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Can neutrophil to lymphocyte ratio and platelet to lymphocyte ratio be used as biomarkers for non-dipper blood pressure?

Nötrofil/lenfosit oranı ve platelet/lenfosit oranı non-dipper kan basıncı için biyobelirteç olarak kullanılabilir mi?

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Abstract

Aim: Hypertension is a major risk factor for cardiovascular diseases and non-dipper status is associated with increased risk for cardiovascular events. Neutrophil lymphocyte ratio (NLR) and platelet lymphocyte ratio (PLR) are related to inflammation and cardiovascular risk. The purpose of the study is to investigate the relationship between NLR and PLR with non-dipper status of hypertensive and normotensive patients.

Methods: A total of 482 patients were enrolled for the study. The study was planned as retrospective cohort study. Four groups were formed according to 24-h ambulatory blood pressure monitoring results. Group 1 was defined as hypertensive, non-dipper patients; group 2 as hypertensive, dipper patients; group 3 as normotensive, non-dipper patients and group 4 as normotensive, dipper patients.

Results: Mean age of the study population was 50.1±15.5 years, 38.1% were male. According to the statistical analysis of Group 1 (n=165), Group 2 (n=88), Group 3 (n=123) and Group 4 (n=91) NLR was statistically different among groups ($p<0.001$). Group 1 had significantly higher values compared to Group 2 ($p=0.001$), Group 3 ($p=0.002$) and Group 4 ($p=0.023$). In hypertensive patient group, PLR values of Group 1 was significantly higher than Group 2 ($p=0.002$). Pearson correlation analysis showed that NLR and PLR were correlated with BP variability ($r=-0.188$, $p<0.001$ for NLR and $r=-0.182$ and $p<0.001$ for PLR). Regression analysis showed NLR ($p=0.040$), PLR ($p=0.021$), age ($p=0.006$) and hypertension ($p<0.001$) were independent predictors of BP variability.

Conclusion: Our findings suggest that NLR and PLR can be used as inexpensive and easily accessible markers to detect non-dipper status in hypertensive patients.

Keywords: Neutrophil to lymphocyte ratio, Platelet to lymphocyte ratio, Hypertension, Ambulatory blood pressure monitoring, Non-dipper blood pressure

Öz

Amaç: Hipertansiyon, kardiyovasküler hastalıklar için önemli bir risk faktörüdür ve non-dipper kan basıncı kardiyovasküler olaylar için artmış risk ile ilişkilidir. Nötrofil lenfosit oranı (NLR) ve platelet lenfosit oranı (PLR) inflamasyon ve kardiyovasküler risk ile ilişkilidir. Bu çalışmanın amacı, hipertansif ve normotansif hastalarda NLR, PLR ve non-dipper kan basıncı arasındaki ilişkiyi araştırmaktır.

Yöntemler: Çalışmaya toplam 482 hasta alındı. Çalışma retrospektif kohort çalışma olarak planlandı. 24 saatlik ayaktan kan basıncı monitorizasyonu sonuçlarına göre dört grup oluşturuldu. Grup 1 hipertansif, non-dipper hastalar, Grup 2 hipertansif, dipper hastalar; Grup 3 normotansif, non-dipper hastalar ve Grup 4 normotansif, dipper hastalar olarak sınıflandırıldı.

Bulgular: Çalışma popülasyonunun yaş ortalaması 50,1±15,5 yıl idi ve %38,1'i erkekti. Grup 1 (n = 165), Grup 2 (n=88), Grup 3 (n=123) ve Grup 4 (n=91) NLR açısından karşılaştırıldığında sonuç istatistiksel olarak anlamlı farklıydı ($p<0,001$). Grup 1'de; Grup 2'ye ($p=0,001$), Grup 3'e ($p=0,002$) ve Grup 4'e ($p=0,023$) göre NLR değeri istatistiksel anlamlı yüksekti. Hipertansif hasta grubunda, Grup 1'in PLR değerleri Grup 2'den anlamlı olarak yüksekti ($p=0,002$). Pearson korelasyon analizine göre NLR ve PLR, diurnal kan basıncı değişkenliği ile korelasyon gösterdi (NLR için $r=-0,188$, $p<0,001$ ve PLR için $r=-0,182$, $p<0,001$). Regresyon analizinde NLR ($p=0,040$), PLR ($p=0,021$), yaş ($p=0,006$) ve hipertansiyon ($p<0,001$), kan basıncı değişkenliğinin bağımsız belirleyicileri olarak saptandı.

