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The Association Between Red Cell Distribution Width and Blood Pressure Variability in Hypertensive Patients

Mehmet Ali Mendi

Department of Cardiology, Near East University Faculty of Medicine, Nicosia, North Cyprus

Abstract

BACKGROUND/AIMS: The relation between blood pressure (BP) variability and inflammation has been demonstrated in numerous types of research. Red cell distribution width (RDW) is independently related to worse cardiovascular consequences. An increased RDW in the circulation may project continuing systemic and vascular inflammatory processes and contribute to the development of hypertension. We aimed to investigate the correlation between RDW and BP variability in hypertensive patients.

MATERIALS AND METHODS: Our research included 210 participants with essential hypertension. The hypertensive participants were identified according to the current guidelines. Twenty-four-hour ambulatory blood pressure monitoring (24-hABPM) was performed for each participant. Since variability values were in a standard deviation distribution, statistical analysis was carried out accordingly. Routine biochemistry analyses and complete blood count were also performed. The contribution of independent variables on BP variability was analyzed by stepwise multivariable linear regression analysis.

RESULTS: A positive statistical correlation was found between RDW levels and daytime systolic blood pressure (SBP) variability, and also diastolic blood pressure (DBP) variability (r=0.198, p=0.002 and r=0.101, p=0.004 respectively). Similarly, positive correlations were found between the variables of gender, DM, and smoking (r=0.202, p=0.002; r=0.130, p=0.042; r=0.181, p=0.004 respectively) both for daytime SBP and DBP variability (r=0.186, p=0.005; r=0.192, p=0.004; r=0.191, p=0.004 respectively). Although a strong positive statistical correlation (p<0.001) was found between age and daytime SBP, no correlation was detected between age and daytime DBP variability.

CONCLUSION: Elevated RDW values predict daytime BP variability in hypertensive patients. This relationship may depend on the underlying inflammation. Further research is needed in order to investigate the influences of strict BP control on adverse cardiovascular events via inflammation and BP variability.

Keywords: Blood pressure variability, inflammation, red cell distribution width, ambulatory blood pressure monitoring

INTRODUCTION

Red cell distribution width (RDW) is a numerical value of versatility in the volume and dimension of red blood cells, and it is in the routine blood cell count which shows anisocytosis.[1] In addition, RDW can be a guide in the differentiation of types of anemia, as well as predicting morbidity and survival rates for many other conditions.[2] RDW has been reported as a predictor of adverse outcomes and mortality in many cardiovascular diseases (CVD) such as stable coronary artery disease,[2,3] heart insufficiency,[1,4] stroke,[5] myocardial infarction,[6] limb atherosclerosis[7] and also in those patients with myocardial infarction.[8] The pathophysiological rationale between the inflammatory process and RDW is based on the hypothesis that chronic systemic inflammation

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ORCID IDs of the authors: M.A.M. 0000-0003-4948-1645.

Address for Correspondence: Mehmet Ali Mendi
E-mail: mendimehmetali@gmail.com
ORCID ID: orcid.org/0000-0003-4948-1645

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in CVD may cause anisocytosis.[9] The RDW value is elevated in hypertensive patients with normotensives[10] and it is raised in non-dipping hypertensive patients with dipper hypertensives[11] as well. A high level of circulating RDW may project continuing vascular inflammatory processes and play a part in the mechanism of hypertension.[12] Elevated blood pressure (BP) aggravates the vascular inflammatory process, leading to endothelial damage and eventually atherosclerosis.[13]

Recent trials have added to the emphasis on 24-hour blood pressure variability (24-hBPV). Hypertensives in those with low 24-hBPV have a lower prevalence and severity of end-organ damage than in those with high 24-hBPV.[14,15]

Based on our hypothesis that there is a positive correlation between BP variability and RDW in hypertensive patients, which has not been investigated before to the best of our knowledge, we aimed to investigate this relationship.

