A RESTROSPECTIVE EVALUATION OF THE ESTIMATION OF VO_{2max} IN INDIVIDUALS WHO ATTAIN PEAK VERSUS INDIVIDUALS THAT ATTAIN MAX DURING A CPET USING A DYNAMIC SYSTEMS MODEL

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ABSTRACT

Kerry Martin: A Retrospective Evaluation of the Estimation of VO_{2max} in Individuals Who Attain Peak Versus Individuals That Attain Max During a CPET Using a Dynamic Systems Model
(Under the direction of Claudio Battaglini)

Due to uncertainty in maximal oxygen uptake (VO_{2max}) determination from a traditional cardiopulmonary exercise test (CPET), dynamic systems models (DSMs) may be used to predict or confirm VO_{2max}. The purpose of this study was to use a DSM to predict VO_{2max} and to compare the difference between individuals who reached maximal criteria (MAX) versus individuals who did not (PEAK). A retrospective analysis was performed on nine male individuals who performed a cycle ergometer CPET. Oxygen uptake, stage power, and fixed cadence values from a CPET were used in the DSM to predict VO_{2max}. Despite a trend to predict VO_{2max} in both groups, there was a significant difference between predicted and obtained VO_{2max} in the MAX group ($p=.045$), and no significant difference between experimental VO_{2peak} and predicted VO_{2max} in the PEAK group ($p=.13$). This study demonstrates the necessity of power and cadence when using a DSM to predict VO_{2max}.

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CHAPTER I

Introduction

The assessment of maximal oxygen uptake (VO_{2max}) using a cardiopulmonary exercise test (CPET) is the gold standard method for the assessment of cardiopulmonary function. It is defined as the maximum amount of oxygen that the body can uptake and utilize during vigorous exercise (Hill & Lupton, 1923). Many times, the results from a cardiopulmonary exercise test (CPET) can be translated into exercise training prescription, quantify and predict aerobic activity performance, and be used as a determinant of health status or mortality risk (Albouaini, Egred, & Alahmar, 2007). Furthermore, VO_{2max} is considered by many experts to be the single-best measurement of overall fitness.

There are many physiological factors that affect VO_{2max} and VO_2 kinetics, such as cardiovascular, pulmonary, and skeletal muscle factors, as well as ambient conditions. However, the culmination of all of these factors yields the final oxygen consumption measurement as a simple number. That is to say that oxygen consumption is a metric that is an indicator for capacity to utilize oxygen, but does not directly reflect differences in individuals' physiological responses during the test (e.g. a-vO_2, hematocrit, etc.). Results that are obtained from a CPET are often used to measure aerobic performance, especially in endurance aerobic activities, such as running or cycling. In a study performed by Noakes et al., VO_{2max} was found to be a strong predictor of running performance in the marathon (Noakes, Myburgh, & Schall, 1990).

In addition to being an indicator of fitness, it is often used for training and exercise prescription, offering a more accurate definition of training intensities than the commonly used heart rate training zones. Often times, training prescription is expressed as a percent of VO_{2max} or percent of VO_2 reserve. When extrapolated from a VO_{2max} test, corresponding workloads to oxygen consumption values may be prescribed using HR or workloads as a percent of VO_{2max}. This allows exercise physiologists to control the dose-response of an individual's exercise session more accurately, which is commonly used in research settings and high-performance athletic training; this is very important when attempting to maximize an adaptation from training known as a training response.

The VO_{2max} measurement has also been used as a determinant for physical wellbeing. Results of a CPET can be used to identify different cardiopulmonary abnormalities that may indicate a clinical disease (Neuberg, Friedman, Weiss, & Herman, 1988), stratify individuals for risk of cardiac events (Albouaini et al., 2007), predict mortality of cancer patients (Wood et al., 2013; Jones et al., 2010; Sawada et al., 2003) as well as many other clinical applications. Despite the value of a CPET in clinical populations, the assessment of VO_{2max} is seldom obtained due to its complex nature, expensive equipment, and the necessity of specialized personnel to administer the test.

When maximal exercise tests are performed, there are predetermined criteria that are analyzed after the test to determine if the individual who underwent the test was able to attain VO_{2max}. The American College of Sports Medicine suggests the following five criteria for the determination of a true VO_{2max}: blood lactate concentration greater than 8.0mmol/L, rating of perceived exertion equal to or greater than 17 on the Borg 6-20 RPE scale, a maximally obtained heart rate that is within 10 beats per minute of the age-predicted maximum heart rate, a respiratory exchange ratio greater than or equal to 1.15, and a failure to see a rise in VO_2 when workload is increased (plateau); if at least three of the aforementioned criteria are met, the individual is considered to have attained a "true" VO_{2max} (American College of Sports Medicine, 2014). It is not uncommon to see a failure to reach the predetermined criteria; in these scenarios, the highest VO_2 value is said to be the peak oxygen uptake (VO_{2peak}). The VO_{2peak}, although the highest VO_2 an individual could attain during the test, is not thought to be the highest VO_2 that the subject can physiologically achieve (true VO_{2max}). This is more often the case in untrained individuals when fatigue sets in prior to exhausting the cardiovascular and pulmonary systems.

Failing to reach a "true" VO_{2max} means different implications for post-testing inferences. Within the context of research studies, if individuals or populations (e.g. clinical populations) fail to reach a true maximal value, the acceptance of the result of the CPET may undermine the usefulness of such an important physiological parameter for the prescription of exercise training (i.e. the prescription would most likely be underestimated) or for the prognostication for treatment complication and mortality. In other words, in training studies, participants may be failing to exercise at intensity high enough to maximize positive changes in cardiopulmonary capacity large enough to be clinically relevant.

To date, there has been little research to attempt to model oxygen kinetics in an individual-specific manner in an attempt to predict VO_{2max}. Stirling, a biological mathematician, produced an equation that is a function of exercise demand, VO_{2max}, resting VO_2, and subject-specific parameters (Stirling, Zakynthinaki, & Saltin, 2005). At the time, the demand function was unknown, thus the modeling was done in fixed-demand (steady state) scenarios, but still was able to capture on- and off-transient oxygen kinetics. Since individuals of different fitness levels have different transient responses to steady state exercise, the subject-specific parameters are adjusted to the individual to best fit the model.

Continuing off of this model, Mazzoleni and colleagues were able to produce a demand function that was based on cycling power and cadence to adjust for a dynamic system, as opposed to steady-state (Mazzoleni, Battaglini, Martin, Coffman, & Mann, 2016). In this correction, the equation is able to adapt to continuously changing power and cadence, making the equation able to predict oxygen kinetics from power, cadence, and the subject-specific parameters. Once power, cadence, and the resulting oxygen kinetics are known, the equation can be solved using a process of best-fit known as a genetic algorithm to solve for the subject-specific parameters. From there, VO_{2max} may be estimated using the subject-specific parameters, which produces accurate estimations of the "true" maximal oxygen uptake capacity of an individual.

