Submaximal and Peak Cardiorespiratory Response After Moderate-High Intensity Exercise Training in Subacute Stroke

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ABSTRACT

Purpose: Reduced cardiovascular fitness post-stroke may negatively impact recovery. There is little information regarding exercise testing performance and cardiorespiratory response to an aerobic exercise intervention in subacute stroke. The purpose of this study was to examine cardiorespiratory response in subacute stroke after an 8-week aerobic exercise intervention using a total body recumbent stepper (TBRS). **Methods:** Nine individuals with mean age 61.2 (SD 4.7) years and mean 66.7 (SD 41.5) days post-stroke completed the exercise intervention. Participants had a mean Fugl-Meyer score of 100.3 (SD 29.3). Outcome measures were obtained at baseline and postintervention. A peak exercise test using a TBRS assessed oxygen consumption, heart rate, and minute ventilation. Participants completed an 8-week exercise intervention on a recumbent stepper 3 times per week at a prescribed heart rate intensity. **Results:** Submaximal VO_2 was significantly lower from baseline to postintervention with a main effect of Study Visit ($F_{1,8} = 8.5$, $p = 0.02$). Heart rate was not significantly different pre- to postintervention. Minute ventilation exhibited no main effect of Study Visit or Test Minute. **Conclusion:** Moderate-high intensity aerobic exercise in subacute stroke appears to be beneficial for improving cardiovascular outcomes during submaximal performance of an exercise test.

Key Words: oxygen uptake, cerebrovascular accident, cardiovascular fitness, submaximal exercise

INTRODUCTION AND PURPOSE

Individuals post-stroke have low cardiorespiratory (CR) fitness measured by VO_2 peak (peak oxygen uptake)

from a metabolic exercise test.¹⁻³ Reduced CR fitness negatively affects performance of basic activities of daily living (ADLs) as well as instrumental ADLs. For example, light to vigorous ADLs can require anywhere between 10.5 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and 17.5 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.⁴ In our previous work, we retrospectively examined exercise testing results from 62 chronic stroke survivors.² We reported all except one participant had VO_2 peak values lower than the first percentile when compared to age and gender-matched normative data. Additionally, most of the participants' VO_2 peak values were below the needed 17.5 $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ to perform vigorous ADLs. These data reinforce the need for improving energy expenditure during daily activity (submaximal effort) as well as increasing VO_2 peak for tolerance of more vigorous activities.

In attempting to improve VO_2 peak in people post-stroke, exercise interventions using various modalities (ie, treadmill, cycle, water aerobics) have been employed.⁵⁻¹¹ These studies have demonstrated that aerobic exercise training can improve VO_2 peak, cardiovascular health (lower resting blood pressure, heart rate) and measures of functional capacity but the majority of research has been performed in chronic stroke. Several studies have emphasized the need for using exercise in the earlier stages of stroke recovery as a preemptive attempt to minimize cardiovascular decline.^{9,12,13} While there is increasing interest in using exercise interventions in the subacute stage of stroke recovery, a paucity of research exists. In addition, little information is available regarding exercise test performance in subacute stroke and the cardiorespiratory response to an aerobic exercise intervention. There is a need to better understand submaximal performance in response to an intervention since reaching maximal effort in clinical populations such as stroke is difficult.^{12,14}

Therefore, the purpose of this study was to examine whether an 8-week aerobic exercise intervention using a total body recumbent stepper (TBRS) would improve cardiorespiratory response in subacute (after one week but less than 6 months post event) stroke patients. We hypothesized after the intervention improvements in oxygen consumption (VO_2), heart rate (HR), and minute ventilation

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(VE) would be observed at submaximal effort during the exercise test. We hypothesized that at peak effort these same measures would demonstrate improved performance. An exploratory aim examined the relationship between peak VO_2 and a predicted VO_2 peak value obtained from a submaximal exercise test we developed for healthy adults.² We hypothesized that the actual VO_2 and predicted VO_2 would have at least a moderate ($r > 0.75$) relationship. The data generated from this initial study will contribute new knowledge regarding aerobic exercise as an early intervention for individuals with stroke. In addition, we will provide preliminary data regarding a new submaximal exercise test for use in subacute stroke.

METHODS

Study Design

A prospective study with a sample of convenience was used for a pretest-posttest design. Adverse events related to exercise testing and the intervention were monitored throughout the study. The Human Subjects Committee at the University of Kansas Medical Center approved the study protocol. Institutionally approved written consent was obtained prior to enrollment and the rights of all subjects were protected.