MATERIALS AND METHODS

Our study included 210 consequent patients with high BP who had applied to the outpatient department of a cardiology clinic. Hypertension was defined as BP ≥140/90 mmHg in-office measurements for at least two repeated readings.[16] Twenty-four-hour ambulatory blood pressure monitoring (24-hABPM) was carried out for all hypertensive participants. Patients with secondary hypertension, hematological system disorders (anemia, leukemia, etc.), renal or hepatic dysfunction, malignancy, or connective tissue diseases were not included in this research. The demographic characteristics of the participants, such as their age, gender, smoking status, and diabetes mellitus (DM) were noted. In addition, fasting serum lipid panels including high-density lipoprotein, triglyceride, low-density lipoprotein, total cholesterol, fasting blood glucose, and creatinine values were also recorded. The Ethics Committee of Ankara Yüksek İhtisas Training and Research Hospital authorized the research protocol (approval number: 2962, date: 16.09.2013) and informed consent was taken from all participants. Lipid profile, glucose and creatinine were designated by standard methods. Hemoglobin, total white blood cell counts, platelet counts, and RDW were calculated using a self-acting blood cell counter (ADVIA 2120i Hematology System, Siemens, USA).

A 24-hABPM device (Stolberg, Mobilograph, Germany) was used on all participants. The device was worn to measure 24 h BP in 15-min periods during the daytime and each 30-min during the nighttime. It was placed on the non-dominant arm. We analyzed the recordings with interactive software. 24-hABPM was repeated if 20% or more of the measurements could not be taken. The daytime, nighttime, and 24-h averages of systolic blood pressure (SBP), diastolic blood pressure (DBP), and mean BP were obtained from all participants based on the hourly averages of the ambulatory BP recordings.

Statistical Analysis

Since the variability values were in standard deviation distribution, statistical analysis was performed accordingly. Statistical analysis was implemented by SPSS 17.0 statistical software (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was performed to establish the distribution of all data. According to the test results, the analysis of normally distributed variables was performed with mean ± standard deviation, and the analyses of non-normally distributed variables were performed with medians. The contributions of independent variables on BP variability were analyzed by stepwise multivariable linear regression analysis. Statistical significance was set at $p<0.05$.

RESULTS

A total of 210 individuals with primary hypertension took part in our research, and the baseline characteristics of these individuals are outlined in Table 1. Office BP measurements and 24-hABPM results are given in Table 2.

A positive statistical correlation was found between RDW levels and daytime SBP variability, and also daytime DBP variability. Similarly, positive correlations were found between the other variables (female gender, DM, smoking) both for daytime SBP and DBP variability. Although a strong positive statistical correlation ($p<0.001$) was found between age and daytime SBP, no correlation was detected between age and daytime DBP variability. Although a positive correlation was found between nighttime SBP standard deviation with type-2 DM alone, a positive correlation was found between nighttime DBP standard deviation with type-2 DM as well as female gender (Table 3).

Table 1. Baseline characteristics

Variable	n (%)/mean or median ± SD
Age	55.1±12.3
Gender (male)	124 (59%)
Type-2 DM	65 (31%)
Smoking	43 (20.5%)
RDW (%)	13.9±1.4
Hgb (g/dL)	14.5±1.5
WBC (10^3/mm^3)	7.5±1.8
Plt (10^3/mm^3)	258 (219-295)
Fasting glucose (mg/dL)	101 (93-128.2)
Creatinine (mg/dL)	0.9±0.2
HDL-cholesterol (mg/dL)	45.1±13.1
LDL-cholesterol (mg/dL)	123.1±32.9
Triglycerides (mg/dL)	138 (113-198)

SD: Standard deviation, DM: Diabetes mellitus, RDW: Red cell distribution width, Hgb: Hemoglobin, WBC: Wight blood cell, Plt: Platelet, HDL: High-density lipoprotein, LDL: Low density lipoprotein.

Table 2. Office and 24-h blood pressure mean and awake and asleep standard deviation values

Variable	Mean ± SD (mmHg)
Office SBP	172.1±21.4
Office DBP	99.3±16.5
24-h mean SBP	142.5±13.7
24-h mean DBP	89.1±10.1
Awake mean SBP	145.3±14.2
Awake mean DBP	94.7±10.5
Asleep mean SBP	133.1±17.1
Asleep mean DBP	80.6±11.6
Awake SBP SD	15.2±4.1
Awake DBP SD	11.1±2.9
Asleep SBP SD	17.1±3.1
Asleep DBP SD	12.4±2.4

SD: Standard deviation, SBP: Systolic blood pressure, DBP: Diastolic blood pressure.

