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Original Article

The predictive significance of red cell distribution width in anterior ST- elevation myocardial infarction and its relationship with hospital mortality

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Abstract

Objectives: The clinical diagnosis of acute myocardial infarction (AMI) involves assessing the patient's medical history and indirect evidence of myocardial necrosis using biochemical, electrocardiogram (ECG), or imaging methods. Ischemia, hypoxia, and myocardial necrosis result from a disrupted blood supply to the coronary arteries, typically due to atherosclerosis, thrombosis, and coronary artery obstruction. Given the rising incidence and healthcare costs of ST-elevation myocardial infarction (STEMI), particularly anterior STEMI (ant-STEMI), this study examines the diagnostic value of red cell distribution width (RDW) in ant-STEMI patients and its impact on hospital and one-year mortality post-primary angioplasty.

Methods: This study focused on patients with ant-STEMI undergoing primary angioplasty at Shahid Madani Hospital, Tabriz, Iran, from 2018 to 2019. Exclusion criteria included patients receiving drug or antithrombotic treatment, undergoing coronary artery bypass grafting (CABG), not receiving primary percutaneous coronary intervention (PPCI), suffering from STEMI types other than anterior STEMI, having a history of thalassemia or anemia, and those with incomplete patient records. In-hospital complications, such as cardiogenic shock, hematoma, bleeding, and heart failure (HF), were recorded and analyzed using SPSS 23.

Results: In this retrospective and analytical study of 300 patients, there was no significant relationship between RDW levels and in-hospital (P-value=0.59) and one-year mortality (P-value=0.68). However, RDW was significantly associated with hospital complications such as HF, cardiogenic shock, angio-hematoma, gastrointestinal bleeding, and stent thrombosis (P-value<0.01).

Conclusions: Our study showed that RDW is not a reliable prognostic factor for mortality in anterior STEMI patients.

Keywords: Acute myocardial infarction, Red cell distribution width, Hospital mortality

Introduction

Acute myocardial infarction (AMI) is a type of acute coronary syndrome (ACS), which can be divided into two groups: ST-elevation myocardial infarction (STEMI) and non-ST-elevation myocardial infarction (NSTEMI) based on whether there is ST segment

