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Aerobic Exercise in Subacute Stroke Improves Cardiovascular Health and Physical Performance

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Abstract

Background and Purpose—Cardiovascular health is often impaired after stroke. Reduced exercise capacity (VO_2 peak) and changes in the vascular system in the stroke-affected limb may impact physical performance such as walking. There is little information regarding the role of prescribed moderate-high intensity exercise in subacute stroke. The purpose of this study was to examine whether an 8-week aerobic exercise intervention would improve cardiovascular health and physical performance.

Methods—Ten subjects were enrolled in the study and 9 completed the intervention. Participants were 61.2 ± 4.7 years old, 66.7 ± 41.5 days post-stroke and had minor motor performance deficits (Fugl-Meyer score, 100.3 ± 29.3). Outcome measures were taken at baseline, post-intervention and one-month follow-up. Brachial artery vasomotor reactivity (flow mediated dilation; FMD) of both arms assessed vascular health and a peak exercise test assessed exercise capacity. The six-minute walk (6-MWT) test was used to assess physical performance. Participants exercised on a recumbent stepper three times per week for eight weeks in a prescribed heart rate (HR) intensity.

Results—At baseline, we report between-limb differences in brachial artery FMD and low VO_2 peak values. After the intervention, significant improvements were reported in FMD in both arms, resting systolic blood pressure (SBP) and the 6MWT. Although we also observed improvements in resting diastolic BP, HR and VO_2 peak values, after the exercise intervention, these were not statistically significant

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Video Abstract available (see Video, Supplemental Digital Content 1) for more insights from the authors.

Discussion and Conclusion—Aerobic exercise in subacute stroke was beneficial for improving cardiovascular health, reducing cardiac risk and improving physical performance (6MWT).

Keywords

Vasomotor reactivity; oxygen uptake; cerebrovascular accident; blood flow; physical fitness

INTRODUCTION

Exercise capacity (peak oxygen consumption, VO_2 peak) rapidly declines in the acute stage of stroke recovery and has been shown to be approximately 60% lower than age and sex-matched peers.[1] Several studies also corroborate these findings with low VO_2 peak levels in chronic stroke survivors.[2-8] The decline in exercise capacity is multi-factorial with stroke-related impairments found in the neuromotor, respiratory, and cardiovascular systems.[1,2,9,10] However, aerobic exercise interventions have consistently shown improvements in VO_2 peak, the six-minute walk test (6-MWT)[7,11-13]and gait[13] in chronic stroke survivors. A limited number of studies have demonstrated improvements in cognition in response to an aerobic exercise intervention in chronic stroke.[11,14] There have been only a few studies that have focused on exercise in subacute stroke, but the evidence supports improved VO_2 peak and walking endurance.[10,15,16]

While overall exercise capacity is reduced after stroke, there are reports that stroke survivors demonstrate unique unilateral adaptations in the stroke-affected limb[17-20] that may further contribute to fatigue with activity and to metabolic dysfunction.[19] These unilateral changes have been observed in the stroke-affected limb for femoral artery diameter,[17,18] vasomotor reactivity,[19,20] blood flow,[17,19-21] and tissue composition.[21-24] Our previous work suggests that unilateral exercise improves femoral artery diameter and blood flow to the hemiparetic limb[17] but does not improve cardiorespiratory fitness.[21] Ivey and colleagues randomized chronic stroke survivors to either a 6-month task-oriented treadmill intervention or the control group, which consisted of stretching exercises. Individuals participating in the treadmill intervention showed significant improvements in VO_2 peak, leg blood flow and vasomotor reactivity when compared to the control group.

