RESEARCH ARTICLE
DOI: 10.4274/cjms.2022.2022-18

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

Mehmet Ali Mendi. Blood Pressure Variability and Red Cell Distribution Width

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Abstract
BACKGROUND/AIMS: The relation between blood pressure 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 purposed to research the correlation between RDW and blood pressure variability in hypertensive patients.
MATERIALS AND METHODS: Our research included 210 participants with essential hypertension. Hypertensive participants were identified according to the current guidelines. Twenty-four-hour ambulatory blood pressure monitoring (24-hABPM) was done for each participant. Since variability values are parallel with standard deviation values, statistical analysis was done over standard deviation. Routine biochemistry analyses and complete blood count were also done. The Contribution of independent variables on blood pressure variability was analyzed by stepwise multivariable lineer regression analysis
RESULTS: A Positive statistical correlation was found between RDW levels and daytime systolic blood pressure variability, and also diastolic blood pressure variability (R=0.198, p=0.002 and R=0.101, p=0.004; in order of), similarly, positive correlation were found between variables (female, DM, smoking) (R=0.202, p=0.002; R=0.130, p=0.042; R=0.181, p=0.004; in order of) both for daytime systolic and diastolic blood pressure variability (R=0.186, p=0.005; R=0.192, p=0.004; R=0.191, p=0.004; in order of). Although a strong positive statistical correlation (p <0.001) was found between age and daytime systolic blood pressure, no correlation was detected between age and daytime diastolic blood pressure variability.
CONCLUSION: Elevated RDW value predicts daytime blood pressure variability in hypertensive patients. This relation may depend on the underlying inflammation. Further research is needed to survey the influences of strict blood pressure control on adverse cardiovascular events via inflammation and blood pressure variability.
Keywords: Blood pressure variability, inflammation, red cell distribution width, ambulatory blood pressure monitoring

To cite this article: Mendi MA. The Association Between Red Cell Distribution Width and Blood Pressure Variability in Hypertensive Patients. Cyprus J Med Sci 2024;

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09.04.2022
24.11.2022

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 and shows anisocytosis[1]. In addition, RDW can be a guide in the differentiation of types of anemia, as well as it also predicts 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 such as stable coronary artery disease[2-3], heart insufficiency [1,4], stroke[5], myocardial infarction [6], limb atherosclerosis [7] and in patients with myocardial infarction [8]. The pathophysiological rationale between the inflammatory process and RDW is based on the hypothesis that chronic systemic inflammation in cardiovascular diseases may cause anisocytosis[9]. RDW value is elevated in hypertensive patients confronted with normotensives [10] and is raised in non-dipping hypertensive patients confronted with dipper hypertensives[11], as well. A high level of circulating RDW may project continuing vascular inflammatory process and takes a part in the mechanism of hypertension [12]. Elevated blood pressure aggravates the vascular inflammatory process, leading to endothelial damage and eventually atherosclerosis [13].

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

Based on our hypothesis that there is a positive correlation between blood pressure variability and RDW in hypertensive patients, which has not been investigated before to our knowledge, we aimed to investigate whether there is a relationship between blood pressure variability and RDW level.

MATERIALS AND METHODS

Our study included 210 consequent patients with high blood pressure who had applied to the outpatient department of the cardiology clinic. Hypertension was defined as blood pressure ≥140/90 mmHg in-office measurements at least repeated two readings[16]. Twenty-four-hour ambulatory blood pressure monitoring (24-hABPM) was carried out for all hypertensive participants. Secondary hypertension, hematological system disorders (anemia, leukaemia, etc.), renal or hepatic dysfunction, malignancy, and connective tissue diseases were not included in the research. Demographic characteristics of the participants like age, sex, smoking status, and diabetes mellitus (DM), were noted. In addition, fasting serum lipid panels including high-density lipoprotein (HDL), triglyceride, low-density lipoprotein (LDL), total cholesterol, fasting blood glucose, and creatinine values were also recorded. The ethics committee of our hospital authorized the research protocol 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 tool (Stolberg, Mobilograph, Germany) was performed on all participants. The tool was worn to measure 24-h blood pressure (BP) each 15-min period during daytime and

each 30-min during nighttime by situated 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. 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 hourly averages of ambulatory BP recordings.

Statistical Analysis

Since variability values are parallel with standard deviation values, statistical analysis was done over standard deviation. Statistical analysis was implemented by handling 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 done over mean±SD, and the analysis of non-normally distributed variables was done over the median. The Contribution of independent variables on blood pressure variability was analyzed by stepwise multivariable lineer regression analysis. Statistical significance was set at $p < 0.05$.

