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ORIGINAL ARTICLE

The Predictive Value of Red Cell Distribution Width and Red Cell Distribution Width to Erythrocyte Count Ratio for Adverse Cardiovascular Events During the Hospitalization of Patients of ST-segment Elevation Myocardial Infarction

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SUMMARY

Background: **High red cell distribution width (RDW) is correlated with poor prognosis in acute coronary syndromes (ACS), including ST-segment elevation myocardial infarction (STEMI). However, the association of red cell distribution width to erythrocyte count ratio (RER) with STEMI undergoing percutaneous coronary intervention (PCI) during hospitalization has not been investigated. Therefore, we performed a retrospective study to investigate whether RER is associated with STEMI patients after PCI during hospitalization.**
Methods: **A total of 331 patients, who were hospitalized for STEMI and underwent PCI, were enrolled. Receiver operating characteristic curve (ROC) analyses were used to find the cutoff value of RER and classify the patients into two groups including higher RER group and lower RER group by cutoff value. Differences between measured parameters in higher RER and lower RER groups were analyzed by the Mann-Whitney *U* test. The evaluation correlation of RDW, red blood cell, and RER with major adverse cardiovascular events was determined by bivariate regression analysis. Univariate logistic regression analysis was used to determine the factors associated with adverse cardiovascular events during the hospitalization of STEMI patients. Multivariate logistic regression analysis was performed to evaluate the potential independent predictors of STEMI.**
Results: **According to ROC analysis, the cutoff value of RER and RDW is 3.10 and 13.9, the sensitivity is 51% and 35%, the specificity is 76% and 80%, respectively. RER showed improved diagnostic capacity compared to RDW in correlation with adverse cardiovascular events during hospitalization in STEMI patients ($p < 0.001$). Compared with the lower RER group, the incidence of adverse cardiovascular events in STEMI patients is elevated in the higher RER group (75% vs. 64.5%, $p < 0.05$). Bivariate regression analysis indicated that RER and RDW showed a good correlation with adverse cardiovascular events, and the difference was statistically significant ($R = 0.10$ $p < 0.05$ vs. $R = 0.05$ $p < 0.05$). Univariate logistic regression analysis showed that age, heart rate, left ventricular ejection fraction, hyperlipidemia, RDW, mean platelet volume, total cholesterol, and RER were correlated with the occurrence of adverse cardiovascular events during the hospitalization of STEMI patients ($p < 0.05$). Multivariate logistic regression analysis demonstrated that RER could be an independent predictor of adverse cardiovascular events in STEMI patients (B: 0.574, OR: 1.776, 95% CI: 1.043 ~ 3.023, $p < 0.05$).**
Conclusions: **RER and RDW demonstrated good correlation with adverse cardiovascular events during hospitalization in STEMI patients. RER is a potential independent predictor of adverse cardiovascular events during hospitalization in STEMI patients.**
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KEY WORDS

red blood cell distribution width, red blood cell distribution width to erythrocyte count ratio, ST-segment elevation myocardial infarction, adverse cardiovascular events

INTRODUCTION

STEMI is characterized by thrombosis formation on the basis of rupture and erosion of unstable plaque in the coronary arteries, which occludes the lumen and coronary blood sharply reduced or interrupted, resulting in severe and lasting myocardial ischemia [1]. Acute coronary syndrome (ACS) is a type of acute coronary artery disease (CAD), including STEMI, unstable angina (UA), and non-ST-elevation myocardial infarction (NSTEMI) [2]. STEMI is a severe type of CAD with high risk of morbidity and mortality [3,4]. It is known that coronary artery disease results from a complex process known as atherosclerosis. Recently, many studies have shown that inflammation plays a role in the pathophysiology of atherosclerosis [5]. According to statistics, the mortality of STEMI in the United States is as high as 71% in men and 22% in women. Every year, about 1.5 million people have an acute myocardial infarction (AMI) and 450,000 people have another myocardial infarction. Moreover, recent mortality data indicates that the mortality of STEMI in China is rising [6-8]. At present, PCI is mostly used in clinical practice to restore myocardial blood perfusion as soon as possible, saving the dying myocardium, preventing the scope of infarction from expanding again, and protecting cardiac function [9,10]. However, PCI significantly increases the incidence of severe arrhythmia, heart failure, cardiogenic shock, and other adverse cardiovascular events in patients of STEMI [11-13]. Hence, it is particularly important to find simple and effective indicators to improve early diagnosis, timely risk stratification, and effective clinical intervention.

Cardiac troponin (cTn) is a sensitive and specific marker of heart muscle injury. However, cTn is only used to predict the acute phase of myocardial injury. Previous study demonstrated that RDW is a simple and economical marker of complete blood count and is often used by clinicians as a routine test for STEMI [14-16]. RDW, a parameter that reflects the volume variability of red blood cells and is detected by automatic hematology analyzer, is mainly used to the diagnosis of anemia and myelodysplastic syndrome [17-19]. Recent studies showed that RDW is an independent predictor for assessing risk of diseases such as pancreatitis, chronic heart failure, anemia, ankylosing spondylitis, and hepatitis B [20-24]. It has been reported that higher RDW value can be used as an independent predictor of the severity of coronary heart disease [25,26]. Research found that high red cell count has important clinical value in the diagnosis and prediction of early-onset coronary heart disease [27].

In this study, we evaluated the correlation of RDW and RDW/RER with STEMI and their utility as independent predictors of STEMI patients after PCI during hospitalization.

MATERIALS AND METHODS

Study design and population

The medical records of 331 (277 males, 54 females, mean age 60.40 ± 11.76 years), who were diagnosed with STEMI undergoing PCI during hospitalization at the Clinical Laboratory Medicine Center, Shenzhen Hospital of Southern Medical University between February 2014 and December 2017, were reviewed. Three hundred thirty-one STEMI patients were enrolled according to the revised Guidelines for the Management of Acute Myocardial Infarction/ST-elevation Myocardial Infarction, 2017 European Society of Cardiology (ESC) [28,29], and chest pain, electrocardiogram, and myocardial infarction indicators were reviewed to make a clear diagnosis. STEMI can be diagnosed when the following are excluded: 1) Patients with congenital heart disease, malignant tumors, autoimmune diseases, inflammatory diseases, cardiomyopathy, acute infectious diseases, hematological disease, diseases of the left main stem, and severe liver and kidney dysfunction; 2) have recently used glucocorticoid and immunosuppressive agents; and 3) have a recent history of surgery or trauma. The study protocol was approved by the University Local Research Ethics Committee.

