Cardiovascular and Blood Lactate Responses to Low, Moderate, and High Intensity Aerobic Exercise in Breast Cancer Patients: Is Exercise Intensity a True Reflection of Perceived Exertion?

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ABSTRACT

ELIZABETH S. EVANS: Cardiovascular and blood lactate responses to low, moderate, and high intensity aerobic exercise in breast cancer patients: Is exercise intensity a true reflection of perceived exertion?
(Under the direction of Claudio Battaglini, Ph.D.)

Exercise prescription guidelines for breast cancer patients have yet to be established. The purpose of this study was to compare the heart rate (HR), rate of perceived exertion (RPE), and post-exercise blood lactate responses to aerobic exercise between post-treated breast cancer patients and apparently healthy controls. Fourteen subjects (7 patients, 7 controls) participated in this study. Three different exercise intensities (40%, 60%, and 70% of VO_{2max}) were examined. No differences were observed in HR, RPE, or post-exercise lactate for the exercise trials, with the exception of lactate after the exercise trial at 70% of VO_{2max}, where the control group had a significantly higher response compared to the experimental group ($p<0.0005$). Post-treated breast cancer patients seem to respond similarly to these 3 exercise intensities compared with apparently healthy controls. However, methodological challenges faced during this study should be addressed for a more clear understanding of the current findings.

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CHAPTER I

INTRODUCTION

Breast cancer is the most common cancer in women, and the second leading cause of cancer deaths in women in the United States (Kim, Kang, Smith, & Landers, 2006). Treatment for breast cancer, including surgery, chemotherapy, and radiation therapy, can cause significant physical and psychological distress that may persist for months or years after the completion of therapy (Kim et al., 2006). Fatigue is the most common physical distress experienced by breast cancer patients, affecting up to 70% of patients during therapy and up to 30% of patients years after the completion of therapy (Dimeo, Rumberger, & Keul, 1998). This type of fatigue is often severe and may limit activities of daily living; therefore, many patients are advised to rest and reduce their level of daily activities (Dimeo et al., 1998). However, inactivity leads to muscular atrophy, and prolonged rest can actually worsen fatigue, thus contributing to a cycle of further muscular atrophy and down-regulation of daily activity levels (Dimeo et al, 1998; Dimeo, Stieglitz, Novelli-Fischer, Fetscher, & Keul, 1999; and Segal et al., 2001).

Aerobic exercise has been shown to improve physical performance in breast cancer patients (Dimeo, Fetscher, Lange, Mertelsmann, & Keul, 1997; Dimeo et al., 1998; Dimeo et al., 1999; Drouin et al., 2006; Fairey et al., 2003; Fairey, Courneya, Field, Bell, Jones, & Mackey, 2005; Fairey, Courneya, Field, Bell, Jones, St. Martin, et al., 2005; Kim, 2006, Mutrie et al., 2007; Nieman et al., 1995; Quist et al., 2006; Saxton

et al., 2006; and Segal et al., 2001). Previous studies have described intervention

programs ranging in intensities of 50-85% of maximal (peak) oxygen uptake $VO_{2max(peak)}$,

maximum heart rate, or heart rate reserve, frequencies of 3-5 days per week, and

durations of 8-26 weeks (Dimeo et al., 1997; Dimeo et al., 1998; Dimeo et al., 1999;

Drouin et al., 2006; Fairey et al., 2003; Fairey, Courneya, Field, Bell, Jones, & Mackey,

2005; Fairey, Courneya, Field, Bell, Jones, St. Martin, et al., 2005; Kim, 2006; Mutrie et

al., 2007; Nieman et al., 1995; Quist et al., 2006; Saxton et al., 2006; and Segal et al.,

2001). Significant increases in cardiovascular endurance and aerobic capacity, decreases

in fatigue, and some improvements in blood parameters and immune function have been

found (Dimeo et al., 1997; Dimeo et al., 1998; Dimeo et al., 1999; Drouin et al., 2006;

Fairey et al., 2003; Fairey, Courneya, Field, Bell, Jones, & Mackey, 2005; Fairey,

Courneya, Field, Bell, Jones, St. Martin, et al., 2005; Kim, 2006; Mutrie et al., 2007;

Nieman et al., 1995; Quist et al., 2006; Saxton et al., 2006; and Segal et al., 2001). These

choices for exercise intervention parameters, particularly intensity, are modeled after the

current guidelines employed for cardiac patients. In two recent reviews, Ko and

McKelvie (2005) and Smart, Fang, and Marwick (2003) reported that most studies

examining the effects of aerobic training on patients with heart failure have used

intensities of 40%-80% VO_{2peak}. Additionally, many studies involving cardiac patients

have also used heart rate (HR) and Borg's rating of perceived exertion (RPE) as

guidelines for aerobic exercise intensity. Intensities ranging from 50-80% of HR

reserve, 60-85% of predetermined peak HR, 40%-65% of maximal HR, and RPE ratings

of 12-14 have successfully been used to study the effects of aerobic exercise on patients

with heart failure (Corvera-Tindel, Doering, Woo, Khan, & Dracup, 2004; European

Heart Failure Training Group, 1998; Ko et al., 2005; Mairoana, O'Driscoll, Cheetham, Collis, Goodman, Rankin, et al., 2000; Oka, De Marco, Haskell, Batvinick, Dae, Bolen, et al., 2000; Smart et al., 2003; and Whellan, O'Connor, Lee, Keteylan, Cooper, Ellis, et al., 2007). Other studies examining the effect of exercise on cardiac patients have also used blood lactate concentration and lactate threshold to describe exercise intensity as aerobic or anaerobic (Mertesdorf & Schmitz, 2005; and Meyer, Samek, Schwaibold, Westbrook, Hajric, & Beneke, 1997).

In the cardiac patient population, it is thought that lower intensities of 40%-50% VO_{2max} may be more advantageous than higher intensities of 70-80% VO_{2max} because the former may reduce the risk of left ventricular dilation, minimizing stress on the left ventricular wall (European Heart Failure Training Group, 1998). However, it is not yet known whether similar exercise intensities currently prescribed for breast cancer patients are the most appropriate for eliciting the desired physiological changes without compromising other physiological functions (i.e., the immune system). Furthermore, it is not yet known whether the currently prescribed exercise intensity levels are even an accurate or consistent measure of a patient's true level of exertion. What is needed are models that describe physiological responses to differing levels of aerobic exercise for cancer patients compared to healthy controls, so that it may be determined whether the currently prescribed exercise intensities are an accurate measure of a patient's true level of exertion, relative to their normal healthy counterparts. The purpose of this study is to compare the response to low, moderate, and high intensity aerobic exercise in breast cancer patients and healthy controls, using three indicators of exercise intensity; i.e., HR, RPE, and post-exercise blood lactate.

Research Questions

Research Question 1): Will there be a differing response in HR between breast cancer patients and healthy controls during a 9 minute low intensity (40% of VO_{2max}) aerobic exercise bout?

Research Question 2): Will there be a differing response in RPE between breast cancer patients and healthy controls during a 9 minute low intensity (40% of VO_{2max}) aerobic exercise bout?

Research Question 3): Will there be a differing response in post-exercise blood lactate between breast cancer patients and healthy controls after a 9 minute low intensity (40% of VO_{2max}) aerobic exercise bout?

Research Question 4): Will there be a differing response in HR between breast cancer patients and healthy controls during a 9 minute moderate intensity (60% of VO_{2max}) aerobic exercise bout?

Research Question 5): Will there be a differing response in RPE between breast cancer patients and healthy controls during a 9 minute moderate intensity (60% of VO_{2max}) aerobic exercise bout?

Research Question 6): Will there be a differing response in post-exercise blood lactate between breast cancer patients and healthy controls after a 9 minute moderate intensity (60% of VO_{2max}) aerobic exercise bout?

Research Question 7): Will there be a differing response in HR between breast cancer patients and healthy controls during a 9 minute high aerobic intensity (70% of VO_{2max}) exercise bout?

Research Question 8): Will there be a differing response in RPE between breast cancer

patients and healthy controls during a 9 minute high intensity (70% of VO_{2max}) aerobic

exercise bout?

Research Question 9): Will there be a differing response in post-exercise blood lactate

between breast cancer patients and healthy controls after a 9 minute high intensity (70%

of VO_{2max}) aerobic exercise bout?

Research Hypotheses

Hypothesis 1): At a low intensity (40% of VO_{2max}), there will be no significant

difference in HR response between breast cancer patients and healthy controls during a 9

minute aerobic exercise bout.

Hypothesis 2): At a low intensity (40% of VO_{2max}), there will be no significant

difference in RPE response between breast cancer patients and healthy controls during a

9 minute aerobic exercise bout.

Hypothesis 3): At a low intensity (40% of VO_{2max}), there will be no significant

difference in post-exercise blood lactate response between breast cancer patients and

healthy controls during a 9 minute aerobic exercise bout.

Hypothesis 4): At a moderate intensity (60% of VO_{2max}), there will be no significant

difference in HR response between breast cancer patients and healthy controls during a 9

minute aerobic exercise bout.

Hypothesis 5): At a moderate intensity (60% of VO_{2max}), there will be no significant

difference in RPE response between breast cancer patients and healthy controls during a

9 minute aerobic exercise bout.

Hypothesis 6): At a moderate intensity (60% of VO_{2max}), there will be no significant difference in post-exercise blood lactate response between breast cancer patients and healthy controls during a 9 minute aerobic exercise bout.

Hypothesis 7): At a high intensity (70% of VO_{2max}), breast cancer patients will exhibit a significantly higher HR response compared to healthy controls during a 9 minute aerobic exercise bout.

Hypothesis 8): At a high intensity (70% of VO_{2max}), breast cancer patients will exhibit a significantly higher RPE response compared to healthy controls during a 9 minute aerobic exercise bout.

Hypothesis 9): At a high intensity (70% of VO_{2max}), breast cancer patients will exhibit a significantly higher post-exercise blood lactate response compared to healthy controls after a 9 minute aerobic exercise bout.

Definition of Terms

Intensity: The magnitude of stress being placed upon the body during exercise. For aerobic exercise, intensity may be expressed as a percentage of maximum oxygen uptake (% of VO_{2max})

Exertion: The physical effort performed by the body in response to an exercise intensity.

Borg's Rate of Perceived Exertion (RPE) Scale: A category scale ranging from 6 to 20, where a rating of 6 is equivalent to "no exertion" and 20 is equivalent to "maximal exertion." Subjects are shown the scale at various intervals during an exercise test, and are instructed to point to the number on the scale which most closely describes how intensely they feel they are working at a given time.

Blood Lactate: Accumulation of lactate in the bloodstream. Lactate is produced by skeletal muscle as a byproduct of anaerobic glycolysis, and the amount produced by the skeletal muscle, which is then transported into the bloodstream, is directly proportional to exercise intensity.

Predicted VO_{2max}: Maximum oxygen uptake (VO_{2max}) calculated from the results of a submaximal exercise test.

International Physical Activity Questionnaire (IPAQ): a questionnaire used to assess a person's current level of physical activity.

Major Cancer Treatment: Surgery, chemotherapy, and radiation therapy.

Adjuvant Trastuzumab Therapy: A drug used to treat women with advanced breast cancer, particularly in tumors that over-express the human epidermal growth factor receptor 2 protein (HER2 protein). Trastuzumab is also known as Herceptin.

Post-Treated Breast Cancer Patients: Patients within six months of completion of all planned surgery, radiation therapy, and chemotherapy.

Get REAL & HEEL Breast Cancer Program: An exercise/recreation therapy program designed to assist post-treated breast cancer patients in the management of side-effects commonly developed with cancer diagnosis and during cancer treatment.

Healthy Controls: Subjects who do not have a history of cancer treatment, and are not currently suffering from any activity-limiting illnesses.

Control Group: Consists of healthy controls recruited from the faculty, staff, and student populations at UNC-Chapel Hill.

Experimental Group: Consists of post-treated breast cancer patients currently enrolled in the Get REAL & HEEL Breast Cancer Program.

Assumptions

1. All subjects enrolled in the study strictly followed the pre-exercise guidelines prior to reporting for exercise sessions.

2. The impact of different cancer treatments and drugs resulted in similar side effects experienced by the subjects in the experimental group enrolled in the study.

3. Subjects accurately answered the IPAQ.

4. Subjects accurately reported RPE

Delimitations

1. All subjects were female.

2. All subjects were within the ages of 30-75 years.

3. Subjects in the experimental group voluntarily participated in the Get REAL & HEEL Breast Cancer Program and were residents in one of the 13 counties of the N.C. Triangle Affiliate of the Susan G. Komen Foundation.

