ACRM
AMERICAN CONGRESS OF REHABILITATION MEDICINE

Archives of Physical Medicine and Rehabilitation

journal homepage: www.archives-pmr.org

Archives of Physical Medicine and Rehabilitation 2016;97:596-603

ORIGINAL RESEARCH

Exercise Induces Peripheral Muscle But Not Cardiac Adaptations After Stroke: A Randomized Controlled Pilot Trial

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Abstract

Objective: To explore the physiological factors affecting exercise-induced changes in peak oxygen consumption and function poststroke.

Design: Single-center, single-blind, randomized controlled pilot trial.

Setting: Community stroke services.

Participants: Adults (N = 40; age >50y; independent with/without stick) with stroke (diagnosed >6mo previously) were recruited from 117 eligible participants. Twenty participants were randomized to the intervention group and 20 to the control group. No dropouts or adverse events were reported.

Interventions: Intervention group: 19-week (3times/wk) progressive mixed (aerobic/strength/balance/flexibility) community group exercise program. Control group: Matched duration home stretching program.

Main Outcome Measures: (1) Pre- and postintervention: maximal cardiopulmonary exercise testing with noninvasive (bioreactance) cardiac output measurements; and (2) functional outcome measures: 6-minute walk test; timed Up and Go test, and Berg Balance Scale.

Results: Exercise improved peak oxygen consumption (18±5 to 21±5mL/(kg•min); $P<.01$) and peak arterial-venous oxygen difference (9.2±2.7 to 11.4±2.9mL of O_2/100mL of blood; $P<.01$), but did not alter cardiac output (17.2±4 to 17.7±4.2L/min; $P=.44$) or cardiac power output (4.8±1.3 to 5.0±1.35W; $P=.45$). A significant relation existed between change in peak oxygen consumption and change in peak arterial-venous oxygen difference ($r=.507$; $P<.05$), but not with cardiac output. Change in peak oxygen consumption did not strongly correlate with change in function.

Conclusions: Exercise induced peripheral muscle, but not cardiac output, adaptations after stroke. Implications for stroke clinical care should be explored further in a broader cohort.

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An audio podcast accompanies this article. Listen at www.archives-pmr.org.

Supported by the Newcastle Centre for Brain Ageing and Vitality, the UK National Institute for Health Research Biomedical Research Centre for Ageing and Age-Related Disease award to the Newcastle upon Tyne Hospitals NHS Foundation Trust, and the Medical Research Council (reference G0802536). Also supported by a senior research fellowship, a Senior Investigator Award from the National Institute for Health Research, and the Centre for Brain Ageing and Vitality, Newcastle University.

Clinical Trial Registration No.: ISRCTN41026907.

Disclosures: none.

Cardiorespiratory fitness (CRF) levels are decreased after stroke,[1] potentially leading to an increased risk of further cardiovascular disease.[2] The criterion standard measure of CRF is peak oxygen consumption, which is the product of the capacity of the cardiovascular system to supply oxygen (ie, cardiac output) and the capacity of skeletal muscles to use oxygen (ie, arterial-venous oxygen difference). In healthy individuals, peak oxygen consumption appears to be limited by the cardiovascular system.[3] The relation between peak oxygen consumption and oxygen supply and oxygen utilization has yet to be established poststroke. Two small cross-sectional studies have presented opposing views on the

http://dx.doi.org/10.1016/j.apmr.2015.12.018

physiological basis of peak oxygen consumption poststroke. The first study[4] indicated that reduced peak oxygen consumption is secondary to a decline in peak and reserve cardiac output. The second, more recent study,[5] demonstrated that peak oxygen consumption and the ability of skeletal muscles to extract oxygen is reduced poststroke, but cardiac function and pumping capability are maintained.

Investigating how exercise mediates central oxygen supply and peripheral oxygen utilization may lead to a greater understanding of peak oxygen consumption poststroke and how it can be improved. Stroke can lead to a number of negative peripheral skeletal muscle adaptations (eg, change in muscle fiber type and vasculature).[6] Central comorbidities such as heart disease and hypertension are also highly prevalent in this population.[7] Exercise is a potential intervention capable of promoting both central and peripheral adaptations, and these changes may affect both function and CRF poststroke.

