Effects of Exercise on Cardiometabolic and Immunological Biomarkers in Men with Prostate Cancer on Active Surveillance: Findings from the ERASE Randomized Controlled Trial

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Background: Men with localized prostate cancer on active surveillance (AS) have a higher risk of death from cardiovascular disease (CVD) than from their cancer. Both cardiometabolic health and immune function are implicated in the progression of cancer and comorbidities. Exercise can modulate these systems, but its effects in the AS population are not well understood. We investigated the effects of a 12-week high-intensity interval training (HIIT) program on key cardiometabolic and immunological biomarkers in men with prostate cancer on AS from the ERASE trial.

Methods: Fifty-two men with localized prostate cancer on AS were randomized 1:1 to a 12-week supervised HIIT intervention or a usual care (UC) control group. The HIIT program consisted of three 28- to 40-minute sessions per week performed at 85-95% of peak oxygen consumption. Fasting blood samples were collected at baseline and post-intervention. Samples were analyzed for cardiometabolic markers (lipids, insulin, IGF-axis) and immunological parameters (complete blood counts, circulating immune cell phenotypes, plasma cytokines, and natural killer [NK] cell cytotoxicity). Between-group differences were analyzed using ANCOVA, adjusting for baseline values.

Results: Participants in the HIIT group attended 96% of the prescribed exercise sessions. Compared to UC, the HIIT group demonstrated significant improvements in several cardiometabolic markers, including total cholesterol (mean difference, -0.40 mmol/L; p=0.011), non-HDL-C (-0.35 mmol/L; p=0.006), insulin (-13.6 pmol/L; p=0.025), IGF-1 (-15.0 ng/mL; p=0.048), and IGFBP-3 (152.3 ng/mL; p=0.033). Immunological analyses revealed that the HIIT group, compared to UC, had a significant increase in the percentage of total NK cells (1.99%; p=0.024) and enhanced NK cell cytotoxicity (2.86%; p=0.031). Furthermore, HIIT led to significant decreases in circulating basophils (-0.04 $x10^9$/L; p=0.011) and plasma levels of IL-4 (-0.02 pg/ml; p=0.011) and IL-12p70 (-0.14 pg/ml; p=0.002). No significant between-group differences were observed for fasting glucose, HbA1c, other major leukocyte populations (e.g., T-cells, B-cells), or other cytokines measured.

Conclusions: A 12-week HIIT intervention is a feasible and effective strategy for improving key cardiometabolic and immunological parameters in men with prostate cancer on AS. The observed improvements in lipid profiles and insulin-related pathways may help reduce the high risk of CVD in this population. Concurrently, the enhancement of NK cell quantity and function suggests an improvement in antitumor immunosurveillance. These dual benefits highlight the potential for HIIT to positively impact both cardiovascular health and cancer-related outcomes in this clinical setting.

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