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Functional Reserve and Sarcopenia Shape Treatment Outcomes After CAR-T Cell Treatment: Results of a Real-World Pilot Study

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Objective
Assessment of patient fitness before CAR-T cell therapy relies on the subjective ECOG performance status (PS), offering limited granularity for clinical decision-making. To establish a more objective reproducible evaluation, we implemented two standardized bedside physical performance tests. In this prospective pilot study, we investigated whether quantitative measures of functional capacity provide discriminatory value for improved risk stratification of CAR-T outcomes.
Methods
90 patients were screened and 66 enrolled for standard-of-care CD19- or BCMA-directed CAR-T cell therapy for LBCL, MCL, B-ALL, or MM between 04/2024–11/2025. In addition to ECOG PS, patients completed a 10-meter walk test and a 30-second sit-to-stand test. Individuals meeting reference values for both tests were classified as fit; failure of one or both tests defined the unfit group. Clinical endpoints included CRS, ICANS, ICAHT, overall survival (OS), progression-free survival (PFS), and non-relapse mortality (NRM). Body composition was quantified on pre-treatment PET/CT scans using an AI-based segmentation tool (Ship-AI), capturing adipose tissue compartments (TAT, VAT, IMAT) and skeletal muscle measures (SMI, SI). Kaplan–Meier analyses assessed survival outcomes.
Results
The cohort comprised 32 fit (48%) and 34 unfit (52%) patients (median age 63, ECOG 0: 23% ECOG 1: 70%, ECOG ≥2: 6%). ECOG PS was similarly distributed between groups (p=0.55) and did not discriminate survival outcomes, whereas the fitness assessment demonstrated a trend toward improved OS (p=0.068). When integrated with sarcopenia metrics, the model provided significantly greater survival discrimination (p=0.037). CRS and ICANS rates did not differ between groups. Fit patients showed higher SMI and SI, indicating better muscle reserves. Gait speed correlated inversely with adipose tissue (IMAT p=0.003; TAT p=0.041; VAT p=0.048).
Conclusions
This study demonstrated feasibility and clinical relevance of standardized fitness metrics before CAR-T therapy. The combination of impaired physical performance and low muscle mass identifies a high-risk phenotype associated with inferior survival.

Keywords

Functional fitness, sarcopenia, real-world, risk stratification

Conflict of Interest & Ethical Approval

yes

Abstract submitters declaration

yes

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