Vasomotor reactivity via flow-mediated dilation (FMD) is calculated as the peak arterial diameter from the baseline value (%FMD) in response to an “acute increase in blood flow”[25] such as exercise or walking. Flow-mediated dilation in the brachial artery is impaired in acute[26] and chronic[27] stroke when compared to persons without stroke. Stroke-related changes in the brain, specifically in areas that regulate autonomic function may have significant implications for BP regulation (vasodilation/constriction of the vessel) and cardiac function during the acute phase of stroke recovery.[28,29] Gaining insight into vascular changes that occur post-stroke may guide rehabilitation professionals to consider exercise interventions aimed at minimizing vascular decline. However, whether an aerobic exercise intervention in the subacute stage of stroke recovery facilitates improvements in vasomotor reactivity has yet to be explored.

Using a task-oriented treadmill exercise model has significant advantages related to physical performance outcomes such as walking in addition to cardiovascular health and prescribing exercise.[19,22] However, we concur with Tang and colleagues[15] that performing aerobic exercise in persons with subacute stroke presents unique challenges related to excluding participants who have limited to no ambulatory function. In the study by Tang and colleauges,[15] individuals were randomly assigned to either the exercise group, which participated in aerobic exercise using a recumbent cycle ergometer in addition to their

inpatient rehabilitation or the control group, which performed usual inpatient rehabilitation. Although both groups improved from baseline, the exercise intervention group demonstrated greater improvements in VO_2 peak and the 6-MWT during inpatient rehabilitation.[15] It is important to note that participants assigned to the exercise group engaged in aerobic exercise for an average of only 9 days. Therefore, when compared to the control group, there was not a significant group-by-time interaction. Their study, however, laid the groundwork for clinicians and researchers to consider initiating exercise early in stroke recovery.

The purpose of this present study was to determine whether an 8-week moderate-high intensity aerobic exercise intervention using a seated exercise modality (total body recumbent stepper; TBRS) would improve cardiovascular health and physical performance in participants with subacute stroke (less than 6 months). We hypothesized that the aerobic exercise intervention would improve our primary outcome measure, brachial artery FMD bilaterally. For our secondary outcome measures, we also hypothesized that there would be a decrease in resting HR, systolic blood pressure (BP) and diastolic BP. From the exercise test, we hypothesized that there would be an increase in peak HR, VO_2 peak, exercise test time, workload (watts) and the distance covered during the 6MWT would increase following the exercise intervention. In addition, we wanted to explore whether any improvements would still be observed at one month post-intervention. We hypothesized that at the one-month follow-up, our outcomes measures would be significantly higher than baseline.

METHODS

Study Design

A prospective study with a sample of convenience was used for a pretest-posttest design and follow-up testing one-month after completion of the exercise intervention. Adverse events related to exercise testing and the intervention were monitored throughout the study. The study was approved by the Human Subjects Committee at the University of Kansas Medical Center. Institutionally approved written consent was obtained prior to enrollment.

Participants

Between December 2010 and January 2012, 40 individuals with a diagnosis of stroke were screened for inclusion into CRESS (Cardiovascular Regulation and Early Exercise Stroke Study). Inclusion criteria were as follows: 1) between 50-70 years of age, 2) diagnosis of a first-time, unilateral stroke that occurred less than 6 months prior to enrollment, 3) ability to walk with or without an assistive device and need only stand-by assist, 4) ability to travel for all testing and exercise sessions. Individuals were not enrolled if the following exclusion criteria were present: 1) acute renal failure, 2) ischemic cardiovascular event or coronary artery bypass surgery less than 3 months ago, 3) severe peripheral artery disease (ABI < 0.40), 4) diagnosis of congestive heart failure, 5) current smoker, and 6) unable to position the upper extremity in 90 degrees of shoulder abduction and elbow extension for optimal access of the brachial artery during ultrasound scanning.

