PHYSIOLOGICAL RESPONSES TO COUNTERWEIGHTED SINGLE-LEG CYCLING IN AN ELDERLY POPULATION

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By

Phillip V. LaScola, Jr.

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A dissertation written by

Phillip V. LaScola, Jr.

B.S., Mount Union College, 2003

M.S., The University of Akron, 2004

Ph.D., Kent State University, 2015

Approved by

_____, Director, Doctoral Dissertation Committee
John McDaniel

_____, Co-Director, Doctoral Dissertation Committee
Ellen Glickman

_____, Member, Doctoral Dissertation Committee
Angela L. Ridgel

_____, Member, Doctoral Dissertation Committee
Jacob Barkley

_____, Outside Member, Doctoral Dissertation
John Gunstad   Committee

Accepted by

_____, Director, School of Health Sciences
Lynne E. Rowan

_____, Interim Dean, College of Education, Health and Human
Mark Kretovics   Services

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Abstract

Phil LaScola., Ph.D., August 2015   School of Health Sciences

PHYSIOLOGICAL RESPONSES TO COUNTERWEIGHTED SINGLE-LEG
CYCLING IN AN ELDERLY POPULATION (63 pp.)

Director of Dissertation: John McDaniel, Ph.D.

Co-Director: Ellen Glickman, Ph.D.

INTRODUCTION: Single-leg cycling allows for a greater muscle specific exercise

capacity and therefore provides a greater stimulus for metabolic and vascular adaptations

when compared to standard double-leg cycling. **PURPOSE:** The purpose of this

investigation was to compare the metabolic, cardiovascular, and peripheral responses of

single-leg cycling with a counterweight to double-leg cycling in a healthy elderly adult

male population. **METHODS:** Eleven healthy males (age 66 ± 8 years) performed two

cycling conditions consisting of double-leg cycling (DL) and single-leg cycling with a

97N counterweight attached to the unoccupied crank arm (CW). For each condition,

participants performed cycling trials (60rpm) at three different work rates (25, 50, 75 W)

for 4 minutes each. Oxygen consumption (VO_2), respiratory exchange ratio (RER), heart

rate (HR), mean arterial pressure (MAP), femoral blood flow, rating of perceived

exertion (RPE), and liking scores were recorded. **RESULTS:** HR was similar between

DL and CW conditions at all three intensities. VO_2 was similar between DL and CW at

25W and 50W, however, at 75W VO_2 was greater during the CW condition compared to DL (p= 0.037). Femoral artery blood flow was significantly greater during CW cycling for the 50W and 75W work rates (p= 0.01, and p<0.001). RPE and liking were similar between both conditions (p= 0.065, p= 0.060). **CONCLUSION:** At least at low and moderate intensities, counterweighted single-leg cycling provides a greater peripheral stress for the same cardiovascular demand as double-leg cycling in a healthy elderly adult male population. Furthermore, enjoyment of single-leg cycling was similar to double-leg. Thus, single-leg cycling with a counterweight may be a feasible exercise modality for a diseased population (i.e. peripheral vascular disease/cardiovascular disease).

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CHAPTER I

INTRODUCTION

High-intensity endurance training has been shown to result in greater improvements in skeletal muscle adaptations, VO_2 peak, and aerobic performance when compared to lower intensity training; however when prescribing exercise to an elderly or diseased individual, high-intensity endurance training may not be safe due to the increased risk of cardiovascular event. Furthermore, high-intensity endurance exercises that incorporate the entire body (running/cycling) are limited by the ability of central circulation to distribute blood and oxygen to the working muscles (Layec, Haseler, & Richardson, 2013). This reduction is more pronounced if the elderly individual does not regularly exercise or has pulmonary or cardiovascular disease (Dolmage & Goldstein, 2008). However, exercise involving smaller muscle mass can maximize the muscle specific exercise intensity resulting in greater positive adaptations while minimizing strain on the cardiovascular system.

Previous investigators have employed single-leg cycling as an exercise modality that utilizes reduced muscle mass and is more efficient than single joint exercises. These investigators have reported that single-leg cycling can generate greater leg specific work rates when compared to double-leg cycling (BJorgen et al., 2009; Dolmage & Goldstein, 2006; Duner, 1958; Magnusson et al., 1997; Rud, Foss, Krustrup, Secher, & Hallen, 2005). Single-leg cycling confines the exercise to a smaller muscle mass and allows the participant to exercise for a longer duration or a much greater limb specific intensity, because blood flow to the active muscle is no longer a limiting factor (blood flow is no

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longer 'shared' by both legs). While research supports the use of single-leg cycling to generate greater leg specific work rates, the biomechanics of single-leg cycling is very different than the biomechanics of double-leg cycling, making the exercise awkward and uncomfortable. Single-leg cycling requires the recruitment of the fatigable hip flexors during the upstroke of the pedal cycle, thus limiting the application of single-leg cycling as an exercise modality. To address the limitations of single-leg cycling, investigators in two recent studies attached a counterweight to the crank arm opposite to the active limb in order to facilitate smooth single-leg cycling (Matin et al., 2012; Burns et al., 2014). The results indicated that, at least in the young healthy population, the counterweighted single-leg cycling allows for greater limb specific exercise intensity without additional cardiovascular stress. It has yet to be determined how elderly or diseased individuals will respond to single-leg cycling with a counterweight.

The purpose of this investigation is to determine if elderly people can tolerate/coordinate single-leg cycling and to compare the cardiovascular responses between double-leg and single-leg cycling. For this study we will recruit 10 healthy male subjects 55-90 years of age to perform normal double-leg cycling (DL) and single-leg cycling (CW) with the use of a counterweight. Each participant will complete the two conditions (CW, DL) with three work rates within each condition (25, 50, 75Watts). All participants will have the following measurements recorded: RPE (whole body and leg), HR, VO_2, and femoral artery blood flow of the exercising limb (GE Doppler Ultrasound).

We hypothesize that single-leg cycling with a counterweight in an elderly population will generate similar cardiovascular, metabolic, and RPE responses compared to double-leg cycling. Additionally, we hypothesize an increased blood flow to the working limb during single-leg cycling when compared to double-leg cycling. If the hypothesizes are correct, single-leg cycling with a counterweight may be beneficial as an exercise modality for individuals with cardiovascular or respiratory impairment. Additionally, single-leg cycling with a counterweight may also be beneficial for peripheral artery disease patients, by increasing limb blood flow and stimulating angiogenesis.

CHAPTER II

REVIEW OF LITERATURE

Physiological Responses to Aerobic Exercise and Aging

Aerobic exercise training has an array of positive effects, including increased cardiovascular fitness and muscular endurance which result in increased functional capacity. Functional capacity has been shown to improve with exercise in a variety of study cohorts, from young healthy subjects to elderly diseased patients (e.g. CHF, CAD, COPD, diabetes, etc.). Pogliaghi et al. (2006) studied the adaptations to endurance training in healthy elderly subjects, using arm cranking and stationary cycling exercises. Subjects were trained for 12 weeks using either an arm ergometer or a stationary cycle for 30 minutes, 3 times per week. At the conclusion of the study, subjects performed maximal exercise tests on both the arm ergometer and the stationary cycle, independent of training protocol. When compared to pre-training maximal exercise tests, subjects in both groups increased VO_{2peak} and ventilatory threshold on both the arm ergometer and the stationary cycle, independent of training conditions. Results demonstrated that improved aerobic functioning, leading to improved functional capacity, had a carry-over effect between exercise modalities in elderly subjects. These findings are beneficial because aging is associated with decreases in exercise tolerance and maximal oxygen consumption during exercise, resulting in a decreased functional capacity (Conley, Jubrias, Cress, & Esselman, 2013; Layec et al., 2012; Pogliaghi et al., 2006 Sagiv, 2011).

Aging is a natural process that affects all biological systems, but significant decreases in muscle mass and cardiovascular function are major contributors to decreased functional capacity in elderly and diseased adults (Conley et al., 2013; Layec et al., 2012; Pogliaghi et al., 2006; Sagiv, 2011). The decreases in muscle mass and cardiovascular function associated with aging and disease can be minimized by maintaining a high level of physical activity, especially aerobic exercise (Pogliaghi et al., 2006). Exercise training increases functional capacity through positive adaptations in the cardiovascular and skeletal muscle systems. Specifically, regular aerobic exercise training places increased stress on the cardiovascular system and metabolic processes within the skeletal muscle. The working muscles during exercise have an increased demand for oxygen resulting in an increased workload on the cardiovascular system. This increased demand is met through increased stroke volume (SV), heart rate (HR), and ultimately cardiac output (CO) to match the demand of the working muscles. Over time, maintaining a regular exercise regimen, the heart adapts to the stress by increasing cardiac muscle size and strength resulting in an increased stroke volume, allowing the heart to function more efficiently at rest (i.e. lower HR at rest).

The stress placed on the cardiovascular and musculoskeletal system by aerobic exercise training also triggers adaptations within the skeletal muscle. Conley et al. (2013) studied the effects of a 24-week endurance training protocol on elderly (65-80 years old) subjects. Subjects trained 3 times per week with 20 minutes of leg exercises (cycling motion exercises) and 20 minutes of upper body exercises (rowing motion exercises) at an intensity of 80-85% heart rate reserve. At the conclusion of the study

power output of the legs (P_{max}) was measured at VO_{2max} and compared to pre-training findings. Results suggest that improved P_{max} benefits from elevations in energy coupling and oxidative phosphorylation capacity (Conley et al., 2013). Increased oxidative phosphorylation capacity can be the result of increased mitochondrial density within the muscle, as a response to exercise (Layec et al., 2012; Sagiv, 2011). Increased mitochondrial density within the muscle will allow for faster utilization of O_2, increasing the amount and speed of ATP production, providing the working muscle with more energy during exercise, resulting in decrease fatigue.

