ABSTRACT
MECHANISMS OF FATIGABILITY IN INDIVIDUALS WITH PREDIABETES AND THE EFFECT OF DIETARY NITRATE SUPPLEMENTATION

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Prediabetes is characterized as elevated blood glucose levels below the clinical threshold for type 2 diabetes. Previous research identified an increased fatigability (exercise-induced reduction in limb force or power) of the lower limb muscles in individuals with prediabetes which can impair physical function and lead to reduced physical activity. The mechanisms of fatigability in people with prediabetes are not known but are likely related to the established vascular dysfunction. An important healthcare goal is to determine effective treatments to offset the increased fatigability in people with prediabetes to improve daily function. The purpose of this dissertation was to determine (1) vascular contributions to the increased fatigability in people with prediabetes and (2) whether dietary nitrate supplementation is an effective treatment to improve lower limb fatigability.

Study 1 investigated resting vascular function and exercise-induced blood flow and muscle oxygenation responses during dynamic, knee extension exercise in people with prediabetes compared with age-, body mass index-, and physical activity-matched controls. Males and females with prediabetes had an attenuated exercise-induced blood flow response compared with controls; however, fatigability was not different between groups. Resting vascular function and muscle oxygenation responses during exercise did not differ between people with prediabetes and controls. Fatigability (reduction in power) was associated with reductions in electrically evoked muscle contractile properties, exercise-induced blood flow, and deoxygenated myo/hemoglobin responses during exercise, but not reductions in voluntary activation. Thus, the mechanisms of fatigability in both groups were muscular in origin with contributions from muscle oxygen delivery and extraction.

Study 2 determined the effect of dietary nitrate supplementation (via beetroot juice) on fatigability in males and females with prediabetes. Nitrate supplementation had no effect on fatigability and measures of resting vascular function, exercise-induced blood flow, and muscle oxygenation. These results suggest dietary nitrate supplementation is not an effective strategy to offset increased fatigability in people with prediabetes. Collectively, lower limb fatigability in people with prediabetes and controls was related to contractile mechanisms involving lower exercise-induced blood flow and oxygen extraction. Dietary nitrate supplementation was not effective in offsetting fatigability indicating other interventions targeting blood flow and oxygen extraction may be more effective.