Increased red cell distribution width level is associated with absence of coronary collateral vessels in patients with acute coronary syndromes

Akut koroner sendromlu hastalarda yüksek eritrosit dağılım genişliği koroner kollaterallerin yokluğu ile ilişkilidir

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ABSTRACT

Objectives: Several studies have evaluated a relationship between increased red cell distribution width (RDW) and morbidity and mortality of acute coronary syndrome (ACS). In this study, we aimed to investigate the association of serum RDW levels and development of coronary collateral vessel (CCV) in patients with ACS.

Study design: We evaluated 226 patients with ACS in this prospective and cross-sectional study. Traditional laboratory and clinical parameters and serum RDW levels were measured on admission. All patients underwent coronary angiography on the first day after admission and patients with >80% stenosis were included in the study. The CCV was graded according to the Rentrop scoring system, and a Rentrop grade 0 was accepted as no CCV development (Group 1), while Rentrop grades 1-2-3 were accepted as presence of CCV development (Group 2).

Results: Only levels of RDW were significantly higher in Group 1 than in Group 2 (Group 1 RDW 14.6±1.9, Group 2 RDW 14.1±1.4, p=0.02). The predictive value of serum RDW level for absence of collaterals (sensitivity of 58% and specificity of 54%, area under the receiver operating characteristic (ROC) curve = 0.573) was 13.90.

Conclusion: We found that high levels of RDW were associated with absence of CCV in patients with ACS.

ÖZET

Amaç: Eritrosit dağılım genişliği (EDG) ile akut koroner sendromların (AKS) morbidite ve mortalitesi arasındaki ilişki çeşitli çalışmalarda araştırılmıştır. Bu çalışmada, AKS'li hastalarda EDG ile koroner kollateral damar (KKD) gelişimi arasındaki ilişki araştırıldı.

Çalışma planı: Çalışmada AKS'li 226 hasta ileriye dönük ve kesitsel olarak incelendi. Geleneksel laboratuvar ve klinik parametreler ve EDG düzeyleri hasta kabul edilirken ölçüldü. Tüm hastalara kabulden sonraki birinci gün içinde koroner anjiyografi yapıldı ve %80 ve üzerinde damar tıkanıklığı olan hastalar çalışmaya alındı. Koroner kollateral damar dereceleri Rentrop skoruna göre değerlendirildi ve Rentrop 0 KKD olmayan grup (Grup 1), Rentrop 1, 2, 3 KKD olan grup (Grup 2) olarak kabul edildi.

Bulgular: Grup 1'de sadece EDG Grup 2'ye göre anlamlı derecede yüksekti (Grup 1 EDG 14.6±1.9, Grup 2 EDG 14.1±1.4, p=0.02). Koroner kollateral damar yokluğunu öngördüren EDG değeri (%58 duyarlılık ve 54 özgüllük ile, ROC [receiver-operating characteristics] eğrisi altındaki alan =0.573) 13.90 idi.

Sonuç: Akut koroner sendromlu hastalarda yüksek EDG düzeylerinin KKD yokluğu ile ilişkili olduğunu bulduk.

Red cell distribution width (RDW) is a laboratory measure of the variability in erythrocyte volume and is a readily available component of the routine complete blood count. Recent studies have shown that high RDW levels were associated with adverse outcomes in patients with ST elevation myocardial

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infarction (STEMI) and heart failure.[1,2] High levels of RDW are also associated with increased mortality in patients with coronary artery disease (CAD) and patients undergoing percutaneous coronary intervention.[3,4] Furthermore, a relationship between RDW and the severity and complexity of CAD was shown in previous studies.[5,6] In spite of these associations, the mechanisms underlying elevated RDW are unclear in these patient groups. Inflammation and neurohumoral mediators may stimulate changes in the red cell membrane, leading to increased RDW.[7]

Coronary collateral vessels (CCVs) can provide a perfusion reserve in case of increased myocardial oxygen demand. Coronary collaterals can limit the myocardial ischemia and can protect the viable myocardium in patients with acute coronary syndrome (ACS).[8] The absence of CCVs is correlated with worse clinical outcomes in patients with ACS.[9] The absence of CCV in patients with ACS who had high levels of serum RDW may explain the relation between elevated serum RDW and worse clinical outcomes in patients with ACS.

