EJMI

DOI: 10.14744/ejmi.2018.75047
EJMI 2018;2(1):29–34

Research Article

Association Between Admission Red Cell Distribution Width and Mortality in Elderly Hip Fracture Patients: A Retrospective Case Control Study

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Abstract

Objectives: Red cell distribution width (RDW) is an index of red blood cell heterogeneity. A high RDW value has been independently associated with increased mortality; however the relationship has been studied very little in the orthopedic literature. The aim of this study was to evaluate the association between RDW and mortality in elderly hip fracture patients.

Methods: First-time hip fracture patients older than 65 years of age were included in this study. Patients with multiple fractures or pathological fractures were excluded. Mortality data were collected via phone call at 3-month and 1-year time points from the fracture surgery. Patients who lived more than 1 year were classified as a control group (Group 1). Group 2 comprised patients who died within 1 year after fracture surgery, and Group 3 consisted of patients who died within a 3-month period after the operation. The primary variable of this study was admission RDW value. Age, gender, fracture type (extracapsular or intracapsular), American Society of Anesthesiologist score, and the Charlson Comorbidity Index were considered secondary preoperative variables. The case groups were statistically compared with the control group in terms of these variables.

Results: The primary result of our study was that patients who died within 3 months and within 1 year after hip fracture surgery had a higher admission RDW value than the survivors.

Conclusion: An elevated admission RDW level was associated with excess mortality in elderly hip fracture patients within postoperative 3 months and 1 year.

Keywords: Elderly, hip fracture, mortality, red cell distribution width

Hip fracture is associated with high mortality among elderly patients.[1] It was reported that 8.4%-36% of these patients die within 1 year.[1] Concomitant medical illness, advanced age, male gender, diabetes, dementia, fracture type, American Society of Anaesthesiologists (ASA) score, low serum albumin level and recently red blood cell distribution width (RDW) were suggested as the predictors of excess mortalit.[2, 3] RDW is an index of red blood cell heterogeneity performed routinely on a full blood count.[4] Erythrocytes differ in size, getting smaller during aging and the variation in size is quantified by RDW. High RDW value indicates greater variation in the cell size and reflects nutritional deficiencies, bone marrow dysfunction, systemic inflammation and oxidative stress.[4] The RDW was initially considered to be a tool to distinguish microcytic anemia but recent studies have suggested RDW has further clinical significance besides its possible utility in the evaluation of anemia.[5] It is also a consistent and strong predictor of

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Submitted Date: January 03, 2018 **Accepted Date:** January 30, 2018 **Available Online Date:** February 19, 2018

total and cause-specific mortality in older adults.[6] It was reported that an increased RDW was independently associated with increased mortality in chronically ill patients.[7] In orthopedic literature, relationship between high RDW and excess mortality has been studied very little. For this reason, the objective of this study was to evaluate the association between RDW level and mortality in elderly hip fracture patients. Our hypothesis was that if an elderly hip fracture patient hadhigh RDW value on admission, increased postoperative mortality could be expected.

Methods

Study Design

This is aretrospective case-control study approved by the ethics commitee of Balikesir University School of Medicine. Medical records of hip fracture patients treated at the Edremit State Hospital during the time period from august 2009 to november 2013 were analyzed. First time hip fracture patients older than 65 years of age were included in this study. Both of the intracapsular and extracapsular fractures were included. Patients with multiple fracture and pathological fracture were excluded. Mortality data were collected via phone call at the 3-month and 1-year time points from fracture date. Patients who lived more than 1 year were classified as 'control' group (group 1). We created 2 'case' group according to the mortality status. Group 2 involves patients who died within one year after the operation. Group 3 consist of patients who died within 3-month period after the fracture. Primary variable of this study was admission RDW value. Age, gender, fracture type (extracapsular or intracapsular), American Society of Anesthesiologist (ASA) score, Charlson Comorbidity Index (CCI) were considered as secondary preoperative variables. CCI has been validated in numerous mortality studies including in hip fracture patients.[8] Case groups were statistically compared to control group in terms of these variables. No informed consent was required for this study, as we used routinely collected medical data.