Demographic data

1) Basic characteristics of patients: age, gender, heart rate, systolic blood pressure, and time from chest pain onset to PCI; 2) Previous medical history and medication history: a history of hypertension, diabetes, hyperlipidemia, old myocardial infarction, long-term use of aspirin, clopidogrel, beta-blockers, adverse cardiovascular events, inhibitors, statins, and nitrates, etc.

Biochemical and hematological measurements

From each subject, 1 mL peripheral venous blood was collected from an elbow vein after 12 hours of fasting, and all samples were sent to examination within 2 hours. Erythrocyte, leukocyte, platelet count, hemoglobin, neutrophil count, lymphocyte count, RDW, and

mean platelet volume were detected from anticoagulated blood samples on an XN-2000 automatic blood routine analyzer from Sysmex. Fasting blood sugar (FBS), creatinine, serum albumin, globulin, total cholesterol, high-density lipoprotein (HDL), low-density lipoprotein (LDL), creatine kinase, creatine kinase isoenzyme, cTnT, and brain natriuretic peptide (BNP) were measured from freshly separated serum at the clinical laboratory of the hospital on a Siemens Advia 1800 automatic biochemical analyzer. Left ventricular ejection fraction (LVEF) was determined by echocardiography.

Angiographic analysis

All patients underwent PCI with either femoral or radial arteries and were given 300 mg aspirin plus 300 mg clopidogrel before the angiography. All patients who had chest pain lasting 30 minutes, underwent PCI within 12 hours at the hospital. PCI should be completed within one and a half hours if chest pain occurs within 12 hours. PCI is performed if the duration of chest pain exceeds the treatment window. All patients were given clopidogrel (75 mg oral 1/day for 12 months) and aspirin (100 mg continuous) maintenance dose, and antiplatelet aggregation, anti-coagulation, lipid-adjusting, and other treatments after PCI. Collecting coronary angiography results of patients: 1) the coronary artery with a stenosis diameter greater than 50% was defined as the lesion vessel; 2) the lesion vessel (anterior descending branch, left lateral branch, right coronary artery, left coronary artery); 3) the number of stent implantations; 4) stent implantation vessels.

Observed indicators

Adverse cardiovascular events were recorded, including death, malignant arrhythmia, heart failure, and cardiogenic shock.

Grouping

RDW and erythrocyte count were obtained from the first blood routine after admission and RER was calculated. The cutoff value of RER for predicting adverse cardiovascular events was determined by ROC and was used to determine the higher RER group and lower RER group.

Statistics

All the statistical data were processed by SPSS version 23.0. Values are expressed as mean ± standard deviation or quantitative variables and counts or percentage for categorical variables. The cutoff value of RER for predicting adverse cardiovascular events was determined by ROC and determining the higher RER group and lower RER group. Meanwhile, ROC curves were also used to compare the sensitivity, specificity, and area under the curve of RER, RBC, and RDW. The correlation evaluation of RDW, red blood cell, and RER with major adverse cardiovascular events was determined by bivariate regression analysis. Univariate logistic regression analysis was used to determine the factors associated with adverse cardiovascular events during the hospitalization of STEMI patients. Multivariate logistic regression analysis was performed to evaluate the potential independent predictors of STEMI. A p-value less than 0.05 was considered to be statistically significant.

RESULTS

The ROC curve analysis of RER, RDW, and RBC

The ROC curve between RER and adverse cardiovascular events in 331 patients of STEMI undergoing PCI during hospitalization was demonstrated in Figure 1A. The cutoff value for RER was 3.10. All patients were divided into either the higher RER group (RER higher or equal than 3.10) or the lower RER group (RER lower than 3.10) according to the cutoff value for RER. The area under the curve (AUCs) of RER was 0.655, and it showed a statistically significant difference in RER levels of AUCs with adverse cardiovascular events in patients of STEMI after PCI during hospitalization ($p < 0.001$) (Figure 1C). The sensitivity and specificity of RER was 51% and 76%, respectively (Figure 1C).

The sensitivity and specificity of RER, RDW, and RBC with adverse cardiovascular events in patients of STEMI undergoing PCI during hospitalization were determined in Figure 1B. The AUCs of RER, RDW, and RBC are 0.655, 0.603, and 0.388, respectively. There were statistically significant differences between RER and RDW levels of AUCs in patients with STEMI ($p < 0.001$) (Figure 1B). However, there was no significant difference in the area under the curve of RBC (Figure 1B). The RER level of the cutoff is 3.10 (sensitivity 51%, specificity 76%, AUCs 0.655, $p < 0.001$), the RDW level of the cutoff is 13.95 (sensitivity 35%, specificity 80%, AUCs 0.603, $p < 0.001$), and RBC level of cutoff is 4.57 (sensitivity 33%, specificity 46%, AUCs 0.388, $p < 0.05$) (Figure 1C).

Basic characteristics of patients with STEMI

Demographic data, past medical history, and laboratory findings of 100 higher RER patients with STEMI and 231 patients with lower RER are presented in Table 1. The mean age of patients is 60.4 years, with a gender distribution of 277 men (83.7%) and 54 women (16.3%). In total, 100 (30%) STEMI patients were divided into the higher RER group, while 231 (70%) were classified as the lower RER group. Table 1 demonstrated age (67.26 ± 10.66 vs. 57.43 ± 10.96, $p < 0.001$), systolic blood pressure (127.49 ± 21.22 vs. 121.61 ± 22.84, $p = 0.02$), history of hypertension (51.0% vs. 44.2%, $p = 0.025$), aspirin history (80.0% vs. 68.0%, $p = 0.026$), Clopidogrel history (81.0% vs. 69.3%, $p = 0.028$), and statins history (80.0% vs. 67.1%, $p = 0.018$) in patients in the higher RER group had significantly higher levels than the lower RER group. On the contrary, a history of old myocardial infarction levels of the higher RER group was significantly lower than the lower RER group (33.0% vs. 67.1%, $p = 0.049$). No differ-

Table 1. Demographic data, past medical history and laboratory findings of patients with STEMI.

