Relationship Between Dipper/Non-Dipper Pattern and Neutrophil-Lymphocyte Ratio and Platelet-Lymphocyte Ratio in Geriatric Patients with Hypertension

Hipertansiyonu Olan Geriatrik Hastalarda Dipper/Non-Dipper Paterni ile Nötrofil-Lenfosit Oranı ve Trombosit-Lenfosit Oranı arasındaki İlişki

[1]Perihan VARIM, [2]Ahmet Can ÇAKMAK

[1]Department of Cardiology, Sakarya University Medicine Faculty, Sakarya, Türkiye

Perihan Varım: https://orcid.org/0000-0002-8827-1280
Ahmet Can Çakmak: https://orcid.org/0000-0001-5168-8907

ABSTRACT

Objective: Neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) are inflammatory markers associated with poor prognoses. Non-dipper hypertension (HT) is linked to a higher risk for cardiovascular events. This study aims to investigate the association between NLR and PLR in geriatric patients with dipper and non-dipper HT.

Materials and Methods: A total of 124 geriatric patients with HT were included in the study. Based on ambulatory blood pressure monitoring, patients were categorized into two groups: non-dippers (n=62, Group 1) and dippers (n=62, Group 2). NLR and PLR were calculated by dividing the absolute neutrophil and platelet counts, respectively, by the absolute lymphocyte count.

Results: There were no significant differences in sex, age, chronic conditions and smoking between the two groups (p>0.005). The NLR was 1.96±0.66 in group 1 and 1.67±0.68 in group 2 (p:0.005). The PLR was 146±42.2 in group 1 and 115±34.2 in group 2 (p:0.001). The NLR and PLR were significantly higher in non-dippers compared to dippers (p<0.005).

Conclusions: Our findings demonstrate that geriatric patients with non-dipper HT have significantly higher NLR and PLR compared to those with dipper HT. This suggests that non-dipper HT is associated with greater inflammation, which may contribute to its higher cardiovascular risk.

Keywords: Dipper, geriatric patients, NLR, non dipper, PLR

ÖZ

Amaç: Nötrofil lenfosit (NLR) ve trombosit lenfosit oranı (PLR), kötü prognozu gösteren bir inflamatuar belirteçtir. Non-dipper hipertansiyon, kardiyovasküler olaylar için daha yüksek risk ile ilişkilidir. Bu çalışmanın amacı, dipper ve non-dipper hipertansiyonu olan hastalarda NLR ve PLR arasındaki ilişkiyi araştırmaktır.

Materyal ve Metot: Çalışmaya hipertansiyonu olan 124 geriatrik hasta dahil edildi. Hastalar ambulatuvar kan basıncı ölçümüne göre non-dipper (n:62, grup 1) ve dipper (n:62, grup 2) olmak üzere iki gruba ayrıldı. Nötrofil lenfosit (NLR) ve trombosit lenfosit oranı (PLR), mutlak nötrofil sayısı ve trombosit sayısının mutlak lenfosit sayısına bölünmesiyle hesaplandı.

Bulgular: İki grup arasında cinsiyet, yaş, kronik hastalıklar e sigara içiciliği açısından anlamlı fark yoktu (p>0,005). Kronik hastalıklar ve sigara kullanımı açısından da anlamlı fark yoktu. NLR grup 1'de 1,96±0,66 iken grup 2'de 1,67±0,68 idi (p:0,005). PLR grup 1'de 146±42,2 iken grup 2'de 115±34,2 idi (p:0,001).

Sonuç: Bulgularımız non-dipper HT'li geriatrik hastaların, dipper HT'li hastalara göre anlamlı derecede daha yüksek NLR ve PLR'ye sahip olduğunu göstermektedir. Bu, non-dipper HT'nin daha yüksek inflamasyonla ilişkili olduğunu ve bunun da daha yüksek kardiyovasküler riske katkıda bulunabileceğini göstermektedir.

