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RESPONSE TO LETTER

Enhancing the Predictive Value of SII and NLR in LAA Stroke: Addressing Unexplored Limitations and Future Directions [Response to Letter]

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Dear editor

We sincerely appreciate your thoughtful comments and constructive suggestions regarding our recent study, Systemic Immune-Inflammation Index (SII) and Neutrophil-to-Lymphocyte Ratio (NLR): A Strong Predictor of Disease Severity in Large-Artery Atherosclerosis (LAA) Stroke Patients.[1]

Your insights have highlighted several important limitations and provided valuable directions for future research, which we will address in our upcoming studies.

Addressing Lifestyle Factors

You rightly pointed out that lifestyle factors such as smoking, alcohol consumption, dietary habits, and physical activity can significantly influence systemic inflammatory responses and potentially confound the association between SII, NLR, and stroke severity. In our next study, we plan to incorporate detailed lifestyle questionnaires to collect comprehensive data on these variables. By adjusting for these factors in our statistical analyses, we aim to reduce potential biases and improve the reliability of our findings. This will allow us to better isolate the effects of SII and NLR on stroke severity.

Medication Use

We acknowledge that medication use, particularly anti-inflammatory agents, statins, antiplatelet therapies, and corticosteroids, can significantly impact inflammation levels and platelet counts, thereby influencing SII and NLR values. In future research, we will systematically collect data on medication histories and incorporate this information as a covariate in our regression models. Additionally, we plan to stratify our analyses based on medication exposure to better understand its impact on inflammatory biomarkers and stroke outcomes.

Subgroup Analyses

Your suggestion to explore differences in inflammatory responses across sex and age groups is well-taken. Hormonal differences and immunosenescence can indeed modulate inflammation levels, and baseline conditions such as diabetes and hypertension may further complicate the interpretation of SII and NLR. In our next study, we will conduct stratified or subgroup analyses to evaluate the predictive value of SII and NLR in diverse patient populations. This approach will help us develop more personalized diagnostic and therapeutic strategies tailored to specific patient subgroups.

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Strengths and Future Directions

While our study demonstrated that SII and NLR are independent risk factors for LAA stroke severity and have high diagnostic and predictive value, we recognize the need for larger, multicenter studies to confirm these findings. In our future research, we plan to collaborate with other hospitals to expand the sample size and enhance the generalizability of our results. Additionally, we will control the timing of blood sample collection more rigorously to account for changes in inflammation levels over time.

We also aim to explore the potential of anti-inflammatory therapies in stroke management, building on the emerging evidence that targeting inflammation can improve stroke outcomes. By integrating these therapeutic insights with our findings on SII and NLR, we hope to contribute to the development of more effective treatment strategies for LAA stroke patients.

Conclusion

Once again, we thank you for your valuable feedback. Your suggestions have provided us with a clear roadmap for addressing the limitations of our current study and enhancing the robustness of future research. We look forward to advancing this important field and contributing to improved patient outcomes through our ongoing investigations.

Disclosure

The authors declare no conflicts of interest in this communication.

Reference

1. Liu K, Yang L, Liu Y, et al. "systemic immune-inflammation index (SII) and neutrophil-to-lymphocyte ratio (NLR): a strong predictor of disease severity in large-artery atherosclerosis (LAA) stroke patients". *J Inflamm Res*. 2025;18:195–202. doi:10.2147/JIR.S500474

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