4. Subjects in the experimental group completed all major cancer treatment within six months.

5. Subjects in the experimental group received permission from their oncology physician to enroll in the Get REAL & HEEL Breast Cancer Program.

6. Subjects in the control group were recruited from the faculty, staff, and student populations at UNC-Chapel Hill.

Limitations

1. All attempts were made to exactly age-match subjects in the experimental and controls groups. If this was not possible, then subjects were matched within an age range.

2. Similarly, it may be difficult to exactly match subjects in the experimental and controls for physical activity level. All subjects in the control group were recruited based on the knowledge that they were not participating in a regular/structured physical activity program for at least the past 3 months.

3. The submaximal test that was used to predict VO_{2max} may present some measurement error since the subjects were not exercising to their actual VO_{2max}, and because some subjects may have never used a treadmill before and may have felt uncomfortable performing the test.

Significance of the Study

Research hypotheses 1-6 of this study state that there will be no significant difference in HR, RPE, and post-exercise blood lactate responses between breast cancer patients and healthy controls at low and moderate exercise intensities. Accepting these hypotheses would indicate that breast cancer patients and healthy controls exhibit similar exertion at low and moderate aerobic exercise intensities of 40% and 60% of VO_{2max}, respectively, and that exercise interventions designed for the normal healthy population at these intensities may also be safe to use with the breast cancer patient population. Research hypotheses 7-9 state that there will be different responses in HR, RPE, and post-exercise blood lactate responses between breast cancer patients and healthy controls at a high intensity of 70% of predicted VO_{2max}, with breast cancer patients exhibiting

greater responses than the healthy controls. Accepting these hypotheses would indicate that there is a potential threshold above which cardiovascular, RPE and blood lactate responses are different between breast cancer patients and healthy controls, and that prescribing exercise intensities at or above 70% of predicted VO_{2max} for breast cancer patients may cause them to experience greater-than-desired exertion levels when compared to healthy matched controls, which should be seen cautiously when prescribing exercise at high intensity in post-treated breast cancer patients. Therefore, accepting the research hypotheses of this study may significantly affect the way in which exercise intensities are measured and prescribed in the breast cancer patient population when considering exercise interventions after completion of major cancer treatment.

CHAPTER II

REVIEW OF LITERATURE

The purpose of this study is to compare the response to low, moderate, and high intensity aerobic exercise in breast cancer patients and healthy controls, using various indicators of exertion; i.e., heart rate (HR), rate of perceived exertion (RPE), and post-exercise blood lactate. For the purpose of organization, this review of literature has been divided into three sections: 1) quantification of exercise intensity and exertion during aerobic exercise, 2) American College of Sports Medicine (ACSM) guidelines for intensities used for cardiopulmonary exercise prescription for the healthy adult, cardiac patient, and elderly populations, and 3) intensities to use when prescribing cardiopulmonary exercise in the breast cancer patient population.

Quantification of Exercise Intensity and Exertion during Aerobic Exercise

Exercise intensity can be defined as the magnitude of stress being placed upon the body during exercise. For aerobic exercise, intensity may be expressed as a percentage of maximum oxygen uptake (% of VO_{2max}). Quantification of exercise intensity is important when formulating exercise prescriptions for individuals ranging from clinical populations to athletes, because it gives an objective evaluation of performance and physiological measures (Brooks, Fahey, & Baldwin, 2005, p. 503). An exercise specialist can monitor how an individual responds to various intensities during, immediately after, or several hours after an exercise session in order to evaluate which intensities do or do

not produce physiological changes that will help the individual reach his/her desired fitness goals. Three parameters that are commonly used to quantify intensity and exertion during aerobic exercise are HR, RPE, and blood lactate.

Heart Rate

During aerobic exercise, HR increases in a relatively linear fashion with exercise intensity and oxygen consumption (Brooks et al., 2005, p. 345; Whaley, Brubaker, & Otto, 2006, p. 143). In the context of a training program, HR can be used to quantify intensity during an exercise session, as well as adequacy of recovery after the session is complete (Brooks et al., 2005, p. 503). Using HR to quantify intensity also gives an immediate and objective measure of how the body responds to a particular workload during exercise training. When writing an exercise prescription, target HR (THR), corresponding to a particular exercise intensity, can be calculated by three different methods: either directly, as a percentage of maximum HR, or by the HR reserve (HRR) method (Whaley et al., 2006, pp. 144-146).

In order to use the direct method to calculate a THR range corresponding to a particular exercise intensity range, a plot of HR as a function of VO_2 is created. These values can be measured during a VO_{2max} test, during which both VO_{2max} and maximum HR could be determined (Whaley et al., 2006, pp. 144-145). One can then calculate a range of percentage of VO_{2max} and then find the corresponding HR range on the plot. This HR range would correspond to the THR range for the exercise prescription. This method is especially appropriate for certain populations, such as cardiac rehabilitation patients who may be taking medications which may affect the HR response to exercise (Whaley et al., 2006, pp. 144-145).

The second method for calculating THR range is to calculate the maximum HR

for an individual and then calculate straight percentages of those values (Whaley et al.,

2006, p. 144). Intensity ranges of 70-80% of maximum HR approximate 50-70%

VO_{2max}, which is within the range to stimulate improvements in VO_{2max} for most

individuals (Whaley et al., 2006, p. 144). However, this method can an inaccurate

quantification of lower intensities because a THR at a low percentage of maximum HR

may yield a result that is actually below the resting HR (Whaley et al., 2006, p. 144).

A third method for calculating THR range is to use the HRR method, also known

as the Karvonen method (Whaley et al., 2006, pp. 144-145). Target HR is calculated by

using the Karvonen formula, where THR = (220-age-resting HR)*(% intensity) + resting

HR (Brooks et al., 2005, p. 713; Whaley et al., 2006, pp. 144-145). This method is often

preferred for calculating exercise intensity ranges for an exercise prescription because it

is closely linked to percentage of VO_2 reserve (the difference between VO_{2max} and resting

VO_2) across the entire range of fitness levels, an important point when considering

individuals of lower fitness levels (Whaley et al., 2006, p. 145).

Rate of Perceived Exertion

Exertion can be defined as the physical effort performed by the body in response

to a particular exercise intensity. An individual's perception of exertion is considered to

be a combination of sensations involving the muscles, joints, cardiopulmonary system,

and the central nervous system during exercise, and may include factors such as HR,

oxygen uptake, respiration rate, minute ventilation, blood lactate concentration, blood

pH, mechanical strain, skin temperature and core temperature (Borg, 1990; Groslambert

& Mahon, 2006). Borg (1990) has shown that perception of exertion increases as

physical workload increases for several modes of aerobic exercise including cycle

ergometry, running, walking, and arm cranking.

In order to quantify perceived exertion, Borg (1982, 1990) has developed a 15-

point scale, commonly named the Borg's Rate of Perceived Exertion (RPE) scale. This

scale was initially constructed to increase linearly with exercise intensity, HR and power

output on the cycle ergometer, (Borg, 1982, 1990; Groslambert et al., 2006). Borg's RPE

scale displays values that range from 6 to 20, where a value of 6 represents "no exertion"

and a value of 20 represents "maximal exertion" (Borg, 1982). Descriptive phrases

including "very light", "somewhat hard", and "very hard" are also included on the scale.

The scale's range of values from 6 to 20 can be used to denote heart rates ranging from

60 to 200 beats per minute (Borg, 1982). This was intended to make the scale easier to

use because by knowing an individual's RPE score, one could make an estimation of HR

during exercise. However, it is difficult to exactly match a certain RPE score to a certain

HR because HR at a given exercise workload can depend on a multitude of factors such

as age, type of exercise, environment, and anxiety (Borg, 1982). Borg's RPE scale has

become a very popular method of quantifying exercise intensity, and has therefore been

translated into many languages (Borg, 1982).

While perceived exertion ratings obtained from Borg's RPE scale do parallel

physiological variables that increase linearly with exercise (i.e. HR), this may not always

be the case for physiological variables that do not increase linearly with exercise (Borg

1982, 1990; Noble 1983). Therefore, Borg and associates have also developed a

category-ratio scale (Borg's CR10 scale) that is appropriate for measuring sensations that

may arise from physiological variables that grow exponentially such as blood lactate or

pulmonary ventilation (Borg 1982, Borg 1990, Noble, 1982; Groslambert et al., 2006). The CR10 scale displays values that range from 0 to 10, where a value of 0 is described as "nothing at all," while a value of 10 is "very, very strong" (Borg, 1982). Verbal expressions are placed next to the values on the scale according to ratio properties, such that a value of 1 (very weak) represents twice the intensity of a value of 0.5 (very, very weak); a value of 2 (weak) represents twice the intensity of a value of 1, and so on (Borg, 1982).

The simplicity of Borg's RPE scale and the high correlation between RPE and exercise workload have also made it a popular tool for controlling intensities in clinical populations, such as in the cardiac rehabilitation patient population (Noble, 1982). Using perceived exertion rating to quantify exercise intensity could be beneficial in this population particularly when the use of certain medications may have altered HR responses to exercise (Whaley, Brubaker, Kaminsky, & Miller, 1997; Whaley et al., 2006, p. 146). Borg and associates have also developed a 9-point scale for cardiac patients to use when rating angina pectoris during graded exercise tests which is similar to the RPE scale (Noble, 1982). Within the context of exercise prescription, perceived exertion is a useful tool because it is closely related to HR, but it also integrates other important strain variables (Borg, 1982).

Blood Lactate

Lactate is produced by skeletal muscle as a byproduct of anaerobic glycolysis, and the amount produced by the skeletal muscle, which is then transported into the bloodstream, is proportional to exercise intensity. Blood lactate refers to the accumulation of lactate in the bloodstream. A blood lactate concentration of 4 mmol/L is often considered to be the

lactate threshold, the level at which lactate production mechanisms surpass lactate clearance mechanisms, and blood lactate levels begin to rise exponentially (Brooks et al., 2005, pp. 503-504). Intensities that elicit lactate production above the lactate threshold become difficult to maintain for extended periods of time and contribute to fatigue. Although 4 mmol/L is often synonymous with the lactate threshold, exercise training can push this threshold to higher levels.

Relationship between HR, RPE, and Blood Lactate

Several studies have investigated the relationship between HR, RPE, and blood lactate as measures of aerobic exercise intensity. Noble, Borg, Jacobs, Ceci, and Kaiser (1983) examined the relationship between perceived exertion ratings from Borg's CR10 scale with blood and muscle lactate levels and HR. Ten physically active males rode a cycle ergometer until voluntary exhaustion while HR, RPE, and lactate levels were measured. The results showed that RPE, HR, and lactate all increased with increasing exercise intensity; HR increased linearly while RPE and blood lactate increased as a quadratic function of intensity.

Borg, Ljunggren, and Ceci (1985) examined the relationship between perceived exertion, perception of aches and pains in the legs, HR, and blood lactate during bicycle ergometry. Twenty-eight healthy males performed an incremental exercise bout on the cycle ergometer, where workload was increased by 40 Watts every 4 minutes until voluntary exhaustion. Heart rate, RPE (on both the Borg's 6-20 point scale and the CR10 scale), and blood lactate were recorded during the last minute of each workload stage, as well as at the point when the subjects terminated the test. The results showed that HR increased linearly as a function of workload, while RPE, perception of aches and pains in

the legs, and blood lactate increased exponentially. Correlation coefficients between HR, RPE, perception of aches and pains in the legs, and blood lactate were high, particularly during the higher workloads of the test.

In a similar study, Borg, Hassmen, and Lagerström (1987) compared HR, RPE, and blood lactate responses to arm crank ergometry with those from cycle ergometry in 8 healthy males. Exercise bouts involved stepwise increases in intensity of 40-70-100-150-200 Watts for the cycle ergometer, and 20-35-50-70-100 Watts for the arm crank ergometer. The subjects exercised at each intensity in 4 minute increments, and at the end of each increment, HR, blood lactate, and RPE (on both the Borg's 6-20 point scale and the CR10 scale) were measured. Heart rate and RPE scores from Borg's 6-20 point scale showed linear increases as a function of exercise intensity for both cycling and arm cranking, while blood lactate and RPE scores from Borg's CR10 scale showed exponential increases as a function of exercise intensity for both cycling and arm cranking. A plot of RPE response from Borg's 6-20 point scale and RPE from the CR10 scale as a function of HR showed nearly-linear relationships, as did RPE responses as a function of blood lactate. A separate analysis was done to investigate the relationship between RPE response from the CR10 scale as a function of a combined HR-blood lactate response, which also showed a positive linear relationship.