Anahtar Kelimeler: Dipper, geriatrik hastalar, NLR, non dipper, PLR

INTRODUCTION

Hypertension (HT) is one of the most common chronic diseases globally and a significant risk factor for cardiovascular diseases, peripheral vascular diseases, stroke, and renal failure. In patients with HT, blood pressure fluctuates throughout the day, typically decreasing by 10% to 20% at night. This physiological reduction is referred to as the dipper pattern or dipper HT. Conversely, patients who do not experience this nocturnal decrease in blood pressure are classified as having a non-dipper pattern or non-dipper HT.[1]

Non-dipper HT is associated with a worse prognosis compared to dipper HT and poses a higher risk for adverse outcomes, including cardiovascular diseases, peripheral vascular diseases, stroke, and renal failure.[1]

Recently, the neutrophil-to-lymphocyte ratio (NLR) and platelet-to-lymphocyte ratio (PLR) have emerged as reliable and easily measurable markers of inflammation. Inflammatory markers such as interleukin (IL) 6, IL-1b and tumor necrosis factor a (TNF-a) have been found to be associated with HT. Increased inflammation increases the number of neutrophils and decreases the number of lymphocytes.[2] Increased platelet activation has an important role in the initiation and progression of atherosclerosis. Inflammatory mediators, such as IL 1 and 6, stimulate megakaryocytic proliferation and cause thrombocytosis.[3] NLR and PLR are cost-effective and straightforward to determine, making them advantageous over other inflammation markers.[4] A growing body of evidence highlights the association of NLR and PLR with cardiovascular diseases, peripheral vascular diseases, heart failure, cancer, and rheumatologic conditions.[5-8]

This study aims to investigate the relationship between NLR and PLR in geriatric patients with dipper and non-dipper hypertension, providing insights into the inflammatory processes associated with these distinct patterns of blood pressure regulation.

MATERIALS AND METHODS

Ethics Committee Approval: The study was approved by the Sakarya University Faculty of Medicine Ethical Committee and conducted in compliance with the Helsinki Declaration (Date:07.05.2024. Decision No:16214662-050.01.04 -28543-101).

This retrospective study included 124 geriatric patients with HT who were under follow-up at the cardiology outpatient clinic between June 2023 and June 2024. HT was defined as systolic blood pressure (BP) ≥140 mmHg and/or diastolic BP ≥90 mmHg, previously diagnosed hypertension, or the use of antihypertensive medications.

Patients were categorized into two groups: non-dipper (n=62, Group 1) and dipper (n=62, Group 2) based on ambulatory BP monitoring. All participants underwent 24-hour ambulatory BP monitoring to determine their dipper or non-dipper status. Measurements were taken every 30 minutes during the 24 hours using a cuff placed around the non-dominant arm. Sleep and wake periods were recorded based on patient self-reports, and measurements were repeated if necessary to ensure accuracy.

Nocturnal BP dipping was calculated using the formula: *Nocturnal BP Dipping (%)=100×[1 -(Sleep Systolic BP/Awake Systolic BP)]*

Dipper hypertension was defined as a nocturnal BP decrease of >10% in systolic and diastolic BP, while non-dipper hypertension was defined as a decrease of <10% in either measurement.

Demographic and clinical data, including hemoglobin, hematocrit, neutrophil, lymphocyte, platelet counts, white blood cell (WBC) counts, and C-reactive protein (CRP) levels, were obtained from hospital records. The neutrophil-to-lymphocyte ratio (NLR) was calculated by dividing the absolute neutrophil count by the absolute lymphocyte count, while platelet-to-lymphocyte ratio (PLR) was calculated by dividing the absolute platelet count by the absolute lymphocyte count.

Exclusion Criteria: Patients were excluded if they had systemic inflammatory or autoimmune diseases (e.g., systemic lupus erythematosus, rheumatoid arthritis), hematologic disorders, cancer, acute infections, or were on antibiotic or steroid therapy. Other exclusions included acute coronary syndrome, chronic renal or liver disease, Cushing's syndrome, and thyroid dysfunction.