Sonuç: Bulgularımız, NLR ve PLR'nin hipertansif hastalarda non-dipper kan basıncı için ucuz ve kolay erişilebilir işaretleyiciler olarak kullanılabileceğini göstermektedir.

Anahtar kelimeler: Nötrofil lenfosit oranı, Platelet lenfosit oranı, Hipertansiyon, Ayaktan kan basıncı monitorizasyonu, Non-dipper kan basıncı

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Introduction

Hypertension is a major risk factor for cardiovascular diseases [1]. There are several methods for the diagnosis of hypertension. Ambulatory blood pressure monitorization (ABPM) is a commonly used method for detection and follow-up of hypertensive patients [2]. This technique also demonstrates the diurnal variability of the blood pressure (BP) so that we can determine the dipper and non-dipper status in patients. Decreased blood pressure variability is associated with hypertensive target organ damage and higher risk for cardiovascular events [3,4].

Inflammatory processes play an important role for pathophysiology of hypertension. There are studies that indicate blood pressure increase causes activation in inflammatory processes and that is the underlying mechanism which explains the relationship between hypertension and atherosclerosis [5,6]. Several inflammatory cytokines are related to blood pressure increase [7]. Also some inflammatory markers like mean platelet volume (MPV), high sensitivity C-reactive protein (hs-CRP), red cell distribution width (RDW) are related to diurnal variability of blood pressure [8,9]. Neutrophil/lymphocyte ratio (NLR) and platelet/lymphocyte ratio (PLR) are easily available, inexpensive markers which are obtained from complete blood count results. Recent studies showed the relationship between NLR, PLR and cardiovascular events [10,11]. We design the study to examine if there is a relationship between NLR, PLR and diurnal variability of BP in hypertensive and normotensive patients.

Materials and methods

Patient Population

The study population was chosen from 482 consecutive patients who admitted to outpatient clinic of cardiology department with ABPM results between October 2016 and October 2017. The study was retrospective cohort study. Patients with previous hypertension diagnosis, acute coronary syndrome, serious valve regurgitation or stenosis, coronary artery disease, echocardiographic findings of reduced left ventricular ejection fraction (LVEF < 55%), congenital heart diseases, abnormal kidney function, chronic liver disorders, chronic inflammatory disease, patients who had a recent history of acute infection were excluded from this study.

Patients were divided into four groups according to their dipping and hypertensive status. Patients with high ABPM results (waking ambulatory SBP/DBP >135/85 mmHg and/or sleeping SBP/DBP >120/70 mmHg) were categorized as hypertensive. Dipper status was defined as 10% or more nocturnal BP fall in systolic blood pressure compared to daytime values. Group 1 was defined as hypertensive, non-dipper patients; group 2 as hypertensive, dipper patients; group 3 as normotensive, non-dipper patients and group 4 as normotensive, dipper patients.

Evaluated Parameters

Demographic, clinical and echocardiographic data were obtained from hospital medical records. Total blood count and biochemical analyses were taken from the results of the admission before the ABPM.

Ambulatory 24-hour blood pressure monitoring

24-hour ambulatory blood pressure values were obtained by using a non-invasive oscillometric system. Blood pressure recordings are obtained every 30 minutes during day-time and one hour intervals during night-time. The cuff was placed around the non-dominant arm of the subjects. Dipper hypertension was defined as 10% or more nocturnal BP fall compared to daytime values.

Statistical Analysis

Data are presented as mean ± standard deviation (SD) and as proportions for categorical variables. The t-test or Chi-square test was used for comparisons of continuous and categorical variables, respectively. Distribution of the data for normality was tested by the Shapiro–Wilk test and homogeneity of group variances were tested by the Levene test. For the parameters which are not normally distributed, Mann Whithey U test is used. ANOVA model was used for comparisons across more than 2 groups. Pearson correlation test was used for correlation analysis. Regression analysis was performed to identify the independent associations of blood pressure variability. P-values <0.05 were considered statistically significant. The data were analyzed using SPSS 20.0 (IBM SPSS Ver. 20.0, IBM Corp, Armonk NY, USA).

