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Original Article

The relationship between platelet to lymphocyte ratio and the diurnal variation of hypertension

Platelet lenfosit oranı ve hipertansiyonun diürnal ritmi arasındaki ilişki

Savas CELEBI*

TOBB Economics and Technology University, School of Medicine, Department of Cardiology, Ankara/ TURKEY

ABSTRACT

Aim: Platelet to lymphocyte ratio (PLR) predicts worse outcome in cardiovascular disease. However data is limitted about the role of PLR in the diurnal variation of hypertension. In this study we evaluated the relationship between the diurnal variation of hypertension and PLR.

Material and Methods: The study included a total of 247 essential hypertensive patients. All patients underwent 24-hour ambulatory blood monitoring. Thereafter hypertensive patients were divided into two groups: 64 dipper patients (30 female, mean age 53.8±12.9 years) and 38 non-dipper patients (18 female, mean age 52.6±12.5years). Complete blood count and biochemistry were measured by standard methods. PLR was measured by dividing platelet count to lymphocyte count.

Results: Non-dipper hypertensives had signifi cantly higher PLR levels than dippers (127.9±32.16 vs 103.4±10.67, p<0.001). There was a negatif correlation between percentage of sistolic and diastolic blood pressure fall and PLR.

Conclusion: We demonstrated that PLR, an inexpensive and easily accessible biomarker, is significantly higher in nondipper hypertensives than the dipper hypertensives.

Keywords: Hypertension; non-dipper; dipper; platelet to lymphocyte ratio

Corresponding Author*: Savas CELEBI, TOBB Economics and Technology University, School of Medical, Department of Cardiology, Ankara/TURKEY
E-mail: draksuyeksavas@yahoo.com
ORCID: 0000-0002-2566-3877
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ÖZ

Amaç: Platelet lenfosit oranı (PLR) kardiyovasküler kötü sonlanımlar için öngördürücüdür. Ancak PLR'nın hipertansiyonun diürnal ritmindeki rolü ile ilgili veri sınırlıdır. Biz bu çalışmada PLR ile hipertansiyonun diürnal ritmi arasındaki ilişkiyi değerlendirmeyi amaçladık.

Gereç ve Yöntemler: Çalışmaya toplamda 247 esansiyel hipertansiyon hastası dahil edildi. Tüm hastalara 24-saat ambulatuar kan basıncı monitorizasyonu yapıldı. Takiben hastalar iki gruba ayrıldı: 64 dipper hasta (30 kadın, ortalama yaş 53.8±12.9) ve 38 non-dipper hasta (18 kadın, ortalama yaş 52.6±12.5). Tam kan sayımı ve biyokimyasl değerlendirme standart metodlarla yapıldı. PLR platelet sayısının lenfosit sayısına bölünmesiyle hesaplandı.

Bulgular: Nondipper hipertansifler dipper hipertansiflere kıyasla daha yüksek PLR'ye sahipti (127.9±32.16'e 103.4±10.67, p<0.001). Sistolik ve diastolik kan basıncının düşüş oranı ile PLR arasında negatif korelasyon mevcuttu.

Sonuç: Ucuz ve kolay ulaşılabilir bir biobelirteç olan PLR, nondipper hipertansiflerde dipper hipertansiflere kyasla daha yüksektir.

Anahtar Kelimeler: Hipertansiyon; non-dipper; dipper; platelet lenfosit oranı

Introduction

Hypertension is considered as an important risk factor for cardiovascular mortality and morbidity. Hypertension shows diurnal variation. A decrease in systolic and diastolic blood pressure of more than 10% in night time compared to daytime is considered as dipper pattern and the absence of this decrease is considered as non-dipper pattern. Current literature shows that non-dipper pattern increases the risk of cardiovascular events and end-organ damage due to hypertension compared to dipper pattern [1-3]. Even though the underlying reason for this situation has not been fully enlightenede, it is known that inflammatory and thrombotic processes are more common in non-dipper patients [4-5].

Both lymphocytes and platelets are important mediators of inflammatory and thrombotic processes. It has been shown that the platelet/lymphocyte ratio (PLR) obtained by dividing the platelet count by lymphocyte count can be used as a predictor for cardiovascular events [6-7]. Increased PLR has been associated with unfavorable coronary events and coronary artery disease [8].

A number of studies have shown that the levels of inflammatory markers are elevated in non-dipper patients. However, data on PLR, a thrombotic marker in inflammatory and thrombotic processes, is limited in hypertensive patients. In this study, our aim was to investigate the relationship between PLR in hypertensive patients and diurnal pattern in hypertension.

