The Significance of Preoperative Neutrophil to Lymphocyte Ratio in Patients with Meningiomas

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Abstract

Objective: This study aims to evaluate the significance of preoperative neutrophil to lymphocyte and platelet to lymphocyte ratios in predicting the pathological grade of supratentorial meningiomas.

Methods: This retrospective study included a total of 94 patients with newly diagnosed supratentorial meningiomas. Preoperative lymphocyte, neutrophil, platelet counts, and neutrophil to lymphocyte and platelet to lymphocyte ratios were obtained.

Results: Of the 94 patients, 73 patients and 21 patients showed low- and high-grade meningiomas, respectively. Among the hematological markers, only neutrophil to lymphocyte ratio showed significantly higher value in high-grade meningioma group and showed diagnostic efficacy in predicting the pathological grade.

Conclusions: The higher the neutrophil to lymphocyte ratio, the higher the grade of meningioma. This can help neurosurgeons to have better treatment plan before the surgical intervention.

Keywords: Inflammatory markers, meningioma, neutrophil to lymphocyte ratio, platelet to lymphocyte ratio

Introduction

Meningiomas are the most commonly encountered primary central nervous system tumors in clinical practice and originate from meningothelial cells.[1] According to the 2016 World Health Organization classification of tumors of the central nervous system, meningiomas are divided into 3 grades based on their histologic pattern and the majority are grade I (benign) meningiomas.[2] Clinical experience has shown us that all 3 grades can recur with different ratios, the higher the grade the higher the recurrence. After surgery, high-grade meningiomas (grades II and III) require radiotherapy but we have to underline that high-grade meningiomas show invasive behavior and have high morbidity and decrease survival.[3] Preoperative differentiation may help clinicians to apply or select optimal therapeutic strategy. So far, there has been no preoperative clue to differentiate among high- and low-grade meningiomas prior to surgery and current studies have focused on preoperative systemic or hematologic inflammatory markers. Inflammation is now accepted as a hallmark for the formation and progression of cancers and finding a hematological marker would be very important for screening the progression of a solid tumor and making an optimal therapeutic strategy. Ongoing studies have exhibited that evaluation of hematological markers like neutrophil to lymphocyte (NLR), lymphocyte to monocyte (LMR), and platelet to lymphocyte ratio (PLR) from a simple venous blood which is routinely obtained before surgery is very simple, cheap, and informative. Preoperative inflammatory markers, especially high NLR and low LMR, have been shown to be associated with tumor grade in several solid cancers[4,5] and also in gliomas.[6,7] Unfortunately, there are a very limited number of studies published in the English literature concerning preoperative systemic inflammatory markers in patients with meningiomas.[8-12] For this reason, in this study, we try to reveal the connection among preoperative hematological inflammatory markers and grades of meningiomas. This study is the extension of our previously published study in which we included 61 patients with supratentorial meningiomas.[9]

Methods

Patients

In this study, patients with supratentorial meningiomas are analyzed retrospectively. All the patients are operated by a single surgeon from April 2010 to July 2022 in Department of Neurosurgery, Cerrahpasa Medical Faculty. The Istanbul University-Cerrahpasa, Cerrahpasa School of Medicine (Date: October 19, 2020, No: 83045809-604.01.02) approved the study protocol. Our brain tumor database contains clinical presentations, radiological findings, pathological results, and laboratory findings of patients. In order to provide homogeneous results and decrease bias, meticulous inclusion criteria for this study were applied. Our including criteria were as follows: (1) patients without signs or symptoms of any infection; (2) without cancer of any organ and anti-tumor treatment; (3) aged > 18 years of age; (4) without steroid treatment; (5) with complete medical records and preoperative hematological data; and (6) with

Table 1. Statistical Summary of Preoperative Systemic Inflammatory Markers in the Groups

Parameters	Low Grade (n = 73)	High Grade (n = 21)	P
Lymphocytes	2.09 ± 0.6	1.92 ± 0.8	.31
Neutrophils	4.31 ± 1.3	4.72 ± 1.2	.22
Platelets	259.86 ± 63.0	243.90 ± 101.3	.50
NLR	2.26 ± 1.3	3.16 ± 2.2	**.02**
PLR	132.2 ± 45.7	149.2 ± 87.7	.23

Values are given as mean ± standard deviation.
NLR, neutrophil-lymphocyte ratio. PLR, platelet-lymphocyte ratio.
($P < 0.05$).

newly diagnosed meningioma. Our meticulous inclusion criteria provide us a total of 94 patients for this retrospective study.

Sample and Data Collection

During preoperative period, a venous blood sample was taken routinely from all patients for preoperative laboratory evaluation. Moreover, patient age, gender, pathological grade, preoperative lymphocyte, neutrophil, and platelet counts are documented. Neutrophil to lymphocyte ratio and PLR are also recorded. We particularly included and focused on NLR and PLR because they are the main interest in recent several studies.