Results

A total of 482 patients were included to the study. Mean age of the study population was 50.1 ± 15.5 years, 38.1% were male and 61.9% were female. Four groups were formed according to hypertension diagnosis and dipper and non-dipper patterns. Group 1 was consisted of 165 patients with hypertensive and non-dipper status; group 2 was consisted of 88 patients with hypertensive and dipper status; group 3 was consisted of 123 patients with normotensive and non-dipper status; and group 4 was consisted of 91 patients with normotensive and dipper status. Comparison and the baseline characteristics of the groups are shown in Table 1. 24-hour ABPM results of the study groups were shown in Table 2.

Table 1: Comparison of the baseline characteristics and laboratory results of the study groups

Variables	Group 1 (n=180)	Group 2 (n=88)	Group 3 (n=123)	Group 4 (n=91)	p
	Mean ± SD	Mean ± SD	Mean ± SD	Mean ± SD	
Men, %	68 (41.2%)	50 (56.8%)	34 (27.6%)	26 (28.6%)	<0.001
Age, years	52.5 ± 15.0	48.7 ± 14.6	49.1 ± 16.2	44.3 ± 15.2	0.001
LVEF, %	58.0 ± 2.3	57.6 ± 1.7	57.9 ± 2.5	58.2 ± 2.3	0.507
FBG, mg/dL	101.6 ± 32.8	103.6 ± 31.6	98.2 ± 26.5	97.6 ± 40.1	0.590
BUN, mg/dL	14.4 ± 4.6	13.7 ± 4.5	13.6 ± 5.2	12.9 ± 4.2	0.180
Creatinine, mg/dL	0.8 ± 0.2	0.8 ± 0.2	0.7 ± 0.1	0.7 ± 0.1	0.070
HDL-C, mg/dL	50.1 ± 12.8	51.7 ± 14.3	53.2 ± 11.6	52.9 ± 12.1	0.433
LDL-C, mg/dL	128.2 ± 38.3	129.2 ± 27.3	121.0 ± 33.6	125.4 ± 45.6	0.050
Triglyceride, mg/dL	172.7 ± 109.0	138.9 ± 48.2	134.6 ± 79.1	138.5 ± 71.6	0.019
Hb, g/dL	14.1 ± 1.8	14.7 ± 1.8	13.6 ± 1.8	13.8 ± 1.7	<0.001
WBC, x10³/mm³	8.3 ± 2.3	8.2 ± 2.1	7.7 ± 1.9	7.8 ± 2.0	0.048
Neutrophils, x10³/mm³	5.5 ± 3.5	4.7 ± 1.7	4.5 ± 1.6	4.7 ± 1.7	0.006
Lymphocytes, x10³/mm³	2.3 ± 0.7	2.6 ± 0.8	2.4 ± 0.8	2.3 ± 0.6	0.006
Eosinophils, x10³/mm³	0.2 ± 0.1	0.2 ± 0.1	0.1 ± 0.1	0.2 ± 0.1	0.092
Platelets, x10³/mm³	280.0 ± 77.6	270.9 ± 65.3	277.8 ± 67.9	268.1 ± 54.5	0.549
RDW, fL	43.0 ± 29.9	40.6 ± 3.4	41.0 ± 4.7	40.4 ± 4.0	0.648
MPV, fL	11.1 ± 7.1	11.6 ± 9.2	11.2 ± 8.4	10.4 ± 0.9	0.756
PDW, fL	12.4 ± 2.9	12.4 ± 2.5	12.2 ± 2.1	12.2 ± 2.1	0.752
NLR	2.696 ± 1.918	1.933 ± 0.916	2.357 ± 3.066	2.177 ± 1.154	<0.001
PLR	133.3 ± 49.9	112.2 ± 45.4	133.5 ± 90.3	121.7 ± 33.5	0.008