This study aims to explore central and peripheral adaptations to exercise poststroke and the physiological mechanisms that are related to exercise-induced changes in peak oxygen consumption and function. Our hypotheses are that after stroke, (1) structured exercise will improve central oxygen supply and peripheral oxygen utilization; (2) exercise-induced change in peak oxygen consumption will be strongly associated with adaptations in both central oxygen supply and peripheral oxygen utilization; and (3) exercise-induced change in peak oxygen consumption and peripheral muscle oxygen utilization will be strongly associated with improvements in function.

Methods

Study design

The study design was a single-center, single-blind, randomized controlled pilot trial. The trial was approved by the County Durham and Tees Valley Research and Ethics Committee. All participants gave informed written consent for the study. The study was performed in accordance with the ethical standards laid down in the 1975 Declaration of Helsinki and as revised in 2013. Primary outcomes for this study have been reported previously.[8] This article presents a subanalysis of the primary findings.

Participants

Eligibility criteria

The inclusion criteria for the study were as follows: (1) age >50 years; (2) stroke diagnosed (>6mo previously) by a stroke specialist; (3) able to complete a 6-minute walk test (6MWT) with or without a stick; (4) living at home; (5) discharged from all conventional physiotherapy interventions; and (6) not already performing regular exercise (≥3times/wk, moderate intensity). The exclusion criteria were as follows: (1) the absolute and relative contraindications to exercise testing as stated by the American Heart Association[9]; (2) diabetes; (3) neurological disorders other than stroke; (4) pain on walking (visual analog scale score, >5); (5) inability to follow 2 stage commands; (6) cognitive impairment (Mini-Mental Scale Examination score, <24); and (7) untreated major depression.

List of abbreviations:

6MWT	6-minute walk test
10MWT	10-meter walk test
BBS	Berg Balance Scale
CRF	cardiorespiratory fitness
SLE	single limb exercise
TUG	timed Up and Go

Setting

Participants were recruited from community stroke services by National Institute for Health North East Stroke Local Research Network clinical trial officers, stroke health professionals, or advert.

Exercise intervention

The intervention was adapted from the Fitness and Mobility Exercise Program designed by Eng in 2006.[10] The intervention was a "mixed" exercise program consisting of functional exercises designed to improve flexibility, strength, aerobic capacity, and balance. The intervention was delivered using a previously described protocol.[8] In brief, classes were delivered in the community for 19 weeks by a fitness instructor and a physiotherapist (3times/wk, 45−60min). Participants wore a heart rate monitor,[a] and the intensity of the exercise was gradually increased, working within a heart rate zone determined using the Karvonen formula[11] (40%−50% of participant's maximum heart rate, with increasing increments of 10% every 4wk up to 70%−80%). Repetition and resistance were used to progress strength and balance exercises.

Control group intervention

The control group completed a matched duration home stretching program. Ten seated stretches were repeated 3 times for the upper and lower body. Participants were given an instruction booklet and diary to record activity and changes in medication/diet/physical activity and telephoned fortnightly for progress.

Outcomes

Primary outcomes have been published previously.[8] Outcomes listed below represent only the variables explored in this secondary analysis: cardiorespiratory and functional performance measures. Outcome assessment was conducted within 2 weeks preintervention and 1 week postintervention by trained assessors blinded to the study hypotheses and group assignment.

Exercise testing

Expired gases (METALYZER 3B[b]) were collected at rest for 5 minutes and continuously during a maximal progressive exercise test conducted with an electromagnetically controlled recumbent bicycle ergometer (Corival[c]). A warm-up was done at 20W for 3 minutes followed by 10-W increments every minute until volitional exhaustion. The 12-lead electrocardiogram (Custo[d]) was continuously monitored, and blood pressure was recorded twice at rest, during exercise, and at peak exercise and recovery. *Peak exercise* was defined as a respiratory exchange ratio of >1.05; the absence of an increase in oxygen consumption despite a further increase in exercise intensity; a rating of perceived exertion of >18 on the category Borg scale or voluntary termination of the test.[12]

Cardiorespiratory fitness

Peak oxygen consumption was calculated as the average oxygen uptake during the last minute of exercise (expressed in milliliters per kilogram per minute). *Peak work rate* was defined as the peak wattage on test termination.