RESEARCH ARTICLE

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Mean platelets volume and neutrophil to lymphocyte ratio as predictors of stroke

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Background: Mean platelets volume (MPV) is a marker, which indicates platelet function, and is a potential link between inflammation and thrombosis. Previous studies have found a relation between high MPV levels and high risk of stroke. Another factor that has been associated with the risk of stroke is neutrophil to lymphocyte ratio (NLR). Several studies have reported an association between increased NLR and increased risk of cerebrovascular disease. It was found that NLR levels have a relation to the prognosis as well. Since both NLR and MPV have been associated with increased risk of cardiovascular disease, together they may predict the risk of stroke and the prognosis with higher sensitivity and specificity.

Methods: This is a descriptive retrospective study. Data were gathered from medical records of patients who applied the Ziv medical center and were diagnosed with stroke. Stroke severity was evaluated using the NIHSS (national institutes of health stroke scale). MPV and NLR levels of patients with stroke were compared to those of 30 healthy individuals.

Results: Neutrophil to lymphocyte ratio levels were found significantly higher in patients with stroke compared with healthy individuals. NLR was also found higher in patients with moderate/severe stroke compared with those with minor stroke. No association was found between MPV level, the risk of stroke, and stroke prognosis. Moreover, an interaction effect between MPV and NLR level was not found.

Conclusion: Neutrophil to lymphocyte ratio is a good predictive factor of stroke and stroke prognosis. Further prospective studies are needed to establish the relationship between the MPV level and the risk of stroke. NLR and MPV interaction effect can be tested again in the future after establishing the association between MPV, the risk of stroke, and stroke prognosis.

KEYWORDS
mean platelet volume, neutrophil to lymphocyte ratio, platelets activation, risk factor, stroke

1 | INTRODUCTION

The primary role of platelets is preventing excess bleeding, but they also play an important role in maintaining the integrity of the endothelium.[1] Improper interaction between platelets and the endothelium is found to be a pathogenic mechanism in the development of atherosclerosis. Platelets attach to the endothelium in response to different inflammatory signals. This attachment stimulates the production of various molecules that provide a positive feedback for further activation of endothelial cells.[2]

Mean platelets volume (MPV) is the most common used measure of platelets size and it is a marker of platelets function.[3] A number of studies have found a relation between MPV and cardiovascular diseases. One study followed 3134 patients with cerebrovascular disease,

and it was found that Stroke rates were greater among individuals with higher measured MPV, both in all stroke types and for ischemic stroke alone.[4] In patients with atrial fibrillation, stroke events rate increased significantly among patients with higher MPV. Moreover, although some patients had a low to intermediate traditional thromboembolic risk (CHADS2 <2), if they had a high MPV level they were at risk for ischemic stroke, especially in cases without anticoagulation treatment.[5] MPV was also found to be related to stroke severity; MPV measured within the first 24 hours of brain stroke was strongly related to the severity of the disease, and effectively discriminate a severe situation from a milder degree of the disorder.[6]

Another factor known as related to cardiovascular disease is neutrophil to lymphocyte ratio (NLR). In a number of studies, NLR was found to be significantly greater in ischemic stroke patients in relation to control.[7,8] There is also evidence to the relation between NLR and prognosis. Among ischemic stroke patients NLR was higher in dead patients.[8,9]

Since both NLR and MPV have been associated with increased risk of cardiovascular disease, together they may predict the risk of stroke and stroke prognosis with higher sensitivity and specificity.

1.1 | Research hypothesis

Neutrophil to lymphocyte ratio and MPV were predicted to be higher among patients with stroke, as found in previous studies. Together, MPV and NLR predict the risk of stroke better than MPV or NLR by themselves. In addition, in patients with severe strokes, MPV and NLR levels will be higher, compared with patients with minor strokes.