	All patients n = 331	Lower RER n = 231	Higher RER n = 100	p-value
Male-gender	277 (83.7%)	201 (87.0%)	76 (76.0%)	= 0.010
Age (years)	60.40 ± 11.76	57.43 ± 10.96	67.26 ± 10.66	< 0.001
Hypertension history	153 (46.2%)	102 (44.2%)	51 (51.0%)	= 0.025
Hyperlipidemia history	66 (19.9%)	50 (21.6%)	16 (16.0%)	= 0.237
Diabetes history	88 (26.6%)	62 (26.8%)	26 (26.0%)	= 0.874
Old myocardial infarction history	188 (56.8%)	155 (67.1%)	33 (33.0%)	= 0.049
Heart rate, beats/min	79.40 ± 16.01	79.26 ± 15.00	79.75 ± 18.20	= 0.917
Systolic Blood Pressure, mmHg	125.76 ± 22.51	121.61 ± 22.84	127.49 ± 21.22	= 0.020
Erythrocyte, T/L	4.61 ± 9.32	4.88 ± 0.61	4.00 ± 0.50	< 0.001
Leukocyte, G/L	16.13 ± 92.69	18.67 ± 110.90	10.26 ± 3.42	= 0.008
Neutrophil, G/L	8.36 ± 5.41	8.25 ± 3.85	8.61 ± 7.95	= 0.732
Platelet, G/L	241.18 ± 110.36	247.30 ± 110.21	227.04 ± 109.95	= 0.007
Lymphocyte, G/L	2.98 ± 15.52	3.56 ± 18.54	1.64 ± 0.92	< 0.001
Hemoglobin, g/L	137.52 ± 18.03	145.09 ± 13.07	120.02 ± 15.63	< 0.001
RDW, %	13.38 ± 1.30	13.10 ± 1.04	14.02 ± 1.59	< 0.001
Mean platelet volume, fL	10.59 ± 9.13	10.82 ± 10.90	10.05 ± 1.33	= 0.791
Globulin, g/L	27.16 ± 4.39	27.59 ± 44.1	26.17 ± 4.19	= 0.004
Albumin, g/L	40.30 ± 4.30	41.28 ± 4.08	38.04 ± 3.92	< 0.001
cTnT, μg/L	11.49 ± 86.35	14.50 ± 103.20	4.53 ± 6.53	= 0.230
BNP, ng/L	2,686.47 ± 6,304.23	1,391.36 ± 2,258.21	5,678.19 ± 1,037.70	< 0.001
Blood glucose, mmol/L	8.84 ± 4.37	8.75 ± 417	9.04 ± 4.81	= 0.960
Total cholesterol, mmol/L	7.06 ± 34.04	8.07 ± 40.72	4.74 ± 1.09	< 0.001
LDL, mmol/L	3.29 ± 1.04	3.45 ± 1.06	2.90 ± 0.87	< 0.001
HDL, mmol/L	1.20 ± 0.34	1.20 ± 0.31	1.20 ± 0.40	= 0.288
Creatinine, μmol/L	111.77 ± 70.91	100.90 ± 29.97	136.78 ± 117.16	= 0.003
Creatine kinase, IU/L	1,024.32 ± 1,321	1,042.6 ± 1,390.54	982.04 ± 1,150.38	= 0.891
Creatine kinase isoenzyme, IU/L	106.79 ± 158.20	111.66 ± 170.47	136.78 ± 117.56	= 0.711
PT, s	13.99 ± 1.84	13.87 ± 1.77	14.27 ± 125.38	= 0.044
Shock Index	0.65 ± 0.19	0.64 ± 0.14	0.67 ± 0.18	= 0.014
LVEF, %	45.97 ± 9.32	47.09 ± 8.31	43.38 ± 10.92	= 0.003
Killip classification	1.87 ± 0.88	1.71 ± 0.81	2.23 ± 0.95	< 0.001
Aspirin history	237 (71.6%)	157 (68.0%)	80 (80.0%)	= 0.026
Clopidogrel history	241 (72.8%)	160 (69.3%)	81 (81.0%)	= 0.028
β−blocker medication history	97 (29.3%)	62 (26.8%)	35 (35.0%)	= 0.135
ACEI/ARB drugs history	96 (29.0%)	70 (30.3%)	26 (26.0%)	= 0.385
Statins history	235 (71.0%)	155 (67.1%)	80 (80.0%)	= 0.018
Nitrate drug history	95 (28.7%)	65 (28.1%)	30 (30.0%)	= 0.544

RER - red cell distribution width/erythrocyte count ratio, RDW - red cell distribution width, PT - prothrombin time, LVEF - left ventricular ejection fraction, ACEI - ACE inhibitor, ARB - arbitration, LDL - low-density lipoprotein, HDL - high-density lipoprotein, BNP - brain natriuretic peptide, cTnT - cardiac troponin T.

ences in other parameters such as heart rate, hyperlipidemia history, diabetes mellitus history, β-blocker medication history, adverse cardiovascular events, ACEI/ARB drugs history, and nitrate drug history were observed between the groups ($p > 0.05$) (Table 1).

Our study showed that platelet count, RDW, BNP, cre-

Table 2. Angiographic comparison of patients with STEMI.

	All patients n = 331	Lower RER n = 231	Higher RER n = 100	p-value
Anterior descending branch	278 (84.0%)	193 (83.5%)	85 (85.0%)	= 0.038
Left circumflex branch	168 (50.8%)	122 (52.8%)	46 (46.0%)	= 0.274
Right coronary artery	214 (64.7%)	156 (67.5%)	58 (58.0%)	= 0.107
Left coronary artery	35 (10.6%)	24 (10.4%)	11 (11.0%)	= 0.868
Number of stents implanted	1.17 ± 0.70	1.17 ± 0.69	1.17 ± 0.73	= 0.861
Single branch	108 (32.6%)	75 (32.5%)	33 (33.0%)	= 0.025
Double branch	72 (21.8%)	52 (22.5%)	20 (20.0%)	= 0.599
Multiple branch	142 (42.9%)	100 (43.3%)	42 (42.0%)	= 0.979

RER - red cell distribution width/erythrocyte count ratio.