Material and Methods

Study Population

A total of 150 patients were screened fort his retrospective cross-sectional study. Fourty eight patients were excluded according to exclusion criterias. The remaining 102 patients (48 women, 54 men) with a history of chronic hypertension and receiving appropriate antihypertensive medications for at least 3 months prior to enrolment were enrolled. Hypertension was defi ned as systolic BP (SBP) 140 mmHg or a diastolic BP (DBP) 90 mmHg and/or use of the anti-hypertensive drug therapy [9]. After diagnosis of hypertension, ambulatory blood pressure monitoring (ABPM) was performed. Exclusion criteria included the presence of the following: Patients with diabetes mellitus, hematopoietic system disorders, histories of malignancy and/or chemotherapy treatment, signs of accompanying infectious diseases, leukocyte disorders (such as an acute infection or chronic inflammatory status), histories of secondary hypertension, known coronary artery or cerebrovascular disease, chronic renal failure, chronic liver disorders, moderate, or severe valvular disease, congenital heart disease, left ventricular systolic and/or diastolic dysfunction on echocardiography and those who had used glucocorticoid therapy within the last 3 months.

Each of the patients signed an informed consent form, and the study protocol was approved by the local ethics committee.

The patients 'clinical and demographic characteristics such as age, sex, smoking habits and antihypertensive drugs were noted. In addition, serum levels of hsCRP, fasting blood glucose level, creatinine level and fasting serum lipid status including total cholesterol, low-density lipoprotein (LDL), high-density lipoprotein (HDL) and triglyceride levels were also recorded. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m 2). Each patient was assessed using 12-lead electrocardiography and transthoracic echocardiography.

Laboratory analysis

All laboratory data were obtained from venous blood samples after 12 h of fasting. Haematologic parameters were measured using an automated haematologyanalyser(XE-2100;Sysmex Corporation, Kobe, Japan). The biochemical measurements were determined using a molecular analyser (Roche Diagnostics, Manheim, Germany).Ambulatory Blood Monitoring

A 24-h ABPM device (Mobilograph, Stolberg, Germany) was applied to each patient. The cuff was placed around the non-dominant arm and it was worn for 24 h with BP readings every 15-min period in the daytime and every 30-min period at nighttime. Daytime and night-time were defi ned using short, fi xed clock intervals, which ranged from 06:00 to 22:00 h and from 22:00 to 06:00 h, respectively. The recordings were analyzed with interactive software. If 20% or more of the measurements could not be taken,re- ambulatory blood monitoring was performed. From the hourly averages of ambulatory BP recordings, daytime, night-time and 24-h averages of SBP, DBP and mean BP were calculated for each patient. Nocturnal blood pressure dipping was calculated using the following formula: (%) 100 [1 – (sleep systolic blood pressure/awake systolic blood pressure)]. Patients with BP decrease of 10% or more during night-time were accepted as dipper hypertensives, whereas patients with BP decreases less than 10% were accepted as non-dipper hypertensives [10].

Transthoracic Echocardiography Protocol

Two-dimensional transthoracic echocardiography (TTE) was performed in all patients at admission and at the end of the first month of the index acute STEMI. The TTE measurements were performed using a Vivid 7 system (Vivid 7, GE Vingmed Ultrasound, Horten, Norway). On echocardiographic evaluation, dimensions of the left ventricular chamber, wall thickness, left ventricular ejection fraction, diameter of the left atrium, and vlvular function were evaluated with 2D, M-mode, Doppler, and tissue Doppler studie.

Statistical Analysis

Statistical analysis was performed using SPSS 22.0 statistical software. (SPSS Inc., Chicago, IL, USA). Continuous variables are described as the means±SD, whereas discrete variables are reported as frequencies and percentages. The equality of the data to the normal distribution was assessed with Shapiro–Wilk test. Normal distributed variables were given as mean SD and non-normally distributed variables were given as medians with interquartile ranges. The chi-square test was used for categorical variables. Mean values of the groups were compared with Student's t-test and Mann – Whitney U test where appropriate. Similarly, Pearson and Spearman correlation coeffi cients were used to test univariate correlations. Statistical significance was set at p 0.05.

Results

According to the 24-hour ambulatory blood pressure monitoring, 64 patients (62.7%) were dipper and 38 patients (37.2%) were non-dipper. ABPM values were shown in Table 1.

