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Exercise training reshapes the systemic immune environment in patients with metastatic breast cancer: results from the PREFERABLE-EFFECT multi-centre randomised-controlled trial

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Background:

The multinational PREFERABLE-EFFECT RCT (NCT04120298) demonstrated beneficial effects of a 9-month supervised exercise program on fatigue and quality of life among patients with metastatic breast cancer (mBC). As a secondary outcome of the study, we investigated the impact of the exercise program (2x/week resistance, aerobic and balance training) on systemic inflammation and lymphocyte subsets, and explored their association with fatigue in patients with mBC.

Methods:

Blood samples were collected at baseline (T0) and at 3 (T1) and 6 months (T2) into the intervention. PBMCs were analysed with multicolour flow cytometry and 92 plasma proteins were measured with the Olink immunology platform. Between-group differences were identified with linear-mixed-models. Associations of physiological and proteomic markers with clinically relevant baseline fatigue (EORTC QLQ-C30) were explored using Ridge logistic regression.

Results:

Consistent trends toward a higher proportion of CD8+T and CD56dim and a lower proportion of CD4+T cells were found in the exercise group(EX). FlowSOM cluster analyses revealed increases of circulating CCR7+CD45RA+KLRGlowCD8+T, CD56-gammadeltaT cell populations and 3 subsets of CD56dim cells compared to controls. Significantly lower levels of inflammatory mediators, including IL-6(T1:-0.28NPX, p=0.01), CSF-1(T1:-0.06NPX, p=0.008), CCL3(T1:-0.15NPX, p=0.008 ; T2:-0.13NPX, p=0.02) and CD8A(T1:-0.15NPX, p=0.01; T2:-0.13NPX, p=0.03) were measured in EX compared to controls. PTN, associated with worse BC survival was lower (T1: -0.19NPX, p=0.04) and two markers involved in cell death TWEAK(T2:+0.08NPX, p =0.04) and CASP-8(T2:+0.24NPX, p=0.007) were increased in EX. At baseline, the exercise-responsive proteins CSF-1, IL-6, TWEAK and PTN were associated with clinically relevant fatigue.

Conclusion:

Our results demonstrate that the PREFERABLE-EFFECT exercise intervention led to a proportional enrichment of specific immune cell subsets, most of which have a cytotoxic potential, and attenuated chronic inflammation. Multiple exercise responsive proteins were also linked to lower clinically relevant fatigue at baseline, thereby advancing mechanistic understanding of exercise effects in patients with mBC.

Keywords

Breast cancer, exercise intervention, systemic inflammation, fatigue

Conflict of Interest & Ethical Approval

yes

Abstract submitters declaration

yes

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