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The relationship between platelet-to-lymphocyte ratio and neutrophil-to-lymphocyte ratio and prognosis in carotid artery endarterectomy

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ABSTRACT

Objectives: In this study, we aimed to analyze the effect of the platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) on prognosis during one-year follow-up after carotid endarterectomy surgery.

Patients and methods: Between October 2012 and December 2019, a total of 250 patients (176 males, 74 females; mean age: 67.7±8.8 years; range, 47 to 94 years) with isolated carotid artery endarterectomies were retrospectively analyzed. All patients' data were obtained from the hospital information management system and hospital archive. The patients were divided into two groups (Group 1, n=232 and Group 2, n=18) according to the one-year mortality rate and the risk factors were analyzed.

Results: During follow-up, the one-year mortality and one-year no mortality groups were compared. Univariate model revealed that there were statistically significant differences between the groups regarding congestive heart failure, platelet count, NLR, and neurological complications ($p<0.05$). Additionally, the multivariate model indicated that congestive heart failure, NLR, and neurological complications were statistically different between the groups ($p<0.05$).

Conclusion: Inflammatory and oxidative stress agents play an important role in the prognosis of cardiovascular diseases. The NLR and PLR may be helpful in understanding carotid artery disease and stroke. The NLR levels, preoperative congestive heart failure, and neurological complications in the early postoperative period seem to be the most important prognostic criteria in terms of mortality during one-year follow-up.

Keywords: Carotid artery endarterectomy, neutrophil/lymphocyte ratio, platelet/lymphocyte ratio.

Stroke is a cerebral injury arising from cerebral perfusion restriction. Carotid artery stenosis is the most important cause. It is associated with increased morbidity and mortality in untreated or unsuccessful cases. Stroke development due to carotid artery stenosis is preventable.[1]

The percentage of atherosclerosis correlates with clinical findings and symptomatology.[2] Therefore, the predisposition factors for atherosclerosis should be evaluated properly in these patients. Hypertension (HT), diabetes mellitus (DM), advanced age, and duration of symptoms are all important risk factors.[3]

The platelet-to-lymphocyte ratio (PLR) and neutrophil-to-lymphocyte ratio (NLR) have a predictive effect on early and late morbidity and mortality in cardiovascular system diseases. It has already been established that the atherosclerosis chronic system progresses through two inflammatory processes. These parameters, which are practical to measure and access, have been assessed as important markers in recent years.[4]

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Platelet count, function, and lymphocyte levels are important markers of chronic inflammation. High platelet levels and low lymphocyte levels are associated with chronic inflammation and a poor prognosis for cardiovascular diseases.[5] In particular, the PLR is a marker that predicts the severity of atherosclerosis, as well as being a marker of inflammation.[6]

In the present study, we aimed to investigate the effects of PLR and NLR on the early period and one-year follow-up results of patients undergoing carotid endarterectomy.

PATIENTS AND METHODS

This single-center, retrospective, cross-sectional, observational study was conducted at Kartal Koşuyolu High Speciality Training and Research Hospital, Department of Cardiovasculary Surgery between October 2012 and December 2019. A total of 250 patients (176 males, 74 females; mean age: 67.7±8.8 years; range, 47 to 94 years) with isolated carotid artery endarterectomies were included in the study. The patients' data were obtained from the hospital information management system and hospital archive. Patients having systemic chronic diseases with end-organ failure, concomitant surgery, severe left ventricular failure (ejection fraction [EF] below 30%), New York Heart Association (NYHA) Class III-IV, decompensated congestive heart failure (CHF), end-stage renal failure disease with hemodialysis, and emergent/urgent surgeries were excluded from the study. All patients' preoperative risk factors were collected. The blood taken for complete blood count analysis was studied in an ethylenediaminetetraacetic acid (EDTA) tube. The XN-1000 device (Sysmex Europe GmbH, Bornbarch 1, 22848 Norderstedt, Germany) was used for the complete blood count analysis.

Symptomatic patients with 50 to 99% stenosis and asymptomatic patients with 60 to 99% stenosis were operated on under the recommendations of the National Vascular and Endovascular Surgery Society, as stated in the guidelines.[1] All patients who did not develop hemorrhagic complications followed with dual antiplatelet therapy in the postoperative period.

