SRP Diabetes Postdoctoral Fellowship Program 2024

Project Title: Dietary Nitrate and Physical Exercise to Prevent Cardiovascular Disease in Diabetes

Project Outline

Background: Physical exercise and dietary improvements are crucial non-pharmacological strategies for patients with metabolic syndrome and diabetes. These lifestyle changes reduce chronic oxidative stress and increase nitric oxide (NO) bioavailability. Our research focuses on inorganic nitrate, found in high levels in green leafy vegetables and beetroot, which converts to bioactive NO. Studies show nitrate positively affects cardiovascular function, reducing blood pressure, improving vascular function, and enhancing exercise parameters like mitochondrial efficiency and oxygen utilization. We hypothesize that dietary inorganic nitrate combined with physical exercise will provide cardiovascular protection for patients with T2D, who are at high risk for CVD. This project involves a clinical trial to study the combined effects of physical exercise and dietary nitrate on cardiovascular health in T2D patients.

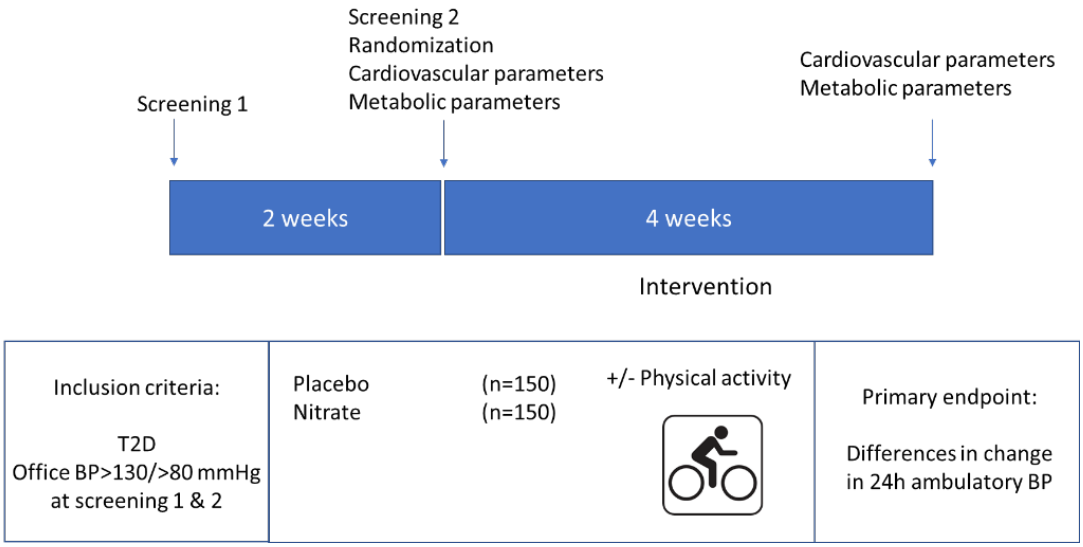

Figure 1.

Overview of study protocol. *Patients with T2D and blood pressure above target value (i.e. 130/80 mmHg) are included. Cardiovascular parameters including blood pressure together metabolic function will be assessed at the time of inclusion, following two weeks of washout (i.e. removal of metformin), and again after 4 weeks intervention with or without exercising three times per week under controlled and supervised conditions. A total of 300 patients will be recruited and each intervention group will contain 150 patients (i.e. 75 with and 75 without physical activity).*

Objectives: We will conduct a randomized controlled trial to explore the effects of dietary nitrate and physical exercise on cardiovascular function in hypertensive T2D patients, hypothesizing that nitrate will enhance the positive effects of exercise.

Work Plan and Methodology: This randomized double-blind placebo-controlled trial involves T2D patients with hypertension. After a two-week medication washout, patients are randomized to four weeks of nitrate or placebo treatment. All patients will perform supervised aerobic exercise thrice weekly. The primary endpoint is the difference in 24h blood pressure changes before and after the intervention.

Participants will receive either 2x 70 ml Beetroot shots (400 mg nitrate) or placebo (beetroot juice with no nitrate) for four weeks. Half of each group will also engage in guided physical exercise via a mobile app, with sessions at 60-70% VO2max, moderate interval training, and intense short sessions. The primary endpoint is the change in 24h ABPM. A power calculation, based on previous studies, requires at least 74 patients per group.

Relevance of Project for Diabetes: Cardiovascular disease is the leading cause of death in over 50% of diabetes patients. This project explores a novel prevention strategy based on nitrate's known cardiovascular benefits. We will test the combined effects of physical exercise and dietary nitrate on cardiovascular risk in T2D patients, potentially offering a straightforward strategy for standard care implementation to reduce CVD risk.

References:

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4. Nilsson LC, et al. Transforming the performance of runners with AI-driven training planning and daily adaptivity. BioRxiv Oct 07, 2023

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