BUN: blood urea nitrogen, FBG: fasting plasma glucose, Hb: hemoglobine, HDL-C: high density lipoprotein cholesterol, LDL-C: low density lipoprotein cholesterol, LVEF: left ventricule ejection fraction, MPV: mean platelet volüme, NLR: neutrophil/lymphocyte ratio, PDW: platelet distribution width, PLR: platelet/lymphocyte ratio, RDW: red cell distribution width, WBC: white blood cell

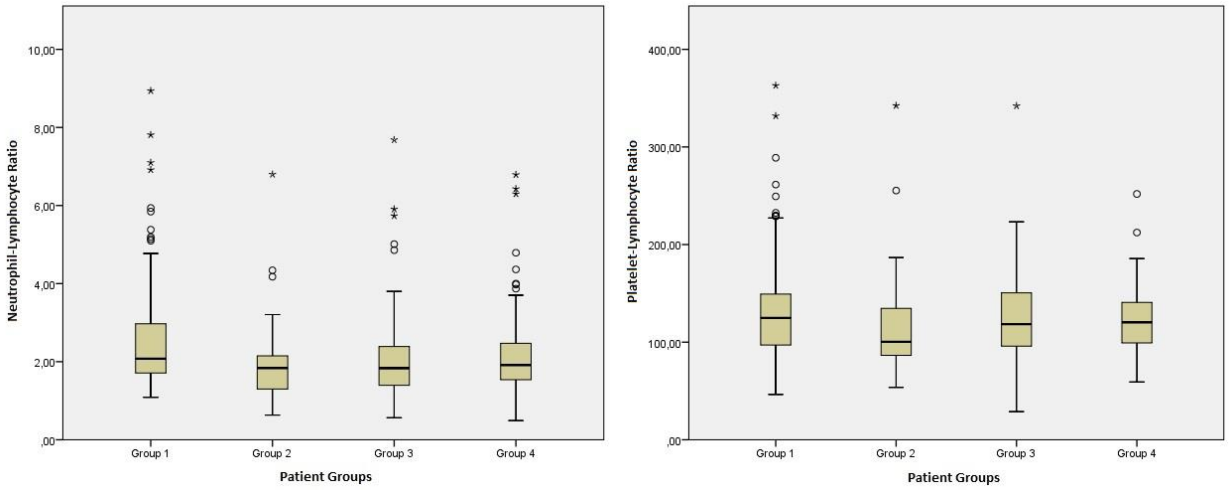

Figure 1: Neutrophil-lymphocyte ratio and platelet/lymphocyte ratio values of four study groups

Neutrophil lymphocyte ratio was statistically different among groups (p<0.001). Group 1 had significantly higher values compared to Group 2 (p=0.001), Group 3 (0.002) and Group 4 (p=0.023). NLR values were similar when values were compared among Group 2, Group 3 and Group 4 within each other (p>0.05). Platelet lymphocyte ratio was significantly different among all groups (p=0.008) (Table 1). Boxplot graph of four investigated groups were seen in Figure 1.

When hypertensive patient group were investigated, PLR values of Group 1 was significantly higher than Group 2 (p=0.002). Also Group 1 and 2 have significant differences in terms of lymphocytes (p=0.001). When normotensive patients were investigated, there were no statistically significant difference between white blood cell parameters between Group 3 and Group 4 (Table 3).

Table 2: 24-h ambulatory blood pressure monitorization results of the study groups

Variables	Group 1 (n=180) Mean ± SD	Group 2 (n=88) Mean ± SD	Group 3 (n=123) Mean ± SD	Group 4 (n=91) Mean ± SD	p
Day SBP, mmHg	138.1 ± 13.6	143.0 ± 10.9	117.4 ± 7.4	123.2 ± 7.0	<0.001
Day DBP, mmHg	81.8 ± 10.5	86.8 ± 9.1	69.5 ± 6.7	73.5 ± 6.0	<0.001
Night SBP, mmHg	136.3 ± 14.1	121.3 ± 9.5	110.9 ± 11.0	105.6 ± 7.3	<0.001
Night DBP, mmHg	79.3 ± 10.6	70.7 ± 8.0	64.1 ± 6.6	60.5 ± 6.3	<0.001
SBP, mmHg	136.9 ± 16.3	138.6 ± 10.5	116.4 ± 6.9	115.5 ± 13.1	<0.001
DBP, mmHg	81.3 ± 10.1	83.7 ± 8.7	68.4 ± 6.5	70.8 ± 6.0	<0.001
BP variability, %	1.1 ± 7.2	14.9 ± 3.9	4.8 ± 3.9	14.3 ± 3.7	<0.001