Green, McLester, Crews, Wickwire, Pritchett, and Lomax (2006) examined the relationship between HR, RPE, and blood lactate responses during repeated high-intensity interval cycling. Twelve physically active males completed a series of high intensity cycling bouts at a workload above what was needed to elicit a 4 mmol/L blood lactate response. The intervals consisted of five 2-minute periods of high-intensity

cycling followed by 3 minutes of recovery cycling Heart rate, RPE (using Borg's 6-20 point scale), and blood lactate were measured at the end of each 2-minute high intensity cycling period and also at the end of each 3-minute recovery cycling period. Significant correlations were found for HR and RPE response as well as blood lactate and RPE response during both the high-intensity period and the recovery period of the interval.

Irving et al. (2006) studied the utility of two different RPE scales as markers of the blood lactate response to exercise in 26 females and 10 males with the metabolic syndrome. Subjects completed a treadmill protocol to determine VO_{2peak} and lactate threshold. Subjects began walking on a treadmill at 60 m/min, which was increased by 10 m/min in 3 minute stages until volitional fatigue. Heart rate and blood lactate were measured at the end of each stage, and RPE scores, using Borg's 6-20 point scale and the OMNI walk/run 0-10 point scale, were measured at 2:15 and 2:45 of each stage. The correlation coefficients within and between the two RPE scales and the treadmill speeds associated with the lactate threshold, blood lactate concentrations of 2.5 mmol/L, 4.0 mmol/L, and peak were 0.82-0.93 (p<0.01). These results indicate that RPE can contribute to the prediction of the blood lactate response to incremental exercise.

ACSM Guidelines for Intensities to use for Cardiopulmonary Exercise Prescription

As mentioned previously, several studies have shown that aerobic exercise can improve physical performance in the breast cancer patient population. The current recommendations for cardiopulmonary exercise prescription in cancer patients are somewhat similar to the ACSM guidelines for exercise prescription in healthy adults; however, they are largely modeled after the current ACSM guidelines for exercise prescription in the cardiac patient population and the elderly adult population. This

section will discuss the current ACSM guidelines for cardiopulmonary exercise prescription in the healthy adult population with respect to exercise intensity, followed by a discussion of the current ACSM guidelines for cardiopulmonary exercise prescription in cardiac patients and the elderly.

Healthy Adult Population

When creating exercise prescriptions for the healthy adult population, the ACSM recommends intensity ranges of 40 or 50% to 85% of oxygen uptake reserve (VO_2R) or HRR, or 64 or 70% to 94% of maximum HR (Whaley et al., 2006, p. 141). This broad range in intensities reflects the fact that lower fitness individuals can demonstrate improved cardiopulmonary fitness when exercising at only 40-50% HRR or 64-70% maximum HR (Whaley et al., 2006, p. 141). Even intensities of 30% of VO_2R can elicit improvements in VO_{2max} for people with a VO_{2max} less than 40 mL/kg/min (Whaley et al., 2006, p. 141). However, for individuals with a VO_{2max} greater than 40 mL/kg/min, exercise intensities above 45% VO_2R should be used in order to stimulate an increase in VO_{2max}, and for individuals who already participate in regular physical activity, exercise intensities at the high end of the recommended range are needed to further elicit improvements in VO_{2max} (Whaley et al., 2006, p. 141). Most individuals can achieve an increased VO_{2max} with intensities of 60-80% HRR or 77-90% of maximum HR when combined with an appropriate training frequency and duration (Whaley et al., 2006, p. 141).

The ACSM also recommends that an RPE range of 12-16 on the Borg RPE scale should be incorporated into the exercise prescription in order to stimulate physiological adaptations to exercise (Whaley et al., 2006, p. 146). This corresponds to a perceived

exertion of "somewhat hard" to "hard." (Borg, 1982). However, it is important to note

that there can be some variation with how exertion is perceived among individuals.

Therefore, it should be expected that RPE for different modes of exercise may not be the

same, and that RPE may not always exactly match the intensity determined by heart rate

methods (Whaley et al., 2006, p. 146).

Cardiac Patient Population

Cardiac rehabilitation exercise programs are designed to help patients return to

their previous vocational and recreational activities, sometimes with the need to modify

or find alternate activities (Whaley et al., 2006, p. 178). They also provide patients with

a safe and effective formal exercise program, and they educate patients and their families

about cardiovascular disease risks and therapies to increase prevention of future cardiac

events (Whaley et al., 2006, p. 178). Cardiopulmonary exercise prescription in this

population is generally similar to that in the healthy adult population with regard to

exercise frequency and duration; while most of the modifications are with regard to

exercise intensity (Whaley et al., 2006, p. 178).

The goals for determine the appropriate aerobic exercise intensities to use in the

cardiac patient population are largely twofold: 1) determine the minimum intensity that

will produce a training effect, and 2) set a safe, upper limit intensity in order to prevent

signs and symptoms representative of an intolerance to exercise (i.e., angina, abnormal

blood pressure increase or decrease, abnormal ECG findings, left ventricular wall motion

abnormalities, and increased ventricular dysrhythmias) (Whaley et al., 2006, p. 178).

Intensities above 45% of VO_2R have been shown to increase VO_{2max} in cardiac patients

(Whaley et al., 2006, pp. 179-180).   Because percent intensity of VO_2R approximates

percent intensity of HRR, calculating THR ranges using the Karvonen method is widely

used when prescribing intensity, and it is effective even for patients who may be taking

medications that can alter the HR response to exercise (Whaley et al., 2006, p. 179).

However, one cannot always rely solely on HR when prescribing exercise intensity; other

variables must be considered, such as onset of angina, blood pressure response to

exercise, ST-segment depression, dysrhythmias, and perceived exertion (Whaley et al.,

2006, p. 180).

Measuring RPE scores along with HR response can be very useful when

prescribing cardiopulmonary exercise intensity, especially if a patient is entering a

rehabilitation program without having done a baseline exercise test, or if clinical status

and medical therapies change (Whaley et al., 2006, p. 180). During the initial phases of

rehabilitation, the ACSM also recommends that an RPE range of 11-13 on the Borg RPE

scale should be incorporated into the exercise prescription (Whaley et al., 2006, p. 180).

This RPE range corresponds to a perceived exertion of "fairly light" to "somewhat hard"

(Borg, 1982). During the later stages of rehabilitation, an RPE range of 14-16

("somewhat hard" to "hard") may be used provided that patients do not exhibit signs and

symptoms of ischemia or serious dysrhythmia (Borg, 1982; Whaley et al., 2006, pp. 180-

181). However, it is important to note that events such as ischemic ST segment

depression or serious ventricular dysrhythmias can occur at a low HR or RPE, indicating

that exercise intensity should be closely monitored in this population (Whaley et al.,

2006, pp. 180-181). Even so, cardiac patients should be encouraged to improve their

exercise capacity through moderate-intensity exercise programs, and provided there are

no contraindications, work towards being able to perform more vigorous exercise (Whaley et al., 2006, p.181).

Elderly Population

The current ACSM guidelines for prescribing cardiopulmonary exercise intensity in the healthy adult population generally apply to the elderly population (Whaley et al., 2006, p. 248). In order to minimize medical problems and promote long-term compliance, initial exercise intensities below 40% of VO_2R or HRR are not uncommon, particularly for inactive elderly adults (Whaley et al., 2006, p. 248). When quantifying intensity, using a measured peak HR may be preferable to using an age-predicted peak HR because of the variability in peak HR in adults older than 65 years and the increased risk of underlying coronary artery disease (Whaley et al., 2006, pp. 248-249). Additionally, elderly adults may be more likely to be taking medications that can affect the HR response to exercise (Whaley et al., 2006, p. 249).

Intensities to use when prescribing Cardiopulmonary Exercise in the Breast Cancer Patient Population

Cardiopulmonary Exercise during Treatment

The first studies examining the effect of cardiopulmonary exercise in breast cancer patients during treatment have occurred only within the past 20 years. These studies primarily focused on outcomes such as changes in fatigue, VO_{2max}, and quality of life. In this body of literature, the reporting of exercise intensity is not always clear or consistent, due to the fact that many of the prescribed interventions were self-paced or home-based, the range of intensities used was quite large, and the quantification of exercise intensity varied from study to study.

There are several studies in which percentage of maximum HR was used to quantify exercise intensity in order to examine the effects of cardiopulmonary exercise on various factors such as physical function, performance, fatigue, treatment-related side-effects, nausea, body composition, psychological well-being, and quality of life in breast cancer patients undergoing treatment. In two studies, Winningham and MacVicar(1988), and Winningham, MacVicar, Bondoc, Anderson, and Minton (1989) investigated the effect of an exercise program on nausea, body weight, and body composition. The first study included 42 breast cancer patients and the second study included 24 breast cancer patients, and in both studies, patients participated in an exercise program which included cycling at intensities of 60-85% of maximum HR. MacVicar, Winningham, and Nickel. (1989) investigated the effects of aerobic interval training on functional capacity in 45 breast cancer patients, which also included an exercise program where patients cycled at intensities of 60-85 % of maximum HR. Dimeo et al. (1998) used an intensity of 80% of maximum HR to examine the effect of treadmill walking on fatigue and performance in 5 cancer patients (including 1 breast cancer patient). Campbell, Mutrie, White, McGuire, and Kearney (2005) conducted a pilot study to investigate the effects of aerobic exercise as an adjunct therapy for women receiving chemotherapy and radiation therapy for early stage breast cancer. In this study, 19 patients participated in supervised aerobic exercise at intensities of 60-75% of maximum HR. Mock et al. (2005) conducted a multi-institutional randomized controlled trial to determine the effects of exercise on fatigue levels in 119 breast cancer patients, for which a home-based walking program at 50-75% of maximum HR was used. Mutrie et al (2007) also used intensities of 50-75% of maximum HR to study the effect of a 12-week supervised group exercise program on 177

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breast cancer patients after 6 months of follow-up. The outcomes of these studies all showed positive changes in physical function parameters including increased VO_{2max}, increased walking distance within a given period of time, and decreased HR and blood lactate during submaximal exercise. Other positive changes including decreased fatigue, nausea, increased satisfaction with life, increased lean body mass, and decreased body fat were also observed.

Other studies have used percentage of HRR to quantify intensity in order to study the effects of cardiopulmonary exercise on similar factors discussed previously. Two studies by Dimeo et al. (1997, 1999) investigated the effects of physical exercise on physical performance, severity of treatment complications, and psychological distress in cancer patients. In the first study, 70 patients (including 46 breast cancer patients) participated in an exercise program that included cycling at 50% of HRR, and in the second study, 59 patients (including 31 breast cancer patients) participated in an exercise program that included interval cycling, also at 50% of HRR. Both studies revealed positive results, including increased physical performance and decreased thrombopenia, neutropenia, psychological distress, and time spent in the hospital.

A third group of studies have used exercise interventions that are described as home-based and self-paced, which do not always clearly state how intensity was quantified. Mock et al. (1997, 2001), Schwartz (1999, 2000), and Schwartz, Mori, Gao, Nail, and King (2001) investigated the effect of home-based, self-paced walking programs on physical function, fatigue, treatment-related symptoms, and emotional distress in cohorts of 27 to 72 breast cancer patients during treatment. The intensities used in these studies are not clearly defined; however, the investigators do report

improvements in 12-minute walk distance and decreases in fatigue and emotional distress.

Lastly, there are several studies that have used percentage of VO_{2max} to quantify cardiopulmonary exercise intensity. Segal et al. (2001) investigated the effect of a self-paced walking intervention along with a supervised exercise program at 50-60% of VO_{2max} on physical function in 123 breast cancer patients. Increased physical function, measured by the Short Form (SF)-36 scale were observed after 26 weeks of exercise intervention. In patients who did not receive chemotherapy, aerobic capacity was significant increased and body weight was significantly decreased ($p=0.01$ and <0.05, respectively) in patients participating in supervised exercise compared with patients receiving usual care.

In a study by Battaglini, Bottaro, Campbell, Novaes, and Simão (2004), a group of 27 patients including 22 breast cancer patients participated in an exercise program where aerobic exercise intensity was set between 50-55% of maximal heart rate. The goal of the study was to examine the relationship between changes in selected physiological parameters and fatigue during a period of 6 months. Even though no significant relationship between selected physiological parameters including % body fat, resting heart rate, and dynamic endurance tests, an improvement in cardiorespiratory endurance of approximately 30% was observed with no adverse effects of the intensity used being reported.

