Elevated Red Blood Cell Distribution Width is Associated with Isolated Systolic Hypertension

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ABSTRACT

Introduction: The aim of this study was to determine the relationship between isolated systolic hypertension and red blood cell distribution width (RDW).

Patients and Methods: Eighty-one patients were included in the study. Blood pressure was measured by a cardiologist using a manual sphygmomanometer, and the patients were divided into 2 groups as isolated systolic hypertensive and normotensive based on the European Society of Hypertension classification. Complete blood counts (CBC) and biochemical values of each patient were measured using standard methods.

Results: There was significant difference between the mean RDW values of the isolated systolic hypertensive and the normotensive groups. While there was a strong association between high RDW values and isolated systolic hypertension, there were no significant differences between the 2 groups for any of the other measured laboratory values.

Conclusion: High RDW value appears to be a strong and independent predictor of isolated systolic hypertension.

Key Words: Red cell distribution width; hypertension; erythrocyte indices

Yükselmiş Kırmızı Kan Hücresi Dağıtım Genişliği İzole Sistolik Hipertansiyon ile İlişkilidir

ÖZET

Giriş: Bu çalışmanın amacı, izole sistolik hipertansiyon ve kırmızı kan hücresi dağılım genişliği (RDW) arasındaki ilişkiyi belirlemektir.

Hastalar ve Yöntem: Toplam 81 hasta çalışmaya dahil edildi. Kan basıncı manuel sfingomanometre kullanarak bir kardiyolog tarafından ölçüldü ve hastalar Avrupa Hipertansiyon Topluluğu sınıflandırmasına dayalı olarak normotansif ve izole sistolik hipertansif olarak iki gruba ayrıldı. Tam kan sayımı ve her hastanın biyokimyasal değerleri standart yöntemler kullanılarak ölçüldü.

Bulgular: İzole sistolik hipertansif ve normotansif grupların ortalama RDW değerleri arasında anlamlı bir fark tespit edildi. Yüksek RDW değerleri ve izole sistolik hipertansiyon arasında güçlü bir ilişki varken, diğer ölçülen laboratuvar değerleri bakımından iki grup arasında anlamlı farklılık yoktu.

Sonuç: Yüksek RDW değeri izole sistolik hipertansiyon için güçlü ve bağımsız bir belirleyici olarak tespit edildi.

Anahtar Kelimeler: Kırmızı kan hücresi dağılım genişliği; hipertansiyon; eritrosit indeksleri

INTRODUCTION

Red blood cell distribution width (RDW) is a laboratory parameter that indicates the anisocytosis of the circulating erythrocytes. This parameter is routinely studied in complete blood count (CBC) examinations[1]. Previous studies have shown that high RDW values are related to increased mortality in heart failure, acute coronary syndromes, and in patients who underwent primary angioplasty or who had a coronary artery bypass graft (CABG)[2-4].

Hypertension is a major health problem. In a comprehensive meta-analysis, both systolic blood pressure (SBP) and diastolic blood pressure (DBP) were shown as predictors for coronary mortality[5]. Increased pulse pressure in middle-aged and elderly hypertensive patients have been reported to be an important determinant of cardiovascular events[6]. SBP increases with age, while DBP remains the same or decreases as a result of a series of

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pathophysiological changes, including a decrease in vascular compliance, an increase in vascular resistance, weakening of the baroreceptor reflex, and a decrease in plasma renin activity in spite of a decrease in plasma volume[7]. For this reason, isolated SBP with a large pulse pressure is observed most frequently in elderly patients[8]. Isolated systolic hypertension is defined as a DBP < 90 mmHg and a SBP ≥ 140 mmHg. Isolated systolic hypertension is related to an increased cardiovascular risk, and its strong relationship with cardiovascular morbidity and mortality has been reported in several studies[9,10]. Hence, in this study we aimed to determine the relationship between RDW and isolated systolic hypertension, which is a powerful predictor of cardiovascular events.