Aerobic exercise training has also been shown to increase vascular conductance and stimulate angiogenesis, both resulting in greater blood flow to active muscles (Lilly, 2003). Additionally aerobic stress on the body stimulates the kidneys to release erythropoietin, a hormone that triggers erythropoiesis (the formation of red blood cells) (Koeppen & Stanton, 2010). Increasing red blood cells in the blood ultimately increases the hemoglobin content in the blood, allowing for more binding sites for O_2 to bind. With increased O_2 carrying capability in the blood, more O_2 will be delivery to the muscles. These positive adaptations of the cardiovascular and musculoskeletal systems generated by aerobic exercise allow the working muscles during exercise to receive and metabolize oxygen at a greater rate.

Intense aerobic exercise has also been shown to maximize the peripheral adaptations typically observed from exercise training. Hottenrott, Ludyga, & Schulze (2012) tested the benefits of high intensity training versus continuous endurance training.

A twelve week training intervention was placed on two study cohorts of middle-aged men and women. The two groups were placed in a high-intensity training or continuous endurance training for twelve weeks, both totaling 2.5 hours of exercise per week. At the conclusion of the study, high-intensity exercise training led to greater improvements in peak VO_2 and led to a greater decrease in resting heart rate when compared to continuous endurance training (Hottenrott et al., 2012). Additionally high-intensity aerobic exercise training can reduce the amount of time needed for exercise, which is attractive to people with time restraints. High-intensity aerobic exercise training has been proven to be superior to long endurance training for time efficiency and health benefits in a healthy young population (Bjorgen et al., 2009; Guiraud et al., 2012). Despite the positive benefits of high-intensity aerobic training in young healthy adults, it is not yet recommended for an elderly or diseased population due to the increased risk of cardiovascular event (Guiraud et al., 2012).

While regular aerobic training (high-intensity or long duration) can elicit improvements in cardiovascular and skeletal muscle function, the ability to distribute and utilize O_2 during whole body exercise steadily declines with age (Layec, Haseler, & Richardson, 2013) resulting in a decrease of aerobic capacity and exercise tolerance. Many factors contribute to the loss of physical performance and loss of aerobic capacity with increasing age including a decline in maximum heart rate, cardiac output, limb blood flow, vascular conductance, and skeletal muscle mitochondrial density (Layec et al., 2013). All of these factors combined contribute to an overall decrease in exercise capacity in an older or elderly individual by reducing oxygen transport to the periphery

(skeletal muscle). Additionally, the elderly population is at a greater risk of developing comorbidities (CHF, COPD, PAD, etc.) that would further impair physical performance.

CHF, PAD, and COPD Exercise Responses

Congestive heart failure (CHF) is a chronic condition that leads to functional impairment of the heart, usually diagnosed with an ejection fraction (LVEF) <40%. Heart failure affects more than 5 million Americans and currently more than 500,000 new cases are reported each year (Lilly, 2003). As CHF progresses, the cardiac muscle weakens, and LVEF further decreases, reducing blood flow to the periphery. The decrease in LVEF is often so great that any form of exercise involving a large muscle mass is too taxing for the cardiovascular system to supply the volume of O_2 required, which leads to exercise intolerance. If the heart cannot match the increased demand of the specific muscle mass, while maintaining MAP, an exaggerated sympathetic response could trigger vasoconstriction in the site-specific muscle, resulting in a further reduction in blood flow to the working muscle. A study conducted by Magnusson and colleagues set out to test this hypothesis. Ten CHF patients and twelve control subjects were recruited for the study. Subjects performed a one and two legged knee extensor exercise, while central and peripheral circulatory responses were monitored. Peak leg blood flow was monitored in all subjects during both exercise conditions. Results showed that peak limb blood flow during peak one-legged knee extensor exercise was consistent among both CHF and control subjects. If muscle mass was increased in CHF patients (using both legs) peak limb blood flow was reduced when compared to control suggesting they

do not have adequate cardiac function to meet the demands of larger muscle mass activity (i.e. two leg cycling) (Magnusson et al. 1997; Jonsdottir et al., 2005; LeJemtel et al., 1986).

Like CHF patients, peripheral arterial disease (PAD) patients also suffer reduced exercise capacity, but this is contributed to claudication pain (a cramping pain in the lower extremity as a result of decreased or limited blood flow to the legs during exercise)(Casillas et al., 2011; Escobar et al., 2011; Parmenter et al., 2010; Spronk et al., 2008; Regensteiner, 2004). Thus, despite the fact that these individuals may have normal cardiac output, PAD patients are severely limited in their ability to walk pain free. The claudication pain during walking will often limit the distance and intensity a PAD patient can walk without stopping. The 6 minute walk test is frequently used to determine the severity of claudication caused by PAD. Bodescu, Jurcau, and Pop (2012) compared the distance PAD patients with claudication and without claudication could achieve on a six-minute walk test. Results demonstrated that PAD patients without claudication achieved a distance of 383 ± 22.9m while PAD patients with claudication achieved a walking distance of 312 ± 54.48m. Similar studies have been conducted in healthy subjects with similar demographics to the previous study. Healthy patients without PAD achieved an average walking distance of 500m or more during a six-minute walk test (Enright & Sherrill, 1998). These findings suggests that PAD with or without claudication can impair walking distance, when compared to healthy subjects (Casillas et al., 2011; Enright & Sherrill, 1998). The impairment in walking makes it difficult for PAD patients

to maintain aerobic exercise for an extending period of time, limiting their ability to achieve cardiovascular benefits from exercise.

Individuals diagnosed with chronic obstructive pulmonary disease (COPD) are limited aerobically by their inability to ventilate or perfuse the lungs, saturate the blood with oxygen, and subsequently meet the metabolic demand during exercise (Dolmage & Goldstein, 2006). COPD is diagnosed using a pulmonary function test in which forced expiratory volume in 1 second (FEV1) is measured. A FEV1 <70% is diagnosed as COPD, and it is estimated that more than 12million people are diagnosed with the disease (Vest et al., 2011). The reduced ventilatory capacity (low FEV1 caused by increased dead space/tidal volume ratio) creates an oxygen deficit, resulting in dyspnea that impairs exercise tolerance (Bjorgen et al., 2009). The decrease in blood oxygen saturation reduces the amount of oxygen available for working skeletal muscle during exercise, causing the muscle to fatigue quickly. While breathing techniques, such as pursed lipped breathing, can be beneficial to overcome dyspnea, exercise tolerance is centrally impaired by COPD. Whether the limitation to exercise is caused by a central or peripheral impairment, patients suffering from CHF, COPD, and PAD will have a reduced ability to see significant improvements in cardiovascular performance.

Reduced Muscle Mass Exercise

Previous investigators have used small muscle mass exercise to overcome the limitations in cardiac output in an attempt to maximize peripheral adaptations. As previously mentioned, high-intensity endurance training is superior to lower intensity exercise for improving aerobic capacity and skeletal muscle adaptations. However, high-intensity endurance exercises that incorporate the entire body (e.g. running and cycling) are limited by the central circulation's ability to distribute sufficient blood to the working muscles (Layec et al., 2013). Additionally peripheral blood flow during high-intensity exercise is limited by sympathetic vasoconstriction initiated by the arterial baroreceptors to prevent a drop in mean arterial blood pressure.

It is well known that when a small muscle mass is used, and cardiac output is not the limiting factor, blood flow to the active muscle is much greater than during large muscle mass activities (Anderson and Saltin, 1985; Richardson, Poole and Knight, 1993; Saltin, 1985). Thus to circumvent this blood flow limitation, researchers have used reduced muscle mass exercises (e.g., leg extension) to maximize peripheral blood flow during exercise. For example, Esposito et al. (2011) used isolated quadriceps training to increase exercise capacity in CHF patients. The study implemented an eight week training period using isolated knee extension exercises to train CHF patients with minimal central hemodynamic challenge. When compared to controls the study subjects displayed increases in capillary and mitochondrial density, an increase in VO_{2peak} across the muscle, and an overall increase in VO_{2peak}. These findings demonstrate that

improvements in muscle structure and oxygen transport can be achieved with minimal central hemodynamic challenge (little change in HR and CO during exercise). This is particularly important for the CHF patient, who has a limited capacity to exercise due to a failing cardiac pump. Traditionally CHF patients are prescribed cardiac rehabilitation, which uses whole body exercise modalities that challenge a large muscle mass and therefore is limited by central circulation (Esposito et al., 2011). Due to low CO and reduced exercise tolerance to whole body exercise, peripheral adaptations may not be maximized in this population. The findings from Esposito and colleagues provide a potential exercise modality for CHF patients that cannot exercise in traditional rehabilitation settings due to poor cardiac functioning. Despite these positive findings for reduced muscle mass exercise, it is not feasible to use isolated joint exercise as an exercise modality due to the time requirement needed to exercise all muscle groups independently. For example, performing knee extension, knee flexion, hip extension, hip flexion, plantar flexion and dorsiflexion for 30 minutes each would require 3 hours: well beyond what time allows for the patient and the rehabilitation specialist.