Statistical Analysis: Data were analyzed using SPSS for Windows 21.0 (SPSS Inc., Chicago, IL, USA). The Kolmogorov-Smirnov test was used to assess data distribution. Continuous variables were compared using the t-test, while categorical variables were analyzed using the Chi-square test. Statistical significance was set at $p<0.05$.

RESULTS

A total of 124 people were analyzed, with 62 patients in each group: Demographic characteristics and medical histories were comparable between the groups. The mean age of the non-dipper group was 68.5 ± 2.8 years, while that of the dipper group was 67.0 ± 2.3 years (p = 0.34). There were no significant differences in sex, chronic conditions such as diabetes mellitus and hyperlipidemia, or smoking status (p>0.005). There were also no significant differences in weight and height between the groups (Table 1).

Table 1. Demographic characteristics and clinical data of the study population.

Parameters	Non-dipper group (n:62)	Dipper group (n:62)	p-value
Age (years)	68.5±2.8	67.0±2.3	0.34
Sex (male/female)	30/32	32/30	0.938
Height (cm)	162.6±10.3	161.1±7.6	0.532
Weight (kg)	67.8±13.7	64.8±12.8	0.254
Diabetes mellitus (n)	16	18	0.418
Hyperlipidemia (n)	22	27	0.256
Smoking (n)	18	13	0.366

Data are expressed as mean ± SD or as number of patients.

Ambulatory BP monitoring revealed higher mean nocturnal systolic and diastolic BP values in the non dipper group compared to the dipper group. Mean BP measurements during wake periods were similar in both groups. Mean BP measurements during sleep periods were higher in the non-dipper group (Table 2).

Hemogram parameters and CRP levels are summarized in Table 3. Significant findings include:

- Neutrophil count: Higher in the non-dipper group (4.0 ± 1.2 K/µL vs. 3.4 ± 1.3 K/µL, p = 0.003).
- Platelet count: Higher in the non-dipper group (282 ± 78 × 10³ K/µL vs. 244 ± 54 × 10³ K/µL, p = 0.01).
- NLR: Higher in the non-dipper group (1.96 ± 0.66 vs. 1.67 ± 0.68, p = 0.005).
- PLR: Higher in the non-dipper group (146 ± 42.2 vs. 115 ± 34.2, p = 0.001).

There were no significant differences in hemoglobin, WBC, lymphocyte counts, or CRP levels between the groups. The hemogram parameters and CRP values of the patients with non-dipper HT and the patients with dipper HT are shown in Table 3. Hemoglobin was 13.1±1.4 g/dL in the patients with non -dipper HT group and 13.4±2.1 g/dL in the patients with dipper HT, respectively, at p= 0.28. Total white blood cell count (WBC) values were 6.8±1.6 K/µL in the patients with non-dipper HT group and 6.3±2.0 K/µL in the patients with dipper HT, respectively, at p= 0.69. Neutrophil counts were 4.0±1.2 K/µL in the patients with non-dipper HT group and 3.4±1.3 K/µL in the patients with dipper HT, respectively, at p= 0.003. Lymphocyte counts were 2.1±0.6 K/µL in the patients with non-dipper HT group and 2.2±0.8 K/µL in the patients with dipper HT, respectively, at p= 0.85. Platelet counts were 282±78 x10³ K/µL in the patients with non-dipper HT group and 244±54 x10³ K/µL in the patients with dipper HT, respectively, at p=0.01. NLR values were 1.96±0.66 in the patients with non-dipper HT group and 1.67±0.68 in the patients with dipper HT, respectively, at p=0.005. PLR values were 146±42.2 in the patients with non-dipper HT group and 115±34.2 in the patients with dipper HT, respectively, at p=0.001. CRP values were 10.1 ± 7.4 mg/L in the patients with non-dipper HT group and 9.6 ± 7.3 mg/L in the patients with dipper HT, respectively, at p=0.421 (Table 3).

Table 2. Ambulatory Blood Pressure Monitoring of the study population.

