Cover Page

Study Title: Creatine Use and Muscle Stretching in Peripheral Artery Disease

NCT Number: NCT04471792

Date of Statistical Analysis Plan: 04-02-2022

Statistical Analysis Plan to follow

PAD- Stretching +Creatine Statistical Analysis

The primary goal of this study is to determine the effects of splint-based passive muscle stretching with and without creatine monohydrate supplementation protocol on changes in microvascular function, walking performance, and subjective measures of walking performance in PAD patients. Based on data from Moraes et al. [129] who reported a 10% increase in post-occlusive reactive hyperemia in participants taking creatine (effect size: 0.78, mean 1: 0.54, mean 2: 0.49, pooled SD 0.02), a sample size of 9 participants per group was needed to detect changes in microvascular reperfusion variables with 80% power and an α of 0.05. Descriptive statistics were calculated for all variables and included means and standard deviations for normally distributed continuous variables and medians, minima and maxima for non-normally distributed continuous variables. Independent t-tests were used to determine if there were differences in baseline variables between groups. If baseline values between groups were significantly different, a secondary analysis was conducted using an analysis of covariance with baseline values as covariates. If sphericity was violated ($\varepsilon < 1$), a Greenhouse-Geisser correction was used. Changes in dependent variables over time were analyzed using repeated measures ANOVA (group by time). When interactions were significant, independent and paired t-tests were used to determine where differences were located. If there were no differences in measured variables between creatine and placebo supplementation, data were pooled, and paired t-tests were used to evaluate pre to post differences in the measured variables of microvascular function, walking performance, and subjective measures of walking performance. Pearson Product Moment Correlations were completed on baseline variables to look at relationships between microvascular function, walking performance, and subjective measures of walking performance. All significance was accepted at $p < 0.05$. Statistical outliers were removed if they exceeded 2 standard deviations from the baseline mean or mean changes from pre to post-intervention. All analyses were performed using the SPSS 27 statistical package.