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Research Article

# Can Neutrophil-Lymphocyte and Platelet-Lymphocyte Ratios Predict the Risk of Developing New Ischemic Lesions After Carotid Stenting?

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**Abstract**

**Aim:** It has been reported that the neutrophil-lymphocyte ratio (NLR) and platelet-lymphocyte ratio (PLR) are associated with carotid artery stenosis rate, risk of restenosis after stenting, and clinical outcome after an ischemic stroke, and are also predictive markers. The objective of this study is to evaluate whether NLR and PLR values and the associated temporal changes are indicators of the risk for newly developing ischemic lesions.

**Material and Methods:** Patients who underwent stenting in our clinic between November 2019 and January 2022 and who had a complete blood count and a diffusion magnetic resonance imaging scan before and after the procedure, were included in the study and evaluated in two groups; patients with and without newly developing ischemic lesions.

**Results:** Newly developing ischemic lesions were detected in 27 of the 50 patients included in the study. There was no difference in baseline and 48th-hour NLR and PLR rates and the temporal variation of these rates between patients with and without newly developing ischemic lesions. Erythrocyte distribution width (RDW) and hemoglobin (HGB) values were higher in the without newly developing ischemic lesions group at 48 hours, but there was only a significant difference between the RDW temporal change between the two groups. In the correlation analysis, no significant correlation was found between NLR, PLR, and their temporal changes, ipsilateral and contralateral stenosis rates, age, and residual stenosis rates.

**Conclusion:** There was no significant relationship between the development of newly developing ischemic lesions and NLR and PLR values and the associated temporal changes.

**Keywords:** Carotid stenosis, stents, neutrophil, lymphocyte, platelet, red cell distribution width

## INTRODUCTION

Atherosclerosis, a systemic inflammatory disease affecting arterial vessels, is one of the common causes of carotid artery stenosis and ischemic stroke (1,2). Although its incidence varies depending on the etiological classification used, carotid artery stenosis is said to cause 15% of all ischemic strokes and transient ischemic attacks (TIA) on average (2,3).

Current guidelines recommend carotid stenting (CAS) for the treatment of carotid stenosis as an alternative to carotid endarterectomy (CEA) in suitable patients (4). It is known that the frequency of minor ischemic stroke is slightly higher in carotid stenting (4). It is also known that after CAS, new ischemic lesions may develop without clinical signs. The studies that addressed newly onset ischemic lesions developing after the CAS procedure by diffusion magnetic resonance imaging (dMRI) reported the incidence of new lesions in a wide range between 18% and 72% (5,6).

It is known that neutrophils and platelets have an important role in the pathophysiology of atherosclerosis, an inflammatory disease (1,7).

Given that these parameters are an indicator of inflammation and are associated with prognosis, it

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was speculated that evaluating them within the scope of neutrophil-lymphocyte ratio (NLR) and the platelet-lymphocyte ratio (PLR) would serve as a better indicator instead of evaluating them individually (8,9). It has been reported that NLR and PLR predict clinical outcomes in many diseases such as cardiovascular, rheumatological and oncological diseases and intensive care unit patients (9,10). Additionally, NLR and PLR were successfully used as a marker in predicting the third-month clinical outcome in acute ischemic stroke (11,12). In studies evaluating the relationship between NLR and PLR values and carotid stenosis rate, plaque morphology, clinical outcome after stenting, and restenosis risk, NLR and PLR values have generally been reported to be good predictive markers (9,13,14).

We could not find a study in the literature that evaluated the relationship between NLR and PLR and the risk of ischemic lesion development after carotid stenting. In the current study, it was aimed to evaluate the relationship between NLR and PLR values and their temporal changes, which were found to be good predictive markers in studies of carotid artery disease ischemic strokes, and the risk of developing newly onset ischemic lesions after carotid stent placement.

