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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

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Abstract

Multiple studies have demonstrated the association of red cell distribution width (RDW) with the ultrasound parameters of both systolic and diastolic heart dysfunction. We aimed to further investigate the clinical associations of RDW in the setting of ST-elevation myocardial infarction (STEMI) and to comparatively evaluate its predictive properties regarding systolic and diastolic dysfunction.

A total of 89 patients with STEMI were prospectively analyzed. RDW was obtained at the time of STEMI and compared to the parameters of systolic and diastolic dysfunction obtained by transthoracic heart ultrasound on the 5th through 7th day post-STEMI.

The median RDW was 13.9%, and among other factors, RDW was significantly associated with older age ($P < .001$), arterial hypertension ($P = .017$), hyperlipoproteinemia 2, nonsmoking ($P = .027$), increased thrombolysis in myocardial infarction score ($P = .004$), and multivessel disease ($P = .007$). A higher RDW was observed in patients with parameters that indicated systolic and diastolic dysfunction (ejection fraction of the left ventricle < 50% [$P = .009$], early/late diastolic filling wave ratio [E/A] < 1 [$P = .001$], ratio of peak early transmitral velocity and early diastolic annular velocity [E/E′] >10 [$P < .001$], and combined E/A < 1 and E/E′ > 10 [$P < .001$]). The best discriminatory properties were observed for combined E/A < 1 and E/E′ > 10. RDW remained significantly associated with the aforementioned parameters in a series of multivariate regression models.

Elevated RDW is significantly associated with the parameters of systolic and diastolic dysfunction even after adjusting for several confounding factors in the setting of STEMI and subsequent percutaneous coronary intervention. RDW seems to be better at discriminating patients with diastolic rather than systolic dysfunction.

Abbreviations: A = peak velocity of the late diastolic filling wave, AMI = acute myocardial infarction, AUC = area under the curve, BMI = body mass index, CABG = coronary artery bypass grafting, CK = creatine kinase, CI = confidence interval, CRP = C-reactive protein, cTnI = cardiac troponin I, CV = cardiovascular, CVI/TIA = cerebrovascular accident/transient ischemic attack, DM = diabetes mellitus, E′ = early diastolic mitral annular velocity, E = peak velocity of the early diastolic filling wave, E/A = ratio of peak velocity flow in early diastole to peak velocity flow in late diastole, E/E′ = ratio of early transmitral velocity and early diastolic annular velocity, EFLV = ejection fraction of the left ventricle, FA = atrial fibrillation, HA = arterial hypertension, HbA1C = glycosylated hemoglobin, HR = hazard ratio, IQR = interquartile range, LVEDD = end-diastolic dimension of the left ventricle, LVESD = end-systolic dimension of the left ventricle, MPV = mean platelet volume, NLR = neutrophil-to-lymphocyte ratio, PCI = percutaneous coronary intervention, PLR = platelet-to-lymphocyte ratio, RDW = red cell distribution width, ROC = receiver operating characteristic, STEMI = ST-elevation myocardial infarction, TIMI = thrombolysis in myocardial infarction, WBC = white blood cells.

Keywords: diastolic dysfunction, red cell distribution width, ST segment elevation myocardial infarction, systolic dysfunction

1. Introduction

Red cell distribution width (RDW) is a measure of the diversity of the size of red blood cells. It is one of the parameters included in routine blood counts and is thus widely available.[1] Along with mean corpuscular volume, RDW is useful in differential diagnosis of various hematological disorders. However, it was shown by Felker et al that elevated RDW is a very strong predictor of morbidity and mortality in patients with chronic heart disease.[2] This association remained after a wide variety of adjustments, and for the first time, RDW was recognized as a marker of adverse outcomes in a disease other than the one for which it was intended. The same finding was shown in the acute setting of heart failure,[3] coronary disease, acute myocardial infarction (AMI), and various other diseases.[4–9] Multiple studies demonstrated an association of RDW with the ultrasound parameters of both systolic and diastolic heart dysfunction in different cardiovascular (CV) settings.[10–16]

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We aimed to further investigate the relationship between RDW and the ultrasonic parameters of systolic and diastolic function of the left ventricle in patients after ST elevation myocardial infarction (STEMI) and percutaneous coronary intervention (PCI) and to compare its properties with clinically and prognostically relevant parameters in this setting.

2. Methods

2.1. Study population

The study was conducted at our institution and in accordance with the principles of the Declaration of Helsinki. It was also approved by the institutional local committee on human research. This study was performed as a single-center prospective cohort study.

All patients <70 years of age admitted to the emergency department with the diagnosis of STEMI from June 2016 until July 2017 were included. A total of 89 patients entered the study. The exclusion criteria were anemic patients (hemoglobin <130 g/L for males and 120 g/L for females), obese patients (body mass index [BMI] > 30), severe renal dysfunction (estimated glomerular filtration rate ≤ 30 mL/min per 1.73 m^2), cardiopulmonary resuscitation or patients with cardiogenic shock after AMI, and previous AMI.

2.2. Study protocol

A 12-lead electrocardiogram was recorded in each patient immediately after hospital admission. STEMI was defined as new ST elevation at the J point in at least 2 contiguous leads of ≥2 mm (0.2 mV) in men or ≥1.5 mm (0.5 mV) in women in leads V_2–V_3 and/or of ≥1 mm (0.1 mV) in other contiguous leads or the limb leads in the absence of left ventricular hypertrophy or left bundle-branch block. Using these electrocardiographic guidelines including elevated biomarkers of myocardial necrosis and positive symptomatology, patients fulfilled the criteria to be included in the study. During the admission process, clinical information was obtained regarding the patients' history of diabetes mellitus (DM), arterial hypertension (HA), hyperlipidemia, and smoking.