Since the model is able to adapt the parameters to each individual's physiological response to exercise, it may be beneficial to use this model to detect what the physiological capabilities are of the individual being tested. In cases where the VO_{2max} is met but a peak VO_2 is attained, the model may be used to detect what the true VO_{2max} is based on the individual physiological response. In cases where max is reached, a valid model could be used to confirm a true VO_{2max}, not relying on the maximal criteria that are currently used.

Statement of Purpose

The purpose of this preliminary study was to evaluate the use of a dynamic systems model to compare predicted VO_{2max} values to VO_{2max} values obtained from a CPET, and to see if the model can detect the true VO_{2max} of individuals who did not reach maximal criteria.

Research Question

Can using a dynamic systems model, shown to accurately predict VO_{2max} in individuals that are able to attain a true VO_{2max} during a CPET test (Manuscript in preparation for publication), confirm VO_{2max} in individuals who reached maximal criteria during a CPET, as well as predict VO_{2max} in individuals who do not attain maximal criteria during a CPET?

Hypotheses

H_0: There will not be a difference between VO_{2max} estimated using dynamic systems modeling and VO_{2max} obtained during the maximal cardiopulmonary exercise test in individuals that did meet the maximal test criteria.

H_1: VO_{2max} estimated by the model from the CPET will be significantly higher than the peak VO_2 obtained during the CPET in individuals that did not meet the maximal test criteria.

Assumptions

- The subjects were motivated to achieve maximal effort during the VO_{2max} test.
- The pre-assessment guidelines have been followed and truthfully answered during pre-testing questioning.
- All subjects have similar experience with exercise and cycling ergometers.

Limitations

- Results will be generalizable only to a young and healthy male population.
- The mathematical model is only valid under the laboratory environmental conditions under which the tests were held.

Delimitations

- Subjects are being used from a study that is limiting subjects to males in order to understand the heart rate response to exercise in the absence of menstrual cycle fluctuations.
- Caffeine consumption was prohibited 24 hours prior to testing to limit diuresis and cardiovascular stimulation.
- Subjects are limited to 18-35 years old and must be cleared by a physician.

Definition of terms

- VO_{2max} – the maximum amount of oxygen able to be utilized by exercising tissues, adjusted for body mass and expressed in ml/kg/min.
- VO_{2peak} – the highest amount of oxygen that the individual was able to consume before during termination of a test that does not meet three of the five criteria for a maximal test.
- CPET – Cardiopulmonary Exercise Test
- Dynamic Systems Model – a model using differential equations to determine oxygen kinetics
- Genetic Algorithm – a process of best fit, where random parameters are tested and assessed for best fit. Parameters deemed fit move to the next generation; the process continued for many generations.

Significance of the Study

It is common when administering a CPET to individuals who are not cycling-trained or are considered to have low fitness level, to result in a failure to reach a true physiological maximum, mainly due to these individuals' inability to pedal at higher workloads without fatiguing prematurely. Many of the maximal criteria that are currently used are heavily debated, and are subject to arbitrary cutoff values. When using a mathematical model that predicts VO_{2max} from individuals' physiological responses, it may be possible to detect if the peak VO_2 value obtained in a CPET is or is not the 'true' VO_{2max}, due to the mathematical model's ability to identify individual transient physiological responses during the test, allowing for the most probable estimation of a maximal response at the end of the bout of the exercise test.

By having a model that can detect an individual's 'true' VO_{2max}, the model could be applied using data from a peak VO_2 test to provide a true max estimation, which would provide better means for using the results of a VO_{2peak} test in many different applications. This would eliminate any uncertainty if the test were a true maximal test or not. Ultimately, this model could be a criterion for maximal tests, either in addition to current criteria, or in place of them.

CHAPTER II

Review of Literature

Cardiorespiratory Function

The process of oxygen consumption is defined by the uptake, transport, and utilization of atmospheric oxygen. During exercise, oxygen consumption increases due to increased reliance on aerobiosis to produce adenosine triphosphate (ATP). There are many processes associated with oxygen consumption, including: alveolar transport, binding of oxygen to hemoglobin, movement of the oxygen-rich hemoglobin to the target tissues, unloading of the hemoglobin, and utilization of oxygen in the mitochondria. These pathways are able to adapt to training, causing an increased ability to utilize oxygen during exercise. Similarly, any disease or condition that alters any of these components will cause a decreased capacity for oxygen consumption.

According to the Fick equation, oxygen consumption can be described as the product of cardiac output and the arteriovenous oxygen difference (Fick, 1870). This takes into account the ability to transport oxygen, as well as to uptake and utilize the oxygen. When increasing exercise demands, both cardiac output and a-vO_2 difference increase and contribute to meet the oxygen demand (De Cort, Innes, Barstow, & Guz, 1991; Skinner, McLellan, & McLellan, 1980). When muscular contractions occur to provide submaximal exercise movement, mostly type I muscle fibers are recruited, which have greater oxidative capacity than type II muscle fibers. The recruited type I fibers require a higher ATP turnover, which comes primarily through oxidative pathways in these tissues sub-maximally. This process converts the O_2 into CO_2, which causes a decline in pO_2 within the muscle. This decline in pO_2 allows for a greater concentration gradient for oxygen to unload in the capillaries. This allows a-vO_2 to increase upon increasing activity level.

Increase of cardiac output can be controlled in multiple different ways. Cardiac output is a function of stroke volume (SV) and heart rate (HR), which are typically under slightly different regulation. Norepinephrine secreted as a result of increased intensity stimulates the beta-adrenergic receptors, causing increased myocardial contraction and acceleration; thus, both HR and SV are increased to increase cardiac output. Stroke volume is also affected by the Frank-Starling mechanism, which is the phenomenon where increased venous return to the heart causes greater diastolic filling and slight myocardium stretching, which has been shown to increase the contractility of the myocardium. Additionally, HR has been shown to respond to increased hydrogen ions, potassium, and CO_2, all of which are metabolic byproducts of exercise. These are just a few factors that affect cardiac output, but these are very important, since much of the increase in VO_2 is typically thought to be through the cardiac output (De Cort et al., 1991).