Postoperative complications were described as transient ischemic attacks, ischemic strokes, hemorrhagic strokes, cranial nerve damage, vascular complications, and cardiac complications. The patients were divided into two groups (Group 1, n=232 and Group 2, n=18) according to the one-year mortality rate and the risk factors were analyzed.

Radiological study

In accordance with the hospital's preoperative algorithm, all of the admitted preoperative elective patients were first checked for carotid lesions with Doppler ultrasonography (USG). For the confirmation step, if the Doppler USG revealed a 50% or higher degree of stenosis in the carotid artery, the patients were studied with either computed tomography angiography or conventional carotid artery angiography. If the degree of the lesion was 70% or higher, the patient underwent carotid endarterectomy surgery.

Surgical procedure

All patients were operated under general anesthesia. Following the skin incision, subcutaneous, and superficial tissue dissections were made, and vessels were explored. The carotid artery and its branches were explorated and fixed using plastic tapes. Anticoagulation was provided with 5,000 IU of heparin via a systemic intravenous. An endarterectomy was performed, and a patch plasty closure was used to ensure arteriotomy repair.

Statistical analysis

Statistical analysis was performed using the IBM SPSS version 26.0 software (IBM Corp., Armonk, NY, USA). Descriptive data were expressed in mean ± standard deviation (SD), median (min-max), or number and frequency. The distribution of variables was measured using the Kolmogorov-Smirnov test. The independent sample t-test and Mann-Whitney U test were used in the analysis of quantitative independent data. The chi-square test was used in the analysis of the qualitative independent data. The impact level was determined using a receiver operating characteristic (ROC) curve. The effect level on a one-year mortality was investigated using the univariate and multivariate logistic regressions. A p value of <0.05 was considered statistically significant.

RESULTS

Symptomatic carotid artery disease was diagnosed in 119 (47.6%) patients, while other patients were also critical, but asymptomatic. The preoperative clinical status and blood sample test results are shown in Table 1. A total of 58 patients had complications after surgery. The cardiovascular complication rate was 15.6% (n=39). Vascular components of the cardiovascular complications were hematoma, reoperation, and reexploration of the surgical site. Acute coronary syndrome was defined as a cardiac complication, and its rate was 3.2%. Neurological complications were observed in 29 (11.6%) patients; seven of these patients (2.8%) had preoperative neurological sequelae. The preoperative data and details regarding these complications are shown in Table 2.

The age and sex distribution of the patients in Group 1 and Group 2 non-significantly differed (p>0.05). However, body mass index (BMI) values did not differ significantly between the groups (p>0.05). In the group with one-year mortality, the rate of CHF (EF >30%) was found to be significantly higher than in the group without one-year mortality (p<0.05). In the inter-group evaluation, the rates of chronic obstructive pulmonary disease (COPD), HT, DM, dyslipidemia, coronary artery disease, operated coronary artery bypass graft (CABG), smoking, atrial fibrillation rhythm (AFR), symptomatic internal carotid artery (ICA) stenosis, and vertebrobasilar insufficiency (VBI) did not significantly differ (p>0.05).

In the one-year mortality group, platelet count, lymphocyte count, and thyroid-stimulating hormone (TSH) values were significantly lower than the one-year non-mortality group (p<0.05). In the group with