2.3. Laboratory testing

On admission, venous blood was obtained from all the patients. RDW, mean platelet volume (MPV), neutrophils, lymphocytes, and white blood cells (WBC) were measured as part of the automated complete blood count before starting any medication; the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) were additionally calculated. All measurements were performed by the Siemens Advia 2120i automatic blood counter (Siemens Healthcare Diagnostics [Shanghai], Walpole, NY). The lipid profile was measured following the first fasting period.

2.4. Echocardiographic measurements

All measurements were performed by 1 single echosonographer. Three consecutive cardiac cycles were recorded, after which the mean value of all of the parameters was calculated. The echosonographer was blinded to the laboratory values. The testing was performed between the 5th and 7th day after the STEMI. Standard echocardiographic views were acquired using Vivid E9. Using M-mode in the parasternal long-axis view, the end-diastolic dimension (LVEDD) and end-systolic dimension (LVESD) of the left ventricle were measured. The ejection fraction of the left ventricle (EFLV) was expressed using modified Simpson method.[17] All patients underwent a comprehensive evaluation with pulsed-wave Doppler imaging in a 4-chamber view. The Doppler gate was placed at the tips of the leaflets of the mitral valve. The variables that were measured included: peak velocity of early diastolic filling wave (E), late diastolic filling wave (A), and deceleration time of the E-wave velocity. Ratio of peak velocity flow in early diastole to peak velocity flow in late diastole (E/A) was calculated afterwards. By means of tissue Doppler imaging, early diastolic mitral annular velocity (E′) was measured. This parameter was obtained from the apical 4-chamber view with a 2- to 5-mm sample volume placed at the septal corner of the mitral annulus, after which the ratio of the peak early transmitral velocity and early diastolic annular velocity (E/E′) was calculated.

2.5. Statistical methods

The normality of the distribution of the numerical variables was tested using the Kolmogorov–Smirnov test. Normally distributed numerical variables were represented as the mean ± standard deviation. Non-normally distributed variables were represented as median and interquartile range (IQR). Categorical variables were represented as proportions.

Non-normally distributed numerical variables were compared between groups using the Mann–Whitney *U* test of the Kruskal–Wallis analysis of variance test when appropriate. The Spearman rank correlation was used to assess correlation between numerical variables. Categorical variables were compared between groups using the chi-squared test or Fisher exact test when appropriate. Receiver operating characteristic (ROC) curve analysis was used to determine optimal cut-off values of numerical variables, area under the curve (AUC), sensitivity, specificity, and positive and negative likelihood ratios. Multivariate analyses regarding the associations of different parameters with the presence of systolic and diastolic dysfunction were performed using logistic regression.

Survival analyses were based on the Kaplan–Meier method. Univariate survival analyses were performed using the Cox–Mantel version of the log-rank test, and screening of factors that potentially affect survival/time-to-event of interest was performed using a custom made MS Excel workbook.[18]

P values < .05 were considered statistically significant. MedCalc statistical program ver. 17.8.1 (MedCalc Software bvba, Ostend, Belgium) was used for the analyses.

3. Results

3.1. Patients' characteristics

A total of 89 patients with STEMI were analyzed. There were 58 (65.2%) males and 31 (34.8%) females with a mean age overall of 59.8 ± 11.2 years. The majority of patients had inferior AMI localization (53/89 [59.6%]), followed by posterior (33/89 [37.1%]), septal (29/89 [32.6%]), anterior (29/89 [32.6%]), and lateral (17/89 [19.1%]) localization. Patients' characteristics are shown in Table 1, and ultrasound characteristics are shown in Table 2.

3.2. RDW and patients' characteristics

RDW values were non-normally distributed and were compared with other parameters using nonparametric statistical tests. The median RDW was 13.9% (IQR 13.4–14.5). A total of 8/89 (9%)

Table 1

Characteristics of all patients stratified according to RDW ≤13.9% and >13.9% (patients separated at median RDW value).

