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LETTER

Comment on "Predictive Value of Advanced Lung Cancer Inflammation Index and Development of a Nomogram for Prognosis in Patients with Cervical Cancer Treated with Radiotherapy" [Letter]

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Dear editor

I have read with great interest the recent article by Yu et al, titled "Predictive Value of Advanced Lung Cancer Inflammation Index and Development of a Nomogram for Prognosis in Patients with Cervical Cancer Treated with Radiotherapy".[1] The study provides compelling evidence for the prognostic utility of Lung Cancer Inflammation Index (ALI) in cervical cancer, highlighting its predictive value in both overall survival (OS) and progression-free survival (PFS). However, we would like to offer some additional insights and considerations that could further enhance the clinical applicability and future research directions of this promising biomarker.

Temporal and Therapeutic Contextualization

The study cohort (2013–2015) predates the integration of immune checkpoint inhibitors into cervical cancer management, which became standard following the 2023 KEYNOTE-A18 trial and 2024 NCCN guidelines.[2,3] While the absence of immunotherapy data reflects historical practice, this limits the model's applicability to contemporary patients. Future validations should incorporate immunotherapy and explore potential interactions between ALI and immune-related biomarkers. Additionally, critical treatment variables, including salvage hysterectomy post-RT and anti-angiogenic therapies, were omitted. As low ALI may correlate with reduced treatment tolerance, multivariate analyses must adjust for therapeutic heterogeneity to isolate ALI's independent prognostic effect.

Unaddressed Prognostic Confounders

The study did not report HPV status, a cornerstone of cervical cancer biology,[4] nor toxicity associated with radiation therapy, particularly gastrointestinal toxicity. Chronic inflammation from unmanaged toxicities or HPV-driven immunosuppression may confound ALI's association with survival. We recommend integrating HPV genotyping (prioritizing HPV16/18) and toxicity profiles in subsequent analyses.

Analytical Rigor and Generalizability

The single-center retrospective design introduces selection bias and limits statistical power for subgroup analyses. Notably, the exclusively Chinese cohort restricts generalizability to populations with divergent HPV subtype prevalence or treatment accessibility. Multicenter prospective cohorts with prespecified subgroup power calculations are imperative. Furthermore, while survival analyses were well-described, the extent of missing data and handling methods were unreported. Transparent reporting of missingness thresholds and sensitivity analysis would strengthen reproducibility.

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Clinical Utility Validation

Although the nomogram demonstrated discrimination (C-index = 0.81), its clinical net benefit remains unquantified. Decision curve analysis (DCA) comparing the model against FIGO staging and ALI alone across mortality risk thresholds is essential to justify clinical implementation.[5]

Mechanistic and Dynamic Perspectives

As acknowledged by the authors, ALI's prognostic value may evolve with treatment response. Serial ALI measurements during therapy could refine risk stratification by capturing dynamic shifts in nutritional-inflammation balance. Mechanistic studies linking ALI components to tumor microenvironment features are needed to identify actionable therapeutic targets.

In summary, Yu et al's work contributes to our understanding of ALI as a prognostic biomarker for cervical cancer.[1] However, the limitations of historical background and methodological deficiencies require us to interpret its clinical translational value with caution. To bridge this gap, we suggest conducting prospective experiments in a multicenter cohort during the era of immunotherapy to validate the prognostic role of ALI and recalibrate its prognostic threshold. Only through rigorous validation can ALI develop from a statistical correlation indicator into a clinically actionable tool.

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