Parameters	Non-dipper group (n:62)	Dipper group (n:62)	p-value
Systolic blood pressure (total) – mmHg	126.5±13.6	124.4±11.1	0.376
Systolic blood pressure (awake) – mmHg	127.2±13.6	130.8±11.5	0.54
Systolic blood pressure (sleep) – mmHg	123.6±14.3	110.5±9.8	**0.001**
Diastolic blood pressure (total) – mmHg	78.8±10.5	78.3±9.2	0.788
Diastolic blood pressure (awake) – mmHg	80.2±10.7	81.6±9.9	0.434
Diastolic blood pressure (sleep) – mmHg	74.4±10.6	67.5±8.5	**0.001**
Mean blood pressure (total) – mmHg	101.2±12.7	99.6±9.6	0.512
Mean blood pressure (awake) – mmHg	102.1±11.6	103.3±10.3	0.496
Mean blood pressure (sleep) – mmHg	97.2 ± 11.1	87.3±9.1	**0.001**

Data are expressed as mean ± SD.

Table 3. Hematological parameters of the study population.

Parameters	Non-dipper group (n:62)	Dipper group (n:62)	Normal Range	p-value
Hemoglobin (g/dl)	13.1±1.4	13.4±2.1	12.2-18.1	0.28
WBC (K/ul)	6.8±1.6	6.3±2.0	4.6-10.2	0.69
Neutrophil (K/ul)	4.0±1.2	3.4±1.3	2.0-6,9	0.003
Lymphocyte (K/ul)	2.1±0.6	2.2±0.8	0.6-3,4	0.85
Platelet x10^3 (K/ul)	282±78	244±54	142-424	**0.01**
NLR	1.96±0.66	1.67±0.68		**0.005**
PLR	146±42.2	115±34.2		**0.001**
CRP (mg/L)	10.1±7.4	9.6±7.3		0.421

Data are expressed as mean ± SD. WBC: White Blood Cell. NLR: Neutrophil lymphocyte ratio. PLR: Platelet lymphocyte ratio. CRP: C-reactive protein

DISCUSSION AND CONCLUSION

This study, to our knowledge, is the first to explore the relationship between NLR and PLR in geriatric patients with dipper versus non-dipper hypertension. Our findings demonstrate significantly higher NLR and PLR values in non-dipper hypertensive patients compared to dipper patients.

Non-dipper hypertension has been linked to autonomic dysfunction and is more commonly associated with conditions such as diabetes, chronic kidney disease, sleep apnea, and hypercortisolism.[9] It carries a higher risk for cerebrovascular events, cardiovascular diseases, sudden death, and end-organ damage due to heightened inflammation and endothelial dysfunction,[10-11] as also suggested by presented work.

Neutrophils are primarily elements of the innate immune system, whereas lymphocytes are elements of an adaptive immune system. Higher neutrophil levels are associated with increased inflammatory response and also cardiovascular diseases.[12-13] Low lymphocyte levels are associated with poor general health and high physiological stress.

Recent studies have shown that lymphocyte counts decrease in acute coronary syndrome and congestive heart failure.[14] Platelets have an important role in the initiation of atherosclerotic lesions. Mediators released from platelets such as thromboxane A2, adenosine diphosphate, serotonin, platelet-activating factor, and platelet-derived growth factor increase platelet activation and aggregation. High platelet levels are associated with cardiovascular events such as acute myocard infarctus and stent thrombosis.[15-16] We found high neutrophil and platelet counts and also low lymphocyte counts in the patients with non-dipper HT.

NLR is an inexpensive and useful marker for inflammation and stress response. High NLR values were found in several acute and chronic diseases such as COVID-19, thyroiditis, fibromyalgia, malignancies and cardiovascular events.[17-20] Cardiovascular events are shown in patients with non-dipper HT than in patients with dipper HT. The high NLR levels we found in our study are consistent with the literature.

PLR is a cost-effective and easy marker for inflammation and thrombosis. High PLR values were found in several cardiovascular diseases, such as MI, heart failure, HT, and peripheral arterial disease.[21-24] Cardiovascular events are shown in patients with non-dipper HT than in patients with dipper HT. The high PLR levels we found in our study are consistent with the literature.