This is the first study that refers to the common effect of NLR and MPV on the risk of stroke and stroke prognosis. Showing the interaction between these two factors may allow predicting the risk of stroke and the prognosis with higher specificity and sensitivity.

2 | MATERIALS AND METHODS

This is a descriptive retrospective study. Data were gathered from medical records of patients who applied the Ziv medical center from January 2012 to May 2015.

Mean platelets volume level was gathered from patients complete blood count, and NLR was calculated as the ratio of lymphocyte and neutrophil counts. Stroke severity was evaluated using the NIHSS (national institutes of health stroke scale). NIHSS was determined by a neurologist at the time of admission. In cases in which the NIHSS was not mentioned in the record, it was calculated according to the physical examination description at the time of admission.

The study includes 200 Patients who were diagnosed with stroke; 160 patients with minor stroke (NIHSS: 1-4), 30 patients with moderate/severe stroke (NIHSS: 16-20), and 10 patients with severe stroke (NIHSS: 21-42). Patients with NIHSS of 16 and above were considered as a single study group.

Mean platelets volume and NLR levels of patients with stroke were compared to those of 30 healthy individuals. Data regarding healthy individuals were obtained from previous studies conducted in the hospital.

The Helsinki committee of Ziv medical center approved the study during March 2015.

2.1 | Statistics

Continuous variables are defined as mean ± standard deviation, and categorical variables are given as percentages. Independent sample t test or Mann-Whitney U test were used for continuous variables, and chi-square test for categorical variables. One-way analysis of variance (ANOVA) or Kruskal-Wallis tests were used to compare more than two groups. Correlations were assessed using Spearman's test. Receiver operating characteristic (ROC) curve analysis was used to determine the optimum cut-off level of NLR to predict stroke. Statistical analyses were performed using Statistical Package for Social Sciences (SPSS) Version 15.0 (SPSS Inc., Chicago, Illinois). Any P value <.05 was considered statistically significant.

Data were analyzed using multiple logistic regression and two-tailed t test with confidence interval of 95% and power of 80%.

3 | RESULTS

3.1 | General characteristics

The study population included 200 patients with stroke, 118 men and 82 women. The mean age was 68.4 years. Among the study population, 199 patients were diagnosed with ischemic stroke and one patient was diagnosed with hemorrhagic stroke.

Data regarding the patients with stroke were compared to a control group of 30 healthy individuals.

3.2 | MPV and NLR levels

Among patients with stroke, the MPV levels ranged from 6.4 fL to 16.6 fL (Median 8.6 fL; Mean 8.73 (SD 1.18 fL)). Nine patients had MPV levels outside the normal range of 6.7-11.1 fL, four patients had MPV level below 6.7, and five patients had MPV level above 11.1 fL. The NLR ranged from 0.45 to 13.6 (Median 2.61; Mean 3.44 (SD 2.56)).

Among the control group, MPV levels ranged from 7.5 fL to 12.6 fL (Median 9 fL; Mean 9.24 (SD 1.28 fL)). One patient had MPV level above the normal range. The NLR ranged from 1.07 to 3.46 (Median 1.7; Mean 1.89 (SD 2.3)).

No differences were found in the levels of MPV and NLR in the men group comparing to the women group.

3.3 | MPV, NLR, and the risk of stroke

Two-tailed t test revealed no significant difference in the MPV levels of the stroke group compared to the controls (t(228)=−1.56; P=.11; Table 1). However, there is a significant difference in the NLR levels of the stroke group compared to the controls (t(228)=2.32; P=.021; Table 1).

TABLE 1 The association between MPV and NLR levels and the risk of stroke

Study group	Mean	SD	t	P value
MPV				
Control	9.24	1.33	−1.56	.11
Stroke	8.73	1.18		
NLR				
Control	1.89	0.61	2.32	.021
Stroke	3.44	2.56		

MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio.

