Published Online: 2024 September 18

Research Article

Red Blood Cell Distribution Width (RDW) During Admission and Anxiety Following Acute Myocardial Infarction

Yasaman Borghei [1], Arsalan Salari [1], Bahare Gholami Chaboki [1], Nasibe Goli [1], Aseme Pourrajabi [1], Samira Arami [1,*]

[1] Department of Cardiology, Cardiovascular Diseases Research Center, Heshmat Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran

[*] ***Corresponding Author:*** Department of Cardiology, Cardiovascular Diseases Research Center, Heshmat Hospital, School of Medicine, Guilan University of Medical Sciences, Rasht, Iran. Email: dr.sarami202@gmail.com ; samiraarami532@gmail.com

Received: 28 April, 2024; **Revised:** 20 May, 2024; **Accepted:** 2 August, 2024

Abstract

Background: Myocardial infarction (MI), a life-threatening event, is often accompanied by an increased risk of anxiety. There is a growing association between anxiety and cardiovascular disease (CVD). Recent studies have shown that anxiety is associated with blood inflammatory markers, such as red blood cell distribution width (RDW).

Objectives: We aimed to evaluate RDW levels during admission and anxiety levels after acute myocardial infarction (AMI).

Methods: In this cross-sectional study, 250 patients with AMI participated during 2023-2024. Demographic information and RDW levels were obtained within 24 hours after admission. The intensity of anxiety was evaluated using the Hamilton Anxiety Rating Scale (HRSA) two weeks after the occurrence of AMI. All data analyses were performed using SPSS version 24.

Results: Of the total participants, 51.6% experienced anxiety two weeks after AMI. The mean age of patients in the anxiety and non-anxiety groups was 59.77 ± 10.10 and 62.68 ± 12.20 years, respectively. Among the laboratory parameters, only blood urea nitrogen was statistically different between the two groups ($P < 0.027$). The RDW level was 13.63 ± 1.20 in the anxiety group and 13.59 ± 1.51 in the non-anxiety group ($P > 0.174$). There was no statistically significant difference between RDW levels and post-AMI anxiety ($P > 0.001$).

Conclusions: This study is the first to investigate the predictive value of RDW for post-AMI anxiety. Based on our findings, no significant relationship was observed between RDW and anxiety following AMI. Therefore, further studies in this field are needed to determine whether this cost-effective and readily available marker should be used for anxiety prediction after AMI.

Keywords: Anxiety, Red Blood Cell Distribution Width, Acute Myocardial Infarction

1. Background

Red blood cell distribution width (RDW) is a parameter that indicates the variation in size of red blood cells (RBCs) (1) and is typically reported as part of a standard complete blood count. RDW, along with other parameters from a complete blood count, is used to identify hematological diseases (2). Recently, it has been shown that RDW can also be used to predict mortality in coronary artery diseases, acute heart failure, and acute myocardial infarction (AMI) (3). One study suggested that RDW may be a reliable marker for mortality in both chronic and acute conditions (4). The majority of cardiovascular deaths occur following AMI (5), which is one of the most serious cardiovascular events (2, 6).

MI is a severe, life-threatening event that is associated with an increased risk of anxiety (7). There is a growing association between anxiety and cardiovascular disease (CVD) (8). Independent of CVD, depression and anxiety are major contributors to disability and mortality, affecting 260 million people globally (8). Recent studies have shown that anxiety is associated not only with serum C-reactive protein levels but also with blood inflammatory markers, including white blood cell (WBC) count and RDW (9). Furthermore, several studies have examined blood indices, including RDW, in psychiatric populations. Measurement of these

parameters is simple and inexpensive, making it an appropriate choice for frequent assessment (10, 11).

2. Objectives

Given the cost-effectiveness, availability, and routine use of the RDW test (12) and the known relationship between anxiety and CVD, including AMI, we decided to investigate the changes in RDW and its relation to anxiety two weeks after AMI.

3. Methods

3.1. Participants

In this cross-sectional study, 250 consecutive patients with AMI who were referred to Dr. Heshmat Hospital in Rasht, Iran, during 2023-2024 were investigated. The study procedure began after obtaining ethical approval with the code IR.GUMS.REC.1402.237 from Guilan University of Medical Sciences. Patients were included in the study if they had a diagnosis of AMI confirmed by a cardiologist, were over 18 years of age, had adequate cognitive ability to answer questions, and did not have mental or physical problems, including neurological and mental diseases such as depression. The exclusion criteria included the presence of fatigue before the occurrence of AMI (according to the patient's statements), failure to measure RDW within 24 hours after admission, presence of blood diseases such as leukemia and myelodysplastic syndrome, and death during hospitalization or within one day of discharge. Informed consent was obtained from all patients who participated in the study.

