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Associations between dynamic metabolic responses to acute exercise and fatigue in survivors of cancer

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Metabolic changes have been consistently observed in survivors of cancer. Despite the strong link between exercise and metabolism, the metabolic effects of exercise in survivors remain largely unknown, especially dynamic responses to acute exercise. This study characterized metabolic changes during and after acute exercise and investigated associations with cancer-related fatigue. METHODS: Survivors of breast, prostate, and colorectal cancers (n=11) who had completed all treatment performed a submaximal walking treadmill test. Speed and grade were adjusted to maintain intensity at 55% heart rate reserve for 36 minutes. Capillary blood (~500μL) was collected before, after, and 30 min after exercise. Fatigue was measured using the Functional Assessment of Chronic Illness Treatment –Fatigue scale (FACIT-Fatigue). Metabolomics and lipidomics were obtained via high-throughput liquid chromatography-mass spectrometry. Metabolite fold changes (FC) were calculated from before to after exercise (acute response) and after to 30 min after exercise (recovery), with significant metabolites identified with linear mixed models. Spearman's correlation coefficients were calculated to investigate associations with FACIT-Fatigue. RESULTS: Participants were 59±11 years old, 70% female, and breast cancer was the most common diagnosis (50%). Acute responses were primarily characterized by increases in fatty acids (FC=1.4-2.1, $p<0.01$) and acylcarnitines (FC=1.2-1.4, $p<0.01$). Recovery was characterized by decreases in fatty acids (FC=0.7-0.8, $p<0.01$), and increases in ketone bodies (FC=1.3-1.4, $p<0.01$) and hydroxy-acylcarnitines (FC=1.3-1.4, $p<0.01$). Acute and recovery responses in lactate and pyruvate were positively correlated with higher fatigue ($\rho=0.6$-0.7, $p<0.05$), as was arachidonic acid during recovery ($\rho=0.7$, $p<0.05$). CONCLUSIONS: Dynamic metabolic responses during exercise displayed patterns of increased fatty acid mobilization and oxidation. Recovery patterns indicated continued beta-oxidation of monolized lipids. Individuals exhibiting markers of impaired fatty acid oxidation and persistent inflammation during and after exercise reported greater cancer-related fatigue. These results reveal associations between dynamic exercise metabolism and fatigue in survivors, providing potential targets for exercise personalization.

Keywords

survivorship, metabolomics, cancer-related fatigue, physical activity

Conflict of Interest & Ethical Approval

yes

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yes

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