Increased neutrophil counts in non-dipper patients may reflect heightened leukocyte activation and cytokine production, contributing to inflammation and vascular damage. High platelet counts in non-dipper patients suggest enhanced platelet activation, a key factor in atherothrombosis and cardiovascular events.

NLR and PLR are simple, cost-effective markers for assessing inflammation and have been linked to various cardiovascular and inflammatory diseases. The elevated NLR and PLR values observed in non-dipper patients align with the literature, supporting their potential utility as indicators of heightened cardiovascular risk.

In conclusion, Non-dipper HT is associated with increased cardiovascular events, likely mediated by inflammation. This study highlights significantly higher NLR and PLR values in non-dipper hypertensive patients, underscoring the role of inflammation in this condition. Our study had some limitations. One of them was the small sample size. We were also not able to evaluate the prognostic value of the NLR and PLR in patients with hypertension. Our study had a cross-sectional design, and it would be better if we had followed the patients and explore the relation between adverse cardiac events and NLR and/or PLR in these patients While our findings are derived from a retrospective study, larger prospective and multicenter studies are needed to elucidate further the relationship between NLR, PLR, and non-dipper hypertension.

Ethics Committee Approval: The study was approved by the Sakarya University Faculty of Medicine

Ethical Committee and conducted in compliance with the Helsinki Declaration (Date:07.05.2024. Decision No:16214662-050.01.04-28543-101).

Conflict of Interest: No conflict of interest was declared by the authors.

Author Contributions: Concept – PV; Supervision – AÇ; Materials – PV; Data Collection and/or Processing – PV; Analysis and/or Interpretation – AÇ; Writing –PV.

Peer-review: Externally peer-reviewed.

REFERENCES

1. Nurkoç SG, Yakışan T. Mean platelet volume/ platelet count ratio and dipper/non-dipper hypertensive patients. Angiology. 2024;22:33197241274825. doi:10.1177/00033197241274825

2. Tosu AR, Demir S, Selcuk M, et al. Comparison of inflammatory markers in non-dipper hypertension vs. dipper hypertension and in normotensive individuals: uric acid, C reactive protein and red blood cell distribution width readings pwki. 2014; 2:98-103.

3. Sarma J, Laan CA, Alam S, et al. Increased platelet binding to circulating monocytes in acute coronary syndromes. Circulation 2002;105:2166e71.

4. Islam MM, Satici MO, Eroglu SE. Unraveling the clinical significance and prognostic value of the neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, systemic immune-inflammation index, systemic inflammation response index, and delta neutrophil index: An extensive literature review. Turk J Emerg Med. 2024;8;24:8-19. doi:10.4103/tjem.tjem_198_23

5. Wu CC, Wu CH, Lee CH, et al. Association between neutrophil percentage-to-albumin ratio (NPAR), neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR) and long-term mortality in community-dwelling adults with heart failure: evidence from US NHANES 2005-2016. BMC Cardiovasc Disord. 2016;21:312. doi:10.1186/s12872-023-03316-6

6. Selvaggio S, Abate A, Brugaletta G, et al. Platelet-to-lymphocyte ratio, neutrophil-to-lymphocyte ratio and monocyte-to-HDL cholesterol ratio as markers of peripheral artery disease in elderly patients. Int J Mol Med. 2020;46:1210-1216. doi:10.3892/ijmm.2020.4644

7. Salciccia S, Frisenda M, Bevilacqua G, et al. Prognostic role of platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio in patients with non-metastatic and metastatic prostate cancer: A meta-analysis and systematic review. Asian J Urol. 2024;11:191-207. doi: 10.1016/ j.ajur.2023.01.002

8. Varim C, Celik F, Sunu C, et al. Inflammatory cell ratios in the patients with fibromyalgia. Georgian Med News. 2021;315:108-113.

