Int J Cardiovasc Sci. 2024; 37:e20230099

ORIGINAL ARTICLE

Hemoglobin/Red Cell Distribution Width Ratio is Associated With Poor Prognosis in Patients With Acute Coronary Syndrome in Long-Term Follow-Up

Oğuz Kılıç,[1] Mehmet Mustu,[2] Hakan Suygun,[2] Enes Con,[1] Ahmet Karakurt,[2] Sümeyye Fatma Özer[1]

Karaman Research and Training Hospital,[1] Karaman – Turkey
Karamanoglu Mehmetbey University,[2] Karaman – Turkey

Abstract

Background: Acute coronary syndrome (ACS) is the most common subtype of coronary artery disease (CAD). It is one of the main reasons affecting the expected life expectancy and quality of life.

Objetives: In this study, we aimed to investigate the relationship between major adverse cardiac events (MACE) and Hemoglobin (Hb)/Red cell distribution width (RDW) in long-term follow-up after ACS.

Methods: A total of 1,146 ACS patients were included in the study, being classified according to the type of myocordial infarction (MI). MACE were recorded in long-term follow-up. The relationship between Hb/RDW and MACE was investigated. The statistical analyses of Mann-Whitney U test for comparison of two independent groups and chi-square test for categorical variables were used. **In order to determine the diagnostic feature of the HB/RDW ratio, the diagnostic ratios were calculated by applying Receiver Operating Characteristic Curve (ROC) analysis. A $p < 0.05$ value was considered statistically significant in all analyses.**

Results: When the patients were analyzed according to MI types — ST segment elevation myocardial infarction (STEMI)/Non-ST segment elevation myocardial infarction (NSTEMI) —, it was observed that Hb/RDW (**$p = 0.038$**) was significantly higher in the STEMI group. The Hb/RDW ratio was statistically significant in predicting mortality. As a result of ROC analysis, **Area Under the Curve (AUC) = 0.654 ($p < 0.001$)** was found. The cut-off value for the Hb/RDW ratio was calculated as **0.947**. The sensitivity and specificity of 76.9% and 48.4% for the diagnostic rates obtained were moderately acceptable.

Conclusion: The Hb/RDW-long-term mortality relationship was found to be significant in ROC analysis. It can be used in clinical practice as it is cheap, easy to apply, and reduces possible bias in post-ACS follow-up.

Keywords: Acute Coronary Syndrome; Hemoglobins; Throcyte Indices; Mortality; Inflammation.

Introduction

Acute coronary syndrome (ACS) is the most common disease of the coronary arteries leading to myocardial ischemia.[1] According to current data, it affects approximately 112 million people over the age of 20 worldwide.[2] Today, although mortality has decreased with the increase in early diagnosis and treatment and complementary health services, it is still one of the most important causes of mortality. It causes high healthcare costs.

It is known that gender, physical activity, follow-up strategies, adherence to treatment, accompanying heart failure (HF), and comorbid conditions affect the prognosis of the preferred treatment method (medical or revascularization).[3] Currently, mortality and morbidity management strategies after ACS focus on stratifying the patient according to their risks and using an appropriate prognostic factor to determine treatment steps.

Cardiac conditions are associated with increased inflammatory burden.[4] Similarly, hemogram-derived markers are considered inexpensive and reliable markers

Mailing Address: Oğuz Kılıç
Department of Cardiology, Karaman Traininng and Research Hospital. Postal code: 20700. Karaman – Turkey
E-mail: dr.kilicoguz@gmail.com

DOI: https://doi.org/10.36660/ijcs.20230099

Manuscript received July 5, 2023; revised manuscript November 12, 2023; accepted December 13, 2023.

Central Illustration: Hemoglobin/Red Cell Distribution Width Ratio is Associated With Poor Prognosis in Patients With Acute Coronary Syndrome in Long-Term Follow-Up

INTERNATIONAL JOURNAL OF Cardiovascular SCIENCES

1,146 ACS patients (423 STEMI patients; 723 NSTEMI patients) were included.

Patients were classified according to the type of treatment after CAG.

Group 1: PTCA and stent implantation
Group 2: stent implantation
Group 3: PTCA
Group 4: medical follow-up
Group 5: coronary artery bypass graft

MACE was defined as all-cause death, non-fatal RMI, and R-TVR.

We examined the association of MACE and Hb/RDW, in both all ACS patients and subgroups (STEMI and NSTEMI group).

EXCLUSION CRITERIA
1-Disseminated infection
2-Major surgery
3-Bleeding
4-Aortic dissection
5-Myocarditis
6-Cardiomyopathy
7-Acute pulmonary embolism
8-Stroke
9-patients with missing data and those with only medical follow-up and those with missing long-term follow-up

RESULTS
- **The Hb/RDW ratio according to MI types was not sufficiently significant for the STEMI patient group.**
- **The Hb/RDW ratio was statistically significant in predicting mortality.**
- **As a result of ROC analysis, AUC = 0.654 (p < 0.001) was found.**

Int J Cardiovasc Sci. 2024; 37:e20230099

Hb: Hemoglobin; RMI: recurrent myocardial infarction; R-TVR: recurrent target vessel revascularization; PTCA: percutaneous transluminal coronary angioplasty; STEMI: ST segment elevation myocardial infarction; NSTEMI: Non-ST segment elevation myocardial infarction; RDW: red cell distribution width; ACS: acute coronary syndrome; MACE: major adverse cardiac events; CAG: coronary angiography; AUC: Area Under the Curve ; ROC: Receiver Operating Characteristic Curve.

