

The Relation Between Blood Pressure Reverse-Dipping and Neutrophil to Lymphocyte Ratio in Hypertensive Patients ***Hipertansif Hastalarda Reverse-dipper Kan Basıncı ile Nötrofil Lenfosit Oranı Arasındaki İlişki***

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Abstract: Reverse dipper hypertension and neutrophil to lymphocyte ratio (NLR) has been investigated as a predictor for cardiovascular risk. The relationship between NLR and other circadian blood pressure (BP) patterns has been showed. The aim of this study was to investigate the relation between NLR and BP reverse dipper pattern in patients with hypertension. 144 hypertensive patients (66 males, 78 females) were enrolled the study. BP patterns were evaluated with 24-h ambulatory BP monitoring (ABPM). Baseline NLR was measured by dividing neutrophil count to lymphocyte count. There was significantly increased NLR in reverse dippers (2,36±1,68) than dippers (1,81±0,69) of hypertension (p=0,040). NLR was negatively correlated with the decline rate of nocturnal systolic BP(r=-0,193;p=0.021) and diastolic BP(r=-0,160; p=0,057). Our study provides a possible association between NLR and reverse dipper pattern, but to report NLR as an independent predictor of reverse dipper pattern further studies are required.

Key Words: NLR, reverse - dipper, ABPM

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Özet: Revers dipper hipertansiyon ve nötrofil/lenfosit oranı (NLR), kardiyovasküler risk öngördürücüsü olarak araştırılmaktadır. NLR ve diğer sirkadyen kan basıncı paternleri arasındaki ilişki gösterilmiştir. Bu çalışmanın amacı hipertansif hastalarda nötrofil lenfosit oranı ile revers dipper kan basıncı paterni arasındaki ilişkiyi değerlendirmektir. Çalışmaya 144 (66 erkek, 78 kadın) hipertansif hasta alındı. Kan basıncı paternleri 24 saat ambulator kan basıncı ile değerlendirildi. Nötrofil lenfosit oranı, nötrofil sayısı lenfosit sayısına bölünerek ölçüldü. Revers dipper hipertansiyonlulara göre nötrofil lenfosit oranında anlamlı artış vardı. (sırasıyla 2.36±1,68 ve 1,81±0,69, p=0,040). Nötrofil lenfosit oranı ile sistolik (r=-0,193;p=0.021 ve diyastolik (r=-0,160; p=0,057) kan basıncı düşme oranları arasında negatif korelasyon vardı. Çalışmamız NLR ve revers dipper patern arasında olası bir ilişki sunmaktadır ancak nötrofil lenfosit oranını, revers dipper paternin bağımsız öngördürücüsü olarak rapor etmek için daha ileri çalışmalar gereklidir.

Anahtar Kelimeler: nötrofil lenfosit oranı, revers dipper, ambulator kan basıncı

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1. Introduction

There is usually circadian variation in blood pressure (BP). Systolic (SBP) and diastolic blood pressure (DBP) are expected to drop > 10% during the night as compared to daytime. Circadian BP patterns were divided into dipper (10% to 20%), extreme dipper (>20%) and nondipper (<10%) based on the nocturnal fall of BP (1-2). Reverse dipper BP pattern a variant of nondipper with higher average nighttime BP than daytime. These different BP patterns are associated with different rates of target organ damage and clinical outcome (2-4). Reverse dipper hypertension was found to be predictor of cardiovascular events (5).

The neutrophil to lymphocyte ratio (NLR), which is calculated from complete blood count is an inexpensive, commonly used, widely available inflammatory marker. NLR has been investigated as a predictor for cardiovascular risk (6). Inflammation is an important etiologic factor of essential hypertension (7). In previous studies, the relationship between NLR and other circadian BP patterns has been showed, but there is no data about the relation between NLR and reverse dipper hypertension. The aim of our study was to explore the association between NLR and reverse dipper pattern.

2. Materials and Method

Ambulatory blood pressure monitoring of 144 patients who admitted to cardiology and nephrology polyclinics of Keçiören Education and Research Hospital because of hypertension suspicion between June 2015 to June 2016 were evaluated retrospectively. Hypertension was diagnosed as daytime SBP>135mmHg and DBP>85 mmHg in ambulatory blood pressure monitoring (ABPM). All patients were divided into three groups according to circadian BP pattern as follows: dippers (average SBP decreased 10-20% of daytime level during sleep), non-dippers (<10% nocturnal SBP fall) and reverse dippers (SBP nocturnal rise). ABPM monitoring was performed with Suntech AccuWin ProV3 (Suntech medical, Inc. Morrisville, NC, USA). Automatic BP

recordings were obtained regularly every 30 minutes during the 24-hour period. The percent change in nocturnal BP decline was calculated as automatically.