Battaglini et al. (2006) investigated the exercise response in a group of 20 breast cancer patients undergoing treatment. Patients assigned to the exercise group, participated in a structured exercise program at an intensity range between 40-60% of VO_{2max}, for a

period of approximately 21 weeks. No adverse effects of the intensity used in this study were reported. Furthermore, significant decreases in fatigue were observed in the exercise group when compared to the control group at the end of the first, second, and final bout of chemotherapy treatment (p=.001, p=.005, and p=.001 respectively).

Courneya et al. (2007) conducted a multicenter trial to study the effects of exercise on body composition, physical function, and quality of life. This study included 78 breast cancer patients who performed aerobic exercise at an intensity range of 60-80% of VO_{2max}, using the treadmill, elliptical, and cycle ergometer. Increased physical function was observed, as well as increased aerobic fitness, increased self esteem, improved body composition, and chemotherapy completion rate without causing lymphadema or other significant adverse events.

Cardiopulmonary Exercise after Treatment

Studies examining the effect of cardiopulmonary exercise on breast cancer patients after the completion of treatment focus on many of the same outcomes as studies conducted during treatment. In addition, endpoints relating to changes in endocrine and immune function are introduced. In many of these studies, exercise intensities are better defined, and most utilize a percentage of maximum HR or percentage of VO_{2peak} to quantify intensity.

Peters, Lötzerich, Niemeier, Schüle, and Uhlenbruck (1994, 1995) conducted two studies examining the effects of aerobic exercise training on immune function, psychological behavior, depression, and anxiety symptoms in 24 post-treated breast cancer patients. Patients cycled at 60% of maximum HR during the aerobic portion of the exercise program. The investigators found no change in natural (NK) cell number,

although there was an increase in NK cell cytotoxic activity. Changes in other immune function parameters included an increase in granulocytes, and a decrease in lymphocytes and monocytes with some increased phagocytic activity in monocytes. Positive changes were also reported for psychological parameters, particularly an increased satisfaction with life.

Nieman et al (1995) investigated the effect of exercise training on NK cell activity in 12 post-treated breast cancer patients. The aerobic portion of the exercise training included walking on an indoor track at 75% of maximum HR. The results showed that patients improved the distance walked during the 6 minutes walk test, while there were no changes in circulating NK cells or NK cell activity.

Segar et al. (1998) evaluated the effect of 10 weeks of aerobic exercise on depressive and anxiety symptoms and self esteem in 24 post-treated breast cancer patients. Patients participated in cardiovascular exercise at 60% of maximum HR. After 10 weeks, patients reported a decrease in depression and anxiety.

Pinto, Frierson, Rabin, Trunzo, and Marcus (2005) examined the efficacy of a home-based physical activity intervention for 86 patients who had completed treatment for early-stage breast cancer. Patients participated in a home-based self-directed exercise program that promoted activities such as biking, swimming, walking, and use of home exercise equipment. Patients were instructed to perform these activities at a moderate intensity corresponding to 55-65% of maximum HR. The results showed positive changes included a decrease in fatigue, improvements in mood and self esteem, and an increase in energy expenditure and total minutes spent performing physical activity.

Several recent studies have turned to using a percentage of $VO2_{peak(max)}$ in order to quantify cardiopulmonary exercise intensity. Fairey et al. (2003, 2005a, 2005b) conducted three studies examining the effect of exercise training on several blood markers including fasting insulin, insulin resistance, insulin growth factors, insulin growth factor binding proteins, NK cell cytotoxic activity, C-reactive protein, and various cardiovascular disease risk factors. Fifty-two post-menopausal post-treated breast cancer patients participated in an exercise program that included cycling at 70-75% of VO_{2peak}. Positive changes were observed for cardiovascular function and disease risk factors, including increased VO_{2max}, and decreased C-reactive protein, resting HR, HRR, blood pressure, and HDL-C. An increase in NK cell activity was also observed as well as changes in levels of insulin-like growth factors and insulin-like growth factor binding proteins.

Kim et al. (2006) studied cardiopulmonary responses and adherence to exercise after an 8-week exercise intervention in 41 post-treated breast cancer patients. Patients participated in supervised aerobic exercise at an intensity of 60-70% VO_{2peak} and/or HRR. Activities consisted of cycling, walking, or jogging on a treadmill. The adherence to the exercise program was 78.3%, and the results showed that patients participating in exercise had decreased resting HR, resting systolic blood pressure, and an increased VO_{2peak}. Patients also reported an increase in voluntary activity, a decrease in sedentary activity.

Cardiopulmonary Exercise Intensity as a Reflection of Exertion

From this review of literature, it is evident that the quantification of cardiopulmonary exercise intensity in the breast cancer patient population is inconsistent

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(self-paced, percentage of maximum HR, HRR, or $VO_{2peak(max)}$)and a wide variety of intensities have been used (50-85%). While many positive changes in psychological and cardiovascular parameters have been observed, the effect of exercise training on immune parameters (i.e., lymphocytes, NK cells, etc.) is not yet clear. Additionally, literature reporting perceived exertion scores and blood lactate responses in the breast cancer patient population is scarce. Therefore, the present study is significant in that it compares HR, RPE, and blood lactate responses to a broad selection of aerobic intensity levels in both breast cancer patients and healthy controls.

CHAPTER III

METHODOLOGY

Subjects

This was a thesis study with the goal of comparing three indicators of exertion (i.e., HR, RPE, and post-exercise blood lactate) in response to low, moderate, and high intensity aerobic exercise in breast cancer patients and healthy controls. There were two study groups: a group comprised of women who were post-treated breast cancer patients (experimental group) and a control group comprised of apparently healthy age-matched women. Subjects in the experimental group were breast cancer patients who were post-treatment and have been enrolled in the Get REAL & HEEL Breast Cancer Program at UNC-Chapel Hill. Subjects in the control group were women recruited from the faculty, staff, and student populations at UNC-Chapel Hill, must not have been enrolled in regular organized physical activity during the past three months, and healthy enough to participate in aerobic exercise. All attempts were made to match subjects in both groups based on age and physical activity level. The sample size for this study was 14 subjects, with 7 subjects in each group.

The criteria for participation in the study for the experimental group are presented below:

1. Confirmed diagnosis of Stage I, II, or III invasive breast cancer;

2. Within 6 months of completion of all major cancer treatment;

3. Ages ranging from 30 to 75 years;

4. Patients receiving adjuvant hormonal therapy or adjuvant trastuzumab were eligible;

5. No presence of metastatic disease;

6. No presence of immune deficiency that would compromise the subject's ability to participate in regular exercise ;

7. Be enrolled in the Get REAL & HEEL Breast Cancer Program.

Participation in this study involved the same risks as any exercise regimen. Given the potential risks involved, all potential participants (both experimental and control group subjects) completed a comprehensive medical history questionnaire, and were thus screened for exclusion based upon the criteria listed below:

1. Cardiovascular disease (unless the disease would not compromise the subject's ability to participate in the exercise rehabilitation program);

2. Acute or chronic respiratory disease (unless the disease would not compromise the subject's ability to participate in the exercise rehabilitation program);

3. Acute or chronic bone, joint, or muscular abnormalities that would compromise the subject's ability to participate in the exercise rehabilitation program.

Demographic Parameters

Age, race, menopausal status, height, weight, percent body fat, and current physical activity level were recorded for all subjects upon enrollment onto the study. Height and weight were be used to calculate body mass index (BMI). Menopausal status was assessed by asking subjects if they would classify themselves as pre-, peri-, or post-menopausal. For subjects in the experimental group, menopausal status before beginning

major cancer treatment was recorded. Percent body fat was estimated using the Pollock 3-site (triceps, suprailiac, and abdomen) skinfold measurement formula for women (Whaley et al., 2006, p. 63). Current physical activity was assessed using the International Physical Activity Questionnaire (IPAQ). For the subjects in the experimental group, breast cancer stage and type of treatment received was also recorded.

Procedure

Each subject participated in a total of 4 sessions, including an initial assessment and 3 aerobic exercise sessions, one at each prescribed aerobic intensity (40%, 60%, and 70% of VO_{2max}). All subjects were asked to follow a set of pre-assessment guidelines before each session, which are as follows:

1. No eating for at least 2 hours prior to testing.

2. No exercise for at least 12 hours prior to testing.

3. Subjects should maintain adequate hydration status.

4. Subjects should refrain from caffeine use for at least 12 hours prior to testing.

5. Subjects should refrain from alcohol use for at least 48 hours prior to testing.

6. Subjects should refrain from using diuretic medications for at least 7 days prior to testing.

All sessions took place in either the Get REAL & HEEL facilities or in the Applied Physiology Laboratory (APL) in the Department of Exercise and Sport Science at UNC-Chapel Hill. For the subjects in the experimental group, these sessions comprised a portion of the aerobic exercise segment of their training session for that day at Get REAL & HEEL. The period of time from the initial assessment to the last exercise session was approximately 1-2 weeks.

Initial Assessment

The Initial Assessment for each subject was conducted in the APL. The Modified Bruce Submaximal Treadmill Protocol was used to predict VO_{2max} for each subject. This was a multistage protocol, where each stage lasted 3 minutes in duration with incremental increases in both treadmill speed and grade. The assessment was terminated when a subject's HR reaches a target heart rate of 75% of HRR, calculated using the Karvonen formula. Heart rate and RPE were recorded at the end of each stage. Borg's Rate of Perceived Exertion Scale (6 to 20 point scale) was used to quantify RPE. The time it took for the subject to complete the assessment was recorded upon termination, and this was used to calculate the predicted the predicted VO_{2max} for each subject, using the following equation:

$$VO_{2max} = 2.282*(time) + 8.545 \text{ (Heyward, 2006, p. 68)}$$

After calculating predicted VO_{2max} for each subject, the training intensities of 40%, 60% and 70% of VO_{2max} were calculated for each subject. To calculate the treadmill speed and grade that corresponded to 40%, 60%, and 70% of VO_{2max}, the horizontal and vertical components of VO_2 were given equal weights of 50% and 50%, respectively.

Aerobic Exercise Sessions

As mentioned previously, each subject participated in 3 aerobic exercise sessions, one at each intensity (40%, 60%, and 70% of VO_{2max}). Each session consisted of a warm-up/stretch period, an exercise trial, and a cool-down period. The warm-up/stretch period was approximately 10 minutes in duration and was standard for all subjects. Each subject walked on the treadmill for 5 minutes at 1.7 miles per hour at 0% grade, which

generally corresponded to an RPE of 6 to 7 (i.e., "no exertion" to "extremely light").

Then, the treadmill was stopped so that the subjects could step off and stretch for

approximately 5 minutes, targeting particularly the muscles of the hips and legs.

After the subjects had properly stretched, they stepped back on the treadmill in

order to start to the exercise trial itself. The exercise trials were each 9 minutes in

duration, and were performed at the prescribed intensity for the day. A duration of 9

minutes had been chosen *a priori* based on a pilot test performed on several patients who

had been currently participating in Get REAL & HEEL, who felt that this was long

enough for them to be able to complete an exercise trial at intensities between 40% and

70% of VO_{2max}. During the exercise trial, the subjects walked or ran on the treadmill

which was set to the appropriate speed and grade to match the desired intensity for the

session. Once the treadmill speed and grade were set, a stopwatch was used to monitor

time.   Heart rate and RPE were recorded minute-by-minute during the sessions (i.e.,

between 1:50-2:00, 2:50-3:00, 3:50-4:00, etc.) using a Polar heart rate monitor and

Borg's RPE scale, respectively. The trials were randomized to prevent an order effect,

and were blinded to the subjects.

After the exercise trial had concluded, the subjects entered the cool-down period,

the purpose of which was to allow the subject's HR to return to below 120 beats per

minute, if needed. At the end of the cool-down period, the treadmill was stopped so that

the subjects could step off. The subjects were then seated in a chair so that a finger-prick

blood sample could be collected, and post-exercise blood lactate could be analyzed using

a Lactate Plus blood lactate analyzer. The post-exercise blood lactate was measured after

the subjects had been seated for 3 minutes, and this was a single specimen analysis. After

analyzing the post-exercise blood lactate, the subjects were allowed to stand up and once again stretch the muscles in the hips and legs.   Heart rate was checked to make sure that the subjects were clear to leave the facility, or for subjects in the experimental group, to continue the rest of their session with a Get REAL & HEEL staff member.

