Neurosurgical Forum

LETTERS TO THE EDITOR

Does preoperative NLR predict brain metastasis resections outcome?

TO THE EDITOR: We have read with great interest the article by Mitsuya et al.⁵ (Mitsuya K, Nakasu Y, Kurakane T, et al: Elevated preoperative neutrophil-to-lymphocyte ratio as a predictor of worse survival after resection in patients with brain metastasis. *J Neurosurg* [epub ahead of print December 2, 2016. DOI: 10.3171/2016.8.JNS16899]). The study showed that 82 patients with a neutrophil-to-lymphocyte ratio (NLR) < 5 had a median overall survival of 14 months, significantly longer survival than 5 months for 23 patients with an NLR ≥ 5, underscoring that an elevated preoperative NLR was a predictor of worse survival after resection of brain metastasis. However, the prognostic value of NLR should be considered cautiously.

Mitsuya et al. conducted a retrospective study of records at a single center with a limited sample size, all of which contributed to selection bias in the study. Medical conditions such as autoimmune disease, underlying inflammations, trauma, blood system diseases, and steroid usage would significantly affect blood cells and NLRs, whereas only patients receiving steroid therapy were excluded from the study. The authors mentioned that blood sampling was performed 1–14 days before surgery. However, NLR is a dynamic variable, which suggests that the specific time during the disease course at which NLR best predicted worse survival was hard to confirm.

Several studies have identified sex, age, performance status, systemic tumor activity, and response to steroid treatment as reliable prognostic factors in patients with brain metastases.^{1–4,6} Jacot et al. have demonstrated that male sex was an independent determinant of a poor outcome with a hazard ratio of 2.29.³ In this study, the number of male patients with an NLR ≥ 5 was significantly higher than it was in those with an NLR < 5 (83% vs 59%, respectively; $p = 0.034$). Meanwhile, patients with an NLR < 5 underwent chemotherapy significantly more frequently than patients with an NLR ≥ 5 (55% vs 17%, $p = 0.001$). However, the authors did not illustrate the association between NLR and worse survival in different groups based on sex and chemotherapy.

To conclude, the predictive value of NLR is controversial. Whether there exists an association between NLR

and worse survival of the patients undergoing brain metastasis resection requires further exploration.

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Disclosures

The authors report no conflict of interest.

Response

We thank Drs. Ren, He, and Xu for their interest and comments regarding our article. We agree that various factors influence NLR in cancer patients. In our study, we analyzed outcome in patients who needed craniotomy for brain metastases. If patients had had serious complica-

tions such as severe infection or blood system diseases, they would never have been considered for surgery.

We acknowledge the issue of timing when we calculate the NLR. If patients had any kind of silent events, peripheral blood counts might reflect them. In patients with rapid deterioration, surgical treatment needs to be performed emergently. In most cases blood sample workup was performed less than 7 days before surgery, and many of the patients were treated with steroids for neurological deterioration just before undergoing surgery.

We also thank Dr. Ren et al. for their comment on the variability of NLR in relation to sex, systemic metastasis, and systemic therapy. Extracranial metastases, systemic therapy, and systemic complications have significant influence on performance status in cancer patients. We regard NLR as one of the indices that demonstrate a systemic condition predicting outcome in candidates for invasive treatment.

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Characteristics influencing preoperative neutrophil-to-lymphocyte ratio

TO THE EDITOR: I read with the great interest the article by Mitsuya et al.¹ in which they retrospectively analyzed the impact of the neutrophil-to-lymphocyte ratio (NLR) on the survival data of patients who had undergone resection of brain metastases (Mitsuya K, Nakasu Y, Kurakane T, et al: Elevated preoperative neutrophil-to-lymphocyte ratio as a predictor of worse survival after resection in patients with brain metastasis. *J Neurosurg* [epub ahead of print December 2, 2016. DOI: 10.3171/2016.8.JNS16899]). They found that an elevated preoperative NLR is a predictor of worse survival after resection for brain metastases. First, although recursive partitioning analysis classification was shown in the paper, the authors did not give detailed information about the extension of extracranial metastases (bone-only vs visceral metastases), which may indirectly increase neutrophil levels resulting in preopera-

tive elevated NLR. Second, solitary versus multiple brain metastases may influence NLR. Cases of solitary metastases were proposed to have low NLR values compared to cases of multiple brain lesions.

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Disclosures

The author reports no conflict of interest.

Response

We thank Dr. Altundag for his attention to our article. We agree that extracranial metastases may influence NLR in cancer patients. A quick detailed workup of systemic metastasis is often difficult for patients with life-threatening brain lesions. Medical oncologists in charge of these patients have difficulties in estimating life expectancy in the individual cancer journey of a specific patient. As discussed in our article, "The decision to perform resection in each patient must be made urgently but cautiously because surgery has a potential concern for morbidity and mortality. The selection criteria should include both the patient's whole systemic condition and the characteristics of the brain metastases." In this study, NLR is a useful, simple marker in emergent situations before thorough systemic examination is undertaken.

We also thank Dr. Altundag for sharing his thoughts on the number of brain metastases and surgical outcome ("solitary versus multiple brain metastases may influence NLR"). It is an interesting hypothesis, which we would like to analyze in the future.

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