Table 1. Blood Pressure Values of Groups

	Nondipper (n=38)	Dipper (n=64)	p
Systolic blood pressure (total) – mmHg	125.7±13.8	123.2±7.16 0.142	0.142
Systolic blood pressure (day)- mmhg	127.16±11.3	126.8±10.8	0.224
Systolic blood pressure (night) – mmHg	122.1 ± 8.17	116.2 ± 8.19	0.001
Diastolic blood pressure (total) – mmHg	84.8±9.7	83.5±8.3	0.125
Diastolic blood pressure (day) – mmHg	85.3±10.1	82.7±9.5	0.002
Diastolic blood pressure (night) – mmHg	79.8±10.3	73.6±9.5	0.026

Patients in the non-dipper group had significantly higher night-time SBP, and daytime DBP compared with the dipper group (122.1 ± 8.17 vs 116.2 ± 8.19 mmHg; P <0 .001; 85.3±10.1 vs 82.7±9.5, p=0.002, respectively). Basal basic clinical and demographic characteristics of the patients are shown in Table 2. There was no statistically significant difference between the dipper and nondipper groups in terms of age, gender , body mass index, antihypertensive medications and smoking status. In the non-dipper group, LDL-C levels and total cholesterol levels were higher than in the dipper groupd. The mean eGFR of the patients in the nondipper group was lower than in the dipper group but statistically insignificant (87.2 ± 19.3 vs. 92.1 ± 14.9, p= 0.186). The platelet counts and PLRs were higher in nondipper group than in dipper group (326.2 ± 65.19 /mm3 vs 277.1 ± 72.5 /mm3; P< 0.001, 127.9 ± 32.16 /mm3 vs 103.4 ± 10.67 / mm3; P <0.001). Patients in the non-dipper group also had higher MPV levels than the dipper group (9.17 ± 0.96 vs 8.59 ± 0.74 fL, P<0.001). The plateletcrit and platelet distribution width were higher in patients with non-dipper hypertension than those in the dipper group (0.26 ± 0.02 % vs 0.22 ± 0.014 %; P <0.001, and 16.2 ± 0.36 vs 15.8 ± 0.57%; P<0.001; respectively).

Table 2. Baseline caharacteristics and the clinical data of the study population.

	Nondipper (n=38)	Dipper (n= 64)	p
Age (years)	52.6±12.5	53.8±12.9	0.149
Sex (female),n(%)	18 (47.3)	30(46.8)	0.338
Body mass index (kg/m2)	28.6±3.2	29.3±3.7	0.271
Current Smokers, n(%)	9 (23.6)	15 (23.4)	0.236
Hyperlipidemia	12(31.5)	19 (29.6)	0.114
Medications (%)			
Betablocker	21.1	21.8	0.310
ACE inhibitor	34.2	35.9	0.217
ARB	28.9	34.3	0.259
CCB	31.5	35.9	0.198
Diüretics	55.2	53.1	0.281
Fasting glocose (mg/dl)	98.7±12.3	93.5±16.7	0.291
eGFR (ml/ min/1.73 m2)	87.2 ± 19.3	92.1 ± 14.9	0.186
Total cholesterol (mg/dl)	246.8±69.3	198.7±75.9	0.023
Triglycerides (mg/ dl)	152.9±80.5	151.3±75.8	0.736
Low dencity lipo-protein (mg/dl)	132.3±45.8	121.7±58.3	0.001
High dencity lipo-protein (mg/dl)	42.7±8.1	44.3±7.7	0.562
Leukocytes (mm3)	6812±1216	6519±1325	0.468
Neutrophils (mm3)	4216±1428	4370±1289	0.429
Lymphocyes (mm3)	1994±697	2418±796	<0.001
Platelets (103 / mm3)	326.2 ± 65.19	277.1 ± 72.5	<0.001
PLR	127.9 ± 32.16	103.4 ± 10.67	<0.001
Mean platelet vol-ume (fL)	9.17 ± 0.96	8.59 ± 0.74	<0.001
Plateletcrit (%)	0.26 ± 0.02	0.22 ± 0.014	<0.001
Platelet distribution width (%)	16.2 ± 0.36	15.8 ± 0.57	<0.001
Hemoglobin (g/dl)	13.8±1.1	13.4±1.7	0.127

ACE, Angiotensin converting enzyme; ARB, Angiotensin receptor blocker; CCB, calcium channel blocker ;eGFR, estimated glomerular filtration rate; PLR, platelet to lymphocyte ratio

Univariate correlation analysis were determined significant negative correlation between the rate of nocturnal SBP and DBP fall and PLR (r =-0. 403, p< 0.001 and r =- 0.307, p < 0.001, respectively) (Figure 1-2).