of inflammation in various inflammatory conditions such as cancer, hepatosteatosis, irritable bowel disease, pancreatitis, and thyroiditis.[4-9] Complete blood count is one of the basic tests used in routine clinical practice in coronary artery patients. The prognostic importance of complete blood count parameters (neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, mean platelet volume, and neutrophil/monocyte) in coronary artery disease (CAD) has been demonstrated in many studies.[10-12] Hemoglobin (Hb) is generally used to define anemia along with other parameters such as hematocrit. However, recent works suggest that Hb is also a predictor of hospital admission of subjects with chronic diseases. Thus, studying these markers in cardiac diseases makes sense.[13] It is known that low Hb levels in the follow-up after acute myocardial infarction (AMI) and percutaneous coronary intervention (PCI) adversely affect the prognosis. Although there are many studies investigating the relationship between Hb level and adverse cardiovascular outcomes, the level of Hb that causes poor prognosis has not been identified.[14-15] Red cell distribution width (RDW), which is an indicator of anisocytosis, is another blood parameter. RDW has been particularly linked with inflammatory diseases, including functional bowel conditions, autoimmune diseases, rheumatoid arthritis, degenerative vertebral conditions, malignancy, autoimmune hepatitis, and even COVID-19.[16-22] In many studies, it has been shown that increased RDW level negatively affects the prognosis of cardiovascular diseases (CVD) and HF.[23-24]

Although the prognostic importance of both Hb and RDW has been proven in CVD and HF, studies on Hb/RDW ratio are limited. In this study, we aimed to investigate the relationship between major adverse cardiac events (MACE) and Hb/RDW in long-term follow-up after AMI.

Materials and methods

Study Population

Our study is retrospective and observational. Patients who underwent coronary angiography (CAG) in our

clinic with the diagnosis of AMI in the last five years were screened consecutively. Demographic characteristics, laboratory values, CAG findings of the patients, and long-term follow-up data were obtained from the computerized database. Patients were included according to the principles of the 4th universal definition of AMI, as defined by the European Society of Cardiology (ESC).[25] A total of 1,146 patients were included. The patients were divided into two groups. ST segment elevation myocardial infarction (STEMI) (423 patients) and Non-ST segment elevation myocardial infarction (NSTEMI) (723 patients). Patients were classified according to the type of treatment after CAG (group 1: percutaneous transluminal coronary angioplasty (PTCA) and stent implantation, group 2: stent implantation, group 3: PTCA, group 4: medical follow-up, group 5: coronary artery bypass graft). Disseminated infection, major surgery, bleeding, aortic dissection, myocarditis, cardiomyopathy, acute pulmonary embolism, and stroke were excluded. In addition, patients with missing data, those with only medical follow-up, and those with missing long-term follow-up were not included. Our study complies with the principles of the Declaration of Helsinki. Local ethics committee approved the study protocol.

Laboratory Parameters

Hemogram and biochemical parameters were studied from fresh blood samples taken after overnight fasting. Glucose was measured in plasma. Other parameters were studied in serum. Triglyceride, complete blood cell count, renal function panel, total cholesterol, low-density lipoprotein (LDL) cholesterol, high-density lipoprotein (HDL) cholesterol, and C-reactive protein (CRP) levels were measured. We calculated the Hb/RDW ratio in all patients.

CAG

CAG was performed via the femoral or radial artery, depending on the operator's experience. A routine Judkins catheter was used in the diagnostic CAG. The left main coronary artery (LMCA), left anterior descending (LAD), and left circumflex artery (LCX) were evaluated from the left caudal, right caudal, left cranial, right cranial, and antero-posterior cranio-caudal poses. The right coronary artery (RCA) was evaluated in the left anterior oblique and left cranial poses. According to the results of the CAG, stenosis of ≥ 50% for the LMCA and ≥ 70% for other epicardial vessels was considered to be an obstructive-severe CAD. After diagnostic CAG, medical follow-up, PCI, and coronary bypass graft decisions were made according to ESC guidelines. The patients were given dual antiaggregants (acetyl salicylic acid and ticagrelor or prasugrel or clopidogrel) for one year. Compliance with medical treatment was standardized during follow-up. MACE during follow-up was recorded.

Primary endpoint

Our aim was to investigate the relationship between MACE and Hb/RDW ratio in AMI patients at 60-month follow-up. MACE was defined as all-cause death, non-fatal recurrent myocardial infarction (RMI), and recurrent target vessel revascularization (R-TVR). We examined the association of MACE and Hb/RDW in all AMI patients and subgroups (STEMI and NSTEMI groups).

Statistical analysis

Statistical analyses of the study were performed with the SPSS 20.0 (IBM Inc, Chicago, IL, USA) program. Descriptive statistics are mean ± standard deviation (SD) for continuous data, presented as absolute and relative frequencies for categorical data. The Kolmogorov-Smirnov test analyzed the conformity of continuous variables to normal distribution. **The Mann-Whitney U test was used to compare groups that did not show normal distribution**. **Continuous variables with normal distribution were defined using mean ± SD. "Continuous variables that were not normally distributed were defined using the median and interquartile range.** The diagnostic ratios were calculated by applying ROC analysis to determine the diagnostic feature of the Hb/RDW ratio. A chi-square analysis was used to determine the relationships between categorical variables. A $p < 0.05$ value was considered statistically significant for a type-I error rate of 5% in all analyses.

