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The Validity of the Six Minute Walk Test in Determining VO_{2peak} in Cancer Survivors: A Pilot Study

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Abstract: Peak oxygen consumption (VO_{2peak}) is critical for developing and implementing an exercise prescription to guide a cancer survivor's rehabilitative exercise program, which will improve physiological and psychological values in cancer survivors. Many clinicians choose a submaximal protocol, the 6 Minute Walk Test (6MWT) to determine VO_{2peak}. The University of Northern Colorado Cancer Rehabilitation Institute's (UNCCRI) treadmill protocol is cancer-specific and accurately determines VO_{2peak}. **PURPOSE:** To determine the validity of VO_{2peak} obtained from the 6MWT compared to the VO_{2peak} obtained by the UNCCRI treadmill protocol. **METHODS:** 34 cancer survivors completed the UNCCRI treadmill protocol and the 6MWT in randomized order one week apart. VO_{2peak} derived from the four commonly used equations for the 6MWT were compared to VO_{2peak} obtained from the UNCCRI treadmill protocol. **RESULTS:** All four 6MWT's equation mean differences significantly underestimated VO_{2peak} compared to the UNCCRI treadmill protocol ($p < 0.001$). Cancer survivors also exercised at a higher intensity executing the UNCCRI treadmill protocol. **CONCLUSION:** The 6MWT significantly underestimates VO_{2peak}, inhibits cancer survivors from training at a higher intensity level, and should not be used in formulating an exercise prescription. Clinicians should utilize the UNCCRI treadmill protocol.

Keywords: *cancer, rehabilitation, VO_{2peak}*

INTRODUCTION

Cancer is a collection of diseases in which cells exhibit uncontrolled cell growth and development; it is among one of the leading causes of death in the world. In 2016 an estimated 1.7 million new cases of cancer will be diagnosed in the United States and 595,690 people will succumb to the disease; this translates to 1,630 Americans dying per day (American Cancer Society, 2016). However, there are nearly 15.5 million cancer survivors living today, and the number of cancer survivors will continue to increase to 20 million by 2026 (National Cancer Institute, 2016). Of those cancer survivors, many will suffer from negative side effects from both the cancer and cancer treatments.

Cancer requires long-term management and there is an exponential need for exercised-based rehabilitation interventions for cancer survivors (Spence, Heesch, & Brown, 2010). Research has affirmed that cancer rehabilitation programs, and specifically the use of exercise prescriptions, have been associated with prolonged survival and combats the negative side effects tied to cancer and cancer treatments (American Cancer Society,

2016). Commonly used as a baseline for post-rehabilitation comparisons, peak volume of oxygen consumption (VO_{2peak}) is used to determine an individual's overall fitness level and health status. Stevens, Kirby, Buckworth, Devor, and Hamlin (2007) utilized VO_{2peak} to train African American females with prehypertension. Using cardiorespiratory fitness, the ability of the body's circulatory and respiratory system to deliver necessary nutrients to the rest of the body during sustained exercise, Stevens et al. were able to compare cardiorespiratory fitness pre and post exercise intervention by training the females at 70% of their VO_{2peak} (Stevens et al., 2007). Likewise, VO_{2peak} is used in developing and administering individualized exercise prescriptions within the cancer population, as well as using percent of VO_{2peak} to regulate intensity. Training at a higher percent of VO_{2peak} elicits a greater intensity.

However, cancer rehabilitation is a growing field with the absence of common practice in cancer-specific standardized protocols. A frequently used protocol utilized in determining VO_{2peak} is the Six Minute Walk Test (6MWT). The 6MWT is infamous for underestimating

VO_{2peak}. Consequently, inaccurate uses of VO_{2peak} can be detrimental to exercise prescriptions due to inhibiting a CS from training at an accurate exercise intensity. By way of contrast, clinics such as the University of Northern Colorado Cancer Rehabilitation Institute (UNCCRI) utilize a treadmill protocol, to obtain a more accurate VO_{2peak} used in exercise prescriptions. Training at an accurate exercise intensity maximizes the physiological benefits from exercised-based prescription training. Therefore, the purpose of this present study is to determine the validity of VO_{2peak} obtained from the 6MWT compared to the VO_{2peak} obtained by the UNCCRI treadmill protocol in working with cancer survivors.

