



## Original Research

# RDW Value may Increase the Diagnostic Accuracy of MPS

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### Abstract

**Objectives:** As the feasibility of obtaining health care has improved in the last decade, there is an increase in the number of performing unnecessary coronary angiogram. Red Cell Distribution Width (RDW), which shows erythrocyte dispersion volume, is associated with coronary artery disease. The present study aims to evaluate the relationship between RDW value and the severity of coronary artery disease in patients who undergo myocardial perfusion scintigraphy (MPS) as an evaluation for coronary ischemia and after which patients had a coronary angiography.

**Methods:** This retrospective study included 452 patients diagnosed as stabile angina that had MPS to evaluate coronary ischemia and after which coronary angiography was performed. Complete blood count was obtained on the same day. Patients were first divided into two groups: patients with and without ischemia on MPS. Then, the group who had ischemia on the MPS where divided into another two groups: patients who had RDW values  $\geq 13.5$  and the others who had RDW value  $< 13.5$ . Patients who had fixed perfusion defect, chronic kidney disease, thyroid dysfunction, hematological disease, those who use iron supplements, and those who had active infectious disease were excluded from this study.

**Results:** The basic characteristics were the same between study groups. We found that severe coronary vessel disease, single vessel, two vessels and three vessels diseases were higher in patients who had ischemia on the MPS and RDW values  $\geq 13.5$  (p-value were 0.032, 0.004, 0.042 respectively). RDW values  $\geq 13.5$  was found to be an independent predictor for the presence of severe coronary artery disease (p<0.001 OR:3.55).

**Conclusion:** Patients who have MPS for ischemic evaluation and RDW values of  $\geq 13.5$  were more severe coronary heart diseases. As a result, the findings suggest that using of RDW value is a cheap and feasible parameter that may prevent performing unnecessary coronary angiography for patients after MPS.

**Keywords:** Coronary artery disease; MPS; RDW.

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Red cell distribution width (RDW) is a parameter that is used to show erythrocyte dispersion volume.<sup>[1]</sup> Although it is a subgroup of erythrocyte count, it has been associated with many diseases rather than anemia.<sup>[2]</sup> Atherosclerosis and coronary artery disease (CAD) are some of these diseases that show an increased value of RDW.<sup>[3]</sup>

As the possibility of obtaining health care has improved in the last decade, there was an increase in the number of performing coronary angiogram.<sup>[4]</sup> As a result, there is an increase in the number of non-occlusive coronary angiography and its financial burden.<sup>[5]</sup> Although Myocardial perfusion scintigraphy (MPS) has high sensitivity and specific-

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ity in detecting coronary artery disease, it cannot prevent performing unnecessary angiogram when used alone.<sup>[6]</sup>

This study aims to evaluate the usefulness of using RDW values in detecting severe CAD in patients that have ischemia on MPS and planned for coronary angiography.

## Methods

### Study Population

In this study, we retrospectively evaluate 452 patients (mean age was 59 and 56% were male gender). All patients had stable angina pectoris. The study group included the patients with ischemia on MPS or patients without ischemia on MPS but had a high clinical suspicion for having myocardial ischemia. Patients who had fixed perfusion defect, chronic kidney disease, thyroid dysfunction, anemia, hematological disease, those who use iron supplements, and those who had the active infectious disease were excluded from the study. Study protocol was approved by the local ethics committee and this study was conducted in accordance with the Declaration of Helsinki.

### Coronary Angiography

All patients had coronary angiography that was administered according to standard technique. Angiography results were interpreted by two different cardiologists who were unaware of patients' clinical status. The presence of epicardial coronary artery stenosis more than 50% was accepted as significant.<sup>[7]</sup>

### Myocardial Perfusion Scintigraphy

All patients had MPS according to standard techniques. Vertical long axis, horizontal long axis and short axis were obtained from the saved stress and rest phase images.

Stress and rest images were divided in to six zones (left ventricle anterior, anterior septum, posterior septum, lateral, inferior, and posterior), and each zone was visually evaluate separately. Evaluation was performed with a scoring between 0-3, (0=no perfusion, 1=marked perfusion loss, 2=mild perfusion loss, 3=normal perfusion). Evaluation of the perfusion ratio for each zone was performed by comparing the scores of stress and rest images. The evaluation was carried out as follow: If the perfusion was normal and there were no difference between both the stress and rest images 'Normal'; if there was one or more difference in between stress and rest images 'ischemia' (reversible- returning perfusion); and if there was a perfusion defect without any scoring change at early and late phase images 'previous myocardial infarction' (constant perfusion defect).

## Laboratory

On the day of angiography, complete blood count and biochemical parameters was obtained from all patients and analyzed according to standard techniques. Coulter Gen-S Hematology Analyzer (Beckman Coulter Corp, Hialeah, Florida) system was used for the complete blood count evaluation. RDW was divided into two groups as follows: RDW  $\geq$ 13.5 and RDW  $<$ 13.5.

