

# The relationship of erectile dysfunction severity with nocturnal blood pressure pattern and RDW

Muzaffer Aslan<sup>1</sup>, Yunus Emre Yavuz<sup>1</sup>, Doğaç Okşen<sup>2</sup>, Erdem Bal<sup>1</sup>

<sup>1</sup>Department of Cardiology, Faculty of Medicine, Siirt Training and Research Hospital, Siirt, Türkiye

<sup>2</sup>Department of Cardiology, Faculty of Medicine, Altınbaş University, İstanbul, Türkiye

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## ABSTRACT

**Aims:** The study aimed to investigate the relationship between the severity of erectile dysfunction (ED), nocturnal blood pressure patterns, and red blood cell width distribution (RDW) in hypertensive patients.

**Methods:** The study involved 106 hypertensive patients, categorized into non-dippers and dippers based on their nocturnal blood pressure patterns. Key parameters including smoking status, RDW, and International Index of Erectile Function (IIEF) scores, were compared between the groups.

**Results:** The demographic data of the patients were similar. RDW was significantly higher in patients with non-dipper hypertension (HT) compared to the dipper group. Moderate and severe ED was seen more frequently in the non-dipper HT group (40.4% vs 20.4%; p=0.025). IIEF score was higher in the dipper HT group ( $17.6 \pm 6.9$  vs  $21.0 \pm 4.5$ ; p=0.004). According to logistic regression analysis, age and smoking habit were significant predictors for moderate or severe ED.

**Conclusion:** The study highlights the significant association between non-dipping blood pressure patterns, elevated RDW, and the severity of ED in hypertensive patients. The findings underscore the importance of monitoring nocturnal blood pressure patterns and RDW in understanding and managing ED in this population.

**Keywords:** Hypertension, erythrocyte indices, erectile dysfunction

## INTRODUCTION

Erectile dysfunction (ED) is a common condition that affects male health and quality of life.<sup>1,2</sup> It has multiple causes, one of which is hypertension (HT), a common comorbidity. HT can contribute to ED by affecting vascular health. Another cause of ED is atherosclerosis, which can impair penile arterial blood flow.<sup>3-5</sup> Red blood cell width distribution (RDW) is an emerging area of interest that may provide insights into the relationship between ED and systemic vascular health.<sup>6-7</sup> Early diagnosis of any underlying medical conditions contributing to ED is crucial for successful treatment. This article explores the intricate connections between ED, HT, and RDW and how these factors interrelate and influence men's health.

HT is a common health issue in the general population.<sup>8,9</sup> There are different ways to diagnose HT, with ambulatory blood pressure monitoring (ABPM) being one of them. ABPM not only diagnoses HT but also provides information about the patient's nocturnal dipping pattern.<sup>10</sup> Non-dippers are those patients whose blood pressure does not fall by more than 10% at night, and they are at a higher risk of morbidity and mortality compared to dippers.<sup>11</sup> Non-dippers are associated with several cardiovascular and non-cardiovascular diseases. It has been suggested that hypertensive patients with a non-dipper profile may have impaired endothelial function.<sup>12</sup> It has

been demonstrated in multiple studies that non-dippers have notably lower levels of endothelium-dependent vasodilation when compared to dippers, due to significantly lower levels of nitric oxide (NO) release.<sup>13</sup>

The International Index of Erectile Function (IIEF) is a score that measures the ability to achieve and maintain an erection. It consists of five questions and is commonly used in clinical trials due to its simplicity. The IIEF is an effective tool for diagnosing ED.<sup>14-15</sup>

RDW is a marker that indicates the destruction of red blood cells and ineffective erythropoiesis. It has prognostic value in various cardiovascular diseases, along with anemia.<sup>16-19</sup> While there are many studies on the relationship between RDW and non-dipping/dipping patterns, there is limited research available on the correlation between RDW values and erectile dysfunction.<sup>20</sup>

The study explores the relationships between ED, HT and RDW. We investigated the correlation between the nocturnal blood pressure dipping pattern in hypertensive patients and ED severity (measured by the International Index of Erectile Function, IIEF) and the potential links between ED, dipping pattern, and RDW values.

Corresponding Author: Yunus Emre Yavuz, yemre91@icloud.com



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## METHODS

The study was carried out with the permission of Siirt University Ethics Committee (Date: 28.02.2024, Decision No: 2024/2/02/06). All procedures were carried out in accordance with the ethical rules and the principles of the Declaration of Helsinki.

This study was designed as a cross sectional observational study. We included 150 patients who referred our cardiology polyclinic between November 2022 and July 2023. This study consisted of male population. Our inclusion criterias are patients who are diagnosed with hypertension and above 18 years old. Exclusion criterias are; i) patients with uncontrolled hypertension which is described as his blood pressure  $>180/100$  mmHg despite optimal antihypertensive treatment, ii) patients with uncontrolled type 1 and 2 diabetes mellitus, iii) patients who diagnosed with erectile dysfunction before admission to our clinic and have treatment for ED. The study was approved by the local ethics committee and written informed consent was obtained from all patients enrolled into the study. 44 patients were ruled out according to exclusion criterias. 106 patients were enrolled in this study.