However, at maximal efforts, both systems are thought to be at maximal capacity, yet there is disagreement about whether or not these systems are being fully taxed. Traditional cardiovascular theory has pointed to cardiac output being the limiting factor (González-Alonso & Calbet, 2003). More recently, evaluations of the limiting factors of VO_{2max} suggest that a-vO_2 difference may be the more important limiting factor. One study in horses demonstrated that erythropoietin usage in horses increased a-vO_2 in horses and VO_{2max}, despite a lack of increase in cardiac output, indicating that a-vO_2 difference may be the limiting factor in maximal oxygen uptake (McKeever, McNally, Hinchcliff, Lehnhard, & Poole, 2016).

By monitoring heart rate, lactate response, respiratory exchange ratio, and the oxygen consumption plateau effect, maximal efforts may be monitored and quantified. If aerobic activity is at or near maximum, heart rate should be maximized in order to maximize the cardiac output, allowing for greater oxygen transportation. If workloads are so high that type II fibers are being recruited heavily, blood lactate should also accumulate faster than it can be cleared, so lactic acid values should rise drastically. This lactic acid buildup causes the blood and tissues to become more acidic due to hydrogen ion buildup, which is countered by bicarbonate buffering in the blood. When these hydrogen ions combine with bicarbonate, formation of carbon dioxide occurs, which can be blown off. This excess carbon dioxide contributes to the RER rising well over a value of one, indicating a large anaerobic contribution. Lastly, oxygen consumption is thought only to increase to a certain point, at which aerobic cannot consume any more oxygen for ATP production. Reaching this point indicates the upward limit of cardiopulmonary function and aerobic contribution to exercise.

VO_{2max} Testing

Maximal oxygen consumption was a concept originally expressed by Hill and Lupton. Using bags to collect expired gas, they were able to quantify the average amount of oxygen that was consumed for different running stages. Each stage was completed by trained runners on a grass track and were discontinuous from one another. As speed increased, Hill and Lupton noticed an increase in oxygen consumption. However, the most notable was that there was a point at which no more oxygen was being consumed, despite an increased running speed. This eventually gave rise to the concept of the physiological maximum oxygen consumption, as well as the VO_2 plateau. Since this study, many exercise physiology studies have included this concept in different forms for different purposes.

VO_{2max} Versus VO_{2peak}

Many exercise physiologists determine whether or not a test was a true maximal effort by use of criteria. The traditional criterion from the study by Hill and Lupton is that a plateau in oxygen consumption should be attained to validate the physiological maximum. In a CPET, this would mean that oxygen consumption does not increase despite an increase in workload. While this is the traditional criterion, there have since been additional criteria that are set forth by the American College of Sports Medicine (ACSM). The ACSM criteria are a plateau in oxygen consumption, a blood lactate level greater than 8.0 mmol, a respiratory exchange ratio greater than 1.10, a rating of perceived exertion greater than or equal to 17 on the Borg 6-20 scale, and a heart rate maximum that is within 10 bpm of age-predicted maximum heart rate (220-age).

ACSM recommends that these criteria be used in conjunction; three or more criteria met indicates a maximal effort, whereas less than three criteria met indicates a peak effort. This peak (VO_{2peak}) is thought to indicate the highest value that the individual could achieve during that particular test, but may not be the highest possible VO_2 value that the individual can achieve physiologically. This is often times the case when subjects reach fatigue at a premature state, which has been theorized to be related primarily to peripheral fatigue.

Often times, VO_{2peak} and VO_{2max} are used interchangeably, which should not be the case. Using a peak value as a true maximal value will lead to undervaluing the importance of the statistic. When used as a way to prescribe exercise, a peak value will lead to a lower VO_2 reserve; in this case, exercise prescription may be less than desired, not reaching the proper dose-response of exercise. In training studies, this may potentially lead to under-valuing the protocol's efficacy in providing a training response. Additionally, in clinical studies using VO_{2max} cut-off values for health or survivorship interpretation, VO_{2peak} values would lower the cut-off. Since the physiological aerobic capacities are being inferred from the VO_{2max} values, then the VO_{2peak} values are not a good marker for a clinical cut-off. In these populations, it is most often a peak value that is being attained, since the individual may not be functionally strong enough to complete the test, fatiguing before the cardiopulmonary system has been completely utilized.

Effects of different types of CPET testing on determination of VO_{2max}

The aim of a CPET is to obtain the true physiological VO_{2max} to understand the physiological capabilities of an individual. Since Hill and Lupton's initial study on VO_{2max}, there have been many different protocols created for the sole purpose of obtaining the true VO_{2max}. Protocols may vary in the type of exercise, ramp rates, and whether or not the test is continuously graded. The selection of protocol has been shown to make a difference in VO_{2max} determination and evidence of maximal criteria, particularly the evidence of a VO_2 plateau.

A study conducted by Froelicher et al. demonstrated that different protocol methods yielded different VO_{2max} values (Froelicher et al., 1974). The comparison of protocols was between continuous protocols (Bruce and Balke) and discontinuous protocols (modified Taylor). Fifteen subjects completed each test a total of three times over 9 weeks, one of each test per three-week period where order was randomized. Results showed that the Bruce and Balke continuous protocols provided VO_{2max} values 6.5% and 9.7% lower than the discontinuous Taylor protocol. It was theorized that the 5 minutes of rest in between the exercise stages in the Taylor protocol allowed for heat dissipation, which allowed for less shunting of blood for thermoregulatory purposes. Regardless of mechanism, the findings of this study suggest that different protocols can provide different outcome measures. This is important when interpreting VO_{2max} values because these are all maximal tests for the purpose of determining the maximal oxygen uptake; however, the Bruce and Balke protocols provide lower values, despite maximal efforts. If these were to be used without the results of the discontinuous Taylor test, the subject's VO_{2max} values may be undervalued.

In order to better understand the effect of testing modalities on the ability to achieve maximal VO_2, Bassett and Boulay examined the VO_{2max} values obtained from running and cycling protocols in three different groups of athletes (Basset & Boulay, 2000). The groups were separated into trained runners, cyclists, and triathletes, consisting of six subjects per group. These groups represented the different levels of familiarity with the modalities used. The tests were both continuous ramp protocols designed to last a similar total duration of time-to-completion. In every group, regardless of familiarity, the treadmill CPET produced significantly higher VO_{2max} values than the cycling CPET. The difference in VO_{2max} between treadmill and cycling was largest in runners and least in the cycling group. These results indicate that the ability to achieve a true maximal effort depends on the modality of testing used, particularly for the athlete's specific abilities. Although the cyclist group performed the closest between the two tests, the treadmill test provided VO_{2max} values that were an average of 4.1 mlO_2/kg/min higher; despite being highly trained on a bicycle, a treadmill test still provided results that were higher. Since cycle ergometers are commonly used for CPET evaluation, it is important to note that the results from this kind of test may not be indicative of the true maximal physiological capability of the subject.