REVIEW OF LITERATURE

Side effects related to cancer and cancer treatments include fatigue, depression, cachexia, decreased quality of life (QOL), and most commonly, cardiovascular diseases (Schneider, Hsieh, Sprod, Carter, & Hayward; Shackelford et al., 2015; Yusuf, Razeghi, Yeh, 2008). Due to diminished cardiovascular capabilities, many cancer survivors also have poor cardiorespiratory function (Myers, O'Neil, Walsh, Hoffmeister, Venzon, & Johnson, 2015). Common symptoms of decreased cardiorespiratory capabilities include wheezing, dyspnea, and shortness of breath (Myers et al., 2005; Raber-Durlacher et al., 2012; Sarna et al., 2004). Lacking the ability to efficiently exchange gases between the heart and lungs further hinders one's cardiovascular capabilities. Cardiorespiratory function and fitness are as influential as the traditional risk factors in cardiopulmonary disease, and is often more strongly associated with mortality (Lee, Artero, Sui, & Blair 2010). One approach to examine cardiorespiratory function is to measure chronic physical activity. By measuring chronic physical activity, physicians can assess how healthy an individual is based on their cardiovascular and respiratory function and efficiency. Clinicians have explored ways to reverse side effects of cancer and cancer treatments such as fatigue and cachexia, increase aspects of cardiovascular capabilities, and increase the QOL for cancer survivors. One way

to increase a cancer survivor's QOL is through exercise-based cancer rehabilitation programs. Cancer rehabilitation encompasses many aspects, all which seek to assist individuals who experience, or are likely to experience disability, to achieve and maintain optimal functioning within the limits imposed by disease and its treatment (Cromes, 1978; Handberg, Lomborg, Nielsen, Oliffe, & Midtgaard, 2015). According to the American Cancer Society (2016), the 5-year survival rate for individuals diagnosed with cancer from 2005-2011 was 69%, which has increased from the 49% survival rate from 1975-1977. The increase survival rate can be attributed to advanced treatments, earlier detection, and the implementation of cancer rehabilitation programs (Shackelford et al., 2015; Thijs et al., 2012).

The majority of cancer rehabilitation clinics, such as UNCCRI, promotes exercise-based cancer rehabilitation through prescriptive exercise. UNCCRI utilizes numerous factors such as, but not limited to: type of cancer, age, medication, treatments, treatment related side-effects, and cardiovascular related functions to create an individualized exercise prescription to help combat the negative side effects resulting from cancer and cancer treatments.

Cancer rehabilitation is a rapidly emerging and evolving medical field in both Europe and the United States, largely because of increases in rates of cancer survival (Stubblefield et al, 2013). However, with the lack of foundation preceding the push for cancer rehabilitation, there seems to be no universal standard protocol among cancer facilities for composing an exercise prescription. In writing an exercise prescription, commonly used assessments for establishing baselines for post-rehabilitation comparisons are muscular strength and endurance, balance, flexibility, and cardiovascular endurance. Cardiovascular exercises play a paramount role in a well-formulated exercise prescription, and cardiovascular exercises can vary from clinic to clinic. According to the National Academy of Sports Medicine (2013), to develop a complete program, the health and fitness professional must assess the client, create a program with specific

goals, and then apply a tool (such as a heart rate measurement) to evaluate the client's training success. An accurate and proper exercise prescription will produce improvements in aerobic fitness, muscular strength, and overall QOL (Ardic, 2014). In addition, exercise prescriptions can potentially prevent some types of cancer and reduce risk of cancer recurrence and cancer-related death (Leiserowitz & Watchie, 2011).

For rehabilitation clinicians to make an adequate program for a client, many initial tests need to be performed, and cardiopulmonary values are required. Blood lactate levels, percent of oxygen saturation, and maximum volume of oxygen consumption (VO_{2max}) are cardiopulmonary values factored into producing an exercise prescription for a client. VO_{2max} is measured via a maximal cardiopulmonary test. The value obtained from VO_{2max} measures the ability of the body to deliver oxygenated blood to active skeletal muscle for ATP re-synthesis after glycogen has been depleted from the active muscle. A higher VO_{2max} value indicates an overall healthier individual. To measure a VO_{2max} value directly, a metabolic cart is necessary. The metabolic cart has been deemed the gold standard in determining VO_{2max}, which uses gas analysis to quantify the amount of oxygen consumed against the amount of carbon dioxide produced. VO_{2max} tests requires an individual to exert themselves to the point of exhaustion, having a respiration exchange ratio (RER) of 1.15 or greater and blood lactate greater than 8 mmol⁻¹. VO_{2max} tests are generally designed for the presumed healthy population, and do not typically cater to the chronically diseased population. Factors such as the expense of the equipment, the lack of trained personnel, physical limitations, minimal motivation, and persistent fatigue, may not make a VO_{2max} test feasible or valid for chronically diseased populations (Jones, Haykowsky, Joy, & Douglas, 2008; Pina & Karalis, 1990; Shackelford et al., 2015; Stone, Lawlor, Nolan, & Kenny, 2011).