Instrumentation

Height and body weight were assessed using a Detecto Model 437 Physician Beam Scale (Webb City, MO). Body fat was analyzed through skinfold measures (Pollock 3 site, see Appendix I) using a Lange C-130 Beta Technology calipers (Cambridge, MD). Current physical activity was assessed using the IPAQ (see Appendix II). The Modified Bruce Submaximal Treadmill Protocol was used to predict each subject's VO_{2max} and to calculate the appropriate speed and grade corresponding to 40%, 60%, and 70% of VO_{2max} for each subject (see Appendix III). During the initial assessment and the exercise trials, a Quinton treadmill was used (Quinton Fitness Equipment, Bothell, WA). Heart rate was measured using a Polar heart rate monitor (Lake Success, NY), and RPE was monitored using Borg's RPE scale (see Appendix IV). Post-exercise blood sampling was performed using a lancet, and blood lactate analysis was assessed using a hand-held Lactate Plus blood lactate analyzer (Sports Resource Group, Hawthorne, NY).

Statistical Analysis

All data was gathered and entered into an electronic database for analysis. Descriptive statistics are presented in the form of means and standard deviations. All data were analyzed on SPSS version 15.0 for Windows, a statistical software program. An alpha level of 0.05 was used for all analyses. Each hypothesis was analyzed as follows:

Hypothesis 1): At a low intensity (40% of VO_{2max}), there will be no significant difference in HR response between breast cancer patients and healthy controls during a 9 minute aerobic exercise bout. A 2x9 mixed-model ANOVA was used to analyze HR response between the experimental group and the control group during the 9 minute exercise trial at 40% of VO_{2max}. If a significant interaction was observed, then post-hoc testing of pair-wise comparisons was made using independent samples t-tests.

Hypothesis 2): At a low intensity (40% of VO_{2max}), there will be no significant difference in RPE response between breast cancer patients and healthy controls during a 9 minute aerobic exercise bout. A 2x9 mixed-model ANOVA was used to analyze RPE response between the experimental group and the control group during the 9 minute exercise trial at 40% of VO_{2max}. If a significant interaction was observed, then post-hoc testing of pairwise comparisons was made using independent samples t-tests.

Hypothesis 3): At a low intensity (40% of VO_{2max}), there will be no significant difference in post-exercise blood lactate response between breast cancer patients and healthy controls during a 9 minute aerobic exercise bout. An independent samples t-test was used to analyze post-exercise blood lactate response between the experimental group and the control group after the 9 minute exercise trial at 40% of VO_{2max}.

Hypothesis 4): At a moderate intensity (60% of VO_{2max}), there will be no significant difference in HR response between breast cancer patients and healthy controls during a 9 minute aerobic exercise bout. A 2x9 mixed-model ANOVA was used to analyze HR response between the experimental group and the control group during the 9 minute exercise trial at 60% of VO_{2max}. If a significant interaction was observed, then post-hoc testing of pair-wise comparisons was made using independent samples t-tests.

Hypothesis 5): At a moderate intensity (60% of VO_{2max}), there will be no significant difference in RPE response between breast cancer patients and healthy controls during a 9 minute aerobic exercise bout. A 2x9 mixed-model ANOVA was used to analyze RPE response between the experimental group and the control group during the 9 minute exercise trial at 60% of VO_{2max}. If a significant interaction was observed, then post-hoc testing of pair-wise comparisons was made using independent samples t-tests.

Hypothesis 6): At a moderate intensity (60% of VO_{2max}), there will be no significant difference in post-exercise blood lactate response between breast cancer patients and healthy controls during a 9 minute aerobic exercise bout. An independent samples t-test was used to analyze post-exercise blood lactate response between the experimental group and the control group after the 9 minute exercise trial at 60% of VO_{2max}.

Hypothesis 7): At a high intensity (70% of VO_{2max}), breast cancer patients will exhibit a significantly higher HR response compared to healthy controls during a 9 minute aerobic exercise bout. A 2x9 mixed-model ANOVA was used to analyze HR response between the experimental group and the control group during the 9 minute exercise trial at 70% of VO_{2max}. If a significant interaction was observed, then post-hoc testing of pair-wise comparisons was made using independent samples t-tests.

Hypothesis 8): At a high intensity (70% of VO_{2max}), breast cancer patients will exhibit a significantly higher RPE response compared to healthy controls during a 9 minute aerobic exercise bout. A 2x9 mixed-model ANOVA was used to analyze RPE response between the experimental group and the control group during the 9 minute

exercise trial at 70% of VO_{2max}. If a significant interaction was observed, then post-hoc testing of pair-wise comparisons was made using independent samples t-tests.

Hypothesis 9): At a high intensity (70% of VO_{2max}), breast cancer patients will exhibit a significantly higher post-exercise blood lactate response compared to healthy controls after a 9 minute aerobic exercise bout. An independent samples t-test was used to analyze post-exercise blood lactate response between the experimental group and the control group after the 9 minute exercise trial at 70% of $VO_{2max.}$

CHAPTER IV

RESULTS

Subjects

This thesis study included a total of 14 subjects divided into two groups: an experimental group and a control group. Subjects in the experimental group were breast cancer patients who were post-treatment and were newly-enrolled in the Get REAL & HEEL Breast Cancer Program at UNC-Chapel Hill. All subjects in the experimental group underwent surgery, chemotherapy, and radiation therapy during treatment for breast cancer. Four subjects in the experimental group received additional adjuvant therapies including Herceptin, Femara, and Tamoxifen. Three subjects in the experimental group had been diagnosed with Stage II breast cancer, and four subjects had been diagnosed with Stage III breast cancer. Subjects in the control group were women who had been recruited from the faculty, staff, and student populations at UNC-Chapel Hill, had not been enrolled in regular organized physical activity during the past three months, had no history of any chronic disease or cancer treatment, and were healthy enough to participate in aerobic exercise. Subject characteristics are presented in Table 1. Descriptive statistics are presented in the form of mean ± standard deviation. Comparisons between the control group and the experimental group were made using independent samples t-tests, where appropriate.

Table 1. Subject Characteristics

Characteristic (mean ± SD)	Control Group (n=7)	Experimental Group (n=7)	p-value
Age (years)	46.0 ± 12.4	53.9 ± 6.7	0.164
Race	Caucasian (7/7)	Caucasian (7/7)	--
Menopausal Status	Pre (2/7) Pre/Peri (2/7) Post (3/7)	Pre (2/7) Peri (1/7) Peri/Post (1/7) Post (3/7)	--
Height (cm)	166.2 ± 5.3	166.0 ± 7.3	0.947
Weight (kg)	75.8 ± 12.9	72.9 ± 14.1	0.692
BMI (kg/m^2)	27.5 ± 5.0	26.3 ± 3.6	0.617
Percent Body Fat (%)	30.1 ± 4.0	29.3 ± 3.8	0.719
Predicted VO_{2max} (mL/kg/min)	36.4 ± 4.4	32.9 ± 2.2	0.082

Hypotheses 1-3

Hypotheses 1-3 stated that at a low intensity (40% of VO_{2max}), there would be no significant difference in either the HR, RPE, or post-exercise blood lactate response between breast cancer patients and healthy controls during a 9 minute aerobic exercise bout. Hypotheses 1 and 2 were analyzed using 2x9 mixed-model ANOVAs to compare the HR response (Hypothesis 1) and the RPE response (Hypothesis 2) between the experimental and the control group during the 9-minute aerobic exercise trial at 40% of VO_{2max}. The descriptive statistics (mean ± standard deviation) for the results of the analyses of Hypotheses 1 and 2 are presented in Table 2. The overall results from the ANOVA showed that there was no significant group x time interaction for either HR or RPE response (p=0.775 and 0.108, respectively). This indicates that there was no significant difference in either HR response or RPE response between the experimental group and the control group at any time during the 9 minute aerobic exercise trial at 40% of VO_{2max}.

Table 2. Minute-by-Minute Heart Rate and Rate of Perceived Exertion Response during the 9 Minute Aerobic Exercise Trial at 40% of VO_{2max}.

Time (minutes)	Study Group	Heart Rate (bpm) (mean ± SD)	Rate of Perceived Exertion (mean ± SD)
1	Control	97 ± 10	7 ± 1
	Experimental	100 ± 12	8 ± 2
2	Control	100 ± 10	7 ± 1
	Experimental	102 ± 12	8 ± 2
3	Control	100 ± 10	8 ± 1
	Experimental	102 ± 9	9 ± 2
4	Control	100 ± 10	8 ± 1
	Experimental	103 ± 12	9 ± 3
5	Control	100 ± 8	8 ± 1
	Experimental	102 ± 11	9 ± 3
6	Control	102 ± 9	8 ± 1
	Experimental	104 ± 11	9 ± 3
7	Control	103 ± 8	9 ± 1
	Experimental	104 ± 15	9 ± 3
8	Control	103 ± 10	9 ± 2
	Experimental	103 ± 13	9 ± 3
9	Control	104 ± 11	9 ± 2
	Experimental	103 ± 12	9 ± 3

Hypothesis 3 was analyzed using an independent samples t-test to compare the post-exercise blood lactate response between the experimental group and the control group after the 9 minute aerobic exercise trial at 40% of VO_{2max}. The descriptive statistics (mean ± standard deviation) for the analysis of Hypothesis 3 are presented in Table 3. There was no significant difference in post-exercise blood lactate response between the experimental group and the control group following the 9 minute aerobic exercise trial at 40% of VO_{2max} (p=0.704).

Table 3. Post-Exercise Blood Lactate Response following the 9 Minute Aerobic Exercise Trial at 40% of VO_{2max}.

Study Group	Post Exercise Blood Lactate (mmol/L) (mean ± SD)
Control	1.11 ± 0.73
Experimental	1.26 ± 0.64

Hypotheses 4-6

Hypotheses 4-6 stated that at a moderate intensity (60% of VO_{2max}), there would be no significant difference in either HR, RPE, or post-exercise blood lactate response between breast cancer patients and healthy controls during a 9 minute aerobic exercise bout. Hypotheses 4 and 5 were analyzed using 2x9 mixed-model ANOVAs to compare the HR response (Hypothesis 4) and the RPE response (Hypothesis 5) between the experimental group and the control group during the 9 minute exercise trial at 60% of VO_{2max}. The descriptive statistics (mean ± standard deviation) for the results of the analyses of Hypotheses 4 and 5 are presented in Table 4. The overall results from the ANOVA showed that there was a significant group x time interaction for both HR and RPE response during the 9 minute aerobic exercise trial at 60% of VO_{2max} ($p=0.014$ and 0.039, respectively). Post-hoc analysis was performed using independent samples t-tests to examine pair-wise comparisons of both HR response and RPE response between the experimental group and the control group during each minute of the exercise trial. (i.e., HR response of the experimental group vs. the control group at Minute 1, HR response of the experimental group vs. the control group at Minute 2, etc.). Based on this analysis, no significant pair-wise differences in either HR response or RPE response were found to exist between the experimental group and the control group during any minute of the 9 minute aerobic exercise trial at 60% of VO_{2max}.

Table 4. Minute-by-Minute Heart Rate and Rate of Perceived Exertion Response during the 9 Minute Aerobic Exercise Trial at 60% of VO_{2max}.

Time (minutes)	Study Group	Heart Rate (bpm) (mean ± SD)	Rate of Perceived Exertion (mean ± SD)
1	Control	112 ± 16	9 ± 2
	Experimental	109 ± 10	10 ± 3
2	Control	122 ± 18	11 ± 2
	Experimental	116 ± 12	10 ± 3
3	Control	124 ± 17	11 ± 2
	Experimental	117 ± 14	10 ± 3
4	Control	127 ± 18	12 ± 2
	Experimental	118 ± 13	10 ± 3
5	Control	130 ± 18	13 ± 3
	Experimental	117 ± 14	10 ± 3
6	Control	131 ± 18	13 ± 2
	Experimental	119 ± 14	11 ± 3
7	Control	132 ± 17	13 ± 2
	Experimental	120 ± 14	11 ± 3
8	Control	133 ± 18	13 ± 2
	Experimental	120 ± 12	11 ± 3
9	Control	136 ± 18	14 ± 3
	Experimental	121 ± 14	11 ± 3

Hypothesis 6 was analyzed using an independent samples t-test to compare the post-exercise blood lactate response between the experimental group and the control group after the 9 minute exercise trial at 60% of VO_{2max}. The descriptive statistics (mean ± standard deviation) for the analysis of Hypothesis 6 are presented in Table 5. There was no significant difference in post-exercise blood lactate response between the experimental group and the control group following the 9 minute aerobic exercise trial at 60% of VO_{2max} (p=0.181).

Table 5. Post-Exercise Blood Lactate Response following the 9 Minute Aerobic Exercise Trial at 60% of VO_{2max}.