Laboratory Analysis

In each patient, venous blood samples were obtained and complete blood cell count (CBC) assessed in our biochemical laboratory. An automated blood cell counter was used for CBC measurement (Beckman Coulter® LH 780, California, USA). The intraassay and interassay quality control procedures and calibration were performed every day. The RDW is an automatically obtained parameter of CBC. The normal range for RDW in our laboratory is 11.5% to 14.5%.

Laboratory Analysis

Statistical analysis of data were performed via IBM SPSS statistics 22.0. Whether the data are normally distributed were studied by Shapiro-Wilk test. Descriptive statistics of the data were expressed as median (minimum, maximum) for variables with an abnormal distribution in continuous data and as frequency, percent (n (%)) for categorical variables. Kruskal Wallis test was used to compare more than two independent groups for abnormally distributed continuous data. Mann-Whitney U test was used to compare independent two groups. Pearson chi-square test, Fisher-Freeman-Halton test, Yate's correction for continuity chi-squared test and Fisher exact chi-square test were used for analyzing of categorical data. Bonferroni correction was performed for correction of type 1 error in pairwise comparison. Receiver operating characteristic (ROC) analysis was performed to determine cut-off value of RDW level and related values, area under the curve and it's standard error, 95% confidence intervals, sensitivity and specifity values were given together. Related cut-off values were calculated according to the Youden index. Binary logistic regression analysis was used to detect of common effect of independent variables on dependent variables with two results. Level of significance was defined as $\propto$=0.05.

Table 1. Comparison of the groups in terms of preoperative variables

	Control group (n=112)	Group 2 (n=54)	Group 3 (n=27)	p
Age (mean)	79.50 (65-97)	84.50 (65-95)	86 (65-95)	0.002
Male n (%)	36 (32.1)	29 (53.7)	15 (55.6)	0.013
Female n (%)	76 (67.9)	25 (46.3)	12 (44.4)	
ASA	2.83 (1-4)	3.24 (2-4)	3.40 (2-4)	<0.001
CCI	2.44 (0-4)	3.03 (1-5)	3.18 (2-6)	<0.001
RDW	14.60 (7.90-49.90)	16.57 (13.20-47.40)	16.30 (13.29-23.83)	0.014
Extracapsularfx n (%)	64 (57.1)	32 (59.3)	17 (63)	0.800
Intracapsularfx n (%)	48 (42.9)	22 (40.7)	10 (37)	

ASA: American society of anaesthesiologists; CCI: Charlson comorbidity index; RDW: Red blood cell distribution width.

Results

One hundred and sixty-six patients were included in this study. Sixtynine (41.56%) of patients were men and 97 (58.44%) were women. Mean age of patients was 79.16 (65-95) years. Extracapsular fracture was detected in 97 (58.44%) patients and intracapsular fracture in 69 (41.56%) patients.

Group 1 (control group) consisted of 112 (67.46%) patients and group 2 consisted of 54 (32.53%) patients. It was detected that 27 patients (16.26%) (group 3) had died within 3 months after the surgery. Thirty-six (32.1%) of group 1 patients were men and 76 (67.9%) were women, 29 (53.7%) of group 2 were men and 25 (46.3%) were women, 15 (55.6%) of group 3 were men and 12 (44.4%) were women. Mean ages were 79.50 (65-97) for group 1, 84.50 (65-95) for group 2, and 86 (65-95) for group 3. Mean ASA scores of groups were 2.83 (1-4), 3.24 (2-4), and 3.40 (2-4) for group 1, 2 and 3 respectively. Mean CCI of groups were 2.44 (0-4), 3.03 (1-5) and 3.18 (2-6) for group 1, 2 and 3 respectively. Mean RDW value of each groups were calculated as 14.60 (7.90-49.90), 16.57 (13.20-47.40) and 16.30 (13.29-23.83) for group 1, 2 and 3 respectively.

