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LETTER

Comment on "Peripheral T Lymphocyte Predicts the Prognosis of Gastric Cancer Patients Undergoing Radical Gastrectomy: a Multicenter Retrospective Cohort Study" [Letter]

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Dear editor

The study by Xiao et al[1] provides valuable insights into the prognostic role of peripheral T lymphocytes in gastric cancer (GC) and highlights their potential utility in guiding adjuvant chemotherapy (AC) decisions. However, several methodological and interpretative limitations raise concerns about the validity and generalizability of the conclusions.

1. Retrospective Design and Selection Bias

The retrospective nature of the study inherently introduces selection bias, particularly in AC administration. As acknowledged, 25% of stage II/III patients did not receive AC, yet reasons for this omission (eg, patient frailty, comorbidities) are unaddressed. Such confounding factors may skew survival outcomes, as shown in Squires et al's analysis of perioperative variables in GC.[2] Furthermore, heterogeneity in chemotherapy regimens (SOX vs CapOx) complicates efficacy assessments. A prospective design, as advocated by the STROCSS criteria,[3] is critical to mitigate these biases.

2. External Validation and Population Specificity

While external validation is a strength, the cohorts were exclusively Chinese, potentially limiting extrapolation to Western populations with distinct GC biology and treatment patterns. Previous research highlighted global disparities in GC incidence and molecular profiles, underscoring the need for multinational validation. Moreover, the median follow-up (26 months) is insufficient to assess long-term recurrence, as 20% of stage II/III GC relapses occur beyond 3 years.[4]

3. Statistical Oversimplification

Using X-tile for cutoff optimization risks overfitting, as dichotomizing continuous variables (eg, T lymphocytes) sacrifices granularity. Camp et al[5] warned that such approaches may inflate false-positive associations. Additionally, the absence of machine learning or interaction analyses (eg, T cells × AC timing) overlooks nuanced biological relationships.

In conclusion, while Xiao et al contribute to the growing interest in immune biomarkers for GC, the study's retrospective design, narrow and methodological oversights limit its translational value. Overreliance on T lymphocytes risks oversimplifying GC prognosis, potentially misguiding clinical decisions. Future research must prioritize prospective validation in diverse cohorts, integrate multi-omics data, and address the intricate interplay between immunity and therapy. Without such advancements, the promise of precision oncology in GC remains unmet.

Disclosure

The author reports no conflicts of interest in this communication.

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