Study Group	Post Exercise Blood Lactate (mmol/L) (mean ± SD)
Control	3.83 ± 2.48
Experimental	2.23 ± 1.65

Hypotheses 7-9

Hypotheses 7-9 stated that at a high intensity (70% of VO_{2max}), breast cancer patients would exhibit significantly higher HR, RPE, and post-exercise blood-lactate responses compared to healthy controls during a 9 minute aerobic exercise bout. Hypotheses 7 and 8 were analyzed using 2x9 mixed-model ANOVAs to compare the HR response (Hypothesis 7) and the RPE response (Hypothesis 8) between the experimental group and the control group during the 9 minute exercise trial at 70% of VO_{2max}. The descriptive statistics (mean ± standard deviation) for the results of the analyses of Hypotheses 7 and 8 are presented in Table 6. The overall results from the ANOVA showed that there was no significant group x time interaction for HR response during the 9 minute aerobic exercise trial at 70% of VO_{2max} (p=0.662). However, there was a significant group x time interaction for RPE response during the 9 minute aerobic exercise trial at 70% of VO_{2max} (p=0.003). Post-hoc analysis was performed using independent samples t-tests to examine pair-wise comparisons of RPE response between the experimental group and the control group during each minute of the exercise trial. (i.e., RPE response of the experimental group vs. the control group at Minute 1, RPE response of the experimental group vs. the control group at Minute 2, etc.). Based on this analysis, no significant pair-wise differences in RPE response were found to exist between the experimental group and the control group during any minute of the 9 minute aerobic exercise trial at 70% of VO_{2max}.

Table 6. Minute-by-Minute Heart Rate and Rate of Perceived Exertion Response during the 9 Minute Aerobic Exercise Trial at 70% of VO_{2max}.

Time (minutes)	Study Group	Heart Rate (bpm) (mean ± SD)	Rate of Perceived Exertion (mean ± SD)
1	Control	130 ± 25	11 ± 2
	Experimental	116 ± 13	11 ± 3
2	Control	145 ± 26	12 ± 2
	Experimental	129 ± 14	12 ± 3
3	Control	149 ± 27	13 ± 1
	Experimental	135 ± 13	12 ± 3
4	Control	152 ± 27	14 ± 1
	Experimental	137 ± 14	13 ± 3
5	Control	155 ± 27	15 ± 2
	Experimental	139 ± 14	13 ± 3
6	Control	156 ± 28	15 ± 2
	Experimental	140 ± 13	13 ± 3
7	Control	157 ± 28	15 ± 2
	Experimental	141 ± 13	13 ± 3
8	Control	158 ± 28	16 ± 2
	Experimental	140 ± 14	13 ± 3
9	Control	158 ± 27	16 ± 2
	Experimental	142 ± 13	13 ± 3

Hypothesis 9 was analyzed using an independent samples t-test to compare the post-exercise blood lactate response between the experimental group and the control group after the 9 minute exercise trial at 70% of VO_{2max}. The descriptive statistics (mean ± standard deviation) for the analysis of Hypothesis 9 are presented in Table 7. The post-exercise blood lactate response was significantly higher in the control group versus the experimental group following the 9 minute aerobic exercise trial at 70% of VO_{2max} (p<0.0005).

Table 7. Post-Exercise Blood Lactate Response following the 9 Minute Aerobic Exercise Trial at 70% of VO_{2max}.

Study Group	Post Exercise Blood Lactate (mmol/L) (mean ± SD)
Control	7.70 ± 1.62
Experimental	3.29 ± 1.08

Summary of Results

A summary of results is presented in Table 8. Brief descriptions of the research

hypotheses and major outcomes are shown, along with the corresponding p-value. Based

on the results of this study, each hypothesis may now be accepted or rejected.

Table 8. Summary of Results

Exercise Trial Intensity	Hypothesis	Study Outcome	p-value	Accept or Reject Hypothesis?
40% of VO_{2max}	1: No significant difference in HR response between groups	No significant difference between groups	0.775	Accept
40% of VO_{2max}	2: No significant difference in RPE response between groups	No significant difference between groups	0.108	Accept
40% of VO_{2max}	3: No significant difference in post-exercise blood lactate between groups	No significant difference between groups	0.708	Accept
60% of VO_{2max}	4: No significant difference in HR response between groups	Significant group x time interaction	0.014, but no significance upon post-hoc analysis	Reject
60% of VO_{2max}	5: No significant difference in RPE response between groups	Significant group x time interaction	0.039, but no significance upon post-hoc analysis	Reject
60% of VO_{2max}	6: No significant difference in post-exercise blood lactate between groups	No significant difference between groups	0.181	Accept
70% of VO_{2max}	7: Experimental group will exhibit a significantly higher HR response	No significant difference between groups	0.662	Reject
70% of VO_{2max}	8: Experimental group will exhibit a significantly higher RPE response	Significant group x time interaction	0.003, but no significance upon post-hoc analysis	Reject
70% of VO_{2max}	9: Experimental group will exhibit a significantly higher post-exercise blood lactate response	Control group exhibited significantly higher response	<0.0005	Reject

CHAPTER V

DISCUSSION

The purpose of this study was to compare the HR, RPE, and post-exercise blood lactate response to low, moderate, and high intensity aerobic exercise in post-treated breast cancer patients and healthy controls. During the course of this study, subjects completed an initial assessment to determine their predicted VO_{2max} from a Modified Bruce Protocol on the treadmill. The results of the initial assessment were used to calculate the speed and grade that corresponded to 40%, 60%, and 70% of predicted VO_{2max}. Subjects then completed three 9-minute aerobic exercise trials, one at each intensity, in random order. During each trial, HR and RPE data were collected during the last 10 seconds of every minute, and blood lactate was collected 3 minutes post-trial. The HR and RPE data were analyzed using 2x9 mixed-model ANOVAs, and post-hoc analyses were carried out using independent samples t-tests, where appropriate. The post-exercise blood lactate data were analyzed using independent samples t-tests.

Heart Rate, RPE, and Post-exercise Blood Lactate Response at 40% of VO_{2max}

Hypotheses 1-3 stated that at a low intensity (40% of VO_{2max}), there would be no significant difference in either the HR, RPE, or post-exercise blood lactate response between breast cancer patients and healthy controls during a 9 minute aerobic exercise bout. The results of this study support these hypotheses, indicating that the physiological and perceived exertion responses are similar between the experimental group and the

control group during short-duration, low-intensity aerobic exercise (HR response: p=0.775; RPE response: p=0.108; post exercise blood lactate response: p=0.708).

Heart Rate, RPE, and Post-exercise Blood Lactate Responses at 60% of VO_{2max}

Hypotheses 4-6 stated that at a moderate intensity (60% of VO_{2max}), there would be no significant difference in either HR, RPE, or post-exercise blood lactate response between breast cancer patients and healthy controls during a 9 minute aerobic exercise bout. The results showed that there was a significant group x time interaction for HR and RPE response (p=0.014, 0.039, respectively). However, post-hoc analysis, minute-by-minute comparisons between the control group and the experimental group for HR and RPE response only occurred in the comparisons that were not of relevance to this study (i.e., HR response at minute 1 for the control group vs. HR response at minute 9 for the experimental group). As for the analyses of blood concentration between groups, again, no significant difference was observed between the two groups (p=0.181).

Even though the post-hoc analyses did not show differences in the pair-wise comparisons of HR and RPE response relevant to the hypotheses tested in this study, the mean differences observed minute-by-minute for HR and RPE may be of clinical relevance. However, according to this study design, many methodological challenges were faced by the investigators during this experiment may somewhat explain these differences. Firstly, the small sample size could have been one of the major limitations in the analysis. Secondly, some subjects held the handrails on the treadmill while others did not. More specifically, 5 of the 7 experimental subjects held the handrails while only 2 of the 7 control subjects held the handrails. By holding the handrails, it is likely that the subjects did not have to work as hard to keep up with the treadmill belt as it was moving.

Since it was mainly the experimental group that used the handrails, this may have contributed to the lower HR and RPE response observed for this group. While post-exercise blood lactate response was not significantly different between the groups, the experimental group did have a lower mean level than did the control group (3.83 mmol/L vs. 2.23 mmol/L), which may also be due in part to the use of the treadmill handrails. During this study, all attempts were made to standardize the protocols used during the initial assessment and during each aerobic exercise trial, but as the study progressed, it became evident that some subjects could not safely or comfortably walk on the treadmill without using the handrails. However, if a subject held the handrails during the initial assessment, then they were instructed to hold the rails for the subsequent aerobic exercise trials.

A third possible reason why the control group displayed a higher HR and RPE response during the exercise trial may be related to the age difference between the two groups. The mean age difference between the control group and the experimental group was not statistically significant (p=0.164); however, the experimental group was older than the control group by 7.9 years. It is known that HR decreases with age during submaximal exercise at a relative exercise intensity (Brooks et al., 2005, p. 839). Muscle biochemistry also changes with age, including decreases in glycolytic enzymes (Brooks et al., 2005, p. 844). This includes the enzyme lactate dehydrogenase (LDH), which is responsible for the production of lactic acid, especially during more intense exercise (Brooks et al., 2005, p. 844). Since the experimental group is older than the control group, this may also explain why HR and post-exercise blood lactate were lower in this group. The small sample size may have also contributed to the statistically non-

significant difference in mean age between the groups. If the sample size were larger, it is possible that a mean difference of 7.9 years could present a different result.

Heart Rate, RPE, and Post-exercise Blood Lactate Responses at 70% of VO$_{2max}$

Hypotheses 7-9 stated that at a high intensity (70% of VO$_{2max}$), breast cancer patients would exhibit significantly higher HR, RPE, and post-exercise blood-lactate responses compared to healthy controls during a 9 minute aerobic exercise bout. The results showed that there was no significant group x time interaction in HR response. There was a significant group x time interaction for RPE response (p=0.003). Post-hoc analysis, minute-by-minute comparisons between the control group and the experimental group for RPE response, as was the case for the moderate intensity trial, indicated that the significant pair-wise differences in RPE response occurred for comparisons that were not of relevance for this study. There was a significant difference in post-exercise blood lactate between the control group and the experimental group, with the control group exhibiting a higher response (p<0.0005).

The fact that there was no significant difference in HR or RPE response during the trial at 70% of VO$_{2max}$ was surprising; however, methodological reasons may have again influenced the results. As was the case during the moderate intensity trial, 5 of the 7 experimental subjects held the handrails on the treadmill while only 2 of the 7 control subjects used the handrails. Even though no statistical significance was observed for HR response between the groups, the differences in mean HR response throughout the 9 minutes ranged from 14-18 bpm, with the control group exhibiting the higher HR response. Additionally, the standard deviations surrounding the mean HR response for

the control group was twice as large as those for the experimental group, which may have also contributed to the non-significant findings.

Another factor that may have contributed to the results for HR and RPE response was the fact that 4 of the 7 control subjects ran for the duration of the trial, while all of the experimental subjects walked. These 4 subjects did not hold the handrails during the exercise trial, and these 4 subjects also had a predicted VO_{2max} greater than the mean for the control group. As such, these 4 subjects were required to perform this exercise trial at a speed of 4.2-5.2 mph. This is quite a fast pace for most people to walk, so it is not surprising that these subjects had to run during the trial. It should be noted that one of the control subjects who held the handrail did walk at a speed of 4.1 mph; however, had she not held the handrail, it is likely that she would have not been able to walk that fast, and would have needed to run during the trial. The differences in running vs. walking, as well as whether or not the subjects held the handrails may have also contributed to the significant RPE findings, where the control subjects reported higher RPE scores than did the experimental group.

A third factor that may have contributed to the findings for HR and RPE response during the exercise trial at 70% of VO_{2max}, may have involved the method that was used to calculate intensity. The Modified Bruce Protocol, which was used during the initial VO_{2max} assessment, terminates at 75% of HRR. In reality, 75% of HRR is a lower intensity than 75% of VO_{2max}. Therefore, when using the results of the Modified Bruce Protocol to calculate the treadmill speed and grade that would correspond to 70% of VO_{2max}, it is possible that subjects may have been exercising at an intensity higher than 70% of VO_{2max}.

The significant difference in post-exercise blood lactate response was surprising, in that it was not expected that the control group would exhibit a higher response than the experimental group. Many of the factors previously discussed, as well as the mean age difference between the two groups, may have contributed to the higher lactate response in the control group. Additionally, the action of running, compared to walking, requires the use of more Type II muscle fibers, which have significant glycolytic capacity and therefore produce lactate in response to higher intensity exercise. However, a mean diff of 4.41 mmol/L between the two groups is intriguing, and it is possible that there are other physiological mechanisms occurring that may have caused the differences in lactate response. The literature describing the effect of cancer treatment on the production of lactate in skeletal muscle is extremely scarce; therefore, it is early to believe that the experimental subjects are in fact producing less lactate than age-matched controls of similar cardiopulmonary fitness.