Single-Leg Cycling

Several studies have investigated single-leg cycling to circumvent both the blood flow limitation during whole body exercise and the time requirements of single-joint exercise. Single-leg cycling reduces the active muscle by half (one leg instead of two) yet would be more efficient than single-joint exercise. Rud, Foss, Krustrup, Secher, & Hallen (2011) examined leg blood flow and O_2 extraction during cycling in one-legged

endurance trained individuals. They implemented a 7 week one-legged training program on 12 young healthy endurance trained volunteers (6 male, 6 female). VO_{2max} was determined prior to training in double-leg and single-leg cycling. One-legged training consisted of 4 training session per week for seven weeks. Cadence during training remained at 80rpm, and workload corresponded to 70-77% of the one-legged maximal heart rate lasting from 40-100minutes. At the conclusion of the 7-week training program results showed that participants displayed a 2% higher power output and a 2.3% higher VO_{2max}, when the trained leg was compared to the untrained leg. Additionally, flow increased 7% and oxygen extraction increased 3.5% when the trained leg was compared to the control leg. These increases resulted in a 21% higher oxygen uptake in the trained leg when compared to the control leg. Rud and colleagues reveal that single-leg cycling training not only increase localized factors (increase trained muscle O_2 extraction), but increase O_2 delivery.

A study conducted by Dolmage & Goldstein (2008) showed that COPD patients were able to tolerate constant-power exercise longer by exercising one-leg at a time versus two-legs at a time. Dolmage and Goldstein applied the same muscle specific workload (50-70% peak power) during both single and double-leg cycling. During the single-leg cycling there was a reduced ventilatory workload, allowing for an overall increase in total work completed in 30 minutes (Dolmage and Goldstein, 2008). Their more recent study involved a 7-week training protocol with COPD patients. Training consisted of either two-legged cycling for 30 continuous minutes or one-legged cycling for 30 continuous minutes (15 minutes per leg) three-days per week. The results from

this investigation indicate that COPD patients assigned to one-legged exercise training significantly improved their peak VO_2 as compared to those assigned to the two-legged training (Dolmage and Goldstein, 2008). The one-legged exercise group was able to exercise at a higher muscle-specific intensity, despite the fact that their overall exercise intensity remained below the two-legged group's overall intensity. By increasing muscle-specific exercise intensity versus overall intensity (reducing respiratory and cardiovascular demand and dyspnea), COPD patients were able to exercise longer. Dolmage and Goldstein conclude that one-legged exercise training is feasible for COPD rehabilitation because it does not require any specific learning and the patients found it to be at least as comfortable as two-legged training, because leg fatigue is tolerated better than dyspnea (Dolmage and Goldstein, 2008).

Overall previous reports suggests that single-leg cycling can be an excellent exercise modality for patients that have central and peripheral limitations, but feasibility of this type of exercise for a larger rehabilitation class remains questionable. Despite these findings, single-leg cycling has yet to become a mainstream exercise modality. Patients may not tolerate single-leg cycling because of muscle fatigue or poor biomechanics. Single-leg cycling requires the recruitment of the fatigable hip flexors during the upstroke of the pedal cycle, thus making single-leg cycling awkward and uncomfortable for the patient. However, in a recent study Burns et al. (2014) attempted to circumvent this limitation of single-leg cycling by utilizing a counterweight attached to the unoccupied crank. The counterweight would help assist the active leg on the upstroke reducing the need to recruit the fatigable hip flexors. They recruited ten young healthy

males and tested them in three cycling conditions; traditional double-leg cycling (DL), non-counterweight single-leg cycling (NCW), and counterweighted single-leg cycling (CW). Within each condition the participants pedaled for 4 minutes at three different work rates (40, 80, and 120W). While the power remained the same in all conditions, the CW and NCW conditions required the pedaling leg to work twice as hard when compared to the DL (one leg now doing the work of two legs). In all exercise conditions heart rate, blood pressure, VO_2, RER, and RPE were recorded. Additionally participants were asked to indicate their liking of the exercise via the liking scale upon completion. Results revealed that CW can produced similar cardiovascular responses compared to DL, specifically; RER, VO_2, HR, and MAP. NCW produced significantly higher HR, MAP, RER and VO_2 values, when compared to CW and DL. Five participants from this study had femoral artery blood flow recorded during CW and DL, in which blood flow increased significantly more in the CW condition when compared to DL.

Burns and colleagues showed not only that cardiovascular response could be similar, but that lower extremity blood flow would increase more in the exercising limb during CW when compared to DL. An increase in blood flow to one limb at a time is a direct result of the single leg now doubling its work rate to accomplish the task of two legs. This direct increase in blood flow could lead to a promotion in angiogenesis, resulting in new blood vessels in the lower extremities. Furthermore, while patients still prefer double-leg cycling to single-leg, the difference is minimal if a counterweight is place on the opposite side to the actively working leg. The counterweight aids in movement of the crank arm, to reduce the need of hip flexor muscles to generate force.

There was a significant difference between groups using a counterweight compared with a group without a counterweight, with liking scores closer to the double- leg group. Thus, the results by Burns indicates that counterweighted single-leg cycling can be used as an exercise modality that will allow for greater limb specific intensity, without additional cardiovascular stress. However, we have yet to establish whether older individuals have the same cardiovascular response to counterweighted single-leg cycling and whether they can coordinate that action similar to their younger counterparts.

Purpose

The use of single-leg counterweighted cycling as an exercise modality for the elderly population has yet to be explored. Thus the purpose of this study is to compare the cardiovascular responses of normal double-leg cycling to single-leg cycling with a counterweight in health elderly men (55-85 years old). Specifically, the dependent variables include; VO_2, RER, heart rate, blood pressure, as well as limb blood flow. Additionally, participants will rate each activity (single-leg and double-leg cycling) on the liking scale to test feasibility. Healthy elderly men have been selected for this study to match the age of patients that will most likely use this protocol in the rehab setting. We hypothesize that older individuals will be able to tolerate single-leg cycling and that the cardiovascular responses between single and double-leg cycling will be similar. Thus, single-leg counterweighted cycling could be used as an exercise modality in the elderly and diseased populations to maximize skeletal muscle adaptations.

CHAPTER III

METHODOLOGY

Participants

Ten healthy elderly males (55-90 years old) will be selected for the study.
Volunteers with heart disease, renal failure, neuro-muscular impairment, and any other
disease or condition that would limit their ability to complete the exercises safely will not
participate in the study.   All participants will have a pre-screening to check blood
pressure, heart rate, and cholesterol. All participants will need physician approval to
continue into the study. Participants will be informed about the risks and benefits of the
study, and an informed consent and health history questionnaire will be obtained prior to
inclusion into the study. This protocol was reviewed and approved by the Kent State
University Institutional Review Board.

Protocol

During the initial visit participants will undergo a series of baseline
measurements. These measurements include; height, weight, resting blood pressure, and
resting heart rate, as well as a semi-fasted (8hrs) blood sample will be taken for
assessment of lipid panel (total cholesterol, LDL, HDL, Triglycerides), CHEM 7 (BUN,
creatinine, glucose, sodium, potassium, chloride, and bicarbonate), and CBC/wdiff.
Following these measurements the participant will perform a YMCA submaximal cycle
ergometry test for assessment of aerobic capacity. After completing the YMCA

submaximal cycling protocol, participants will be familiarized with single-leg cycling. This is to allow for a smooth transition into single-leg cycling upon their subsequent visit.

The second visit, subjects will have all resting measurements repeated prior to the start of the cycling protocol. The experimental cycling protocol will require participants to pedal a Monark Ergomedic 828E cycle ergometer (Monark Exercise AB, Vansbro, Sweden) at two conditions and three different work rates within each condition. The two cycling conditions to be used are: traditional double-leg cycling (DL) and counterweighted single-leg cycling (CW). The CW condition will have a 10kg weight placed on the left crank arm of the cycle. The purpose of the counterweight is to help assist the active limb back to the top of the pedal stroke; this will reduce the need to recruit hip flexor muscles, thus mimicking the mechanics of standard double leg cycling (Thomas and Martin, 2009).

Within each condition the participants will pedal for 4 minutes at three different work rates (25, 50, and 75 W). Although the total work rate will remain the same across both conditions, the active limb during the CW condition will perform twice as much work compared to the DL condition: work performed during the DL condition will be divided across two legs. Work rates will be performed in increasing order, while cycling conditions will be counterbalanced to eliminate an order effect. While cycling participants will be required to maintain a pedaling rated of 60 RPM. A 5 minute rest will be given between the two conditions to allow the participant to recover.

During the exercise protocols participants will wear a heart rate monitor (Suunto, Vantaa, Finland) which will transmit data to a Schoberer Rad Messtechenik (SRM) power meter 7 which will measure and record power (Colorado Springs, Colorado, USA). The Parvo metabolic cart will be used to measure VO_2 and RER during the exercise trials. During the last 30 seconds of each work rate BP will be manually measured by a trained technician using an aneroid sphygmomanometer and participants will be asked to report their perceived exertion for total body fatigue and also for leg fatigue, using the Borg RPE scale (Borg, 1970). Upon completion of each condition, participants will be asked to indicate their liking of the exercise using a liking scale. The liking scale asked participants to place an X on a 10cm line, with the far left marked "did not like at all", the middle with "neutral", and the far right with "liked a lot" (Dacey, Baltzell, Zaichkowsky, 2008; McArthur, Raedeke, 2009; Williams, Papandonatos, Mapolitano 2006). The average VO_2 and RER will be used to calculate rate of caloric expenditure and metabolic cost using the regression equation reported by Zuntz (Zuntz 1901) (metabolic cost= Absolute VO_2 x (1.2341 x RER + 3.8124) which is based upon the thermal equivalent of O_2 for non-protein respiratory equivalent. The metabolic cost of exercise will then be used to calculate metabolic power: metabolic power = metabolic cost x 69.7. Gross efficiency will then be determined by dividing mechanical power by metabolic power.