The complex mechanisms in the development of CCV are not well understood. Some mediators (such as C-reactive protein, uric acid, and circulating endothelial progenitor cells) were investigated to explain the development of CCV, but there is not yet conclusive evidence. Moreover, as serum RDW predicted the risk of CAD and cardiac mortality, it may also be interesting to examine whether serum RDW predicts the presence of coronary collaterals (especially via oxidative stress), one of the major predictors of mortality in patients with ACS. In this study, we aimed to investigate the association of serum RDW levels and development of CCV in patients with ACS.

PATIENTS AND METHODS

Patients

This was a prospective and cross-sectional study. A total of 370 consecutive patients who had admitted to the hospital between February 2010 and May 2011 with ACS defined as either unstable angina (UA) or non-ST elevation myocardial infarction (NSTEMI) and undergone coronary angiography were examined. UA was diagnosed according to the following criteria: typical chest pain and/or electrocardiographic changes indicating myocardial ischemia with negative cardiac enzymes. NSTEMI diagnosis was based on elevated cardiac enzymes with typical chest pain and/or electrocardiographic changes suggestive of myocardial ischemia. Typical chest pain was evaluated as follows: more than 20 minutes (min) in duration, new-onset angina, and an increase in its frequency and duration or severity. Each subject was questioned about major risk factors for CAD and development of CCV including diabetes (defined as a fasting blood glucose level >110 mg/dl or using antidiabetic drugs), hypertension (defined as blood pressure of 140/90 mmHg or more or taking antihypertensive medications), chronic obstructive pulmonary disease, and current smoking and alcohol status.

Abbreviations:

ACS	*Acute coronary syndrome*
CAD	*Coronary artery disease*
CCVs	*Coronary collateral vessels*
NSTEMI	*Non-ST elevation myocardial infarction*
RDW	*Red cell distribution width*
ROC	*Receiver operating characteristics*
ROS	*Reactive oxygen species*
STEMI	*ST elevation myocardial infarction*
UA	*Unstable angina*

Patients with histories of coronary intervention/coronary artery bypass, cardiac failure, renal disease (or serum creatinine level >1.5 mg/dl), or inflammatory rheumatic disease; anemia; clinical evidence of active infection; active cancer; hematological proliferative diseases; active or chronic inflammatory or autoimmune diseases; pregnancy; recent blood transfusion; a history of chronic obstructive pulmonary disease; or severe arrhythmia were excluded. The patients with less than 80% stenosis in the coronary angiography were also excluded from the study. Finally, 226 patients (UA, 93 patients and NSTEMI, 133 patients) were included in the study.

Anemia was defined as hemoglobin levels lower than 13 g/dl in men and 12 g/dl in women, in accordance with the World Health Organization criteria.[10]

Informed consent was obtained from all patients. The study was approved by our local ethical committee. All demographic and clinical data were collected prospectively.

Laboratory analysis

In all cases, blood samples were drawn at admission before starting any medication and were collected in tripotassium EDTA tubes. All measurements were performed 30 min after blood collection by an automatic blood counter (A Sysmex XE-2100, Symex, Kobe, Japan).

Coronary angiography

Quantitative coronary angiography was performed by the Judkins technique via the right femoral artery by two experienced interventional cardiologists who had no knowledge of the patients' clinical information. Coronary arteries were imaged by utilizing right and left anterior oblique views with cranial and caudal positions. Injection of contrast medium (Iopromide, Ultravist-370; Schering AG, Berlin, Germany) was carried out by an automatic injector at a speed of 3-4 ml/seconds (sec) for the left coronary artery and 2-3 ml/sec for the right coronary artery. Arteriographies were recorded at a speed of 25 frames/sec. Coronary vessel disease was described as degree of diameter stenosis of 80% or greater in at least one coronary artery. Collateral circulation was graded according to the Rentrop classification. The collateral circulation was based on the injection that best opacified the occluded vessel: 0= no visible filling of any collateral vessels, 1= filling of side branches of the artery to be perfused by collateral vessels without visualization of the epicardial segment, 2= partial filling of the epicardial segment by collateral vessels, and 3= complete filling of the epicardial segment by collateral vessels. [11] Rentrop grade 0 was accepted as no development of CCV (Group 1) and Rentrop grade ≥1 was accepted as presence of CCV (Group 2).