Results

The study was completed with 1,146 ACS patients, 68.8% of them being male and 63.1% were NSTEMI. The most common comorbidities were hyperlipidemia (HL) (56.8%) and hypertension (HT) (53.9%) (Table 1). The mean age of the patients was 68.21 ± 12.31 years (29-96). The mean time for R-MI was calculated as 211.5 ± 355.2 days (0-1564) (Table 2). When the patients were examined according to the treatment type, PTCA and stent implantation were performed in 77.4%, medical

Table 1 – Demographic characteristics of patients

		STEMI (n%)	NSTEMI (n%)	TOTAL	P value
GENDER	Male	321 (75.9%)	468 (64.7%)	789 (68.8%)	**< 0.001***
	Female	102 (24.1%)	255 (35.3%)	357 (32.2%)	
SMOKING	No	307 (72.6%)	616 (85.2%)	923 (80.5%)	**< 0.001***
	Yes	116 (27.4%)	107 (14.8%)	223 (19.5%)	
HT	No	222 (52.5%)	306 (42.3%)	528 (46.1%)	**0.001***
	Yes	201 (47.5%)	417 (57.7%)	618 (53.9%)	
DM	No	319 (75.4%)	501 (69.3%)	820 (71.6%)	**0.027***
	Yes	104 (24.6%)	222 (30.7%)	326 (28.4%)	
CAD	No	385 (91.0%)	567 (78.4%)	952 (83.1%)	**< 0.001***
	Yes	38 (9.0%)	156 (21.6%)	194 (16.9%)	
HL	No	173 (40.9%)	322 (44.5%)	495 (43.2%)	0.230
	Yes	250 (59.1%)	401 (55.5%)	651 (56.8%)	
HF	No	421 (99.5%)	717 (99.2%)	1138 (99.3%)	0.484
	Yes	2 (0.5%)	6 (0.8%)	8 (0.7%)	
CRF	No	414 (97.9%)	714 (98.8%)	1128 (98.4%)	0.246
	Yes	9 (2.1%)	9 (2.1%)	18 (1.6%)	
TREATMENT	PTCA+ SI	389 (92.6%)	496 (68.6%)	885 (77.2%)	**< 0.001***
	SI	5 (1.2%)	8 (1.1%)	13 (1.1%)	
	PTCA	1 (0.2%)	7 (1.0%)	8 (0.7%)	
	MEDICAL	10 (2.4%)	50 (6.9%)	60 (5.2%)	
	CABG	15 (3.6%)	162 (22.4%)	177 (15.4%)	
LONG TERM EX	No	351 (83.0%)	613 (84.8%)	964 (84.1%)	0.419
	Yes	72 (17.0%)	110 (15.2%)	182 (15.9%)	
LONG TERM RMI	No	399 (94.3%)	691 (95.6%)	1090 (95.1%)	0.344
	Yes	24 (5.7%)	32 (4.4%)	56 (4.9%)	
LONG TERM R-TRV	No	396 (93.6%)	694 (96.0%)	1090 (95.1%)	0.072
	Yes	27 (6.4%)	29 (4.0%)	56 (4.9%)	

Categorical variables were summarized as frequency and percentages. HT: Hypertension; DM: Diabetes Mellitus; CAD: Coronary Artery Disease; HL: Hyperlipidemia; HF: Heart Failure; CRF: Chronic Renal Failure; PTCA: Percutaneous Transluminal Coronary Angioplasty; SI: Stent Implantation; CABG: Coronary Artery Bypass Graft; RMI: Recurrent Myocardial Infarction; R-TRV: Recurrent Target Vessel Revascularization; STEMI: ST segment elevation myocardial infarction; NSTEMI: Non-ST segment elevation myocardial infarction.

follow-up was given in 5.2%, and CABG was decided in 15.5% (Table 1). Mortality was 15.9%, while R-TRV was 4.9% in long-term follow-up (Table 1). The mean Hb of the patients was 13.78 ± 1.76 g/dL, and the mean RDW was 14.89 ± 1.78%. The mean value of the Hb/RDW ratio was calculated as 0.938 ± 0.162 (Table 2).

When the patients were analyzed according to MI types (STEMI/NSTEMI), it was observed that both WBC and Hb/RDW were significantly higher in the STEMI group. Hb values were found to be significantly lower in patients with ex (12.82 ± 1.59 gr/dL). Similarly, while the Hb/RDW ratio was 0.951 ± 0.162 in survivors, it decreased significantly to 0.865 ± 0.143 in ex-patients (Table 3).

The Hb/RDW ratio according to MI types was not sufficiently significant for the STEMI patient group. However, the Hb/RDW ratio was statistically significant in predicting mortality. As a result of ROC analysis, **AUC = 0.654 (p < 0.001)** was found. The cut-off value for the Hb/RDW ratio was calculated as **0.947**. The sensitivity and specificity of 76.9% and 48.4% for the diagnostic rates obtained were moderately acceptable (Figure 1). The Hb/RDW ratio was not significant in predicting R-MI and R-TVR (Table 4 and 5).

Discussion

In our study, we investigated the relationship between MACE and Hb/RDW in the long-term follow-up of patients who underwent CAG for STEMI and NSTEMI. Our average follow-up was 60 months. The Hb/RDW ratio was lower only in the mortality group. ROC analysis also showed that low Hb/RDW has a high predictive value for MACE in both NSTEMI and STEMI patients. However, no statistically significant correlation was found for R-MI and R-TRV.

