

CT-derived body composition as a prognostic and predictive biomarker in high-risk/metastatic hormone-sensitive prostate cancer: exploratory analysis of the STAMPEDE trials

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Background

CT-derived body composition (BC) can be quantified opportunistically from routine imaging and may provide insights into disease phenotype, prognosis and treatment response. However, its clinical significance and longitudinal evolution following treatment intensification in high-risk hormone-sensitive prostate cancer (HSPC) remain unclear. We evaluated associations between BC and disease presentation, clinical outcomes, treatment benefit and longitudinal changes across multiple treatment intensification strategies evaluated in the STAMPEDE trials.

Methods

We retrospectively analysed clinician directed baseline and follow-up CT imaging from patients with HSPC enrolled in nine randomised STAMPEDE platform trials. Treatment comparisons included docetaxel ± zoledronic acid, abiraterone acetate and prednisolone (AAP) ± enzalutamide, prostate radiotherapy, and metformin, each added to standard of care (SOC). Docetaxel and prostate radiotherapy comparisons included metastatic (M1) patients only. Skeletal muscle index (SMI), intramuscular adipose tissue (IMAT), subcutaneous adipose tissue (SAT) and visceral adipose tissue (VAT) were quantified using an automated toolkit with expert quality assurance. Associations with baseline characteristics were evaluated using linear regression. Cox models assessed overall survival (OS) in M1 disease and metastasis-free survival (MFS) in M0 disease, adjusting for primary analysis defined covariates. Treatment effect modification was evaluated within individual trials using BC-by-treatment interactions reporting likelihood-ratio tests (LRTs). Longitudinal trajectories were assessed using linear mixed-effects models accounting for repeated measurements, with treatment-by-time interactions.

Results

We analysed 7,289 CT scans from 3,825 patients (M1, n=3,134; M0, n=691). Lower SMI and higher IMAT, SAT and VAT were associated with older age, higher grade and stage, greater metastatic burden, and poorer performance status (false discovery rate-adjusted $q \leq 0.008$). Only SMI was independently associated with OS in M1 disease (HR per 10 cm²/m² 0.84; 95% CI 0.76–0.91; $p < 0.001$). Higher VAT showed weak evidence of longer OS (HR 0.98; 95% CI 0.97–1.00; $p = 0.06$). No BC measure was independently prognostic for MFS in M0 disease. BC did not modify treatment benefit in M1 disease. In M0 disease, SMI (interaction LRT $\chi^2 = 9.95$; $p = 0.006$) and SAT ($\chi^2 = 7.89$; $p = 0.03$) showed evidence of modifying the MFS benefit associated with AAP ± enzalutamide.

Among 963 patients with follow-up imaging, SMI decreased by 7.5% annually, while IMAT, SAT and VAT increased by 14.2%, 10.9% and 8.0%, respectively. Compared with SOC, SMI decline was greater with metformin (additional –3.7% annually; interaction $p = 0.03$) and docetaxel ± zoledronic acid (–4.3% annually; interaction $p = 0.02$). AAP ± enzalutamide and prostate radiotherapy did not significantly alter BC trajectories.

Conclusions

Lower SMI at diagnosis was independently associated with poorer OS in M1 disease. BC did not modify treatment benefit in M1 disease, while exploratory interactions in M0 disease require validation. Substantial muscle loss and fat gain during treatment support trials of interventions to preserve skeletal muscle and mitigate fat gain.

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