elevation on the (1). STEMI typically arises when there is a sudden reduction in coronary blood flow due to thrombotic blockage of a coronary artery that has already been narrowed by atherosclerosis, resulting in complete blockage of the artery. Conversely, a reduction in oxygen supply or an increase in oxygen demands in the myocardium related to coronary obstruction can trigger NSTEMI. The primary clinical indication of STEMI is chest pain, usually experienced in the region below the sternum or occasionally in the epigastric area (2). The World Health Organization (WHO) and the American Heart Association (AHA) have identified at least two of the following criteria as essential for diagnosing STEMI: characteristic clinical symptoms of a myocardial infarction (MI); changes in the electrocardiogram (ECG); and expected elevations followed by reductions in biochemical markers (1). Reperfusion treatment for AMI tries to reduce mortality rates (3).Consequently, it is crucial to establish stable and improved conditions for coronary arteries affected by infarction. By restoring blood flow in the blocked artery within 12 hours of the onset of pain, complications and mortality rates diminish. Restoration can be accomplished either mechanically through primary percutaneous coronary intervention (PPCI) or by administering thrombolytics (4, 5). Red cell distribution width (RDW) has emerged as a significant predictor of mortality in cardiovascular diseases (CVD). RDW is a marker for anisocytosis, indicating the variation in red blood cell (RBC) size. High RDW levels are linked to impaired red blood cell (RBC) production, often resulting from inflammation and pathophysiological processes. In CVD, elevated RDW is associated with poor outcomes due to several mechanisms (6). Elevated RDW is associated with a reduced ability to clear old RBCs from circulation, resulting from inflammation and oxidative stress. Smaller and less functional RBCs persist in circulation, resulting in a greater distribution of the size of RBCs, leading to a higher RDW value. Moreover, this increased RDW is associated with poor prognoses in conditions such as heart failure and coronary artery disease. The higher levels of RDW in the present study signify a non-specific indicator of systemic inflammation, which represents an overstimulated hematopoietic activity in patients with CVD and may increase the overall mortality risk in patients with CVD (7). Several more recent biochemical investigations have looked at relations between RDW and other proteins related to the inflammatory and pathological changes seen in cardiovascular disease, including growth differentiation factor 15 (GDF-15) and the matrix metalloproteinases, which are both involved in tissue remodeling and inflammation, all showing that increased levels of RDW are again indicative of increased mortality for CVD disease patients. RDW is an indicator of an elevated inflammatory state of oxidative stress and abnormal regulation of RBC, which makes this marker valuable for risk assessment and prognosis in diseases related to atherosclerotic CVD and a chronic immune response (8-10).Research indicates that elevated RDW levels in individuals with STEMI undergoing percutaneous coronary intervention (PCI) are linked to a higher likelihood of serious cardiac complications and that evaluating both factors together enhances the capacity to predict risk (11-13). In a separate case-control study, Karakas et al. investigate how RDW and the neutrophil-lymphocyte ratio (NLR) can forecast left ventricular (LV) dysfunction in patients experiencing anterior ST-segment elevation myocardial infarction (STEMI). The findings from this research suggest that elevated levels of RDW and NLR in anterior STEMI patients undergoing primary percutaneous coronary intervention (PPCI) are associated with left ventricular systolic dysfunction (LVSD) (14). RDW is a potential marker for inflammation and cardiovascular risk. However, its prognostic value for hospital and one-year mortality in STEMI patients remains inconsistent. This research adds to the growing body of evidence by exploring RDW's association with mortality and hospital complications in a specific clinical context. Understanding these relationships is critical, given the increasing healthcare burden of STEMI and the need for cost-effective, accessible biomarkers to enhance risk stratification and patient management. Considering this information, this study was designed to examine the diagnostic value of RDW in predicting outcomes for ant-STEMI patients undergoing primary angioplasty.

Materials and Methods

2.1. Study Design and Setting

The current investigation is a retrospective analytical study aimed at assessing the diagnostic

significance of RDW in patients with anterior STEMI and its correlation with in-hospital and one-year mortality rates among individuals undergoing primary angioplasty during 2017-2018 at Shahid Madani Hospital in Tabriz, Iran. The study involved 300 patients diagnosed with anterior STEMI. The criteria for exclusion included those receiving drug or antithrombotic treatments, individuals undergoing coronary artery bypass grafting (CABG), cases of STEMI other than anterior STEMI, patients with a history of thalassemia or anemia, as well as individuals with incomplete medical records or missing essential information. Inclusion criteria were patients diagnosed with anterior ST-elevation myocardial infarction (ant-STEMI), and who underwent primary percutaneous coronary intervention (PPCI).

2.2. Data collection

After approval from the ethics committee of Tabriz University of Medical Sciences with the ethics code IR.TBZMED.REC. 1399.1061, a list of patients diagnosed with anterior - STEMI who underwent primary angioplasty was prepared. The checklist for the study included demographic factors such as age and gender, risk indicators like diabetes mellitus, hypertension, and smoking status, along with a history of laboratory results: hemoglobin (HBG), white blood cell count (WBC), and platelets (PLT). Additionally, echocardiog raphic criteria such as ejection fraction (EF), as well as in-hospital and one-year mortality rates, were documented. Lastly, complications occurring during hospitalization, which included cardiogenic shock (CS), hematoma, bleeding, and heart failure (HF), were examined using the information from the patient's file and logged in the study checklist.