Hb is a protein that carries oxygen to the tissues and carbon dioxide from the tissues to the lungs.[26] A low Hb level is called anemia.[26] As a result of acute or chronic anemia, the amount of oxygen carried to the tissues decreases. Hb has an important prognostic significance in

Table 2 – Biochemical characteristics of patients according to Myocardial Infarction types

VARIABLES	STEMI (mean ± SD)	NSTEMI (mean ± SD)	TOTAL (mean ± SD)	P value
Follow-up time (day)	199.54 ± 336.52	219.5 ± 368.05	211.5 ± 355.2	0.663
Age (years)	67.67 ± 12.61	68.53 ± 12.13	68.21 ± 12.31	0.257
WBC (µl/ml)	10.53 ± 3.35	9.43 ± 2.92	9.84 ± 3.13	**< 0.001***
HB (g/dL)	13.92 ± 1.74	13.71 ± 1.78	13.79 ± 1.77	0.059
RDW (%)	14.82 ± 1.61	14.95 ± 1.88	14.9 ± 1.78	0.225
Neutrophil (10^3/L)	7.82 ± 9.7	6.77 ± 11.58	7.16 ± 10.93	0.115
Lymphocyte (10^3/L)	2.43 ± 1.23	2.38 ± 1.05	2.4 ± 1.12	0.470
Platelet (10^3/L)	231.37 ± 73.28	226.69 ± 63.41	228.42 ± 67.23	0.255
Glucose (mg/dL)	127.75 ± 40.29	142.12 ± 57.15	135.49 ± 50.29	0.210
Triglyceride (mg/dL)	160.42 ± 107.11	153.95 ± 78.58	156.9 ± 92.1	0.758
TC (mg/dL)	202.78 ± 48.42	204.94 ± 56.74	204.3 ± 54.33	0.800
HbA1c (mmol/mol)	6.12 ± 1.34	6.48 ± 1.2	6.31 ± 1.27	0.255
LDL (mg/dL)	115.84 ± 37.75	115.74 ± 38.27	115.78 ± 38.06	0.965
Creatine (mg/dL)	1.06 ± 0.4	1.19 ± 5.31	1.14 ± 4.22	0.618
CRP (mg/L)	14.68 ± 24.45	12.68 ± 22.29	13.42 ± 23.12	0.159
Hb/RDW	0.95 ± 0.16	0.93 ± 0.16	0.94 ± 0.16	**0.038***

**p < 0.05 statistically significant difference; Continuous variables were summarized as mean ± SD. WBC: White Blood Cell; HB: Hemogram; RDW: Red Cell Distribution Width; TC: Total Cholesterol; HbA1c: Glycated Hemoglobin; LDL: Low-density Lipoprotein; CRP: C-reactive Protein; STEMI: ST segment elevation myocardial infarction; NSTEMI: Non-ST segment elevation myocardial infarction; Hb: Hemoglobin; SD: standard deviation.*

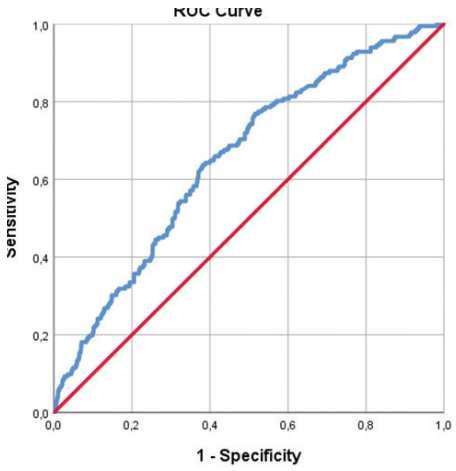

Figure 1 – ROC analysis of Hb/RDW ratio for mortality. The cut-off value for the Hb/RDW ratio was calculated as 0.947. Sensitivity and specificity levels were at 76.9% and 48.4%, respectively. Diagonal segments are produced by ties.
ROC: Receiver Operating Characteristic Curve

CVD.[27] AMI may develop as myocardial oxygen demand-delivery balance will be disrupted after acute anemia.[28] The hemodynamic changes that occur with chronic anemia cause eccentric left ventricular hypertrophy (LVH) and left ventricular dilatation (LVD).[29] Increased LVH and LVD cause HF in the future.[29] In the TIME study, which examined the relationship between anemia and major cardiovascular events, patients were followed for an average of four years for cardiovascular death, non-fatal MI, and hospitalization for CAD. As a result of the study, a 1 g/dl reduction in Hb was associated with a significantly increased risk of cardiovascular death and MACE.[30] In another study, which included 6,116 patients who underwent PCI, it was found that as the severity of anemia increased, the MACE rate increased, and the one-year survival rate decreased.[31]

Additionally, there are many studies investigating the relationship between Hb -derived markers and CAD. In a study conducted in 2020 with 290 unstable angina pectoris (UAP), STEMI, and NSTEMI patients, the relationship between MI groups and eosinophil levels was examined. An inverse relationship between blood eosinophil count and severity of ACS subgroups in elderly patients was found; this number was higher in the UAP than in the MI groups.[32] In another study aiming to compare hemogram parameter values in patients with sufficient or inadequate coronary collateral development (CCD) presenting with NSTEMI, it has been shown that platelet distribution width may be a marker of CCD in NSTEMI patients.[33] In our study, we also found a lower Hb value in the group with mortality.

RDW width is formulated with a SD of (red blood cell volume/mean cell volume) × 100.[34] It is a parameter measured in a CBC. It represents anisocytosis. Felker et al. investigated its role in CVD for the first time.[35] Many similar studies have been published since then.[36-38] Tonelli et al. showed that increased RDW level is a risk factor for stroke, HF, and recurrent AMI in patients with CAD.[39] In another study, in-hospital and long-term mortality after AMI was found to be correlated with RDW levels.[40] Lippi et al. observed that RDW has a diagnostic value in patients followed in the intensive care unit with the suspicion of AMI.[41] Our findings were higher in the group with mortality, as in the literature.