Table 3. Comparing the incidence of adverse cardiovascular events between groups.

	All patients n = 331	Lower RER n = 231	Higher RER n = 100	p-value
Death	3 (0.9%)	1 (0.4%)	2 (2.0%)	= 0.387
Malignant arrhythmia	59 (17.8%)	41 (17.7%)	18 (18.0%)	= 0.969
Heart failure	133 (40.2%)	87 (37.7%)	46 (46.0%)	= 0.017
Cardiogenic shock	63 (19.0%)	44 (19.0%)	19 (19.0%)	= 0.934
Adverse cardiovascular events	224 (67.7%)	149 (64.5%)	75 (75%)	= 0.033

RER - red cell distribution width/erythrocyte count ratio.

Table 4. The relationship between RER, RDW, and RBC with adverse cardiovascular events.

	RER	RDW	Adverse cardiovascular events
RER	-	R = 0.29, p < 0.001	R = 0.10, p = 0.038
RDW	R = 0.29, p < 0.001	-	R = 0.05, p = 0.026
RBC	R = -0.64, p < 0.001	R = 0.04, p = 0.304	R = -0.89, p = 0.052

RER - red cell distribution width/erythrocyte count ratio, RDW - red cell distribution width, RBC - red blood cell.

atinine, prothrombin time (PT), shock index, Killip classification, and time from chest pain onset to PCI in the higher RER group were significantly higher than in the lower RER group ($p < 0.05$), while erythrocyte, leukocyte, lymphocyte count, hemoglobin, serum albumin, globulin, total cholesterol, LDL, and LVEF in the higher RER group were significantly lower than in the lower RER group ($p < 0.05$). No differences in other parameters such as neutrophil count, mean platelet volume, fasting blood sugar (FBS), creatinine, HDL, creatine kinase, creatine kinase isoenzyme, and cTnT were seen in the groups ($p > 0.05$) (Table 1).

Angiographic analysis of patients with STEMI

Angiographic analysis between the higher RER group and the lower RER group of patients with STEMI were compared in Table 2. Compared with the lower RER group, the percentage of lesion vessels in the anterior descending branch and single branch in the higher RER group were higher than in the lower RER group (85.0% vs. 83.5% $p < 0.05$, 33.0% vs. 32.5%, $p < 0.05$, respectively). No differences in other parameters such as lesion vessels in the left branch, right coronary artery, double branch, multiple branch, and left coronary artery were compared between the groups ($p > 0.05$) (Table 2).

Comparison of adverse cardiovascular events between groups

Table 3 compared the incidence of adverse cardiovascular events after PCI during hospitalization between the higher and lower RER groups. The incidence of adverse cardiovascular events in the higher RER group were significantly higher than in the lower RER group (75% vs. 64.5%, $p < 0.05$). The incidence of heart failure in

Table 5. Univariate logistic regression analysis of patients with STEMI.

	B	OR	95% CI-upper	95% CI-lower	p-value
Age	0.007	1.007	1.036	0.979	= 0.036
Heart (rate)	0.001	1.001	1.020	0.982	= 0.028
Systolic blood pressure, mmHg	0.002	1.002	1.016	0.989	= 0.723
LVEF	0.014	1.014	1.047	0.983	= 0.038
Killip classification	0.053	1.055	1.477	0.754	= 0.755
Hyperlipidemia	0.058	1.060	2.092	0.537	= 0.008
Aspirin history	0.440	1.553	9.972	0.242	= 0.643
Leukocyte	0.002	1.002	1.013	0.991	= 0.763
Neutrophil	0.024	1.025	1.095	0.959	= 0.473
Platelet	0.001	1.001	1.005	0.998	= 0.530
RDW	0.412	1.509	3.861	0.590	= 0.039
Mean platelet volume	0.896	2.450	10.210	0.588	= 0.022
Albumin	0.053	1.055	1.264	0.880	= 0.563
Blood glucose	0.019	1.019	1.099	0.946	= 0.616
Total cholesterol	0.025	1.025	1.638	0.642	= 0.009
LDL	0.006	1.006	1.659	0.610	= 0.982
RER	0.264	0.768	7.276	0.081	= 0.008

B - regression coefficients, OR - odds ratio, RER - red cell distribution width/erythrocyte count ratio, RDW - red cell distribution width, RBC - red blood cell, LDL - low-density lipoprotein, LVEF - left ventricular ejection fraction.

Table 6. Multivariate logistic regression analysis of patients with STEMI.

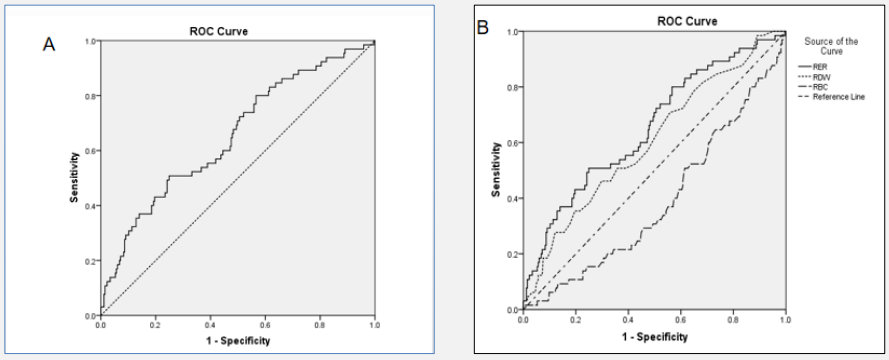
	B	OR	95% CI-upper	95% CI-lower	p-value
B-blocker medication history	-0.679	0.507	0.961	0.507	= 0.037
Hyperlipidemia history	0.307	2.028	3.867	1.064	= 0.032
Statins history	-0.578	0.561	0.966	0.326	= 0.037
Higher leukocyte	0.185	2.259	3.634	1.405	= 0.001
Higher mean platelet volume	0.677	1.968	3.902	0.993	= 0.052
Higher RER	0.574	1.776	3.023	1.043	= 0.034
cTnT	0.006	0.994	1.002	0.986	= 0.124
BNP	0.019	1.019	1.099	0.946	= 0.616
Shock Index	0.058	1.060	2.092	0.537	= 0.867
LVEF	0.014	1.014	1.047	0.983	= 0.382

B - regression coefficients, OR - odds ratio, RER - red cell distribution width/erythrocyte count ratio, LVEF - left ventricular ejection fraction, BNP - brain natriuretic peptide, cTnT - cardiac troponin T.

the higher RER group were significantly higher than in the lower RER group (46.0% vs. 37.7%, p = 0.017. The incidence of adverse cardiovascular events including death, malignant arrhythmia, and cardiogenic shock were not significant between groups (p > 0.05) (Table 3).