Table 1. Sociodemographic and laboratory parameters

	n	%	Mean±SD	Median	Min-Max
Age (year)			67.7±8.4	68.0	47.0-94.0
Sex					
Female	74	29.6			
Male	176	70.4			
Body mass index (kg/cm^2)			27.8±4.8	27.3	17.7-48.3
Bilateral lesion	89	35			
Congestive heart failure	10	4.0			
Chronic obstructive pulmonary disease	26	10.4			
Hypertension	173	69.2			
Diabetes mellitus	93	37.2			
Dyslipidemia	97	38.8			
Coronary artery disease	155	62.0			
Operated coronary artery bypass graft	51	20.4			
Smoking	96	38.4			
Atrial fibrillation rhythm	12	4.8			
Symptomatic internal carotid artery stenosis	119	47.6			
Vertebrobasilar insufficiency	26	10.4			
White blood cell (×10^3)			7.9±2.0	7.7	3.7-13.5
Hemoglobin			12.8±1.8	13.0	4.3-17.4
Hematocrit			38.8±5.3	39.1	26.5-53.6
Platelet (×10^3)			236.0±66.0	230.5	89.0-579.0
Mean platelet volume			8.6±1.1	8.5	6.2-12.5
Neutrophile			5.0±1.6	4.9	1.9-10.7
Lymphocyte			2.0±0.8	1.9	0.5-5.4
Neutrophil-to-lymphocyte ratio			2.9±1.5	2.6	0.8-13.0
Platelet-to-lymphocyte ratio			136.4±66.5	120.7	28.3-574.0
Monocyte			0.7±0.4	0.6	0.1-6.0
Eosinophile			0.2±0.2	0.2	0.0-0.8
Basophile			0.0±0.0	0.0	0.0-0.2
Platelet distribution width			17.4±3.6	16.9	15.6-50.3
C-reactive protein			6.0±16.9	1.3	0.1-207.0
fT3			4.0±1.2	3.9	2.1-8.3
fT4			9.4±5.1	11.0	0.8-20.9
Thyroid stimulating hormone			1.9±2.0	1.3	0.0-21.4

SD: Standard deviation.

Table 2. Postoperative complications

	n	%	Mean±SD	Median	Min-Max
Right ICA stenosis rate			56.3±35.3	70	0.0-100
Left ICA stenosis rate			67.5±33.5	80	0.0-100
Complication					
No	192	76.8			
Yes	58	23.2			
Neurological complication	29	11.6			
Preoperative neurological complication*	7	2.8			
Transient ischemic attack	3	1.2			
Ischemic stroke	9	3.6			
Hemorrhagic stroke	2	0.8			
Cranial nerve injury/convulsion	8	3.2			
Vascular complication	31	12.4			
Cardiac complication	8	3.2			
Operation time			109.1±33.4	105.0	45.0-300.0
Extubation time			7.0±9.1	5.0	1.0-92.0
Intensive care unit stay			43.0±98.1	24.0	9.0-1100.0
Hospital stay			5.3±5.6	4.0	1.0-44.0
30 days mortality	4	1.6			
1 year mortality	8	7.2			

SD: Standard deviation; ICA: Internal carotid artery; * Patients with neurological sequelae in the preoperative period.

one-year mortality, the NLR values and C-reactive protein (CRP) values were significantly higher than the one-year non-mortality group ($p<0.05$). In the one-year mortality follow-up group, platelet count, lymphocyte count, CRP, and TSH values were statistically significantly higher than in the one-year non-mortality follow-up group ($p<0.05$). The NLR values were higher in the one-year follow-up mortality group and statistically different compared to the non-mortality group ($p<0.05$) (Figure 1). However, the PLR value was not different between the groups ($p>0.05$). Age, sex, BMI, COPD, DM, and HT were not statistically different between the groups ($p>0.05$) (Table 3).

The complication rate and neurological complications were higher in Group 1 ($p<0.05$).

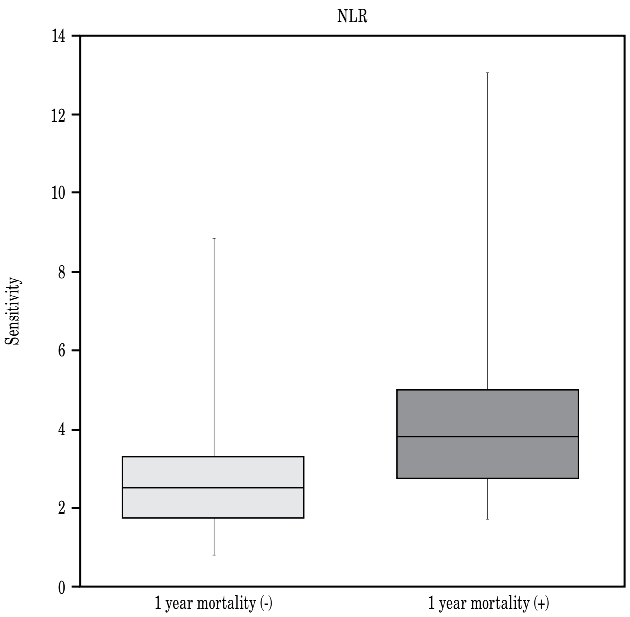

Figure 1. NLR in one year mortality.