Table 3. Stepwise multivariable linear regression analysis

	Awake SBP SD		Awake DBP SD		Asleep SBP SD		Asleep DBP SD	
	r^2=0.469		r^2=0.387		r^2=0.176		r^2=0.156	
	r	p	r	p	r	p	r	p
Age	0.265	<0.001						
Female	0.202	0.002	0.186	0.005			0.154	0.025
RDW	0.198	0.002	0.101	0.004				
Smoking	0.181	0.004	0.191	0.004				
Type-2 DM	0.130	0.042	0.192	0.004	0.176	0.011	0.162	0.03

SD: Standard deviation, SBP: Systolic blood pressure, DBP: Diastolic blood pressure, RDW: Red cell distribution width, DM: Diabetes mellitus.

DISCUSSION

Our research revealed that RDW was positively correlated with daytime BP variability but no correlation was found between nighttime BP variability and RDW.

Hypertension has been reported as one of the major causes of coronary artery disease, cerebrovascular events, and renal insufficiency.[17] With the increasing availability of 24-hABPM, it has become possible not only to measure the BP during 24 h, but also 24-hABPM can contribute to more information about BP, such as the average level, fluctuations, and the circadian rhythm of BP.[18]

The effects of BP variability on adverse cardiovascular outcomes have been demonstrated by recent research. Suchy-Dicey et al.[19] put forward that SBP variability is independently associated with high mortality ratios and myocardial infarctions. In addition, BP variability is related to increased end-organ damage.[12] The association between BP variability and inflammation has been demonstrated in many types of research using different inflammatory biomarkers, such as high sensitive-C-reactive protein, sE-selectin, and IL-6.[13,20,21]

The clinical importance of RDW in hypertension has been defined in various trials. Tanindi et al.[10] demonstrated a strong correlation between high levels of RDW and high SBP and DBP levels. It has been reported that increased RDW levels were associated with higher BP levels in two major community-based cohorts.[3,22] In this study, we attempted to establish whether there was any possible association between BP variability and RDW levels in current essential hypertension. Our results indicate that RDW is associated with daytime BP variability in essential hypertension.

Increased RDW shows a strong and independent association with poor cardiovascular outcomes in CVD and so it is suggested as a new predictor of mortality.[1,7] The association between RDW and CVD may be based on underlying inflammations.[2,23,24] According to our results, increased RDW levels in patients with high BP variability may suggest a greater inflammatory load. There was no correlation between nighttime BP variability and RDW and this may be explained by a decrease in sympathetic activity at nighttime. An elevated RDW level may be a marker which demonstrates increased BP variability in hypertensive patients.

Study Limitations

One of the main limitations of our study was that it was single-centered and did not include normotensive individuals. In addition, the results cannot be generalized to the entire hypertensive population due to the lack of black origin among the participants. Also, morning BP fluctuation was not evaluated. Body mass index and waist circumference were not measured. Other biomarkers which have been proven to be associated with inflammation were not included in this study. Despite these limitations, this was the first study to draw attention to the association of BP variability with RDW.

CONCLUSION

Elevated RDW value predicts daytime BP variability in hypertensive patients. This relation may depend on the underlying inflammation. Further research is needed to investigate the influences of strict BP control on adverse cardiovascular events via inflammation and BP variability.

MAIN POINTS

- Elevated RDW values predict blood pressure variability.
- Blood pressure variability is associated with a raised inflammatory process.
- The inflammatory process takes part in the setting of worse cardiovascular outcomes.

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ETHICS

Ethics Committee Approval: The Ethics Committee of Ankara Yüksek İhtisas Training and Research Hospital authorized the research protocol (approval number: 2962, date: 16.09.2013).

Informed Consent: Informed consent was taken from all participants.

DISCLOSURES

Financial Disclosure: The author declared that this study had received no financial support.

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