Statistical analysis

All analyses were performed using the Statistical Package for the Social Sciences (SPSS) v 16.0 for Windows (version 16.0, SPSS, Chicago, IL, USA). Quantitative variables were expressed as mean value ± SD for continuous variables and median and minimum-maximum levels for categorical variables/string variables. Comparison of continuous values between two groups was performed by means of independent-samples t test. Comparison of categorical variables/string variables between two groups was performed by Mann-Whitney U-test. Categorical variables were compared by the chi-squared test. Pearson test was used for correlation parametric variables and Spearman test for non-parametric variables. Two-tailed p value <0.05 was considered statistically significant. In the univariate analysis, only levels of RDW were associated with absence of CCV. Multiple logistic regression analysis was not performed. Receiver operating characteristics (ROC) analysis was performed. The best cutoff value of RDW was determined, and the sensitivity and specificity at that point were determined.

RESULTS

The baseline demographic and clinical patient characteristics are presented in Table 1. There was no significant difference in the presence of diabetes mellitus, hypertension, smoking, gender, age, and systolic-diastolic blood pressure between Groups 1 and 2. Only levels of RDW were significantly higher in Group 1 than in Group 2 (Group 1 RDW 14.6±1.9, Group 2 RDW 14.1±1.4, p=0.02). Other laboratory parameters were similar between the two groups (Table 2).

Table 1. Relation between presence of coronary collaterals and baseline characteristics of patients

	All (n=226)			Group 1 (n=110)			Group 2 (n=116)			*p*
	n	%	Mean±SD	n	%	Mean±SD	n	%	Mean±SD	
Age (years)			62±11			62±11			61±11	0.5
Gender (male)	171	75.7		82	74.5		89	76.7		0.7
Smoking	127	56.2		65	59.1		62	53.4		0.4
Hypertension	39	17.3		17	15.5		22	19.0		0.4
Diabetes	31	13.7		11	10.0		20	17.2		0.1
USAP	93	41.2		50	45.0		43	37.1		0.1
NSTEMI	133	58.8		60	54.5		73	62.9		0.2
Systolic BP (mmHg)			110.2±16.0			115.6±14.5			114.2±17.3	0.6
Diastolic BP (mmHg)			70.1±11.9			72.6±12.0			70.7±11.9	0.4

USAP: Unstable angina pectoris; NSTEMI: Non-ST elevation myocardial infarction; BP: Blood pressure.

Table 2. Relation between presence of coronary collaterals and baseline laboratory findings of patients

	Group 1	Group 2	*p*
Red cell distribution width (%)	14.6±1.9	14.1±1.4	0.02
Glucose (mg/dl)	105 (57-455)	109 (59-463)	0.2
Hemoglobin (mg/dl)	14.2±1.9	14.3±1.3	0.6
White blood cell (x10^9/L)	9.5±3.3	9.9±3.0	0.3
Platelet count (x10^6)	235.1±68.1	230.0±59.1	0.5
Blood urea nitrogen (mg/dl)	18 (5-36)	18 (9-43)	0.8
Creatinine (mg/dl)	0.9±0.2	0.9±0.2	0.8
Troponin (ng/ml)	1.9 (0-50)	2.2 (0-50)	0.3
Creatinine kinase-MB fraction (IU/L)	21 (5-159)	26 (7-360)	0.1
Total cholesterol (mg/dl)	178.3±40.3	189.1±42.2	0.06
Low density lipoprotein cholesterol (mg/dl)	114.1±32.9	121.0±36.1	0.1
High density lipoprotein cholesterol (mg/dl)	35.0 (17-79)	35.1 (18-64)	0.8
Triglyceride (mg/dl)	118.5 (29-510)	122.5 (28-648)	0.6
Total protein (g/dl)	6.4±0.6	6.6±0.5	0.06
Albumin (g/dl)	3.7±0.5	3.8±0.5	0.3

The predictive value of serum RDW level for absence of collaterals (sensitivity of 58% and specificity of 54%, area under the ROC curve = 0.573) was 13.90 (Fig. 1).

