Nature and Science of Sleep

Elevate Series

Open Access Full Text Article

LETTER

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

Xiang Ma, Qing-qing Shan

Department of Respiration, Chengdu Integrated TCM & Western Medicine Hospital, Chengdu, People's Republic of China

Correspondence: Qing-qing Shan, Department of Respiration, Chengdu Integrated TCM & Western Medicine Hospital, No. 18, Wangxiang North Road, High-Tech Zone, Chengdu, Sichuan, 610041, People's Republic of China, Tel +86-028-85311622, Email shanqingqing52377@126.com

Dear editor

We read with great interest the article by Hou et al[1] published in Nature and Science of Sleep. While we appreciate the authors' exploration of inflammation as a potential risk marker, we have significant concerns regarding the methodological rigor and the interpretation of the findings, which we believe substantially limit the validity and clinical applicability of the proposed model.

Omission of Critical Confounding Variables

Our primary concern is the severe omission of key clinical confounders. The development of CIF is multifactorial, driven by well-established risk factors such as hypertension, diabetes mellitus, dyslipidemia, atrial fibrillation, and prior coronary artery disease.[2] These factors are highly prevalent in OSA populations and are themselves potent drivers of systemic inflammation, including elevated NLR.[3] Furthermore, the model neglects the crucial role of body mass index (BMI) and medication history. Obesity is a cornerstone of OSA pathophysiology and a primary driver of chronic inflammation. The trend towards a higher BMI in the CIF group ($P = 0.08$) strongly warrants its inclusion as a covariate. Its exclusion makes it impossible to discern if NLR is an accurate predictor or merely an epiphenomenon of obesity.

Unrigorous Variable Selection Process

The variable selection criteria- "$P < 0.10$ or clinical relevance" -are highly subjective and lack statistical rigor. This approach risks cherry-picking variables that favor a desired outcome. A variable with a strong clinical rationale, such as BMI ($P = 0.08$), was excluded, while others were included based on an arbitrary P-value threshold. A more robust approach would be to pre-specify variables based on clinical knowledge, forcing all established risk factors into the initial model regardless of univariate significance, and then using penalized regression techniques (eg, LASSO) for selection to avoid overfitting, especially in a small sample with only 68 events.

Misinterpretation of Correlation as Causation

The authors' discussion repeatedly implies a causal role for inflammation, stating that it plays a "crucial role in the pathogenesis".[1] This is an overinterpretation of data from a retrospective, cross-sectional study.

In conclusion, the proposed nomogram, despite its high AUC, is built on a statistically and clinically unstable foundation. Future studies will be prospective, adequately powered, and meticulously adjusted for the full spectrum of clinical confounders to determine if inflammatory markers offer any incremental predictive value beyond established risk factors.

Received: 7 September 2025
Accepted: 26 September 2025
Published: 8 October 2025

Data Sharing Statement

Data sharing is not applicable to this communication as no data were created or analysed in this communication.

Author Contributions

Xiang Ma: Conceptualization, Writing – original draft. Qing-qing Shan: Conceptualization, Writing – original draft.

All authors approved the final version accepted for publication; agreed on the journal to which this communication was submitted; and agreed to take responsibility and be accountable for the contents of this communication.

Funding

No funding was received.

Disclosure

There are no relevant financial or non-financial competing interests to report.

References

1. Hou Z, Chen C, Liu H, et al. Predictive value of neutrophil-to-lymphocyte ratio for cerebral infarction in obstructive sleep apnea: a nomogram-based analysis. *Nat Sci Sleep*. 2025;17:1777–1787. doi:10.2147/NSS.S536799
2. Virani SS, Newby LK, Arnold SV, et al. 2023 AHA/ACC/ACCP/ASPC/NLA/PCNA guideline for the management of patients with chronic coronary disease: a report of the American Heart Association/American College of Cardiology Joint Committee on Clinical Practice Guidelines. *Circulation*. 2023;148(9):e9–e119. doi:10.1161/CIR.0000000000001168
3. Adamstein NH, Macfadyen JG, Rose LM, et al. The neutrophil-lymphocyte ratio and incident atherosclerotic events: analyses from five contemporary randomized trials. *Eur Heart J*. 2021;42(9):896–903. doi:10.1093/eurheartj/ehaa1034

https://doi.org/10.2147/NSS.S565515