Patient's blood samples were collected at the same day of ABPM records. NLR was calculated as the ratio of neutrophil count to lymphocyte count from complete blood count.

The exclusion criteria included age<18, patients with secondary hypertension, under antihypertensive treatment, night workers, patients with systemic disease and using of medical treatment that can affect the white blood cell counts (history of glucocorticoid therapy, history of malignancy or chemotherapy), inflammatory disease, heart failure, acute coronary syndromes, chronic renal or hepatic disease, diabetes mellitus and cerebrovascular disease.

Patients were evaluated in the study under an institutionally approved protocol.

Statistical analysis

All statistical analyses were performed using the SPSS 15 (SPSS INC, Chicago, Illinois, USA). Analysis of variance (ANOVA) test was used for statistical comparison of data. Descriptive statistics are presented as mean ± Standard deviation, Binary logistic regression was used for to evaluate association of NLR with ABPM results. Bivariate correlation analysis was used to examine the association between NLR and systolic and diastolic blood pressure decline rate. A calculated difference of $p<0.05$ was considered to be statistically significant.

3. Results

The clinical characteristics of patients in different groups according to circadian variations of BP were shown in table 1. In our study, a total of 49 patients (34%) had the reverse-dipper BP pattern. The nondipper pattern was observed in 48 patients with hypertension (33,3%) and the dipper pattern in 47 patients (32,6%). Patients of the reverse-dipper group are older than dipper and non-

dipper group's. There was significantly increased NLR in reverse dipper ($2,36 \pm 1,68$) than in dipper ($1,81 \pm 0,69$) ($p= 0,040$). There was no significant difference of NLR between the non-dipper and reverse dipper groups.

Table 1.
Characteristics of the study population according to circadian blood pressure patterns.

| Variable | Dipper | Non-dipper | Reverse dipper | P value |
|----------------------------------|--------------|--------------|----------------|---------|
| Patients, n | 47 | 48 | 49 | |
| Age, years | 48,74±13,83 | 46,64±17,45 | 61,68±14,90 | <0,001 |
| Male/female, n | 21/26 | 24/25 | 21/27 | 0,626 |
| 24 h SBP, ABPM, mmHg | 122,16±11,94 | 117,78±11,68 | 125,83±19,56 | 0,032 |
| SBP awakening, mmHg | 127,22±12,36 | 119,84±11,95 | 123,00±26,53 | 0,149 |
| SBP bedtime, mmHg | 107,34±18,30 | 112,92±11,76 | 131,42±21,18 | <0,001 |
| Decline rate of nocturnal SBP, % | 13,94±3,36 | 5,75±3,64 | -4,69±6,17 | <0,001 |
| 24 h DBP, ABPM, mmHg | 72,65±9,57 | 69,08±11,03 | 70,28±11,82 | 0,268 |
| DBP awakening, mmHg | 76,10±10,13 | 70,26±11,59 | 69,30±11,66 | 0,007 |
| DBP bedtime, mmHg | 63,73±9,30 | 65,59±11,11 | 72,79±12,86 | <0,001 |
| Decline rate of nocturnal DBP, % | 16,00±7,64 | 6,38±8,13 | -4,10±7,86 | <0,001 |
| NLR | 1,81±0,69 | 1,91±0,69 | 2,36±1,68 | 0,047 |

ABPM, ambulatory blood pressure monitoring; SBP, systolic blood pressure; DBP, diastolic blood pressure; NLR: neutrophil to lymphocyte ratio

Bivariate correlation analysis was performed to investigate the relationship between NLR and different circadian BP patterns. We found that NLR was negatively correlated with the decline rate of nocturnal SBP ($r=-0,193$; $p=0,021$) and DBP ($r=-0,160$; $p=0,057$) (figure 1).