The correlation between RBC, RDW, and RER with adverse cardiovascular events in the higher RER and lower RER groups

The correlation between RBC, RDW, and RER with adverse cardiovascular events in patients of STEMI are shown in Table 4. Bivariate regression analysis (Kendall's tau b(K)) showed that RER and RDW had significant correlation with adverse cardiovascular events (R =



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	RER	RDW	RBC
Cutoff value	**3.10**	**13.95**	**4.57**
Sensitivity	**51%**	**35%**	**33%**
Specificity	**76%**	**80%**	**46%**
AUCs	**0.655**	**0.603**	**0.388**
p-value	**< 0.001**	**= 0.010**	**= 0.005**

Figure 1. The ROC curve analysis of RER, RDW, RBC.

(A) The ROC curve analysis of RER. (B) The ROC curve analysis of RER, RDW, RBC. (C) Statistical data obtained from the ROC curves of RER, RDW and RBC. AUCs - area under the curve, RER - red blood cell distribution width/erythrocyte count ratio, RDW - red cell distribution width, RBC - red blood cell.

0.10 $p < 0.05$, R = 0.05 $p < 0.05$, respectively). Meanwhile, RER had a statistically significant correlation with RDW (R = 0.29 $p < 0.001$). On the contrary, RBC had negative correlation with adverse cardiovascular events (R = -0.89 p = 0.052). RBC had no statistically significant correlation with RDW (R = 0.04 p = 0.304) (Table 4).

Univariate logistic regression analysis of adverse cardiovascular events during the hospitalization of STEMI patients

A multivariate analysis model was established for adverse cardiovascular events during hospitalization, and the results of univariate logistic regression analysis was shown in Table 5. Univariate logistic regression analysis showed that age (OR: 1.007, 95% CI: 0.979 ~ 1.036, p = 0.036), heart rate (OR: 1.001, 95% CI: 0.982 ~ 1.020, p = 0.028), hyperlipidemia (OR: 1.060, 95% CI: 0.537 ~ 2.092, p = 0.008), RDW (OR: 1.509, 95% CI: 0.590 ~ 3.861, p = 0.039), mean platelet volume (OR: 2.450, 95% CI: 0.588 ~ 10.210, p = 0.022), total cholesterol (OR: 1.025, 95% CI: 0.642 ~ 1.638, p = 0.009) and RER (OR: 1.633, 95% CI: 0.975 ~ 2.736, p = 0.026) had significant correlation with adverse cardiovascular events. On the contrary, systolic blood pressure, Killip classification, erythrocyte, platelet, serum albumin, globulin, neutrophil, LDL, and aspirin history had no significant correlation with adverse cardiovascular events ($p > 0.05$) (Table 5).

Multivariate logistic regression analysis of patients with STEMI

Multivariate logistic regression analysis of adverse cardiovascular events with patients of STEMI were shown in Table 6. Our results demonstrated that β-blocker medication history (B: -0.679, OR: 0.507, 95% CI: 0.507 ~ 0.961, p = 0.037), statins history (B: -0.578, OR: 0.561, 95% CI: 0.326 ~ 0.966, p = 0.037), hyperlipidemia history (B: 0.307, OR: 2.028, 95% CI: 1.064 ~ 3.867, p = 0.032), higher leukocyte (B: 0.185, OR: 2.259, 95% CI: 1.405 ~ 3.634, p = 0.001), time from chest pain onset to PCI (B: 0.518, OR: 1.431, 95% CI: 1.046 ~ 2.849, $p < 0.05$), and higher RER (B: 0.574, OR: 1.776, 95% CI: 1.043 ~ 3.023, $p < 0.05$) were potential independent predictors of adverse cardiovascular events during hospitalization in STEMI patients. However, higher RER (B = 0.574) had the highest contribution in all above. Meanwhile, Table 6 indicated that cTnT (B: 0.006, OR: 0.994, 95% CI: 0.986 ~ 1.002, p = 0.124), BNP (B: 0.019, OR: 1.019, 95% CI: 0.946 ~ 1.099, p = 0.616), shock index (B: 0.058, OR: 1.060, 95% CI: 0.537 ~ 2.092, p = 0.867), and LVEF (B: 0.014, OR: 1.014, 95% CI: 0.983 ~ 1.047, p = 0.382) were not significantly correlated in adverse cardiovascular events during hospitalization in STEMI patients ($p > 0.05$).

DISCUSSION

In this study, the relationship between RDW and RER with adverse cardiovascular events during hospitalization in STEMI patients was investigated. We found that RER and RDW had significant correlation with adverse cardiovascular events, and higher RER is a potential independent predictor of adverse cardiovascular events during hospitalization in STEMI patients.

With the change of human lifestyle, the risk factors of cardiovascular diseases such as smoking, high blood lipid, and hypertension are gradually increasing, and the morbidity of coronary atherosclerosis has also significantly increased and patients tend to be younger [30, 31]. Meanwhile, the morbidity of STEMI increased and the prognosis of adverse cardiovascular events became worse [12,32,33]. It is well known that the atherosclerosis first damages the arterial intima and incorporates multiple pathological changes, which is its pathogenesis [32,33]. In time, the gradual degeneration of the middle layer of the artery leads to bleeding within the plaque, plaque rupture, and local thrombosis [34-37]. Studies have found that the mechanism of plaque rupture is closely related to inflammatory response and coagulation mechanism [38-41].

RDW is a parameter reflecting the consistency of red blood cell volume, size, and shape. Elevated RDW indicates elevated volume heterogeneity of peripheral red cells [42-45]. Previous studies showed that higher RDW had significant correlation with STEMI [46]. When STEMI occurs, the activation of inflammatory factors inhibits red blood cell maturation, causing a large number of immature red blood cells to enter the bloodstream, which in turn stimulates an increase of RDW [47,48]. Hence, elevated RDW may have a significant relationship with the inflammatory mechanism of STEMI.