Femoral artery blood flow will be measured for each participant using the right femoral artery. The right femoral artery was chosen, because it will be the side that is active in both conditions. Femoral artery blood flow will be measured prior to the start of

the exercise condition (with participants seated on the stationary cycle) to provide a baseline value. A Logiq 7 ultrasound Doppler transducer (GE Healthcare, New York, NY) will be used to assess all femoral artery measurements. Blood flow measurements will be measured immediately (within 3-4 seconds) following the completion of each 4-minute stage of exercise (25W, 50W, 75W) for each exercise condition (DL and CW). At the completion of a 4-minute stage, participants will be asked to stop cycling and to extend the right leg while remaining seated on the stationary cycle so that an ultrasound transducer can be place above the right femoral artery. Blood flow measurements will be measured for 10 seconds upon which time the subjects will be advised to begin peddling to start the next stage. In total, subjects will remain stopped for less than 30seconds between stages to allow for blood flow measurements. To calculate blood flow the femoral artery radius and blood velocity obtained from the Logiq 7 will be placed in the following equation: Blood Flow= $(radius)^2(3.14)(2*blood\ velocity)$.

Data Analysis

The dependent variables to be assessed are VO_2, HR, MAP, RPE (body and leg), metabolic cost, gross efficiency, RER, liking score and femoral artery blood flow. Statistical analysis will be performed using two-way repeated measures ANOVA on condition (DL and CW) and work rate (25, 50, 75 W) followed by post-hoc comparisons using SPSS software (SPSS version 22, SPSS Inc., Chicago Illinois). The level of significance will be set at $p \leq 0.05$. All data will be reported as mean $\pm$ sd.

CHAPTER IV

PHYSIOLOGICAL RESPONSES TO COUNTERWEIGHTED SINGLE-LEG CYCLING IN AN ELDERLY POPULATION

Background

High-intensity endurance training has been shown to result in greater improvements in skeletal muscle adaptations (Whyte, Gill, & Cathcart 2010), VO_2 peak (Hottenrott, Ludyga, & Schulze 2012), and aerobic performance (Hottenrott, Ludyga, & Schulze 2012) when compared to lower intensity training; however when prescribing exercise to an elderly or diseased individual, high-intensity endurance training may not be safe due to the increased risk of cardiovascular event. Furthermore, high-intensity endurance exercises that incorporate the entire body (running/cycling) are limited by the ability of central circulation to distribute blood and oxygen to the working muscles (Saltin 1985; Layec, Haseler, & Richardson, 2013) while maintaining adequate blood pressure (Collins 2001). However, exercise involving smaller muscle mass can maximize the muscle specific exercise intensity resulting in greater positive adaptations while minimizing strain on the cardiovascular system.

Previous investigators have employed single-leg cycling as an aerobic exercise modality. These investigators have reported that single-leg cycling can generate greater leg specific work rates when compared to double-leg cycling (BJorgen et al., 2009; Dolmage & Goldstein, 2006; Duner, 1958; Magnusson et al., 1997; Rud, Foss, Krustrup, Secher, & Hallen, 2005). Specifically, single-leg cycling confines the exercise to a smaller muscle mass and allows the participant to exercise for a longer duration or a

much greater limb specific intensity because blood flow to the active muscle is much greater compared to double-leg cycling (Burns et al., 2014) (i.e.blood flow is no longer 'shared' by both legs). While research supports the use of single-leg cycling to generate greater leg specific work rates, the biomechanics of single-leg cycling is very different than the biomechanics of double-leg cycling, making the exercise awkward and uncomfortable. Single-leg cycling requires the recruitment of the fatigable hip flexors during the upstroke of the pedal cycle, thus limiting the application of single-leg cycling as an exercise modality. To overcome this limitation, previous investigators have either used a motor (Koga et al., 2001) or a fixed gear ergometer to facilitate smooth single-leg cycling (Dolmage & Goldstein, 2006; Dolmage & Goldstein, 2008). More recently a counterweight was mounted on the non-occupied crank arm such that the counterweight assists with the upward phase of the active limb and thereby reducing the need to recruit hip flexors (Martin et al., 2012; Burns et al., 2014, Abiss et al., 2011, Elmer et al., 2013). The results indicated that, at least in the young healthy population, the counterweighted single-leg cycling allows for greater limb specific exercise intensity without additional cardiovascular stress (Burns et al., 2014). It has yet to be determined how elderly or diseased individuals will respond to single-leg cycling with a counterweight.

The purpose of this investigation was to determine if an elderly population could tolerate/coordinate single-leg cycling that is assisted with a counterweight and to compare the cardiovascular responses between double-leg and counterweighted single-leg cycling in the elderly population. Based on previous results, we hypothesized that single-leg cycling with a counterweight will be well tolerated in an elderly population

and will generate similar cardiovascular, metabolic, and RPE responses compared to double-leg cycling. Additionally, we hypothesized an increased blood flow to the working limb during single-leg cycling when compared to double-leg cycling.

Methods

Participants

Eleven healthy elderly men (age 66 ±8 years; body mass 87.5 ± 13.5 kg; height 1.8 ± .05 m) volunteered to participate in the study. Volunteers with pulmonary or cardiovascular disease, neuro-muscular impairment or any condition that would limit their ability to complete the exercises safely were excluded from this investigation. Initially, participants were informed about the risks and benefits of the study. An informed consent, health history questionnaire and physician's clearance to participate was obtained prior to inclusion into the study. This protocol was reviewed and approved by the Kent State University Institutional Review Board.

Protocol

During the initial visit a series of baseline measurements were obtained from the participants. These measurements included; height, weight, resting blood pressure, resting heart rate, as well as a semi-fasted (8hrs) blood sample for assessment of lipid panel (total cholesterol, LDL, HDL, Triglycerides), CHEM 7 (BUN, creatinine, glucose, sodium, potassium, chloride, and bicarbonate), and CBC/wdiff. Following these measurements the participant performed a YMCA submaximal cycle ergometry test to estimate aerobic capacity. After completing the YMCA submaximal cycling protocol,

participants were familiarized with single-leg cycling. This was to allow for a smooth transition into single-leg cycling upon their subsequent visit. Subject characteristics are displayed in Table 1.

The experimental cycling protocol required participants to pedal a Monark Ergomedic 828E cycle ergometer (Monark Exercise AB, Vansbro, Sweden) across two conditions. The two cycling conditions were traditional double-leg cycling (DL) and counterweighted single-leg cycling (CW). The CW condition used a 10kg weight placed on the unoccupied crank arm of the ergometer. The purpose of the counterweight was to help assist the active limb back to the top of the pedal stroke; this reduced the need to recruit hip flexor muscles, thus mimicking the mechanics of standard double-leg cycling (Thomas and Martin, 2009; Burns et al., 2014). During single-leg cycling, the non-active limb remained at rest to the side of the ergometer and supported by a wooden box.

Within each condition the participants pedaled for 4 minutes at 60 RPM at three different work rates (25, 50, and 75 W) in increasing order. Although the total work rate remained the same across both conditions, the active right limb during the CW condition performed twice as much work as it did during the DL condition: work performed during the DL condition was divided across two active legs. Cycling conditions were counterbalanced to eliminate an order effect and a 10 minute recovery period was included between the two conditions.

During the exercise protocols participants wore a heart rate monitor (Suunto, Vantaa, Finland) that transmitted data to a Schoberer Rad Messtechenik (SRM) power

meter 7, which measured and recorded power (Colorado Springs, Colorado, USA). A

Parvo metabolic cart was used to measure VO_2 and RER during the exercise trials.

During the last 30 seconds of each work rate BP was manually measured by a trained

technician using an aneroid sphygmomanometer and participants were asked to report

their perceived exertion (RPE) for total body exertion as well as RPE specific to their

legs, using the Borg RPE scale (Borg, 1970). Upon completion of each condition,

participants were asked to indicate their liking of the exercise using a liking scale. The

liking scale asked participants to place an X on a 10cm line, with the far left marked "did

not like at all", the middle with "neutral", and the far right with "liked a lot" (Dacey,

Baltzell, Zaichkowsky, 2008; McArthur, Raedeke, 2009; Williams, Papandonatos,

Mapolitano 2006). The average VO_2 and RER were used to calculate rate of caloric

expenditure and metabolic cost using the regression equation reported by Zuntz (Zuntz

1901) (metabolic cost= Absolute VO_2 x (1.2341 x RER + 3.8124) which is based upon

the thermal equivalent of O_2 for non-protein respiratory equivalent. Lipid and

carbohydrate oxidation were then calculated in grams per liter of oxygen, to assess fuel

utilization during both conditions.

A Logiq 7 GE ultrasound Doppler and linear M12 transducer (GE Healthcare,

New York, NY) was used to assess femoral artery blood flow. Specifically, femoral

artery blood flow was measured prior to the start of the exercise condition (with

participants seated on the stationary cycle) to provide a baseline value and immediately

following the completion of each 4-minute stage of exercise. At the completion of a 4-

minute stage, participants were asked to stop cycling and to extend the right leg while

remaining seated on the stationary cycle so that an ultrasound transducer could be placed above the right femoral artery. Following the measurement subjects resumed peddling to start the next stage. In total, subjects remained stopped for less than 30 seconds between stages to allow for blood flow measurements. Consistent and timely probe placement (within 3-4 seconds following pedaling termination) was made possible by marking the location for probe placement on the skin prior to testing. Femoral artery blood flow was ultimately calculated as: Blood Flow (ml/min) = $radius^2 * 3.14 * blood\ velocity * 60$. Conductance was then calculated as: Blood Flow (ml/min)/ MAP.