RESULTS

A total of 210 individuals with primary hypertension were received our research, and the baseline characteristics of the individuals are outlined in Table-1. Office blood pressure measurements and 24-hABPM results are given in Table-2.

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

Discussion

Our research put forth that RDW was positively correlated with daytime blood pressure variability but it wasn't found between nighttime blood pressure 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 became possible not only to measure the blood pressure during 24 h, but also 24-hABPM can contribute to more information about BP, such as the average level, fluctuation, and the circadian rhythm of BP [18].

The effect of blood pressure variability on adverse cardiovascular outcomes has been demonstrated by recent research. Suchy-Dicey AM et al. [19] put forth that systolic blood pressure variability has been independently associated with high mortality ratio and myocardial infarction. In addition, blood pressure variability has been related to increased end-organ damage[12]. The association between blood pressure variability and inflammation has been demonstrated in many types of research using different inflammatory biomarkers, such as high sensitive-CRP [13, 20], sE-selectin[13], and IL-6[21].

The clinical importance of RDW in hypertension has been defined in various trials. Tanındı et al.[10] demonstrated a strong correlation between the high level of RDW and high systolic and diastolic blood pressure 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 any possible association between blood pressure variability and RDW levels in current essential hypertension. Our results propose that RDW is associated with daytime blood pressure variability in essential hypertension.

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

Study Limitations

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

CONCLUSION

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

MAIN POINTS

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

Acknowledgments: I would like to express my gratitude, especially to our founding rector Professor Doctor Suat Günsel and, Professor Doctor Hamza Duygu, and Professor Doctor Levent Cerit for their contributions.

REFERENCES

1. Felker GM, Allen LA, Pocock SJ, Shaw LK, McMurray JJV, 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(1):40-47. doi:10.1016/j.jacc.2007.02.067
2. Lappe JM, Horne BD, Shah SH, May HT, Muhlestein JB, Lappe DL, et al. Red cell distribution width, C-reactive protein, the complete blood count, and mortality in patients with coronary disease and a normal comparison population. Clin Chim Acta, 2011. 412(23-24):2094-9. doi:10.1016/j.cca.2011.07.018
3. Tonelli M, Sacks F, Arnold M, Moye L, Davis B, Pfeffer M. Relation Between Red Blood Cell Distribution Width and Cardiovascular Event Rate in People With Coronary Disease. Circulation, 2008. 117(2):163-168. doi:10.1161/CIRCULATIONAHA.107.727545
4. Zalawadiya SK, Zmily H, Farah J, Daifallah S, Ali O, Ghali JK. Red cell distribution width and mortality in predominantly African-American population with decompensated heart failure. J Card Fail, 2011. 17(4):292-8. doi:10.1016/j.cardfail.2010.11.006