Outcome Measures

Flow Mediated Dilation (FMD)—Participants were asked to refrain from food or caffeine for 12 hours and from vigorous activity for 24 hours prior to the FMD procedure. The participant was resting supine for 20 minutes prior to the FMD procedure in a temperature controlled (22-24 degrees Celsius) and a quiet, dimly lit room.[1] HR was monitored continuously using a 3-lead EKG while resting BP was taken in supine after the 20-minute rest period. An automated cuff with rapid inflation system (D.E. Hokanson, Bellevue, Washington) was placed just distal to the olecranon process.[30,31] The arm to be scanned was placed on a stabilizing device to allow for optimal scanning of the brachial artery and avoid

arm movements during the ultrasound imaging. The brachial artery was identified longitudinally always at the same reference point, 2-3 cm proximal to the antecubital fossa using an ultrasound system and a 7.5 MHz linear array transducer (Siemens Medical Solutions, Malvern, Pennsylvania). Once a satisfactory image of the brachial artery was obtained, the transducer was stabilized using a custom-designed holder. If needed, minor adjustments were made to the transducer placement for optimal imaging. We also captured Doppler velocity measurements at an insonation angle of 60 degrees using the ultrasound system. Baseline diameter and blood flow velocity was recorded continuously for 10 seconds. The pneumatic cuff was then inflated to suprasystolic pressure (220 mmHg) and maintained for 5 minutes. Twenty seconds prior to cuff deflation, recording of diameter and blood flow velocity was resumed. At 5 minutes, the cuff was deflated while ultrasound images continued to be recorded for another 3 minutes. All images were stored on a computer and analyzed off-line using specialized software (Brachial Analyzer, Medical Imaging Applications, Coralville, Iowa). This edge-detection software allows the operator to identify a region of interest at a specific, designated area of the vessel. The automated software identified the near and far wall properties of the vessel and track diameter changes. Using an automated software system minimized investigator bias and more accurately detected changes in FMD.[32] In addition, using computerized edge-detection and wall-tracking systems to detect changes in FMD improve the validity and intra-relater reliability variation for the automated systems than for the manual technique.[33-35]

Six-minute walk test (6-MWT)—The 6-MWT is a valid and reliable test of assessing physical performance for people with stroke.[5] The 6-MWT was performed on the same day but following the FMD procedure. The 6-MWT was performed in a 100-foot corridor with minimal distractions and was marked every 3 meters to measure distance.[36] A stopwatch was used to keep time and standardized verbal cues were given.[36] Participants were allowed to use their assistive device if needed during the test but were required to use the same assistive device for all testing sessions.

Cardiovascular Health and Peak Exercise Test—Exercise testing was conducted on a separate day from the FMD procedures and 6-MWT. Participants were asked not to consume food or drink (except water) within 2-3 hours of the exercise tests and to avoid caffeinated products for 6 hours prior to the exercise test. Participants were asked to avoid vigorous physical activity for 24 hours prior to testing. All participants had an opportunity to use the exercise device (total body recumbent stepper, TBRS (NuStep, T5XR, NuStep, Inc., Ann Arbor, Michigan) to practice the alternating, reciprocal movement pattern, step rate (80spm) and were familiarized with the Borg Rating of Perceived Exertion (RPE) Scale. This was performed prior to the maximal exercise testing day.

Prior to each exercise test and after 15-minutes of sitting quietly, resting HR, SBP and DBP measures were obtained and recorded. Oxygen uptake was measured and analyzed through collection of expired gases using the ParvoMedics metabolic measurement system (Parvomedics Inc., Sandy, UT). Gas and flowmeter calibrations were performed on the metabolic cart according to the specifications of the manufacturer. The calibration of the metabolic cart was performed by the same individual to reduce the likelihood of operator error. We used identical exercise testing methodology and the mTBRS-XT protocol.[6] Briefly, the mTBRS-XT is a 2-minute incremental exercise test to assess VO_2 peak and other metabolic parameters. The mTBRS-XT has been shown to be a valid exercise test for people post-stroke[6] and has been sensitive enough to detect change in VO_2 peak.[11] A physician was present for all exercise tests.