Data Analysis

The dependent variables assessed were VO_2, HR, MAP, RER, rate pressure product, lipid and carbohydrate oxidation, RPE (body and leg), metabolic cost, liking score and femoral artery blood flow. Statistical analysis was performed using two-way repeated measures ANOVA on condition (DL and CW) and work rate (25, 50, 75 W) followed by post-hoc comparisons using SPSS software (SPSS version 22, SPSS Inc., Chicago Illinois). The level of significance was set at $p \leq 0.05$. All data are reported as mean ± sd.

<div align="center">

Results

</div>

Results from the blood analysis indicate that all participants were within normal range for CBC w/diff and are presented in table 1 (N=8). Cholesterol screening suggests that 3 subjects have elevated cholesterol values (total cholesterol and LDL) and elevated glucose values. Mean values from the blood analysis are within normal range for all

measures, and blood analysis was conducted in a semi-fasted state (8hrs). Mean VO_{2max} estimated from the YMCA cycling protocol was 33.4 ± 4.9 ml*kg^{-1}*min^{-1}. Mean VO_2 estimates from the YMCA submaximal cycle ergometry test indicate that participants had an overall fitness level rating of average with fitness levels ranging from below average (N=1) to good (N=3). During double-leg cycling, the three work rates utilized in this study (25, 50, and 75W) elicited approximately $26.6 \pm 3.5\%$, $36.5 \pm 4.0\%$, and $43.1 \pm 5.7\%$ of estimated VO_{2max}.

Cardiovascular Responses

There was no significant difference in VO_2 between single and double-leg cycling at the 25W and 50W intensity, however while cycling at 75watts, VO_2 was $11.5 \pm 3.8\%$ greater during the CW compared to DL (p= 0.037) (Figure 1A). Although HR increased with exercise intensity, it was not significantly different between conditions in all three work rates (p≥0.160) (Figure 1B). Like HR, there was no significant difference in MAP at the 25W and 75W intensities between single and double-leg cycling (p= 0.090, p= 0.159). However, there was a significant difference in MAP between the two conditions at the 50W intensity (p= 0.047) (Figure 1C).

Femoral artery blood flow was measured in nine subjects during both cycling conditions (140.1 ± 69.7 Ml/min), two subjects were excluded from analysis due to operational error. There was a significant difference between DL and CW cycling during the 50W and 75W intensities (p= 0.01, p< 0.001) (25W, p= 0.09) (Figure 1 D). Specifically, compared to DL, CW cycling increased right femoral artery blood flow by

17.1 ± 27.9% at 25W intensity, 31.35 ± 20.49% % at 50W, and 31.5 ± 15.05% at 75W.

Furthermore, we examined conductance to determine if increases in femoral artery blood

flow was strictly the result of increased cardiovascular demand or caused by increased

local demand and delivery. There was a significant increase in conductance when

comparing CW to DL cycling at 50W and 75W (p=0.01, p<0.001).

Metabolic Responses

RER was significantly greater during single-leg cycling compared to double-leg

cycling across all three workloads (p≤ 0.018) (Figure 2). Carbohydrate oxidation was

0.33 ± 0.23, 0.71 ± 0.28, 0.98 ± 0.35 g/min. at 25W, 50W, and 75W during double-leg

cycling and 0.47 ± 0.20, 0.88 ± 0.35, and 1.4 ± 0.45 g/min at 25W, 50W, and 75 W

during single-leg cycling, however these were only significant at 50W (25W p= 0.213,

50W p= 0.028, 75W p= 0.065).

Perceptual Reponses

Total body RPE measured at 25W was not significantly different between DL and

CW cycling groups (p= 0.068), however RPE at 50W and 75W was significantly greater

in the CW group when compared to the DL group (p= 0.05, p= 0.009) (Figure 3A). Leg

RPE scores were significantly different for all intensities (Figure 3B). Liking scores were

not significantly different between conditions. Mean liking score was 7.47 ± 2.17 for

CW cycling and 7.95 ± 1.86 DL cycling. Both liking scores indicate that participants had

a moderate liking for the exercise conditions (Figure 4).

Discussion

This investigation examined the cardiovascular and perceptual responses of traditional double-leg cycling to single-leg cycling with a counterweight in a healthy elderly male population. The results from this investigation indicate that healthy elderly men tolerated and perceived CW cycling as well as traditional DL cycling. Furthermore, the results from this investigation are similar to the results of previous investigations of DL and CW tested in a young healthy male population (Burns et al., 2014). Single-leg cycling with a counterweight in both studies revealed that CW cycling doubled the work performed by the muscles of the lower limb, while maintaining nearly similar cardiovascular stress to normal double-leg cycling. These results have implications to exercise rehabilitation for those with lower limb injury/amputation or diseases in which oxygen delivery is severely limited.

Metabolic and Cardiovascular Responses

Results of this study indicate that single-leg cycling with a counterweight produces metabolic and cardiovascular responses that are similar to that of traditional double-leg cycling, while doubling the work performed by the lower limb. There was no significant difference in VO_2 between groups at the 25W and 50W intensity, however VO_2 was significantly greater for CW during the 75W intensity ($48.1 \pm 8.2\%$ estimated VO_{2max}) compared to DL. Burns et. al. (2014) noted in a young male population, that at the highest intensity of single-leg cycling, VO_2 significantly increased compared to double-leg cycling at the same intensity. At lower intensities (25W and 50W) VO_2

remained almost identical to that of double-leg cycling. It is possible that at the higher intensities participants had to recruit more hip flexors or stabilizing muscles in the core or upper body, causing an increase in VO_2 beyond what is required for normal double-leg cycling. This is likely also why metabolic cost was slightly higher during CW at the highest intensity compared to the double leg condition.

Heart rate was not significantly different between conditions for all three intensities, and MAP was only greater during CW cycling at the 50 watt stage when compared to DL. However, femoral artery blood flow of the active limb was significantly greater during the CW cycling condition for all intensities when compared to DL cycling due to the increased metabolic demand of sole active limb that is producing all the external work. Together these data suggest that with minimal extra cardiovascular demand, external workload can be doubled and blood flow to the active limb increased by more than approximately 30% during single-leg counterweighted cycling. The increase in femoral artery blood flow can be contributed to the combination of increased metabolic demand of the working muscle and by the increase in the release of local vasodilators (nitric oxide/prostacyclin) from the endothelium. The increase in conductance that occurred during CW cycling is an indicator that the increase in femoral artery blood flow during CW cycling is due to peripheral vasodilation, and not caused by an increase in MAP. The increase in local blood flow during CW cycling is promising for clinical application in peripheral artery disease therapy, as the increase in shear stress would promote improvements in endothelial function and angiogenesis.

In addition to the greater femoral blood flow across all intensities with CW cycling, substrate utilization also differed between the two cycling modalities. Specifically RER was significantly greater for CW compared to DL across all intensity levels suggesting greater glucose oxidation. This difference is expected based on the doubling of the leg-specific work rate. For example, during the 50W condition, each leg would effectively contribute 25W. However, during CW cycling all 50W was produced by the active leg resulting in greater glucose utilization and subsequently increased RER compared to normal double-leg cycling. Although numerically these data suggest carbohydrates were utilized more during single-leg cycling across all workloads, the only significant difference occurred at the 50W stage. It is likely that a significant difference was not observed during the 25W cycling trial because resistance was so low that the cost of simply moving both legs (cost of unloaded cycling) offset the extra metabolic stress added to the sole active leg during CW cycling. In addition, at 75 watts there were several subjects that exceeded an RER of 1.0 during the CW condition which makes the energy expenditure calculations invalid. For those individuals carbohydrate utilization was calculated as if RER was at 1.0 and therefore likely underestimated their true carbohydrate oxidation during the CW condition. The elevated RER during CW agrees with Burns et al. (2014) who also reported greater RER values at 40, 80, and 120 watts CW compared to DL for young healthy individuals. This could have implications for acute glucose control in diabetic patients, providing an aerobic exercise modality that has greater glucose oxidation, and therefore may help stabilize post prandial blood glucose compared to traditional exercise modalities. In fact, Abbiss et al. (2011) found that 6

weeks of single-leg cycling training increased leg-specific power that resulted in GLUT-4 and AS160 content, which could improve long term glucose control.

Perceptual Responses

Previous reports indicate that single-leg cycling without a counterweight is poorly perceived as an exercise modality (Burns et al., 2014), while participants perceive single-leg cycling with a counterweight much better. This result is likely because single-leg cycling with a counterweight reduces the amount of work required during the upstroke phase of cycling, thus reducing the amount of work the fatigable hip flexor muscles are required to produce during the exercise. In addition, the counterweight allows for a more fluid movement during cycling, and produces similar cycling biomechanics to that of double-leg cycling. Despite the similarity in biomechanics between the two conditions, there was a significant difference in RPE for both body and leg, however participants did not indicate a preference to either double or single-leg cycling. Specifically, liking scores were not significantly different between the two conditions. This suggests that single-leg cycling with a counterweight is well perceived and tolerated well among healthy elderly male subjects. Furthermore, liking score results suggest that participants are just as willing to perform single-leg cycling with a counterweight as double-leg cycling making single-leg cycling a possible exercise modality for elderly or diseased individuals.

Single-Leg Cycling

Single-leg cycling has been successfully used in previous studies with COPD patients using a fixed gear cycle ergometer with much success (Dolmage & Goldstein,

2006; Dolmage & Goldstein 2008). Fixed gear cycle ergometers likely also facilitate natural cycling biomechanics for single-leg cycling as the inertial load of the flywheel assists the active leg on the upstroke similar to the counterweight in our model. It is likely that in a clinical population such as COPD and heart failure in which power produced by the subject is relatively low (25-75 watts single-leg) and therefore resistance on the flywheel is also low, the kinetic energy stored within the flywheel may be sufficient to assist with hip flexion with minimal deviation in the angular velocity of the crank. Thus single-leg cycling with a fixed gear ergometer is a great alternative to the counterweight for a clinical setting with patients that have a low exercise capacity (<75W). However, if the mass of the flywheel is small or the power output is large (200 watts single-leg), kinetic energy may be insufficient to assist with leg flexion without large scale changes in instantaneous crank angular velocity. A future study comparing the single-leg cycling biomechanics using either a fixed gear ergometer or counterweight could alleviate these concerns.