5. Ani C, Ovbiagele B. Elevated red blood cell distribution width predicts mortality in persons with known stroke. J Neurol Sci, 2009. 277(1-2):103-8. doi:10.1016/j.jns.2008.10.024
6. Dabbah S, Hammerman H, Markiewicz W, Aronson D. Relation between red cell distribution width and clinical outcomes after acute myocardial infarction. Am J Cardiol, 2010. 105(3):312-7. doi:10.1016/j.amjcard.2009.09.027
7. Ye Z, Smith C, Kullo IJ. Usefulness of red cell distribution width to predict mortality in patients with peripheral artery disease. Am J Cardiol, 2011. 107(8):1241-5. doi:10.1016/j.amjcard.2010.12.023
8. 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(1):68-72. doi:10.1097/MCA.0b013e32834f1188
9. Salvagno GL, Sanchis-Gomar F, Picanza A, Lippi G. Red blood cell distribution width: A simple parameter with multiple clinical applications. Crit Rev Clin Lab Sci. 2015;52(2):86-105. doi: 10.3109/10408363.2014.992064. Epub 2014 Dec 23. PMID: 25535770.
10. Tanindi A, Topal FE, Topal F, Celik B. Red cell distribution width in patients with prehypertension and hypertension. Blood Press, 2012. 21(3):177-81. doi:10.3109/08037051.2012.645335
11. Ozcan F, Turak O, Durak A, İşleyen A, Uçar F, Giniş Z, et al. Red cell distribution width and inflammation in patients with non-dipper hypertension. Blood Press, 2013. 22(2):80-5. doi:10.3109/08037051.2012.707336
12. Fici F, Celik T, Balta S, Iyisoy A, Unlu M, Demitkol S, et al. Comparative Effects of Nebivolol and Metoprolol on Red Cell Distribution Width and Neutrophil/Lymphocyte Ratio in Patients with Newly Diagnosed Essential Hypertension. J Cardiovasc Pharmacol, 2013 Oct;62(4):388-93. doi:10.1097/FJC.0b013e31829f716a
13. Tatasciore A, Zimarino M, Rende G, Zurro M, Soccio M, Prontera C, et al. Awake blood pressure variability, inflammatory markers and target organ damage in newly diagnosed hypertension. Hypertens Res, 2008. 31(12):2137-46. doi:10.1291/hypres.31.2137
14. Parati G, Pomidossi G, Albini F, Malaspina D, Mancia G. Relationship of 24-hour blood pressure mean and variability to severity of target-organ damage in hypertension. J Hypertens, 1987. 5(1):93-8. doi:10.1097/00004872-198702000-00013
15. Mancia G, Parati G, Hennig M, Flatau B, Omboni S, Glavina F. Relation between blood pressure variability and carotid artery damage in hypertension: baseline data from the European Lacidipine Study on Atherosclerosis (ELSA). J Hypertens, 2001. 19(11):1981-9. doi:10.1097/00004872-200111000-00008
16. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC Guidelines for the management of arterial hypertension: The Task Force for the management of arterial hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). J Hypertens, 2013. 31(7):1281-357. doi:10.1097/01.hjh.0000431740.32696.cc
17. Kannel, W.B., Blood pressure as a cardiovascular risk factor: prevention and treatment. JAMA, 1996. 275(20):1571-6. doi:10.1001/jama.1996.03530440051036
18. Kanbay M, Turkmen K, Ecder T, Covic A. Ambulatory blood pressure monitoring: from old concepts to novel insights. Int Urol Nephrol, 2012. 44(1):173-82. doi:10.1007/s11255-011-0027-6

19. Suchy-Dicey AM, Wallace ER, Mitchell SVE, Aguilar M, Gottesman RF, Rice K, et al. Blood Pressure Variability and the Risk of All-Cause Mortality, Incident Myocardial Infarction, and Incident Stroke in the Cardiovascular Health Study. Am J Hypertens, 2013 Oct;26(10):1210-7. doi:10.1093/ajh/hpt092
20. Chen SH, Liu YH, Cai J, Wang AT, Ma YJ, Li XL, et al. [Impact of systolic blood pressure on visit-to-visit blood pressure variability in middle-aged and elderly people]. Zhonghua Xin Xue Guan Bing Za Zhi, 2013. 41(3):219-23. doi:10.3760/cma.j.issn.0253-3758.2013.03.010
21. Kim KI, Lee JH, Chang HJ, Cho YS, Youn TJ, Chung WY, et al. Association between blood pressure variability and inflammatory marker in hypertensive patients. Circ J, 2008. 72(2):293-8. doi:10.1253/circj.72.293
22. 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(6):588-94. doi:10.1001/archinternmed.2009.55
23. Semba RD, Patel KV, Ferrucci L, Sun K, Roy CN, Guralnik JM, et al. Serum antioxidants and inflammation predict red cell distribution width in older women: the Women's Health and Aging Study I. Clin Nutr, 2010. 29(5):600-4. doi:10.1016/j.clnu.2010.03.001
24. Forhecz Z, Gombos T, Borgulya G, Pozsonyi Z, Prohaszka Z, Janoskuti 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(4):659-66. doi:10.1016/j.ahj.2009.07.024

Table 1. Baseline characteristics	
Variable	**n(%)/mean or median/ ± standard deviation**
Age	55.1±12.3
Sex (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)
Creatinin (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)
DM: Diabetes mellitus, HDL-cholesterol: High density lipoprotein cholesterol, Hgb: Hemoglobin, LDL-cholesterol: Low density lipoprotein cholesterol, Plt: Platelet, RDW: Red cell distribution width, WBC: Wight blood cell.	

Table 2. Office and 24-h blood pressure mean and awake and asleep standard deviation values	
Variable	**Mean ± standard deviation (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
DBP: diastolic blood pressure, SBP: systolic blood pressure, SD: Standard deviation	

Table 3. Stepwise multivariable lineer 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
DBP: diastolic blood pressure, DM: Diabetes mellitus, SBP: Systolic blood pressure, SD: Standard deviation, RDW: Red cell distribution width								