	All patients	RDW ≤ 13.9%	RDW > 13.9%	P
Number of patients	89	47	42	—
Age, y	59.8±11.2	56±11	64±10.1	.001*
Gender				.291
Male	58/89 (65.2%)	33/47 (70.2%)	25/42 (59.5%)	
Female	31/89 (34.8%)	14/47 (29.8%)	17/42 (40.5%)	
Family history of CV disease	67/89 (75.3%)	36/47 (76.6%)	31/42 (73.8%)	.761
HA	60/89 (67.4%)	27/47 (57.4%)	33/42 (78.6%)	.034*
DM	25/89 (28.1%)	13/47 (27.7%)	12/42 (28.6%)	.924
Hyperlipoproteinemia	52/89 (58.4%)	22/47 (46.8%)	30/42 (71.4%)	.019*
CVI/TIA prior to AMI	6/89 (6.7%)	2/47 (4.3%)	4/42 (9.5%)	.415
Peripheral artery disease	31/89 (34.8%)	16/47 (34%)	15/42 (35.7%)	.869
Smoking	63/89 (70.8%)	36/47 (76.6%)	27/42 (64.3%)	.202**
FA prior to AMI	4/88 (4.5%)	2/47 (4.3%)	2/41 (4.9%)	1.000
WBC	10.2 IQR (8.8–12.5)	10.8 IQR (9.2–12.7)	9.9 IQR (7.6–12.1)	.148**
Hemoglobin	144 IQR (136–151)	147 IQR (139–158)	139.5 IQR (131.3–146.8)	.004*
Platelets	232 IQR (196–299)	236 IQR (193–297)	227.5 IQR (200.8–312.5)	.622
CRP	5.1 IQR (2.4–7.7)	5.1 IQR (2.1–7)	5 IQR (3.2–7.9)	.359
BMI	28.7 IQR (25.8–32.5)	28.6 IQR (26.3–32.3)	29.3 IQR (25.7–32.7)	.837
cTnI	0.3 IQR (0.1–1.1)	0.4 IQR (0.1–1.4)	0.2 IQR (0.1–1)	.535
AMI localization				.141***
Inferior	53/89 (59.6%)	32/47 (68.1%)	21/42 (50%)	.083
Posterior	33/89 (37.1%)	20/47 (42.6%)	13/42 (31%)	.258
Lateral	17/89 (19.1%)	6/47 (12.8%)	11/42 (26.2%)	.108
Septal	29/89 (32.6%)	12/47 (25.5%)	17/42 (40.5%)	.133
Anterior	29/89 (32.6%)	12/47 (25.5%)	17/42 (40.5%)	.133
ASCVD score	0.1 IQR (0.1–0.3)	0.1 IQR (0.1–0.2)	0.2 IQR (0.1–0.3)	.110**
TIMI score	3 IQR (1–5)	2 IQR (1–4)	3 IQR (2–6)	.021*
Extension of coronary disease				
SVD	53/86 (61.6%)	36/47 (76.6%)	17/39 (43.6%)	.002*
MVD	33/86 (38.4%)	11/4 (23.4%)	22/3 (56.4%)	
Dominantly affected vessel				.624***
Right coronary artery	39/89 (43.8%)	22/47 (46.8%)	17/42 (40.5%)	.548
Circumflex artery	13/89 (14.6%)	8/47 (17%)	5/42 (11.9%)	.495
Left anterior descending artery	32/89 (36%)	14/47 (29.8%)	18/42 (42.9%)	.200
Other	5/89 (5.6%)	3/47 (6.4%)	2/42 (4.8%)	1.000

AMI = acute myocardial infarction, ASCVD = atherosclerotic cardiovascular disease, BMI = body mass index, CRP = C-reactive protein, cTnI = cardiac troponin I, CV = cardiovascular, CVI/TIA = cerebrovascular accident/transient ischemic attack, DM = diabetes mellitus, FA = atrial fibrillation, HA = arterial hypertension, IQR = interquartile range, MVD = multivessel disease, RDW = red cell distribution width, SVD = single-vessel disease, TIMI = thrombolysis in myocardial infarction, WBC = white blood cells.

* Statistically significant at $P < .05$.

** Statistically significant at $P < .05$ when RDW is used as a continuous variable.

*** Overall P value.

Table 2

Ultrasound characteristics of all patients stratified according to red cell distribution width ≤13.9% and >13.9% (patients separated at median red cell distribution width value).

	All patients	RDW ≤ 13.9%	RDW > 13.9%	P
Number of patients	89	47	42	—
EFLV	53.1±9.1	54.7±7.6	51.2±10.4	.074**
EFLV < 50%	33/89 (37.1%)	13/47 (27.7%)	20/42 (47.6%)	.052**
LVEDD	52±5.3	51.7±5.4	52.3±5.2	.602
LVESD	36.9±5.4	36.4±5.1	37.6±5.7	.297
E	0.6 IQR (0.5–0.8)	0.6 IQR (0.6–0.8)	0.6 IQR (0.5–0.8)	.368
A	0.7 IQR (0.6–0.9)	0.7 IQR (0.5–0.8)	0.8 IQR (0.7–1)	.001*
E/A	0.8 IQR (0.6–1.1)	1 IQR (0.7–1.2)	0.7 IQR (0.6–0.9)	.006*
E/A < 1	57/89 (64%)	24/47 (51.1%)	33/42 (78.6%)	.007*
E/E′	8.9 IQR (6.9–12.8)	7.3 IQR (6.7–10.2)	12.2 IQR (8.5–14)	<.001*
E/E′ > 10	57/89 (64%)	12/47 (25.5%)	29/42 (69%)	<.001*
TAPSE	20 IQR (18–21)	20 IQR (18–21.5)	20 IQR (18–21)	.232

A = peak velocity of the late diastolic filling wave, E = peak velocity of the early diastolic filling wave, E/A = ratio of peak velocity flow in early diastole to peak velocity flow in late diastole, E/E′ = ratio of early transmitral velocity and early diastolic annular velocity, EFLV = ejection fraction of the left ventricle, IQR = interquartile range, LVEDD = end-diastolic dimension of the left ventricle, LVESD = end-systolic dimension of the left ventricle, RDW = red cell distribution width, TAPSE = tricuspid annular plane systolic excursion.

* Statistically significant at $P < .05$.