3.2. Data Collection

Demographic information such as age, sex, systolic and diastolic blood pressure (BP), and history of diseases was obtained from patients' medical records. Laboratory parameters, including fasting blood sugar (FBS), total cholesterol, triglycerides, low-density lipoprotein (LDL), high-density lipoprotein (HDL), creatinine, blood urea nitrogen (BUN), and RDW (our main variable), were collected within 24 hours after admission from the laboratory test results. The intensity of anxiety was evaluated using the Hamilton Anxiety Rating Scale (HRSA) at baseline and two weeks after the occurrence of AMI. The HRSA consists of 14 questions, each scored up to 4 points, with a maximum total score of 56. We considered a total score of less than 25 as indicative of no anxiety and a score of 25 or greater as indicative of anxiety.

3.3. Statistical Analysis

Qualitative variables were reported as frequency and percentage. The Kolmogorov-Smirnov test was used to check the normality of quantitative variables. If these variables were normally distributed, they were reported with the mean and standard deviation; otherwise, they were reported with the median and interquartile range. After collecting the data, based on the results of the HRSA, the data were divided into two groups: With anxiety and without anxiety. The initial investigation of the research variables in these two groups was performed using independent *t*-tests, Mann-Whitney tests, chi-square tests, or Fisher's exact tests. Finally, to assess the relationship between RDW and anxiety while adjusting for auxiliary variables, a logistic regression model was fitted to the data. Data analysis was performed using SPSS version 24 software.

4. Results

Based on our findings, 129 (51.6%) patients in our study experienced anxiety two weeks after the occurrence of AMI. Of the total 250 participants, 69.8% were male and 30.2% were female. The mean ± SD age of patients in the anxiety and non-anxiety groups was 59.77 ± 10.10 and 62.68 ± 12.20 years, respectively. Among the laboratory parameters, only blood urea nitrogen (BUN) was statistically different between the two groups (P = 0.027). The RDW was 13.63 ± 1.20 in patients with anxiety and 13.59 ± 1.51 in the non-anxiety group (P = 0.174). Other patient information is shown in Table 1.

Figure 1 shows the violin plot for RDW distribution in the anxiety and non-anxiety groups. The median and the first and third quartiles are nearly identical in both groups. The violin plot also identifies an outlier in the anxiety group.

Multivariable regression was used to assess the relationship between RDW and anxiety. In model 1 (unadjusted model) [OR (odds ratio), 0.978; 95% CI, 0.816 - 1.173; P = 0.809], model 2 (adjusted for age and gender) [OR, 0.960; 95% CI, 0.798 - 1.154; P = 0.661], model 3 (adjusted for age, gender, and BUN) [OR, 0.949; 95% CI, 0.787 - 1.144; P = 0.584], and model 4 (adjusted for age, gender, BUN, previous AMI, and CVD) [OR, 0.932; 95% CI, 0.769 - 1.130; P = 0.475], no significant relationship was found between RDW and anxiety (Table 2).

5. Discussion

Cardiovascular disease, depression, and anxiety are prominent contributors to disability and mortality, affecting 260 million individuals globally (8). Recent

Table 1. Baseline Information of Patients in Patients with Anxiety and Without It [a]

Variables	Anxiety 129 (51.6)	Non-anxiety 121 (48.4)	P-Value
Gender			
Male	90 (69.8)	92 (76)	0.266
Female	39 (30.2)	29 (24)	
Age	59.77 ± 10.10	62.68 ± 12.20	0.040 [b]
Laboratory parameters			
FBS	137.99 ± 62.52	138.65 ± 64.34	0.932
Chol	155.71 ± 52.91	152.65 ± 44.14	0.971
TG	202.92 ± 150.21	189.69 ± 146.6	0.152
BUN	19.85 ± 6.76	18.38 ± 6.05	0.027 [b]
Cr	1.12 ± 0.37	2.3 ± 10.66	0.061
RDW	13.63 ± 1.20	13.59 ± 1.51	0.174
Underlying diseases			
HTN	77 (59.7)	66 (54.5)	0.411
HLP	57 (44.2)	53 (43.8)	0.951
DM	39 (30.2)	49 (40.5)	0.090
Arthritis	1 (0.8)	3 (2.5)	0.357
CVDs			
Previous	11 (8.5)	3 (2.5)	0.038
AMI	6 (4.7)	0 (0)	0.30 [b]
Systolic BP	134.34 ± 20.04	136.72 ± 22.31	0.274
Diastolic BP	79.51 ± 17.21	79.92 ± 11.08	0.659

Abbreviations: AMI, acute myocardial infraction; BP, blood pressure; Bun, blood urea nitrogen; Cr, creatinine; Chol, cholesterol; CVDs, cardiovascular diseases; DM, diabetes mellitus; FBS, fasting blood sugar; RDW, red blood cell distribution width; TG, triglyceride; RDW, red blood cell distribution width.

