Effects of Peripheral Vertigo on Inflammatory and Immunologic Laboratory Markers

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Abstract
The neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV) are markers of subclinical inflammation and atherothrombosis. We investigated whether these easily accessible blood count parameters are affected by peripheral vertigo (PV). We studied 142 patients who were diagnosed with PV and referred to our hospital along with 135 healthy patients who were free of inflammation as a control group. The patient group was divided into 3 study groups depending on the presence of benign paroxysmal positional vertigo (BPPV): BPPV, vestibular dysfunction (VD), and BPPV + VD. The total patient group and 3 subgroups were compared to the control group with respect to the NLR, PLR, and MPV. The NLR and PLR were calculated by dividing the neutrophil and platelet values by the lymphocyte value. Of 142 patients, 43, 71, and 28 patients comprised the BPPV, VD, and BPPV + VD groups, respectively. There was no statistically significant difference (P > .05) in the NLR, PLR, or MPV between the main patient group or the individual patient subgroups and the control group. Our findings suggest that NLR, PLR, and MPV do not change significantly either in BPPV or in other peripheral vestibular disorders.

Keywords
peripheral vertigo, videonystagmography, neutrophil-to-lymphocyte ratio, platelet-to-lymphocyte ratio, mean platelet volume, vestibulopathy

Introduction
The complete blood count (CBC), commonly performed in clinical practice, is a very informative laboratory test. Recently, it is seen that interests of clinicians are increased to certain parameters of the CBC including the neutrophil-to-lymphocyte ratio (NLR), platelet-to-lymphocyte ratio (PLR), and mean platelet volume (MPV). The NLR, an established marker of subclinical inflammation, has been defined as a novel parameter to detect inflammation in patients with facial paralysis, cardiac disease, and several neoplastic disorders. Moreover, the relationship between the NLR and MPV and inner ear diseases, particularly those characterized by sudden hearing loss and peripheral vertigo (PV), was recently found to be significant.

The PLR is a novel index reflecting systemic inflammation that combines prognostic values of an individual’s platelet and lymphocyte counts. Increases in the NLR and PLR may indicate atherosclerosis as well as inflammation in microvascular structures.

Vertigo is one of the most common reasons for patients to consult a physician. Vertigo is estimated to affect 20% to 30% of people at some point in their lifetime. Vertigo refers to a feeling of rotation, swaying, or tilting of the body or surrounding environment. The causes of vertigo may be central (involving the brainstem or cerebellum) or peripheral (involving the inner ear or vestibular nerve); PV is the more common type.

Given the above findings, this study aimed to investigate the role of inflammation and atherothrombosis in PV patients using the NLR, MPV, and PLR.

Patients and Methods
Subjects
We retrospectively reviewed the medical records of 1046 consecutive patients who were diagnosed with PV at Safa Hospital and treated from January 2014 to February 2016. The inclusion
criteria for this study were patients aged 18 to 65 years, diagnosis of PV confirmed by videonystagmography (VNG), and a CBC performed at the first visit with no indicators of infection (elevated erythrocyte sedimentation rate, elevated c-reactive protein, or a white blood cell [WBC] count > 10 000 or < 3500). The exclusion criteria were a history or clinical findings of any inflammatory, autoimmune, acute, or chronic infectious diseases; any malignant neoplasia; cardiac or coronary artery disease; diabetes mellitus; metabolic syndrome; chronic obstructive pulmonary disease; amyloidosis; chronic renal insufficiency; or active otologic disease such as chronic otitis media or otosclerosis. Of 1046 patients, 142 were ultimately included in our study based on these criteria.

The patients were divided into 3 groups depending on their clinical diagnosis of benign paroxysmal positional vertigo (BPPV; all types of BPPV), vestibular dysfunction (VD; unilateral and/or bilateral), or BPPV with VD (BPPV + VD). To compare biomarker profiles, 135 age- and sex-matched healthy patients with no acute inflammation or the diseases mentioned above were included in the study as a control group.