Participants

Between December 2010 and January 2012, a total of 40 individuals with a diagnosis of stroke were screened for inclusion into CRESS (Cardiovascular Regulation and Early Exercise Stroke Study). The inclusion and exclusion criteria for CRESS have been reported previously.¹⁵ Briefly, individuals were enrolled if they were between 50 and 70 years of age and had a diagnosis of a first-time, unilateral stroke that occurred less than 6 months prior to enrollment. They also needed to be able to walk (with or without an assistive device) with stand-by assist. Individuals were excluded if they had a recent cardiac event, acute cardiac or renal failure, or were current smokers.

Peak Exercise Testing

Since individuals may not be familiar with the reciprocal movement of the recumbent stepper, all participants had an opportunity to use the exercise device (total body recumbent stepper, TBRS [NuStep, T5XR, NuStep, Inc., Ann Arbor, MI]) to practice the movement pattern and step rate (80 spm). They were also instructed on the Borg Rating of Perceived Exertion (RPE) Scale. This was performed prior to the exercise testing day. Participants were informed not to

consume food or drink (except water) within two to 3 hours of the exercise tests and 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.

Oxygen uptake was measured and analyzed through collection of expired gases using a metabolic measurement system (Parvomedics Inc., Sandy, UT). Gas and flow meter 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.¹⁴ Briefly, the mTBRS-XT is a two-minute incremental exercise test to assess VO_2 peak and other metabolic parameters. We have used this exercise testing protocol in previous work and have reported that the mTBRS-XT has been shown to be a valid exercise test for people post-stroke.¹⁴

The exercise testing sessions were held at the Clinical and Translational Science Unit (CTSU) at the University of Kansas Medical Center and a physician was present for all exercise tests. A 12-lead electrocardiograph (ECG) was attached to each participant's chest and used to continuously monitor HR and rhythm throughout the exercise test. The VO_2 peak was defined as the highest observed value during the test.

Submaximal Exercise Testing

We recently developed a submaximal exercise test in healthy adults with low to moderate cardiac risk using the YMCA protocol¹⁶ for the TBRS (Table 1).² Because of timing and motor coordination difficulties often seen in stroke survivors, individuals were given a range and asked to maintain a step rate between 90-100 spm. The participants completed the submaximal exercise test within one to two days after the peak exercise test and prior to the commencement of the exercise intervention.

Participants started the test at 30 watts and resistance was increased every 3 minutes according to the protocol² until completion of the test, volitional fatigue, or 85% of age-predicted maximal HR was achieved ($0.85 [220 - \text{age}]$). As reported in our previous work,² HR was recorded 10 seconds prior to the end of the second and third minute of each stage. If the two HR measures were within 5 bpm of each other, participants progressed to the next stage.¹⁷ However, if the difference was greater than 5 bpm, an additional minute was performed to ensure a steady-state. The workload in watts and HR at the end of the submaximal

Table 1. Submaximal Exercise Test Protocol Stages Based on Heart Rate. Reprinted with permission from Billinger S, Van Swearingen E, McClain M, Lentz A, Mathew G. Recumbent stepper submaximal exercise to predict oxygen uptake. *Med Sci Sports Exerc.* 2012;44(8):1539-1544. Copyright 2012, Wolters Kluwer Health.

Stage 1 begins at 30 Watts				
	If HR < 80 bpm:	If HR 80-89 bpm:	If HR 90-100 bpm:	HR >100 bpm:
Stage 2	125 Watts	100 Watts	75 Watts	50 Watts
Stage 3	150 Watts	125 Watts	100 Watts	75 Watts
Stage 4	175 Watts	150 Watts	125 Watts	100 Watts

exercise test were used in the prediction equation. The prediction equation used to determine VO_2 peak ($\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) = $125.707 + (-0.476)(\text{age}) + (7.686)(\text{sex [0=female; 1= male]}) + (-0.451)(\text{weight in Kg}) + (0.179)(\text{Watts}_{\text{end_submax}}) + (-0.415)(\text{HR}_{\text{end_submax}})$.² Upon completion of the exercise test, the individual continued to step at a self-selected speed with resistance at 25 watts for two minutes or until HR returned to near baseline levels.