This investigation has several limitations. First, participants that volunteered for this study were healthy elderly men that were regularly active. While the results appear to have a clear clinical application, we cannot exclude the possibility that the results may be different in a diseased population. In addition, finding the appropriate counterweight and exercise intensity is crucial to determine optimal effectiveness for a clinical application. Finally, exercise intensity was selected based on previous pilot data. To get optimal results for a rehabilitation study, exercise intensity should be selected according

to an individualized exercise prescription based on maximal/submaximal exercise tests, activity levels, health, and tolerance of the exercise.

In conclusion, results from this study indicate that single-leg cycling with the use of a counterweight will significantly increase femoral artery blood flow to the working limb (with a minimal increase in cardiovascular demand) when comparted to traditional double-leg cycling.   Additionally, participants in this study report no significant difference in liking scores, indicating that single-leg cycling with a counterweight can be easily implemented into an exercise program. The positive results from this study, suggest that single-leg cycling with a counterweight would be feasible to use in a rehabilitation program (COPD, CAD, PAD). Due to the increase in femoral artery blood flow, single-leg cycling with a counterweight may promote angiogenesis and/or arterial adaptations that may be beneficial to PAD patients. Further research is needed to determine if single-leg cycling with a counterweight will have a similar effect in PAD patients.

CHAPTER V

**COUNTER-BALANCED SINGLE-LEG CYCLING: USES IN PERIPHERAL
ARTERY DISEASE REHABILITATION**

Introduction

Peripheral artery diseases (PAD) is a narrowing of the arteries that supply blood

to the extremities and other areas of the body beyond the coronary arteries. PAD is

similar to coronary artery disease (CAD), both diseases are a result of plaque build-up in

the arterial walls, leading to narrowing of the artery (arteriosclerosis). With a narrowing

of the artery, blood flow is limited in the region the artery is supplying. PAD most

commonly affects the arteries serving the legs, and produces claudication (a cramping

pain) in the legs while exercising, due to the reduced blood flow/oxygenation to the

working muscles. PAD often goes undiagnosed, which is troublesome, because PAD

increases the likelihood of developing CAD, myocardial infarction (heart attack), stroke,

and transient ischemic attack (mini-stroke) (NIH 2006). PAD currently affects 8 to 12

million people in the United States, with those who are 50 years of age or older at higher

risk (NIH 2006; Hamburg & Balady, 2011). Risk factors for PAD include; age 50 or

older, smoking, diabetes, hypertension (high blood pressure), hypercholesterolemia (high

blood cholesterol), history of vascular disease (heart attack/stroke), and being of African

American decent (NIH 2006).

When left untreated PAD can lead to decreased mobility and an increased risk of

heart attack and stroke (Escobar et al., 2011). This makes PAD not only critical to

diagnoses, but critical to treat as well. A comprehensive treatment plan that reduces risk

factors for PAD, will also reduce the risk of CAD and stroke. Treatment plans for PAD

include pharmacotherapy (hypolipidemic, antihypertensive, and anticoagulant medications), surgery/angioplasty, and lifestyle changes (smoking cessation, nutritional changes, and exercise) (Regensteiner 2004). Of the treatment plans provided for PAD patients, rehabilitation is often overlooked and or not covered by medical insurance, but provides the greatest increase in mobility and function (Regensteiner, 2004).

Current treatment for PAD patients includes cardiac rehabilitation (if CAD is present), with the primary goal of achieving an improved aerobic capacity. Medicare cardiac rehabilitation guidelines recommend a program that consists of 36 rehabilitation sessions spread out over 12-15 weeks. This allows for three one-hour rehabilitation sessions per week. Current rehabilitation modalities are focused on Coronary Artery Disease (CAD) rehabilitation. Typically CAD patients do not express the peripheral limitations to exercise that PAD patients experience (Spronk et al. 2008). In recent years there has been a shift in rehabilitation programing to address the specific issues that face PAD patients, but a diagnosis of PAD without CAD typically does not qualify for rehabilitation coverage.

Claudication is the primary symptom reported by PAD patients, but only 10-15% of PAD patients report having intermittent claudication (Hamburg & Balady, 2011). Many individuals with PAD contribute claudication pain to normal aging or do not recognize the pain as claudication. Additionally, up to 50% of PAD patients have atypical leg symptoms that interfere with mobility (Hamburg & Balady, 2011). In both circumstances, PAD patients suffer reduced exercise capacity, with or without the presence of classic claudication (Casillas et al., 2011; Escobar et al., 2011; Parmenter et

al., 2010; Spronk et al., 2008; Regensteiner, 2004). Thus, despite the fact that these individuals may have normal cardiac output, PAD patients are severely limited in their ability to walk pain free. The claudication pain during walking will often limit the distance and intensity a PAD patient can walk without stopping. The six-minute walk test is frequently used to determine the severity of claudication caused by PAD. Bodescu, Jurcau, and Pop (2012) compared the distance PAD patients with claudication and without claudication could achieve on a six-minute walk test. Results demonstrated that PAD patients without claudication achieved a distance of $383 \pm 22.9m$ while PAD patients with claudication achieved a walking distance of $312 \pm 54.48m$. Similar studies have been conducted in healthy subjects with similar demographics to the study conducted by Bodescu, Jurcau, and Pop. Healthy patients without PAD achieved an average walking distance of 500m or more during a six-minute walk test (Enright & Sherrill, 1998). These findings suggests that PAD with or without claudication can impair walking distance, when compared to healthy subjects (Casillas et al., 2011; Enright & Sherrill, 1998). The impairment in walking makes it difficult for PAD patients to maintain aerobic exercise for an extending period of time, limiting their ability to achieve cardiovascular benefits from exercise.

New strategies for PAD rehabilitation programing is focused on inducing claudication while walking on a treadmill. The rehabilitation program consists of 30-60 minutes of exercise 2-3 times per week (Regensteiner 2004). Before beginning the program, patients will perform a treadmill test to determine the maximal walking distance they can achieve before stopping due to severe claudication (Regensteiner 2004). Based

on their performance, a rehabilitation program will be prescribed to elicit aerobic improvement and increase walking distance without claudication. To address the limiting factor of claudication, the rehabilitation session will consist of short bouts of exercise (treadmill walking), ranging from several seconds to a few minutes according to the patient's tolerance. When claudication pain is too severe (3/4 on the claudication pain scale) the patient will rest, until the pain subsides. Once the pain dissipates, the patient begins walking again until the claudication becomes unbearable once more. This process will be repeated several times during the rehabilitation session. Improvement in maximal walking distance has been demonstrated in rehabilitation programs of this nature, but improvements in aerobic capacity (VO_2 peak) are limited, often because target heart rate is not maintained for an extended period of time (Spronk et al. 2008). Other forms of rehabilitation have been implemented for PAD (resistance training, unsupervised walking), but all have failed to increase walking distance and aerobic capacity to the same extent of frequent mini-bouts of treadmill walking. Furthermore, researchers have found that supervised rehabilitation programs have the greatest success at treating claudication. This effect could be due to the increased program adherence for supervised rehabilitation versus unsupervised rehabilitation.

Recent studies have looked at single-leg cycling as a possible rehabilitation modality for patients with various disease conditions   A study conducted by Dolmage & Goldstein (2008) showed that COPD patients were able to tolerate constant-power exercise longer by exercising one-leg at a time versus two-legs at a time. Dolmage and Goldstein applied the same muscle specific workload (50-70% peak power) during both

single and double leg cycling. During the single-leg cycling there was a reduced ventilatory workload, allowing for an overall increase in total work completed in 30 minutes (Dolmage and Goldstein, 2008). Their more recent study involved a 7-week training protocol with COPD patients. Training consisted of either two-legged cycling for 30 continuous minutes or one-legged cycling for 30 continuous minutes (15 minutes per leg) three-days per week. The results from this investigation indicate that COPD patients assigned to one-legged exercise training significantly improved their peak VO_2 as compared to those assigned to the two-legged training (Dolmage and Goldstein, 2008). The one-legged exercise group was able to exercise at a higher muscle-specific intensity, despite the fact that their overall exercise intensity remained below the two-legged group's overall intensity. By increasing muscle-specific exercise intensity versus overall intensity (reducing respiratory and cardiovascular demand and dyspnea), COPD patients were able to exercise longer. Dolmage and Goldstein conclude that one-legged exercise training is feasible for COPD rehabilitation because it does not require any specific learning and the patients found it to be at least as comfortable as two-legged training (Dolmage and Goldstein, 2008).