Historical studies found that the neutrophil/lymphocyte ratio, platelet/lymphocyte ratio, mean platelet volume, and prognostic nutritional index were independent predictors of adverse cardiovascular events during hospitalization in patients of STEMI [49-53]. Studies demonstrated that higher neutrophil/lymphocyte ratio and platelet/lymphocyte have a statistically significant relationship with adverse cardiovascular events in STEMI patients. Meanwhile, the researchers suggest that these indicators may also be involved in the development of inflammatory mechanisms in tumors [54-57].

Our study also has some limitations. Since our study is a single-center retrospective study, it is necessary to further explore the correlation between RER and long-term adverse cardiovascular events in STEMI patients with a large sample size to confirm the conclusion, not only the relationship between adverse cardiovascular events during hospitalization with patients of STEMI. Secondly, RER was not compared with traditional myocardial infarction markers (troponin T, brain natriuretic peptide, CRP, etc.) in this study. The exact cutoff value of RER needs to be further determined by a large sample size.

CONCLUSION

In summary, RER is an independent predictor of adverse cardiovascular events in STEMI patients during hospitalization, but further studies are needed to make long-term predictions of adverse cardiovascular events in STEMI patients using this simple indicator.

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Reference:

1. Zegre-Hemsey Jk, Patel Md, Fernandez Ar, Pelter MM, Brice J, Rosamond W. A Statewide Assessment Of Prehospital Electrocardiography Approaches Of Acquisition And Interpretation For St-Elevation Myocardial Infarction Based On Emergency Medical Services Characteristics. Prehosp Emerg Care 2019 Oct 31:1-7 (PMID: 31593496).

2. Roffi M, Patrono C, Collet JP, et al. [2015 Esc Guidelines For The Management Of Acute Coronary Syndromes In Patients Presenting Without Persistent St-Segment Elevation: Task Force For The Management Of Acute Coronary Syndromes In Patients Presenting Without Persistent St-Segment Elevation Of The European Society Of Cardiology (Esc)]. G Ital Cardiol (Rome). 2016 Oct;17(10):831-72 (PMID: 27869901).

3. Hajizadeh R, Ghaffari S, Salehi R, Mazani S, Aghavali S. Association Of Serum Uric Acid Level With Mortality And Morbidity Of Patients With Acute St-Elevation Myocardial Infarction. J Cardiovasc Thorac Res 2016;8(2):56-60 (PMID: 27489597).

4. Jibran Ms, Habib Sa, Khan Sb. Hypertensive Retinopathy: A Prognostic Factor For Morbidity And Mortality After Acute St Elevation Myocardial Infarction. J Coll Physicians Surg Pak 2019;29(3):205-9 (PMID: 30823942).

5. Perez De LA Hoz RA, Swieszkowski SP, Cintora FM, et al. Neuroendocrine System Regulatory Mechanisms: Acute Coronary Syndrome And Stress Hyperglycaemia. Eur Cardiol 2018;13(1): 29-34 (PMID: 30310467).

6. Brener Sj, Westerhout Cm, Fu Y, et al. Contribution Of Angiographic And Electrocardiographic Parameters Of Reperfusion To Prediction Of Mortality And Morbidity After Acute St-Elevation Myocardial Infarction: Insights From The Assessment Of Pexelizumab In Acute Myocardial Infarction Trial. Am Heart J 2009; 158(5):755-60 (PMID: 19853693).

7. Amlani S, Nadarajah T, Afzal R, Pal-Sayal R, Eikelboom JwW, Natarajan MK. Mortality And Morbidity Following A Major Bleed In A Registry Population With Acute St Elevation Myocardial Infarction. J Thromb Thrombolysis 2010;30(4):434-40 (PMID: 20213257).

8. Santos AR, Picarra BC, Celeiro M, Bento Â, Aguiar J; Investigadores Do Registo Nacional De Síndromes Coronárias Agudas. Multivessel Approach In St-Elevation Myocardial Infarction: Impact On In-Hospital Morbidity And Mortality. Rev Port Cardiol 2014;33(2):67-73 (PMID: 24502933).

9. Tiller C, Reindl M, Holzknecht M, et al. Relationship Between Admission Q Waves And Microvascular Injury In Patients With St-Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention. Int J Cardiol 2019 Dec 15;297:1-7 (PMID: 31629564).

10. Ciolek AM, Ma K, Garan AR, Eisenberger Ab, Jennings Dl. Use Of Cangrelor During Venoarterial Extracorporeal Membrane Oxygenation Following Percutaneous Coronary Intervention. Artif Organs 2019 (PMID: 31602658).

11. Akturk E, Askin L, Tasolar H, Türkmen S, Kaya H. Comparison Of The Predictive Roles Of Risk Scores Of In-Hospital Major Adverse Cardiovascular Events In Patients With Non-St Elevation Myocardial Infarction Undergoing Percutaneous Coronary Intervention. Med Princ Pract 2018;27(5):459-65 (PMID: 29672288).

12. Mccutcheon K, Triantafyllis AS, Marynissen T, et al. Major Adverse Cardiovascular Events While Awaiting Staged Non-Culprit Percutaneous Coronary Intervention After St-Segment Elevation Myocardial Infarction. Acta Cardiol 2019;74(1):60-4 (PMID: 29560788).

13. Akkus O, Topuz M, Koca H,et al. The Relationship Between Low Thiol Levels And Major Adverse Cardiovascular Events After Primary Percutaneous Coronary Intervention In Patients With Stemi. Turk Kardiyol Dern Ars 2018;46(4):248-59 (PMID: 29853692).

14. Sahin O, Akpek M, Sarli B, et al. Association Of Red Blood Cell Distribution Width Levels With Severity Of Coronary Artery Disease In Patients With Non-St Elevation Myocardial Infarction. Med Princ Pract,2015,24(2):178-183 (PMID: 25531370).

15. Sun XP, Chen W M, Sun Z J, 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 (PMID: 24970296).

16. Arbel Y, Shacham Y, Finkelstein A, et al. Red Blood Cell Distribution Width (RDW) And Long-Term Survival In Patients With St Elevation Myocardial Infarction. Thromb Res 2014;134(5):976-9 (PMID: 25213710).