Aerobic Exercise Training

Details outlining exercise prescription used in this study have been reported elsewhere.¹⁵ Briefly, each exercise session began with pre-exercise vital signs and any changes in medication(s) were recorded in the exercise log. The exercise session began with stretching, followed by a 5-minute warm-up at 15 to 25 watts at a comfortable, self-selected pace. After 5 minutes, the exercise intensity was increased to the prescribed workload. 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 target heart rate range (THRR). We documented in the exercise log the amount of time spent in the prescribed THRR. Heart rate, blood pressure (BP), and RPE were assessed within one minute prior to the end of the exercise training to capture exercise response. A 5-minute cool-down was then employed followed by stretching. After 5 minutes of resting, post-exercise vitals were taken to ensure a return to pre-exercise values. The exercise sessions were held at the University of Kansas Medical Center Research in Exercise and Cardiovascular Health (REACH) Laboratory. Limited data is available to guide exercise prescription for moderate to high-intensity aerobic exercise in subacute stroke. Therefore, we used the following exercise prescription parameters: (1) systolic BP less than 220 mmHg and diastolic BP below 100 mmHg, (2) RPE between 12-16/20, and (3) exercise intensity was prescribed at 50% to 59% of HR reserve (derived from the exercise test) for 4 weeks and then increased to 60% to 69% of HR reserve (HRR) for the remaining 4 weeks. Individuals wore 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.

Sample Size Justification

The sample size was based upon a primary outcome measure (blood flow). Briefly, we conducted a power analysis based on previous work¹⁵ that had an effect size of $d = 4.37$ and a power of 0.95. Therefore, 5 people were needed to determine significant changes ($p \leq 0.05$). However, to account for attrition, we over-enrolled to 10 participants. The sample for this secondary analysis was taken from the 10 individuals enrolled in CRESS.¹⁵

Statistical Analysis

Submaximal performance on the exercise test was assessed using an analysis of variance (ANVOA), with Test Minute (minutes 1-6) and Study Visit (baseline, post-exercise) as within subject factors. Since peak exercise testing is difficult in this clinical population, we hoped to gain additional insight into exercise testing response over each minute for the first 6 minutes of the test.¹⁸ In order to address violations of sphericity, $\alpha = 0.05$ was used. Paired t-tests were used to determine differences at peak effort between baseline and post-exercise outcomes. Pearson correlation coefficient was calculated to determine the relationship between the measured VO_2 peak value and the predicted value from the submaximal exercise test. All analyses were conducted using SPSS statistical software (Version 20; SPSS, Inc, Chicago, IL) with the alpha level < 0.05.

RESULTS

Ten people (mean age: 61.2 years, SD 4.7; mean Fugl-Meyer score: 100.3/126, SD 29.3) 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. Therefore, when comparing pre- to posttesting results, only participants with a complete data set were analyzed ($n = 9$). We report that individuals in the subacute stage of stroke recovery tolerated peak exercise testing and moderate-high exercise training. No serious cardiac or other adverse events occurred that were related to the peak exercise test or the intervention. Since medications can affect physiologic measures during peak exercise testing as well as exercise performance, we tracked participant medication use and any changes. There were no additions of medications for blood pressure, cardiac arrhythmias, or cholesterol; and for these medications, no changes in dosage were reported during the study period. Participant demographics are presented in Table 2.

Exercise Response

Data presented in the following section are the submaximal (minutes 1-6 of the exercise test) and peak responses of the group during the peak exercise test at baseline and postintervention. We chose minute 6 as the last data point for the submaximal effort since not everyone completed 7 minutes in the peak exercise test. For clarity, we have organized the information by outcome measure.

Oxygen consumption

We report a significantly lower submaximal VO_2 from baseline to postintervention (main effect of Study Visit) ($F_{1,8} = 8.5$, $p = 0.02$) which may suggest a reduced work effort during the exercise test. Additionally, VO_2 increased as expected during the exercise test, evident by the main effect of Test Minute ($F_{5,40} = 96.1$, $p < 0.001$). There was no interaction ($F_{5,40} = 0.95$, $p = 0.40$) between Study Visit and Test Minute. During submaximal effort, the largest decrease in VO_2 values between pre- and posttest was at Test Minute 1 with a 14% reduction ($p = .042$). Minutes

Table 2. Baseline Participant Demographics

Characteristics	n = 10	Number or Group Mean (SD)	Range
Male		6	
Age (years)		61.2 (4.7)	52-70
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	
Days Post Stroke		68.6 (40.1)	(10 – 123)
Regular Exercisers Pre-stroke		4	
Diabetes			
Type 1		0	
Type 2		4	
Overall ABI		0.98 (0.11)	
Medications			
Anticoagulants		8	
ACE Inhibitors		6	
Antidepressant		2	
Angiotensin II Receptor Blockers		2	
Beta-Blockers		2	
Calcium Channel Blockers		3	
Cholesterol		3	
Diabetes		2	
Diuretic		2	
Vitamins		3	
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)

Abbreviations: ABI, ankle brachial index; ACE, angiotensin converting enzyme

2 and 3 demonstrated a reduction in VO_2 by 9.3% ($p = .015$) and 8.9% ($p = .022$), respectively. Minutes 4-6 had smaller differences pre- to postintervention and were nonsignificant ($p > 0.05$). The VO_2 for each Test Minute is represented in Figure 1. At peak effort, we report a significant increase in VO_2 peak from baseline (mean 15.8, SD 3.9) to postintervention (mean 17.5, SD 6.2, $p = 0.04$).