In addition to modalities causing different outcome measurements, a study by Kang et al. revealed that different protocols, all of which were continuous-ramp tests on a treadmill, may provide different VO_{2max} values for trained individuals (Kang, Chaloupka, Mastrangelo, Biren, & Robertson, 2001). The study consisted of untrained males, untrained females, and trained male runners. Tests were assigned in a random order and completed over three weeks. In untrained males and females, there was no difference between VO_{2max} values for any of the testing procedures. However, in male trained runners, there was a difference in obtained VO_{2max} values between testing procedures. There was no difference between Astrand and Costill/Fox protocols despite the Astrand test lasting approximately 4 minutes longer on average, but the VO_{2max} obtained from the Bruce protocol was significantly less than the Astrand and Costill/Fox protocols. The researchers suggested that this may be due to the rather small increase in speed relative to the increase in incline through the test, causing premature peripheral fatigue. Regardless, this study demonstrates that there can indeed be a difference between tests based on ramp rates and styles even within a continuously graded treadmill protocol.

Problems with Current Criteria

By using criteria set forth by ACSM for maximal determination, the classification of a maximal effort is assumed to be open to less error. However, many of these criteria are fundamentally arbitrary, which does not allow for a clear-cut assessment of whether or not an effort was a true maximal effort. While the observation of a plateau is often considered the clearest criteria, the presence of a plateau does not always occur (Bassett & Howley, 1997). Furthermore, the definition of a plateau is often debated in terms of quantification and cutoff values (Howley, Bassett, & Welch, 1995). Blood lactate and RER have been shown to correspond well (Howley et al., 1995), but the cutoff value for what is a true “maximal” effort are still arbitrarily chosen, and can change based on how stringent an exercise physiologist wishes to be. It stands to reason that the blood lactate response and RER are going to be different among individuals, as the ability to recruit type II muscle fibers and utilize one’s anaerobic capacity will vary among different types of athletes and different levels of training. For example, an individual who does little anaerobic training could potentially fatigue after the test maximizes oxidative muscle fibers, with less of an anaerobic contribution near the end of the test, altering the RER and blood lactate response.

The initial criterion, a failure to see increased oxygen consumption upon increasing workload (i.e. a VO2 "plateau"), has been considered by many to be the clearest definition of a true maximal test. While the observation of this phenomenon would indicate the maximal aerobic contribution, the absence of a VO_2 plateau would not necessarily indicate a peak test. This leads to confusion when including this criterion in maximal determination, because the VO_2 plateau is not always clear or even present.

Rossiter and colleagues performed a study to assess the plateau prevalence and interpretation (Rossiter, Kowalchuk, & Whipp, 2006). Following a cycling ramp-wise incremental test (RI), seven subjects were instructed to cycle at 105% of the final workload from the RI test after a 6 minute recovery period. Results showed that despite a workload that was higher than the end of the RI test, the maximal oxygen consumption was not difference between the two (r = .98). In 12 maximal RI tests, a plateau in VO_2 was not observed prior to termination of the test. However, the completion of a workload that was higher than the maximal effort during the RI test (105% of maximal power) demonstrated that an increase in workload did not illicit an increase in oxygen consumption, which agree with the original assessment by Hill and Lupton confirming the physiological maximum of oxygen consumption. Given the results of this study, the VO_2 plateau is not a good indicator of a true maximal effort.

Similarly to Rossiter, Day et al. found that there was no difference between the continuous and constant-load protocols (Day, Rossiter, Coats, Skasick, & Whipp, 2003). As a part of their study, 38 subjects completed an incremental ramp test on a cycle ergometer for VO_{2max} assessment as well as a constant load test that was 90% of peak power attained during the ramp test, performed until the limit of tolerance. When comparing the two peak VO_{2max} values, there was no significant difference between them. Additionally, six subjects completed five additional constant-load tests at "very heavy" workloads, three of which were different than the 90% peak workload. When comparing the results of the constant-workloads and the ramp test, there was still no significant difference; that is to say that there was not an ability to achieve a different VO_{2max} that was higher than the ones obtained from the traditional ramp-incremental test. Additionally, in the maximal tests done on a total of 71 subjects, only 17% of the subjects achieved a plateau-like response in the final stages of the maximal test. Day suggests that since there was no difference between the constant-load tests and the ramp-incremental tests as well as a failure to achieve a plateau-like response in 83% of ramp tests, the plateau-response is not a good maximal criterion.

In addition to the plateau phenomenon, Mier et al. investigated criteria cutoff values for heart rate and respiratory exchange ratio (RER) (Mier, Alexander, & Mageean, 2012). Maximal CPETs were performed on 35 Division II college athletes until volitional fatigue. Subjects also performed a verification stage at the next consecutive workload from when they ended the testing session after a 10-minute active recovery window. The verification stage provided confirmation of VO_{2max} in each individual, while max HR and RER were collected and analyzed for cutoff values. Cutoff values tested for HR max were greater than 85% age-predicted MHR, within 10 bpm of age-predicted MHR, and achieving age predicted MHR. For RER, cutoff values assessed were ≥ 1.05, ≥ 1.10, and ≥ 1.15. Plateau cutoff values were also divided into ≤ 2.0 ml/kg/min and ≤ 2.2 ml/kg/min. Of individuals who met a plateau criterion, significantly less people met the most stringent criteria, despite a verified VO_{2max} and a plateau phenomenon. Mier and colleagues do not recommend that graded exercise tests be used for VO_{2max} determination, and that use of HR and RER as secondary criterion for maximal determination is not effective.

Use of the plateau as well as secondary criteria are meant to enhance the ability to determine if an effort was maximal or not. However, it appears that the interpretation of such values may limit the ability to use these criteria, especially depending on the type of test method used. Therefore, additional means to determine VO_{2max} accurately are needed in order to eliminate uncertainty in the maximum versus peak debate.

Mathematical Modeling

To date, there are few models that attempt to model oxygen consumption. Very few of these models are able to predict oxygen consumption in response to dynamic systems (i.e. changing workloads). Additionally, few mathematical models are able to predict oxygen consumption on an individual basis. The use of dynamic systems models has allowed researchers to understand and mathematically describe complex systems and behaviors. Being able to use dynamic systems models can incorporate the ability to adapt to individuals, rather than aggregate responses. Many of the mathematical equations used to predict oxygen consumption, such as the equations set forth by the American College of Sports Medicine, have relied on aggregate data across a wide population at a steady state. This doesn't allow for an accurate estimation of oxygen consumption, as oxygen consumption economy and biomechanical efficiency have been shown to be different among individuals; nor does this allow for accurate predictions in scenarios where the exercise demand changes throughout.

