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Machine-learning based body composition analysis in patients receiving CD19-directed CAR-T cell therapy

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Cancer-associated cachexia (CAC) is associated with adverse outcomes in diffuse large B cell lymphoma (DLBCL). However, exact quantification of CAC remains challenging. Here, we assess the utility of machine learning-based body composition analysis (BCA) using a convolutional neural network for outcome prognostication in patients receiving CD19-directed CAR-T cell therapy for relapsed or refractory LBCL.

BCA parameters were obtained from whole-body CT slides obtained during pre-lymphodepletion PET/CT imaging using a pre-trained pipeline. The pipeline determines absolute values for muscle mass, bone mass, total adipose tissue volume, and adipose tissue volume from different compartments, which were normalized to patient height for further analysis.

Progression-free survival (PFS) was the primary endpoint, with overall survival (OS), probability of grade ≥ 2 cytokine release syndrome (CRS), and probability of grade ≥ 2 immune effector cell-associated neurotoxicity syndrome (ICANS) being secondary endpoints.

Our cohort included 45 patients who received CAR-T cell therapy with either Tisa-cel (n = 28), Axi-cel (n = 14), or Liso-cel (n = 3). Median PFS was 5.1 months and median OS was 9.9 months. Grade ≥ 2 CRS occurred in 21 patients with one fatal event, and ICANS grade ≥ 2 occurred in 10 patients, with one patient succumbing to neurotoxicity.

In univariable analysis using Cox proportional hazards regression, we found no association of BCA parameters with the primary endpoint. International prognostic index (IPI) at the time of CAR T cell infusion (HR + 95% CI: 1.72 [1.22; 2.41] p = 0.0017) and number of prior lines of therapy (1.61 [1.11;2.35] p = 0.013) were significantly associated with PFS. IPI at infusion (2.05 [1.34;3.15] p = 0.001) and reduced muscle-to-bone ratio (MBR, 0.27 [0.08;0.90] p = 0.033) were prognostic for OS. No association between BCA parameters and CRS or ICANS could be determined. In multivariable analysis using best subset selection from all parameters included in univariable analysis, encompassing BMI at infusion, IPI, and lines of therapy, the IPI at infusion retained its prognostic value for PFS (1.67 [1.18;2.36] p = 0.0037) and OS (HR 2.01, [1.31;3.08] p = 0.0013).

Although reduced MBR identifies patients with impaired OS, our study suggests a limited prognostic value of BCA in CD19-directed CAR-T cell therapy. The IPI, incorporating both patient- and disease-specific features, remains robust in identifying high-risk patients.