2.3. Statistical analysis

The study used SPSS version 16 software for statistical analysis. Quantitative results were presented as means and standard deviations (±SD) for symmetrical distributions, while medians and interquartile ranges were used for asymmetric data. The normality of the dataset was assessed using the K-S test. Parametric tests were employed for normally distributed data, whereas non-parametric tests were used for non-normally distributed data. Descriptive statistics, including mean, standard deviation, and percentage counts, were reported. Furthermore, objectives 3 to 9 were pursued following the normality assessment with the K-S test, utilizing the T-student or U-Mann-Whitney tests based on the normality of the data to evaluate the objectives. The receiver operating characteristic (ROC) curve is appropriate even when an index, like RDW, has a known normal range, as it provides an optimal cut-off value for predicting specific clinical outcomes. In studies involving RDW and cardiovascular risk, ROC analysis helps identify the threshold that maximizes the sensitivity and specificity of RDW for predicting mortality risk, even if a single variable alone (in univariate analysis) is not significant. This approach enhances the clinical utility by defining a specific level at which RDW becomes a strong predictor of risk. ROC-derived cut points are especially helpful in capturing variations in sensitivity and specificity that could go unnoticed if we had used a general normal range. This method allows for precision in assessing risks for cardiovascular patients, where even subtle changes can carry predictive value. A p-value less than 0.05 was considered significant (15, 16).

Results

Table1. Presents the frequency and percentage of qualitative variables among 300 patients.Of these, 232 (77.3%) were male, while 68 (22.7%) were female. A total of 148 patients (49.3%) reported a history of smoking. Furthermore, 72 patients (24%) were diagnosed with diabetes mellitus (DM), and 154 patients (51.2%) had high blood pressure. Among the patients, 80 (26.7%) had single-vessel (1VD) coronary artery disease (CAD), while 96 patients (32%) had two-vessel (2VD) involvement, and 124 patients (41.3%) had three-vessel (3VD) involvement. In the event of complications occurring during hospitalization, 14.7% of patients experienced stent thrombosis, 46 patients (15.3%) suffered from gastrointestinal bleeding, and 15 patients (5%) had hematomas at the angiographic site Table 1.

Table1. Frequency and percentage of qualitative variables

Variables	Group		Frequency	Percentage
Gender	Male		232	77.3
	Female		68	22.7
Risk factors	Diabetes Mellitus	Yes	72	24
		No	228	76
	Hypertension	Yes	158	51.2
		No	146	48.7
	Smoking	Yes	148	49.3
		No	152	50.7
	Number of vessels involved	1	80	26.7
		2	96	32
		3	124	41.3
	In-hospital complications	Stent thrombosis	44	14.7
		Gastrointestinal bleeding	46	15.3
		Angio site hematoma	15	5

The cut-off value for the RDW index was established at 12.75, and the area under the receiver operating characteristic curve was calculated to be 0.69, which showed statistical significance (P-value = 0.003). The identified cut-off point demonstrated a sensitivity of 81% and a specificity of 44%, which falls within an acceptable range. In this research, 57 patients (19%) had an RDW of less than 12.75, while 243 patients (81%) had an RDW above 12.75 (high) Figure 1.

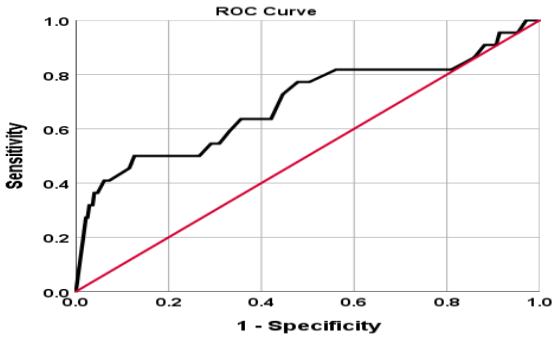

Figure1. ROC for red cell distribution width sensitivity and specificity

The relationship between RDW and in-hospital mortality and one-year mortality, and also, the relationship between RDW and in-hospital complications, was analyzed. As shown in Table 2, during their hospital stay, 22 patients (7.3%) died from their condition, of which 18 patients (81.8%) had elevated RDW levels, while 4 (18.2%) had normal RDW levels. However, this association was statistically insignificant (P-value=0.59). Furthermore, out of 300 patients, 123 (41%) died within one year, of which 101 patients (82.1%) had high RDW, while 22 patients (17.9%) had low RDW. As indicated in Table 2, this relationship was also statistically insignificant (P-value=0.68).