Stirling, a biological mathematician, was able to create a mathematical model to describe the on- and off-transient kinetics of oxygen consumption in response to a steady-state exercise demand(Stirling et al., 2005). Understanding that individuals have different physiological responses of oxygen consumption to the same exercise demand, Stirling included parameters that allowed the equation to be adapted to best fit the individual's physiological response. This model, however, was unable to account for a dynamic system. The demand function was set at an arbitrary value, without a method of exercise quantification.

Mazzoleni and colleagues were able to solve this problem by creating a demand function that is dependent upon workload (watts) and pedaling cadence on a cycle ergometer (Mazzoleni et al., 2016). This demand function can then change over the course of time, which allows the original Stirling model to work in a dynamic system. Using this model, oxygen consumption measured in response to a cycling protocol can be used to solve for the individual-specific parameters. Once these parameters are known, the model is able to be used to simulate the individual's physiological response of oxygen consumption to synthetic protocols or to simulate the physiological response to recorded power and cadence (i.e. a commercially available power meter for bicycles).

CHAPTER III

Methods

Subjects

For this retrospective preliminary study, data from 8 subjects between 18-35 years recruited from a larger study, *Prediction and Uncertainty in Cycling Performance* (Principal Investigators: Claudio Battaglini and Brian Mann IRB #14-0967) were used. Since the mathematical model has not been previously compared to physiological data, effect size and power may not be computed *a priori.* Subjects in the larger study were recruited from a university in central North Carolina by word of mouth and emailing those expressing verbal interest. Subjects must have been considered healthy and classified as low-risk for maximal exercise participation by guidelines of the American College of Sports Medicine (American College of Sports Medicine, 2014), free of any cardiovascular, pulmonary, lung, kidney, or orthopedic condition, and not have been on any medication that could alter heart rate response (screened by telephone call prior to initial screening). The PAR-Q (Physical Activity Readiness Questionnaire), a medical history questionnaire, and clearance from a physician were all used for further health indication. Prior to the study, the subjects must have been regularly exercising a minimum of 30 minutes, 3 times per week, at a moderate intensity but not have been a cyclist in training. The I-PAQ (International Physical Activity Questionnaire) were used to assess the level of physical activity of all subjects.

Instrumentation

Health status and participation eligibility was assessed using the PAR-Q and general medical history form. Previous physical activity levels were collected using the IPAQ. The Pre-assessment Guidelines were used to prepare the subject for exercise sessions. A sphygmomanometer (American Diagnostics Corporation, Hauppage, NY) and a Littman stethoscope (3M, St. Paul, MN) was used to manually assess resting blood pressure by auscultation. Height was measured with a stadiometer (Detecto, Webb City, MO), and a balance beam scale (Detecto, Webb City, MO) was used to measure subject weight. Hydration status was verified using refractometer (TS Meter, American Optical Corp., Keene, NH, USA) prior to testing. A GE CASE Exercise Testing System (GE Healthcare, Buckinghamshire, United Kingdom) was used for a 12 lead resting ECG as one of the criterion for participation eligibility. Oxygen uptake was measured using a Parvo Medics TrueMax® 2400 Metabolic system (Parvo Medics, Salt Lake City, UT, USA). A Garmin heart rate monitor (Garmin International, Inc., Olathe, KS) was used to collect instantaneous heart rate data during testing. The CEPT was performed on a Lode Corival electronically braked cycle ergometer (Lode B.V, Groningen, Netherlands). Garmin Vector power meter pedals (Garmin International, Inc., Olathe, KS) were used to quantify and transmit power and cadence data, paired with and recorded by a Garmin 810 cycling computer (Garmin International, Inc., Olathe, KS). The Borg 6-20 RPE scale (Borg, 1970) was used to assess perceived exertion during the maximal exercise test. Blood lactate measurements were conducted using a Lactate Plus handheld analyzer (Sports Resource Group, Hawthorne, NY). A genetic algorithm developed by Dr. Brian Mann (Duke University, Durham, NC) was used to estimate maximal oxygen from the submaximal test by the process of parameter estimation.

General Procedures

For this study, data from the initial CPET obtained from a larger study, *Prediction and Uncertainty in Cycling Performance* (Principal Investigators: Claudio Battaglini and Brian Mann IRB #14-0967) was used for analyses. Therefore, only the procedures up to completion of the initial CPET is presented. The current study consisted of two total visits, occurring two to seven days apart. Subjects reported to the Exercise Oncology Research Lab (EORL) in Fetzer Hall on the campus of the University of North Carolina at Chapel Hill for both visits. After expressing verbal interest in the study to one of the research team members, the subject was contacted by email and phone to participate in a health screening for participation (Visit -1). After subjects signed an informed consent approved by the University of North Carolina Institutional Review Board (IRB), and were cleared and agreed to be in the study, they were scheduled for a second visit to undergo the initial VO_{2max} test.

Visit 1(Health Screening for participation)

Upon arrival to the lab for the first visit, subjects were provided with informed consent and were assigned a coded identification number. Then subjects completed the IPAQ, PAR-Q, and a general medical history questionnaire and underwent a 12-lead resting ECG. Subjects were then instructed to sit quietly for approximately 5 minutes, after which resting blood pressure, height, and weight were recorded. The results of all the initial screening assessments were reviewed by a physician part of the research team. After being approved by the research team physician, subjects were given pre-assessment guidelines, and instructed to follow these guidelines strictly prior to reporting to the lab for the second visit.

Visit 2 (CPET)

Upon arrival to the EORL, subjects were asked about adherence to the pre-assessment guidelines, sleep, and current fatigue state. Then, the subject's height, weight, and hydration status were assessed using the specific gravity method. For the assessment of hydration status, subjects were provided with a sterilized cup for urine collection, which assessed hydration using a refractometer. A specific gravity value of 1.028 was used as the cutoff for euhydration. If the subject did not meet the hydration criteria, then the subjects were scheduled to perform the CPET on another day.

Before testing began subjects were given instructions about the stages of the test, safety, and termination of the test. Once a subject was ready for testing, a heart rate monitor, electronically braked ergometer, helmet, nose clip, and mouthpiece were fitted to the subject. Subjects were allowed a five-minute warm-up period during which the subject were instructed to pedal at 50W and maintain cadences between 60 and 100RPM to become accustomed to the bike. Upon completion of the warm-up, the test began at an intensity of 100W, with wattage increasing by 50W every two minutes. After reaching 250W, test wattage increased in intervals of 30W per minute.

