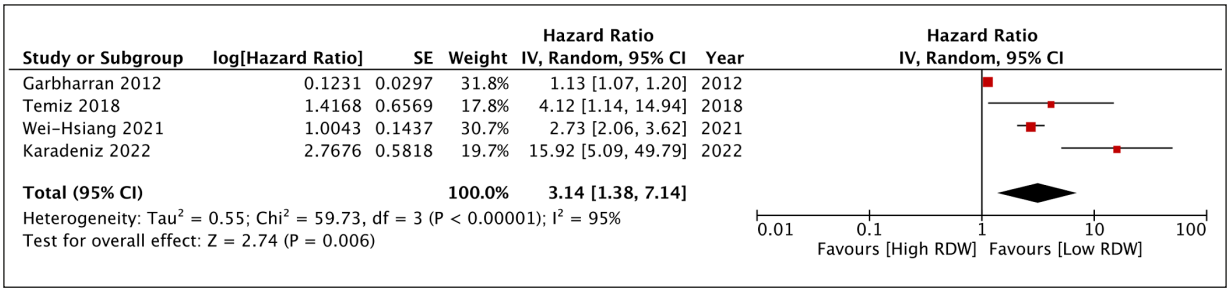

Figure 4. Meta-analysis of adjusted mortality rates between patients with high *vs*. low RDW.

The first part of the meta-analysis was based on crude mortality data which can be confounded due to variations amongst high and low RDW groups. Lack of baseline matching could be an important source of error as other variables influencing the outcome were not catered for. Research has shown that survival after hip fracture depends on several factors like age, gender, comorbidities, pre-injury functional status, cognitive status, type of fracture, delay in surgery, etc.[32,33]. Hence, it is important to examine adjusted data to support the results of crude mortality rates. While the analysis of adjusted data also showed significantly increased mortality rates with high RDW, it must be noted that data was derived only from four studies[15,17,20,23]. Stronger conclusions on the independent prognostic ability of RDW would require further studies reporting multivariable adjusted data.

The results of our review are similar to other meta-analysis studies[8-12] examining the prognostic effect of high RDW on outcomes of other diseases. Recently, Frentiu et al[12] in a pooled analysis of 26 studies, showed that elevated preoperative RDW was associated with increased mortality and acute kidney injury following cardiac surgery. Xing et al[11] combined evidence from seven studies to show higher mortality rates with elevated RDW in pulmonary embolism. Wen et al[10] have noted poor overall survival and disease-free survival in colorectal cancer patients with high RDW. Zhang et al[9], in a meta-analysis of nine studies, have demonstrated an increased risk of all-cause mortality in chronic kidney disease patients with higher RDW. Similar results have been noted by Zhang et al[8] in sepsis patients with higher RDW being an independent predictor of mortality.

The exact cause of increased mortality with high RDW has not been conclusively established; however, several hypotheses have been proposed. Increased RDW corresponds to the dysregulated state of erythrocyte homeostasis and impaired red blood cell production, which may interfere with the healing of hip fractures[7]. High RDW also correlates with chronic baseline inflammation, which is a risk factor for fractures34. Elevated RDW is indicative of an oxidative state in the individual which is associated with endothelial cell injury resulting in poor healing of tissues[35]. Furthermore, nutritional deficiencies are common amongst older individuals and can affect RDW and patient prognosis. Folate, vitamin B12, and iron, which are elementary for the generation of red blood cells, can be deficient in the elderly resulting in anemia and higher RDW[36,37]. Therefore, higher RDW can be due to a combined effect of inflammation, undernutrition status, and other factors which causes anisocytosis and gives an accumulative indication of increased mortality after hip fracture.

Strengths and Limitations

The strength of this review is that it is the first meta-analysis to generate evidence on the utility of RDW in predicting mortality after hip fracture. After a detailed literature search, nine studies with data from more than five thousand patients were combined to establish the role of RDW as a prognostic indicator. Meta-analysis was conducted for both crude and adjusted data, along with several subgroup analyses to provide comprehensive evidence. However, there are limitations as well, like the predominance of retrospective studies, which are a source of bias. Studies included only those patients with complete laboratory values and follow-up. It is plausible that patients with less severe injuries with incomplete investigations could have been missed. Secondly, the RDW cut-off across studies was uncommon, which could have introduced bias. Thirdly, data were derived from only nine studies restricted to a few countries across the world, which may limit the generalizability of evidence.

Conclusions

Within the limitations of the review, RDW was found to be an indicator of mortality in hip fracture patients. High RDW was significantly associated with increased mortality despite different cut-offs among studies. Further research is needed to generate more rigorous evidence.

Conflict of Interest
The authors have nothing to disclose.

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Not applicable.

Authors' Contributions
XZ conceived and designed the study. HW and SH collected the data and performed the literature search. XZ was involved in the writing of the manuscript. All authors have read and approved the final manuscript. All authors confirm the authenticity of all the raw data.

Ethics Approval and Informed Consent

Not applicable.

