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Investigating the effects of dietary nitrate supplementation on coronary and leg outcomes in peripheral artery disease: Rationale, methods, and feasibility

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Peripheral artery disease (PAD) severely limits exercise tolerance and confers significant coronary event risk. Dietary nitrate supplementation may be a particularly effective intervention for patients with PAD due to its ability to enhance oxygen supply to ischemic tissues; however, little is known about its' impact on oxygen supply in the heart or leg muscles during exercise in these patients. **PURPOSE:** This pilot and feasibility double-blinded RCT (NCT0255733) aimed to determine if short-term dietary nitrate supplementation improves oxygen supply-demand responses in the heart and leg muscles during acute exercise in patients with PAD. **METHODS:** Six PAD patients (ABI < 0.9, Fontaine \leq 2) were randomized to consume either nitrate-rich or nitrated depleted (placebo) beetroot juice for 4 to 6 days, followed by a 7 to 14-day washout before crossing over to the other treatment. Coronary blood velocity (transthoracic ultrasound) and calf muscle oxygenation (NIRS) were measured during handgrip and plantar flexion exercise (Day 4), while claudication onset time, systemic blood pressure, and calf oxygenation were measured during graded treadmill exercise (Day 5 or 6). **RESULTS:** Beetroot juice-delivered nitrate supplementation in these patients was well tolerated and safe (0.7 to 1.8% methemoglobin). Plasma nitrite (NO₂⁻) concentrations increased 12-fold following nitrate supplementation and remained high during laboratory testing, with negligible increases observed following placebo juice consumption. Compared to the placebo visit, dietary nitrate supplementation increased peak coronary blood velocity during plantar flexion (5 vs. 15 cm/sec, p<0.05) and attenuated peak diastolic blood pressure during treadmill exercise (89 vs. 79 mmHg, p=0.02). No other variables were significantly different between visits (all p>0.05). **CONCLUSION:** In this small short-term pilot study, dietary nitrate supplementation lowered treadmill diastolic blood pressure and increased coronary hyperemia during isolated calf exercise. This novel, ischemia-targeted intervention has the potential to combat PAD symptoms, and should therefore continue to be studied in depth.