** Statistically significant at $P < .05$ when RDW is used as a continuous variable.

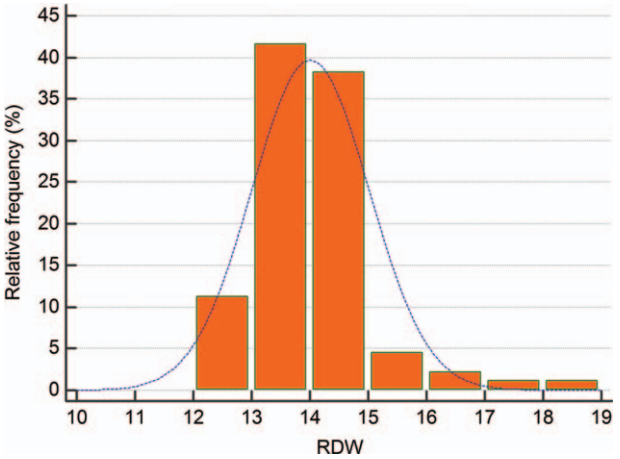

Figure 1. RDW values were non-normally distributed. RDW = red cell distribution width.

of the patients had RDW values >15%, which is above the upper limit of the reference range used in our laboratory. The distribution of RDW values is shown in Fig. 1.

RDW was statistically significant higher in older patients ($P < .001$, Rho = 0.43), in patients with HA (median 14.2% vs. 13.5% for patients with and without HA, $P = .017$), in patients with hyperlipoproteinemia (median 14.2% vs. 13.6% for patients with and without hyperlipoproteinemia, $P = .037$), in nonsmokers (median 14.4% vs. 13.8% for nonsmokers and smokers, $P = .027$), and in patients with lower WBC ($P = .026$, Rho = −0.24), lower hemoglobin ($P = .001$, Rho = −0.34), and lower lymphocytes ($P = .013$, Rho = −0.26). RDW was positively correlated with the thrombolysis in myocardial infarction (TIMI) score ($P = .004$, Rho = 0.31) as shown in Fig. 2A and the atherosclerotic cardiovascular disease score ($P = .042$, Rho = 0.23).

We found no statistically significant association regarding gender ($P = .281$), positive family history for CV diseases ($P = .475$), DM ($P = .667$), cerebrovascular accident/transient ischemic attack (CVI/TIA) prior to AMI ($P = .176$), peripheral artery disease ($P = .433$), atrial fibrillation (FA) prior to AMI ($P = .361$), glycosylated hemoglobin (HbA1C) ($P = .525$), total cholesterol ($P = .704$), low-density lipoprotein cholesterol ($P = .361$), high-density lipoprotein cholesterol ($P = .067$), triglycerides ($P = .152$), platelets ($P = .630$), C-reactive protein (CRP) ($P = .064$), fibrinogen ($P = .282$), body height ($P = .684$), body weight ($P = .566$), BMI ($P = .824$), or waist circumference ($P = .993$).

3.3. RDW and coronary disease characteristics

Patients with multivessel disease had statistically significant higher RDW values than patients with single-vessel disease (median 14.3% vs. 13.6%, $P = .007$). RDW did not differ significantly with regard to dominantly affected coronary vessel