## Statistical Analysis

Statistical analysis was performed using SPSS 16 software (SPSS Inc, Chicago, Illinois). Data with homogeneous distribution were evaluated using Kolmogorov-Smirnov test. Independent samples t-test or Mann-Whitney U test was used to evaluate numerical data. Chi square and Fisher exact test were used for the evaluation of categorical data. The p-value for the standard error of type 1 was accepted as 0.05. Univariate and multivariate analysis were performed to predict severe coronary artery disease. Age, fasting glucose, creatinine level, LDL-C, diabetes, hypertension and RDW  $\geq$ 13.5 were included in Univariate and multivariate analysis.

## Results

As shown in Table 1, basic characteristics of two groups were similar ( $p>$ 0.05) except for gender ( $p=$ 0.032). There were no difference at left ventricular ejection fraction (LVEF), severe coronary lesion, single vessel disease, two-vessel disease, three-vessel disease and LMCA disease in between two groups.

Table 2 shows the comparison of two groups with RDW  $\geq$ 13.5 and RDW  $<$ 13.5 that had ischemia on MPS. Patients group that increased RDW values were lower LVEF ( $p<$ 0.001). Patients group with increased RDW values had severe coronary lesions, as well as much more single vessel, two vessel, and three vessel diseases ( $p$ -value  $<$ 0.001, 0.036, 0.029, 0.005, respectively). Table 3 shows univariate and multivariate analysis that were performed to show severe coronary artery disease in patients who had ischemia on MPS. RDW  $\geq$ 13.5 was an independent predictor of severe coronary artery disease ( $p<$ 0.001 OR:3.55).

## Discussion

Our study showed that in patients that have ischemia on MPS, when the RDW value is  $\geq$ 13.5 there is an increase in the number of severe coronary lesions, as well as much more single vessel, two vessel and three vessel diseases on coronary angiography. RDW value  $\geq$ 13.5 was an independent predictor for severe coronary diseases. Patients group with high RDW values had a decrease in LVEF.

Recent studies showed that RDW value increases not only in anemia but also in many other diseases like CAD.<sup>[2]</sup>

CAD is the first leading cause of morbidity and mortality in

**Table 1.** Demographic, laboratory, echocardiographic and coronary angiographic findings of patients with and without ischemia in MPS

	No-Ischemia (n=56)	Ischemia (n=396)	p
Age (years)	59.41±10.00	58.72±10.79	0.672
Male, n (%)	39 (69.4)	215 (54.3)	0.032
Family history, n (%)	16 (28.6)	80 (19.5)	0.116
Diabetes, n (%)	11 (19.6)	84 (21.2)	0.863
Hypertension, n (%)	18 (32.1)	134 (33.8)	0.880
Fasting glucose (mg/dl)	106.00	111.00	0.211
Creatinine (mg/dl)	0.88	0.90	0.285
TSH (µIU/ml)	1.50	1.38	0.532
LDL-C (mg/dl)	117.00	126.00	0.386
Triglycerides (mg/dl)	108.50	143.50	0.268
Hemoglobin	13.66±1.32	13.70±1.31	0.826
LVEF (%)	49.64±11.64	51.50±9.92	0.064
Severe coronary lesion, n (%)	41 (73.2)	243 (61.4)	0.104
Single vessel disease, n (%)	15 (26.8)	85 (21.5)	0.391
Two-vessel disease, n (%)	14 (25.0)	66 (16.7)	0.136
Three-vessel disease, n (%)	12 (21.4)	97 (23.6)	0.866
LMCA disease, n (%)	2 (3.6)	6 (1.5)	0.260
RDW (%)	14.21±1.65	14.40±1.64	0.214

MPS: Myocardial perfusion scintigraphy; TSH: Thyroid stimulating hormone; LDL-C: Low-density lipoprotein cholesterol; LVEF: Left ventricular ejection fraction; LMCA: Left main coronary artery; RDW: Erythrocyte distribution width.

the world.<sup>[8]</sup> Optimal evaluation and detection of risky lesions is an important factor that prevents secondary injuries from CAD.<sup>[9]</sup> Diagnosing CAD should be made using physical examination, laboratory non-invasive and invasive tests.<sup>[10]</sup>

MPS is a non-invasive test that is used to diagnose CAD. A positive MPS is obtained when there is severe CAD and atherosclerotic changes.<sup>[11]</sup> On the other hand, MPS may not always detect severe coronary lesions.<sup>[12]</sup> To increase the ability of MPS to detect CAD and to prevent unnecessary coronary angiography, there is a need for new, cheap, easily available and reliable tests.