The research conducted by Dolmage and Goldstein suggests that single-leg cycling can be an excellent exercise modality for patients that have central and peripheral limitations. Despite these findings, single-leg cycling has yet to become a mainstream exercise modality. Patients may not tolerate single-leg cycling because of muscle fatigue or poor biomechanics. Single-leg cycling requires the recruitment of the fatigable hip flexors during the upstroke of the pedal cycle, thus making single-leg cycling awkward

and uncomfortable for the patient.   However, in a recent study Burns et al. (2014) attempted to circumvent this limitation of single- leg cycling by utilizing a counterweight attached to the unoccupied crank. The counterweight would help assist the active leg on the upstroke reducing the need to recruit the fatigable hip flexors. They recruited ten young healthy males and tested them in three cycling conditions; traditional double leg cycling (DL), non-counterweight single-leg cycling (NCW), and counterweighted single-leg cycling (CW). Within each condition the participants pedaled for 4 minutes at three different work rates (40, 80, and 120W). While the power remained the same in all conditions, the CW and NCW conditions required the pedaling leg to work twice as hard when compared to the DL (one leg now doing the work of two legs). Results revealed that CW can produced similar cardiovascular responses compared to DL, specifically; RER, VO_2, HR, and MAP. NCW produced significantly higher HR, MAP, RER and VO_2 values, when compared to CW and DL. Five participants from this study had femoral artery blood flow recorded during the CW and DL cycling, and their data indicate that femoral blood flow was approximately 65% greater during CW condition when compared to DL. Thus, Burns and colleagues showed not only that cardiovascular response could be similar, but that lower extremity blood flow would increase more in the exercising limb during CW when compared to DL.

In a similar study LaScola et al. (2015) examined the cardiovascular responses to double and single leg cycling in an elderly male population. Participants in this study cycled at three different intensities (25, 50, and 75w) for 4 minutes at each intensity. Subjects maintained a pedal rate of 60 RPM and completed both single-leg cycling with a

counterweight and standard double-leg cycling. Results showed that all subjects tolerated both cycling conditions well (liking) and produced similar cardiovascular responses (HR). Right femoral artery blood flow was significantly greater in the single-leg cycling condition (50 and 75W) when compared to double leg cycling. Again, this study demonstrates that single-leg cycling is tolerated well and produces a similar cardiovascular response as double-leg cycling, while increasing blood flow to the working limb.

The increase in blood flow to the working limb creates an increase in the amount of shear stress applied to the blood vessel walls serving the isolated area. An increase in shear stress has been shown to increase the release of endothelial nitric oxide, which causes vasodilation of blood vessels (Green, 2009). This increase in vasodilation can lead to peripheral adaptations in the working limbs that may result in increased blood vessel diameter over time (Zeppilli et al. 1995). Additionally, shear stress can cause adaptations to the apical endotheilial cell surface, causing the cells to flatten, resulting in an increased blood vessel diameter (Ballermann, et al. 1998). Thus increased shear stress induced by single-leg cycling may further increase adaptations to the arterioles serving the working muscles.

Angiogenesis (growth of new blood vessels) is also stimulated by an increase in shear stress along the vessel wall (Ballermann, et al. 1998). Shear stress causes endothelial cells to release a variety of growth factors (PDGF, TGF, and cyclooxygenase). The increased release of growth factors, serves as a stimulant for the development of new blood vessels. By establishing new blood vessels, blood flow can

increase to a working muscle during exercise, resulting in improved performance. Collectively the increase in blood vessel diameter and increased angiogenesis in the working limb could serve to decrease claudication symptoms in the PAD patient.

In addition to the greater shear stress, single-leg cycling may also allow patients to maintain a more constant exercise session. Specifically, PAD patients may experience greater cardiovascular improvement via single-leg cycling, because they would not require complete cessation of exercise for claudication pain to dissipate. Single-leg cycling would allow the PAD patient to continue to exercise while one leg is experiencing claudication. PAD patients would be able to exercise one leg at a time, and rest one leg at a time when claudication pain continues. This would allow PAD patients to increase their overall exercise time, potentially leading to greater cardiovascular benefits.

Objectives

To test and determine if a 12 week counterweighted single-leg cycling rehabilitation program in PAD patients provides greater improvement in vascular blood flow and relief of claudication compared to a traditional PAD rehabilitation program. Participants will come from four local cardiac rehabilitation programs and will be conducted at the patient's local site. Twenty-five subjects will be recruited for this study over a 12 month time period. All participants will complete the training program in a 12 week time period, exercising 3 days per week. Participants will be randomly assigned to one of two groups, single-leg cycling or control (traditional treadmill protocol). Results

will be compared between the two groups to determine any improvements in claudication/symptoms, arterial blood flow, functional capacity, and walking distance.

Hypothesis

We hypothesize that after the completion of the 12 week rehabilitation program, patients in the counterweighted single-leg cycling program will have significant improvements in claudication, ABI, arterial blood flow, functional capacity, and walking distance when compared to the control.

Methods

Thirty PAD patients from two northeast Ohio cardiovascular rehabilitation programs (Aultman Hospital and Cleveland Clinic) will be recruited for participation in a 12-week single-leg cycling rehabilitation program. The program will be conducted by rehabilitation staff at the patients selected program site. Participants will be required to have a physician's referral and insurance approval to be accepted into the rehabilitation program. Participants will have a diagnosis of PAD, and may also have documented cardiovascular disease (to allow for insurance approval). All participants will have a pre-screening to check blood pressure, heart rate, and cholesterol. Participants will be informed about the risks and benefits of the study, and an informed consent and health history questionnaire will be obtained prior to inclusion into the study. This protocol will be reviewed and approved by the Kent State University Institutional Review Board and any participating hospital's institutional review boards prior to the start of the rehabilitation program.

Participants will complete pre-screening testing before participating in the rehabilitation program. Participants will complete a six-minute walk test, to determine a maximal distance walked in six minutes prior to the start of rehabilitation. Additionally participants will complete a metabolic cycle-ergometer maximal stress test, to monitor any adverse cardiovascular complications and to serve as a measurement of cardiovascular fitness. During both testing procedures claudication pain will be assessed. Other initial testing will include a complete lipid panel, resting and exercising blood pressure, and ABI. A physician will complete a full physical and subjects will also complete a health history questionnaire and informed consent prior to any testing.

Rehabilitation will consist of 30-60 minute exercise sessions 3 days per week for a total of 12 weeks. Participants will be prescribed a target heart rate to achieve and maintain while exercising, this prescribed target heart rate will be determined by the patient's individual fitness level, medical condition, and performance on the maximal exercise stress test. Rehabilitation sessions will consist of single-leg cycling with a counterweight or traditional mini-bouts of treadmill walking. Participants in the single-leg cycling group will cycle at a desired pedal rate and intensity to achieve the recommended exercising heart rate, as prescribed from initial testing. When/if claudication pain in the exercising leg reaches a ¾ on the claudication scale or becomes intolerable by the patient, the participant will switch legs. This will reduce the amount of rest time and will allow the participant to achieve the desired heart rate for a longer period of time. Participants will maintain the target heart rate for the 60 minute exercise prescription.

Participants selected for the treadmill walking protocol will walk at an appropriate speed to achieve the recommended exercising heart rate, as prescribed from initial testing. Participants will walk on the treadmill until their claudication pain in the legs reaches a ¾ on the claudication scale or the walking becomes intolerable by the patient, at this point the patient will be provided a chair to rest in until the claudication pain subsides. Mini-bouts of walking will range from 3-5 minutes in length. When the claudication pain dissipates or is tolerated by the participant, walking will again resume. In total the participant will walk for 60 minutes. Upon completion of the twelve week protocol, participants in both exercise groups will have lipids, BP, HR, weight, ABI, femoral blood flow, six-minute walk test, and cycling metabolic stress test reassessed. All pre and post rehabilitation dependent variables will be assessed using a paired sample t-test using SPSS software (SPSS version 22, SPSS Inc., Chicago Illinois). The level of significance will be set at $p<0.05$. All data will be reported as mean ± sd.

Personnel and Facilities

Two Northeast Ohio hospitals will be targeted as potential rehabilitation centers. These centers include; Aultman Hospital and Cleveland Clinic. The research conducted will be a collaboration of all participating hospitals and Kent State University. All facilities selected currently operated PAD and/or CAD rehabilitation programs. Potential PAD rehabilitation candidates will come from physician referrals that are submitted to each program site. Once medical clearance and insurance coverage is verified the potential participant will be contacted regarding the study. Participation will be on a voluntary basis and risks and potential benefits will be discussed with all participants

prior to joining the study. Pre-screening criteria for inclusion into the study, will follow

hospital and insurance guidelines for inclusion into a PAD/CAD rehabilitation program.

Exercise rehabilitation sessions will be monitored by hospital staff, which includes;

clinical exercise physiologists, nurses, and physicians.

CHAPTER VI

SUMMARY

Single-leg cycling with the use of a counterweight has proven to be an accepted exercise modality by elderly male participants. Likability scores indicate that there is no significant difference between single-leg cycling with a counterweight and traditional double-leg cycling at the same exercise intensity. This is likely due to the counterweight providing assistance with the upstroke phase of cycling, allowing reduced hip flexor muscle recruitment, thus decreasing fatigue during exercise. By demonstrating that single-leg cycling with a counterweight is as likable as double-leg cycling, indicates that it would be feasible to use as a training exercise modality for a diseased population.

In addition to the positive results for likeability, single-leg cycling with a counterweight significantly increases blood flow to the exercising limb, when compared to traditional double-leg cycling at the same exercise intensity. This increase in blood flow came at minimal cardiovascular cost. By not increasing demand on the cardiovascular system, the exercising individual could potentially exercise for a longer duration and improve overall cardiovascular fitness. The increase in blood flow to the working limb during single-leg cycling with a counterweight could promote angiogenesis and arterial adaptations due to an increase in shear stress. This increase in shear stress has been shown to cause local vasodilation in the blood vessels supplying blood to the working muscles. Overtime the increased shear stress will promote vascular health and angiogenesis, which could potentially assist peripheral artery disease patients to reduce claudication pain and improve mobility.

