NCT number not yet given.

Protocol Synopsis

On testing days, patients start with a baseline blood-draw and 15-min supine rest period, then blood pressure will be taken from each arm in duplicate and measured throughout testing (Finapres medical systems, The Netherlands). We will then use a non-invasive doppler probe to assess carotid-femoral arterial stiffness. Next, following reported guidelines, flow-mediated vasodilation of the popliteal artery and near-infrared microvascular function tests will be performed to assess arterial reactivity and endothelial function of the lower leg. The popliteal artery and calf of the most effected leg will be used. Diameters will be analyzed using commercially available vascular analyzing software (Quipu cardiovascular suit, Italy). Next, we will perform two bouts of calf plantar flexion exercise, separated by 15-min, for calf mitochondrial function. Finally, we will perform out primary outcome measurements (six-minute walk test) and a final blood draw. We anticipate these testing to take approximately 2-3 hours.

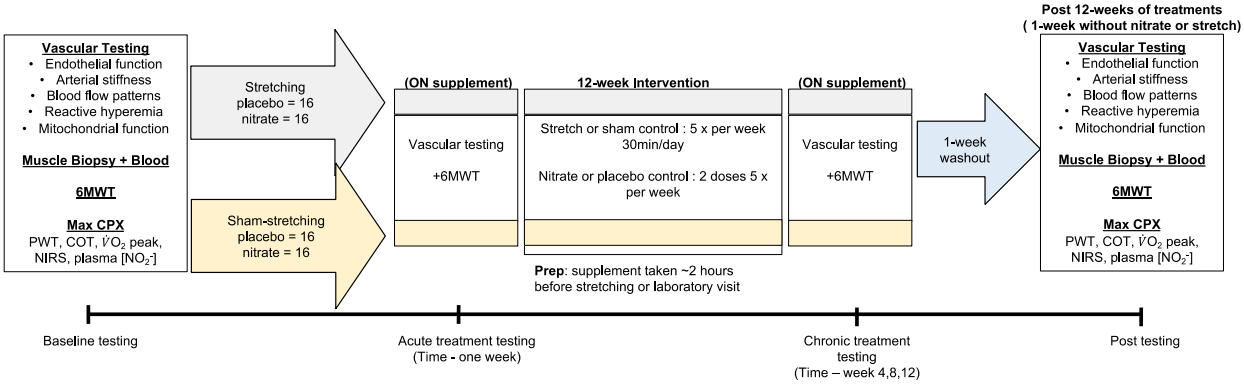

Figure 6. Study design with visit timeline and corresponding assignments. Prior to intervention, patients will complete a battery of tests, including a 6MWT, muscle biopsy and blood draw, and a series of vascular measurements. Patients will then be randomized into four study groups, which includes a true control. The intervention will proceed for 12-weeks. A modified testing battery (no CPX) will be performed and repeated every month for the duration of the study. The complete testing battery will be performed after a 1-week washout from nitrate supplementation and stretching to minimize any residual effect of dietary nitrate or stretching. Please see figure 8 for complete graphical representation. PL: placebo; NR: nitrate-rich; CPX: cardiopulmonary exercise test; PWT: peak walking time; COT: claudication onset time; NIRS: near-infrared spectroscopy; 6MWT: six-minute walk test; $\dot{V}O_2$peak: peak oxygen uptake.