**Vestibular Examination**

We used VNG equipment from Otometrics (ICS Chart 200; Taastrup, Denmark) and a computerized system. PC-videoystagmography was used for automatic analysis of the recordings.

Also considered in the analysis were the presence of spontaneous nystagmus and results of the Saccade test, tracking test, optokinetic test, gaze test, Dix-Halpike maneuver, position test, head shake test, air-stimulated binaural bithermal caloric test, fixation suppression test, baseline shift, gain asymmetry measurement, and directional preponderance assessments.

**Hematologic Examinations**

We included in our analysis only hemogram values that were measured (including the WBC, neutrophil count, lymphocytes, platelets, and MPV) in our hospital laboratory on the day of admission.

The NLR and PLR were calculated as a simple ratio between the absolute neutrophil and lymphocyte counts and between the absolute platelet and lymphocyte counts. An automated blood cell counter (Sysmex XN-1000; Kobe, Japan) was used for CBC measurements. All samples were run in duplicate; mean values were used for statistical analysis. The laboratory data were analyzed and compared between the patient and control groups.

### Statistical Analyses

Statistical analyses of quantitative data were performed using SPSS version 22.0. The mean, median, lowest, and highest values and standard deviation were measured. The distribution of variations was measured using the Kolmogorov-Smirnov test while the Mann-Whitney *U* test was used to analyze quantitative data.

### Results

Of 142 patients, 41, 71, and 28 were diagnosed with BPPV, VD, and BPPV + VD, respectively. The patient and healthy control groups were similar in terms of age and sex (*P* > .05). The hemogram parameters, particularly the WBC, neutrophil count, lymphocytes, platelets, and MPV, were in the normal range and did not differ significantly between the study groups (refer to Tables 1-3 for *P* values). When the NLR and PLR of the patients were calculated both together and separately according to subgroup, there was no statistically significant difference in comparison with the control group (refer to Tables 1-3 for *P* values).

### Discussion

As markers of inflammation and immune responses, the NLR, PLR, and MPV are highly repeatable, inexpensive, and widely available; indeed, they are as valuable as some inflammatory

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**Table 1. Comparison of the BPPV and Control Groups.**

|                  | BPPV Mean ± SD/n (%) | BPPV Med (min-max) | Control Group Mean ± SD/n (%) | Control Group Med (min-max) | P       |
|------------------|-----------------------|--------------------|--------------------------------|----------------------------|---------|
| Age              | 45.5 ± 15.01          | 49                 | 42.2 ± 12                      | 42                         | .087 m  |
| Sex              |                       |                    |                                |                            |         |
| Female           | 25 (58.1)             |                    | 71 (67.6)                      |                            | .273    |
| Male             | 18 (41.9)             |                    | 34 (32.4)                      |                            |         |
| WBC              | 7.6 ± 1.6             | 7.5                | 7.5 ± 1.3                      | 7.7                        | .904 m  |
| Lymphocyte       | 2.6 ± 1.03            | 2.5                | 2.6 ± 0.6                      | 2.5                        | .919 m  |
| Neutrophil       | 4.5 ± 1.6             | 4.1                | 4.3 ± 0.9                      | 4.4                        | .570 m  |
| PLT              | 235.0 ± 59.2          | 230                | 245.2 ± 60.4                   | 234                        | .385 m  |
| MPV              | 9.2 ± 1.1             | 9.0                | 9.1 ± 1.4                      | 9.1                        | .949 m  |
| NLR              | 2.1 ± 1.8             | 1.7                | 1.7 ± 0.4                      | 1.7                        | .928 m  |
| PLR              | 98.4 ± 32.6           | 93                 | 97.4 ± 32.8                    | 91                         | .677 m  |