We foundstatistically significant difference between groups in terms of age, gender, ASA score, CCI and RDW value. No significant difference was found in terms of fracture type. (Table 1) Patients with low and high RDW value were compared in each group andstatistically significant difference was found in group 2 and 3 only. (Fig. 1) Paired comparison was performed in terms of admission RDW value and statistically significant difference was found between group 1 (control)–group 2 (1 year mortality) and group 1 (control)–group 3 (3 months mortality) (p=0.001, p=0.002). Statistically significant difference was found between group 1 and 2 in terms of age, gender (1 year mortality is higher in male gender), ASA score and CCI. When group 1 compared to the group 4 (3 monhts mortality), statistically significant difference was found in terms of age, ASA score, CCI. ROC analysis results are seen in table 2 and figure 2. Cut-off value was detected as 14.5 for 1 year and 3 months mortality in ROC analysis. Results of binary logistic regression analysis are seen in table 3 and 4.

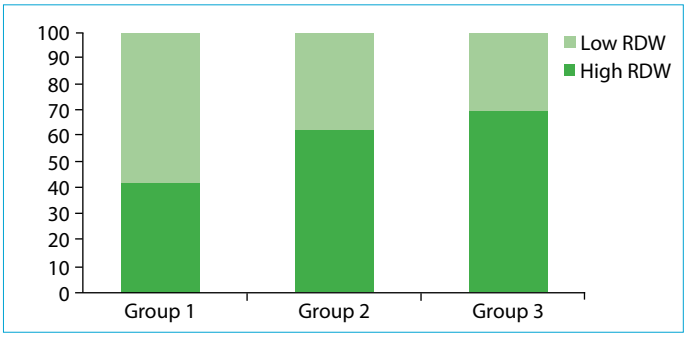

Figure 1. Intragroup comparison of patients with high and low RDW value (cut-off=14.5, p=0.0014).

Discussion

Primary result of our study is that patients who died within 1 year and 3 months period after the hip fracture surgery have higher admission RDW value than survivors. When intragroup comparison of high and low RDW patients were performed, statistically significant difference was detected only in group 2 (1 year mortality group) and group 3 (3 months mortality group). Between groups, statistically significant difference was detected in terms of age, gender, ASA score and CCI but there was no significant difference regarding the fracture type.

An association between high RDW value andexcess mortality especially in patients with heart failure, acute myocardial infarction, community acquired pneumonia, pulmonary hypertension and in the general population has been reported in the literature.[7] The relationship between high RDW value and increased mortality has been investigated in hip fracture patients.[2, 9, 10] Garbharran et al.[9] reported

Table 3. Result of logistic regression analysis for 1 year mortality. Odds ratios and P values of statistically significant variables as indicated as bold

	Odds Ratio	95% confident interval for odds ratio	p
Gender (female reference)	2.306	1.210-4.396	0.011
Age	1.034	0.987-1.084	0.158
RDW (refence <14.5)	3.044	1.432-6.474	0.004
Fracture type (refernce extracapsular)	1.139	0.595-2.179	0.695
ASA	2.405	1.279-4.520	0.006
CCI	1.055	0.665-1.673	0.821

ASA: American society of anaesthesiologists; CCI: Charlson comorbidity index.

Table 2. ROC analysis results. Statistically significant cut-off values were indicated as bold

	Area under the curve	Standart error	95% confident interval	p	Cut-off	Sensitivity	Specificity
1 year mortality	0.675	0.038	0.605-0.740	<0.001	14.5	83.72	47.32
3 months mortality	0.636	0.636	0.565-0.703	0.004	14.5	90.62	38.55