NLR: Neutrophil-to-lymphocyte ratio.

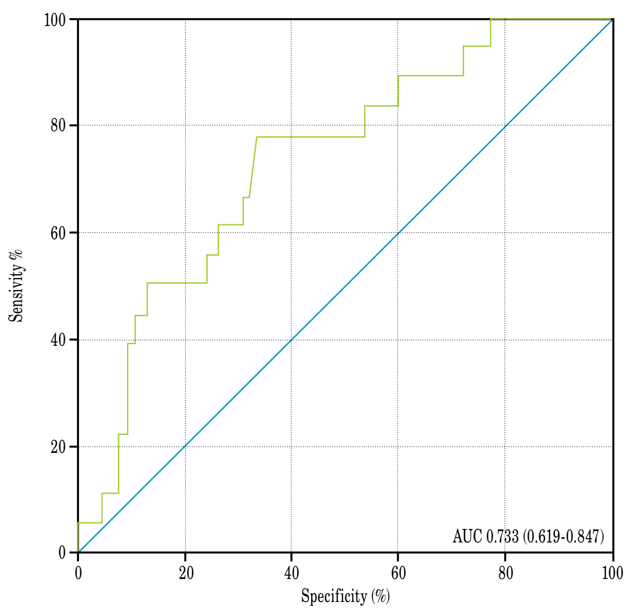

Figure 2. ROC curve analysis.

However, other complications, length of intensive care unit (ICU) stay, total length of hospital stay, extubation time, and total operation time were not statistically different between the groups (Table 4).

Univariate model revealed a statistically significant difference between the groups for CHF, platelet count, NLR, and neurological complications ($p<0.05$). Additionally, the multivariate model indicated that CHF, NLR, and neurological complications were statistically different between the groups (Table 5). When the effect on one-year mortality was examined (Figure 2), a significant effect was observed using a

Table 3. Effect of preoperative parameters on one-year mortality

	1 year mortality (-)				1 year mortality (+)				
	n	%	Mean±SD	Median	n	%	Mean±SD	Median	*p*
Age (year)			67.4±8.3	68.00			71.3±9.3	69.50	0.059*
Sex									0.212‡
Female	71	30.6			3	16.7			
Male	161	69.4			15	83.3			
Body mass index (kg/cm^2)			27.9±4.9	27.34			27.2±3.4	28.13	0.906†
Bilateral lesion	80	89.9			9	10.1			0.075‡
Congestive heart failure	7	3.0			3	16.7			**0.027**‡
Chronic obstructive pulmonary disease	22	9.5			4	22.2			0.102‡
Hypertension	161	69.4			12	66.7			0.809‡
Diabetes mellitus	85	36.6			8	44.4			0.509‡
Dyslipidemia	91	39.2			6	33.3			0.621‡
Coronary artery disease	143	61.6			12	66.7			0.672‡
Operated coronary artery bypass graft	48	20.7			3	16.7			0.683‡
Smoking	88	37.9			8	44.4			0.584‡
Atrial fibrillation rhythm	10	4.3			2	11.1			0.210‡
Symptomatic ICA stenosis	110	47.4			9	50.0			0.832‡
Vertebrobasilar insufficiency	24	10.3			2	11.1			1.000‡
White blood cell (×10^3)			7.9±2.1	7.7			7.7±1.5	7.4	0.642*
Hemoglobin			12.9±1.8	13.0			12.3±2.0	12.1	0.173*
Hematocrit			39.0±5.2	39.4			36.8±6.1	36.4	0.089*
Platelet (×10^3)			238.3±65.8	231.5			206.2±63.2	185.5	**0.019**†
Mean platelet volume			8.6±1.1	8.50			8.82±1.17	8.60	0.527†
Neutrophile			4.98±1.58	4.80			5.23±1.31	4.99	0.352†
Lymphocyte			2.0±0.8	1.93			1.44±0.53	1.39	**0.001**†
Neutrophil-to-lymphocyte ratio			2.8±1.4	2.52			4.24±2.51	3.81	**0.001**†
Platelet-to-lymphocyte ratio			134.2±63.3	117.9			165.0±96.7	136.7	0.156†
Monocyte			0.7±0.4	0.60			0.70±0.19	0.69	0.097†
Eosinophile			0.2±0.2	0.20			0.24±0.19	0.20	0.843†
Basophile			0.0±0.1	0.00			0.02±0.04	0.00	0.407†
Platelecrit			0.3±1.4	0.20			0.18±0.04	0.19	0.068†
Platelet distribution width			17.4±3.7	16.85			17.39±0.75	17.45	0.052†
C-reactive protein			5.3±16.0	1.22			14.8±24.7	1.94	**0.039**†
sT3			4.0±1.3	4.03			3.74±0.78	3.52	0.511*
sT4			9.5±5.0	11.01			8.70±5.91	12.61	0.582†
Thyroid stimulating hormone			1.9±2.0	1.37			1.3±1.6	0.71	**0.017**†
Indication side									0.717‡
Right	93	40.1			8	44.4			
Left	139	59.9			10	55.6			
Right ICA stenosis rate			56.2±35.5	70.0			58.1±33.8	70.0	0.981†
Left ICA stenosis rate			66.5±34.2	80.0			80.1±18.8	85.0	0.200†