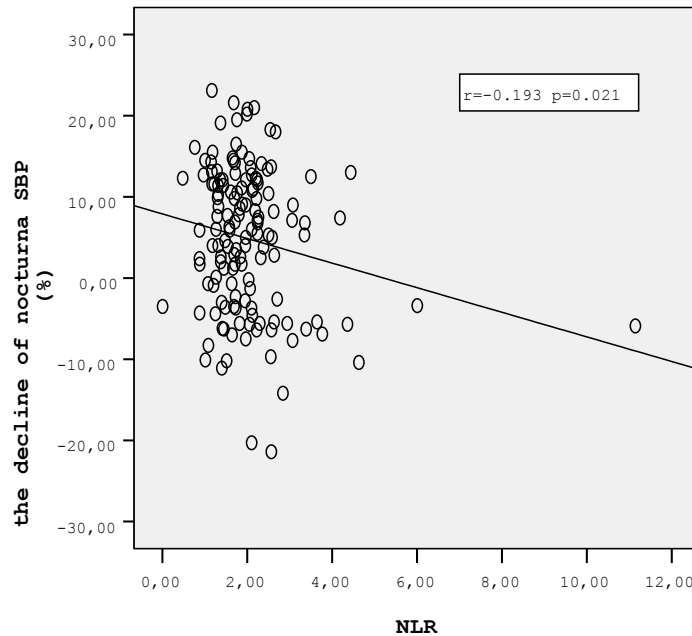


Figure 1. Correlation of NLR with the decline rate of nocturnal systolic blood pressure (SBP)

In the two year follow up period, a total of 8 (5.5%) deaths and 3 (2.2%) cerebrovascular events(CVE) occurred in the study population. The number of deaths according to groups were respectively 1 (2,1%) in dipper group, 4 (8,3%) in non-dipper group and 3 (6.1%) in reverse dipper group. While there was no CVE in dipper group, there were 2 (4.1%) CVEs in non-dipper group and 1 (2%) CVE in reverse dipper group. However in the binary logistic regression analysis there was no statistically significant effect of reverse dipper pattern on death (OR 1.286, 95%CI 0.251 to 0,754, $p=0.739$) and CVE (OR 1.044, 95%CI 0,043 to 1,238, $p=0,972$).

4. Discussion

In our study we aimed to investigate the relation between NLR and blood pressure abnormal dipping in patients with essential hypertension. We found abnormal dipping was associated with NLR.

Ambulatory blood pressure monitoring is a noninvasive examination used for evaluating 24-h blood pressure. ABPM can provide detailed information about variability and circadian dipping status (1, 8). The common circadian variation is the physiological decline in nocturnal BP. Reverse dipper pattern is opposite to circadian rhythm which is defined as an increase in BP at night. The loss of physiological decline in nocturnal blood pressure is related to target organ damage and high risk for cardiovascular mortality (9). Especially the night-time BP have a significant predictive role for clinical events in hypertensive patients (10). Maintenance of a high BP at night overloads cardiovascular system. For this reason new clinical trials have drawn attention to reverse dipper hypertension where nighttime blood pressure increases are seen. Our study is one of them. We evaluated the relationship between reverse dipper pattern and NLR as an inflammatory marker.

Studies showing the relationship between reverse dipper hypertension and cerebral and renal damage have been reported. Kario et.al found that reverse dippers had twice risk for

stroke compared with dippers and non-dippers (11). Besides reverse dipping has also been shown to be associated with early carotid plaque formation in hypertensives (12). Chang Wang et al. showed prognostic value of reverse dipper pattern in chronic kidney disease patients in their studies (13). However there was limited data involving cardiovascular effects of reverse dipper pattern. Dan Su et al. showed the relation between red blood cell distribution width and reverse dipper pattern (14). RDW is an inflammatory marker derived from hemogram parameters like MPV, NLR and PLR. Since inflammation plays an important role in the pathogenesis of atherosclerotic cardiovascular diseases, it is important to evaluate the inflammatory state. NLR has been investigated as a new predictor for cardiovascular risk (6). Therefore, it is important to assess NLR in the hypertensive population where increased cardiovascular risk is seen . the correlation between NLR and hypertension especially the non-dipper pattern has been demonstrated in many studies previously. Our study is the first study to report the association between NLR and reverse dipper pattern in hypertensive patients.

We found that NLR levels were significantly higher in the reverse dipper group than in the dipper group. However, in logistic regression analysis we could not report NLR was an independent predictor of reverse dipper. We thought small sample size of our study groups effect the results and it was the major limitation of our study.

The other limitations of our study include lack of evaluation of the relationship between other inflammation markers, lack of extreme-dipper group. All patients underwent only one ABPM and NLR was calculated from only one blood sample.

In conclusion, our study provides a possible association between NLR and reverse dipper pattern, but to report NLR as an independent predictor of reverse dipper pattern further studies are required.

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