Table2. Frequency and percentage of quantitative variables

Variable	Mean	Standard deviation
Age	.65	2.73
WBC	11.4	4.1
HGB	14.45	2.27
PLT	237.13	84.94
RDWCV	13.78	2.72
MPV	10.45	6.14
NEUT	21.54	3.63
LVEF	36.94	7.88

WBC: White blood count
HGB: Hemoglobin
PLT: Platelets
RDW-CV: (Red Cell Distribution Width MPV: Mean Platelet Volume)
NEUT: Neutrophil
LVEF: Left ventricular ejection fraction

Table 3 shows the association between hospital complications such as stent thrombosis, angiohematoma, gastrointestinal (GI) bleeding, and RDW. The results clearly indicate a statistically significant relationship (P-value = 0.006) among these variables. In the group of 44 patients with stent thrombosis, the results indicate that 29 individuals (representing 65.9%) had elevated RDW levels, while the other 15 patients (34.1%) displayed normal RDW values.

Table3. RDW levels in relation with different complications

RDW LEVEL	High	Normal	Total	P-value
Hospital mortality	18	4	22	0.591
One year mortality	22	101	123	0.682
Hematoma	13	2	15	
GIB	37	9	46	0.006
Stent thrombosis	29	15	44	
Heart failure	74	33	107	0.001
Cardiac shock	42	4	46	

RDW: Red cell distribution width
GIB: Gastrointestinal bleeding

Additionally, among the cohort of 46 patients suffering from gastrointestinal bleeding (GIB), the results indicate that a significant majority, specifically 37 individuals, representing approximately 80.1%, had an increased RDW value. However, only a minor proportion of nine patients, about 19.9%, had a low RDW value. Furthermore, among the total number of patients exhibiting angio site hematoma, which consisted of around 15 cases, it was noted that a vast majority, particularly 13 patients, accounting for roughly 88.2%, had elevated RDW values; in contrast, only two individuals, making up about 11.8%, displayed low RDW values. The relationship between other hospital complications, such as heart failure (HF) and circulatory shock (CS) related to RDW levels was analyzed using a chi-square test. The findings indicate that in the 107 patients diagnosed with HF, 74 individuals (69.2%) had high RDW levels, whereas 33 patients (30.8%) had low RDW. Additionally, within the subset of 46 individuals who encountered cardiac shock (CS), a substantial majority of 42 patients (91.3%) exhibited elevated

RDW levels, while only four cases (8.7%) showed low RDW measurements.