PATIENTS and METHODS

After approval from the Ethics Committee, 81 consecutive patients were evaluated at the Cardiology Polyclinic. Thirty-three patients (17 males, 16 females) were included in the isolated systolic hypertension group, and 48 patients (19 males, 29 females) were included in the normotensive group. The classification criteria accepted by the European Society of Hypertension and the European Society of Cardiology (ESH/ESC) were used for grouping the patients. According to these criteria, isolated systolic hypertension was accepted as SBP equal to or greater than 140 mmHg, and DBP lower than 90 mmHg. Normotension was defined as SBP < 140 mmHg, and DBP < 90 mmHg.

Blood pressure measurements were taken from both arms and from the brachial artery by a cardiologist (E.Y.) after the patients have been in a sitting position for about 5 min at the Cardiology Polyclinic. A standard sphygmomanometer cuff was utilized to take the measurements, each patient's blood pressure was evaluated twice and the average results were calculated and recorded. Demographic characteristics, cardiovascular history, and risk factors (smoking, hypercholesterolemia, diabetes mellitus, hypertension, and alcohol use) were obtained from each patient. CBC and biochemical tests were done using a Beckman Coulter LH-750 and a Beckman Coulter L × 20, respectively. White blood cell (WBC), hemoglobin, platelet, RDW, mean platelet volume (MPV), creatinine, total cholesterol, low-density lipoprotein cholesterol, high-density lipoprotein cholesterol, and triglyceride levels of each patient were recorded. Glomerular Filtration Rate (GFR) was calculated by using Modification of Diet in Renal Disease MDRD formula. Standard 12-lead Electrocardiogram (ECG) recordings were taken, and transthoracic echocardiography was performed by a cardiology specialist. Patients who had systolic or diastolic heart failure, hemodynamically significant valvular heart disease, coronary artery disease, heart rhythm problem, diabetes, chronic renal failure, malignancy, anemia or hematologic disease, and regular medicine users were excluded from the study. For the diagnosis of anemia, the lower limit of hemoglobin was taken to be 11.5 g/dL.

Statistical Analysis

Pearson's chi-square test was used to compare the incidence of the categorical variables (gender) that are presented numerically. Kolmogorov-Smirnov test was used to evaluate the normality of the distribution of the continuous variables. Two independent sample t-tests or the Mann-Whitney U-tests were used to compare the continuous variables between 2 groups. Continuous variables were presented as mean and standard deviation (SD) or as median and interquartile range (Q1-Q3). The associations between the study parameter (RDW) with baseline demographic characteristics were determined by the Pearson or the Spearman correlation test. SPSS software 15.0 for Windows was used for all statistical analyzes. Calculated p-values < 0.05 were considered statistically significant.

RESULTS

The baseline characteristics of both groups are shown in Table 1. The mean age of the patients in the isolated systolic hypertensive group was higher than the normotensive group (67 ± 10 years vs. 51 ± 11 years, p< 0.001). The mean GFR of the patients in the isolated systolic hypertensive group was lower than in the normotensive group (109.4 ± 19.8 vs. 95.7 ± 16.9, p= 0.002). However, in multivariate regression analysis; there was no significant association between the RDW and other variables, including GFR, age, creatinine and sex (p= 0.871). There was no significant difference in the distribution of gender between the groups. The SBP and DBP of the isolated systolic hypertension group were significantly higher than those of the normotensive group [160 (150-170) mmHg vs. 115 (110-120) mmHg, p< 0.001; 80 (80-85) mmHg vs. 70 (70-80) mmHg, p< 0.001].