BP: blood pressure, DBP: diastolic blood pressure, SBP: systolic blood pressure

Table 3: Comparison of white blood cell parameters between Group 1-2 and Group 3-4

Variables	p value of Group 1 compared to Group 2	p value of Group 3 compared to Group 4
WBC	0.657	0.759
Neutrophils	0.056	0.578
Lymphocytes	0.001	0.595
Eosinophils	0.349	0.226
Platelets	0.377	0.285
RDW	0.478	0.408
MPV	0.637	0.357
PDW	0.965	0.998
NLR	<0.001	0.564
PLR	0.002	0.454

MPV: mean platelet volume, NLR: neutrophil/lymphocyte ratio, PDW: platelet distribution width, PLR: platelet/lymphocyte ratio, WBC: white blood cell

Pearson correlation analysis showed that NLR and PLR were correlated with blood pressure variability between night and day (r=-0.188, p<0.001 for NLR and r=-0.182 and p<0.001 for PLR). NLR levels were significantly correlated with night SBP (r=0.141, p=0.003) and night DBP (r=0.113, p=0.020). Pearson correlation analysis between NLR, PLR and ABPM results were shown in Table 4.

Table 4: Pearson correlation analysis of NLR, PLR and 24-hour ABPM values

	NLR		PLR	
	r	p	r	p
Day SBP	0.023	0.630	-0.033	0.495
Day DBP	-0.006	0.904	-0.065	0.180
Night SBP	0.141	0.003	0.095	0.050
Night DBP	0.113	0.020	0.051	0.295
SBP	0.054	0.267	-0.001	0.989
DBP	0.021	0.673	-0.042	0.387
BP variability	-0.188	<0.001	-0.182	<0.001

BP: blood pressure, DBP: diastolic blood pressure, NLR: neutrophil/lymphocyte ratio, PLR: platelet/lymphocyte ratio, SBP: systolic blood pressure

Regression analysis showed that NLR (p=0.040), PLR (p=0.021), age (p=0.006) and hypertension (p<0.001) were independent predictors of diurnal blood pressure variability.

Discussion

In this study we demonstrated that NLR is significantly higher in hypertensive non-dipper patients than hypertensive and non-dipper; normotensive and non-dipper; and normotensive and dipper patients. Also in hypertensive patient group; PLR is significantly higher in patients with non-dipper status compared to patients with dipper status.

24-hour ambulatory blood pressure monitorization is used for the diagnosis and follow-up of hypertension. It also gives valuable information about dipper and non-dipper status of patients. Non-dipper blood pressure pattern is defined as less than 10% drop of blood pressure in night-time blood pressure compared to day-time blood pressure [12]. Non-dipper blood pressure pattern is associated with cardiovascular mortality, end-organ damage and autonomic dysfunction [13-15]. There is evidence that number of endothelial progenitor cells is decreased in hypertensive non-dipper status meaning vascular repair mechanisms and endothelial homeostasis is disturbed [16]. Elevated blood pressure and decreased blood pressure variability may stimulate inflammation by increased expression of endothelial cytokines [6].

Chronic inflammation plays an important role in atherosclerosis, cardiovascular diseases, malignancy, chronic kidney disease, rheumatologic diseases and diabetes mellitus [17-22]. Neutrophils play a major role in inflammation by releasing cytokines and triggering immune system mechanisms. Increased NLR values are associated with atherosclerosis, severity of coronary artery diseases and worse cardiac outcome [23,24]. Increased platelet count is an indicator of increased platelet activity and increased platelet activity is in correlation with the severity of inflammation [25,26].

Increased platelet counts and decreased lymphocyte counts are associated with worse cardiac outcomes. No reflow after stent implantation after ST segment elevation myocardial infarction is more common in patients with high PLR values [27]. In non-ST segment elevated myocardial infarction patients, mortality outcome is higher with increased PLR values [28].