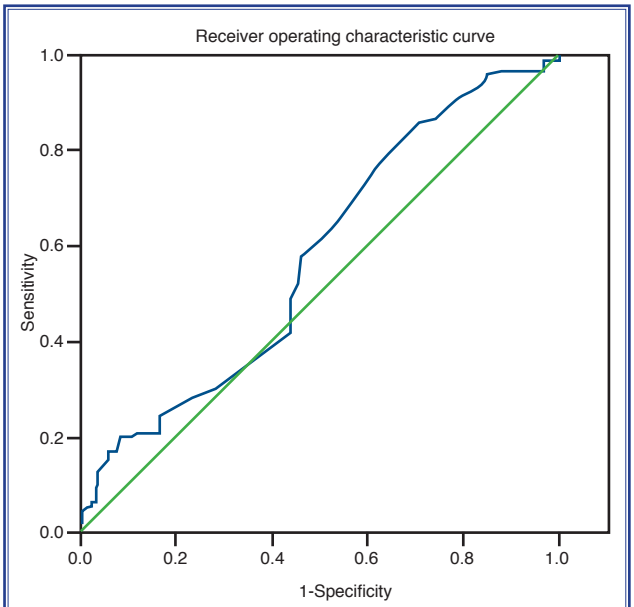

Figure 1. The receiver operating characteristic curve for RDW for predicting absence of CCV.

DISCUSSION

To our knowledge, this is the first study to evaluate the relationship between RDW and the development of coronary collateral circulation. Our observations suggest that elevated levels of RDW are associated with absence of CCVs in patients with ACS.

Well-developed CCVs can limit the myocardial ischemia, may minimize the infarct size and can protect the viable myocardium in patients with ACS.[8] The absence of CCV is correlated with bad clinical outcomes in patients with ACS.[9] Resting distal coronary pressure consistently falls as stenosis severity exceeds 70%.[12]

Myocardial ischemia, growth factors and shear stress are factors that likely contribute to initiating and remodeling for collateral development during the tissue hypoxia.[13] The severity of CAD and the duration of myocardial ischemic symptoms were described as influencing the development of coronary collaterals.[14] Vascular growth is usually categorized as angiogenesis (new capillaries from pre-existing ones) or arteriogenesis (the *in situ* development of vessels from angioblasts).[15] The underlying mechanisms of this collateral growth depend on the expression of numerous growth factors and signaling cascades.[16] Reactive oxygen species (ROS), which are free radicals, contain lots of molecules produced in all aerobic cells including molecular oxygen and its derivatives. In pa-

tients with CAD, ischemia and reperfusion lead to an increase in the production of ROS.[17] Increase in the production of ROS is related with increasing biological functions of the cells. Oxidative stress can result in oxidation of biological macromolecules.[18] Oxidative stress also corrupts the signal transduction of growth factors.[18] A variety of physiological molecules, such as fibroblast growth factors (FGF) and vascular endothelial growth factors (VEGF), have been identified that appear to promote angio- and arteriogenesis.[19,20] As a result, inflammation and oxidative stress are also proposed as key mechanisms of atherosclerosis and collaterals.[21-23]

Red cell distribution width is a marker of the variability in erythrocyte volume and is a routinely available component of the complete blood count. Elevated RDW reflects the heterogeneity of cell sizes in the peripheral blood smear.[24] Elevated RDW levels can be seen in conditions of ineffective red cell production (such as iron deficiency, B12 or folate deficiency and hemoglobinopathies), increased red cell destruction (such as hemolysis), and with blood transfusion.[25]