Abbreviations: BPPV, benign paroxysmal positional vertigo; m, Mann-Whitney U test; max, maximum value; Med, median value; min, minimum value; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; PLT, platelet; PLR, platelet-to-lymphocyte ratio; SD, standard deviation; WBC, white blood cell. $\chi^2$. Chi-square test.
markers that are more expensive to assess, including interleukin (IL)-6, IL-1β, IL-8, and tumor necrosis factor-α.6,10

The NLR and PLR are inflammatory parameters that are associated with a poor prognosis due to their association with atherosclerosis and atherothrombosis in peripheral arterial occlusive disease.11-13

The NLR has advantages compared to other WBC subtype parameters (eg, neutrophil, lymphocyte, and total leukocyte counts); namely, its stability compared to other WBC subtype counts, which can be affected by various physiological and pathological conditions. Furthermore, NLR may indicate both inflammatory and immunological processes.1 Mean platelet volume, an indicator of platelet activation, is also used as a marker of atherothrombosis.14 Larger platelets are often younger, metabolically and enzymatically more active, and produce more thrombogenic factors. Mean platelet volume is one of the most extensively studied platelet activation markers.1,14

Demirin et al15 found the normal range of MPV in healthy Turkish people to be 8.9 ± 1.4 fL; 95% of the individuals had an MPV between 7.2 and 11.7 fL. The MPV of both the patient and control groups in our study (9.2 ± 1.2 and 9.1 ± 1.4 fL, respectively) were in the normal range and were similar to the findings of Demirin et al.15

Recently, Ozbay et al3 investigated the NLR in PV patients and found a significantly higher NLR value in PV patients compared with healthy people. They concluded that the higher NLR was due to a stress-related inflammatory mechanism in PV patients. Therefore, they suggested that the NLR may be a novel marker for monitoring patients with PV during follow-up.

Peripheral vertigo is a symptom rather than a primary disease that can be caused by many disorders with various pathophysiologies. Therefore, the NLR and/or PLR of some PV patients who have obvious inflammatory or neoplastic diseases (eg, labyrinthitis or acoustic neuroma) possibly may be high. But until now, no published study has investigated this issue. In view of their relatively small amount, we could not include the vertigo patients with diagnosis of labyrinthitis, acoustic

### Table 2. Comparison of the Vestibular Dysfunction (VD) and Control Groups.

|                      | VD                  | Control Group         | P       |
|----------------------|---------------------|-----------------------|---------|
|                      | Mean ± SD/n (%)     | Med (min-max)         |         |
| Age                  | 44.2 ± 12.5         | 48 20 65              | .088 m  |
| Male                 | 22 (31.0)           | 34 (32.4)             | .845    |
| Gender               |                     |                       |         |
| Female               | 49 (69.0)           | 71 (67.6)             |         |
| Male                 | 22 (31.0)           | 34 (32.4)             |         |
| WBC                  | 7.3 ± 1.6           | 7.3 3.7 11.0          | .154 m  |
| Lymphocyte           | 2.5 ± 0.8           | 2.4 0.8 4.4           | .064 m  |
| Neutrophil           | 4.3 ± 1.2           | 4.0 2.0 7.5           | .431 m  |
| PLT                  | 244.3 ± 64.8        | 246 53 439            | .695 m  |
| MPV                  | 9.2 ± 1.0           | 9.0 7.5 12.0          | .937 m  |
| NLR                  | 2.0 ± 1.1           | 1.7 0.0 6.8           | .616 m  |
| PLR                  | 109.0 ± 43.2        | 103 41 272            | .051 m  |

Abbreviations: m, Mann-Whitney U test; max, maximum value; Med, median value; min, minimum value; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; PLT, platelet; PLR, platelet-to-lymphocyte ratio; SD, standard deviation; WBC, white blood cell; χ², Chi-square test.