9. Wang H, Hu Y, Geng Y, et al. The relationship between neutrophil to lymphocyte ratio and artery stiffness in subtypes of hypertension. J Clin Hypertens (Greenwich). 2017;19:780-785. doi:10.1111/jch.13002

10. Jhuang YH, Kao TW, Peng TC, et al. Neutrophil to lymphocyte ratio as predictor for incident hypertension: a 9-year cohort study in Taiwan. Hypertens Res. 2019;42:1209-1214. doi:10.1038/ s41440-019-0245-3

11. Tatsukawa Y, Hsu WL, Yamada M,et al. White blood cell count, especially neutrophil count, as a predictor of hypertension in a Japanese population. Hypertens Res. 2008;31:1391-1397. doi:10.1291/hypres.31.1391

12. De Servi S, Landi A, Gualini E,et al. Neutrophil count as a risk factor for cardiovascular diseases: how can we manage it? J Cardiovasc Med (Hagerstown). 2024;25:759-765. doi:10.2459/ JCM.0000000000001668

13. De Servi S, Landi A, Gualini E, et al. Neutrophil count as a risk factor for cardiovascular diseases: how can we manage it? J Cardiovasc Med (Hagerstown). 2024;25:759-765. doi:10.2459/ JCM.0000000000001668

14. Núñez J, Miñana G, Bodí V, et al. Low lymphocyte count and cardiovascular diseases. Curr Med Chem. 2011;18:3226-3233. doi:10.2174/092986711796391633

15. Ferroni P, Vazzana N, Riondino S, et al. Platelet function in health and disease: from molecular mechanisms, redox considerations to novel therapeutic opportunities. Antioxid Redox Signal. 2012;17:1447-1485. doi:10.1089/ars.2011.4324

16. Amraotkar AR, Song DD, Otero D, et al. Platelet count and mean platelet volume at the time of and after acute myocardial ınfarction. Clin Appl Thromb Hemost. 2017;23:1052-1059. doi:10.1177/1076029616683804

17. Nalbant A, Kaya T, Varim C, et al. Can the neutrophil/lymphocyte ratio (NLR) have a role in the diagnosis of coronavirus 2019 disease (COVID-19)? Rev Assoc Med Bras (1992). 2020;66:746-751. doi:10.1590/1806-9282.66.6.746

18. Cengiz H, Varim C, Demirci T, et al. Hemogram parameters in the patients with subacute thyroiditis. Pak J Med Sci. 2020;36:240-245. doi:10.12669/pjms.36.2.1063

19. Cupp MA, Cariolou M, Tzoulaki I, et al. Neutrophil to lymphocyte ratio and cancer prognosis: an umbrella review of systematic reviews and meta-analyses of observational studies. BMC Med. 2020;18:360. doi:10.1186/s12916-020-01817-1. PMID: 33213430; PMCID: PMC7678319

20. Zhang X, Wei R, Wang X, et al. The neutrophil-to-lymphocyte ratio is associated with all-cause and cardiovascular mortality among individuals with hypertension. Cardiovasc Diabetol. 2024;23:117. doi:10.1186/s12933-024-02191-5

21. Pruc M, Peacock FW, Rafique Z,et al. The Prognostic Role of Platelet-to-Lymphocyte Ratio in Acute Coronary Syndromes: A Systematic Review and Meta-Analysis. J Clin Med. 2023;12:6903. doi:10.3390/jcm12216903

22. Vakhshoori M, Bondariyan N, Sabouhi S,et al. The impact of platelet-to-lymphocyte ratio on clinical outcomes in heart failure: a systematic review and meta-analysis. Ther Adv Cardiovasc Dis. 2024;18:17539447241227287. doi:10.1177/17539447241227287

23. Meng X, Sun H, Tu X, et al. The Predictive Role of Hematological Parameters in Hypertension. Angiology. 2024;75:705-716. doi: 10.1177/00033197231190423

24. Uzun F, Erturk M, Cakmak HA, et al. Usefulness of the platelet-to-lymphocyte ratio in predicting long-term cardiovascular mortality in patients with peripheral arterial occlusive disease. Postepy Kardiol Interwencyjnej. 2017;13:32-38. doi:10.5114/aic.2017.66184