Statistical Analysis

In this study, Statistical Package for Social Sciences software version 20.0 (IBM SPSS Corp., Armonk, NY, USA) was used for statistical analysis. The "Student's *t*-test" or "Mann–Whitney *U*"-test were used to compare continuous variables. The area under the curve (AUC) for the NLR and PLR with a receiver operating characteristics (ROC) curve analysis was used for the diagnostic performance. A *P*-value (<.05) was considered statistically significant.

Ethical Approval

The ethics committee approval was received for this study from Istanbul University-Cerrahpasa, Cerrahpasa School of Medicine (Date: October 19, 2020, No: 83045809-604.01.02) concordant with the Declaration of Helsinki.

Results

A total of 94 patients with pathologically proven supratentorial meningioma were included in our study. The patient group is composed of 25 males and 69 females with a mean age of 53.15 ± 11.5 years (29-75 years). A total of 73 of the patients were diagnosed with low-grade (grade I) and 21 of the patients were diagnosed with high-grade (grade II) meningiomas histopathologically. During the study period, we had only one patient with grade III meningiomas and that patient was excluded.

No difference was seen regarding the hematological inflammatory markers such as lymphocyte, neutrophil, and platelet counts and PLR (*P* > .05), between low- and high-grade meningioma groups. On the other hand, NLR in the high-grade meningioma group was significantly higher than those of the low-grade meningioma group (*P* = .02) (Table 1).

When low-grade meningioma group was tested against high-grade meningioma group, the AUCs for the NLR were 0.66 (95% CI = 0.52-0.80, *P* = .02) and 0.54 (95% CI = 0.40-0.69, *P* = .07) for the PLR (Figure 1). The cut-off value was found as 3.29 (*P* = .02) for NLR. The findings suggest that NLR was more accurate than other parameters studied here for predicting the meningioma grade.
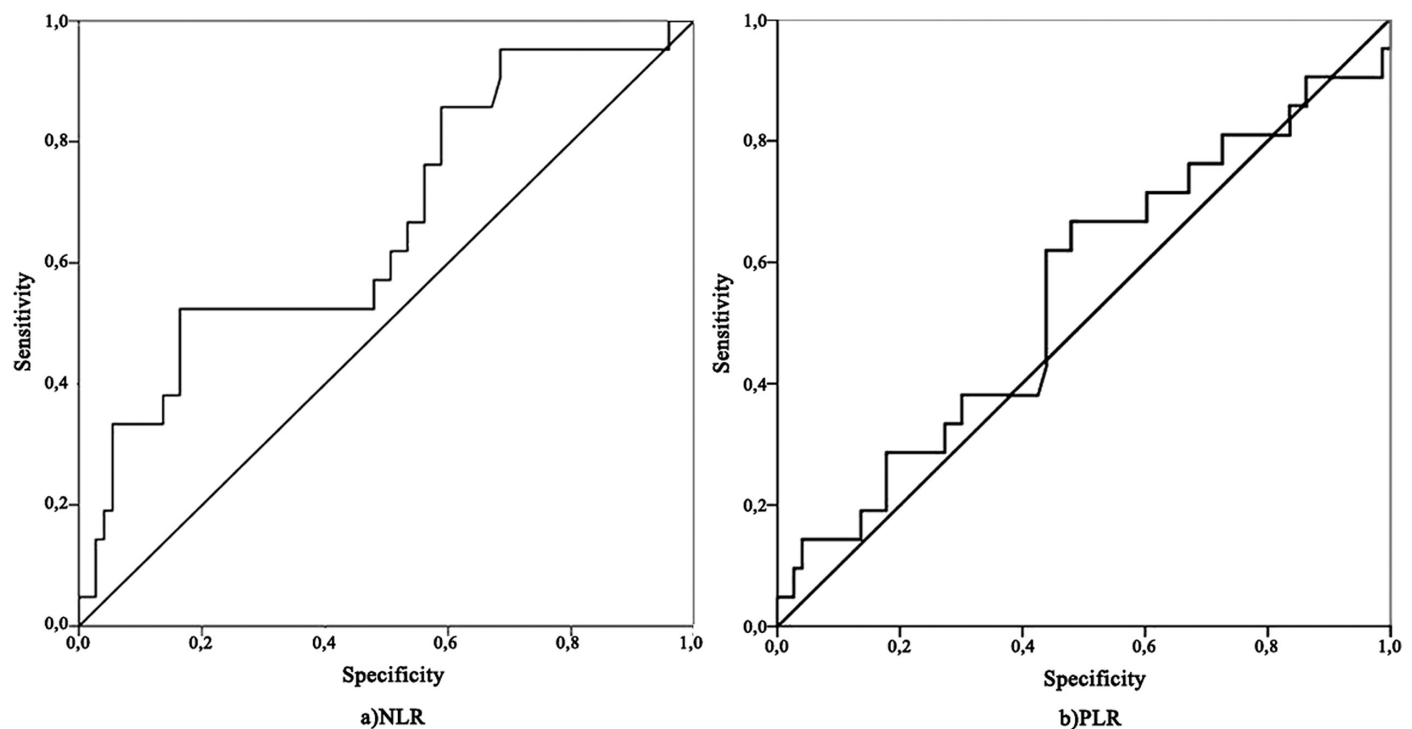

Figure 1. ROC analysis showing diagnostic accuracy for NLR (A; AUC = 0.66, 95% CI = 0.52-0.80) and PLR (B; AUC = 0.54, 95% CI = 0.40-0.69). NLR shows more diagnostic accuracy in differentiating low-grade meningioma (grade I) from high-grade meningioma (grade II). AUC, area under the curve; NLR, neutrophil-lymphocyte ratio; PLR, platelet-lymphocyte ratio; ROC, receiver operator characteristic.