The IIEF-5 score is a diagnostic tool used to assess erectile dysfunction. All patients filled IIEF score form for the evaluation of the ED presence and severity. IIEF score contains 5 question about ability and maintain penile erection. It is determined by the sum of ordinal responses to five items. The scoring range and corresponding levels of erectile dysfunction are as follows: a score between 22 to 25 indicates no erectile dysfunction; a score of 17 to 21 suggests mild erectile dysfunction; a score of 12 to 16 signifies mild to moderate erectile dysfunction; a score between 8 to 11 is indicative of moderate erectile dysfunction; and a score of 5 to 7 is associated with severe erectile dysfunction.

After the physical examination, if the patient's blood pressure  $>140/80$  mmHg and have not been diagnosed with hypertension before, we take control measurement after 15-minute resting state, and if BP is still above 140/80 mmHg, we perform 24-hour ABPM on the patient. ABPM was performed directly on patients with a previous diagnosis of hypertension. Twenty-four-hour ambulatory BP and heart rate monitoring were performed. Heart rate, systolic blood pressure and diastolic blood pressure were recorded every 15 minutes in the day-time and 30 minutes at night-time (22:00-07:00 accepted as night). Patients' clinic BP and ABPM measurements were recorded respectively.

Complete blood count and routine biochemistry, including lipid profile, are taken from all patients. Patients' White blood count, red blood cell count, hemoglobin, hematocrit, RDW, platelet count, and creatinine measurements were recorded. Echocardiography Epiq 7 ultrasound system (Philips Medical Systems; Andover, MA). Basic echocardiographic parameters, left ventricular ejection fraction and valvular pathologies were evaluated in all patients included in our study.

### Statistical Analysis

SPSS 20.0 was used for statistical analysis. Continuous variables were reported as mean $\pm$ SD for parametric data and median

(25-75%) for nonparametric data. Categorical variables were expressed as frequency and percentage (%). Data distribution was assessed using the Kolmogorov-Smirnov test. The study compared variables between groups using the Student's t-test. Normal distribution was observed for most variables, while the Mann-Whitney-U test was used for variables that didn't meet the normality assumption. Categorical variables were compared using chi-square test. Univariate and multivariate logistic regression models were used to identify independent predictors of ED. A significance level of P<0.05 was used for all statistical analyses.

## RESULTS

The information about the groups involved in the study is presented in Table 1. There was not any significant difference patients characteristics except smoking habits. Patients who had non-dipper HT smoked more frequently rather than dipper group (48.1% vs 27.8%; p=0.031). Patients, who had non-dipper HT, had a higher RDW percentage ( $15.3\pm2.6$  vs  $14.0\pm1.4$ ; p=0.001), lower IIEF score ( $17.6\pm6.9$  vs  $21.0\pm4.5$ ; p=0.004) and more frequent moderate to severe ED (40.4% vs 20.4%; p=0.025) compared to dipper group.

Table 1. Basic demographic characteristics of patients

Variables	Non-dipper HT (n=52)	Dipper HT (n=54)	p-value
Age (years)	$55.7\pm11.5$	$52.4\pm10.8$	0.139
BMI (kg/m <sup>2</sup> )	$29.4\pm3.6$	$29.7\pm4.0$	0.349
Smoker n(%)	25(48.1)	15(27.8)	0.031
Systolic blood pressure (mmHg)	$139\pm18$	$136\pm16$	0.485
Diastolic blood pressure (mmHg)	$82\pm10$	$84\pm10$	0.241
WBC (x10 <sup>3</sup> /ul)	$8.5\pm2.3$	$8.3\pm2.3$	0.545
HGB (g/dl)	14.5(13.1-15.8)	14.9(13.5-16.0)	0.222
PLT (10 <sup>3</sup> /ul)	$250\pm62$	$265\pm66$	0.208
Creatinine (mg/dl)	$1.05\pm0.24$	$1.02\pm0.17$	0.549
eGFR (ml/min)	83.7(69.2-95.6)	90.2(75.3-98.0)	0.263
Total cholesterol (mg/dl)	$178\pm44$	$191\pm40$	0.122
HDL (mg/dl)	$47.7\pm15.1$	$51.5\pm12.5$	0.164
LDL (mg/dl)	$111\pm28$	$117\pm33$	0.277
Triglyceride(mg/dl)	144(126-185)	136(98-184)	0.595
Neutrophil	$5.4\pm1.9$	$5.0\pm1.8$	0.271
Lymphocyte	$2.4\pm0.8$	$2.5\pm0.7$	0.463
RDW (%)	$15.3\pm2.6$	$14.0\pm1.4$	0.001
IIEF score	$17.6\pm6.9$	$21.0\pm4.5$	0.004
Moderate-severe ED n(%)	21(40.4)	11(20.4)	0.025