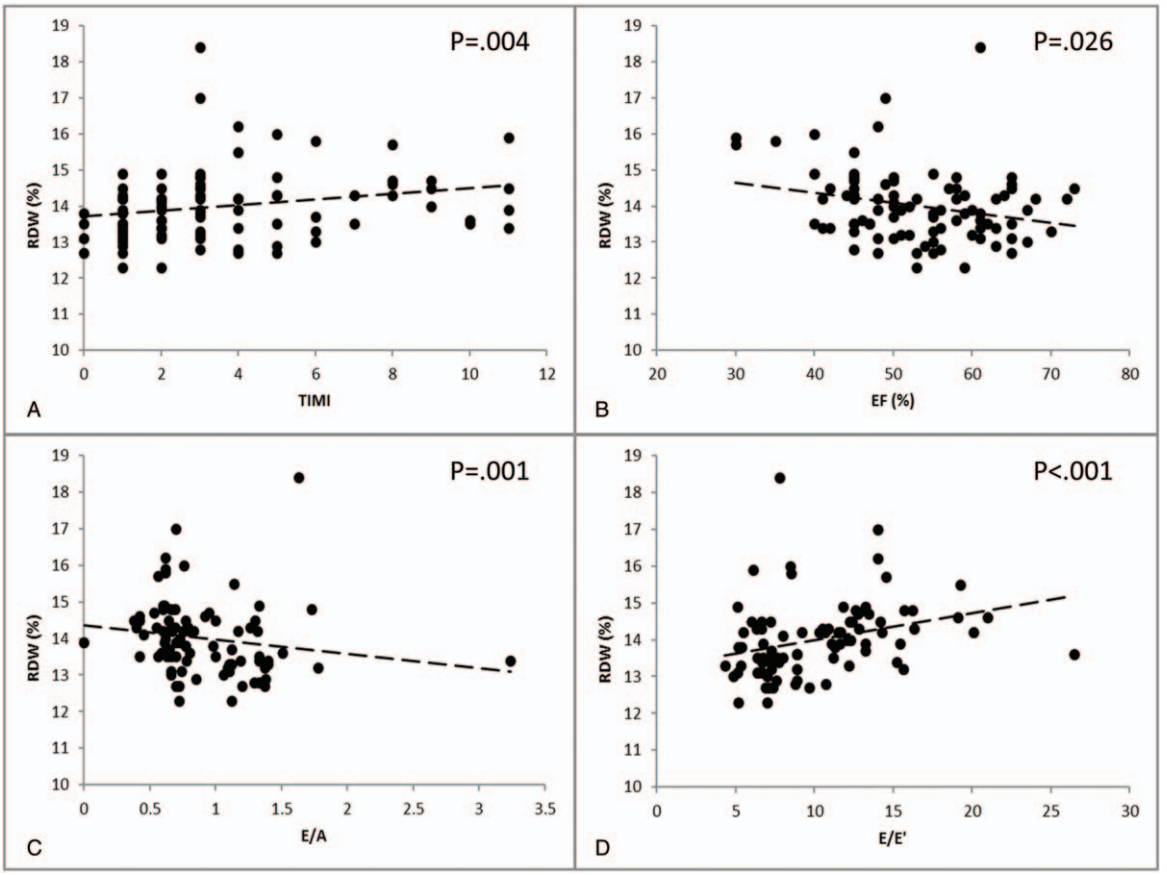

Figure 2. (A) RDW values were positively correlated with TIMI score, (B) negatively correlated with EFLV, (C) negatively correlated with E/A, and (D) positively correlated with E/E′. E/A = ratio of peak velocity flow in early diastole to peak velocity flow in late diastole, E/E′ = ratio of early transmitral velocity and early diastolic annular velocity, EFLV = ejection fraction of the left ventricle, RDW = red cell distribution width, TIMI = thrombolysis in myocardial infarction.

($P=.603$), cardiac troponin I (cTnI) levels ($P=.845$), peak creatine kinase (CK) levels ($P=.904$), pain-to-balloon time ($P=.508$), or AMI localization ($P=.138$).

There was a statistically significant difference in the proportion of patients with high RDW between different TIMI flow categories ($P=.035$) after coronarography was performed; there was a statistically significant trend in the proportion of patients with high RDW with declining TIMI flow category ($P=.010$), suggesting that lower RDW might predict coronarography success.

3.4. RDW and ultrasound characteristics

RDW values showed a statistically significant negative correlation with EFLV ($P=.026$, Rho $=-0.24$) and E/A ($P=.001$, Rho $=-0.36$) and a positive correlation with E/E′ ($P<.001$, Rho $=0.43$), as shown in Fig. 2B–D. Accordingly, statistically significant higher RDW values were observed in patients with EFLV <50% (median 14.3% vs. 13.8% for patients with EFLV <50% and ≥50%, $P=.009$), patients with E/A < 1 (median 14.2% vs. 13.4% for patients with E/A <1 and ≥1, $P=.001$), patients with E/E′ >10 (median 14.3% vs. 13.5% for patients with E/E′ >10 and ≤10, $P<.001$) and patients with both E/A < 1 and E/E′ > 10 (median 14.4% vs. 13.5% for patients with and without both parameters, $P<.001$).

In addition, we observed a positive correlation between RDW and A ($P=.001$, Rho $=0.36$). We detected no statistically significant correlation between RDW and LVEDD ($P=.725$), LVESD ($P=.404$), E ($P=.330$), tricuspid annular plane systolic excursion ($P=.242$), degree of aortal regurgitation ($P=.794$), degree of mitral regurgitation ($P=.093$), degree of tricuspid regurgitation ($P=.100$), or degree of pulmonal regurgitation ($P=.247$).

Using ROC curve analysis, we determined optimal RDW cut-off points to discriminate between patients with and without systolic/diastolic dysfunction (Fig. 3A–D). RDW values >14.1% were able to identify patients with EFLV < 50% (AUC 0.667, $P=.007$) with a sensitivity of 60.6%, 95% confidence interval (CI) (42.1–77.1); a specificity of 66.1%, 95% CI (52.2–78.2); a positive likelihood ratio of 1.79, 95% CI (1.1–2.8); and a negative likelihood ratio of 0.6, 95% CI (0.4–0.9). RDW values >13.4% were able to identify patients with E/A < 1 (AUC 0.708, $P<.001$) with a sensitivity of 85.5%, 95% CI (74.2–93.7); a specificity of 59.4%, 95% CI (40.6–76.3); a positive likelihood ratio of 2.12, 95% CI (1.4–3.3); and a negative likelihood ratio of 0.24, 95% CI (0.1–0.5). RDW values >13.8% were able to identify patients with E/E′ > 10 (AUC 0.765, $P<.001$) with a sensitivity of 80.5%, 95% CI (65.1–91.2); a specificity of 70.8%, 95% CI (55.9–83.0); a positive likelihood ratio of 2.76, 95% CI (1.7–4.4); and a negative likelihood ratio of 0.28, 95% CI (0.1–0.5). RDW values >13.8% were able to identify patients with combined E/A < 1 and E/E′ > 10 (AUC 0.806, $P<.001$) with a sensitivity of 93.3%, 95% CI (77.9–99.2); a specificity of 67.8%, 95% CI (54.4–79.4); a positive likelihood ratio of 2.9, 95% CI (2.0–4.2); and a negative likelihood ratio of 0.098, 95% CI (0.03–0.4).

RDW remained statistically significant associated with determinants of systolic (EFLV < 50%) and diastolic dysfunction (E/A < 1, E/E′ > 10, combination of both) in a series of logistic regression models adjusted for potential confounders (age, gender, TIMI score, hemoglobin level, pain to balloon time, TIMI flow, peak CK levels were included in the models as shown in Table 3), showing that RDW bears additional predictive properties and is able to predict the development of systolic and diastolic dysfunction after adjusting for the aforementioned parameters.

In addition, we investigated how RDW performs in predicting determinants of systolic and diastolic dysfunction when compared with other "inflammatory biomarkers" with known CV associations, such as MPV, NLR, and PLR, in a series of logistic regression models (Table 4). Predictive properties of RDW remained statistically significant in all models, suggesting that RDW performs best among the aforementioned parameters in terms of predicting systolic and diastolic dysfunction.