[a] Values are expressed as mean ± SD or No. (%).

[b] Significant.

evidence has revealed that high levels of anxiety are associated with poor prognosis in patients with MI (13). Additionally, anxiety is associated with blood inflammatory markers such as RDW (9). Given the importance of this issue, in this study, we decided to evaluate RDW as a predictive serum marker for post-AMI anxiety. Based on different analyses, our results showed no significant correlation between RDW and anxiety after AMI.

In line with our findings, Vulser et al. found no significant association between depressive and anxiety symptoms and inflammatory markers (14). In contrast, in the study by Peng et al., which investigated the relationship between RDW and post-stroke fatigue, a relation between RDW and anxiety was shown (15). It should be noted that they also used the HRSA. The study by Shafiee et al. revealed that higher anxiety scores are associated with higher hematological inflammatory markers, including RDW (16). However, they used the Beck Depression and Anxiety Inventories (BDI) to assess anxiety.

In contrast to our findings, several recent studies have hypothesized that high RDW levels among individuals with anxiety may predict the risk of CVDs (17, 18). Moreover, Fábián et al. indicated that RDW has no predictive impact on patients with anxiety based on BDI (11). In our study, most of the patients who experienced anxiety were men, whereas in other studies, anxiety following AMI seems to disproportionately impact women (8).

A previous study indicated that increased RDW may result from an underlying inflammatory state associated with negative outcomes in patients (19). Some studies have demonstrated that RDW measurements are useful in differentiating individuals with various psychiatric disorders (20, 21). A significant finding in our study was the higher BUN level in patients with post-AMI anxiety. Interestingly, consistent with our findings, Qawaqzeh et al. showed that a decreased BUN level was a predictor of increased depressive and anxiety symptoms (22). Since no similar study has investigated the relationship between anxiety,

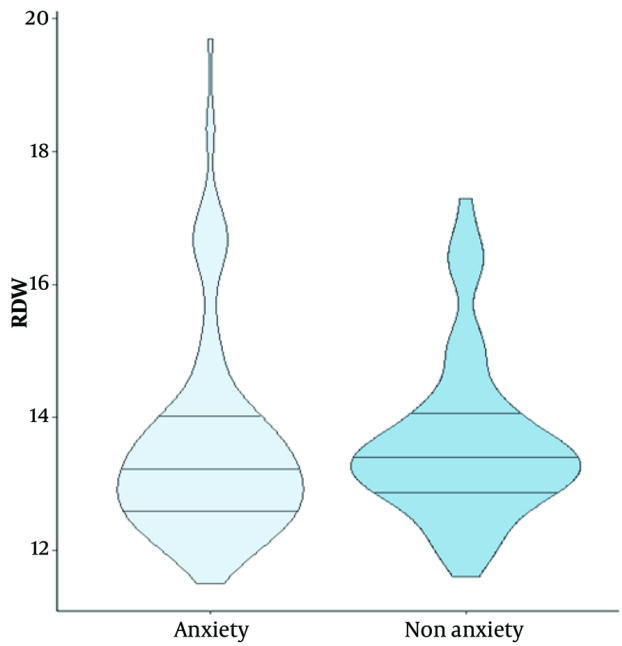

Figure 1. The violin plot for anxiety and non-anxiety distribution

Table 2. Logistic Regression Analysis of Relation Between Anxiety and Red Blood Cell Distribution Width [a]

Model	SE	Wald	OR (95%CI)	P-Value
Model 1	0.093	0.058	0.978 (0.816 - 1.173)	0.978
Model 2	0.094	0.192	0.960 (0.798 - 1.154)	0.661
Model 3	0.095	0.299	0.949 (0.787 - 1.144)	0.584
Model 4	0.098	0.511	0.932 (0.769 - 1.130)	0.932

[a] Model 1 unadjusted model; model 2 was adjusted for age and gender; model 3 was adjusted for age, gender and Bun; model 4 was adjusted for age, gender and bun, previous AMI, CVD.

RDW, and AMI, we could not accurately compare the results of our study with others.

