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RESPONSE TO LETTER

Letter to the Editor Regarding "Predictive Value of Neutrophil-to-Lymphocyte Ratio for Cerebral Infarction in Obstructive Sleep Apnea: A Nomogram-Based Analysis" [Response to Letter]

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Dear editor

We sincerely thank Xiang Ma and Qing-qing Shan for their interest in our study and for their thoughtful comments on our recently published article "Predictive Value of Neutrophil-to-Lymphocyte Ratio for Cerebral Infarction in Obstructive Sleep Apnea: A Nomogram-Based Analysis".[1,2] We truly appreciate the opportunity to clarify and further discuss several important issues.

On Omission of Confounders

We agree that cardiovascular comorbidities (hypertension, diabetes, dyslipidemia, atrial fibrillation, coronary artery disease) and obesity are important contributors to systemic inflammation and cerebral infarction (CIF). In our dataset these variables were collected, but not all were consistently represented or statistically significant in univariate or multivariate analyses. Although obesity would be expected, on theoretical and clinical grounds, to be more prevalent among patients with both OSA and CIF, the number of participants meeting criteria for obesity in our cohort was relatively small and the BMI difference only showed a non-significant trend ($P = 0.08$). This limited representation likely reduced the statistical power to detect an independent effect of BMI and may have biased estimates. To remain faithful to the observed data we based the multivariable model on variables supported by our sample rather than forcing inclusion of under-represented factors; nevertheless, we acknowledge this limitation. Future multi-center studies with larger samples that include sufficient numbers of obese patients — and that perform subgroup and sensitivity analyses — are warranted to clarify the independent role of BMI in OSA-related cerebrovascular risk. We appreciate the reviewer's comment and will emphasize this point more clearly in the revised manuscript.

On Variable Selection

We appreciate the concerns regarding our variable selection process. We adopted the approach of including variables with $P < 0.10$ or strong clinical relevance to balance statistical feasibility with clinical plausibility, given the relatively small number of events (n = 68). We agree that penalized regression methods (eg, LASSO) would be more robust for variable selection and should be considered in future studies with larger samples.

On Causality

We acknowledge that the retrospective and cross-sectional nature of our study precludes causal inference. Our goal was to identify a potential biomarker that could provide new diagnostic and therapeutic insights into OSA-related cerebrovascular risk. However, we recognize that our wording was not sufficiently precise and may have implied causality. In future work, we will use larger sample sizes while also improving the clarity of our scientific expression.

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Conclusion

Once again, we thank Shan et al for their constructive feedback. Their comments help to improve the clarity of our work and highlight important directions for future studies.

Data Sharing Statement

Data availability is not applicable as no data was generated in this communication.

Author Contributions

All authors gave final approval of the version to be published; have agreed on the journal to which the article has been submitted; and agree to be accountable for all aspects of the work.

Ziwei Hou: Writing – Original Draft, Writing – Review & Editing, Methodology, Investigation, Conceptualization. Chen Chen: Writing – Review & Editing, Formal Analysis. Hong Liu: Writing – Review & Editing, Methodology. Yunpeng Wang: Writing – Review & Editing, Conceptualization. Zongxuan Li: Writing – Review & Editing, Conceptualization.

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Disclosure

All authors declare no conflict of interest in this communication.

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