3.5. RDW and clinical outcomes

Using survival analysis methods, we detected that patients with higher RDW had a statistically significant higher risk of developing FA in the post-STEMI period (optimal cut-off value > 14.5%, $P=.001$, hazard ratio [HR] $=3.99$) and clinical signs of heart failure (optimal cut-off value > 14.3%, $P=.003$, HR $=5.98$).

RDW did not show a statistically significant association with length of hospitalization ($P=.303$) or with stent thrombosis ($P=.388$). Although patients with elevated RDW had a tendency to develop other adverse outcomes, the results did not reach statistical significance for overall survival ($P=.082$), major adverse cardiac and cerebrovascular events ($P=.07$), bleeding ($P=.098$), reinfarction ($P=.116$), coronary artery bypass grafting (CABG) ($P=.207$), or CVI ($P=.083$). Lack of statistically significant results does not mean that the investigated associations do not exist, and our study is likely underpowered to detect a statistical significance due to the relatively small numbers of both events and included patients.

4. Discussion

To the best of our knowledge, our study is the first to compare the predictive properties of RDW between the contexts of systolic and diastolic dysfunction in patients with acute STEMI and PCI and to compare the strength of RDW with other inflammatory biomarkers derived from complete blood counts.

At the moment, particular mechanism by which RDW is directly related to ventricular dysfunction is unknown, but many possible indirect associations exist. Older patients in our study had elevated values of RDW, a finding consistent with the findings of Hoffmann's study, who termed this strong correlation between age and elevated RDW a "universal biological feature."[19] Other author groups have confirmed the association of aging with an increase in RDW in the general population.[20,21] We observed that RDW was significantly associated with some of the classic CV risk factors, such as HA and hyperlipoproteinemia, but it was also somewhat surprisingly associated with nonsmoking. It could be that both smoking and RDW reflect a high risk for the development of a CV incident, and patients who did not smoke were otherwise burdened with CV risk (manifested with high RDW) and developed STEMI despite positive lifestyle habits. Interestingly, despite the fact that we were not able to prove a statistically significant association between HbA1C and RDW, several other studies have confirmed this association in patients without DM[22] or in an unselected population of elderly patients.[23] HbA1C had an impact on the severity of coronary disease, as is also seen with RDW, and a potential linking mechanism could therefore exist.[24–26] In our study, there was no statistically significant correlation between CRP and RDW. However, a significant and graded correlation between RDW and