The mean RDW of the isolated systolic hypertensive group was significantly higher than the normotensive group [14.2

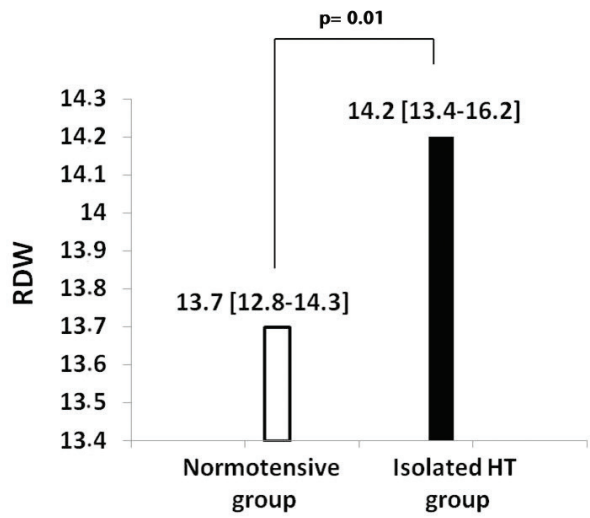

Figure 1. The mean RDW levels in the study groups (RDW, red blood cell distribution width).

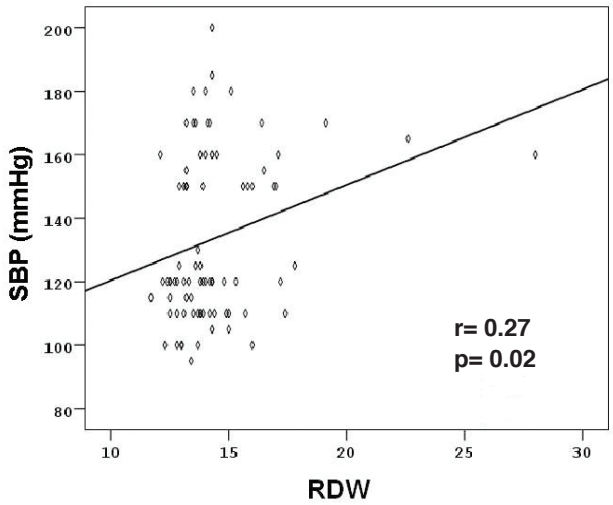

Figure 2. The relationship between RDW with systolic blood pressure in patients with isolated hypertension (RDW, red blood cell distribution width; SBP, systolic blood pressure).

(13.4-16.2) vs. 13.7 (12.8-14.3)], p= 0.01, respectively, (Figure 1). There was a correlation between the RDW and SBP (r= 0.27, p= 0.02, Figure 2). Laboratory values such as creatinine, total cholesterol, HDL, LDL, triglycerides, WBC, hemoglobin, platelet count, and MPV were similar in both groups.

DISCUSSION

The results indicated that the mean RDW of the isolated systolic hypertensive group was significantly higher than the normotensive control group. However, in patients with isolated systolic hypertension, a correlation was observed between the RDW and SBP.

The most recent Joint National Committee (JNC) 7 hypertension guidelines state that particularly after the age of 50, the prevalence of isolated systolic hypertension increases with increasing SBP, and it is the most common form of hypertension in elderly patients[11]. Isolated systolic hypertension increases mortality, predominantly for patients older than 50 years[12]. The mean age of the isolated systolic hypertensive group was significantly higher than the normotensive group, which is compatible with these previous studies and guidelines.

The relationship between isolated systolic hypertension and stroke, heart failure and increased cardiovascular risk has been demonstrated[13,14]. Previous studies have shown a relationship between high RDW and increased mortality and morbidity in short term follow up of patients with acute and chronic heart failure[15,16]. A study by Gul et al. reported that RDW was related to long-term mortality in patients with acute coronary syndrome[17]. In a study by Uyarel et al., high RDW was shown to be related with in-hospital and long-term increased cardiovascular mortality in 2506 patients with ST segment elevated myocardial infarction that underwent primary angioplasty[2]. It has also been shown that RDW is increased in coronary artery ectasia and slow coronary flow patients[18,19]. These studies are important for us because they show the close relationship between RDW and cardiovascular problems.