The underlying mechanism by which high levels of RDW are associated with development of CCVs in ACS is unclear. Inflammation has an important role in the atherosclerotic process and coronary collateral circulation.[26] Inflammatory cytokines, which are activated in ACS, have been found to suppress the erythrocyte maturation, so juvenile erythrocytes enter into the circulation.[27] Also, elevated levels of neurohumoral mediators stimulate erythropoiesis; for example, angiotensin II may affect the erythroid progenitor cells with direct stimulation.[7] In addition, levels of erythropoietin increase independent of hemoglobin levels, and adrenergic activation may act on bone marrow response in patients with ACS.[28] There is a substantial genetic contribution to red cell size in the general population.[29] The variability in circulating red cell sizes may increase with these mechanisms. Investigators have shown a relationship between elevated levels of RDW and both generalized inflammation and oxidative stress, which are proposed as key mechanisms of atherosclerosis and absence of collaterals, and have also demonstrated an association of RDW with high-sensitive C-reactive protein and erythrocyte sedimentation rate, which are indicators of inflammation.[30]

Several studies have evaluated the relationship between increased RDW and morbidity and mortality of CAD. Investigators showed that an increased RDW was independently associated with in-hospital and long-term all-cause mortality and coronary events in STEMI and NSTEMI in an unselected population of male patients referred for coronary angiography.[2,31,32] Also, in other studies, a high admission RDW was independently associated with worse reperfusion and increased risk of in-hospital and long-term cardiovascular mortality in patients with STEMI undergoing primary percutaneous intervention.[33] In a study of 7556 adult participants (divided into 3 categories according to their 10-year Framingham risk of hard CAD events, as <10%, 10-20%, >20%), it was found that a higher RDW might be a powerful independent predictor of future coronary heart disease risk.[34] Isik et al.[5] demonstrated that RDW was independently associated with the presence of CAD and coronary complexity of CAD as assessed by the SYNTAX score.

Only hemoglobin levels were measured in this study and not other factors such as levels of iron, vitamin B12, folate, and mean corpuscular volume. However, we did not include the patients with anemia in our study. We believe that this makes it highly unlikely that the predictive value of RDW was related to iron deficiency. Furthermore, the incidence of clinically significant vitamin B12 and folate deficiency is low in a modern population. In a study of 15852 adult participants, RDW was found to be an independent predictor of mortality, and the investigators concluded that the relationship between RDW and mortality was not confounded by anemia-related deficiencies such as vitamin B12, folate or iron.[35]

In conclusion, we found that high levels of RDW were associated with absence of CCVs in patients with ACS. We also think that RDW is a widely available marker with no additional costs, in contrast to other novel markers of cardiovascular risk.

Limitations

There are several limitations to our study. We did not evaluate other novel risk factors for STEMI in young patients, such as fibrinogen, CD 40 ligand, factor V Leiden, protein C, and antithrombin III, and could not evaluate the medical history of patients. Only hemoglobin levels were measured in this study and not other factors such as levels of iron, ferritin, vitamin B12, and folate. We also did not evaluate the duration of angina or degrees of exercise capacity, which are important for development of CCVs.