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References

1) Li L, Bennett-Brown K, Morgan C, Dattani R. Hip fractures. Br J Hosp Med (Lond) 2020 Aug 2;81: 1-10.
2) Veronese N, Maggi S. Epidemiology and social costs of hip fracture. Injury 2018; 49: 1458-1460.
3) Guzon-Illescas O, Perez Fernandez E, Crespí Villarias N, Quirós Donate FJ, Peña M, Alonso-Blas C, García-Vadillo A, Mazzucchelli R. Mortality after osteoporotic hip fracture: incidence, trends, and associated factors. J Orthop Surg Res 2019; 14: 203.
4) Pang C, Aqil A, Mannan A, Thomas G, Hossain FS. Hip fracture patients admitted to hospital on weekends are not at increased risk of 30-day mortality as compared with weekdays. J Orthop Traumatol 2020; 21: 23.
5) Min K, Beom J, Kim BR, Lee SY, Lee GJ, Lee JH, Lee SY, Won SJ, Ahn S, Bang HJ, Cha Y, Chang MC, Choi JY, Do JG, Do KH, Han JY, Jang IY, Jin Y, Kim DH, Kim DH, Kim IJ, Kim MC, Kim W, Lee YJ, Lee IS, Lee IS, Lee J, Lee CH, Lim SH, Park D, Park JH, Park M, Park Y, Ryu JS, Song YJ, Yang S, Yang HS, Yoo JS, Yoo JI, Yoo SD, Choi KH, Lim JY. Clinical Practice Guideline for Postoperative Rehabilitation in Older Patients With Hip Fractures. Ann Rehabil Med 2021; 45: 225-259.
6) Evans TC, Jehle D. The red blood cell distribution width. J Emerg Med 1991; 9 Suppl 1: 71-74.
7) Salvagno GL, Sanchis-Gomar F, Picanza A, Lippi G. Red blood cell distribution width: A simple parameter with multiple clinical applications. Crit Rev Clin Lab Sci 2015; 52: 86-105.
8) Zhang L, Yu CH, Guo KP, Huang CZ, Mo LY. Prognostic role of red blood cell distribution width in patients with sepsis: a systematic review and meta-analysis. BMC Immunol 2020; 21: 40.
9) Zhang T, Li J, Lin Y, Yang H, Cao S. Association Between Red Blood Cell Distribution Width and All-cause Mortality in Chronic Kidney Disease Patients: A Systematic Review and Meta-analysis. Arch Med Res 2017; 48: 378-385.
10) Wen ZL, Zhou X, Xiao DC. Is red blood cell distribution width a prognostic factor for colorectal cancer? A meta-analysis. Front Surg 2022; 9: 945126.
11) Xing X, Deng Y, Zhu Y, Xu S, Liu J, Zhang C, Xu S, Yang J. Red cell distribution width for prognosis in patients with pulmonary embolism: A systematic review and meta-analysis. Clin Respir J 2020; 14: 901-907.
12) Frentiu AA, Mao K, Caruana CB, Raveendran D, Perry LA, Penny-Dimri JC, Ramson DM, Segal R, Bellomo R, Smith JA, Liu Z. The Prognostic Significance of Red Cell Distribution Width in Cardiac Surgery: A Systematic Review and Meta-Analysis. J Cardiothorac Vasc Anesth 2023; 37: 471-479.
13) Montagnana M, Danese E. Red cell distribution width and cancer. Ann Transl Med 2016; 4: 399.
14) Lippi G, Mattiuzzi C, Cervellin G. Learning more and spending less with neglected laboratory parameters: The paradigmatic case of red blood cell distribution width. Acta Biomed 2016; 87: 323-328.
15) Karadeniz S, Yurtbay A. Predicting mortality rate in elderly patients operated for hip fracture using red blood cell distribution width, neutrophil-to-lymphocyte ratio, and Nottingham Hip Fracture Score. Jt Dis Relat Surg 2022; 33: 538-546.
16) Marom O, Paz I, Topaz G, Ohana N, Yaacobi E. Red cell distribution width-A mortality predictor in older adults with proximal femoral fracture. Arch Gerontol Geriatr 2022; 100: 104623.
17) Wei-Hsiang H, Zhu Y, Zhang J, Zhang Y. Pretreatment red blood cell distribution width as an efficient predictor of survival in older patients undergoing hip fracture surgery. Int J Clin Pract 2021; 75: e14791.
18) Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD, Shamseer L, Tetzlaff JM, Akl EA, Brennan SE, Chou R, Glanville J, Grimshaw JM, Hróbjartsson A, Lalu MM, Li T, Loder EW, Mayo-Wilson E, McDonald S, McGuinness LA, Stewart LA, Thomas J, Tricco AC, Welch VA, Whiting P, Moher D. The PRISMA 2020 statement: An updated guideline for reporting systematic reviews. Int J Surg 2021; 88: 105906.
19) Wells G, Shea B, O'Connell D, Peterson J, Welch V, Losos M, Tugwell P. The Newcastle-Ottawa Scale (NOS) for assessing the quality of nonrandomized studies in meta-analyses. Available at: http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed October 30, 2020.
20) Garbharran U, Chinthapalli S, Hopper I, George M, Back DL, Dockery F. Red cell distribution width is an independent predictor of mortality in hip fracture. Age Ageing 2013; 42: 258-261.
21) Zehir S, Sipahioğlu S, Özdemir G, Şahin E, Yar Ü, Akgül T. Red cell distribution width and mortality in patients with hip fracture treated with partial prosthesis. Acta Orthop Traumatol Turc 2014; 48: 141-146.
22) Lv H, Zhang L, Long A, Mao Z, Shen J, Yin P, Li M, Zeng C, Zhang L, Tang P. Red Cell Distribution Width as an Independent Predictor of Long-Term Mortality in Hip Fracture Patients: A Prospective Cohort Study. J Bone Miner Res 2016; 31: 223-33.