## MATERIAL AND METHOD

After receiving the ethics committee's approval, the files of patients who underwent carotid stenting at our clinic between November 2019 and January 2022 were retrospectively reviewed (2022/245, 11.10.2022). Patients with symptomatic ICA stenosis of 50% or more and patients with asymptomatic ICA stenosis of 70% or more were included in the study. Of 118 patients who had carotid stenting during the study period, 45 were excluded from the study due to lack of control blood count examination and 23 because control dMRI was not performed, and 50 patients were included in the study. The study comprised patients who were older than 18 and who had undergone a complete blood count and dMRI before and within 48 hours (24-48 hours) of the procedure. Patients who had acute stent insertion, whose data could not be accessed, and who missed their follow-up visits were excluded from the study.

Patients' age, gender, vascular risk factors, stented ICA side, ipsilateral and contralateral stenosis rates, and whether they were symptomatic or not were noted. ICA stenosis rates were calculated from DSA images according to the NASCET method. Patients who had a stroke or TIA on the same side as the stenosis within the last six months were considered symptomatic.

Patients who underwent carotid stenting had been receiving dual antiplatelet therapy (acetylsalicylic acid and clopidogrel or ticagrelor) for at least five days. There were no patients receiving anticoagulant therapy. Statin therapy was initiated in patients with hyperlipidemia. Whether a balloon angioplasty was performed or not, at what stage it was performed and residual stenosis rates were noted. The patients were split into two groups as those with newly developing ischemic lesions and those without newly developing ischemic lesions in the dMRIs at the 48th-hour post-procedure. Entry data of the patients were expressed as NLR1, PLR1 and RDW1, and 48th hour values were expressed as NLR2, PLR2 and RDW2. The temporal variation in these values was specified as NLR2-NLR1, PLR2-PLR1 and RDW2-RDW1.

### Statistical Analysis

Data were evaluated with SPSS 21.0 (IBM Corp., Armonk, NY, U.S., 2012) software. Categorical variables as numbers and percentages; numerical data were expressed as mean±standard deviation (SD). Whether the data met the criteria for normal distribution was evaluated with the Shapiro wilk test. Independent sample t-test or Mann-Whitney U test was used to compare two independent groups. Spearmen and Pearson correlation analysis test was used to determine the level and direction of the relationship between dependent variables. Chi-square test was used to evaluate the relationship between categorical variables. Significance level was accepted as $p<0.05$.

## RESULTS

Among the 118 patients who had carotid stenting during the study date range, 50 patients who met the inclusion criteria were included in the study. In the 48th-hour dMRI examination, newly developing ischemic lesions were detected in 27 patients (54%), but not in 23 (46%) patients.

Age and gender information, vascular risk factors and procedures-related data of the patients in both groups are given in Table 1. The mean age of the patients with newly developing ischemic lesions was significantly higher than that of the patients without newly developing ischemic lesions ($p=0.017$). The two groups did not differ from one another in terms of other variables.

The data pertaining to the complete blood counts of the patients performed both before and 48 hours after the stenting are given in Table 2. When the postoperative complete blood count data was compared, the HGB2 and RDW2 values in patients with newly developing ischemic lesions were significantly lower than those without newly developing ischemic lesions (respectively $p= 0.032, 0.000$). When the HGB change values were compared between the two groups, no significant difference was found. Comparing the RDW change values, it was discovered that patients without newly developing ischemic lesions had much higher values ($p=0.000$). Between the groups, there was no significant difference in NLR1, NLR2, PLR1 and PLR2 values. In addition, regarding the temporal variations in NLR and PLR values, there was similarly no significant difference between the groups.

In the correlation analysis, no significant correlation was found between NLR, PLR, and their temporal changes, ipsilateral and contralateral stenosis rates, age, and residual stenosis rates (Table 3).