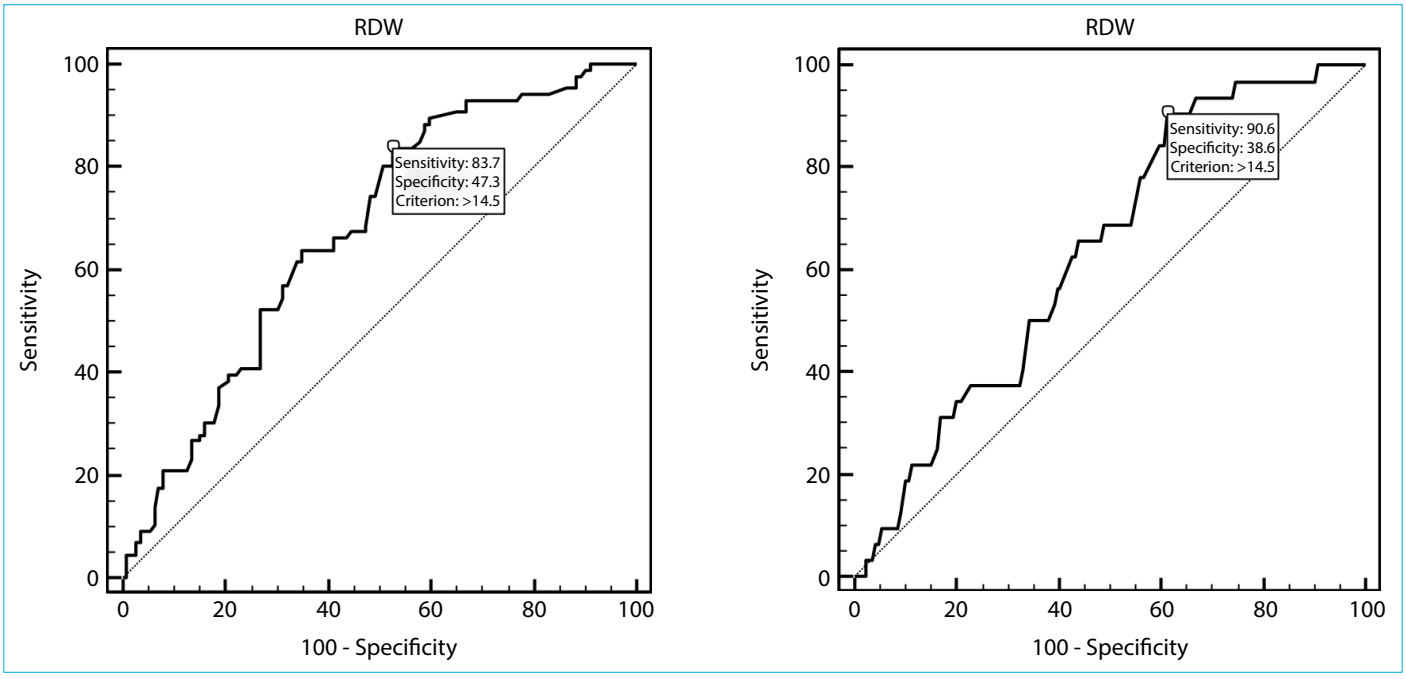

Figure 2. ROC analysis graphics of 1 year and 3 months mortality.

Table 4. Result of logistic regression analysis for 3 months mortality Odds ratios and P values of statistically significant variables as indicated as bold

	Odds Ratio	95% confident interval for odds ratio	p
Gender (female reference)	1.396	0.625-3.118	0.416
Age	1.029	0.970-1.091	0.344
RDW (refence <14.5)	4.124	1.138-14.948	0.031
Fracture type (refernce extracapsular)	1.199	0.526-2.733	0.665
ASA	2.271	1.040-4.959	0.040
CCI	1.060	0.586-1.916	0.848

ASA: American society of anaesthesiologists; CCI: Charlson comorbidity index; RDW: Red blood cell distribution width.

that high RDW value has a significant independent association with 'in-hospital', 120-day and 1-year mortality. Zehir et al.[2] found a significant correlation between an elevated RDW level and mortality in hip fracture patients treated with partial prosthesis. Recently, in study of Lv et al.,[10] a strong and independent association between admission RDW value and the risk of long-term all-cause mortality has been detected in hip fracture patients. Our study agrees with the finding of previous studies. We also think that high RDW value may be a risk factor for 3-months and 1-year mortality in elderly hip fracture patient.