23) Temiz A. Association between admission red cell distribution width and mortality in elderly hip fracture patients: A Retrospective Case Control Study. EJMI 2018; 2: 29-34.

24) De La Cruz-Vargas JA, Benel FCV, Perez MA, Correa-Lopez LE. Red cell distribution width as mortality prognostic factor in patients 65 and older with hip fracture. Salud Uninorte 2019; 35: 13-28. Available at: http://www.scielo.org.co/scielo.php?pid=S0120-55522019000100013&script=sci_abstract&tlng=es. Accessed January 27, 2023.

25) Hamdan M, Haddad BI, Jabaiti M, Alryalat SA, Abdulelah AA, Alabed SH, Alabdullah TF, Aouant AN, Shahein HE, Dweik HI, Matar K, Alisi MS. Does Red Cell Distribution Width Predict Hip Fracture Mortality Among the Arab Population? A Single-Center Retrospective Cohort Study. Int J Gen Med 2021; 14: 10195-10202.

26) Fisher A, Fisher L, Srikusalanukul W, Smith PN. Usefulness of simple biomarkers at admission as independent indicators and predictors of in-hospital mortality in older hip fracture patients. Injury 2018; 49: 829-840.

27) Chen YH, Chou CH, Su HH, Tsai YT, Chiang MH, Kuo YJ, Chen YP. Correlation between neutrophil-to-lymphocyte ratio and postoperative mortality in elderly patients with hip fracture: a meta-analysis. J Orthop Surg Res 2021; 16: 681.

28) Lizaur-Utrilla A, Gonzalez-Navarro B, Vizcaya-Moreno MF, Lopez-Prats FA. Altered seric levels of albumin, sodium and parathyroid hormone may predict early mortality following hip fracture surgery in elderly. Int Orthop 2019; 43: 2825-2829.

29) Jonsson MH, Hommel A, Todorova L, Melander O, Bentzer P. Novel biomarkers for prediction of outcome in hip fracture patients-An exploratory study. Acta Anaesthesiol Scand 2020; 64: 920-927.

30) Gulin T, Kruljac I, Kirigin Biloš LS, Gulin M, Grgurević M, Borojević M. The role of adipokines as prognostic factors of one-year mortality in hip fracture patients. Osteoporos Int 2017; 28: 2475-2483.

31) Button KS, Ioannidis JP, Mokrysz C, Nosek BA, Flint J, Robinson ES, Munafò MR. Power failure: why small sample size undermines the reliability of neuroscience. Nat Rev Neurosci 2013; 14: 365-376.

32) Yong EL, Ganesan G, Kramer MS, Howe TS, Koh JSB, Thu WP, Logan S, Cauley JA, Tan KB. Risk Factors and Trends Associated With Mortality Among Adults With Hip Fracture in Singapore. JAMA Netw Open 2020; 3: e1919706.

33) Miralles-Muñoz FA, Perez-Aznar A, Gonzalez-Parreño S, Sebastia-Forcada E, Mahiques-Segura G, Lizaur-Utrilla A, Vizcaya-Moreno MF. Change in 1-year mortality after hip fracture surgery over the last decade in a European population. Arch Orthop Trauma Surg 2022: 1-7.

34) Cauley JA, Barbour KE, Harrison SL, Cloonan YK, Danielson ME, Ensrud KE, Fink HA, Orwoll ES, Boudreau R. Inflammatory Markers and the Risk of Hip and Vertebral Fractures in Men: the Osteoporotic Fractures in Men (MrOS). J Bone Miner Res 2016; 31: 2129-2138.

35) Lippi G, Targher G, Montagnana M, Salvagno GL, Zoppini G, Guidi GC. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Arch Pathol Lab Med 2009; 133: 628-632.

36) Sun H, Weaver CM. Decreased Iron Intake Parallels Rising Iron Deficiency Anemia and Related Mortality Rates in the US Population. J Nutr 2021; 151: 1947-1955.

37) Koury MJ, Ponka P. New insights into erythropoiesis: the roles of folate, vitamin B12, and iron. Annu Rev Nutr 2004; 24: 105-131.