Intervention

Aerobic exercise training—The exercise sessions were held at the University of Kansas Medical Center Research in Exercise and Cardiovascular Health (REACH) Laboratory. Since few studies have performed moderate- to high-intensity aerobic exercise[37] in subacute stroke, we used the following exercise prescription guidelines: 1) systolic BP less than 220 mmHg and diastolic BP below 100mmHg; 2) RPE between 12-16/20 and 3) exercise intensity was prescribed at 50-59% of HR reserve (derived from the exercise test) for 4 weeks and then increased to 60-69% of HR reserve for the remaining 4 weeks. Individuals wore Polar HR monitors (Polar Electro Oy, Oulu, Finland) and were given cueing, if needed and encouragement to maintain exercise intensity to stay in the prescribed target HR range for the duration of the session. Exercise sessions were 3 times per week for 8 weeks. Exercise compliance for attendance was recorded in the exercise log.

Each exercise session began with pre-exercise vital signs, for those with diabetes, blood glucose was recorded and we inquired whether there were any changes in medication(s). If a medication was added or removed or if the dosage was changed, we documented this in the exercise log. Ten stretching exercises for the upper and lower body were performed prior to commencement of the exercise session. After stretching, each session began with a 5 minute warm-up at 15-25 watts at a comfortable, self-selected pace. After 5 minutes, the exercise intensity was increased to the prescribed workload. Exercise intensity for each session began at the low end-range of the targeted HR range (THRR) and increased in intensity so that the remaining 10 minutes was spent at the upper portion of the THRR (i.e. ~ 59% of HR reserve). Once 20 minutes of exercise was performed with an RPE <13, the duration was increased to 30 minutes. No aerobic exercise session exceeded 40 minutes in duration. Intensity was adjusted according to physiologic response but did not exceed the THRR. We documented in the exercise log, the amount of time spent in the prescribed HRR. Heart rate, BP and RPE were assessed within 1 minute prior to the end of the exercise training to capture exercise response. A 5-minute cool-down was then employed.

Follow-up—No specific information related to exercise or physical activity was provided for the 4-week period. Once the time period had elapsed, individuals returned for final testing.

Sample Size Justification—The primary outcome of interest for the proposed work was the percent change in vasomotor reactivity after the exercise program. No data exists regarding brachial artery vasomotor reactivity response to an exercise intervention in people post-stroke. The sample size for the present study was based on our previous work using a within-group treatment design and the outcome measure was a change in blood flow after unilateral exercise training.[17] Based on the power analysis with an effect size ($d = 4.37$, power of 0.95), we needed 5 people to determine significant changes. However, since we are examining a different outcome (vasomotor reactivity), and expected a smaller effect size, we chose a conservative approach and over enrolled to include 10 participants.

Data Analysis

Data analysis was performed with SPSS Version 18.0 (SPSS Inc, Chicago, Illinois) for Windows. For each of the outcome measures, descriptive statistics were performed. For our primary outcome, we tested FMD in bilateral brachial arteries. For our secondary outcomes, we assessed resting HR, SBP and DBP. From the exercise test, we assessed peak HR, VO_2 peak, exercise test time, workload (watts) and the distance covered during the 6MWT. Baseline and 1) post-intervention data and 2) one-month follow-up comparisons were made using a one-tailed paired t-test. Due to multiple comparisons and the risk of inflating our type I error, we adjusted our p-value to be significant when p was ≤ than 0.02.

RESULTS

Ten people completed the initial screening and consented to participate. One individual had an echocardiogram prior to her discharge from inpatient hospitalization and a blood clot was found in the aorta. The individual was no longer eligible for participation in the study. Therefore, an additional person was screened and enrolled. Ten people completed the initial testing and began the training intervention. One person after completion of week 4 discontinued the training due to schedule conflicts and could not commit to attending the training session 3 times per week. For the remaining nine participants exercise adherence was 85% (range: 75-100%). The primary reason for missing a session for those below 80% adherence was transportation. Average time in the prescribed HR zone was 66% for the 8-week intervention. The first four weeks approximately 70% of the exercise session was spent in the THRR (50-59% of peak HR) while the last 4 weeks were 63% of THRR (60-69% of peak HR). No serious cardiac or other adverse events related to exercise testing or the intervention were reported. There were no additions of medications for BP, cardiac arrhythmias, or cholesterol. In addition, for those taking cardiovascular medications, no changes in medication dosage were reported. One individual began taking pregabalin (Lyrica) after week 3 of the exercise intervention. Since a known side effect of this medication is weight gain, this may have contributed to the 20 pound increase in weight that was observed at the post-intervention testing. This likely affected the group mean value for body weight (kg). Participant demographics are presented in Table 1.