VO_{2peak} can be defined as the highest level of oxygen consumption achieved during a graded treadmill test, regardless of whether maximum

criteria are met (Heyward & Gibson, 2014). VO_{2peak} is often used as a cardiopulmonary value for chronic diseased populations, such as CS, to determine and evaluate one's cardiopulmonary system. It has been observed that there is no significant variability in the values of VO_{2peak} compared to VO_{2max} (Coquart et al., 2014; Jones et al., 2011). Tests utilizing VO_{2peak} are generally used with chronic diseased populations because VO_{2peak} protocols are generally less taxing on the participant and requires minimal equipment. In fact, it has been observed that there are no significant differences in final VO₂ values between a VO_{2peak} and a VO_{2max} test (Day, Rossiter, Coats, Skasick, & Whipp, 2003; Eldridge, Ramsey-Green, & Hossack, 1986; Hawkins et al., 2006; Howley, 2007; Jones et al., 2011).

There are numerous exercise protocols that measure VO_{2peak} directly or indirectly, such as the Bruce treadmill protocol (BTP) (Pinkstaff et al., 2011) and the Six Minute Walk Test (6MWT) (Fuentes et al., 2014). The BTP has been deemed a valid and accurate measurement of VO_{2peak} (Akinpelu et al., 2014). The BTP uses equations from the American College of Sports Medicine's running and walking equations during the multi-stage treadmill protocol to estimate VO_{2peak} (American College of Sports Medicine, 2013; Heyward & Gibson, 2014). Treadmill protocols, such as the BTP, are more applicable for the presumed healthy populations, such as athletes, and do not cater to the specific needs of the chronically diseased population. The BTP increases in speed and incline very rapidly, and for an individual to keep up with the demands of the rigorous stages in the BTP, muscular strength of the participant is also required. During these intense treadmill protocol tests, CS may fatigue quicker due to reasons other than cardiovascular, or may have an increased risk of injuring themselves trying to complete the protocol due to the negative side effects of cancer and cancer treatments. Research has shown up to 50% of cancer patients suffer from cancer cachexia, a progressive atrophy of adipose tissue and skeletal muscle, resulting in weight loss, a reduced QOL,

and a shortened survival time (Tisdale, 2009). The degeneration of skeletal muscle can contribute to the reason cancer survivors cannot advance far in demanding treadmill protocols such as the BTP.

With the accumulation of cancer treatments and the cancer itself, cancer survivors are less likely to achieve accurate VO_{2peak} values from apparently healthy treadmill protocols. Protocols such as the BTP, with greater increments in magnitudes between stages, can result in an overestimation of VO_{2peak} , and show greater variability (Bader, Maguire, & Balady, 1999; Shackelford et al., 2015). Researchers have also found that although the BTP is a valid way to calculate VO_{2max} in above average athletic populations between 20 and 40 years of age, it overestimates VO_{2max} by $4 \text{ mL}\cdot\text{kg}^{-1}\cdot\text{min}^{-1}$ in chronic diseased populations (Pollock, Foster, Schmidt, Hellman, Linnerud, & Ward, 1982). It stands to reason the BTP is not a suitable protocol to estimate VO_{2peak} in chronically diseased populations, particularly in cancer survivors. On the opposite end of the spectrum regarding VO_{2peak} protocols, there is the 6MWT. The 6MWT is one of the most familiar cardiovascular tests used with chronic diseased populations (cardiac and pulmonary) for VO_{2peak} or with the geriatric population for distance (American Thoracic Society, 2012). Using the 6MWT with regards to distance, is a prognostic value and is effective to exhibit progress from prescribed interventions. The 6MWT is utilized, owing to the fact the protocol is very untroublesome, inexpensive, and due to the belief that the geriatric population, as well as the chronic diseased populations cannot sustain higher intensities while exercising. During the 6MWT, a participant walks a designated hallway spanning a specified number of meters, usually 100 meters, at any pace they deem suitable for a six-minute period. The participant may also dictate when he or she would like to slow down and/or stop during the test. The distance the participant ambulates in meters during the six minutes is factored into equations to determine VO_{2peak} . However, the 6MWT has been shown to greatly underestimate VO_{2peak} . Comparing VO_{2peak} values derived from the