BMI: Body mass index, eGFR: Estimate glomerular filtration rate, HDL: High density lipoprotein, LDL: Low density lipoprotein, RDW: Red cell distribution width, IIEF: International Index of Erectile Function, ED: Erectile dysfunction

According to multivariate logistic regression analysis models, smoking (OR:3.27, p:0.021) and age (OR:1.09, p:0.001) were independent predictors of moderate to severe ED ([Table 2](#)).

**Table 2. Independent predictors of moderate-severe ED in patients in a univariate and multivariate logistic regression analysis model**

Variables	Univariate analysis			Multivariate analysis		
	OR	95% CI	p	OR	95% CI	p
Age	1.103	1.051-1.158	<0.001	1.094	1.038-1.154	0.001
Non-dipper HT	2.648	1.117-6.279	0.027	1.980	0.714-5.491	0.189
Smoking	3.039	1.288-7.168	0.011	3.266	1.194-8.934	0.021
RDW (%)	1.000	0.999-1.000	0.036	1.000	1.000-1.000	0.329

ED: Erectile dysfunction, OR: Odds ratio, CI: Confident interval, RDW: Red blood cell width distribution

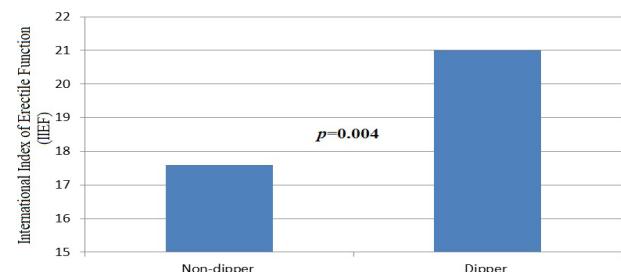
## DISCUSSION

The findings suggests a strong association between non-dipping blood pressure patterns in hypertensive patients and increased prevalence of ED. Smoking status and higher RDW values were found significantly associated with ED. The study underscores the importance of considering nocturnal blood pressure patterns and RDW values in the clinical evaluation of ED in hypertensive patients. These results highlight the multifactorial nature of ED, emphasizing the need for a comprehensive approach to its diagnosis and management, especially in hypertensive patients.

The relationship between hypertension, specifically non-dipper hypertension HT, high RDW and ED is complex and multifaceted. Non-dipper HT is characterized by a diminished nocturnal decrease in blood pressure, leading to sustained high blood pressure that can impair vascular health. This impairment is crucial in the context of ED, as erectile function relies heavily on vascular integrity and blood flow.<sup>21,22</sup> In previous studies, it has been shown that Non-dipper HT adversely affects sleep quality.<sup>23</sup> This is known to be a factor that increases the risk of ED. The sustained high blood pressure in non-dippers can damage the vascular endothelium, reducing nitric oxide availability, a key mediator in erectile function.<sup>24</sup> In a previous study, it was shown that the IIEF score was higher in dipper HT patients than in non-dipper hypertensive patients.<sup>25</sup> Similarly, the study by Yildirim et al.<sup>26</sup> found that the severity of ED in newly diagnosed hypertensive patients is associated with the nondipper pattern, establishing nondipper HT as an independent predictor of ED. The study by Yuvaç et al.<sup>27</sup> investigated the effects of Nebivolol on ED in patients with nondipper hypertension, showing a significant improvement in ED according to the International Index of Erectile Function (IIEF) scores before and after treatment in the nondipper group. Another study by Yuvaç et al.<sup>28</sup> examined the effects of nocturnal blood pressure patterns on ED functions and found that nondipper hypertensive patients are more prone to developing ED. These findings underscore the significant role of the nondipper pattern in the relationship between cardiovascular risk factors and ED.

The study by Ateş et al.<sup>29</sup> investigated the relationship between masked arterial hypertension and ED, demonstrating that the nondipper pattern increases the risk of ED. Finally, the study by Kumaran et al.<sup>30</sup> examined the relationship between