Brachial Artery Diameter and FMD

Baseline brachial artery diameter was significantly smaller in the stroke-affected arm when compared to the other side. Furthermore, the stroke-affected side demonstrated a significantly reduced FMD response when compared to the other limb ($p < 0.02$). After the 8-week exercise intervention, significant improvements were reported bilaterally for both artery diameter ($p < 0.01$) and FMD ($p < 0.01$). At the one-month follow-up, no significant differences were found for artery diameter when compared to baseline values ($p > 0.05$). However, FMD remained higher than baseline bilaterally but this was not statistically significant ($p > 0.02$). One person experienced significant bouts of coughing during the scan which increased his tone in the stroke-affected arm. We tried several rest breaks but ultimately, he was unable to maintain a quiet, resting position for the duration of the scans. Therefore, due to excessive movement, we were unable to capture a continuous, clear image of the brachial artery for the duration of the ultrasound scan. Therefore, this individual's ultrasound data was not included in the follow-up (Table 2).

6MWT

From baseline to post-intervention, we observed a 12.7% (38.7 meters) increase in the distance walked (304.1 ± 167.5 to 342.8 ± 185.6 meters, $p < 0.002$). For the 8 individuals who returned for the follow-up visit, there was an additional gain of 9.8 meters between the mean distance walked at post-intervention compared to the one-month follow-up. However, when the one-month follow-up was compared to baseline, participants significantly increased ($p < 0.005$) the distance walked by 44.9 meters.

Cardiovascular Health and Peak Exercise Testing

Baseline values for resting HR, SBP, DBP and exercise testing outcomes are listed in Table 3. This group of stroke survivors could tolerate higher workloads during the exercise test than those in our previous work. [6] Therefore, we added an additional two stages (Stage 9 = 145 watts; Stage 10 = 160 watts) to the mTBRS-XT protocol.

Resting HR, SBP and DBP all decreased after the exercise intervention but SBP was significantly lower. Neither peak VO_2 ($p = 0.04$) nor peak HR ($p = 0.25$) was significantly improved after the intervention and RER was essentially unchanged (1.1 ± 0.1, $p = 0.44$). The perception of their exertion level following the intervention was lower with RPE at 17.7 ± 2.8 but non-significant ($p = 0.08$). Mean exercise test time increased from the initial assessment at baseline while peak workload was significantly higher. At the one-month follow-up, only RPE and peak watts remained significantly different from baseline (Table 3).

DISCUSSION

This study examined whether an 8-week aerobic exercise intervention using a recumbent exercise device could improve cardiovascular health and physical performance during the subacute stage of stroke recovery. This is the first investigation to demonstrate that brachial artery vasomotor reactivity was improved after exercise in both the stroke-affected and non-affected side. As hypothesized, we found that the intervention improved cardiovascular health and physical performance (6-MWT). Further, we chose a one-month follow-up to assess whether any improvements gained from the exercise intervention would be maintained, and found this to be the case for some of the outcome measures.

Vasomotor Reactivity

Even in the early stages post-stroke, we report between-limb differences in vasomotor reactivity. Since blood flow regulation and vessel wall diameter are controlled by both metabolic demand and autonomic control,[38] these unilateral changes may be in part, a result of the stroke rather than only due to decreased physical inactivity or muscle loss. Since this study did not examine the influence of any mechanistic factors (i.e. inflammation, or lesion location such as the insula), it may be premature to suggest these unilateral changes are an absolute, direct result of the stroke. Further study is warranted to identify the underlying mechanisms contributing to unilateral vascular differences or whether beginning exercise within days post-stroke would mitigate these differences.