Criteria for test termination used included:

1. Volitional fatigue;
2. The subject requested to stop at any time point;
3. The researcher stops the test due to a medical issue; or
4. Oxygen consumption does not increase despite an increase in workload.

After test termination, subjects were instructed to rest for three minutes on the bike. After three minutes of rest, a drop of blood was collected using a standardized finger prick technique and analyzed for blood lactate concentration with a lactate plus analyzer.

For the determination of a maximal effort during the test (VO_{2max}), three of five criteria below had to be met:

1. A blood lactate greater than or equal to 10.0mmol;
2. A lack of increase in oxygen uptake with increasing workload;
3. A heart rate maximum within 10 beats per minute of age-predicted maximum heart rate (220-age)
4. A respiratory exchange ratio greater than or equal to 1.15; and
5. An RPE greater than or equal to 18

If three of the five criteria were not met, the test was considered a VO_{2peak} test, instead of a VO_{2max} test (American College of Sports Medicine, 2014).

After the lactate measurement, subjects were assisted off the bike and into a chair to complete the recovery process. Subjects rested until resting blood pressure returned within 10 mmHg and heart rate returned to within 30 bpm of resting values. After that, subjects were cleared to leave the laboratory.

Data Processing

Results from the Parvo Medics TrueMax® 2400 Metabolic system were converted into eight-breath averaging, exported as an Excel file, and downloaded into MatLab (MathWorks, Natick, MA). Average power from each stage, a fixed cadence, and oxygen kinetics data were used in a heuristic algorithm in MatLab to estimate parameters for the subject. Since cadence was not recorded in the CPET, an assumed cadence of 50RPM was given to all subjects. Then, parameters were used to calculate a VO_{2max} value from the submaximal test protocol as well as the submaximal stages of the maximal exercise test.

Research Design and Statistical Analyses

The study design was a retrospective study, with the subjects acting as their own controls. Descriptive statistics, including mean and standard deviations of predicted and obtained VO_{2max} values, were computed. The obtained VO_{2max} values and values obtained from the dynamic model prediction were compared using a two-tailed paired-samples t-test. Comparison of the VO_{2peak} values and the predicted VO_{2max} values from the system dynamic model were evaluated using a one-tailed paired-samples t-test. Data was analyzed using Microsoft SPSS version 22.0 (IBM Solutions, Durham, NC). An *a priori* alpha level of $p < .05$ was used to declare statistical significance for all analyses.

CHAPTER IV

Manuscript

Introduction

Use of cardiopulmonary exercise tests (CPET) are commonly used to determine maximal oxygen uptake (VO_{2max}), which is defined by the maximal amount of oxygen that the body can uptake and utilize during exercise (Hill & Lupton, 1923). Use of a CPET for VO_{2max} determination is often used to evaluate athletic performance, cardiopulmonary health (Albouaini et al., 2007), and even survivorship in clinical settings (Wood et al., 2013), among many other uses. Additionally, the determination of VO_{2max} allows for quantification of aerobic exercise intensity, usually expressed as a percentage of VO_{2max}, or percent of VO_2 reserve.

It is important that the subject undergoing the CPET achieves a maximal effort for accurate VO_{2max} determination. There are many differing criteria to assess whether the effort was a true maximal effort or not, but the most widely used criteria are those set forth by the American College of Sport Medicine (ACSM) recommendations (American College of Sports Medicine, 2014). These recommendations state that if three of the following five criteria are met during the CPET, effort VO_{2max} was achieved: 1. Heart rate (HR) maximum is within 10 bpm of age-predicted maximal heart rate (220-age), 2. Blood lactate $\geq$ 8.0 mmol, 3. Respiratory exchange ratio $\geq$ 1.10, 4. Rating of perceived exertion > 17, and 5. A plateau in oxygen uptake, with an increase in workload during the test. However, if three of the five criteria are not met, the highest value obtained is called a *peak* oxygen consumption (VO_{2peak}); in other words, the peak oxygen uptake attained by the individual during the test. It is accepted within the exercise physiology community that this VO_{2peak} value is considered not to be the maximal physiological capability of an individual, whereas a true VO_{2max} is often accepted as the current maximal cardiopulmonary capacity of an individual during a maximal exercise effort. The reason an individual may attain a peak value instead of a maximal value may be due to many different factors. It is often thought that, peripheral muscle fatigue sets in before cardiopulmonary systems are fully demanded, thus not allowing the individual to continue with the test, terminating it prematurely prior to achieving $VO_{2max.}$ This scenario is believed to be even more accentuated in sedentary and older individuals experiencing sarcopenia (Neder, Nery, Silva, Andreoni, & Whipp, 1999).

Interpretation and use of the VO_{2max} criteria may help with practical classification of maximal versus peak tests, but may not provide the most accurate determination of the "true" maximum oxygen uptake during a CPET. Some exercise physiologists deviate from the ACSM guidelines, and vary their cutoff values or number of overall criteria used to be more stringent in the evaluation of a "true" max test. For example, RER $\geq$ 1.15 instead of 1.10 is not uncommonly seen. Although these altered cutoff points may assist in a more precise evaluation of the results of a CPET, this does not help guarantee that results from the CPET are truly maximal. However, the biggest issue facing the certainty of maximal tests is that many of these aforementioned criteria are arbitrary in nature, and are subject to much debate (Howley et al., 1995). Cutoff values for RER and HR that change slightly have been shown to affect the total percentages of people meeting the criteria, despite verification of VO_{2max} (Mier et al., 2012). Certainty in whether or not a value is a true physiological maximum attained during a CPET is quite debatable. This issue becomes even more evident in CPETs conducted in cycle ergometers, where most oxygen being up-taken during the exercise comes from the muscle action of the legs, neglecting other tissues of the body. Also, the specificity of the cycling test, potentially leading to premature fatigue in those who are not used to cycle or are sedentary or have decreased leg muscle strength (Neder et al., 1999).

The implication of using a VO_{2peak} in place of a VO_{2max} value may overvalue the intensity of the exercise being quantified as a percent of VO_{2max}, or may undervalue the dose-response relationship when used as exercise prescription in training. This may be more pronounced in less athletic populations, where the physiological responses are more variable than trained athletic populations. Similarly, clinical populations have much less reliable responses to the test, which makes the use of maximal criteria more complicated to be interpreted. The goal of CPET testing should therefore be to increase certainty of the physiological maximum value in order to better understand cardiovascular function and to provide a more precise mean for the quantification of aerobic exercise intensity for training.