TABLE 2 The association between MPV and NLR levels and stroke severity

Study group	Mean	SD	t	P value
MPV				
Minor stroke	8.74	1.16	.16	.86
Moderate/severe stroke	8.71	1.28		
NLR				
Minor stroke	3.18	2.19	−2.91	.004
Moderate/severe stroke	4.48	3.53		

MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio.

3.4 | MPV, NLR, and the stroke severity

Two-tailed t test revealed no significant difference in the MPV levels of the minor stroke group compared to the moderate/severe stroke group (t(198)=0.16; P=.86; Table 2). However, there is a significant difference in the NLR levels of the minor stroke group compared to the moderate/severe stroke group (t(198)=32.91; P=.004; Table 2).

3.5 | MPV and NLR interaction effect

Multiple logistic regression was used to examine the interaction between MPV and NLR levels and their effect on stroke severity. It was found that the model is not statistically significant (chi-square=9.27, P=.026; Table 3).

4 | DISCUSSION

In this study, no association was found between the MPV level, the risk of stroke, and stroke prognosis. Previous studies show inconsistent results; some studies have found a relation between high MPV level and high risk of stroke.[4–6] However, there are also studies in which such association was not found. In one study, the MPV level measured within the first 24 hours after stroke onset was not found to be associated with stroke severity or outcome.[10] Another study compared the MPV level in patients with cerebrovascular event, patients with different degrees of carotid stenosis, and healthy volunteers. No difference was found between the MPV levels of the groups.[11]

TABLE 3 MPV and NLR interaction effect

	B	Wald	P value	Exp(B)
MPV	.31	1.45	.22	1.37
NLR	.86	2.74	.097	.37
MPV & NLR	−.82	1.81	.17	.92

MPV, mean platelet volume; NLR, neutrophil to lymphocyte ratio.

The MPV level is influenced by a number of factors; a randomized controlled trail measured a lower MPV level after 4 weeks of antiplatelet drugs treatment.[12] Since 163 of the patients included in our study had at least one background disease (previous stroke, hypertension, diabetes mellitus, atrial fibrillation, etc.), some of them may have been under antiplatelet drugs treatment at the time of admission, a fact that could have affected their MPV level. Another explanation to the inconsistency in the results is the different methods used to measure MPV level in different laboratories. Further studies, neutralizing factors that affect the MPV level, are needed to establish the relationship between the MPV level and the risk of stroke. One possibility is to include only patients who are not treated with antiplatelet drugs.

In agreement with previous reports, this study shows an association between the NLR level, the risk of stroke, and stroke prognosis. NLR levels were found higher in patients with stroke than in controls. In addition, NLR levels were found higher in patients with moderate/severe stroke than in patients with minor stroke. This results support the notion that NLR is a good predictive factor of stroke and stroke prognosis. It is important to note that this study included patients with stroke in different areas of the brain, this fact could affect the results since the severity of stroke was determined by the NIHSS, which has a good correlation with the middle cerebral artery infracts but underestimates severity of posterior circulation strokes.[13]

Finally, several studies also showed that lower levels of MPV, were observed in patients with active or chronic inflammation such as rheumatoid arthritis, familial Mediterranean fever (FMF) and other conditions, of which MPV may be used as a negative acute-phase reactant.[3,14] In our study, there was an inversely significant correlation between MPV and NLR, this new finding was not observed before, in patients with stroke, but no conclusions can be made of these data at this point, it is obvious that we need more prospective studies with large sample to determine whether there is an increase level of MPV in addition to NLR in patients with stroke without treatment or decrease level of MPV as negative acute case reactant.

5 | CONCLUSION

This study is the first to assess the interaction effect of MPV and NLR in predicting stroke risk and stroke prognosis; however, this effect has not been shown. These results are not surprising since no difference in the MPV level between the study groups was found. This interaction effect can be tested again in the future after establishing the association between MPV, the risk of stroke, and stroke prediction, but

the study showed that NLR is a good predictive factor of stroke and stroke prognosis.

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