

Effects of a Home-Based Walking Intervention on Serum Metabolomic Profiles in Men with Prostate Cancer on Active Surveillance

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Background: The potential for long-term exercise to affect the metabolome in healthy individuals is well established. Given the metabolic underpinnings of prostate cancer, it is important to investigate whether long-term exercise similarly alters the metabolome in disease-affected men. This study is among the first to characterize metabolic changes in individuals with prostate cancer, comparing those assigned to a home-based walking program to those assigned to printed materials with physical activity recommendations.

Methods: Fifty-one men with prostate cancer on active surveillance were randomly allocated to the exercise or control intervention. Metabolomic profiling of primary metabolism, complex lipids, and biogenic amines was performed at the West Coast Metabolomics Center on serum samples collected at baseline and after the 16-week interventions; data were successfully generated for 22 participants in the exercise arm and 23 participants in the control arm. To identify intervention-related differences in metabolic changes, we performed hierarchical clustering and fit mixed-effects models including an arm x time interaction.

Results: Hierarchical clustering indicated limited separation in metabolic profiles between the exercise and control groups at 16 weeks. Although none of the 1,220 named metabolites exhibited statistically significant differences in change between the two groups ($q < 0.10$), 85 (7.0%) demonstrated nominal significance ($p < 0.05$). Among the 15 metabolites with the smallest p-values, six (40%) were sphingolipids – specifically sphingomyelins – though sphingolipids comprised only 11% of all named metabolites. All six sphingomyelins decreased more over time in the exercise group than in the control group.

Conclusions: Although metabolic profiles were not significantly altered overall, a walking intervention may promote the reduction of sphingomyelins, thereby shifting lipid signaling toward pathways that enhance mitochondrial function and reduce inflammation. Such changes are consistent with biologically plausible mechanisms through which exercise could favorably influence prostate cancer biology, even in the absence of broad metabolomic shifts.