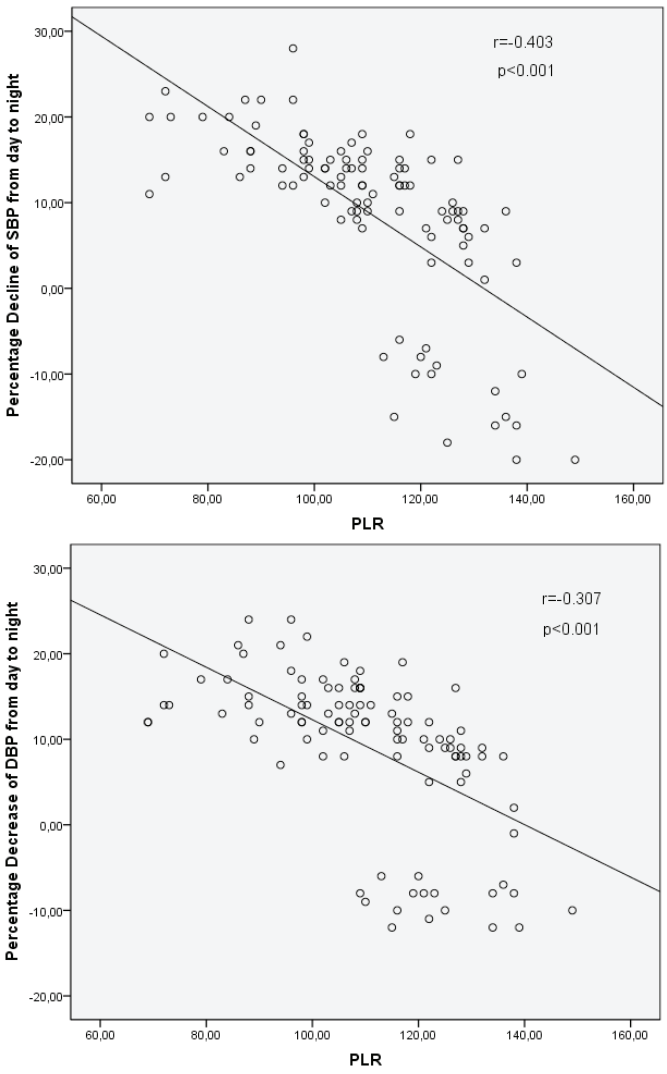

Figure 1-2: *The negative correlation between platelet to lymphocyte ratio (PLR) and nocturnal blood pressure fall. SBP, systolic blood pressure; DBP, diastolic blood pressure.*

Discussion

In this study we have found that PLR is significantly higher in the non-dipper HT groups compared with those of the dipper HT group.

It is known that the diurnal rhythm of hypertension is associated with hypertension-related end organ damage and unfavorable cardiovascular outcomes [11-13].

It has been shown that non-dipper hypertension which is defined as a decrease in blood pressure of less than 10 mmHg during the night hours causes more undesirable cardiovascular events in non-hypertensive patients and in dipper hypertensive patients whose blood pressure decreases 10 mmHg or more [14-15]. This situation in non-dipper hypertensive patients has been tried to be explained by endothelial damage and abnormalities in inflammatory process. Studies have shown elevated levels of inflammatory

markers and deterioration of platelet functions in non-dipper hypertensive patients [16-17]. However, the exact pathophysiological process is still unknown.

Recent studies have shown that PLR may be used as a predictor of cardiovascular risk. Zhou et al. have demonstrated that PLR is associated with the prevalence of coronary artery disease and that increased PLR is a predictor of poor prognosis in coronary artery disease [7]. Ye et al. haveshown that increased PLR in patients with acute heart failure is associated with poor clinical outcomes and it can be used as a marker in treatment of acute heart failure [18]. Kurtul et al. have reported that PLR was associated with the severity of coronary artery disease in patients with acute coronary syndrome [19]. Thomas et al. have reported that risk of adverse events increases in parallel with increased PLR in patients with peripheral artery disease [20]. In literature, many publications have shown that the levels of inflammatory markers have increased in patients with non-dipper hypertension compared to dipper hypertensive patients. However, the number of studies investigating the relationship between PLR and diurnal rhythm is very limited [7,21]. In our study, we demonstrated that diurnal rhythm of hypertension is associated with PLR. Therefore, increased PLR, an inflammatory and thrombotic marker, may be associated with an increased incidence of adverse events in non-dipper hypertensive patients. Large-scale randomized studies are necessary to clarify this subject.

Conclusion

We can state a close relationship between increased cardiovascular risk and non-dipper status in hypertensive patients. Data in literature suggests that this condition is related to increased inflammation and platelet aggregation in non-dipper status. In addition, it is known that increased platelet count promotes inflammation. Therefore, the results of our study supports the hypothesis that the increased risk of cardiovascular events in non-dipper status is associated with abnormalities in inflammation and thrombogenesis.

Declaration of conflict of interest

The authors received no financial support for the research and/or authorship of this article. There is no conflict of interest.

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