RDW is a parameter that used to show erythrocyte dispersion volume, in other words, it is a parameter that shows anisocytosis.<sup>[13]</sup> Recent studies showed that RDW value increases not only in anemia but also is associated with many other diseases.<sup>[14]</sup> RDW value increased in atherosclerosis, which is a chronic inflammatory disease that leads to CAD.<sup>[15]</sup> Çetin et al.,<sup>[3]</sup> showed that RDW value is associated with the severity of coronary artery lesions in patients with stable CAD. Gul et al.,<sup>[16]</sup> at their three years follow up study found that an increased RDW leads to an increase in the mortality in patients who had NSTEMI and USAP. In a study, Sun et al.<sup>[17]</sup> evaluated NSTEMI patients who did not have heart failure and found that in patients who had RDW value more than 13 there is an increase in all may cause mortality. The relationship between elevated RDW value and CAD exactly is unknown. However, oxidative stress, inflammatory cytokines and neurohormonal factors may be the cause. Inflammatory cytokines are known to be associated with chronic inflammation. This

**Table 2.** Demographic, laboratory, echocardiographic and coronary angiographic findings of patients with ischemia on MPS according to RDW

	Total (n=396)	RDW<13.5 (n=132)	RDW>13.5 (n=264)	p
Age (years)	58.81±10.69	58.06±10.37	59.10±11.03	0.362
Male, n (%)	215 (54.3)	71 (53.8)	144 (54.5)	0.915
Diabetes, n (%)	84 (21.2)	27 (20.5)	57 (21.6)	0.896
Hypertension, n (%)	134 (33.8)	47 (35.6)	87 (33)	0.652
Fasting glucose (mg/dl)	107.0	106.00	110.00	0.055
Creatinine (mg/dl)	0.90	0.88	0.91	0.039
TSH (µIU/ml)	1.45	1.64	1.37	0.409
LDL-C (mg/dl)	122.00	126.00	120.00	0.624
Triglycerides (mg/dl)	149.50	152.00	144.00	0.715
LVEF (%)	51.76±10.08	50.56±10.08	54.13±8.73	0.001
Severe coronary lesion, n (%)	243 (61.4)	55 (41.7)	188 (71.2)	<0.001
Single vessel disease, n (%)	99 (21.9)	21 (15.9)	64 (24.2)	0.036
Two-vessel disease, n (%)	66 (16.7)	15 (11.4)	51 (19.3)	0.029
Three-vessel disease, n (%)	102 (22.6)	19 (14.4)	71 (26.9)	0.005
LMCA disease, n (%)	8 (1.9)	0 (0.0)	6 (2.3)	0.185

RDW: Erythrocyte distribution width; MPS: Myocardial perfusion scintigraphy; TSH: Thyroid stimulating hormone; LDL-C: Low-density lipoprotein cholesterol; LVEF: Left ventricular ejection fraction; LMCA: Left main coronary artery.

**Table 3.** Univariate and multivariate logistic regression analysis which shows severe vessel disease in patients with detected ischemia on MPS

	Univariate Analysis		Multivariate Analysis	
	Odds Rate (95% CI)	p	Odds Rate (95% CI)	p
Age	1.04 (1.02-1.07)	0.001		
Fasting glucose	1.00 (0.99-1.00)	0.093		
Creatinine	1.02 (0.76-1.38)	0.886		
LDL-C	1.0 (0.99-1.01)	0.037		
RDW>13.5+mps ischemia	3.46 (2.24-5.36)	<0.001	3.55 (2.24-5.62)	<0.001
Diabetes	1.17 (0.71-1.93)	0.536		
Hypertension	1.14 (0.74-1.76)	0.545		

MPS: Myocardial perfusion scintigraphy; CI: Confidence interval; LDL-C: Low-density lipoprotein cholesterol; RDW: Erythrocyte distribution width.

inflammation by affecting erythrocyte growing and production from bone marrow may cause anisocytosis.<sup>[18]</sup>

This study showed that there is relationship between increase RDW value and the severity of CAD. Patients with RDW value of  $\geq 13.5$  had more frequent CAD. Therefore, RDW value can be used to detect severe coronary artery stenosis in patients who had ischemia on MPS.

### Limitations

First limitation is that this study is retrospective. Thus, we could not evaluate inflammatory and oxidative markers. Also, lacking some parameters like smoking and BMI that may affect RDW value is one of the limitations in this study. Another limitation is that echocardiography was not administered by the same person.

### Conclusion

Patients with high RDW values have more severe CAD. RDW value may be used to prevent performing unnecessary coronary angiography for patients evaluated for ischemia by MPS.

### Disclosures

**Ethics Committee Approval:** The study was approved by the Local Ethics Committee and this study was conducted in accordance with the Declaration of Helsinki.

**Peer-review:** Externally peer-reviewed.

**Conflict of Interest:** None declared.

**Authorship Contributions:** Concept – S.C., S.S.Y., K.K., S.S., A.B., I.S.; Design – S.C., S.S.Y., K.K., S.S., A.B., I.S.; Supervision – S.C., S.S.Y., K.K., S.S., A.B., I.S.; Data collection &/or processing – S.C., S.G.; Analysis and/or interpretation – K.K., I.S.; Literature search – S.S.Y., S.C.; Writing – S.C.; Critical review – A.B., I.S.

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