A variety of mechanism have been proposed for the association between RDW and mortality. One of the possible explanations is that an increased RDW is caused by a state of inflammation.[11] Perlstein et al.[6] found an association between RDW and C-reactive protein (CRP) in a community-based cohort. Chronic subclinical inflammation may alter red blood cell circulation half-life, erythropoiesis and red blood cell membrane deformability, factors that might lead to a more mixed population of red blood cell volumes in the circulation.[12] Exposure to greater oxidative stress might be another potential contributing mechanism. In patients with conditions characterized by increased level of oxidative stress such as poor pulmonary function and dialysis, RDW values are elevated.[13] Iron, folate and vitamin B12 deficiencies can cause an increased RDW but Perlstein et al.[6] found RDW to be an independent predictor of mortality even after correction for vitamin deficiencies. Bone marrow dysfunction, haemodilution, renal insufficiency and abnormalities of erythropoietin response have also been mentioned as possible explanations.[14] Anemia might affect RDW value and hemoglobine level should be adjusted when detecting the independent value of RDW.[10] In the study of Lv et al.,[10] RDW was higher in anemic patients than non-anemic patients. Furthermore, anemia itself is a significant negative prognostic factor for mortality in hip fracture patients.[15] We did not account anemia and nutritional deficiencies as confounding factors for RDW value. For this reason, we can not say that RDW is an 'independent' risk factor for excess mortality in elderly hip fracture patient.

Advanced age and male gender have been identified as strong evidence mortality predictors in the study of Hu et al.[1]

Forsen et al.[16] found that patients older than 85 years had excess mortality especially 3 months postoperatively. Sener et al.[3] reported that advanced age increased the mortality rate after hip fracture. Based on our study results, we think that there is a relationship between advanced age and excess mortality after hip fracture surgery. However, Ozturk et al.[17] established no association between age and mortality.

The effect of gender on mortality after hip fracture is debatable.[17] Franzo[18] and Jiang[19] detected the mortality rate was higher in males, whereas Alegre-Lopez[20] reported a higher rate in females. Ozturk et al.[17] reported that the mortality rate was higher in female patients but the difference was not significant. We detected that 1 year mortality rate is higher in male.

Association between comorbidities and mortality in elderly hip fracture patients is established.[1] We also detected that both of the 1 year and 3 months mortality rates were associated with the ASA score and CCI. In study of Hu et al.,[1] intertrochanteric fracture (versus femoral neck fracture)has been reported as moderate evidence mortality predictor. In spite of that, Smith et al.[21] reported that intracapsular fracture was associated with increased risk of mortality following hip fracture surgery. There was no relationship between fracture type and mortality in our study.

Current study hadseveral limitations. This is a retrospective, observational study of small patient population. Observational studies are prone to selection, attrition and detection bias. It is also possible that recall bias has influenced the mortality information of patients. The existance of other confounding factors for RDW level (anemia, nutritional status) and mortality (surgical delay) cannot be ruled out in our study. In our study, single RDW value (admission) was evaluated. Serial measurements of RDW may allow better characterization of the associations of RDW with mortality risk.

Despite these limitations, we conclude that elevated admission RDW level is associated with the excess 1 year and 3 months postoperative mortality in elderly hip fracture patients. We think that RDW, a readily available laboratory biomarker, may be a prognostic variable for risk stratification in the elderly hip fracture patients.

Disclosures

Ethics Committee Approval: The study was approved by the Local Ethics Committee.

Peer-review: Externally peer-reviewed.

Conflict of Interest: None declared.

Authorship contributions: Concept – A.T., M.D.; Design – A.T., M.D.; Supervision – A.T., M.D.; Materials – A.T., M.D.; Data collection &/or processing – A.T., M.D.; Analysis and/or interpretation – A.T., M.D.; Literature search – A.T., M.D.; Writing – A.T., M.D.; Critical review – A.T., M.D.

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