Application of Results to Aerobic Exercise Prescription in Breast Cancer Patients

As stated before, the purpose of this experiment was to compare the HR, RPE, and post-exercise blood lactate response to low, moderate, and high intensity aerobic exercise in post-treated breast cancer patients and apparently healthy controls. Changes in physiological /psychological function over the duration of a long-term exercise program were not assessed; therefore, this study does not really attempt to evaluate whether 40%, 60%, and 70% of VO_{2max} are intensities that are truly appropriate for exercise prescription in the breast cancer patient population. However, the results of this study may begin to shed some light on how post-treated breast cancer patients respond to acute bouts of low, moderate, and high intensity aerobic exercise compared with

individuals who have never been through major cancer treatment. As more studies are conducted, this knowledge will be useful when assessing the appropriateness of different intensities in order to formulate safe and effective exercise prescriptions for this population.

The results of the exercise trials at 40% and 60% of VO_{2max} indicate that the experimental group responded similarly to the control group with respect to HR, RPE, and post-exercise blood lactate. During the exercise trial at 70% of VO_{2max}, the experimental group again responded similarly to the control group with respect to HR and RPE response, and the post-exercise blood lactate response was significantly lower in the experimental group. These results may infer that it could be appropriate to use a wide range of intensities similar to those used for healthy adult, cardiac patient, and elderly adult populations when formulating exercise prescriptions for post-treated breast cancer patients. A closer look at the results of the exercise trial at 60% of VO_{2max} showed that the levels of exertion reported by the experimental group seemed to be tolerable (mean RPE range of 10-11 or "light"), and the subjects did not report any extreme difficultly, when exercising on the treadmill holding the hand rails. Therefore, it is likely that the subjects would be able to continue at this intensity for an extended period of time before volitional fatigue. Similarly, the subjects in the experimental group seemed to tolerate the exercise trial at 70% of VO_{2max} for the 9 minute period without adverse effects, but it is possible that they may not have been able to maintain that intensity for much longer. This is suggested by the mean RPE scores for the experimental group for each minute of the trial, which ranged from 11 to 13 ("light" to "somewhat hard") with standard deviations of ± 3 around the mean RPE scores of 13, as well as from anecdotal feedback

from subjects in the experimental group. It is also important to note that the subjects within the experimental group were within 6 months of completion of major cancer treatment. Patients who are currently undergoing in-hospital treatment, or who are suffering from more severe side effects may not respond the same way the subjects in the current study did; nor might they be able to tolerate an intensity of 60% of VO_{2max}. Therefore, the results of this study should be interpreted cautiously, especially when considering intensities of above 60% of VO_{2max}.

The existing literature reporting the effects of aerobic exercise in the breast cancer patient population is encouraging, in that aerobic exercise of various intensities seems to elicit many positive responses in physiological and psychological parameters. When considering low intensity aerobic exercise, Dimeo et al. (1997, 1999) investigated the effects of physical exercise on physical performance, severity of treatment complications, and psychological distress in cancer patients, using an exercise intensity of 50% of HRR, which may be similar to 40% of VO_{2max}. In the first study, 70 patients (including 46 breast cancer patients) participated in an exercise sessions that included alternating bouts of 1 minute of cycling and 1 minute of rest, for a total of 30 minutes. In the second study, 59 patients (including 31 breast cancer patients) participated in an exercise program that included the same type of interval cycling. Both studies revealed positive results, including increased physical performance and decreased thrombopenia, neutropenia, psychological distress, and time spent in the hospital. In a study by Battaglini et al. (2004), a group of 27 patients including 22 breast cancer patients participated in an exercise program where aerobic exercise intensity was set between 50-55% of maximal heart rate, which may also be similar to 40% of VO_{2max}. The goal of the

study was to examine the relationship between changes in selected physiological parameters and fatigue during a period of 6 months. Even though no significant relationship between selected physiological parameters including % body fat, resting heart rate, and dynamic endurance tests, an improvement in cardiorespiratory endurance of approximately 30% was observed with no adverse effects of the intensity used being reported.

Moving towards the literature examining the effect of moderate aerobic intensity on breast cancer patients, another study by Battaglini et al. (2006) investigated the exercise response in a group of 20 breast cancer patients undergoing treatment. Patients assigned to the exercise group, participated in a structured exercise program at an intensity range between 40-60% of VO_{2max}, for a period of approximately 21 weeks. No adverse effects of the intensity used in the Battaglini et al. study were reported. Furthermore, significant decreases in fatigue were observed in the exercise group when compared to the control group at the end of the first, second, and final bout of chemotherapy treatment ($p=0.001$, $p=0.005$, and $p=0.001$ respectively). Segal et al. (2001) investigated the effect of a self-paced walking intervention along with a supervised exercise program at 50-60% of VO_{2max} on health-related quality of life in 123 breast cancer patients. Increases in physical functioning, measured by the Short Form (SF)-36 scale were observed after 26 weeks of exercise intervention. In patients who did not receive chemotherapy, aerobic capacity was significant increased and body weight was significantly decreased ($p=0.01$ and <0.05, respectively) in patients participating in supervised exercise compared with patients receiving usual care.

Several studies have used intensities of 70% of VO_{2max} and above to examine the impact of exercise on various endpoints in breast cancer patients. Fairey et al. (2003, 2005a, 2005b) conducted three studies examining the effect of exercise training on several blood markers including fasting insulin, insulin resistance, insulin growth factors, insulin growth factor binding proteins, NK cell cytotoxic activity, C-reactive protein, and various cardiovascular disease risk factors. Fifty-two post-menopausal post-treated breast cancer patients participated in an exercise program that included cycling at 70-75% of VO_{2peak}. Patients trained 3 times per week for 15 weeks, starting with a duration of 15 minutes during weeks 1-3 and increasing by 5 minutes every 3 weeks thereafter up to a total of 35 minutes for weeks 13-15. Positive changes were observed for cardiovascular function and disease risk factors, including increased VO_{2max}, and decreased C-reactive protein, resting HR, HRR, blood pressure, and HDL-C. An increase in NK cell activity was also observed as well as changes in levels of insulin-like growth factors and insulin-like growth factor binding proteins. Kim et al. (2006) studied cardiopulmonary responses and adherence to exercise after an 8-week exercise intervention in 41 post-treated breast cancer patients. Patients participated in supervised aerobic exercise at an intensity of 60-70% VO_{2peak} and/or HRR for 30 minutes per day, 3 days per week. Activities consisted of cycling, walking, or jogging on a treadmill. The results showed that patients participating in exercise had decreased resting HR, resting systolic blood pressure, and an increased VO_{2peak}. Patients also reported an increase in voluntary activity, a decrease in sedentary activity. Courneya et al. (2007) conducted a multicenter trial to study the effects of exercise on body composition, physical function, and quality of life. The study included 78 breast cancer patients who performed aerobic exercise at an intensity range

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of 60-80% of VO_{2max}, using the treadmill, elliptical, and cycle ergometer. Patients participated in an exercise program for 3 days per week for the duration of their chemotherapy regimen, plus 2 weeks before and 3 weeks afterwards. Exercise duration began at 15 minutes during weeks 1-3, and it increased by 5 minutes every 3 weeks until the total duration reached 45 minutes. During weeks 1-6, patients exercised at 60% of VO_{2max}, which progressed to 70% of VO_{2max} during weeks 7-12, and then to 80% of VO_{2max} beyond week 12. Increases in aerobic fitness and self esteem, and improved body composition and chemotherapy completion rate without causing lymphadema or other significant adverse events were observed.

Therefore, according to the current literature, physiological responses to aerobic exercise comparable to the intensities used in the current study seem to be well-tolerated by the breast cancer patient population, while also attaining positive changes in physiological and psychological parameters. Even though no significant adverse effects were observed in the studies cited above, several investigators used intensities that were quite high, and therefore these results should be interpreted cautiously, particularly when considering the potential impact of high intensity aerobic exercise on the immune system in breast cancer. Very few studies have examined the impact of exercise on immune markers and therefore, up to now, the results of these studies are somewhat inconclusive. Also, according to the results of the Segal et al. (2001) study, the type of treatment, phase of treatment, and the level of side effects experienced should all be taken into consideration before prescribing exercise dosage.

Limitations

This is the first study that has attempted to understand the physiological responses to various levels of aerobic exercise intensity in post-treated breast cancer patients, compared with apparently healthy age-matched controls that have never gone through treatment for breast cancer. Many challenges were faced during this experiment, which may have impacted our results. These limitations should be addressed in order to precisely understand the impact of different intensities on the physiology of these patients.

The first limitation of this study is the small sample size. There were 7 subjects in the experimental group and 7 subjects in the control group, and while statistically significant differences in some physiological parameters were observed between the groups, it is difficult to know whether these differences would persist with a larger sample size. Similarly, it is difficult to know whether the statistically non-significant differences that were observed between the groups would still be non-significant with the addition of more subjects.

The second limitation of this study is the difference in the mean ages of the groups. The mean age of the experimental group was 53.9 years, and the mean age of the control group was 46.0 years, which is a mean difference of 7.9 years. This difference was not statistically significant (p=0.164); however, the older age of the experimental group may have contributed to the lower HR responses observed in this group during the trials at 60% and 70% of VO_{2max}.

A third limitation of this study was that some subjects walked on the treadmill using the handrails while some did not. While every attempt was made to standardize the

protocol, it became evident that some subjects were not able to comfortably or safely walk on the treadmill without holding the handrails. Since it was mainly the experimental group that used the handrails, it may still be difficult to compare the physiological responses between the two groups, and this may partially account for the attenuated HR, RPE, and post-exercise blood lactate responses in the experimental group during the moderate and high-intensity aerobic exercise trials.

A fourth limitation of this study was the protocol during the initial assessment to predict VO_{2max}, as well as the method used to calculate predicted VO_{2max}. The Modified Bruce Protocol was chosen for this study because it is the same protocol that is currently used to assess cardiopulmonary endurance of participants in the Get REAL & HEEL Breast Cancer Program; therefore, it was familiar to the investigators, and it would be used to re-assess the subjects in the experimental group throughout their time as participants in Get REAL & HEEL. Additionally, the Modified Bruce Protocol is recommended for use in high risk, cardiac patient, and elderly adult populations; therefore, it should be a suitable protocol to use with post-treated breast cancer patients (Heyward, 2006, p. 67). As mentioned previously, the test terminates when the subject reaches a THR of 75% of HRR. Since an intensity of 75% of HRR is most likely lower than an intensity of 75% of VO_{2max}, the mathematical formula used to determine the intensities for the aerobic exercise trials may not have been entirely accurate, particularly when determining the treadmill speed and grade for the high-intensity exercise trial.

The following equation was used to calculate predicted VO_{2max}:

$$VO_{2max} = 2.282*(\text{total time on treadmill}) + 8.545$$

This equation is currently used at Get REAL & HEEL, as recommended by the Rocky Mountain Cancer Rehabilitation Institute (Schneider, Dennehy, Roozeboom & Carter, 2002), to calculate predicted VO_{2max} during cardiopulmonary physiological assessments, and it is recommended for use in the cardiac patient and elderly adult populations (Heyward, 2006, p. 68). However, this prediction equation was mostly intended for use when the subject is holding the handrails while walking on the treadmill (Heyward, 2006, p. 68). Since not all subjects held the handrails, this equation may not have been the most appropriate choice for calculating predicted VO_{2max}.

A fifth limitation of this study was that some subjects in the experimental group had been considered post-treated for a longer time period than others (all were within 6 months of completion of major cancer treatment). It is possible that patients who have just finished treatment may experience side effects to a higher degree than those who have been finished with treatment for a longer period of time. Future studies should control for this; for example, a post-treatment window of 1-2 months rather than a window of 6 months should be used.

A sixth limitation of this study may have related to the amount of time that the control group had been considered sedentary before enrolling onto the study. As mentioned in the Methodology, the control subjects who had not participated in regular organized physical activity during the past 3 months were eligible for this study. While this was true for all subjects in the control group, 4 of these subjects did have a prior history of being physically active, either as a recreational or competitive athlete, and it was these same 4 subjects who ran for the duration of the exercise trial at 70% of VO_{2max}. It is possible that some of the physiological adaptations experienced during previous

training may still exist, even if the subject is currently sedentary. For this reason, it may be better to use control subjects who have been physically inactive for at least 1 year for future studies. Also, a longer period of not participating in regular physical activity beyond the 3-month criteria used in the current study should be revised.

