

ORIGINAL RESEARCH

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Can neutrophil-lymphocyte ratio be a predictor of cerebral vasospasm in patients with subarachnoid hemorrhage?

Huseyin Ulas Pinar¹, Enes Duman², Suleyman Deniz¹, Ilker Coven³, Omer Karaca¹, Rafi Dogan¹¹Baskent University Konya Research Center, Department Anesthesiology, Ankara, Turkey²Baskent University Konya Research Center, Department Radiology, Ankara, Turkey³Konya Education and Research Hospital, Department Neurosurgery, Ankara, Turkey

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Abstract

This study aimed to investigate the relationship between neutrophil-lymphocyte ratio (NLR) and development of vasospasm in patients with aneurysmal subarachnoid hemorrhage (SAH). **Materials and Methods** The study was performed by retrospectively analyzing the data of 170 aneurysmal SAH patients who admitted to the intensive care unit of our hospital between 2011 and 2017. We investigated the ability of NLR values calculated from the blood samples taken at the time of admission to predict for vasospasm. Results Thirty-five percent of the patients developed vasospasm. NLR values were associated with the development of vasospasm (OR 1.15; 95% confidence interval, 1.09-1.22; $p < 0.0001$). When the ability of NLR to predict for vasospasm was analyzed, the area under curve (AUC) of ROC curve was 0.776 (95% confidence interval: 0.70-0.85). The optimal cut-off point was 14.48 using the Youden index. The sensitivity and specificity for this cut-off point were 61.7% and 83.6%, respectively. **Conclusion** NLR can be used as an independent predictor of vasospasm development as a cheap and practical method, along with other predictive factors.

Keywords: Aneurysmal subarachnoid hemorrhage, vasospasm, neutrophil-lymphocyte ratio

Introduction

Cerebral vasospasm is one of the most important causes of morbidity and mortality in patients with subarachnoid hemorrhage (SAH). Vasospasm is detected angiographically in two-thirds of the patients after aneurysmal SAH, while almost half of these patients develop delayed ischemia due to vasospasm, leading to neurological disorder [1]. Therefore, after treatment of aneurysm by surgical and endovascular interventions, prevention of vasospasm which may cause secondary damage is of critical importance. Effective treatment and preventive approaches can be used earlier if post-SAH vasospasm can be predicted.

In the recent years, neutrophil-lymphocyte ratio (NLR), one of the economical markers of systemic inflammation, started to be used as a prognostic factor in several diseases such as cancers, infections, and acute coronary syndromes [2-5]. Moreover, studies on NLR in cerebrovascular events were also conducted in the recent years. High NLR was associated with an increase in 30-day mortality in

patients with intracerebral hemorrhage [5] and in a meta-analysis, increased NLR was found to be associated with worse functional outcomes and increased mortality based on 3-month results in this patient group [6].

Based on these data, we aimed to evaluate if NLR values were associated with the development of vasospasm in aneurysmal SAH patients followed in our intensive care unit.

Material and Method

This study was performed retrospectively on 170 patients followed in our clinic for aneurysmal SAH between 2011 and 2017. Inclusion criteria were as follows: aneurysmal SAH diagnosis made with cerebral computed tomography (CCT) and confirmed with cerebral angiography; admission at the hospital within 24 hours of the onset of initial symptoms; surgical or endovascular treatment of aneurysm within 2 days of the event; complete blood count performed at the time of admission; and patients at the age range of 18-80 years. Patients were excluded if they had acute or chronic infections, known malignancies, uremia, chronic hepatic failure, or heart or lung diseases.

Data of patients including age, gender, smoking, alcohol intake,

*Corresponding Author: Huseyin Ulas Pinar, Baskent University Konya Research Center, Department Anesthesiology, Ankara, Turkey
E-mail: huseyinpinar2002@gmail.com

and medical histories were recorded at the time of admission. Neutrophil and lymphocyte counts were determined in the blood samples of the patients and NLR values were calculated and recorded. The neurological status at the time of admission was evaluated using World Federation of Neurosurgical Societies (WFNS) score, while modified Fisher scale was used for radiological classification. Digital subtraction angiography (DSA) was used to assess the localization and size of the aneurysm. Ruptured aneurysm treatment was performed by Interventional Radiology and Neurosurgery teams in 48 hours and the patients were followed in our intensive care unit for at least 14 days.

Patients received standard treatments after aneurysmal SAH. Cerebral vasospasm development was defined as neurological deterioration as hemiparesis, aphasia, apraxia, hemianopia or sudden reduction at least two points in the Glasgow Coma Scale. Patients who developed cerebral vasospasm treated with appropriate treatment modalities like intra-arterial vasodilators or medical interventions.

Statistical analysis

Frequencies and percentages were presented for categorical variables. Means and standard deviation statistics were given for continuous variables. ROC analysis was performed and the optimal cut-off based on Youden Index was determined to investigate the power of NLR to predict vasospasm. Moreover, the effect of NLR on vasospasm was investigated by using simple and multiple regression models by controlling for age and gender and uncorrected odds ratio (OR) and corrected OR were presented. Sequential logistic regression models were used to investigate the association of NLR with clinical and radiological scores. Analyses were performed using the SAS (University Edition) software package (version 9.4; SAS Institute Inc., Cary, NC, USA) and a p value of <0.05 was considered significant.