In our study we investigated the association between NLR, PLR and dipper, non-dipper status of hypertensive and normotensive patients. NLR values were highest in hypertensive non-dipper group when compared to hypertensive dipper, normotensive non-dipper and normotensive dipper groups. When the hypertensive patient group was examined separately, the lymphocyte count was significantly lower; NLR and PLR were significantly higher in non-dipper patient group. When non-dipper and dipper patients were compared in normotensive patients, no statistically significant difference was found in terms of whole blood count parameters, NLR and PLR. Correlation analysis revealed a statistically significant relationship between NLR and night systolic, night diastolic blood pressures and blood pressure variability. When the PLR was analyzed in the correlation analysis, a statistically significant relationship was found between this value and the night systolic blood pressure and BP variability. Moreover, NLR and PLR along with hypertension and age found to be an independent predictor for BP variability and non-dipper status. Kılıçaslan et al. [29] investigated NLR values in hypertensive and normotensive patients. This study included 150 subjects and NLR values were highest in non-dipper hypertensive patients. Sunbul et al. [30] found out that in hypertensive patients, PLR and NLR values are higher in non-dipper patients and PLR but not NLR was an independent predictor for non-dipper status. In our study both NLR and PLR values were independent predictors for BP variability. The difference may be caused because our study included normotensive patients and in our regression model, normotensive patients were not excluded and our sample size is wider.

Our study had some limitations. It would be better to compare inflammation markers like hs-CRP with our findings. We excluded conditions that would cause inflammation but still it would be better to include CRP levels to our regression model.

In conclusion, our findings suggest that NLR and PLR can be used as inexpensive and easily accessible markers to detect non-dipper status in hypertensive patients. Further investigations are needed to find the mechanism behind this relationship.