SD: Standard deviation; ICA: Internal carotid artery; * Student t-test; † Mann-Whitney U test; ‡ Ki-kare test.

Table 4. Effect of postoperative parameters on one-year mortality

	1 year mortality (-)				1 year mortality (+)				
	n	%	Mean±SD	Median	n	%	Mean±SD	Median	*p*
Complication									**0.027†**
No	182	78.4			10	55.6			
Yes	50	21.6			8	44.4			
Neurological complication	24	10.3			5	27.8			**0.026†**
Transient ischemic attack	3	1.3			0	0.0			1.000†
Ischemic stroke	8	3.4			1	5.6			0.495†
Hemorrhagic stroke	1	0.4			1	5.6			0.139†
Cranial nerve injury/convulsion	7	3.0			1	5.6			0.455†
Vascular complication	27	11.6			4	22.2			0.189†
Cardiac complication	6	2.6			2	11.1			0.106†
Operation time			108.9±33.7	105.0			110.7±30.8		0.680‡
Extubation time			7.10±9.29	5.00			6.1±4.9		0.817‡
Intensive care unit stay			38.4±69.1	24.0			109.5±285.9		0.223‡
Hospital stay			5.1±5.0	4.00			7.7±10.7		0.685‡

SD: Standard deviation; † Ki-kare test; ‡ Mann-Whitney U test.

Table 5. Independent predictive factors affecting mortality

	One variable model			One variable model		
	OR	95% CI	*p*	OR	95% CI	*p*
Congestive heart failure	6.43	1.51-27.41	**0.012**	7.97	1.66-38.23	**0.009**
Platelet	1.00	1.00-1.00	**0.045**			
Lymphocyte	0.24	0.09-0.61	**0.003**			
Neutrophil-to-lymphocyte ratio	1.48	1.16-1.88	**0.001**	1.57	1.21-2.04	**0.001**
Complication	2.91	1.09-7.77	**0.033**			
Neurological complication	3.33	1.09-10.16	**0.034**	3.78	1.13-12.69	**0.031**

OR: Odds ratio; CI: Confidence interval.

cut-off value of the NLR of 8.67 (area under the curve [AUC] 0.733: 0.6191-0.847).

DISCUSSION

Carotid artery endarterectomy is still the most valuable therapy option for carotid artery stenosis. Some authors argue against any intervention for carotid artery disease due to limitations. Survival rate, restenosis, and stroke odds should be provided to candidates for surgery. An evaluation of the pre- and postoperative status is useful for elective surgery patients. It is well known that inflammatory and oxidative stress agents play an important role in cardiovascular disease prognosis. Many inflammatory proteins, such as interleukins and CRP, predict inflammation, and complete blood count tests provide valuable information for the prognosis of atherosclerosis and cardiovascular diseases.[7,8]