6MWT and a portable metabolic cart, the 6MWT underestimated VO_{2peak} by 20% compared to a metabolic cart (Faggiano et al., 1997). According to Cahalin et al. (1996), the 6MWT is inferior to other measures, such as bicycle ergometer exercise testing, in predicting long-term survival in cancer patients. An accurate measure of VO_{2peak} in creating a beneficial exercise prescription is essential. Variability in overestimation and underestimation of VO_{2peak} can do potentially more harm than good. Overtraining can cause numerous changes in immunity that possibly reflects physiological stress and immune suppression (Gholamnezhad et al., 2014), while undertraining can decrease an already inadequate fitness level. As VO_{2peak} also evaluates cardiovascular abilities such as the intensity that can be sustained, training at an inaccurate intensity level can limit the benefits of physiological responses to chronic resistance training while following an exercise prescription (Hickson et al., 1985).

Until recently, there was no standard way to assess a cancer survivor's VO_{2peak} effectively without the use of a metabolic cart. To alleviate this problem, UNCCRI created a treadmill protocol specific for cancer survivors. Unlike the BTP, the UNCCRI treadmill protocol increases intensity at a moderate and more manageable rate. The gradual increases in magnitude allows not only for a much safer cardiopulmonary endurance test, but also allows cancer survivors to advance further in the protocol to elicit a more accurate VO_{2peak} value. The correlation between the UNCCRI treadmill protocol and a metabolic cart in predicting VO_{2peak} was very high ($r = 0.93$; Shackelford et al. 2015). Literature has shown that the UNCCRI treadmill protocol is the most accurate treadmill test next to a metabolic cart in determining VO_{2peak} in cancer survivors (Shackelford et al., 2015).

Compared to the widely used BTP which can overestimate VO_{2peak} , there has been minimal research done on the accuracy of the 6MWT with cancer survivors, which is hypothesized to underestimate VO_{2peak} . Submaximal VO_2 prediction such as the 6MWT, are generally

outperformed by peak workloads, like the UNCCRI treadmill protocol. A submaximal VO₂ is derived from steady-state exercise (Loe, Nes, & Wisløff, 2016), whereas peak workloads are obtained at the optimal amount of effort exhausted at a given exercise bout. The 6MWT is prevalent as a submaximal cardiopulmonary test to assess the outcome measure in exercise rehabilitation due to its simple nature (Alison et al., 2012). The purpose of this present study was to determine the validity of VO_{2peak} obtained from the 6MWT compared to the VO_{2peak} obtained by the UNCCRI treadmill protocol for cancer survivors. It was hypothesized that the 6MWT would underestimate VO_{2peak} in cancer survivors, leading to a lesser exercise intensity, which would further substantiate the UNCCRI treadmill protocol as the standard cardiopulmonary exercise protocol for VO_{2peak} in the cancer population.

METHOD

Participants

Participants for this study ($N = 34$) included clients who were currently enrolled in UNCCRI's program. Participants met the following criteria: (a) diagnosed with cancer, (b) at least 18 years of age, (c) absence of severe cardiorespiratory difficulties, such as chronic obstructive pulmonary disease, (d) and or severe arterial hypertension (resting systolic blood pressure >200 mmHg, resting diastolic blood pressure 110, or both). Potential participants' oncologists or physicians faxed medical histories directly to UNCCRI. All clients training at UNCCRI signed an informed consent, agreeing to engage in research for the institute upon entering the program. Over the course of four months, all clients of UNCCRI who entered the rehabilitation program took part in this study; as well as clients who were already training at UNCCRI and wanted to participate in the study. Before engaging in the study, a detailed explanation was given on the protocols and what was expected from the participant. Upon demonstrating they understood the tasks being asked of them, participants engaged in both the UNCCRI treadmill protocol and the 6MWT during two of

their upcoming training sessions. The protocols used in this study had been approved by the University of Northern Colorado's Institutional Review Board.