Heart rate

There was no main effect of Study Visit ($F_{1,8} = 2.7$, $p = 0.14$) on heart rate. Test Minute was significant ($F_{5,40} = 48.1$, $p < 0.001$) as HR linearly increased during the exercise test. There was not a significant interaction between Study Visit and Test Minute ($F_{5,40} = 0.28$, $p = 0.92$). Heart rate for each Test Minute appears lower after the intervention when compared to baseline (Figure 2). Peak HR was not significantly different pre- to postintervention (baseline mean HR = 142.9, SD 18.0 and postintervention mean HR = 144.2, SD 20.4, $p = 0.40$).

Minute ventilation

Minute ventilation (VE) increased similarly across Test Minute between the Study Visits. No interaction of Study Visit and Test Minute was evident nor was there a main effect of Study Visit or Test Minute. The VE for each Test Minute is represented in Figure 3. At peak effort, VE was higher but this increase was not statistically significant (baseline mean VE = 51.3, SD 15.6 and postintervention mean VE = 52.0, SD 17.1, $p = 0.87$).

Submaximal Exercise Test to Predict VO_2 Peak

The 10 participants initially enrolled in CRESS performed both maximal and submaximal exercise tests. We found that predicted VO_2 peak generated from the submaximal exercise test equation had a strong correlation to the measured VO_2 peak ($r = 0.80$, $p = 0.006$). Mean measured peak VO_2 from the exercise test was 17.6 (SD 6.1) $\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ and the predicted mean value was 22.9 (SD 7.3) $\text{ml} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. Paired t-test revealed a statistically

Figure 1. Oxygen consumption for each test minute of peak exercise test.

Figure 2. Heart rate for each test minute of peak exercise test.

Figure 3. Minute ventilation for each test minute of peak exercise test.

significant difference between these two values ($p = 0.005$).

DISCUSSION

To our knowledge, this is the first study to examine both the submaximal and peak cardiorespiratory adaptations to an 8-week moderate-high intensity aerobic exercise intervention in subacute stroke patients. Because information regarding when to perform exercise testing after stroke is limited,¹⁹ we provide information that peak exercise testing can begin in the subacute stages of stroke recovery. Two of the participants were less than 20 days

post-stroke and had no cardiac or serious adverse events related to testing or the exercise intervention. Our findings support the few studies available that exercise testing can safely be performed in subacute stroke.⁹ Further, the current American Heart Association/American Stroke Association *Physical Activity and Exercise Recommendations for Stroke Survivors* suggest using guidelines similar to those “post-myocardial infarction with pre-determined endpoints of 120 bpm or 70% of age-predicted HR max.”^{19,20} Although our sample size is small and more studies are needed in these earlier stages of stroke recovery, we demonstrated peak HR response during the exercise test to reach up to 142 bpm at baseline, which we believe allowed for accurate exercise prescription. The results from this study will extend the current literature and contribute novel information regarding moderate-high intensity exercise in subacute stroke. In addition to the exercise intervention, we have examined the relationship between predicted VO_2 peak from a submaximal exercise test and the measured values from a peak exercise test.

Exercise Response Oxygen consumption

After the training intervention, we observed a decrease in VO_2 at each Test Minute except minute 6. However, we did not find a significant interaction between Test Minute and Study Visit. We find the results encouraging that there was a reduction in oxygen consumption (measured by VO_2) during submaximal effort of the exercise test. Macko and colleagues²¹ demonstrated that 6 months of treadmill exercise training can reduce submaximal effort and improve economy of gait. We used a recumbent stepper for both exercise testing and the intervention and did not assess whether this would transfer to improved economy of gait. Future work should examine whether different training modalities would elicit improvements in gait economy.

