Pericardial irradiation dose may be strongly associated with grade 4 lymphopenia and affect prognosis in patients with locally advanced esophageal cancer receiving definitive concurrent chemoradiotherapy

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Abstract

Background: The immune system may influence prognosis, and lymphopenia is a frequent side effect of concurrent chemoradiotherapy (CCRT). Radical irradiation for locally advanced esophageal cancer (LA-EC) exposes significant vascular and heart volumes. In this study, we hypothesized that lymphopenia is linked to cardiac and pericardial doses and affects patient prognosis.

Methods and materials: We identified 190 LA-EC patients who received radical CCRT. Multivariate analysis (MVA) was performed to correlate clinical factors and dosimetric parameters with overall survival (OS). We collected lymphocyte-related variables and ratios before and during CCRT. MVA was performed to correlate hematologic toxicity with OS. The relationship between dosimetric parameters and G4 lymphopenia was determined using logistic stepwise regression. Finally, a nomogram of G4 lymphopenia was developed and validated externally.

Results: Median follow-up time for all patients was 27.5 months. On MVA for OS, higher pericardial V_{30} (PV_{30}) was linked to worse survival (HR: 1.013, 95% CI: 1.001-1.026, p = 0.039). The median OS stratified by PV_{30} > 55.3% and PV_{30} ≤ 55.3% was 24.0 months and 54.0 months, respectively (p = 0.004). G4 lymphopenia was shown to be linked with worse OS in the MVA of hematological toxicity with OS (HR: 2.042, 95% CI: 1.335-3.126, p = 0.001). Thirty of the 100 patients in the training set had G4 lymphopenia. Logistic stepwise regression was used to identify variables associated with G4 lymphopenia, and the final model consisted of stage-IVA (p = 0.017), platelet-to-lymphocyte ratio during CCRT (p = 0.008), Heart V50 (p = 0.046), and PV_{30} (p = 0.048). Finally, a nomogram predicting G4 lymphocytopenia were constructed and externally validated. The ROC curve showed an AUC for internal validation of 0.775 and external validation of 0.843.

Conclusion: Higher doses of pericardial radiation might affect LA-EC patients' prognosis by inducing G4 lymphopenia during CCRT. Further prospective studies are warranted to confirm these findings, especially in the era of immune-checkpoint inhibitor treatment.