Procedures

Within a two-week period, the participants either completed the 6MWT or the UNCCRI treadmill protocol during week one, and then completed the other protocol during the following week. For the UNCCRI treadmill protocol, an explanation stated that this was a test used to measure VO_{2peak}, and the participants should try to reach their self-perceived maximum threshold of fatigue; when they reached exhaustion, the test was concluded. Participants were encouraged not to use the handrails during the test, but if they did choose to use the handrails, they would have to grasp the handrails from the start of the protocol to the termination of the protocol. Participants were also informed that they would be asked their Rating of Perceived Exertion (RPE) every three minutes during the test. Additionally, a 3M™ Littmann® Classic II SE Stethoscope with Prestige Medical Basics Sphygmomanometer Kit was used on the participant's arm to take blood pressure every three minutes, a Clinical Guard® pulse oximeter was on the participant's finger to read oxygen saturation every minute, and a Polar® heart rate monitor was strapped to each participant's chest to measure heart rate every minute. Subsequently, once each patient reached their perceived maximal exertion, a cool-down period was administered to lower their vitals close to resting measures. The test concluded when: (a) participants could no longer keep up with the demand of work needed to keep up with the treadmill protocol stage; (b) participants' heart rate or systolic blood pressure did not increase with increased intensity; (c) diastolic blood pressure varied more than 10 mmHg from resting measures; (d) oxygen saturation dropped below 80%; and/or (e) participants felt the need to stop due to any safety issues. Once participants understood what was being asked of them, the test began.

The UNCCRI treadmill protocol required at least three trained Cancer Exercise Specialists, (CES) to be present during the test. A CES was in charge of increasing the treadmill intensity every minute to the appropriate speed and grade. This same CES was in charge of using the Clinical Guard® pulse oximeter to record heart rate and oxygen saturation. The second CES was in charge of taking the client’s blood pressure on the treadmill. The third CES was in charge of spotting the participant, and observing any signs of distress, indicators of safety and or health problems. After the test concluded each participant was given a guided cool-down. During the cool-down, oxygen saturation and heart rate were taken every minute. Every three minutes during the cool-down period RPE and blood pressure were also taken. Once the values reached near resting measures, the treadmill was stopped, and the test was terminated. A final heart rate measurement was taken at the conclusion of the test. VO_{2peak} was calculated using the American College of Sports Medicine's running/walking equations: (a) the last stage the cancer survivor successfully completed, (b) if the individual was running or walking at the termination of the protocol, (c) and if the individual was holding onto the treadmill handrails (Appendix B). The equations to derive VO_{2peak} by the UNCCRI treadmill protocol are as follows:

- Cancer survivor walking at the termination point of the test without the use of handrails:

$$VO_{2peak} = (0.1 \times S) + (1.8 \times S \times G) + 3.5$$

- Cancer survivor walking and holding onto the handrails at the termination of the test:

$$VO_{2peak} = 0.694 [(0.1 \times S) + (1.8 \times S \times G) + 3.5] + 3.33$$

- Cancer survivor running at the termination of test without the use of handrails:

$$VO_{2peak} = (0.2 \times S) + (0.9 \times S \times G) + 3.5$$

- Cancer survivor running and holding onto the handrails at the termination of the test:

$$VO_{2peak} = 0.694 [(0.2 \times S) + (0.9 \times S \times G) + 3.5] + 3.33$$

(S, Speed in meters/min; G, grade of treadmill in %)

Alternatively, the 6MWT required very little equipment. The 6MWT was conducted in a 12.6-meter-long hallway at UNCCRI. There were two chairs, one at both ends of the hallway, with a cone placed one foot in front of each chair indicating the end of the walkway. The participants were told prior to the test that the goal was to walk as far as possible in the six-minute time period. If at any time participants felt the need to stop and or sit down at any point during the test they could do so at either end of the hallway. Slightly different from the American Thoracic Society (ATS) 6MWT protocol guidelines, participants were notified at three minutes that the test was half-way completed, and at five minutes that there was only one-minute remaining, opposed to being warned every minute that had elapsed. During the test, verbal encouragement was given, such as “Great Job.” The participants were reminded they were able to sit and rest when signs of distress appeared. Signs of distress include excessive sweating, heavy breathing, and dizziness. Once the six minutes came to an end, the ambulated distance in meters, rate pressure product (max heart rate* max systolic blood pressure), final blood pressure, and heart rate were measured using the Clinical Guard® pulse oximeter and the Polar® heart rate monitor were recorded. The forced expiratory volume and forced vital capacity (volume/liters) were measured by the MIR Spirolab III Portable Desktop Spirometer®. Along with the forced vital capacity and forced expiratory values, weight (kg), height (cm), and other values were obtained from the participants’ initial or reassessment using the InBody770®. The 6MWT equations are as follows:

- Equation 1: $VO_{2peak} = 0.03 \times \text{distance (m)} + 3.98$
- Equation 2: $VO_{2peak} = 0.02 \times \text{distance(m)} - 0.191 \times \text{age(year)} - 0.07 \times \text{weight(kg)} +$

$$0.09 \times \text{height(cm)} + 0.26 \times \text{RPP} \times 10^{-3} + 2.45$$

- Equation 3: $\text{VO}_{2\text{peak}} = 0.02 \times \text{distance(m)} - 0.14 \times \text{age(year)} - 0.07 \times \text{weight(kg)} + 0.03 \times \text{height(cm)} + 0.23 \times \text{RPP} \times 10^{-3} + 0.10 \times \text{FEV}_1 \text{ (L)} - 1.19 \times \text{FVC (L)} + 7.77$
- Equation 4: $\text{VO}_{2\text{peak}} = 4.948 + 0.023 * \text{distance (m)}$

(RPP, Rate Pulse Pressure; FVC, Forced vital capacity; FEV₁, Forced expiratory volume in 1 second) (see Appendix A).

Statistical Analysis

The VO₂peak values from the four 6MWT equations were compared to the UNCCRI treadmill protocol VO₂peak value by a repeated measures ANOVA test using the IBM Statistical Package for the Social Sciences 23. The repeated measures ANOVA test examined any differences in the 6MWT’s ability to determine VO₂peak compared to the UNCCRI treadmill protocol. Paired T-tests were used to compare the differences in mean systolic and diastolic blood pressure values, and heart rate for the 6MWT compared to the UNCCRI treadmill protocol. Lastly, a Pearson *r* correlation was used to see if there was an appropriate correlation between equation three from the 6MWT compared to the UNCCRI treadmill protocol VO₂peak. Equation three was elected for the Pearson *r* correlation by virtue of possessing the most variables, eliciting the most accurate and individualized VO₂peak. The significance for each of the analysis was set at *p* < 0.05.

RESULTS

Table 1 displays the mean significant differences for VO₂peak calculated using the four 6MWT equations against the UNCCRI treadmill protocol. All 6MWT equations significantly underestimated VO₂peak compared to the UNCCRI treadmill protocol (*p* < 0.001). Table 2 displays the averages for heart rate, systolic and diastolic blood pressure recorded during each protocol. There was a significant difference in the heart rate and systolic blood pressure between the 6MWT and the UNCCRI treadmill protocol (*p* < 0.001)

collectively, while there was no significant difference in diastolic blood pressure between the two groups (*p* = 0.874). Figure 1 displays the correlation (*r* = 0.86) between the VO₂peak value from the UNCCRI treadmill protocol and equation three from the 6MWT. The average time for a cancer survivors engaging in the UNCCRI treadmill protocol was 10:45 (minutes, seconds), while the average distance for the 6MWT was 485 meters.

Table 1. Mean differences of the 6MWT equations compared to the UNCCRI treadmill protocol