17. Hong N, Kim CO, Youm Y, Choi JY, Kim HC, Rhee Y. Elevated Red Blood Cell Distribution Width Is Associated With Morphometric Vertebral Fracture In Community-Dwelling Older Adults, Independent Of Anemia, Inflammation, And Nutritional Status: The Korean Urban Rural Elderly (KURE) Study. Calcif Tissue Int 2019;104(1):26-33 (PMID: 30159752).

18. Sargento L, Simoes AV, Longo S, Lousada N, Palma Dos Reis R. Red Blood Cell Distribution Width Is A Survival Predictor Beyond Anemia And Nt-ProBNP In Stable Optimally Medicated Heart Failure With Reduced Ejection Fraction Outpatients. Clin Hemorheol Microcirc 2017;65(2):185-94 (PMID: 27716652).

19. Shi Z, Li B, Huang H, et al. Prognostic Impact Of Red Blood Cell Distribution Width In Myelodysplastic Syndromes. Br J Haematol 2019;186(2):352-5 (PMID: 30836422).

20. Yilmaz EM, Kandemir A. Significance Of Red Blood Cell Distribution Width And C-Reactive Protein/Albumin Levels In Predicting Prognosis Of Acute Pancreatitis. Ulus Travma Acil Cerrahi Derg 2018;24(6):528-31 (PMID: 30516251).

21. Liu S, Wang P, Shen PP, Zhou JH. Predictive Values Of Red Blood Cell Distribution Width In Assessing Severity Of Chronic Heart Failure. Med Sci Monit 2016;22:2119-25 (PMID: 27324271).

22. Liu XM, Dong JZ, Liu XH, et al. [The Impact Of Red Blood Cell Distribution Width On Outcome Of Elective Percutaneous Coronary Intervention In Non-Anemia Patients]. Zhonghua Nei Ke Za Zhi 2016;55(12):937-40 (PMID: 27916048).

23. Lin F, Wang X, Liang Y, et al. Red Blood Cell Distribution Width In Rheumatoid Arthritis, Ankylosing Spondylitis And Osteoarthritis: True Inflammatory Index Or Effect Of Anemia? Ann Clin Lab Sci 2018;48(3):301-7 (PMID: 29970432).

24. Fan X, Deng H, Wang X, et al. Association Of Red Blood Cell Distribution Width With Severity Of Hepatitis B Virus-Related Liver Diseases. Clin Chim Acta 2018;482:155-60 (PMID: 29627486).

25. Loprinzi PD. Comparative Evaluation Of Red Blood Cell Distribution Width And High Sensitivity C-Reactive Protein In Predicting All-Cause Mortality And Coronary Heart Disease Mortality. Int J Cardiol 2016;223:72-3 (PMID: 27543696).

26. Li Y, Xiao Q, Zeng W, et al. Red Blood Cell Distribution Width Is Independently Correlated With Diurnal Qtc Variation In Patients With Coronary Heart Disease. Medicine (Baltimore) 2015;94(23):E822 (PMID: 26061304).

27. Simonenko VB, Siuch NI, Vokuev IA. [Diagnostic Implications Of Changed Red Cell Count In Low-Intensity Laser Radiation Of Blood In Elderly Patients With Coronary Heart Disease]. Klin Med (Mosk) 2002;80(4):31-3 (PMID: 12043259).

28. Wagner M, Wanner C, Kotseva K, et al. Prevalence Of Chronic Kidney Disease And Its Determinants In Coronary Heart Disease Patients In 24 European Countries: Insights From The Euroaspire Iv Survey Of The European Society Of Cardiology. Eur J Prev Cardiol 2017;24(11):1168-80 (PMID: 28503987).

29. Pogosova N, Kotseva K, De Bacquer D, et al. Psychosocial Risk Factors In Relation To Other Cardiovascular Risk Factors In Coronary Heart Disease: Results From The Euroaspire Iv Survey. A Registry From The European Society Of Cardiology. Eur J Prev Cardiol 2017;24(13):1371-80 (PMID: 28534422).

30. Tutun U, Cicekcioglu F, Budak B, et al. Coronary Atherosclerosis Distribution And The Effect Of Blood Glucose Level On Operative Mortality/Morbidity In Diabetic Patients Undergoing Coronary Artery Bypass Grafting Surgery: A Single Center Experience. Anadolu Kardiyol Derg 2007;7(2):158-63 (PMID: 17513212).

31. Akdemir O. High Blood Glucose Concerns Heart Specialist Very/Coronary Atherosclerosis Distribution And The Effect Of Blood Glucose Level On Operative Mortality/Morbidity In Diabetic Patients Undergoing Coronary Artery Bypass Grafting Surgery: A Single Center Experience. Anadolu Kardiyol Derg 2007;7(3):338-9 (PMID:17785239).

32. Mangion K, Carrick D, Carberry J, et al. Circumferential Strain Predicts Major Adverse Cardiovascular Events Following An Acute St-Segment-Elevation Myocardial Infarction. Radiology 2019;290(2):329-37 (PMID: 30457480).

33. Khorramirouz R, Corban MT, Yang SW, et al. Microvascular Obstruction In Non-Infarct Related Coronary Arteries Is An Independent Predictor Of Major Adverse Cardiovascular Events In Patients With St Segment-Elevation Myocardial Infarction. Int J Cardiol 2018;273:22-8 (PMID: 30131228).

34. Ma L, Zheng H, Zhang T. Il-10 Suppress Vascular Smooth Muscle Cell Apoptosis Via JAK2/STAT3 Signaling Pathway And Its Mechanism Of Action In Atherosclerosis. Minerva Endocrinol 2019 (PMID: 31359747).

35. Andreou I, Stone PH, Ikonomidis I, Alexopoulos D, Sabaté M. Recurrent Atherosclerosis Complications As A Mechanism For Stent Failure. Hellenic J Cardiol 2019 (PMID: 31034959).

36. Puca A A, Carrizzo A, Spinelli C, et al. Single Systemic Transfer Of A Human Gene Associated With Exceptional Longevity Halts The Progression Of Atherosclerosis And Inflammation In Apoe Knockout Mice Through A Cxcr4-Mediated Mechanism. Eur Heart J 2019 (PMID: 31289820).