Results suggest that further research is needed to determine if single-leg cycling with the use of a counterweight will have the same positive effects in diseased populations, other than PAD. Single-leg cycling has been shown to reduce the amount of muscle mass needed to complete the exercise, allowing participants with central limitations (CHF, COPD) to maintain the exercise for a longer duration to achieve greater peripheral adaptations. Results from this study also indicate that single-leg cycling may be beneficial for diabetic patients, as single-leg cycling was shown to increase the use of carbohydrates as a fuel source, ultimately leading to greater blood glucose control.

Table 1 *Physical Characteristics of Participants*

|	
Age	65.8 ± 8.3
Height	1.8 ± .05m
Weight	87.5 ± 13.5kg
BMI	26.48 ± 3.8
MAP	91.8 ± 10.98mmHg
Systolic	122.2 ± 16.58mmHg
Diastolic	76.6 ± 9.2mmHg
HR	73 ± 15.2bpm
BF	140.11 ± 69.74ml/min.
YMCA	33.4 ± 4.9mL/kg
Blood characteristics	**(n=8)**
Total Chol.	193.88 ± 36.72mg/dL
LDL	116.75 ± 24.59mg/dL
HDL	49.25 ± 7.48mg/dL
WBC	7.16 ± 1.99K/mm3
RBC	4.49 ± .38M/mm3
Hemoglobin	14.64 ± 1.1g/dl
Hematocrit	43.37 ± 3.68%
Platelets	229.29 ± 38.88K/mm3
Trigly	127.43 ± 64.8mg/dL
BUN	19.14 ± 4.79mg/dL
Creatine	1.14 ± .22 mg/dL
Potassium	4.2 ± .26mmol/L
Chloride	104 ± 2.78mmol/L
Glucose	96.29 ± 15.25mg/dL
Sodium	138.43 ± 2.92mmol/L
Age	65.8 ± 8.3
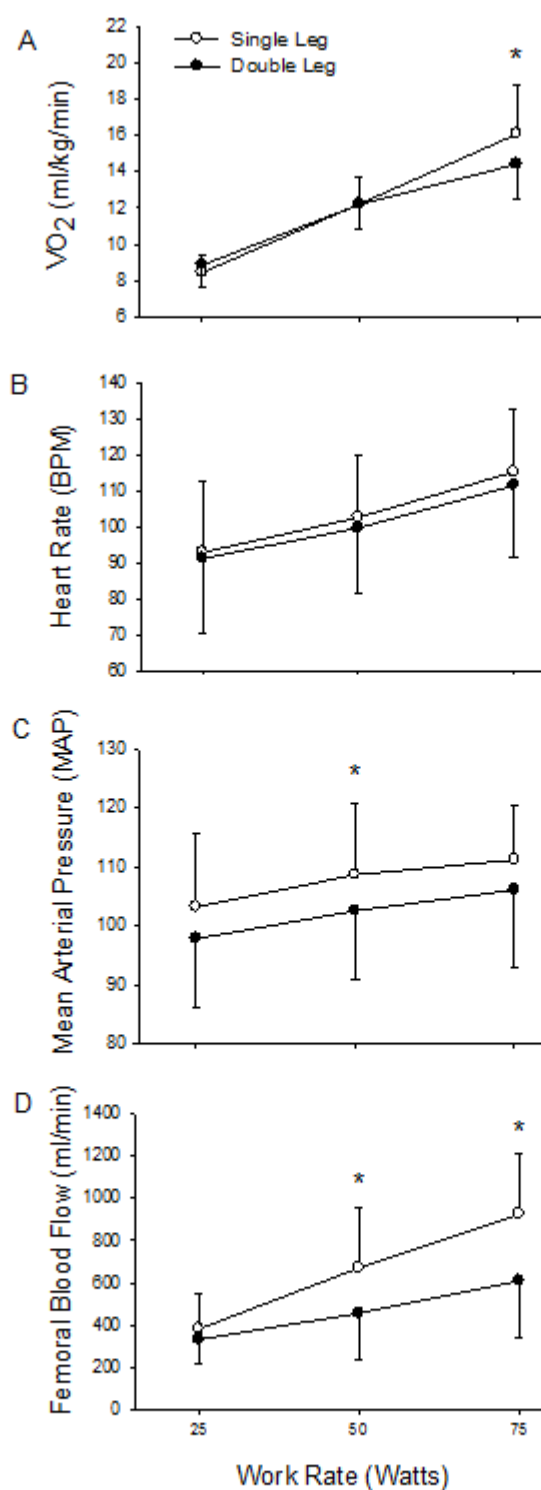
Figure 1: VO^2, HR, MAP, and femoral artery blood flow during double-leg and single-leg cycling across three workrates. * indicates a significant difference between conditions (p≤0.05).

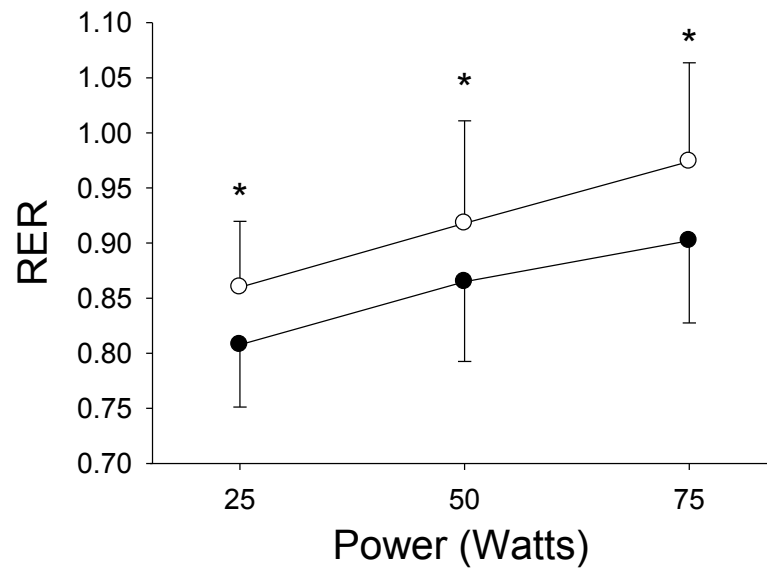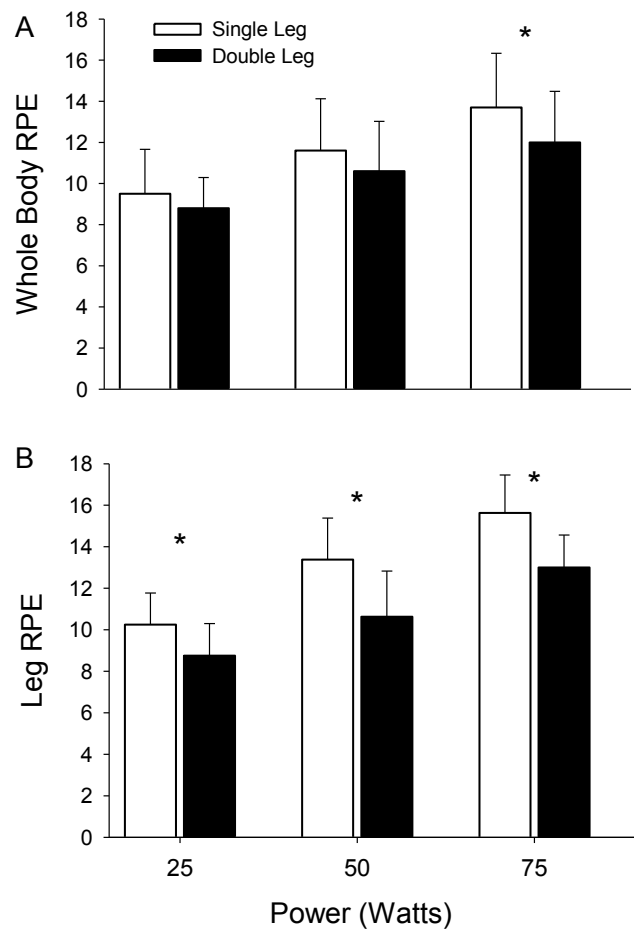*Figure 2:* RER during double-leg and single-leg cycling across three work rates. * indicates a significant difference between conditions (p≤0.05).

Figure 3: RPE for the whole body and legs during double-leg and single-leg cycling across three work rates. * indicates a significant difference between conditions (p≤0.05).
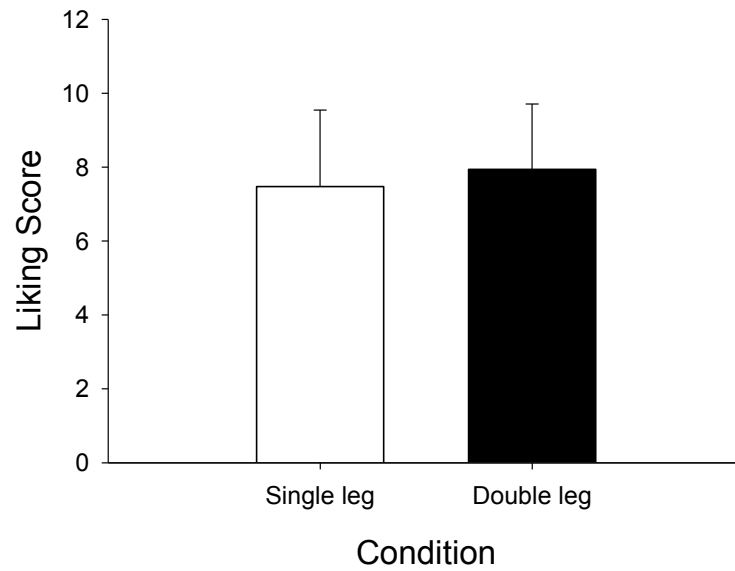
Figure 4: Liking score following double-leg and single-leg cycling that included three work rates. There was no difference in liking score between single-leg and double-leg cycling.

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