### Table 3. Comparison of the BPPV + Vestibular Dysfunction (VD) and Control Groups.

|                      | BPPV + VD            | Control Group         | P       |
|----------------------|----------------------|-----------------------|---------|
|                      | Mean ± SD/n (%)      | Med (min-max)         |         |
| Age                  | 43.0 ± 15.8          | 44 18 65              | .720 m  |
| Male                 | 8 (28.6)             | 34 (32.4)             | .700    |
| Gender               |                     |                       |         |
| Female               | 20 (71.4)            | 71 (67.6)             |         |
| Male                 | 8 (28.6)             | 34 (32.4)             |         |
| WBC                  | 7.5 ± 1.6            | 7.8 4.0 9.8           | .871 m  |
| Lymphocyte           | 2.4 ± 0.7            | 2.5 0.8 3.7           | .211 m  |
| Neutrophil           | 4.6 ± 1.2            | 4.7 1.8 6.3           | .203 m  |
| PLT                  | 228.3 ± 76.1         | 225 4 393             | .259 m  |
| MPV                  | 9.3 ± 1.1            | 9.1 7.7 12.5          | .751 m  |
| NLR                  | 2.1 ± 1.0            | 1.8 0.9 6.3           | .065 m  |
| PLR                  | 102.9 ± 43.6         | 101 1 251             | .320 m  |

Abbreviations: BPPV, benign paroxysmal positional vertigo; m, Mann-Whitney U test; max, maximum value; Med, median value; min, minimum value; MPV, mean platelet volume; NLR, neutrophil-to-lymphocyte ratio; PLT, platelet; PLR, platelet-to-lymphocyte ratio; WBC, white blood cell; χ², Chi-square test.
The most common type of PV is BPPV, which affects 2.4% of the population.\textsuperscript{8} Benign paroxysmal positional vertigo causes more than half of all cases of PV.\textsuperscript{3} Other common causes of PV are Meniere disease, vestibular neuritis, and, less frequently, acoustic neuroma, infection, or trauma.\textsuperscript{16}

To the best of our knowledge, neither immune nor inflammatory mechanisms play a role in the pathogenesis of BPPV, which is caused by the accumulation of calcium crystals in the semicircular canals.\textsuperscript{16,17} The crystals hinder the movement of endolymph in the semicircular canals, leading to vertigo. Interestingly, vasospasm and atherosclerosis are thought to predispose individuals to BPPV.\textsuperscript{17} Therefore, we separated the vertigo patients into 3 groups depending on the presence of BPPV: BPPV only, BPPV along with another peripheral vestibular disorder (BPPV + VD), and those with a peripheral vestibular disorder without BPPV (VD). Despite this, there was no statistically significant difference between the patient groups and the control groups regarding the NLR, PLR, or MPV. Additionally, there was no statistically significant difference between the control group and each patient group when they were analyzed separately. Although the NLRs and PLRs of the patient groups were higher than those of the control group, this difference was not statistically significant.

Unlike our results, Ozbay et al found a statistically significant higher NLR value in PV (\(P < 0.05\)). However, NLR values of their study groups were very close to ours (PV group: 2.2, and control group: 1.8) and were in normal range which is reported as 0.78 to 3.53.\textsuperscript{18} This discrepancy of results may be due to the small number of samples.

While an increase in NLR and PLR is expected in inflammatory processes and the PLR and MPV are increased in immune and vascular pathologies, the fact that there was no significant change in any of these parameters in patients with PV regardless of their final diagnosis demonstrates that no systemic reaction is given by the organism to this condition.

To the best of our knowledge, this is the first study to investigate the NLR, PLR, and MPV in patients with PV; our findings suggest that the NLR, PLR, and MPV are not affected in the PV.

Authors’ Note

1. The English in this document has been checked by at least 2 professional editors, both native speakers of English. For a certificate, please see: http://www.textcheck.com/certificate/e0153092. All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards. Informed consent was obtained from all individual participants included in the study.

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Declaration of Conflicting Interests

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References

1. Kum RO, Ozcan M, Baklaci D, et al. Investigation of neutrophil-lymphocyte ratio and mean platelet volume in sudden hearing loss. Braz J Otorhinolaryngol. 2015;81(6):636-641.