Use of individualized models has been shown to describe oxygen kinetics to a non-dynamical demand function (i.e. using steady state exercise to model oxygen kinetics) (Stirling et al., 2005). However, during exercise oxygen kinetics behave in a non-linear fashion, with transient alterations in physiological parameters occurring constantly to account for the stress being imposed in the body. Thus, models using non-dynamical demand functions to estimate individualized oxygen kinetics responses during exercise may not be as precise for the evaluation of cardiopulmonary function. This would inherently limit the use of submaximal exercise models for physiological parameter estimation, which may be used for the prediction of VO_{2max} in individuals who most likely won't be able to achieve a maximal effort during a test. By modifying this non-dynamical model of estimation, Mazzoleni et al. (2016) first works, was able to describe the individual heart rate kinetics in a dynamic system, where the demand function adapts in a changing system as a function of cycling power output and pedaling cadence (Mazzoleni et al., 2016). Further adapting this dynamical model to describe oxygen consumption kinetics, it is possible to model the individualized response of one subject and obtain individual-specific parameters using a heuristic algorithm. Using this method, a VO_{2max} prediction may allow for verification of maximal tests, or predictions in peak tests. Therefore, a first step using data from a traditional CPET conducted using a cycle ergometer may assist in the development and evaluation of the potential use of dynamic system modeling in accurately determining a maximum oxygen uptake of an individual during a CPET. Thus, the purpose of this study was to evaluate a dynamic system model estimation of VO_{2max} using data from a traditional CPET test conducted using a cycle ergometer to compare the results of the dynamic system model prediction with results of individuals who attained VO_{2max} versus individuals who attained VO_{2peak} during the CPET.

Methods

A retrospective analysis of nine males from the *Uncertainty in Cycling Performance Study* (PI's: Claudio Battaglini and Brian Mann; IRB #14-0967) was performed. The subjects were divided into two groups, those who achieved maximal effort during a CPET (VO_{2max}) and those who achieved peak effort during a CPET (VO_{2peak}). Maximal determination was considered meeting three or more of the ACSM maximal CPET criteria (American College of Sports Medicine, 2014), otherwise the test was considered a peak test.

Subjects from the study were cleared by a medical physician after a screening visit consisting of an electrocardiogram, completion of a general medical history questionnaire, International Physical Activity Questionnaire, and a Physical Activity Readiness Questionnaire, and reviewing the informed consent. The testing visit consisted of a maximal CPET conducted on a Lode Corival electronically-braked cycle ergometer (Lode B.V., Groningen, Netherlands). Expired gas was measured using a Parvomedics TrueOne 2400 (Parvo Medics, Salt Lake City, UT, USA) for the determination of oxygen uptake. Subjects were given a five-minute warm-up period at 50W, and then began the test at 100W. Workload was increased by 50W from the initial 100W every two minutes until the 250W stage was achieved. After that, workload was increased by 30W every minute until volitional fatigue. Rating of perceived exertion (RPE) on the Borg 6-20 scale (Borg, 1970) was collected during the last 20 seconds of each stage. Heart rate was recorded using a Polar Heart Rate monitor synced via telemetry to the metabolic cart. Three minutes after CPET termination, blood lactate was performed on the fourth digit of the non-dominant hand using a lancet and Lactate Plus (Sports Resource Group, Hawthorne, NY).

Data from the Parvomedics were exported using eight-breath averaging. The maximum VO_2 used for analyses was determined by averaging the highest VO_2 values attained during the last stage of the test. Using a heuristic algorithm, power output and oxygen uptake data from the CPET, as well as an assumed constant cadence, were used to determine the individual parameters for each subject. Because the cadence was not recorded during the maximal tests, even though an electric-braked cycle ergometer was used, for the purpose of this retrospective study, an assumed cadence of 50RPM was used in the dynamic system model. Using the parameters obtained from this heuristic algorithm, predicted maximal oxygen uptake values were determined for all subjects.

For the MAX group, a two-tailed paired-samples t-test was performed to test the hypothesis that there would be no difference between predicted (pVO_{2max}) and experimental (eVO_{2max}) relative maximal oxygen uptake values. In the PEAK group, pVO_{2max} and experimental VO_{2peak} (eVO_{2peak}) values were compared using a one-tailed paired-samples t-test to test the hypothesis that the predicted VO_{2max} value would be higher than the VO_{2peak} value obtained from the CPET.

Results

Nine young, healthy male subjects had an average age of 21.4 ± 2.9 years, height of 178.9 ± 12.9 cm, and weight of 81.9 ± 11.6 kg. Six individuals achieved VO_{2max} during the CPET and were placed in the MAX group, while three individuals who did not achieve VO_{2max} were placed in the PEAK group. The average VO_{2max} in the MAX group as determined by the CPET was 47.59 ± 3.51 ml/kg/min, and the average VO_{2peak} in the PEAK group was 49.54 ± 4.60 ml/kg/min.

In individuals in the MAX group, there was a significant difference between eVO_{2max} and pVO_{2max} ($p = .046$) using the dynamic system model. The average predicted VO_{2max} was 51.75 ± 5.95 ml/kg/min, with a mean absolute error in the MAX group of 4.13 ml/kg/min. However, no significant difference was found between the pVO_{2max} and eVO_{2peak} in individuals who achieved peak values (PEAK) ($p = .130$). The average VO_{2max} prediction for the PEAK group was 56.41 ± 3.76 ml/kg/in, with a mean absolute error for the PEAK group was 6.87 ml/kg/min.

Table 1. Obtained and predicted maximal VO_2 values for MAX and PEAK groups.

Group	Number of Subjects (n)	Maximal VO2 From CPET (ml/kg/min ± SD)	Predicted VO2max (ml/kg/min ± SD)	Significance (p)
MAX	6	47.59 ± 3.51	51.75 ± 5.95	0.045
PEAK	3	49.54 ± 4.60	56.41 ± 3.76	0.130

Table 2. Individual subjects' obtained peak VO_2 versus predicted VO_{2max}. Lactate – blood lactate in mmol, RPE – last stage RPE from Borg's 6-20 scale, Max. HR - maximum heart rate in beats per minute, Plateau – evidence of a lack of increase in VO_2 despite increased workload, and RER – respiratory exchange ratio. (*values that did not fit the expected trend, when factoring in the 1-3.0 ml/kg/min error of the equipment; italicized values represent criteria that were not met using ACSM guidelines)