An eighth limitation of this study may have related to the menopausal status and menstrual cycle phase of the subjects during the completion of the exercise trials. High levels of estrogen decreases carbohydrate metabolism and increases lipid metabolism; therefore, women who are in the luteal phase of the menstrual cycle experience decreased glucose oxidation and consequently lower lactate production during exercise (Brooks et al., 2005, p. 790). On the other hand, women who are experiencing oligomenorrhea or amenorrhea due to the onset of menopause, have decreased levels of estrogen, and therefore increased carbohydrate metabolism and lactate production during exercise. It is possible that the differences in menopausal status between subjects, as well as menstrual cycle phase, may have also contributed to the post-exercise blood lactate results of the two study groups in response to the exercise trials.

Recommendations for Future Studies

The basis for the current study is the need to better understand the impact of exercise intensity in breast cancer patients so that prescriptions can be made more safely and efficiently. Prescriptions for cancer patients are variable and should be individualized based on the physiological state of the patient prior to each session. Furthermore, while the impact of exercise on immune function in breast cancer patients is not clearly understood, it is known that exercise can act as a stressor on the body's physiological systems, including the immune system. Since some breast cancer patients

may be starting an exercise program with compromised immune function, it is important to ensure that the exercise prescription does not further suppress the immune system, but instead, helps to stimulate recovery. Therefore, the need for a better understanding of aerobic exercise intensity is paramount.

In light of the limitations previously mentioned, some recommendations for future studies are provided below.

1. A larger sample size of patients and controls should be obtained so that the impact of aerobic exercise intensity can be evaluated in a greater number of individuals.

2. Subjects in the experimental and control groups should be age-matched more closely. Additionally, a smaller age range should be used (i.e. 40-50 years of age rather than 30-75 years of age). This may help to minimize the effect of age differences on cardiovascular responses and lactate production during exercise.

3. A more accurate assessment of menopausal status should be considered, since estrogen levels may impact the carbohydrate metabolism and the production of lactate during exercise. Similarly, menstrual cycle phase should be controlled for more closely when scheduling the exercise trials.

4. Since some subject held the handrails on the treadmill while others did not, it may be best to recommend that all subjects hold the handrails during the initial VO_{2max} assessment, as well as during the individual exercise trials. This may help to further standardize the testing protocol, as well as to ensure that all subjects feel as safe and comfortable as possible. Alternatively, a cycling protocol such as the YMCA Cycle Ergometer Test could be used in order to predict VO_{2max}, with subsequent exercise sessions taking place on a cycle ergometer. By using a

cycling protocol, all subjects would be required to perform the same technique for each session; i.e., there would be no discrepancies concerning running vs. walking, or holding vs. no holding handrails.

5. A post-treatment window of 1-2 months, rather than 6 months should be considered when recruiting experimental subjects in order to more closely control for the type and severity of side effects experienced by the experimental group which may affect performance during the initial assessment and exercise trials.

6. A window of physical inactivity of at least 1 year, should be considered when recruiting control subjects in order to more closely control for potential physiological changes from previous exercise training.

7. Since the termination intensity for the initial VO_{2max} assessment was lower than the highest intensity used during the exercise trials, it may be more useful to perform a VO_{2peak} test to more accurately determine baseline cardiopulmonary fitness and to calculate workloads to be used for the different intensities during the aerobic exercise trials. If this option were chosen, all subjects should be thoroughly screened for any medical contraindications to completing a VO_{2peak} test, and HR, RPE, blood pressure, and a 12-lead ECG should be recorded during and after the test (Heyward, 2006, p 60). Additionally, the presence of a physician would be necessary, which would follow the recommendation of the ACSM when administering VO_{2max} tests in clinical populations (Whaley et al., 2006, p. 29). Since expired gases are collected during a VO_{2peak} test, patients may feel more comfortable wearing a mask rather than a mouthpiece.

Once studies have been conducted that help clarify the impact of aerobic exercise intensity on post-treated breast cancer patients, studies utilizing patients who are undergoing treatment should be considered. Knowing that HR during treatment varies tremendously from day to day, confirming the results of this experiment plus exploring the possibility of using other quantifiers for aerobic exercise may be of importance.

Conclusion

Low, moderate and high-intensity aerobic exercise does not seem to elicit significant differences in HR or RPE response in breast cancer patients compared with apparently-healthy controls. Likewise, low and moderate intensity aerobic exercise does not seem to elicit significant differences in post-exercise blood lactate response; however, controls had a significantly higher response after high-intensity aerobic exercise. Small sample size, methodological issues and mean age difference between the two groups may have contributed to the differing physiological responses seen in this study. It appears that exercise intensities of 40% and 60% of VO_{2max} are tolerable to use when prescribing exercise for breast cancer patients, even more so when exercising while holding the handrails on a treadmill. However, it is unclear whether exercise intensities of 70% of VO_{2max} are appropriate to use when prescribing exercise for breast cancer patients, particularly when considering the possible impact of high intensity aerobic exercise on the immune system. Further investigation with a larger sample size and a more standardized protocol is needed in order to better understand the impact of aerobic exercise intensity on the physiological function of breast cancer patients compared with healthy controls. Such an understanding will aid in the development of guidelines that

are both safe and effective in improving physical function in breast cancer patients after

the completion of major cancer treatment.

Appendix I

Pollock 3-site method for measuring skinfold thickness

Skinfold Measurement Sites for Women

1. Measure sites in triplicate

Triceps): Vertical fold over triceps, halfway between the shoulder and the elbow.

Abdomen): Horizontal fold 3 cm lateral and 1cm inferior to the umbilicus.

Suprailiac): Diagonal fold posterior to the midaxillary line and superiorly to the

iliac crest along the natural cleavage of the skin.

Thigh): Vertical fold on the front of the thigh, halfway between the knee and

inguinal fold

2. Average the two closest measurements for each site

3. Sum the three averages (triceps, abdomen, suprailiac, or triceps, suprailiac, thigh).

4. If using triceps, abdomen, and suprailiac sites, calculate Percent Body Fat using the

equation below. (Whaley et al., 2006, p. 62)

Computation of Percent Body Fat (Triceps, Abdomen, Suprailiac Sites)

% Body Fat = [0.41563*(sum of skinfolds)] – [0.00112*(sum of skinfolds)^2] +

[0.03661*(age)] + 4.03653

5. If using triceps, suprailiac and thigh sites, calculate Body Density, then Percent Body

Fat using the equations below.

Computation of Body Density Equation for Women (Triceps, Suprailiac, Thigh Sites)

Body Density = 1.0994921 – [0.0009929*(sum of skinfolds)] + [0.0000023*(sum of

skinfolds)^2] – [0.0001392*(age)]

Computation of Percent Body Fat

% Body Fat = [(4.95/(Body Density)) – 4.500]*100

(Whaley et al., 2006, p. 63)

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE
(August 2002)

SHORT LAST 7 DAYS SELF-ADMINISTERED FORMAT

FOR USE WITH YOUNG AND MIDDLE-AGED ADULTS (15-69 years)

The International Physical Activity Questionnaires (IPAQ) comprises a set of 4 questionnaires. Long (5 activity domains asked independently) and short (4 generic items) versions for use by either telephone or self-administered methods are available. The purpose of the questionnaires is to provide common instruments that can be used to obtain internationally comparable data on health–related physical activity.

Background on IPAQ
The development of an international measure for physical activity commenced in Geneva in 1998 and was followed by extensive reliability and validity testing undertaken across 12 countries (14 sites) during 2000. The final results suggest that these measures have acceptable measurement properties for use in many settings and in different languages, and are suitable for national population-based prevalence studies of participation in physical activity.

Using IPAQ
Use of the IPAQ instruments for monitoring and research purposes is encouraged. It is recommended that no changes be made to the order or wording of the questions as this will affect the psychometric properties of the instruments.

Translation from English and Cultural Adaptation
Translation from English is supported to facilitate worldwide use of IPAQ. Information on the availability of IPAQ in different languages can be obtained at www.ipaq.ki.se. If a new translation is undertaken we highly recommend using the prescribed back translation methods available on the IPAQ website. If possible please consider making your translated version of IPAQ available to others by contributing it to the IPAQ website. Further details on translation and cultural adaptation can be downloaded from the website.

Further Developments of IPAQ
International collaboration on IPAQ is on-going and an *International Physical Activity Prevalence Study* is in progress. For further information see the IPAQ website.

More Information
More detailed information on the IPAQ process and the research methods used in the development of IPAQ instruments is available at www.ipaq.ki.se and Booth, M.L. (2000). *Assessment of Physical Activity: An International Perspective*. Research Quarterly for Exercise and Sport, 71 (2): s114-20. Other scientific publications and presentations on the use of IPAQ are summarized on the website.

SHORT LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised August 2002.

INTERNATIONAL PHYSICAL ACTIVITY QUESTIONNAIRE

We are interested in finding out about the kinds of physical activities that people do as part of their everyday lives. The questions will ask you about the time you spent being physically active in the **last 7 days**. Please answer each question even if you do not consider yourself to be an active person. Please think about the activities you do at work, as part of your house and yard work, to get from place to place, and in your spare time for recreation, exercise or sport.

Think about all the **vigorous** activities that you did in the **last 7 days**. **Vigorous** physical activities refer to activities that take hard physical effort and make you breathe much harder than normal. Think *only* about those physical activities that you did for at least 10 minutes at a time.

1. During the **last 7 days**, on how many days did you do **vigorous** physical activities like heavy lifting, digging, aerobics, or fast bicycling?

    _____ days per week

    ☐ No vigorous physical activities ➡ *Skip to question 3*

2. How much time did you usually spend doing **vigorous** physical activities on one of those days?

    _____ hours per day

    _____ minutes per day

    ☐ Don't know/Not sure

Think about all the **moderate** activities that you did in the **last 7 days**. **Moderate** activities refer to activities that take moderate physical effort and make you breathe somewhat harder than normal. Think only about those physical activities that you did for at least 10 minutes at a time.

3. During the **last 7 days**, on how many days did you do **moderate** physical activities like carrying light loads, bicycling at a regular pace, or doubles tennis? Do not include walking.

    _____ days per week

    ☐ No moderate physical activities ➡ *Skip to question 5*

SHORT LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised August 2002.

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4. How much time did you usually spend doing **moderate** physical activities on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

Think about the time you spent **walking** in the **last 7 days**. This includes at work and at home, walking to travel from place to place, and any other walking that you might do solely for recreation, sport, exercise, or leisure.

5. During the **last 7 days**, on how many days did you **walk** for at least 10 minutes at a time?

_____ **days per week**

☐ No walking ➡️ **Skip to question 7**

6. How much time did you usually spend **walking** on one of those days?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

The last question is about the time you spent **sitting** on weekdays during the **last 7 days**. Include time spent at work, at home, while doing course work and during leisure time. This may include time spent sitting at a desk, visiting friends, reading, or sitting or lying down to watch television.

7. During the **last 7 days**, how much time did you spend **sitting** on a **week day**?

_____ **hours per day**

_____ **minutes per day**

☐ Don't know/Not sure

This is the end of the questionnaire, thank you for participating.

SHORT LAST 7 DAYS SELF-ADMINISTERED version of the IPAQ. Revised August 2002.

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Modified Bruce Submaximal Treadmill Protocol

Test Termination

The test is terminated when the subject reaches a target heart rate (THR), which is 75%

of the subject's heart rate reserve using the Karvonen Formula.

THR = [(220 – Age) – Resting HR]*0.75 + Resting HR

Table of Protocol Stages

Stage	Time (min)	Speed (mph)	Grade (%)	HR	RPE	Total Time Spent in Stage
Warm-up	3	1.7	0			
1	3	1.7	5			
2	3	1.7	10			
3	3	2.5	12			
4	3	3.4	14			
5	3	4.2	16			
6	3	5.0	18			

Formula to calculate VO_{2max}

VO2max = 2.282*(total time, in minutes) + 8.545

Formula to calculate VO_2, speed, and grade for the aerobic exercise trials

Horizontal VO_2 (in mL/kg/min) = speed (in m/min) * (0.1 mLO_2/kg/min)

Vertical VO_2 (in mL/kg/min) = % grade * speed (in m/min) * (1.8 mLO_2/kg/min)

Rest VO_2 = 3.5 mL/kg/min

Total VO_2 = Horizontal VO_2 + Vertical VO_2 + Rest VO_2

Conversion Factor

1 mph = 26.8 m/min

(Heyward, 2006, p. 64, 68)

Appendix IV

Borg's Rate of Perceived Exertion Scale

6	No exertion at all
7	Extremely light
8	
9	Very light
10	
11	Light
12	
13	Somewhat hard
14	
15	Hard (heavy)
16	
17	Very hard
18	
19	Extremely hard
20	Maximal exertion

(Borg, 1982)

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