Moreover, some prognostic laboratory studies, such as the NLR and PLR, may be helpful in understanding carotid artery disease and stroke. There is a great deal of data about NLR and PLR that affect inflammatory response in the literature. Also, these novel markers are used for the acute phase and inflammatory response for diagnosis and prognosis.[9]

In addition, NLR and PLR are low-cost and easily accessible tests. The relationship between increasing NLR values and worsening atherosclerosis prognosis has been described in the literature.[10,11] Deşer et al.[3] reported that PLR and NLR ratios were positively correlated with the degree of carotid artery stenosis in their study in 361 patients. Corriere et al.[12] clearly demonstrated a relationship between NLR and plaque growth progression and prognosis in the carotid artery. Our study showed that, in determining the prognosis after endarterectomy, a statistically significant difference was found in NLR levels in patients in the one-year mortality group and in patients in the non-mortality group at one-year follow-up.

Prabhu[13] described the role of cytokines in modulating left ventricular functions. The inflammatory response that occurs in the pathophysiology of both acute and chronic heart failure may help in the prognosis of ventricular dysfunction. Uthamalingam et al.[14] also reported risk stratification with NLR follow-up in decompensated heart failure. According to these findings, CHF alone may affect mortality and cardiovascular disease prognosis. In our clinical study, when NLR values were evaluated in terms of CHF, a statistically significant difference was found between the groups with and without mortality within one-year, and the effect of CHF on one-year mortality was demonstrated.

Post-stroke disability is a significant health problem. Although carotid artery stenosis is treated to prevent stroke, there is a risk of developing a stroke following a carotid endarterectomy. A stroke is one of the most important criteria for prognosis after an endarterectomy. Alternative treatments are available, such as medical therapy and stenting into the carotid artery. Published meta-analyses and systematic reviews have shown that a carotid endarterectomy is less risky in terms of stroke incidence in early- and long-term follow-ups compared to stenting.[15,16] However, Dharmakidari et al.[17] reported in their study that risk stratification should be done well in patient selection, and that high-risk patients for possible strokes should be given priority in the selection of patients to be revascularized. Reddy et al.[18] also strongly recommended completing preoperative risk assessments to avoid perioperative strokes. Although perioperative and postoperative early stroke risks were emphasized as in these studies, the early postoperative period and one-year follow-up results were also examined in our study.

Friedlander et al.[19] clearly reported in their cross-sectional study that imaged carotid atheroma plaques in a male population were correlated with the increased NLR. Paying attention to the increased NLR levels in the outpatient setting may be useful in identifying the possible carotid artery disease in the elderly and male populations.

Although it is accepted that NLR values are typically high in patients with carotid artery lesions, our study demonstrated a statistically significant relationship between neurological complications in the early postoperative period and mortality in the one-year period.

Nonetheless, there are some limitations to this study. Further clinical studies are needed to clearly investigate the effects of inflammatory markers on prognoses. Although NLR levels have been shown to be associated with cardiovascular events, there is no clear consensus on the cut-off values, normal, or high values. In this study, we used NLR levels between the groups and in a selected patient population as criteria for long-term mortality. A study with a different design is needed to reveal the differences between NLR and PLR levels among healthy and patient populations. Future clinical studies may provide more valuable information about NLR and PLR levels.

In conclusion, carotid artery disease is an important clinical entity that affects morbidity and mortality. With the recommendations of the guidelines, carotid endarterectomy is an alternative method that can be applied together with percutaneous interventions. However, the NLR level, preoperative CHF, and neurological complications in the early postoperative period seem to be the most important prognostic factors in terms of mortality during one-year follow-up.

Ethics Committee Approval: An ethical committee of non-interventional clinical trials (No:2020/13/380, 8/12/2020) in 'Kosuyolu High Specialty Training and Research Hospital Ethical Committee' approved. The study was conducted in accordance with the principles of the Declaration of Helsinki.

Patient Consent for Publication: A written informed consent was obtained from each patient.

Data Sharing Statement: The data that support the findings of this study are available from the corresponding author upon reasonable request.

Author Contributions: Study design: T.B., D.Ç.; Data collection: H.H., A.Z.; Writing: T.B., R.A.; Supervising: B.Ö., K.K.; Final approval by all authors. All authors have read and approved the manuscript.

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