2. Ozler GS, Gunak G. Neutrophil–lymphocyte ratio: a new predictive and prognostic factor in patients with Bell palsy. J Craniofac Surg. 2014;25(3):944-945.

3. Ozbay I, Kahraman C, Balikci HH, et al. Neutrophil-to-lymphocyte ratio in patients with peripheral vertigo: a prospective controlled clinical study. Am J Otolaryngol. 2014;35(6):699-702.

4. Seo YJ, Jeong JH, Choi JY, Moon IS. Neutrophil-to-lymphocyte ratio and platelet-to-lymphocyte ratio: novel markers for diagnosis and prognosis in patients with idiopathic sudden sensorineural hearing loss. Dis Markers. 2014;2014:702-807.

5. Osadnik T, Wasilewski J, Lekston A, et al. The platelet-to-lymphocyte ratio as a predictor of all-cause mortality in patients with coronary artery disease undergoing elective percutaneous coronary intervention and stent implantation. J Saudi Heart Assoc. 2015;27(3):144-151.

6. Gasparyan AY, Ayvazyan L, Mikhailidis DP, Kitas GD. Mean platelet volume: a link between thrombosis and inflammation? Curr Pharm Des. 2011;17(1):47-58.

7. Petri M, Chirila M, Bolboaca S, Cosgarea M. Unilateral peripheral vestibular disorders in the emergency room of the ENT department of Cluj-Napoca, Romania. Clujul Med. 2015;88(2):181-187.

8. M von Brevern M, Radtke A, Lezius F, et al. Epidemiology of benign paroxysmal positional vertigo: a population based study. J Neurol Neurosurg Psychiatry. 2007;78(7):710-715.

9. Chang TP, Lin YW, Sung PY, Chuang HY, Chung HY, Liao WL. Benign paroxysmal positional vertigo after dental procedures: a population-based case-control study. PLoS One. 2016;11(4):e0153092.

10. Turkmen K, Guneý I, Yerlikaya FH, Tonbul HZ. The relationship between neutrophil-to-lymphocyte ratio and inflammation in end-stage renal disease patients. Ren Fail. 2012;34(2):155-159.

11. Papa A, Emdin M, Passino C, Michelassi C, Battaglia D, Cocci F. Predictive value of elevated neutrophil-lymphocyte ratio on cardiac mortality in patients with stable coronary artery disease. Clinica Chimica Acta. 2008;395(1-2):27-31.
12. Tamhane UU, Aneja S, Montgomery D, Rogers EK, Eagle KA, Gurm HS. Association between admission neutrophil to lymphocyte ratio and outcomes in patients with acute coronary syndrome. *Am J Cardiol.* 2008;102(6):653-657.

13. Gary T, Pichler M, Belaj K, et al. Platelet-to-lymphocyte ratio: a novel marker for critical limb ischemia in peripheral arterial occlusive disease patients. *Plos One* 2013;8(7):e67688.

14. Ozkan B, Uysal OK, Duran M, et al. Relationship between mean platelet volume and atherosclerosis in young patients with ST elevation myocardial infarction. *Angiology.* 2013;64(5):371-374.

15. Demirin H, Ozhan H, Ucgun T, et al. Normal range of mean platelet volume in healthy subjects: insight from a large epidemiologic study. *Thromb Res.* 2011;128(4):358-360.

16. Dommaraju S, Perera E. An approach to vertigo in general practice. *Aust Fam Physician.* 2016;45(4):190-194.

17. Cohen HS, Kimball KT, Stewart MG. Benign paroxysmal positional vertigo and comorbid conditions. *ORL J Otorhinolaryngol Relat Spec.* 2004;66(1):11-15.

18. Forget P, Khalifa C, Defour JP, Latinne D, Van Pel MC, De Kock M. What is the normal value of the neutrophil-to-lymphocyte ratio? *BMC Res Notes.* 2017;10(1):12.