Exercise has been shown to be beneficial in improving brachial artery vasomotor reactivity in those with acute myocardial infarction,[37] heart transplant recipients,[39] and hypothryoidism[40] but has not been assessed in subacute stroke. We chose to use a recumbent stepper for the exercise intervention versus treadmill due to the potential challenges in balance and walking in people post-stroke. After the intervention, our findings demonstrate improvements in FMD in the stroke-affected and non-affected (18.5%, 19.4%) limbs. These results are similar to those reported in chronic stroke.[19] It is important to note that greater changes in brachial artery FMD have been observed in other clinical populations using a higher intensity of prescribed exercise.[39,41,42] Taking into account that stroke survivors have existing cardiovascular disease and the exercise intervention was well-tolerated by our small group of participants, future work should expand upon this study and consider a randomized-controlled trial further examining exercise dose and intensity to improve vasomotor reactivity.[39]

Walking endurance

Aerobic exercise training has been effective at improving endurance and distance walked during 6-MWT in subacute and chronic stroke. After the exercise intervention, participants increased their 6-minute walking distance by 38.7 meters. These results fall between a small and moderate meaningful change for stroke survivors.[43] We found these results to be noteworthy since the exercise intervention was not walking but rather a recumbent stepper. Since the TBRS has been a preferred exercise modality for older adults[44] and can

accommodate a variety of people with neurologic impairments,[6,45,46] we believe this information will be useful to clinicians in stroke rehabilitation settings.

Cardiovascular Health and Exercise Testing

As stated by our lab[2] and others,[1,47,48] stroke survivors have very poor levels of exercise capacity. VO_2 peak values for our group of stroke survivors were in the very poor fitness category.[37] Although improvements for mean VO_2 peak were observed, only 2 participants increased their fitness level sufficient enough to move upward into another category. However, these values were considered "poor" when compared to age- and gender-matched counterparts.[37] This study further highlights the need for continued, aggressive exercise programming during stroke rehabilitation and continuing into community programming.

We used a one-month follow-up to examine whether improvements from the exercise intervention would be maintained above baseline measures. At the follow-up testing we noticed improvements in some of our measures. When we started asking what they did during this follow-up, many continued to be physically active. Since, we were not expecting the participants to continue to be physically active, we did not collect information regarding activity levels.

Certainly, we were encouraged by their desire to continue to exercise, and in our future studies, we plan to collect this information.

There are challenges associated with exercise testing in the stroke population and VO_2 peak should not be the only outcome measure when examining exercise performance. After the exercise intervention, VO_2 peak values increased 9% while power output (watts) increased 26.3% with a perception of reduced exertion using the RPE. The participants gave good effort with mean RER values at 1.1 at all timepoints.[49] In addition, we report improvements in resting HR and BP after the exercise intervention. It has been suggested that a little as a 5mm Hg decrease in SBP could reduce mortality associated with stroke by 14%.[50] After the exercise intervention, our findings showed an 11mmHg decrease in resting SBP and a 1.4 mm Hg drop in DBP. Since stroke survivors are considered high cardiac risk,[37] it is advantageous to consider interventions that modify these risk factors. While many issues may contribute to fluctuations in HR and BP, we monitored medications for dose and frequency changes. We recognize that this is a small sample size with a pre/post-test design. Therefore, data need to be interpreted with caution. Based on the results of the study, individuals in the subacute phase of stroke recovery tolerated moderate-high aerobic exercise. No serious or cardiac adverse events were reported as a result of this intervention. The findings of this study are encouraging and demonstrate the need to extend this work to a randomized-controlled trial.