In this study, we showed that high RDW is a predictor for isolated systolic hypertension. Some earlier studies have reported the relationship between RDW and hypertension. Tanindi et al. demonstrated that RDW is higher in pre-hypertensive and hypertensive patients than in healthy controls, and that RDW values have a strong relationship with SBP and DBP[20]. However, that study did not include an isolated systolic hypertension group. Gunebakmaz et al. monitored the

Table 1. Baseline characteristics in the study groups

	Normotensive group (n= 48)	Isolated HT group (n= 33)	p
Age (years)	51 ± 11	67 ± 10	< 0.001
Sex (male/female)	19/29	17/16	NS
Systolic blood pressure (mmHg)	115 (110-120)	160 (150-170)	< 0.001
Diastolic blood pressure (mmHg)	70 (70-80)	80 (80-85)	< 0.001
Creatinine (mg/dL)	0.69 ± 0.21	0.76 ± 0.20	NS
Total cholesterol (mg/dL)	192 ± 52	194 ± 31	NS
HDL-cholesterol (mg/dL)	39 ± 10	43 ± 10	NS
LDL-cholesterol (mg/dL)	123 ± 49	124 ± 26	NS
Triglycerides (mg/dL)	152 ± 87	139 ± 85	NS
WBC count ($10^3/\mu L$)	6.9 ± 1.9	7.2 ± 2.3	NS
Platelet count ($10^3/\mu L$)	238 ± 61	252 ± 73	NS
Hemoglobin (g/dL)	13.5 ± 1.3	13.2 ± 1.6	NS
MPV (fL)	8.3 ± 0.9	8.4 ± 0.9	NS

HDL: High-density lipoprotein, LDL: Low-density lipoprotein, WBC: White blood cell, MPV: Mean platelet volume.

ambulatory blood pressure of 123 hypertensive patients, and found that RDW was significantly higher in the non-dippers patients than in the dipper hypertensive and normotensive patients[21]. Also, the relationship between high RDW in hypertensive patients has been reported to be related to Carotid intimal-medial thickness[22]. These studies support our findings, because this study indicates that there is a relationship between hypertension and RDW.

The pathophysiological explanation indicating why RDW increases in isolated systolic hypertensive patients is not fully known; however, some hypotheses have been made. Fornal et al. hypothesized that inflammation causes the development of target organ damage in hypertension that is accompanied by increased degradation in erythropoiesis[23]. Similarly, Ozcan et al. demonstrated that in non-dipper hypertension patients, high RDW was associated with high hs-CRP values, and that there was a close relationship between inflammatory activity and high RDW[24]. Inflammation may cause RDW to increase by disrupting iron metabolism, reducing the production of erythropoietin, reducing the erythropoietin response, or by shortening the lifespan of erythrocytes[25,26]. Therefore, the effects of inflammation on erythropoiesis in the renin-angiotensin-aldosterone system may be affecting RDW values[27]. Pathophysiological mechanisms are outside the scope of our study and inflammatory markers were not examined in our study. On the other hand, impaired kidney function is a well-known risk factor for cardiovascular disease and hypertension. Previous studies showed that there is an inverse, graded, association between RDW and kidney function tests in a large cohort of unselected adult outpatients[28]. However, our study's analyses show that there is no significant association between the RDW and GFR.

The limitations of this study are threefold: 1) It was a single-center study with a small number of patients. Therefore, the results should be confirmed with larger sample size.

2) Although patients with anemia were excluded from this study, iron, vitamin B12 and folic acid levels were not measured, and they may affect RDW. 3) Another important issue is that RDW is a dynamic variable and supposed to depend on the inflammatory status. The inflammatory marker was not assessed and RDW was assessed only on a single occasion instead of serial measurements.

CONCLUSION

The average RDW was significantly higher in the isolated systolic hypertension group compared to the normotensive group. High RDW value appears to be a strong and independent predictor of isolated systolic hypertension.

CONFLICT of INTEREST

The author reported no conflict of interest related to this article.

AUTHORSHIP CONTRIBUTIONS

Concept/Design: EY
Analysis/Interpretation: EY
Data Acquisition: EY
Writing: EY
Critical Revision: EY
Final Approval: EY

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