At peak effort, a 10.1% increase was found in VO_2 after the training intervention and was similar with other studies in subacute stroke.³ A recent study by Jakovljevic and colleagues²² suggests that in individuals with mild stroke, VO_2 peak may be limited by the ability of the skeletal muscle to extract and use oxygen during exercise. They found that arterial-venous oxygen differences were significantly lower in stroke versus control participants while peak cardiac output was similar between the two groups. More information is needed to elucidate factors within the peripheral and central cardiovascular systems that may contribute to reduced VO_2 peak.²²⁻²⁴

Heart rate

Although we did not observe a significant interaction between Test Minute and Study Visit, HR response appeared to be decreased at each Test Minute during the exercise test. This work provides initial support for the possibility of improved HR response during submaximal activity after an exercise intervention. We did not test HR response to functional activities such as gait or other activities of daily living. We hope that future research will extend our initial work to examine whether improved HR response

at submaximal effort translates to functional activities in stroke survivors.

We observed a nonsignificant improvement in peak HR from the exercise test. We reported higher mean peak HR in our cohort (baseline HR 143 to 144 bpm) than previous studies that were approximately 120-126 bpm³ or 107-119 bpm.⁹ This may be due to differences in medications, exercise modality, stroke severity, or motivation by the individual participants. We used a recumbent stepper with reciprocal bilateral upper and lower extremity movement versus a semi-recumbent cycle ergometer used by other researchers. It is possible that incorporation of the upper extremities during the exercise test elicits a higher HR response. Six of 9 people reached 85% of age-predicted HR maximum and all but one person reached 80% of this value. Individuals enrolled in this study were considered minimally impaired by their Fugl-Meyer (FM) score. In a study by Chang and colleagues³ they report mean lower extremity FM scores. Our participants may have had less motor coordination difficulties in performing the bilateral reciprocal motion of the stepper, which may have allowed them to exercise longer during the exercise test.

Minute ventilation

Minute ventilation during submaximal effort did not demonstrate a similar pattern to VO₂ and HR. Rather, postintervention VE almost matched baseline values at each Test Minute with the exception of Test Minute 1 where a 3% decrease was reported. Few exercise training studies have examined VE as an outcome measure in people with stroke but physiologic impairments in pulmonary function may contribute to lower peak VO₂ values.² A study in individuals with heart failure that participated in a 16 to 24 week exercise training study found a decrease in VE during submaximal performance of an incremental exercise test and a significant decrease in VE during a constant load submaximal protocol.²⁵ Although the sample size was relatively small (n = 12), the exercise intervention was longer in duration (16-24 weeks) and the intensity was higher (75% of peak HR). These exercise prescription parameters may have had a greater effect on VE than the protocol used in our study.

After the 8-week exercise intervention, peak VE was slightly higher but was not significantly different between baseline and post-exercise training. Our findings for peak VE are similar to a recent study that used robot-assisted gait training.³ In the intervention, participants with subacute stroke used a robot-assisted exercise device 5 times a week for two weeks. The shorter intervention time (two weeks) may have influenced their findings at peak effort. A more comprehensive pulmonary profile such as measures obtained from pulmonary function testing may provide greater insight into the physiologic impairments of pulmonary function in stroke survivors.

Submaximal Exercise Test to Predict VO₂ Peak

Submaximal exercise testing can be an attractive alternative to peak testing especially in clinical environments where a metabolic cart and medical staff may not be readily

available.^{2,26} Recently, our laboratory determined the YMCA cycle protocol using the TBRS could predict VO₂ peak (r = 0.92, p < 0.001) in healthy adults ranging from 20 to 60 years of age.² The submaximal exercise test in our subacute stroke survivors was easy to administer and all participants were able to perform and complete the test. We report that the predicted VO₂ peak and measured VO₂ peak values were moderately and significantly related. Previous literature using submaximal exercise tests in people with stroke have found weak to strong relationships (r = 0.37-0.84) in various walking tests (ie, 6-minute walk test); however, none were performed using the TBRS.^{12,13,27,28} We believe these early findings are important and should be considered meaningful to clinicians since the predicted and measured VO₂ peak were closely related. In addition, the various motor and coordination deficits that can result from a stroke make exercise testing challenging. Since all of our participants were able to complete the TBRS submaximal exercise test, we believe these initial results are encouraging.

CONCLUSIONS

An 8-week aerobic exercise intervention using the TBRS in subacute stroke participants resulted in improved VO₂ peak and HR at submaximal effort during the exercise test. The finding that VE did not improve after exercise training is interesting and requires further investigation. A future randomized trial should be performed to investigate the effect of aerobic exercise training on the parameters of cardiovascular and pulmonary function early after stroke. The submaximal exercise test used in this study shows promise to predict VO₂ peak for individuals with subacute stroke but requires further exploration.

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