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Prognostic Value of Sarcopenia in Head and Neck Squamous Cell Carcinoma treated with Immune Checkpoint Inhibitors: A Systematic Review and Meta-Analysis

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Abstract

Background

Sarcopenia, the loss of skeletal muscle mass and function, is increasingly recognised as a prognostic biomarker in solid tumours. Immune checkpoint inhibitors (ICIs) are now established therapy for recurrent or metastatic head and neck squamous cell carcinoma (HNSCC), but reliable pre-treatment predictors of outcome remain scarce. Whether body composition-defined sarcopenia predicts survival in ICI-treated HNSCC has not been quantitatively synthesised.

Methods

We performed a PRISMA-guided systematic review and meta-analysis (PROSPERO CRD420261334507). PubMed, Cochrane Library and Scopus were searched from inception to March 2026, supplemented by reference-list screening. Observational studies reporting survival by body composition-defined sarcopenia in adults with HNSCC receiving PD-1, PD-L1 or CTLA-4 inhibitors were eligible. Two reviewers independently screened, extracted data (multivariable-adjusted estimates preferred) and appraised quality using the Newcastle–Ottawa Scale (NOS). Hazard ratios (HRs) for overall survival (OS, primary) and progression-free

survival (PFS, secondary) were pooled using random-effects models with Hartung–Knapp–Sidik–Jonkman adjustment in R 4.5.2, with subgroup, leave-one-out and publication-bias analyses.

Results

Seven observational studies comprising 713 patients (NOS 7–8) were included. Sarcopenia was associated with significantly worse OS (pooled HR 1.94, 95% CI 1.37–2.75; $I^2 = 30.2\%$) and worse PFS across three studies (HR 1.87, 95% CI 1.64–2.12; $I^2 = 0\%$). Leave-one-out analysis for OS yielded pooled HRs of 1.80–2.16, indicating robustness; PFS estimates were directionally consistent but less stable. Subgroup analysis by assessment method showed no significant difference ($p = 0.99$), with the L3 CT-based subgroup yielding HR 2.08 (95% CI 1.74–2.49; $I^2 = 0\%$). Funnel plot inspection showed no marked asymmetry.

Conclusion

Body composition-defined sarcopenia is associated with approximately two-fold higher mortality in HNSCC patients treated with ICIs, independent of the imaging method used. Muscle status assessed on routinely available imaging may aid baseline risk stratification, though

retrospective designs and heterogeneous definitions warrant prospective validation.

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