Although the prognostic significance of RDW and Hb after AMI has been reported separately in many studies, the prognostic significance of Hb/RDW in this patient group is unclear. Our study is the first study to investigate the prognostic significance of Hb/RDW in post-AMI long-term follow-up. There is only one study in the literature investigating the prognostic significance of Hb/RDW in CVD. In this study, which was published in 2022 and included 6,888 HF patients, Hb/RDW was found to be an important prognostic tool in predicting HF mortality and cardiovascular hospitalization.[42] In our study, we observed that the incidence of MACE increased as the Hb/RDW ratio decreased. Considering that the prognostic significance of Hb and RDW is shown separately in many

Table 3 – Biochemistry measurements of patients according to mortality status

LONG-TERM MORTALİTY			
VARIABLES	**NO (mean ± SD)**	**YES (mean ± SD)**	**P value**
Follow-up time (day)	325.36 ± 376.92	167.71 ± 337.43	**0.003***
Age (years)	66.35 ± 11.8	78.08 ± 10.09	**< 0.001***
WBC (µl/ml)	9.3 ± 2.57	12.66 ± 4.15	**< 0.001***
HB (g/dL)	13.97 ± 1.74	12.82 ± 1.6	**< 0.001***
RDW (%)	14.88 ± 1.79	15 ± 1.76	0.428
Neutrophil (10^3/L)	6.58 ± 11.72	10.2 ± 3.8	**< 0.001***
Lymphocyte (10^3/L)	2.53 ± 1.12	1.71 ± 0.85	**< 0.001***
Platelet (10^3/L)	225.96 ± 63.66	241.39 ± 82.62	0.018*
Glucose (mg/dL)	127.6 ± 47.09	161.78 ± 52.98	**0.021***
Triglyceride (mg/dL)	159.95 ± 95.58	146.56 ± 80.8	0.591
TC (mg/dL)	211.97 ± 47.01	161.37 ± 71.23	**0.001***
HbA1c (mmol/mol)	6.29 ± 1.11	6.39 ± 1.74	0.780
LDL (mg/dL)	117.62 ± 37.69	105.81 ± 38.66	**< 0.001***
Creatine (mg/dL)	1.12 ± 4.59	1.24 ± 0.52	0.728
CRP (mg/L)	11.29 ± 19.69	24.69 ± 34.19	**< 0.001***
HB/RDW RATIO	0.95 ± 0.16	0.87 ± 0.14	< 0.001*

**p < 0.05 statistically significant difference; Continuous variables were summarized as mean ± SD. WBC: White Blood Cell; HB: Hemogram; RDW: Red Cell Distribution Width; TC: Total Cholesterol; HbA1c: Glycated Hemoglobin; LDL: Low-density Lipoprotein; CRP: C-reactive Protein; SD: standard deviation.*

Table 4 – Biochemistry measurements of patients according to target vessel revascularization status

Target Vessel Revascularization In Long-Term Follow-Up			
VARIABLES	**NO (mean ± SD)**	**YES (mean ± SD)**	**P value**
Follow-up time (day)	189.92 ± 359.48	296.55 ± 327.41	0.055
Age (years)	68.17 ± 12.32	69.02 ± 12.14	0.615
WBC (µl/ml)	9.76 ± 3.09	11.36 ± 3.46	**0.001***
HB (g/dL)	13.78 ± 1.77	13.94 ± 1.71	0.510
RDW (%)	14.89 ± 1.77	15.02 ± 1.97	0.602
Neutrophil (10^3/L)	6.9 ± 9.6	12.2 ± 25.19	0.122
Lymphocyte (10^3/L)	2.42 ± 1.1	2 ± 1.44	**0.036***
Platelet (10^3/L)	228.34 ± 67.35	229.86 ± 65.54	0.870
Glucose (mg/dL)	132.34 ± 47.71	149.86 ± 60.63	0.240
Triglyceride (mg/dL)	150.91 ± 96.32	184.71 ± 64.9	0.215
TC (mg/dL)	204.58 ± 54.87	196.86 ± 38.7	0.713
HbA1c (mmol/mol)	6.32 ± 1.3	6.26 ± 1.17	0.872
LDL (mg/dL)	116.5 ± 38.24	102.05 ± 31.9	**0.002***
Creatine (mg/dL)	1.15 ± 4.32	0.99 ± 0.44	0.786
CRP (mg/L)	13.33 ± 23.15	15.21 ± 22.66	0.554
HB/RDW RATIO	0.94 ± 0.16	0.94 ± 0.16	0.850

**p < 0.05 statistically significant difference; Continuous variables were summarized as mean ± SD. WBC: White Blood Cell; HB: Hemogram; RDW: Red Cell Distribution Width; TC: Total Cholesterol; HbA1c: Glycated Hemoglobin; LDL: Low-density Lipoprotein; CRP: C-reactive protein; SD: standard deviation.*

CAD and HF studies, the result obtained from our study may not be striking. However, Hb and RDW can be affected by nutrition, infection, and other factors. Hb/RDW can minimize potential bias. It can be used as a more reliable diagnostic parameter than Hb and RDW. Finally, Hb and RDW are both cost-effective and easy to apply, and they can be used frequently. We believe that this procedure will make a significant contribution to long-term mortality prediction.

Our study has several limitations. The first is that it is single-centered and retrospective, because we cannot exclude factors that may affect the outcome, such as nutrition and autoimmune conditions. Second, we cannot generalize the results as it was performed in a small patient population. For this reason, our results should be supported by multicenter prospective studies with large participation.