5.1. Conclusions

The present study is the first to determine the predictive value of RDW on post-AMI anxiety. Based on our findings, no significant relationship was observed between RDW and anxiety following AMI. Therefore, conducting more studies in this field would be helpful in determining whether this marker should be used for anxiety prediction after AMI.

Footnotes

Authors' Contribution: Study concept and design: Yasaman Borghei and Arsalan Salari; acquisition of data: Arsalan Salari and Nasibe Goli; analysis and interpretation of data: Bahare Gholami Chaboki; drafting of the manuscript: Yasaman Borghei; critical revision of the manuscript for important intellectual content: Samira Arami and Aseme Pourrajabi; statistical analysis: Bahare Gholami Chaboki; administrative, technical, and material support: Samira Arami.

Conflict of Interests Statement: The authors declared no conflict of interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author

during submission or after publication.

Ethical Approval: The study procedure began after obtaining ethical approval with code of IR.GUMS.REC.1402.237 from Guilan University of Medical Sciences.

Funding/Support: Authors declared no fund was received for this study.

Informed Consent: Informed consent was obtained from all patients who participated in the study.

References

1. Yu XS, Chen ZQ, Hu YF, Chen JX, Xu WW, Shu J, et al. Red blood cell distribution width is associated with mortality risk in patients with acute respiratory distress syndrome based on the Berlin definition: A propensity score matched cohort study. *Heart Lung*. 2020;**49**(5):641-5. [PubMed ID: 32434701]. https://doi.org/10.1016/j.hrtlng.2020.04.008.
2. Chen M, Liao L, Yan J, Lin FQ. Predictive Value of Red Blood Cell Distribution Width for 1-Year All-Cause Mortality in Critically Ill Patients with Acute Myocardial Infarction. *Int J Gen Med*. 2022;**15**:465-71. [PubMed ID: 35046707]. [PubMed Central ID: PMC8760980]. https://doi.org/10.2147/ijgm.S345109.
3. Ye WY, Li J, Li X, Yang XZ, Weng YY, Xiang WW, et al. Predicting the One-Year Prognosis and Mortality of Patients with Acute Ischemic Stroke Using Red Blood Cell Distribution Width Before Intravenous Thrombolysis. *Clin Interv Aging*. 2020;**15**:255-63. [PubMed ID: 32110004]. [PubMed Central ID: PMC7039056]. https://doi.org/10.2147/cia.S233701.
4. Oh HJ, Park JT, Kim JK, Yoo DE, Kim SJ, Han SH, et al. Red blood cell distribution width is an independent predictor of mortality in acute kidney injury patients treated with continuous renal replacement therapy. *Nephrol Dial Transplant*. 2012;**27**(2):589-94. [PubMed ID: 21712489]. https://doi.org/10.1093/ndt/gfr307.
5. Blakeman JR, Woith WM, Astroth KS, Jenkins SH, Stapleton SJ. A qualitative exploration of prodromal myocardial infarction fatigue experienced by women. *J Clin Nurs*. 2020;**29**(19-20):3882-95. [PubMed ID: 32730655]. https://doi.org/10.1111/jocn.15432.
6. Nikfarjam S, Borghei Y, Salari A, Miraftabi SM, Gholami-Chaboki B, Fakhr-Moosavi SA. Short-term Clinical Outcomes of Ticagrelor versus Clopidogrel after Percutaneous Coronary Intervention in Patients with Myocardial Infarction: A Randomized Clinical Trial Study. *Res Cardiovascular Med*. 2023;**12**(2):56-60. https://doi.org/10.4103/rcm.rcm_24_23.
7. Figueiredo JHC, Silva N, Pereira BB, Oliveira GMM. Major Depression and Acute Coronary Syndrome-Related Factors. *Arq Bras Cardiol*. 2017;**108**(3):217-27. [PubMed ID: 28443957]. [PubMed Central ID: PMC5389871]. https://doi.org/10.5935/abc.20170028.
8. Liblik K, Mulvagh SL, Hindmarch CCT, Alavi N, Johri AM. Depression and anxiety following acute myocardial infarction in women. *Trends Cardiovasc Med*. 2022;**32**(6):341-7. [PubMed ID: 34363978]. https://doi.org/10.1016/j.tcm.2021.07.005.