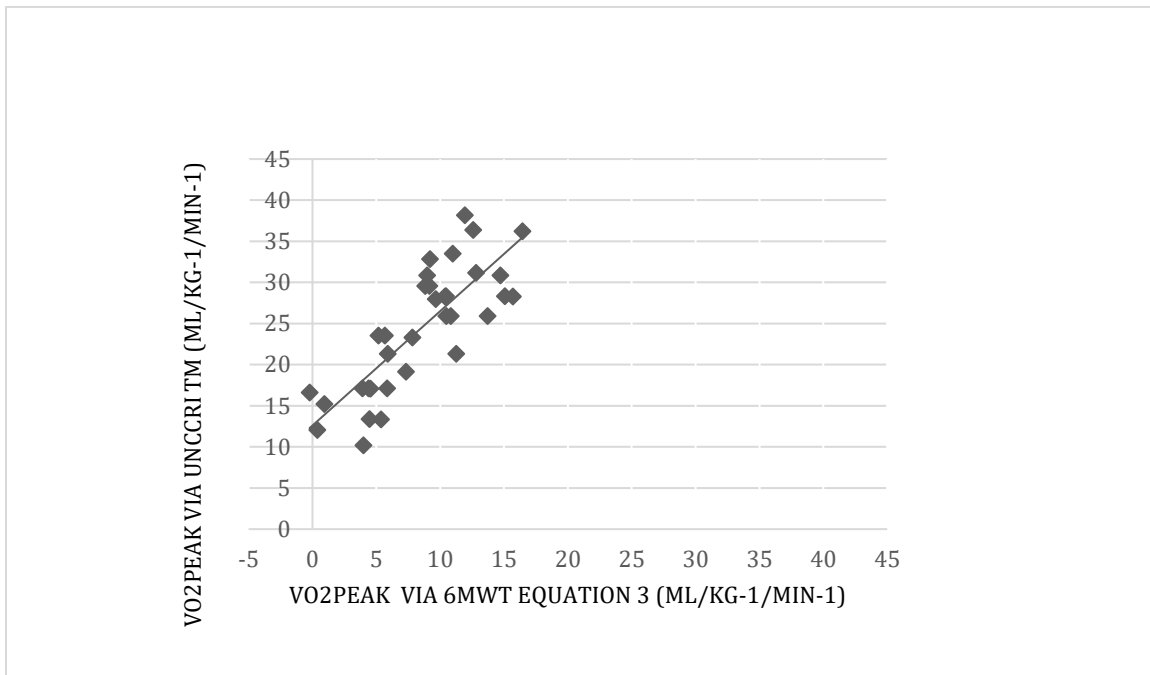
	VO ₂ Peak (mL/kg-1/min-1)	Mean Difference (mL/kg-1/min-1)	<i>p</i> -value
UNCCRI TP	24.4		
Equation 1	18.3	6.2	<0.001
Equation 2	14.2	10.2	<0.001
Equation 3	8.5	15.9	<0.001
Equation 4	15.9	8.3	<0.001

Note: UNCCRI TP = University of Northern Colorado Rehabilitation Institute Treadmill Protocol

Table 2. Average peak heart rate, systolic blood pressure, and diastolic blood pressure of the UNCCRI Treadmill Protocol compared to the 6MWT

	UNCCRI treadmill protocol	6MWT	<i>p</i> -value
Avg. heart rate (bpm)	150.6	111.9	<0.001
Peak systolic blood pressure (mmHg)	143.8	138.7	<0.001
Peak diastolic blood pressure (mmHg)	77.3	75.4	<0.874

Figure 1. Correlation between the 6MWT equation 3 and UNCCRI treadmill protocol VO_{2peak} values



DISCUSSION

The present study examined the validity of the 6MWT compared to the standard UNCCRI treadmill protocol in determining cancer survivors' VO_{2peak} . As hypothesized, the 6MWT significantly underestimated VO_{2peak} in cancer survivors. This hypothesis was supported when the mean difference between UNCCRI treadmill protocol and equations 1, 2, 3, and 4 for the 6MWT had a significant mean difference ($p < 0.001$) compared to the UNCCRI treadmill protocol. With the consistent underestimation of VO_{2peak} in each of the 6MWT equations, the commonly used 6MWT does not appear to be a reliable nor an accurate way to obtain VO_{2peak} in cancer survivors for the use in an exercise prescription. Not only accuracy of the protocol, but safety should also be an important consideration in protocol choice, as it will affect the efficacy and thereby the outcome measures of the exercise program implemented (Kirkham, Campbell, & McKenzie, 2013). The UNCCRI treadmill protocol was able to measure VO_{2peak} in the cancer survivors more accurately than the 6MWT. In addition to the significant underestimated mean differences in all four

6MWT equations, the 6MWT produced a significantly lower mean heart rate and mean systolic blood pressure than the UNCCRI treadmill protocol; the lower mean heart and mean systolic blood pressure is an indicator of a lesser intensity. Exercise intensity refers to the rate at which activity is being performed and the required amount of energy needed to sustain the particular effort. The increase in heart rate and systolic blood pressure during exercise is due to the increased demand of oxygen by active muscles throughout the body. The amount of oxygen needed by the muscles is directly related to the amount of oxygen consumed at a given moment. Accordingly, the peak volume of oxygen being consumed in the body establishes the intensity for a structured and formulated exercise prescription. The presence of intensity in a cancer rehabilitating intervention requires precision in its application to maximize its health benefits and to reduce risk of adverse events in cancer survivors (Kirkham et al., 2013).