CONCLUSIONS

Individuals in the subacute stage of stroke participated in an 8-week moderate-high exercise training intervention using a recumbent stepper; after the exercise intervention, improvements were reported in brachial artery vasomotor reactivity as well as cardiovascular and physical performance. Future work should focus on examining the effects of an exercise intervention on cardiovascular health through a randomized-controlled trial.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1

Baseline Participant Demographics

Characteristics n = 10	Number or Group Mean (SD)	Range
Male	6	
Age (years)	61.2 (4.7)	52-70
Weight (kg)	**78.1 (10.6)**	**60.4-95.5**
Race		
African American	3	
Caucasian	6	
Native American	1	
Ethnicity		
Hispanic	1	
Non-Hispanic	9	
Marital Status		
Married/Partner	9	
Single	1	
Stroke Lesion		
Right	5	
Left	5	
Overall ABI	0.98 (0.11)	
Fugl-Meyer		
Lower	27.4 (8.8)	(7 – 34)
Upper	51.2 (19.6)	(10 –66)
Sensation	21.7 (3.4)	(18 – 24)
Total	100.3 (29.3)	(35 – 124)
Days Post Stroke	68.6 (40.1)	(10–123)
Diabetes		
Type I	0	
Type II	4	
Regular Exercisers Pre-Stroke	4	
Medications		
Blood Thinners	8	
ACE Inhibitors	6	
Antidepressant	2	
Angiotensin II Receptor Blockers	2	
Beta-Blockers	2	
Calcium Channel Blockers Cholesterol	3 3	
Diabetes	2	
Diuretic	2	
Vitamins	3	

Table 2

Brachial Artery Measures

	Baseline n = 9	Post-Intervention n = 9	Change %	p-value	1-month follow-up n = 7	p-value baseline to follow-up
$FMD_{affected}$(%)	4.7 (2.5)*	5.4 (2.4)*	18.5	0.001	5.4 (2.5)*	0.05
$FMD_{nonaffected}$ (%)	6.5 (2.2)	7.7 (2.3)	19.4	0.001	7.1 (2.9)	0.03
$Diameter_{affected}$ (mm)	3.7 (0.5)*	3.9 (0.6)*	5.0	0.01	3.7 (0.5)	0.26
$Diameter_{nonaffected}$ (mm)	4.0 (0.6)	4.2 (0.7)	6.3	0.01	4.0 (0.4)	0.14

Data expressed as mean (SD) unless otherwise stated. FMD = flow-mediated dilation

* indicates $p \leq 0.02$ for between-limb differences for the outcome measure at each timepoint (baseline, post-intervention and follow-up)

Table 3

Cardiovascular Health and Exercise Testing Outcomes.

	Baseline n=9	Post-Intervention n=9	p-value	1-month follow-up n=8	p-value
Resting					
HR (bpm)	81.2 (14.1)	78.7 (12.9)	0.25	74.8 (10.1)	0.08
SBP (mmHg)	134.1 (8.6)	122.4 (11.1) *	0.001	131.4 (12.6)	0.27
DBP (mmHg)	78.2 (10.2)	76.8 (6.3)	0.34	77.3 (5.5)	0.25
Peak Exercise					
VO_{2peak} ($mL^{*}kg^{-1}{}^{*}min^{-1}$)	15.8 (3.9)	17.5 (6.2)	0.04	17.4 (7.4)	0.18
HR (bpm)	142.9 (18.0)	144.2 (20.4)	0.40	143.3 (20.1)	0.40
RER	1.1(0.1)	1.1(0.1)	0.44	1.2 (0.1)	0.20
RPE	18.9 (1.7)	17.4 (2.8)	0.08	17.4 (2.1) *	0.01
Work (Watts)	66.7 (26.5)	83.3 (32.9) *	0.004	90.6 (33.2) *	0.01
Ex Time (sec)	654.1 (215.2)	700.9 (212.5)	0.10	707.9 (225.7)	0.09

Data expressed as mean (SD). HR = heart rate; SBP = systolic blood pressure; DBP = diastolic blood pressure; RER = respiratory exchange ratio; (VCO_2 ($L^{*}min^{-1}$)/VO_2($L^{*}min^{-1}$)); RPE = rate of perceived exertion.

* indicates significance ($p \leq 0.02$) between baseline and 1) post-intervention and 2) 1 month follow-up.