Table 2. Studies Including Meningioma Only Published so far in the English Literature

No.	Year	Authors	Main Findings	Reference
1	2017	Karimi et al	Neutrophilia was associated with tumor recurrence and a significant predictor of poor outcome.	8
2	2018	Kemerdere et al	Higher NLR was associated with the grading of meningioma and a predicting factor for progression.	9
3	2019	Lin et al	Preoperative SIMs had a limited ability to differentiate low- and high-grade meningioma.	10
4	2019	Liang et al	High leukocyte count and low LMR could be used in the assessment of the grade of meningioma.	11
5	2020	Chen et al	NLR could be used as a predictor to evaluate the recurrence risk of atypical meningioma.	12

LMR, lymphocyte-to-monocyte ratio; NLR, neutrophil-to-lymphocyte ratio; SIMs, systemic inflammatory markers.

Discussion

Inflammation is an important process for initiation, progression, and malignant conversion of cancers.[13] It has clearly been shown that inflammation-related neutrophils and lymphocytes can participate in angiogenesis and proliferation of tumors.[14] The reason(s) behind the increased neutrophil and decreased lymphocyte counts in malignant tumors is poorly understood. One possible reason is that cytokines and chemokines released from tumor cells can induce neutrophil infiltration and increased neutrophil count which inhibits lymphocyte activity and lymphocyte apoptosis in high-grade tumors.[15,16]

Our study showed that higher NLR was associated with higher meningioma grade and more than or equal to 3.29 of NLR can predict higher grade in meningiomas: the higher the NLR the higher the meningioma grade. The high NLR means an increased amount of neutrophil count or relatively decreased amount of lymphocyte count obtained from peripheral blood sample. This may reflect the favorable effect of lymphocyte which can migrate into the tumor microenvironment to build a defensive barrier. Depending on our results, the determination of NLR prior to surgery can help clinicians to make a better treatment plan.

Preoperative inflammatory markers have been the focus of several cancer researches and the majority of studies interestingly have focused on several other organ system tumors[4,5] and studies including primary brain tumors are rare. Furthermore, there is very limited number of studies focused on meningiomas in the English literature (Table 2). Diagnostic efficacy of preoperative inflammatory markers, especially NLR and LMR, has been shown in glial tumors and the common notion is that glioma grade is closely related with a higher NLR and can be utilized as an indicator for glioma progression and NLR showing ≥ 4 prognosticates a poor prognosis.[6]

The current results actually are in line with the limited number of studies included meningioma only. Karimi et al[8] demonstrated that increased peripheral blood neutrophil counts is a strong indicator of decreased recurrence-free survival rate and only a unit increase in neutrophil counts can cause almost 10% increase in the tumor recurrence rate. Kemerdere et al[9] found that grade II meningiomas showed higher neutrophil and lower lymphocyte and platelet counts compared to grade I meningiomas and underlined that a higher NLR exhibited the best accuracy for meningioma grade of meningiomas. However, Lin et al[10] in their 672 patients demonstrated that preoperative systemic inflammatory markers had limited adequacy to discriminate meningioma grade and they underlined as many others that the inflammatory reactions around the tumor microenvironment could be different from those in the periphery and could be over demonstrated or under demonstrated in the periphery. An important study by Liang et al[11] including largest number of patients (944 patients) with meningioma reported so far found that leukocyte, neutrophil, monocyte counts, and the NLR in the high-grade meningioma group were significantly higher than those in the low-grade meningioma group and highlighted that high leukocyte count and low LMR were other independent predictors of high-grade meningiomas. Lastly, Chen et al[12] confirmed that NLR can be used as a predictor to assess the recurrence risk of atypical or grade II meningiomas.

In summary, limited studies regarding preoperative systemic inflammatory markers in intracranial meningiomas have similar results like the studies including other organ tumors and brain gliomas. Almost all studies underline the role of inflammation in cancers and the usefulness of some of the preoperative inflammatory markers especially higher NLR and lower LMR in the prediction of malignancy and grade of tumor. Our findings support the notion that higher NLR could be used as an indicator of meningioma grade before surgery and to help or to give an idea about making a better decision on treatment planning.

We underline that the leading limitation of our study is that this is a retrospective study that may cause selection bias although we had strict selection criteria. Another limitation may be the number of patients included here. The future studies should be prospective with a higher cohort of patients with meningioma.

In conclusion, high-grade meningiomas have significantly higher NLR compared to the low-grade meningiomas and higher NLR is associated with better accuracy for predicting meningioma grade: higher the NLR, the higher the grade of meningioma. This can help neurosurgeons to have better treatment plan before the surgical intervention.

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