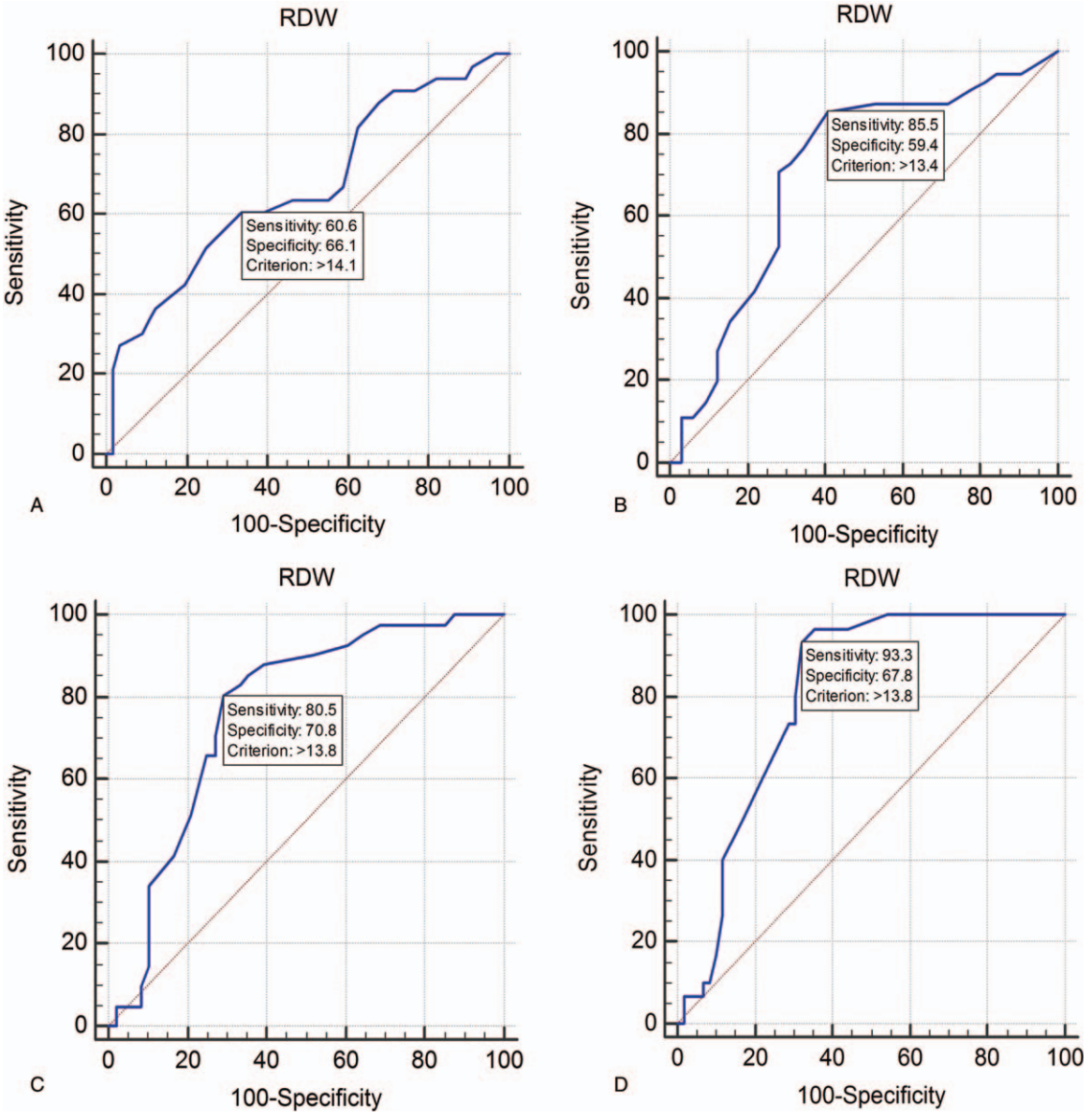

Figure 3. ROC curves for RDW in the context of identifying patients with (A) EFLV < 50%, (B) E/A < 1, (C) E/E′ > 10, and (D) a combination of E/A < 1 and E/E′ > 10. E/A = ratio of peak velocity flow in early diastole to peak velocity flow in late diastole, E/E′ = ratio of early transmitral velocity and early diastolic annular velocity, EFLV = ejection fraction of the left ventricle, RDW = red cell distribution width, ROC = receiver operating characteristic.

Table 3

Overview of logistic regression models showing that elevated RDW remains associated with the parameters of systolic and diastolic dysfunction after adjustments for potential confounders.

	Model predicting EFLV < 50%	Model predicting E/A < 1	Model predicting E/E′ > 10	Model predicting E/A < 1 and E/E′ > 10
Elevated RDW	OR = 1.15, 95% CI (4.48–17.43), $P = .031$*	OR = 2.85, 95% CI (9.63–32.56), $P < .001$*	OR = 2.63, 95% CI (10.7–43.54), $P = .001$*	OR = 5.41, 95% CI (37.23–256.37), $P < .001$*
TIMI score	OR = 1.07, 95% CI (1.39–1.8), $P = .014$*	OR = 0.91, 95% CI (1.17–1.51), $P = .229$	OR = 0.86, 95% CI (1.1–1.42), $P = .454$	OR = 0.88, 95% CI (1.16–1.53), $P = .278$
Hemoglobin level	OR = 0.99, 95% CI (1.04–1.1), $P = .135$	OR = 0.98, 95% CI (1.01–1.05), $P = .436$	OR = 0.98, 95% CI (1.04–1.1), $P = .176$	OR = 0.96, 95% CI (1.02–1.08), $P = .476$
Pain to balloon time	OR = 0.99, 95% CI (1–1.01), $P = .605$	OR = 0.99, 95% CI (1–1), $P = .261$	OR = 0.99, 95% CI (1–1.01), $P = .465$	OR = 0.99, 95% CI (1–1), $P = .328$
TIMI flow	OR = 0.17, 95% CI (0.51–1.6), $P = .249$	OR = 0.41, 95% CI (1.22–3.67), $P = .725$	OR = 0.27, 95% CI (0.89–2.9), $P = .843$	OR = 0.33, 95% CI (1.21–4.39), $P = .777$
Peak CK	OR = 1, 95% CI (1–1), $P = .044$*	OR = 1, 95% CI (1–1), $P = .439$	OR = 1, 95% CI (1–1), $P = .761$	OR = 1, 95% CI (1–1), $P = .894$
Age	OR = 0.91, 95% CI (0.97–1.04), $P = .384$	OR = 0.91, 95% CI (0.97–1.03), $P = .275$	OR = 0.97, 95% CI (1.04–1.11), $P = .263$	OR = 0.9, 95% CI (0.97–1.05), $P = .467$
Male gender	OR = 0.15, 95% CI (0.7–3.18), $P = .644$	OR = 0.13, 95% CI (0.49–1.83), $P = .290$	OR = 0.12, 95% CI (0.54–2.52), $P = .434$	OR = 0.08, 95% CI (0.47–2.6), $P = .383$

CI = confidence interval, CK = creatine kinase, E/A = ratio of peak velocity flow in early diastole to peak velocity flow in late diastole, E/E′ = ratio of early transmitral velocity and early diastolic annular velocity, EFLV = ejection fraction of the left ventricle, OR = odds ratio, RDW = red cell distribution width, TIMI = thrombolysis in myocardial infarction.

* Statistically significant at $P < .05$.

Table 4

Overview of logistic regression models showing that elevated RDW remains associated with the parameters of systolic and diastolic dysfunction after adjusting for MPV, NLR, and PLR.

	Model predicting EFLV < 50%	Model predicting E/A < 1	Model predicting E/E′ > 10	Model predicting E/A < 1 and E/E′ > 10
RDW	OR 1.95, 95% CI (1.14–3.34), $P=.016^*$	OR 1.93, 95% CI (1.06–3.52), $P=.033^*$	OR 1.99, 95% CI (1.14–3.49), $P=.016^*$	OR 2.38, 95% CI (1.31–4.31), $P=.004^*$
MPV	OR 1.12, 95% CI (0.67–1.9), $P=.66$	OR 1.79, 95% CI (1–3.21), $P=.05$	OR 1.38, 95% CI (0.81–2.34), $P=.231$	OR 1.31, 95% CI (0.74–2.31), $P=.349$
NLR	OR 1.1, 95% CI (0.91–1.32), $P=.336$	OR 1, 95% CI (0.83–1.2), $P=.993$	OR 0.9, 95% CI (0.72–1.14), $P=.381$	OR 0.76, 95% CI (0.51–1.13), $P=.179$
PLR	OR 1, 95% CI (0.99–1.01), $P=.569$	OR 1, 95% CI (0.99—1.01), $P=.625$	OR 1.01, 95% CI (1–1.02), $P=.266$	OR 1.01, 95% CI (0.99–1.02), $P=.38$