Discussion

The current research is a descriptive correlational study aimed at assessing the diagnostic significance of RDW in patients with anterior STEMI who are undergoing primary angioplasty, as well as its connection to hospital and one-year mortality rates. Findings from this study indicated that there was no significant correlation between blood RDW levels and the in-hospital and one-year mortality rates of patients with anterior STEMI undergoing primary angioplasty. In contrast, prior studies in this area have indicated a noteworthy association between the one-year mortality rate in patients diagnosed with anterior STEMI and their blood RDW levels. (12, 17-19), Osadnik et al. (2013) demonstrated that the oldest patients had the highest RDW values, frequently presenting with diabetes mellitus (DM), heart failure (HF), and other chronic illnesses. The results suggested that RDW is an independent predictor of mortality among individuals with stable coronary artery disease (CAD) (20). In line with the present study, Xin-Min Liu and colleagues (2015) discovered that elevated preoperative RDW was notably linked to an increase in all-cause mortality after surgery. Additionally, the findings suggested that a rise in RDW serves as an independent indicator of higher mid-term all-cause mortality in older CAD patients following elective PCI (21). In the same line, Khaki et al. (2016) indicated that the mortality rate after six months was notably elevated in patients experiencing myocardial infarction (MI) who had high red cell distribution width (RDW). They determined that RDW represents a cost-effective and easily accessible laboratory test to evaluate mortality risk and monitor patients for better management of other modifiable risk factors (22). Sun et al. (2014) in their study indicated that elevated RDW is statistically linked to higher cardiac and all-cause mortality rates in patients with STEMI who were initially not experiencing heart failure. Nevertheless, RDW is a marker with limited prognostic accuracy, which lacks clinical utility (23). In line with this, Arbel et al. (2014) found that an RDW value exceeding 14 is independently linked to a rise in long-term all-cause mortality among STEMI patients undergoing PCI (24).Moreover, the cohort study by Uyarel et al. in 2011 revealed a significant connection between elevated RDW levels and the risk of cardiovascular mortality. Additionally, increased RDW emerged as an independent predictor of cardiovascular mortality among non-anemic patients. The findings indicated that higher RDW levels correlate with an elevated risk of cardiovascular death in STEMI patients undergoing PPCI (17). All these studies have highlighted the association between RDW and a poorer prognosis in individuals with cardiovascular diseases. However, the reasons behind this poorer prognosis remain unclear. In contrast, the current study did not find a notable link between high RDW levels and elevated in-hospital or one-year mortality rates in STEMI patients. The precise pathophysiological mechanisms leading to an elevated RDW in heart failure (HF) are not completely understood (25), however, research indicates that inflammation and the activation of the neurohormonal and adrenergic systems may cause alterations in red blood cell (RBC) maturation by affecting the red cell membrane, resulting in increased RDW among HF patients (26). Our findings mirrored those of patients with anterior ST-elevation myocardial infarction (ant-STEMI) who exhibited higher serum RDW levels. Tunçez et al. found that elevated RDW values may have an independent association with the emergence of stent thrombosis in STEMI patients. They propose that this relationship may stem from heightened ischemia, oxidative stress, neurohumoral activation, and inflammation, all of which could contribute to stent thrombosis (11). Similarly, in our study, we observed a significant correlation between elevated serum RDW levels and stent thrombosis in patients with ant-STEMI. Prior research has indicated that inflammatory cytokines, such as interleukin-6, -7, -8, and -10, serve as prognostic indicators in acute myocardial infarction (AMI) complicated by cardiogenic shock (CS) (27). Additionally, the results suggested that pro-inflammatory cytokines may disrupt the erythrocyte maturation process, potentially leading to increased serum RDW levels (28, 29). hus, this could be a plausible pathophysiological link between elevated RDW and cardiogenic shock. The present study noted a significant relationship between high RDW levels and CS in patients with ant-STEMI. Lastly, in research conducted by Liao et al., elevated RDW levels were associated with a greater risk of

gastrointestinal bleeding (GIB) following coronary artery bypass grafting (CABG) (30). Although the exact mechanism linking RDW to GIB is not clearly understood, studies suggest that indirect factors such as oxidative stress, erythropoietin deficiency, and deficiencies related to iron and vitamin D3 may heighten the risk of major bleeding (6, 31-33). We also found a significant relation between high serum RDW and increased GIB in ant-STEMI patients.

Limitations and suggestions

The study was a retrospective analysis with inherent limitations such as incomplete or missing data and lack of control over confounding factors. Conducting the study at a single hospital may limit the generalizability of the findings to a broader population. The study suggests that conducting a prospective, multicenter study with a larger sample size would enhance the generalizability of the findings and allow for better control of confounding factors. Extending the follow-up period beyond one year could provide valuable information on the long-term prognostic significance of RDW in patients with anterior STEMI. Evaluating the diagnostic and prognostic value of RDW alongside established biomarkers, such as troponin, C-reactive protein (CRP), and natriuretic peptides, may clarify RDW's additional value in managing anterior STEMI patients. Conclusion In conclusion, the study found no significant association between elevated RCD Width RDW levels and in-hospital or one-year mortality among ant-STEMI patients undergoing PPCI. However, a significant relationship was observed between high RDW levels and various in-hospital complications, including HF, CS, stent thrombosis, GIB, and angio-site hematoma. This suggests that although RDW is not a dependable predictor of mortality in these patients, it could serve as an essential marker for identifying patients at risk of complications. To better understand the prognostic value of RDW in ant-STEMI patients and to strengthen the evidence, more prospective multicenter studies are recommended.

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Consent for publication

Not applicable

Availability of data and materials

The dataset analyzed the current study is available from the corresponding author on a reasonable request.

Conflicts of Interest

None

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None

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