Conflict-of-interest issues regarding the authorship or article: None declared

REFERENCES

1. Felker GM, Allen LA, Pocock SJ, Shaw LK, McMurray JJ, Pfeffer MA, et al. Red cell distribution width as a novel prognostic marker in heart failure: data from the CHARM Program and the Duke Databank. J Am Coll Cardiol 2007;50:40-7. [CrossRef]
2. Uyarel H, Ergelen M, Cicek G, Kaya MG, Ayhan E, Turkkan C, et al. Red cell distribution width as a novel prognostic marker in patients undergoing primary angioplasty for acute myocardial infarction. Coron Artery Dis 2011;22:138-44.
3. Anderson JL, Ronnow BS, Horne BD, Carlquist JF, May HT, Bair TL, et al. Usefulness of a complete blood count-derived risk score to predict incident mortality in patients with suspected cardiovascular disease. Am J Cardiol 2007;99:169-74. [CrossRef]
4. Poludasu S, Marmur JD, Weedon J, Khan W, Cavusoglu E. Red cell distribution width (RDW) as a predictor of long-term mortality in patients undergoing percutaneous coronary intervention. Thromb Haemost 2009;102:581-7.
5. Isik T, Uyarel H, Tanboga IH, Kurt M, Ekinci M, Kaya A, et al. Relation of red cell distribution width with the presence, severity, and complexity of coronary artery disease. Coron Artery Dis 2012;23:51-6. [CrossRef]
6. Akin F, Köse N, Ayça B, Katkat F, Duran M, Uysal OK, et al. Relation Between Red Cell Distribution Width and Severity of Coronary Artery Disease in Patients With Acute Myocardial Infarction. Angiology 2012 Oct 15. [CrossRef]
7. Weiss G, Goodnough LT. Anemia of chronic disease. N Engl J Med 2005;352:1011-23. [CrossRef]
8. Sabia PJ, Powers ER, Ragosta M, Sarembock IJ, Burwell LR, Kaul S. An association between collateral blood flow and myocardial viability in patients with recent myocardial infarction. N Engl J Med 1992;327:1825-31. [CrossRef]
9. Prêtre R, Rickli H, Ye Q, Benedikt P, Turina MI. Frequency of collateral blood flow in the infarct-related coronary artery in rupture of the ventricular septum after acute myocardial infarction. Am J Cardiol 2000;85:497-9, A10.
10. World Health Organization. Nutritional Anemia: Report of a WHO Scientific Group World Health Organization. Geneva: World Health Organization, 1968.
11. Rentrop KP, Cohen M, Blanke H, Phillips RA. Changes in collateral channel filling immediately after controlled coronary artery occlusion by an angioplasty balloon in human subjects. J Am Coll Cardiol 1985;5:587-92. [CrossRef]
12. Bonow RO, Mann DL, Zipes DP, Libby P. Braunwald's Heart Disease A Textbook of Cardiovascular Medicine, Part VII, p. 1064-6, 9th ed., Saunders, an imprint of Elsevier Inc, International Edition 2012.
13. Yun J, Rocic P, Pung YF, Belmadani S, Carrao AC, Ohanyan V, et al. Redox-dependent mechanisms in coronary collateral growth: the "redox window" hypothesis. Antioxid Redox Signal 2009;11:1961-74. [CrossRef]
14. Piek JJ, Koolen JJ, Hoedemaker G, David GK, Visser CA, Dunning AJ. Severity of single-vessel coronary arterial stenosis and duration of angina as determinants of recruitable collateral vessels during balloon angioplasty occlusion. Am J Cardiol 1991;67:13-7. [CrossRef]
15. Schaper W, Ito WD. Molecular mechanisms of coronary collateral vessel growth. Circ Res 1996;79:911-9. [CrossRef]
16. Matsunaga T, Warltier DC, Weihrauch DW, Moniz M, Tessmer J, Chilian WM. Ischemia-induced coronary collateral growth is dependent on vascular endothelial growth factor and nitric oxide. Circulation 2000;102:3098-103. [CrossRef]
17. Griendling KK, Sorescu D, Ushio-Fukai M. NAD(P)H oxidase: role in cardiovascular biology and disease. Circ Res 2000;86:494-501. [CrossRef]
18. Pung YF, Chilian WM. Corruption of coronary collateral growth in metabolic syndrome: Role of oxidative stress. World J Cardiol 2010;2:421-7. [CrossRef]
19. Seiler C. The human coronary collateral circulation. Heart 2003;89:1352-7. [CrossRef]
20. Celik T, Celik M, Iyisoy A. Coronary collateral circulation. Turk Kardiyol Dern Ars 2010;38:505-14.
21. Sahinarslan A, Kocaman SA, Topal S, Erçin U, Bukan N, Timurkaynak T. The relation of serum monocyte chemoattractant protein-1 level with coronary atherosclerotic burden and collateral degree in stable coronary artery disease. Turk Kardiyol Dern Ars 2011;39:269-75. [CrossRef]
22. Selçuk MT, Selçuk H, Temizhan A, Maden O, Ulupinar H, Baysal E, et al. The effect of plasma asymmetric dimethylarginine (ADMA) level and L-arginine/ADMA ratio on the development of coronary collaterals. Turk Kardiyol Dern Ars 2008;36:150-5.
23. Kadı H, Ceyhan K, Karayakalı M, Koç F, Celik A, Onalan O. The relationship between coronary collateral circulation and blood high-sensitivity C-reactive protein levels. Turk Kardiyol Dern Ars 2011;39:23-8.
24. Marsh WL Jr, Bishop JW, Darcy TP. Evaluation of red cell volume distribution width (RDW). Hematol Pathol 1987;1:117-23.
25. Förhécz Z, Gombos T, Borgulya G, Pozsonyi Z, Prohászka Z, Jánoskuti L. Red cell distribution width in heart failure: prediction of clinical events and relationship with markers of ineffective erythropoiesis, inflammation, renal function, and nutritional state. Am Heart J 2009;158:659-66. [CrossRef]
26. Libby P. What have we learned about the biology of atherosclerosis? The role of inflammation. Am J Cardiol 2001;88:3J-6J. [CrossRef]
27. Pierce CN, Larson DF. Inflammatory cytokine inhibition of erythropoiesis in patients implanted with a mechanical circulatory assist device. Perfusion 2005;20:83-90. [CrossRef]
28. Ferrario M, Massa M, Rosti V, Campanelli R, Ferlini M, Ma-