9. Shafiee M, Ahmadnezhad M, Tayefi M, Arekhi S, Vatanparast H, Esmaeili H, et al. Depression and anxiety symptoms are associated with prooxidant-antioxidant balance: A population-based study. *J Affect Disord*. 2018;**238**:491-8. [PubMed ID: 29935471]. https://doi.org/10.1016/j.jad.2018.05.079.
10. Pariante CM. Why are depressed patients inflamed? A reflection on 20 years of research on depression, glucocorticoid resistance and inflammation. *Eur Neuropsychopharmacol*. 2017;**27**(6):554-9. [PubMed ID: 28479211]. https://doi.org/10.1016/j.euroneuro.2017.04.001.
11. Fábián B, Horváth IF, Shemirani AH, Csiki Z. Depression and Anxiety Symptoms Are Associated with Mean Platelet Volume in Autoimmune Disorders. *Int J Environ Res Public Health*. 2022;**19**(17). [PubMed ID: 36078719]. [PubMed Central ID: PMC9518376]. https://doi.org/10.3390/ijerph191711006.
12. Khorasanchi Z, Azarpajouh M, Ferns G. Depression and anxiety symptoms are associated with white blood cell count and red cell distribution width: a sex-stratified analysis in a population-based study. *Iran J Psychiatry Clinical Psychol*. 2017;**3**(62).
13. Wen Y, Yang Y, Shen J, Luo S. Anxiety and prognosis of patients with myocardial infarction: A meta-analysis. *Clin Cardiol*. 2021;**44**(6):761-70. [PubMed ID: 33960435]. [PubMed Central ID: PMC8207975]. https://doi.org/10.1002/clc.23605.
14. Vulser H, Wiernik E, Tartour E, Thomas F, Pannier B, Czernichow S, et al. Smoking and the Association Between Depressive Symptoms and Absolute Neutrophil Count in the Investigations Préventives et Cliniques Cohort Study. *Psychosom Med*. 2015;**77**(9):1039-49. [PubMed ID: 26461856]. https://doi.org/10.1097/psy.0000000000000243.
15. Peng M, Chen Y, Chen Y, Feng K, Shen H, Huang H, et al. The relationship between red blood cell distribution width at admission and post-stroke fatigue in the acute phase of acute ischemic stroke. *Front Neurol*. 2022;**13**:922823. [PubMed ID: 35968310]. [PubMed Central ID: PMC9366669]. https://doi.org/10.3389/fneur.2022.922823.
16. Shafiee M, Tayefi M, Hassanian SM, Ghaneifar Z, Parizadeh MR, Avan A, et al. Depression and anxiety symptoms are associated with white blood cell count and red cell distribution width: A sex-stratified analysis in a population-based study. *Psychoneuroendocrinology*. 2017;**84**:101-8. [PubMed ID: 28697416]. https://doi.org/10.1016/j.psyneuen.2017.06.021.
17. Blumenthal JA. Depression and coronary heart disease: association and implications for treatment. *Cleve Clin J Med*. 2008;**75 Suppl 2**:S48-53. [PubMed ID: 18540147]. https://doi.org/10.3949/ccjm.75.suppl_2.s48.
18. Montagnana M, Cervellin G, Meschi T, Lippi G. The role of red blood cell distribution width in cardiovascular and thrombotic disorders. *Clin Chem Lab Med*. 2011;**50**(4):635-41. [PubMed ID: 22505527]. https://doi.org/10.1515/cclm.2011.831.
19. Khorasanchi Z, Mayvan MR, Hasanzadeh E, Allahyari M, Moghadam RR, Asadiyan-Sobhan P, et al. The Association of Hematological Inflammatory Markers and Psychological Function Among in COVID-19 Patients: a Cross Sectional Study. *Res Square*. 2022. https://doi.org/10.21203/rs.3.rs-1174423/v1.
20. Demircan F, Gözel N, Kılınç F, Ulu R, Atmaca M. The Impact of Red Blood Cell Distribution Width and Neutrophil/Lymphocyte Ratio on the Diagnosis of Major Depressive Disorder. *Neurol Ther*. 2016;**5**(1):27-33. [PubMed ID: 26686339]. [PubMed Central ID: PMC4919129]. https://doi.org/10.1007/s40120-015-0039-8.
21. Gundogmus İ, Algul A, Karagöz A, Kıyançiçek M. PDW and RDW are new parameters for bipolar episodes and unipolar depression. *Psychiatry Clinical Psychopharmacol*. 2019;**29**(4):520-6.
22. Qawaqzeh DTA, Masa'deh R, Hamaideh SH, Alkhawaldeh A, A. LBashtawy M. Factors affecting the levels of anxiety and depression among patients with end-stage renal disease undergoing hemodialysis. *Int Urol Nephrol*. 2023;**55**(11):2887-96. [PubMed ID: 36995556]. [PubMed Central ID: PMC10061404]. https://doi.org/10.1007/s11255-023-03578-1.