37. Therapeutic Target Identified For Slowing Early Atherosclerosis In Progeria: Researchers Have Identifi Ed A New Molecular Mechanism Involved In The Premature Development Of Atherosclerosis In Progeria. Am J Med Genet A 2019;179(6):881-2 (PMID: 31033169).

38. Hiro T. [Pathogenesis Of Acute Coronary Syndrome: Mechanism Of Plaque Rupture]. Nihon Rinsho 2011;69 Suppl 9:286-93 (PMID: 22724217).

39. Abela GS, Aziz K. Cholesterol Crystals Cause Mechanical Damage To Biological Membranes: A Proposed Mechanism Of Plaque Rupture And Erosion Leading To Arterial Thrombosis. Clin Cardiol 2005;28(9):413-20 (PMID: 16250264).

40. Brezinski ME, Harjai KJ. Longitudinal Necrotic Shafts Near Tcfas-A Potential Novel Mechanism For Plaque Rupture To Trigger Acs?. Int J Cardiol 2014;177(3):738-41 (PMID: 25449500).

41. Weitz JI. Activation Of Blood Coagulation By Plaque Rupture: Mechanisms And Prevention. Am J Cardiol 1995;75(6):18b-22b (PMID: 7863966).

42. Loprinzi PD. Effects Of Light-Intensity Physical Activity On Red Blood Cell Distribution Width: Implications For A Novel Mechanism Through Which Light-Intensity Physical Activity May Influence Cardiovascular Disease. Int J Cardiol 2016;203:724-5 (PMID: 26587727).

43. Nightingale TE, Bhangu GS, Bilzon JLJ, Krassioukov AV. A Cross-Sectional Comparison Between Cardiorespiratory Fitness, Level Of Lesion And Red Blood Cell Distribution Width In Adults With Chronic Spinal Cord Injury. J Sci Med Sport 2019 (PMID: 31558360).

44. Wang P, Huang C, Meng Z, et al. No Obvious Association Exists Between Red Blood Cell Distribution Width And Thyroid Function. Biomark Med 2019 (PMID: 31599643).

45. Wang B, Aihemaiti G, Cheng B, Li X. Red Blood Cell Distribution Width Is Associated With All-Cause Mortality In Critically Ill Patients With Cardiogenic Shock. Med Sci Monit 2019;25: 7005-15 (PMID: 31530796).

46. Catic J, Jurin I, Lucijanic M, Jerkić H, Blažeković R. High Red Cell Distribution Width At The Time Of St Segment Elevation Myocardial Infarction Is Better At Predicting Diastolic Than Systolic Left Ventricular Dysfunction: A Single-Center Prospective Cohort Study. Medicine (Baltimore) 2018;97(18):E601 (PMID: 29718862).

47. Lappegard J, Ellingsen T S, Hindberg K, et al. Impact Of Chronic Inflammation, Assessed By Hs-Crp, On The Association Between Red Cell Distribution Width And Arterial Cardiovascular Disease: The Tromso Study. TH Open 2018;2(2):E182-E189 (PMID: 31249941).

48. Targonski R, Sadowski J, Starek-Stelmaszczyk M, Targoński R, Rynkiewicz A. Prognostic Significance Of Red Cell Distribution Width And Its Relation To Increased Pulmonary Pressure And Inflammation In Acute Heart Failure. Cardiol J 2018 (PMID: 30234 900).

49. Yaylak B, Ede H, Baysal E, et al. Neutrophil/Lymphocyte Ratio Is Associated With Right Ventricular Dysfunction In Patients With Acute Inferior St-Segment Elevation Myocardial Infarction. Cardiol J 2016;23(1):100-6 (PMID: 26412608).

50. Celik T, Balta S, Demir M, et al. Predictive Value Of Admission Red Cell Distribution Width-Platelet Ratio For No-Reflow Phenomenon In Acute St Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention. Cardiol J 2016;23(1):84-92 (PMID: 26503078).

51. Erratum: Relationship Of Admission Mean Platelet Volume, Platelet Distribution Width And White Blood Cells With St Resolution In Patients With Acute St Segment Elevation Myocardial Infarction Treated With Streptokinase Without History Of Previous Cardiovascular Surgery. Perspect Clin Res 2017;8(4):198 (PMID: 29109940).

52. Avci E, Kiris T, Celik A, et al. Prognostic Value Of Rising Mean Platelet Volume During Hospitalization In Patients With St-Segment Elevation Myocardial Infarction Treated With Primary Percutaneous Coronary Intervention. BMC Cardiovasc Disord 2018; 18(1):226 (PMID: 30526502).

53. Chen QJ, Qu HJ, Li DZ, et al. Prognostic Nutritional Index Predicts Clinical Outcome In Patients With Acute St-Segment Elevation Myocardial Infarction Undergoing Primary Percutaneous Coronary Intervention. Sci Rep 2017;7(1):3285 (PMID: 286074 42).

54. Sun G, Li Y, Peng Y, et al. Impact of the preoperative prognostic nutritional index On Postoperative And Survival Outcomes In Colorectal Cancer Patients Who Underwent Primary Tumor Resection: A Systematic Review And Meta-Analysis. Int J Colorectal Dis 2019;34(4):681-9 (PMID: 30680451).

55. Ozyurek B A, Ozmen O, Ozdemirel T S, et al. Relation Between Neutrophil/Lymphocyte Ratio And Primary Tumor Metabolic Activity In Patients With Malign Pleural Mesothelioma. Clin Respir J 2018;12(2):646-51 (PMID: 27768834).

56. Wodarczyk M, Kasprzyk J, Sobolewska-Wodarczyk A, et al. Mean Platelet Volume As A Possible Biomarker Of Tumor Progression In Rectal Cancer. Cancer Biomark 2016;17(4):411-7 (PMID: 27802192).

57. Tumturk A, Ozdemir MA, Per H, et al. Pediatric Central Nervous System Tumors In The First 3 Years Of Life: Pre-Operative Mean Platelet Volume, Neutrophil/Lymphocyte Count Ratio, And White Blood Cell Count Correlate With The Presence Of A Central Nervous System Tumor. Childs Nerv Syst 2017;33(2): 233-8 (PMID: 27942922).