Overall, clinicians utilize the 6MWT because it is less strenuous on individuals who may have a compromised cardiovascular system due to cancer and cancer treatments. Previous literature has

demonstrated that the UNCCRI treadmill protocol is a safe and accurate protocol for cancer survivors, and demonstrates cancer survivors can perform more vigorous protocols to establish a more valid VO_{2peak} value (Shackelford et al., 2015). Accurate VO_{2peak} values for exercise prescriptions are critical because the precise intensity in which an individual exercises can positively affect one's cardiovascular functions which are indicative of overall health, QOL, and a predictor of death. This study suggests the 6MWT is an inaccurate way to obtain VO_{2peak}, and therefore clinicians should not use the 6MWT in the cancer population. Instead, the UNCCRI treadmill protocol should remain the standard method of obtaining VO_{2peak} in cancer rehabilitation clinics and facilities.

Limitations and Future Directions

There were minimal limitations to this study. First, the sample size was fairly small. Having a larger number of participants could have strengthened the significant difference between the VO_{2peak} values. In addition to the participant's enrollment at UNCCRI, many of the participants had already partaken in the UNCCRI treadmill protocol for assessments and reassessments for the cancer rehabilitation program. Having being familiarized to the UNCCRI treadmill protocol could have primed the participants to do well in the UNCCRI treadmill protocol. Adversely with participants being unfamiliar with the 6MWT, therefore not obtaining accurate results from the 6MWT protocol. The unfamiliarity of the participants to the 6MWT did not seem to play a contributing role in the results, but is a factor to examine in the future. Lastly, one of the limitations of the study was that the VO_{2peak} from the 6MWT was compared to the very accurate VO_{2peak} value from the UNCCRI treadmill protocol and not compared to actual gas analysis. Even though the UNCCRI treadmill protocol is the most accurate treadmill protocol made specifically for cancer survivors to get VO_{2peak} and has a high correlation ($r = 0.93$) with gas analysis, it does not elicit identical values to gas analysis. For future studies, gas analysis needs to be incorporated to have an indefinite value to

compare VO_{2peak} from the 6MWT to for absolute accuracy.

For future research, a greater sample size is suggested, and not only from participants who currently train at UNCCRI. Having cancer survivors who do not train at UNCCRI to also partake in the UNCCRI treadmill protocol and the 6MWT would eliminate the experience factor, thus generating the most accurate results. Additionally, Dr. Larry Cahalin recommended comparing a linear regression for the most accurate 6MWT VO_{2peak} value with the UNCCRI treadmill protocol VO_{2peak} value (L. Cahalin, personal communication, March 31, 2016). The mean underestimation of VO_{2peak} by the 6MWT could aid in making a correction equation for the 6MWT equations to be more valid way to obtain VO_{2peak} like the highly accurate UNCCRI treadmill protocol.

CONCLUSION

The number of cancer survivors are increasing, controversially are often left coping with adverse side effects from both the cancer and cancer treatments. Side effects related to cancer and cancer treatments include fatigue, depression, cachexia, decreased QOL, and, most commonly, cardiovascular diseases. The plethora of negative side effects that are coupled with cancer not only effects one's physical health, but their mental health as well. Previous literature has demonstrated cancer rehabilitation programs have reversed and minimized the negative side effects from cancer and cancer treatments (Spence et al., 2010). Extremely effective cancer rehabilitation programs use an individualized exercise prescription to aid cancer survivors in returning to their normal functioning capabilities pre-cancer diagnosis. To have an effective exercise prescription, accurate cardiopulmonary values such as VO_{2peak} are needed to train patients at a precise intensity level to maximize the benefits from chronic endurance training. Chronic endurance training benefits the cardiopulmonary system and ultimately improves overall QOL. Based on the findings of the present study, the 6MWT is not an accurate/valid measure of

VO₂peak, which may limit physiological benefits. Therefore, the treadmill protocol should remain the standard. As a result of VO₂peak values being a critical component in exercise prescription and intensity, inaccurate measures may limit the physiological benefits of chronic exercise training (Hickson et al., 1985). The UNCCRI treadmill protocol should remain the standard protocol to determine VO₂peak in cancer survivors for the use of an exercise prescription.

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