Table 5 – Biochemistry measurements of patients according to RMI status

RMI in Long-Term Follow-up			
VARIABLES	NO (mean ± SD)	YES (mean ± SD)	P value
Follow-up time (day)	184.65 ± 350.79	314.77 ± 356.47	**0.021***
Age (years)	68.15 ± 12.3	69.39 ± 12.51	0.461
WBC (µl/ml)	9.74 ± 3.09	11.74 ± 3.25	**< 0.001***
HB (g/dL)	13.8 ± 1.78	13.62 ± 1.58	0.467
RDW (%)	14.9 ± 1.77	14.89 ± 1.97	0.964
Neutrophil (10^3/L)	7.05 ± 11.18	9.27 ± 2.8	0.138
Lymphocyte (10^3/L)	2.43 ± 1.12	1.81 ± 0.99	**< 0.001***
Platelet (10^3/L)	228.42 ± 67.33	228.3 ± 66	0.990
Glucose (mg/dL)	133.44 ± 47.5	146.75 ± 64.86	0.403
Triglyceride (mg/dL)	151.88 ± 96.26	184.92 ± 59.51	0.255
TC (mg/dL)	204.6 ± 54.91	198.8 ± 43.77	0.743
HbA1c (mmol/mol)	6.3 ± 1.26	6.39 ± 1.34	0.835
LDL (mg/dL)	116.35 ± 38.18	104.82 ± 34.38	**0.018***
Creatine (mg/dL)	1.15 ± 4.32	1.03 ± 0.44	0.837
CRP (mg/L)	13.4 ± 23.38	13.85 ± 17.67	0.887
HB/RDW RATIO	0.94 ± 0.16	0.93 ± 0.15	0.646

**p < 0.05 statistically significant difference; Continuous variables were summarized as mean ± SD. WBC: White Blood Cell; HB: Hemogram; RDW: Red Cell Distribution Width; TC: Total Cholesterol; HbA1c: Glycated Hemoglobin; LDL: Low-density Lipoprotein; CRP: C-reactive Protein; RMI: recurrent myocardial infarction.*

Conclusion

In conclusion, our study is the first to investigate the predictor of Hb/RDW for MACE in long-term follow-up after AMI. The Hb/RDW long-term mortality relationship was found to be significant in ROC analysis. It can be used in clinical practice as it is cheap, easy to apply, and reduces possible bias in post-AMI follow-up.

Author Contributions

Conception and design of the research: Kılıç O, Mustu M; acquisition of data: Mustu M, Suygun H, Com E; analysis and interpretation of the data: Kılıç O, Özer SF; statistical analysis: Com E, Özer SF; writing of the manuscript: Kılıç O, Suygun H, Özer SF; critical revision of the manuscript for intellectual content: Kılıç O.

Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

Sources of Funding

There were no external funding sources for this study.

Study Association

This study is not associated with any thesis or dissertation work.

Ethics Approval and Consent to Participate

This study was approved by the Ethics Committee of the Karamanoglu Mehmetbey University under the protocol number 10-2022/09. All the procedures in this study were in accordance with the 1975 Helsinki Declaration, updated in 2013. Informed consent was obtained from all participants included in the study.

References

1. Montalescot G, Sechtem U, Achenbach S, Andreotti F, Arden C, Budaj A, et al. 2013 ESC Guidelines on the Management of Stable Coronary Artery Disease: The Task Force on the Management of Stable Coronary Artery Disease of the European Society of Cardiology. Eur Heart J. 2013;34(38):2949-3003. doi: 10.1093/eurheartj/eht296.
2. Konigstein M, Giannini F, Banai S. The Reducer Device in Patients with Angina Pectoris: Mechanisms, Indications, and Perspectives. Eur Heart J. 2018;39(11):925-33. doi: 10.1093/eurheartj/ehx486.
3. Ho PM, Lambert-Kerzner A, Carey EP, Fahdi IE, Bryson CL, Melnyk SD, et al. Multifaceted Intervention to Improve Medication Adherence and Secondary Prevention Measures After Acute Coronary Syndrome Hospital Discharge: A Randomized Clinical Trial. JAMA Intern Med. 2014;174(2):186-93. doi: 10.1001/jamainternmed.2013.12944.
4. Sincer I, Gunes Y, Mansiroglu AK, Cosgun M, Aktas G. Association of Mean Platelet Volume and Red Blood Cell Distribution Width with Coronary Collateral Development in Stable Coronary Artery Disease. Postepy Kardiol Interwencyjnej. 2018;14(3):263-9. doi: 10.5114/aic.2018.78329.
5. Sit M, Aktas G, Ozer B, Kocak MZ, Erkus E, Erkol H, et al. Mean Platelet Volume: An Overlooked Herald of Malignant Thyroid Nodules. Acta Clin Croat. 2019;58(3):417-20. doi: 10.20471/acc.2019.58.03.03.

6. Aktas G, Duman TT, Kurtkulagi O, Tel BMA, Bilgin S, Kahveci G, et al. Liver Steatosis is Associatedboth with Platelet Distribution Width, Neutrophil/Lymphocyte and Monocyte/Lymphocyte Ratios. Prim Health Care Open Access. 2020;10(1):1-4.

7. Aktas G, Duman TT, Atak BM, Kurtkulagi O, Bilgin S, Basaran E et al. Irritable Bowel Syndrome is Associated with Novel Inflammatory Markers Derived from Hemogram Parameters. Fam Med Prim Care Rev. 2020;22(2):107-10. doi: 10.5114/fmpcr.2020.95311.