rinoni B, et al. Early haemoglobin-independent increase of plasma erythropoietin levels in patients with acute myocardial infarction. Eur Heart J 2007;28:1805-13. [CrossRef]

29. Lin JP, O'Donnell CJ, Jin L, Fox C, Yang Q, Cupples LA. Evidence for linkage of red blood cell size and count: genome-wide scans in the Framingham Heart Study. Am J Hematol 2007;82:605-10. [CrossRef]
30. Lippi G, Targher G, Montagnana M, Salvagno GL, Zoppini G, Guidi GC. Relation between red blood cell distribution width and inflammatory biomarkers in a large cohort of unselected outpatients. Arch Pathol Lab Med 2009;133:628-32.
31. Azab B, Torbey E, Hatoum H, Singh J, Khoueiry G, Bachir R, et al. Usefulness of red cell distribution width in predicting all-cause long-term mortality after non-ST-elevation myocardial infarction. Cardiology 2011;119:72-80. [CrossRef]
32. Cavusoglu E, Chopra V, Gupta A, Battala VR, Poludasu S, Eng C, et al. Relation between red blood cell distribution width (RDW) and all-cause mortality at two years in an unselected population referred for coronary angiography. Int J Cardiol 2010;141:141-6. [CrossRef]
33. Karabulut A, Uyarel H, Uzunlar B, Çakmak M. Elevated red cell distribution width level predicts worse postinterventional thrombolysis in myocardial infarction flow reflecting abnormal reperfusion in acute myocardial infarction treated with a primary coronary intervention. Coron Artery Dis 2012;23:68-72. [CrossRef]
34. Zalawadiya SK, Veeranna V, Niraj A, Pradhan J, Afonso L. Red cell distribution width and risk of coronary heart disease events. Am J Cardiol 2010;106:988-93. [CrossRef]
35. Perlstein TS, Weuve J, Pfeffer MA, Beckman JA. Red blood cell distribution width and mortality risk in a community-based prospective cohort. Arch Intern Med 2009;169:588-94. [CrossRef]

Key words: Acute coronary syndrome; biological markers; coronary circulation; erythrocyte indices; red cell distribution width.

Anahtar sözcükler: Akut koroner sendrom; biyolojik belirteç; koroner dolaşım; eritrosit indeksi; eritrosit dağılım genişliği.