




Comment on “Association of the Cumulative Inflammatory Index and Long-Term Mortality in Stroke-Associated Pneumonia” [Letter]

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Dear editor

We read with great interest the paper evaluating the prognostic value of the inflammatory index (IIC) in stroke-associated pneumonia.¹ The topic is clinically important, and the authors are to be commended for assembling a substantial cohort. Nevertheless, we have several methodological concerns that may affect the robustness and interpretation of the reported associations.

The key determinants of stroke-associated pneumonia and post-stroke outcome, such as baseline stroke severity, dysphagia, aspiration risk, and intensity of supportive care (eg, mechanical ventilation or enteral feeding), appear insufficiently accounted for in the multivariable models. Contemporary evidence shows that post-stroke dysphagia and aspiration are strongly linked to pneumonia and mortality and thus are major confounders when evaluating biomarkers in this setting.^{2,3} Incomplete adjustment for these factors may overstate the independent prognostic value of IIC. Then, if patients who died very early or were discharged rapidly were excluded from analysis, the study may be vulnerable to survivor (immortal time) bias, whereby individuals must survive long enough to have IIC measured and pneumonia diagnosed.⁴ Such bias can induce spurious protective or harmful associations in observational prognostic research.

While the handling of missing data is not fully described. Complete-case analysis and ad hoc exclusions are known to yield biased estimates unless data are missing completely at random, a condition rarely satisfied in clinical datasets.⁵ Methodological guidance recommends explicit reporting of the missingness mechanism and, where appropriate, the use of principled approaches such as multiple imputation with sensitivity analyses. The multivariable models seem to include many covariates relative to the number of outcome events. Simulation studies suggest that low events-per-variable ratios lead to unstable regression coefficients, exaggerated effect sizes, and poor reproducibility. To reduce overfitting, prediction-model guidelines encourage careful pre-specification of predictors, shrinkage methods, and internal validation (eg, bootstrapping) according to TRIPOD recommendations. Finally, categorising IIC into several groups sacrifices information and may introduce arbitrary cut-points, with well-documented loss of power and residual confounding. Modelling IIC as a continuous variable, potentially using flexible functions (eg, splines), would provide a more nuanced description of its relationship with outcomes.

Addressing these issues, perhaps through additional analyses and clearer reporting, would considerably strengthen the credibility and clinical applicability of the findings. We hope these comments are helpful in refining the paper.

Data Sharing Statement

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

Author Contributions

Xiang Deng – Conceptualization, Formal analysis, Writing – original draft, Writing – Review & Editing; Chengjie Wang – Conceptualization, Data curation, Validation, Writing – Review & Editing; Zhongsong Zhang – Conceptualization, Data curation, Validation, Writing – Review & Editing. All authors agreed to the journal where this communication was submitted, agreed to the final version submitted for publication and agreed to be accountable for the contents of this communication.

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Disclosure

The authors declare that they have no competing interests in this communication.

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