Results

A total of 207 patients who admitted to our clinic for aneurysmal SAH between 2011 and 2017 were included in our study. Thirty-seven of these patients were excluded due to meeting exclusion criteria or having missing data. Ninety-five patients (55.8%) were female and 75 patients (44.2%) were male. The mean age of the patients was 56.51 ± 12.41 years. When CCT scans of the patients were examined, 23 patients (13%) had Grade 1, 57 patients (23%) had Grade 2, 43 patients (25%) had Grade 3 and 47 patients (27%) had Grade 4 SAH. When clinical scores the patients were examined, 61 patients (35%) had Grade 1, 48 patients (28%) had Grade 2, 16 patients (9%) had Grade 3, 39 patients (22%) had Grade 4 and 6 patients (3%) had Grade 5 SAH. Correlations were found between NLR and both WFNS score and Fisher's Grade by logistic regression analysis ($p < 0.0001$).

Vasospasm developed in 35% of the patients (60 patients) at some point during the clinical course. Our total mortality rate was 31% (54 patients).

When the power of NLR to predict vasospasm was analyzed, the area under curve (AUC) of ROC curve was 0.776 (95% CI: 0.70 - 0.85). The optimal cut-off point was 14.48 using the Youden index. The sensitivity, specificity, positive predictive value and negative predictive value for this cut-off point were 61.7%, 83.6%, 67.3%, and 80%, respectively [Figure 1].

Table 1. Association between NLR and vasospasm

	Simple Logistic Regression OR (95% Confidence Interval)	Multiple Logistic Regression OR (95% Confidence Interval)	p value
NLR	1.15 (1.09-1.22)	1.16 (1.10-1.23)	<0.0001
Gender (Male)		0.44 (0.20-0.96)	0.039
Age		1.04 (1.0-1.07)	0.02

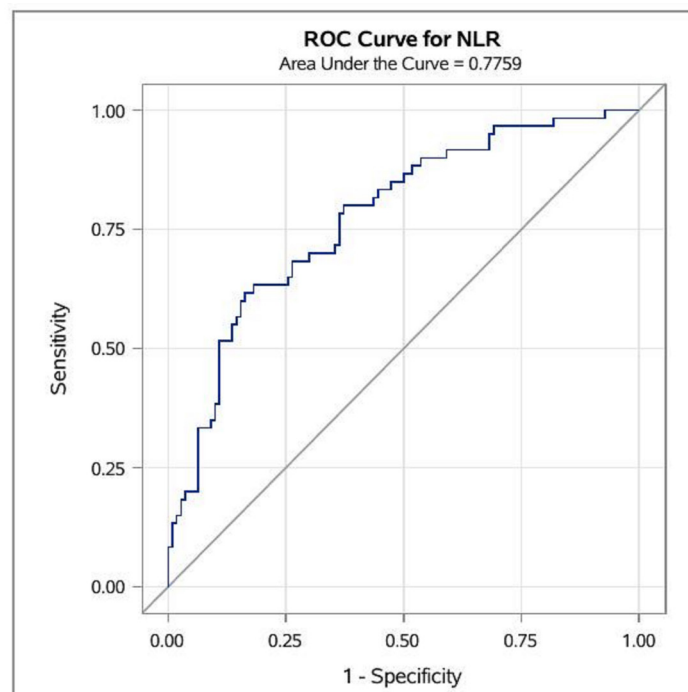


Figure 1. ROC curve for NLR

Discussion

Our study results show that increase in NLR values was independently associated with the development of vasospasm [Table 1] and increased NLR values correlated with the Fisher and WFNS values of the patients. Tao et al. investigated the clinical value of NLR in patients with aneurysmal SAH and demonstrated that high NLR values were associated with poor functional outcomes at 3 months and delayed cerebral ischemia caused by cerebral vasospasm. The authors stated that more correlated results were obtained when NLR and platelet-lymphocyte ratio were used together [7]. In a study conducted in our country, among the patients admitted to emergency service, NLR values were significantly higher in SAH patients compared to those in patients presenting with migraine and other headaches [8].

Neuro-inflammation is seen after any cerebral damage and thus inflammatory reaction is also inevitable in SAH patients. Similar to the study by Tao et al., other studies also reported that inflammatory parameters may have a prognostic value in SAH patients [9,10]. Höllig et al. also showed that inflammatory parameters such as increased levels of IL-6 during the early phase after SAH are associated with poor outcomes [11]. The blood in the subarachnoid space initiates the inflammatory cascade involving vascular and cellular components, leading to leukocyte migration and expression of cell adhesion molecules in the endothelial cells [12]. Accordingly, the increase in NLR appears to be related to

the initiation of neuroprotective mechanisms and inflammatory processes after SAH.

Conclusion

Younger age, smoking, low baseline clinical score, and presence of thick subarachnoid and intraventricular hemorrhage on cerebral CT were found to be the factors associated with cerebral vasospasm and delayed cerebral ischemia [13]. These factors together with the severity of the inflammatory reaction, which was also determined in our study and reported in other studies, may be considered as an increased risk for cerebral vasospasm. In conclusion, more vigorous monitoring and more aggressive treatment for cerebral vasospasm in patients with increased NLR will be clinically useful.

Competing interests

The authors declare that they have no competing interest

Financial Disclosure

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