**Table 1. Comparison of vascular risk factors, demographic data and procedural data**

| | New ischemic lesions Yes (27) | New ischemic lesions No (23) | p |
|---|---|---|---|
| **Age** | 71.03±8.02 (54-90) | 64.13±11.65 | 0.017*[1] |
| **Gender M/F (%)** | 15 (55.6) / 12 (44.4) | 18 (78.3) / 5 (21.7) | 0.091[2] |
| **HT yes/no (%)** | 23 (85.2) / 4 (14.8) | 14 (60.9) / 9 (39.1) | 0.051[2] |
| **DM yes/no (%)** | 16 (59.3) / 11 (40.7) | 8 (34.8) / 15 (65.2) | 0.084[2] |
| **HL yes/no (%)** | 17 (63) / 10 (37) | 17 (73.9) / 6 (26.1) | 0.408[2] |
| **CAD yes/no (%)** | 12 (44.4) /15 (55.6) | 9 (39.1) / 14 (60.9) | 0.704[2] |
| **Previous stroke history (%)** | 9 (33.3) / 18 (66.7) | 6 (26.1) / 17 (73.9) | 0.577[2] |
| **Smoker yes/no** | 12 (44.4) /15 (55.6) | 13 (56.5) / 10 (43.5) | 0.395[2] |
| **Symptomatic/ asymptomatic (%)** | 22 (81.5) / 5 (18.5) | 18 (78.3) / 5 (21.7) | 1.000[3] |
| **Stenosis rate** | 75.37±12.69(55-90) | 79.73±11.44 (61-95) | 0.211[1] |
| **Contralateral stenosis rate** | 27.70±32.96(0-100) | 18.69±22.62 (0-80) | 0.270[1] |
| **Left/Right** | 16/11 | 16/7 | 0.449[2] |
| **Angioplasty yes/no** | 18/9 | 19/4 | 0.200[2] |
| **Residual stenosis rate** | 14.22±10.46 | 11.04±10.65 | 0.294[1] |

HT: hypertension, DM: diabetes mellitus, HL: hyperlipidemia,
CAD: coronary artery disease
*p<0.05 [1]Independent Sample T Test, [2]Chi Square test, [3]Fisher Exact test

**Table 2. Comparison of the blood count parameters of the patients**

| New ischemic lesions | Yes | No | p |
|---|---|---|---|
| **WBC1 ($10^3/mm^3$)** | 7.79±1.79 | 8.32±1.83 | 0.312[1] |
| **HGB1** | 12.75±2.02 | 13.47±1.67 | 0.181[1] |
| **Neutrophil1 ($10^3/mm^3$)** | 5.06±1.46 | 5.19±1.25 | 0.742[1] |
| **Lymphocyte1 ($10^3/mm^3$)** | 1.84±.87 | 2.03±0.82 | 0.424[1] |
| **Platelet1 ($10^3/mm^3$)** | 252.37±91.31 | 242.60±57.72 | 0.861[2] |
| **RDW1** | 14.04±1.45 | 13.61±1.93 | 0.073[2] |
| **WBC2 ($10^3$/mm3)** | 8.92±2.46 | 8.88±2.16 | 0.958[1] |
| **HGB2 ($10^3/mm^3$)** | 11.78±1.29 | 12.66±1.50 | 0.032*[1] |
| **Neutrophil2 48th hour ($10^3/mm^3$)** | 6.02±2.17 | 6.29±1.76 | 0.643[1] |
| **Lymphocyte2 48th hour ($10^3/mm^3$)** | 1.88±0.85 | 1.64±0.80 | 0.318[1] |
| **Platelet2 48th hour ($10^3/mm^3$)** | 230.14±56.91 | 212.30±81.25 | 0.368[1] |
| **RDW2 48th hour** | 13.50±0.77 | 16.33±3.99 | 0.000*[2] |
| **NLR1** | 3.27±1.48 | 2.96±1.53 | 0.472[1] |
| **PLR1** | 163.87±105.47 | 141.43±61.41 | 0.633[1] |
| **NLR2** | 4.68±5.94 | 4.75±3.60 | 0.158[2] |
| **PLR2** | 162.01±108.98 | 149.54±69.28 | 0.704[2] |
| **NLR2-NLR1** | 1.47±6.67 | 1.79±4.14 | 0.083[2] |
| **PLR2-PLR1** | -1.80±158.42 | 10.19±94.41 | 0.397[2] |
| **RDW2-RDW1** | -0.55±1.63 | 2.63±4.57 | 0.000*[2] |