Subject	Group	Maximal VO_2 From CPET (ml/kg/min)	Predicted VO_{2max} (ml/kg/min)	Difference (ml/kg/min)	Maximal Criteria				
					Lactate	RPE	Max. HR	Plateau	RER
1	MAX	46.37	56.69	10.31*	13.6	19	210	*No*	1.25
2	MAX	51.22	58.49	7.26*	10.7	*17*	*176*	Yes	1.16
3	PEAK	49.28	53.37	4.10	9.7	*15*	*170*	Yes	*1.09*
4	MAX	46.88	49.18	2.31	11	*16*	201	Yes	1.23
5	MAX	41.51	41.75	0.24	11.8	*17*	*184*	Yes	1.18
6	PEAK	54.27	55.23	0.95*	*7.9*	*16*	196	*No*	1.13
7	MAX	49.64	52.34	2.71	13.4	18	210	Yes	1.27
8	MAX	49.89	51.85	1.96	12.5	18	192	Yes	1.26
9	PEAK	45.08	60.62	15.54	9.8	*17*	195	*No*	*1.07*

Discussion

Use of a dynamic systems model has the potential to accurately predict VO_2 kinetics as well as VO_{2max}. By using this methodology, a comparison of obtained and predicted VO_{2max} values may enhance the certainty of a true maximal test. The purpose of this study was to evaluate the use of a dynamic systems model to confirm VO_{2max} in individuals who obtained maximal efforts, as well as predicting VO_{2max} in individuals who were not able to achieve maximal criteria.

The results of this initial study were quite surprising, yet not totally unexpected. The hypothesis stated that there would be no significant difference between the dynamic systems model predicted VO_{2max} value when compared to the VO_{2max} results achieved by the MAX group, was not observed.

Although the model has been shown to correlate extremely well with time series predictions, extrapolating VO_{2max} has yet to be refined with the proper protocol. In this study, the methodology inherently limits the parameter estimation, which is the most important step in predicting VO_{2max} for this study.

One of the biggest affecters that limited parameter estimation was the lack of instantaneous cadence acquisition during the CPET. The demand function was calculated using a fixed cadence of 50 RPM, but cadence was neither fixed nor near 50 RPM for any of the tests. Using real-time cadence allows the dynamic systems model to adapt to changes in cadence, despite a fixed-workload. That is to say that the current parameter estimation assumed a fixed demand function for each stage, as opposed to allowing the model to account for a changing demand function in each stage; which is the major advantage of the dynamic system model when compared to non-dynamical models for precise estimation of physiological responses during exercise.

In a similar respect, instantaneous power is necessary to collect and use, even when using an electronically braked cycle ergometer. The electronically braked cycle ergometer controls the power by adapting the torque of each pedal stroke based on the cadence. Due to the time delay from the detection of cadence to the adjustment of torque, instantaneous power output tends to fluctuate, despite the cycle ergometer reporting a steady workload. These small changes in torque, due to slight changes in cadence during the test, have the potential to alter the physiological response to a stage, and are accounted for in the demand function of the model. By collecting both instantaneous power and cadence, the demand function plays a more dynamic role than in the current study, which most likely explains the inaccuracies in VO_{2max} prediction found in the current study.

There was also a large source of error by using the continuously graded CPET, since the parameter estimation works best when oxygen off-kinetics are incorporated. By using a continuously graded test, the oxygen on-kinetics, which is only part of the dynamic systems model, is only being assessed. By having a dynamic exercise protocol, it may be possible to achieve a more inclusive assessment of oxygen kinetics, which would provide a more accurate parameter estimation and VO_{2max} prediction. Given the nature of dynamic systems modeling, it is possible that the inclusion of oxygen off-kinetics would be more important than pushing to maximal workloads, which would allow for submaximal tests to predict VO_{2max}, but that has yet to be validated.

It is worth noting that although the parameter estimations and VO_{2max} predictions are individualized for each subject, having a larger sample in both the maximal and submaximal groups could help with the interpretation of the study results, due to the fact that the way the data was analyzed using paired-samples t-tests. Most likely, the analyses were underpowered, thus potentially producing erroneous interpretation of the data. The average difference for the MAX group between tests was 4.16 ml/kg/min, whereas the PEAK group demonstrated a difference of 6.87 ml/kg/min. Since the total number of individuals in each group was low, the two individuals in the max group and one in the PEAK group that did not follow the expected trend had a large influence on the standard deviation of each group. Despite the error in methodology, inclusion of more subjects may reveal a more normally distributed sample in each of the groups, increasing the statistical power. Further analysis should attempt to increase the sample size in order to see if the data becomes more normally distributed.

Despite the effect that the outliers in the data may have had in the results of the analyses, there is a trend for the model to potentially detect the differences in the PEAK group and verify the data in the MAX group. The PEAK group, containing three individuals, provided absolute errors of 0.96 $ml \cdot kg^{-1} \cdot min^{-1}$, 4.10 ml/kg/min and 15.54 ml/kg/min. Given that the error of the metabolic system used is can be between 1- 3.0 ml/kg/min, it may be important to note that only one subject remained within this margin of error. In the MAX group, two of the six individuals did not have absolute errors inside of 1-3.0 $ml \cdot kg^{-1} \cdot min^{-1}$ (Table 2), which does support that the model could predict inside the margin of error of the equipment. The two individuals in the MAX group who fall outside of this margin are enough to change the statistical significance of the group as a whole, and for these individuals, the instantaneous power and cadence demand functions could potentially be the major source of error of estimation.

It is essential that additional studies using the dynamic systems model include the instantaneous power and cadence data from the exercise session as well as off-kinetic stages when estimating the individual parameters. Without these inclusions, the parameter estimation appears to produce a larger error or estimation. Parameter estimation can, in some individual cases, provide VO_{2max} predictions that appear to be accurate. However, more tightly controlled studies are necessary in order to validate the use of a dynamic systems model for the purpose of predicting VO_{2max}.

Conclusion

To our knowledge, this is the first study that attempted to predict VO_{2max} with a dynamic systems model using data obtained from a traditional CPET. The results suggest that instantaneous cadence and power, parameters usually not collected during a CPET, should be used when estimating physiological parameters for the dynamic systems model. This inclusion may allow for the system to capture transient alterations on the physiology of an individual during testing maximizing the accuracy of estimation. It is also important to note that since the dynamic systems model incorporates factors that account for off-transient oxygen kinetics, parameter estimation may be more accurate with inclusion of stages that allow for decreases in physiological responses, which provides a more inclusive assessment of cardiopulmonary capacity. Therefore, it is concluded that using the physiological data from a traditional CPET may not be the best exercise test to estimate VO_{2max} using dynamic systems modeling, and therefore, future studies which attempt to predict VO_{2max} using a dynamic systems model should not only include instantaneous power and cadence parameters, but also explore other exercise protocols which include more transient behavior to maximize the ability of the model to precisely predict VO_{2max}.

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