8. Balci SB, Aktas G. A Comprehensive Review of the Role of Hemogram Derived Inflammatory Markers in Gastrointestinal Conditions. 2022;10:75-86. doi: 10.30476/ACRR.2022.97244.1160.

9. Erge E, Kiziltunc C, Balci SB, Atak Tel BM, Bilgin S, Duman TT, et al. A Novel Inflammatory Marker for the Diagnosis of Hashimoto's Thyroiditis: Platelet-Count-to-Lymphocyte-Count Ratio. Diseases. 2023;11(1):15. doi: 10.3390/diseases11010015.

10. Yang YL, Wu CH, Hsu PF, Chen SC, Huang SS, Chan WL, et al. Systemic Immune-Inflammation Index (SII) Predicted Clinical Outcome in Patients with Coronary Artery Disease. Eur J Clin Invest. 2020;50(5):e13230. doi: 10.1111/eci.13230.

11. Szolc P, Niewiara Ł, Kawulak M, Szkodoń K, Ostrowska-Kaim E, Nosal M, Krzanowski M, Żmudka K, Legutko J, Guzik B. Neutrophil-Lymphocyte Ratio and Platelet-Lymphocyte Ratio as Predictors of Coronary Microcirculatory Disease Occurrence and Outcome in Patients with Chronic Coronary Syndrome and No Significant Coronary Artery Stenosis. Wiad Lek. 2020;73(12 cz 1):2598-2606.

12. Şahin A, Sisli E. Retrospective Evaluation of the Pre- and Postoperative Neutrophil-Lymphocyte Ratio as a Predictor of Mortality in Patients Who Underwent Coronary Artery Bypass Grafting. Heart Surg Forum. 2021;24(5):E814-20. doi: 10.1532/hsf.4099.

13. Tel BM, Kahveci G, Bilgin S, Kurtkulagi O, Taslamacioglu Duman T, Demirkol M et al. Haemoglobin and Red Cell Distribution Width Levels in Internal Medicine Patients Indicate Recurrent Hospital Admission During COVID-19. Family Medicine & Primary Care Review. 2022;24(1):32-36. doi: 10.5114/fmpcr.2022.113011.

14. Sarnak MJ, Tighiouart H, Manjunath G, MacLeod B, Griffith J, Salem D, et al. Anemia as a Risk Factor for Cardiovascular Disease in The Atherosclerosis Risk in Communities (ARIC) Study. J Am Coll Cardiol. 2002;40(1):27-33. doi: 10.1016/s0735-1097(02)01938-1.

15. Reinecke H, Trey T, Wellmann J, Heidrich J, Fobker M, Wichter T, et al. Haemoglobin-Related Mortality in Patients Undergoing Percutaneous Coronary Interventions. Eur Heart J. 2003;24(23):2142-50. doi: 10.1016/j.ehj.2003.09.008.

16. Aktas G, Alcelik A, Tekce BK, Tekelioglu V, Sit M, Savli H. Red Cell Distribution Width and Mean Platelet Volume in Patients with Irritable Bowel Syndrome. Prz Gastroenterol. 2014;9(3):160-3. doi: 10.5114/pg.2014.43578.

17. Aktas G, Sit M, Dikbas O, Tekce BK, Savli H, Tekce H, et al. Could Red Cell Distribution Width be a Marker in Hashimoto's Thyroiditis? Exp Clin Endocrinol Diabetes. 2014;122(10):572-4. doi: 10.1055/s-0034-1383564.

18. Cakir L, Aktas G, Mercimek OB,Enginyurt O. Are Red Cell Distribution Width and Mean Platelet Volume Associated with Rheumatoid Arthritis? Biomed Res. 2016;27(2):292-4.

19. Dagistan Y , Dagistan E , Gezici AR , Halicioglu S , Akar S , Özkan N , et al . Could Red Cell Distribution Width and Mean Platelet Volume be a Predictor for Lumbar Disc Hernias? Ideggyogy Sz. 2016;69(11-12):411-4. doi: 10.18071/isz.69.0411.

20. Aktas G, Sit M, Karagoz I, Erkus E, Ozer B, Kocak MZ, et al. Could Red Cell Distribution Width be a Marker of Thyroid Cancer? J Coll Physicians Surg Pak. 2017;27(9):556-8.

21. Ustaoglu M, Aktas G, Avcioglu U, Bas B, Bahceci BK. Elevated Platelet Distribution Width and Red Cell Distribution Width are Associated with Autoimmune Liver Diseases. Eur J Gastroenterol Hepatol. 2021;33(1 Suppl 1):e905-8. doi: 10.1097/MEG.0000000000002296.

22. Aktas G. Hematological Predictors of Novel Coronavirus Infection. Rev Assoc Med Bras (1992). 2021;67(Suppl 1):1-2. doi: 10.1590/1806-9282.67.Suppl1.20200678.

23. Ye Z, Smith C, Kullo IJ. Usefulness of Red Cell Distribution Width to Predict Mortality in Patients with Peripheral Artery Disease. Am J Cardiol. 2011;107(8):1241-5. doi: 10.1016/j.amjcard.2010.12.023.

24. Perlstein TS, Weuve J, Pfeffer MA, Beckman JA. Red Blood Cell Distribution Width and Mortality Risk in a Community-Based Prospective Cohort. Arch Intern Med. 2009;169(6):588-94. doi: 10.1001/archinternmed.2009.55.