WBC: White blood cells HGB: Hemoglobin, RDW: Red cell distribution width, NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio,
*P<0.05 [1]Independent Sample T test, [2]Mann Whitney U test

**Table 3. Correlation analysis**

| Pearson correlation | | NLR | PLR | NLR2-NLR1 | PLR2-PLR1 |
|---|---|---|---|---|---|
| Stenosis rate | r | -0.045 | -0.167 | 0.025 | 0.142 |
| | p | 0.758 | 0.246 | 0.862 | 0.325 |
| Contralateral stenosis rate | r | 0.153 | 0.024 | -0.139 | -0.128 |
| | p | 0.287 | 0.871 | 0.335 | 0.374 |
| Residual stenosis rate | r | 0.078 | 0.069 | -0.045 | 0.028 |
| | p | 0.589 | 0.634 | 0.755 | 0.845 |
| Age | r | -0.70 | -0.46 | 0.195 | 0.037 |
| | p | 0.631 | 0.750 | 0.175 | 0.796 |

NLR: Neutrophil-lymphocyte ratio, PLR: Platelet-lymphocyte ratio

## DISCUSSION

In this study, no significant correlation was found between the development of newly developing ischemic lesions after carotid stenting, pre-procedural and 48th-hour NLR and PLR values, and the temporal changes of these rates.

Hyun et al. (15) reported a significant relationship between carotid intima thickness and NLR values in patients who had suffered a stroke due to carotid artery disease. Corriere et al. (13) reported that there was a significant relationship between NLR values and the detection of plaque in the carotid artery. Jiang et al. (16) reported a significant correlation between the NLR value and the rate of carotid stenosis in patients who underwent digital subtraction angiography (DSA). In our study, however, no significant relationship was observed between the rate of carotid stenosis and NLR.

In another study, Deşer et al. (17) found that NLR and PLR values were significantly higher in patients with >70% stenosis and detected a significant relationship between stroke risk after CEA and increased PLR values. In a study by Varım et al. (14), mean PLR was found to be significantly higher in patients with stenosis greater than 50% in symptomatic patients and more than 80% in asymptomatic patients. In our study, however, no significant relationship was observed between the rate of carotid stenosis and PLR.

Keskin et al. (18) evaluated patients who underwent carotid stenting and reported that there was an independent relationship between mortality and major cardiovascular events and the systemic immune-inflammation index. On the other hand, in the study reported by Zhengze Dai et al. (19), a significant relationship was found between stent restenosis and NLR value in asymptomatic patients, but not in symptomatic patients. Yet in another study, stent restenosis was found to be positively correlated with NLR (20). In our study, only the relationship between silent new ischemic lesions and NLR and PLR was evaluated, and no significant relationship was found.

It is known that the risk of a periprocedural stroke increases in carotid stenting in patients aged over 70 (21). In our study, the mean age of the patients with newly developing ischemic lesions was significantly higher, which was consistent with the literature.

Furere et al. (22) reported a significant relationship between carotid intima media thickness and RDW and concluded that a high RDW value is an indicator of severe carotid atherosclerosis. Similarly, in another study, a significant relationship was found between elevated RDW values and the risk of having a symptomatic plaque (23). Studies that investigated the RDW values in patients who have suffered an ischemic stroke have also reported a relationship between RDW values and the severity and clinical outcome of the stroke (24). In our study, no correlation was observed between RDW and the rate of carotid stenosis. It was observed that the postoperative RDW increase was significantly higher in patients who did not develop new ischemic lesions. Although it is difficult to explain this situation, it may be related to the younger age of the patients who do not develop new ischemic lesions.

### Limitations of the Study

Apart from its strengths, such as being the first study that addressed the relationship between the development of newly onset ischemic lesions after the CAS procedure and NLR and PLR values, there were also some limitations, such as its retrospective nature and its relatively small sample size.

## CONCLUSION

Contrary to what has been hypothesized initially, no significant relationship was found between the development of newly onset ischemic lesions after carotid stenting and the NLR and PLR values and the associated temporal changes. These findings may be attributed to the retrospective nature of the study and its relatively small sample size. Hence, large-scale randomized controlled studies are needed.

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