CI = confidence interval, E/A = ratio of peak velocity flow in early diastole to peak velocity flow in late diastole, E/E′ = ratio of early transmitral velocity and early diastolic annular velocity, EFLV = ejection fraction of the left ventricle, MPV = mean platelet volume, NLR = neutrophil-to-lymphocyte ratio, OR = odds ratio, PLR = platelet-to-lymphocyte ratio, RDW = red cell distribution width.
* Statistically significant at $P<.05$.

a high sensitive CRP exists independently from numerous confounding factors in a large cohort of unselected patients.[27] Therefore, RDW is considered to represent subclinical inflammation and is accepted as an inflammatory biomarker, which potentially explains its strong prognostic properties in different benign and malignant diseases.

In our study, elevated RDW was a predictor of systolic and diastolic dysfunction after STEMI and PCI. There were significant univariate and multivariate correlations between elevated RDW and systolic and diastolic dysfunction parameters. According to our data, RDW seems to be better at discerning patients with diastolic rather than systolic dysfunction, and RDW values $\leq$13.8% could be useful for ruling out a combined E/A < 1 and E/E′ > 10 state due to a good negative likelihood ratio. In multivariate analyses, RDW remained statistically significant associated with determinants of systolic (EF < 50%) and diastolic dysfunction (E/A < 1, E/E′ > 10, combination of both) in a series of logistic regression models adjusted for age, gender, TIMI score, and other potential confounders, showing that RDW bears additional predictive properties for TIMI score and is able to predict the development of systolic and diastolic dysfunction after adjusting for the aforementioned parameters. Along with our study, Karakas determined that elevated RDW on admission was connected with systolic dysfunction after STEMI and subsequent PCI,[10] which is consistent with our results. Myocardial ischemia produces diastolic dysfunction as well. The evaluation of diastolic dysfunction also has both diagnostic and prognostic roles in the management of coronary disease.[28,29] Our study shows that elevated RDW could help discern patients who may be particularly affected by myocardial ischemia. However, in light of the most recent study, there are many people with subclinical diastolic dysfunction,[16] and it is unknown how many patients had asymptomatic diastolic dysfunction before they suffered from STEMI and entered our study.

Atherosclerosis is a progressive disease of an inflammatory nature.[30] Several studies have confirmed the association between inflammatory biomarkers and the severity of coronary disease.[31–34] Elevated NLR predicts long-term mortality after PCI.[35] Elevated MPV, an indicator of enlarged and activated platelets,[36] correlates with unstable angina and AMI.[37] Uysal et al suggested that NLR and MPV were predictors of severe atherosclerosis using the Genzini score.[38] Recently, a novel inflammatory biomarker, PLR, has been connected to the severity of coronary disease.[39] In cases of sustained inflammation, lymphocyte counts decrease due to increased lymphocyte apoptosis. In our study, we also confirmed that RDW was significantly elevated in patients with lymphopenia. We examined the correlation of the abovementioned inflammatory biomarkers and confirmed that RDW remained the strongest predictor of systolic and diastolic dysfunction of the left ventricle after STEMI and PCI.

In our study, there was no significant difference between cohorts with regard to localization of AMI, "pain to balloon" time, and range of myocardial damage expressed by cTnI and peak CK. Some authors took only proximal and mid-segment left anterior descending artery localization of AMI into consideration, as well as TIMI flow III after PCI and "pain to balloon" time of <6 h.[10]

Moreover, we mentioned that elevated RDW was associated with worse clinical outcomes in patients suffering from coronary disease, acute coronary syndrome, or AMI.[4–7] RDW is related to the severity of coronary disease.[24,25] Consistent with the study by Karabulut, we found a statistically significant increasing trend in the proportion of patients with elevated RDW toward lower TIMI flow after PCI. In this study, RDW was an independent predictor of abnormal reperfusion.[40] On the contrary, Ilhan et al determined a relationship between elevated RDW and intrahospital mortality after STEMI, but not worse postinterventional TIMI flow.[41]

Consistent with Dabbah's study,[5] our study confirmed a significant increase in acute heart failure after STEMI. The incidence of FA after STEMI can reach up to 13.3%.[42] RDW predicts new onset FA after CABG.[43] There are very few studies reporting a relationship between elevated RDW and the incidence of FA after STEMI,[44] but our results support this claim. On the other hand, there was no association between RDW and stent thrombosis, as Tuncez demonstrated in his study.[45] Limitations of the study are small number of patients and the use of a single center. Another limitation could be the fact that all sites of STEMI were included in the study, although we did not find statistically significant differences regarding the localization of the AMI, "pain to balloon" time, or the range of myocardial damage. Nevertheless, we performed a prospective study that provides interesting observations regarding the usefulness of RDW in the setting of AMI.

5. Conclusion

Elevated RDW, even after adjusting for several confounding factors, remained significantly associated with the parameters of systolic and diastolic dysfunction after STEMI and subsequent PCI. This relationship is especially interesting when considering RDW and the combination of the parameters of diastolic dysfunction, where it has good potential as a screening test for predicting nondevelopment of this complication. Compared with other inflammatory biomarkers, RDW performs best in predicting systolic and diastolic dysfunction.

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