25. Thygesen K, Alpert JS, Jaffe AS, Chaitman BR, Bax JJ, Morrow DA, et al. Fourth Universal Definition of Myocardial Infarction (2018). J Am Coll Cardiol. 2018;72(18):2231-64. doi: 10.1016/j.jacc.2018.08.1038.

26. ASTRUP P. Haemoglobin [Hemoglobin]. Ugeskr Laeger. 1958;120(6):198-9. Norwegian.

27. Ishigami J, Grams ME, Naik RP, Caughey MC, Loehr LR, Uchida S, et al. Hemoglobin, Albuminuria, and Kidney Function in Cardiovascular Risk: The ARIC (Atherosclerosis Risk in Communities) Study. J Am Heart Assoc. 2018;7(2):e007209. doi: 10.1161/JAHA.117.007209.

28. Uyarel H, Ergelen M, Cicek G, Kaya MG, Ayhan E, Turkkan C, et al. Red Cell Distribution Width as a Novel Prognostic Marker in Patients Undergoing Primary Angioplasty for Acute Myocardial Infarction. Coron Artery Dis. 2011;22(3):138-44. doi: 10.1097/MCA.0b013e328342c77b.

29. Horwich TB, Fonarow GC, Hamilton MA, MacLellan WR, Borenstein J. Anemia is Associated with Worse Symptoms, Greater Impairment in Functional Capacity and a Significant Increase in Mortality in Patients with Advanced Heart Failure. J Am Coll Cardiol. 2002;39(11):1780-6. doi: 10.1016/s0735-1097(02)01854-5.

30. Muzzarelli S, Pfisterer M; TIME Investigators. Anemia as Independent Predictor of Major Events in Elderly Patients with Chronic Angina. Am Heart J. 2006;152(5):991-6. doi: 10.1016/j.ahj.2006.06.014.

31. Lee PC, Kini AS, Ahsan C, Fisher E, Sharma SK. Anemia is an Independent Predictor of Mortality After Percutaneous Coronary Intervention. J Am Coll Cardiol. 2004;44(3):541-6. doi: 10.1016/j.jacc.2004.04.047.

32. Sincer I, Gunes Y, Mansiroglu AK, Aktas G. Differential Value of Eosinophil Count in Acute Coronary Syndrome Among Elderly Patients. Aging Male. 2020;23(5):958-61. doi: 10.1080/13685538.2019.1643310.

33. Sincer I, Mansiroglu AK, Aktas G, Gunes Y, Kocak MZ. Association between Hemogram Parameters and Coronary Collateral Development in Subjects with Non-ST-Elevation Myocardial Infarction. Rev Assoc Med Bras. 2020;66(2):160-5. doi: 10.1590/1806-9282.66.2.160.

34. Karnad A, Poskitt TR. The Automated Complete Blood Cell Count. Use of the Red Blood Cell Volume Distribution Width and Mean Platelet Volume in Evaluating Anemia and Thrombocytopenia. Arch Intern Med. 1985;145(7):1270-2. doi: 10.1001/archinte.145.7.1270.

35. Felker GM, Allen LA, Pocock SJ, Shaw LK, McMurray JJ, Pfeffer MA, et al. Red Cell Distribution Width as a Novel Prognostic Marker in Heart Failure: Data from the CHARM PROGRAM and the Duke Databank. J Am Coll Cardiol. 2007;50(1):40-7. doi: 10.1016/j.jacc.2007.02.067.

36. Ye Z, Smith C, Kullo IJ. Usefulness of Red Cell Distribution Width to Predict Mortality in Patients with Peripheral Artery Disease. Am J Cardiol. 2011;107(8):1241-5. doi: 10.1016/j.amjcard.2010.12.023.

37. Osadnik T, Strzelczyk J, Hawranek M, Lekston A, Wasilewski J, Kurek A, et al. Red Cell Distribution Width is Associated with Long-Term Prognosis in Patients with Stable Coronary Artery Disease. BMC Cardiovasc Disord. 2013;13:113. doi: 10.1186/1471-2261-13-113.

38. Sun XP, Chen WM, Sun ZJ, Ding XS, Gao XY, Liang SW, et al. Impact of Red Blood Cell Distribution Width on Long-Term Mortality in Patients with ST-Elevation Myocardial Infarction. Cardiology. 2014;128(4):343-8. doi: 10.1159/000359994.

39. Tonelli M, Sacks F, Arnold M, Moye L, Davis B, Pfeffer M, et al. Relation between Red Blood Cell Distribution Width and Cardiovascular Event

Rate in People with Coronary Disease. Circulation. 2008;117(2):163-8. doi: 10.1161/CIRCULATIONAHA.107.727545.

40. Huang S, Zhou Q, Guo N, Zhang Z, Luo L, Luo Y, et al. Association between Red Blood Cell Distribution Width and in-Hospital Mortality in Acute Myocardial Infarction. Medicine. 2021;100(15):e25404. doi: 10.1097/MD.0000000000025404.

41. Lippi G, Filippozzi L, Montagnana M, Salvagno GL, Franchini M, Guidi GC, et al. Clinical Usefulness of Measuring Red Blood Cell Distribution Width on Admission in Patients with Acute Coronary Syndromes. Clin Chem Lab Med. 2009;47(3):353-7. doi: 10.1515/cclm.2009.066.

42. Rahamim E, Zwas DR, Keren A, Elbaz-Greener G, Ibrahimli M, Amir O, et al. The Ratio of Hemoglobin to Red Cell Distribution Width: A Strong Predictor of Clinical Outcome in Patients with Heart Failure. J Clin Med. 2022;11(3):886. doi: 10.3390/jcm11030886.