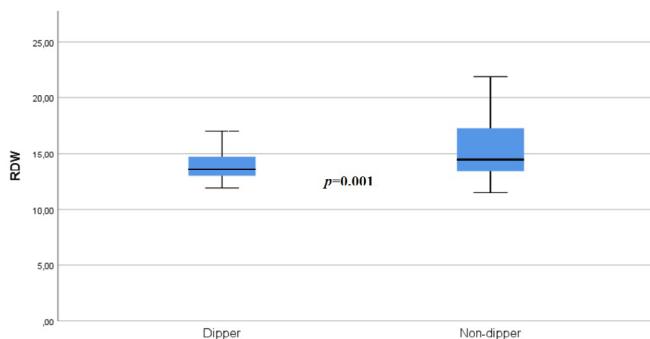
nocturnal systolic blood pressure patterns and ED in type 2 diabetic hypertensive men, showing that the nondipper status increases the risk of ED. In our study, it was consistent with previous studies ([Figure 1](#)). In addition, medium-high ED scores were significantly higher in non-dipper patients. However, in the multivariate logistic regression analysis, non-dipper HT may not have an independent effect on the risk of ED. Our study confirms these associations and provides new insights into the interplay between these factors in hypertensive patients. Our study extends these findings by demonstrating that patients with non-dipper HT not only have higher ED severity but also exhibit significantly higher RDW levels compared to dipper HT patients. This underscores the importance of RDW as a potential marker for vascular health and its role in ED pathophysiology.



**Figure 1. IIEF score distribution in Dipper and Non-Dipper HT patients**

On the other hand, high RDW rates are indicative of anisocytosis (variation in RBC sizes), which is often a marker of systemic inflammation and oxidative stress.<sup>31</sup> These conditions are known to contribute to endothelial dysfunction, a common pathway in both cardiovascular diseases and ED. RDW, an independent prognostic marker in heart failure patients, has gained significant interest in current clinical practice.<sup>32</sup> It is associated with atherosclerosis and the presence and severity of CAD.<sup>33</sup> Moreover, a positive correlation between RDW level and cardiovascular events in CAD patients has been reported.<sup>34</sup> Elevated RDW levels may reflect a broader state of vascular pathology that could exacerbate the effects of hypertension on erectile function. In one study, a strong significant relationship was found between ED and RDW, and it was shown that there may be a prognostic value in diagnosis. A previous study comparing normotensive patients and non-dipper HT patients showed that RDW was significantly higher in non-dipping HT patients than in normotensive patients.<sup>35</sup> Our study corroborates these findings by showing a strong association between higher RDW values and ED severity in non-dipper HT patients ([Figure 2](#)). This highlights the potential of RDW as a prognostic marker for ED and its utility in clinical practice. A unique contribution of our study is the simultaneous evaluation of both RDW and the International Index of Erectile Function (IIEF) scores in hypertensive patients. While previous studies have examined these factors independently, our research provides a comprehensive understanding of their combined effects on ED. This dual assessment offers deeper insights into the interaction between cardiovascular and erectile health, emphasizing the multifactorial nature of ED in hypertensive

patients. Also in our study, unlike the literature, multivariate logistic regression analysis shows that RDW does not have a significant effect on the risk of intermediate- and high-risk ED.



**Figure 2.** Relationship of Dipper and Non-Dipper HT groups to RDW

The statistical significance of the findings in this study, particularly regarding RDW and non-dipper HT, underscores their potential importance in the pathophysiology of ED. The strong association between higher RDW values and non-dipper blood pressure pattern in ED patients suggests that these parameters could serve as indicators of vascular health and erectile function. This insight is crucial for clinicians, as it highlights the need for comprehensive cardiovascular evaluation in ED patients, particularly those with hypertension. Additionally, these results pave the way for further research into targeted therapies that address these specific physiological mechanisms, potentially leading to more effective management of ED in hypertensive patients.

### Limitations

Although univariate and multivariate logistic regression analyses are used, the selection of variables used in the analyses and the inclusion criteria of the patients may have an impact on the results. In this study, the independent effects of specific factors such as non-dipper HT and RDW on moderately-severe ED were investigated. However, the loss of significance of non-dipper HT in multivariate analysis may lead to the oversight of the effect of other non-included variables. This may be due to insufficient sample size or high variance in the data set. Studies of larger and more heterogeneous populations could improve the accuracy and reliability of these findings.

### CONCLUSION

The study highlights the significant association between non-dipping blood pressure pattern, elevated RDW, and the severity of ED in hypertensive patients. However, this study's simultaneous evaluation of both IIEF and RDW provides a more comprehensive understanding of their combined effects on erectile dysfunction, increasing the depth of our insights into the interaction of cardiovascular and erectile health in hypertensive individuals.

### ETHICAL DECLARATIONS

#### Ethics Committee Approval

The study was carried out with the permission of Siirt University Ethics Committee (Date: 28.02.2024, Decision No: 2024/2/02/06).

### Informed Consent

All patients signed and free and informed consent form.

### Referee Evaluation Process

Externally peer-reviewed.

### Conflict of Interest Statement

The authors have no conflicts of interest to declare.

### Financial Disclosure

The authors declared that this study has received no financial support.

### Author Contributions

All of the authors declare that they have all participated in the design, execution, and analysis of the paper, and that they have approved the final version.

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