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RESPONSE TO 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" [Response to Letter]

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Dear editor

We are grateful for Li's thoughtful comments regarding our study, "Predictive Value of Advanced Lung Cancer Inflammation Index and Development of a Nomogram for Prognosis in Patients with Cervical Cancer Treated with Radiotherapy".[1,2] We appreciate the opportunity to address these valuable points, which highlight critical areas for refining the clinical applicability of our findings. Below, we respond to each concern constructively.

We acknowledge that our cohort predates recent advances in immunotherapy. However, there are a few points that we would like to clarify. The NCCN 2024 guidelines recommend immunotherapy as the first-line treatment for cervical cancer, and the KEYNOTE-A18 trial has shown excellent results. Nevertheless, the decision to choose immunotherapy for patients with cervical cancer treated with chemoradiotherapy remains constrained.[3,4] First, immunotherapy is only recommended for patients with FIGO Stage III–IVA cervical cancer. It is not recommended for patients with stage II. Second, the results from CALLA trial showed that durvalumab did not significantly improve the progression-free survival rate in a biomarker unselected, all-comers population. Only for patients with high-risk locally advanced cervical cancer with tumor PD-L1 expression (Tumor Area Positivity $\geq$ 20%) might benefit from the durvalumab.[5] Third, due to economic constraints, some patients are unable to undergo immunotherapy. Thus, not all patients with cervical cancer treated with chemoradiotherapy receive immunotherapy. Consequently, the predictive framework proposed in our research continues to offer clinical utility within contemporary medical practice. However, attention should be paid to the predictive role of the Advanced Lung Cancer Inflammation (ALI) Index in the prognosis of patients receiving concurrent immunotherapy and chemoradiotherapy in future studies.

Furthermore, as a single-center retrospective study, some factors that affected prognosis were unable to be collected, such as HPV status and critical treatment variables, etc. Additionally, some short-term results related to radiotherapy (toxicity of the radiation therapy, etc) could not be evaluated due to incomplete records. These are significant limitations of the article. However, after considering age, pathological type, and FIGO stage, the findings from our study showed that ALI still had good predictive efficacy. Considering that these factors are easily obtainable in clinical practice, we consider that ALI and the prediction model based on ALI are promising predictive tools to predict survival times. This conclusion has also been widely studied and verified in other cancer types.[6] Notably, to improve the applicability of the results, we agree with Dr. Li's viewpoint. We need more multi-center prospective studies to further verify the conclusion.

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In addition, the degree of missing data was presented in the Figure S1, and the analysis and verification of the data were carried out by experienced researchers. The author mentioned that decision curve analysis is necessary for comparing models with FIGO staging and ALI. However, the primary aim was focused on internal validation of the ALI model rather than comparative performance assessment. And the staging factor was taken into account in the analyses.

In summary, Dr. Li's insights underscore key translational gaps in our work. We agree that ALI's prognostic value must be re-evaluated in the immunotherapy era and validated through rigorous multicenter collaboration. Our team is committed to addressing these limitations via multicenter prospective study integrating HPV genotyping, toxicity profiles, and treatment heterogeneity data. More mechanistic studies linking ALI components to tumor microenvironment features are also needed to identify actionable therapeutic targets. In conclusion, current research has confirmed the prognostic predictive efficacy of ALI and we posit that future research will transform ALI from a statistical indicator into a clinically valuable tool.

Disclosure

The authors report no conflicts of interest in this communication.

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