

Comment on: the relationship between systemic inflammation response index and gastric cancer features

Comentario sobre: la relación entre el índice de respuesta inflamatoria sistémica y el cáncer gástrico

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To the editor,

We read with great interest the article by Pehlevan-Özel et al., in which authors evaluated the prognostic significance of the Systemic Inflammation Response Index (SIRI) among patients with gastric adenocarcinoma undergoing elective gastric surgery¹. Investigating inflammation-based biomarkers in oncology is undoubtedly a clinically relevant topic. However, several methodological aspects of the study warrant clarification to better assess the validity and generalizability of the findings.

While authors indicate they aimed to explore the association between SIRI and 3- and 5-year survival, as well as various demographic, clinical, and pathological features, the manuscript does not clearly state a primary objective. This omission is critical, as the absence of a prespecified primary endpoint raises concerns regarding the statistical power of results. In studies involving survival outcomes, clearly defining a primary endpoint is crucial for calculating an appropriate sample size and conducting hypothesis testing.

Furthermore, the methodology used to define the optimal SIRI cutoff raises essential concerns. Authors appear to have constructed a receiver operating characteristic (ROC) curve using mortality as the outcome and subsequently applied the resulting threshold to generate Kaplan-Meier survival curves for the same

endpoint. This approach introduces a form of analytical circularity, as the cutoff is derived and tested on the same dataset using the same outcome variable. Without external validation or appropriate statistical correction (e.g., cross-validation), this strategy may overestimate the prognostic value of SIRI. Moreover, standard ROC analysis is suboptimal for survival data, as it does not account for censoring or time-to-event information. The use of time-dependent ROC curves or Cox-based modeling would provide a more robust assessment of the discriminatory capacity of SIRI in this context.

In addition, the generalizability of the proposed cutoff value deserves further discussion, as numerous studies have reported different SIRI thresholds depending on tumor type, patient population, and analytic method. For instance, Li et al. identified a cutoff of greater than 0.82 using ROC analysis to predict disease-free survival in patients with localized or regional gastric cancer². In contrast, Gao et al. used X-tile software to determine a cutoff of ≥ 1.2 in a similar population^{3,4}. These discrepancies illustrate that SIRI cutoffs are not universally applicable and underscore the importance of external validation. Acknowledging this variability and its implications would enhance the study's relevance to broader clinical practice.

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In conclusion, Pehlevan-Özel et al., contribute valuable data to the growing literature on systemic inflammation markers in gastric cancer. Nonetheless, clarifying the study's primary objective, detailing the methodology used to derive the SIRI cutoff, and addressing the issue of generalizability would enhance the clarity and clinical utility of their findings. In addition, we question whether Kaplan–Meier analysis was the most appropriate method to evaluate survival differences based on the SIRI cutoff, given that the threshold was derived from the same cohort using the same endpoint⁵. A multivariate Cox regression model would offer a more rigorous assessment of SIRI's independent prognostic significance. We hope these comments are received as constructive and helpful for ongoing discussions in this field.

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Conflicts of interest

The authors declare no conflicts of interest.

Ethical considerations

Protection of humans and animals. The authors declare that no experiments involving humans or animals were conducted for this research.

Confidentiality, informed consent, and ethical approval. The authors have followed their institution's confidentiality protocols, obtained informed consent from patients, and received approval from the Ethics Committee. The SAGER guidelines were followed according to the nature of the study.

Declaration on the use of artificial intelligence. The authors declare that no generative artificial intelligence was used in the writing of this manuscript.

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