References

1. Lewington S, Clarke R, Qizilbash N, Peto R, Collins R. Age-specific relevance of usual blood pressure to vascular mortality: a meta-analysis of individual data for one million adults in 61 prospective studies. Lancet. 2002;360:1903-13.
2. Roush GC, Fagard RH, Salles GF, Pierdomenico SD, Reboldi G, Verdecchia P, et al. Prognostic impact from clinic, daytime, and night-time systolic blood pressure in nine cohorts of 13,844 patients with hypertension. J Hypertens. 2014;32:2332-40.
3. Mancia G, Parati G. Ambulatory blood pressure monitoring and organ damage. Hypertension. 2000;36:894-900.
4. Salles GF, Reboldi G, Fagard RH, Cardoso CR, Pierdomenico SD, Verdecchia P, et al. Prognostic effect of the nocturnal blood pressure fall in hypertensive patients: The ambulatory blood pressure collaboration in patients with hypertension (ABC-H) meta-analysis. Hypertension. 2016;67:693-700.
5. Savoia C, Schiffrin EL. Inflammation in hypertension. Curr Opin Nephrol Hypertens. 2006;15:152-8.
6. Chae CU, Lee RT, Rifai N, Ridker PM. Blood pressure and inflammation in apparently healthy men. Hypertension. 2001;38:399-403.
7. Yamada S, Gotoh T, Nakashima Y, Kayaba K, Ishikawa S, Nago N, et al. Distribution of serum C-reactive protein and its association with atherosclerotic risk factors in a Japanese population: Jichi Medical School Cohort Study. Am J Epidemiol. 2001;153:1183-90.
8. Ozcan F, Turak O, Durak A, Işleyen A, Uçar F, Giniş Z, et al. Red cell distribution width and inflammation in patients with non-dipper hypertension. Blood Press. 2013;22:80-5.
9. Kaya MG, Yarlioglues M, Gunebakmaz O, Gunturk E, Inanc T, Dogan A, et al. Platelet activation and inflammatory response in patients with non-dipper hypertension. Atherosclerosis. 2010;209:278-82.
10. Li H, Zhou Y, Ma Y, Han S, Zhou L. The prognostic value of the platelet-to-lymphocyte ratio in acute coronary syndrome: a systematic review and meta-analysis. Kardiol Pol. 2017;75:666-73.
11. Arbel Y, Finkelstein A, Halkin A, Birati EY, Revivo M, Zuzut M, et al. Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography. Atherosclerosis. 2012;225:456-60.
12. Mancia G, Fagard R, Narkiewicz K, Redon J, Zanchetti A, Böhm M, et al. 2013 ESH/ESC Guidelines for management of arterial hypertension. Eur Heart J. 2013;34:2159-219.
13. Mancia G, Parati G. The role of blood pressure variability in end organ damage. J Hypertens Suppl. 2003; 21:S17-23.
14. Liu M, Takahashi H, Morita Y, Maruyama S, Mizuno M, Yuzawa Y, et al. Non-dipping is a potent predictor of cardiovascular mortality and is associated with autonomic dysfunction in haemodialysis patients. Nephrol Dial Transplant. 2003;18:563–9.
15. Ino-Oka E, Yumita S, Sekino H, Ohtaki Y, Takahashi T, Inooka H, et al. The effects of physical activity and autonomic nerve tone on the daily fluctuation of blood pressure. Clin Exp Hypertens. 2004;26:129–36.
16. Kim S, Kim NH, Kim YK, Yoo JH, Shin SN, Ko JS, al. The Number of Endothelial Progenitor Cells is Decreased in Patients With Non-Dipper Hypertension. Korean Circ J. 2012;42:329-34.
17. Ross R. Atherosclerosis--an inflammatory disease. N Engl J Med. 1999;340:115-6.
18. Stenvinkel P, Alvestrand A. Inflammation in end-stage renal disease: sources, consequences, and therapy. Semin Dial. 2002;15:329-37.
19. Garcia C, Feve B, Ferre P, Halimi S, Baizri H, Bordies L, et al. Diabetes and inflammation: fundamental aspects and clinical implications. Diabetes Metab. 2010;36:327-38.
20. Feldmann M, Brennan FM, Maini RN. Role of cytokines in rheumatoid arthritis.Annu Rev Immunol. 1996;14:397-440.
21. Coussens LM, Werb Z. Inflammation and cancer. Nature. 2002;420:860-7.
22. Mangge H, Becker K, Fuchs D, Gostner JM. Antioxidants, inflammation and cardiovascular disease. World J Cardiol. 2014;6:462-77.
23. Wang H, Hu Y, Geng Y, Wu H, Chu Y, Liu R, et al. The relationship between neutrophil to lymphocyte ratio and artery stiffness in subtypes of hypertension. J Clin Hypertens (Greenwich). 2017;19:780-5.
24. Arbel Y, Finkelstein A, Halkin A, Birati EY, Revivo M, Zuzut M, et al. Neutrophil/lymphocyte ratio is related to the severity of coronary artery disease and clinical outcome in patients undergoing angiography. Atherosclerosis. 2012;225:456-60.
25. Projahn D, Koenen RR. Platelets: key players in vascular inflammation. J Leukoc Biol. 2012;92:1167-75.
26. Kaito K, Otsubo H, Usui N, Yoshida M, Tanno J, Kurihara E, et al. Platelet size deviation width, platelet large cell ratio, and mean platelet volume have sufficient sensitivity and specificity in the diagnosis of immune thrombocytopenia. Br J Haematol. 2005;128:698-702.
27. Yildiz A, Yuksel M, Oylumlu M, Polat N, Akyuz A, Acet H, et al. The Utility of the Platelet-Lymphocyte Ratio for Predicting No Reflow in Patients With ST-Segment Elevation Myocardial Infarction. Clin Appl Thromb Hemost. 2015;21:223-8.
28. Azab B, Shah N, Akerman M, McGinn JT Jr. Value of platelet/ lymphocyte ratio as a predictor of all-cause mortality after non- ST-elevation myocardial infarction. J Thromb Thrombolysis. 2012;34:326-34.
29. Kılıçaslan B, Dursun H, Kaymak S, Aydın M, Emekçi Ç, Susam İ, et al. The relationship between neutrophil to lymphocyte ratio and blood pressure variability in hypertensive and normotensive subjects. Turk Kardiyol Dern Ars. 2015;43:18-24.
30. Sunbul M, Gerin F, Durmus E, Kivrak T, Sari I, Tigen K, et al. Neutrophil to lymphocyte and platelet to lymphocyte ratio in patients with dipper versus non-dipper hypertension. Clin Exp Hypertens. 2014;36:217-21.