Similarity between predicted and obtained oxygen consumption during incremental cardiopulmonary exercise test in healthy men and chronic heart failure patients

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ABSTRACT | Cardiopulmonary exercise testing (CPX) is a noninvasive method for assessing physiological changes during physical exercise. Functional capacity has been evaluated using prediction equations. However, this evaluation method may yield different outcomes when applied to a healthy male population and patients with chronic heart failure (HF). This study aimed to compare the estimated and obtained values of oxygen consumption (VO₂) during CPX both at the ventilatory anaerobic threshold (VAT) and at peak exercise for healthy men and HF patients. For that, 56 men were divided into 3 groups: (1) 18 young and healthy (YG) (27±6.01 years); (2) 14 healthy older adults (OG) (61±6.3 years); and (3) 24 chronic HF patients (HFG) (53±13.6 years). CPX in cycle ergometer was administered to all individuals for determining VO₂ at the VAT and peak exercise. Then, VO₂ was estimated at the two moments using a prediction equation, and estimated values were compared to those obtained. Estimated VO₂ was significantly higher than obtained VO₂ in OG (16.9±1.8 vs. 13.1±2.1mL/kg/min) and HFG (12±6.9 vs. 8.7±2.5mL/kg/min). We found no difference between estimated and obtained VO₂ for the YG (22.6±5.5 vs. 23±8.7mL/kg/min). The prediction equation overestimated VO₂ values for older adults and HF patients. However, the YG obtained similar values than those estimated.

Keywords | Exercise Test; Oxygen Consumption; Heart Failure, Anaerobic Threshold.

RESUMO | O teste exercício cardiopulmonar (CPX) é uma metodologia não invasiva de avaliação global da integridade dos ajustes fisiológicos durante o exercício físico. Como alternativa, a avaliação da capacidade funcional foi realizada por meio de fórmulas preditivas. No entanto, esse método de avaliação pode ter resultados diferentes quando usado em uma população de homens saudáveis e pacientes com insuficiência cardíaca (IC) crônica. Compararam-se os valores de consumo de oxigênio (VO₂) obtidos e estimados durante o CPX no limiar anaerobio ventilatório (LAV) e no pico do exercício para homens saudáveis e pacientes com IC crônica. Cinquenta e seis homens foram divididos em 3 grupos: (1) 18 eram jovens saudáveis (GJ) (27±6,01 anos);
(2) 14 eram idosos saudáveis (GE) (61±6,3 anos); e, (3) 24 com IC crônica (HFG) (53±13,6 anos). Todos foram submetidos ao CPX em cicloergômetro para determinação do VO2 no LAV e no pico do exercício. Posteriormente, a estimativa do VO2 foi realizada na potência do LA e no pico do exercício por meio de uma fórmula de predição para exercício físico em cicloergômetro. Os valores de VO2 obtidos e a carga estimada foram comparados. O VO2 estimado foi significativamente maior que o VO2 obtido no GE e no HFG (16,9±1,8 vs. 13,1±2,1mL/kg/min e 12±6,9 vs. 8,7±2,5mL/kg/min, respectivamente). Por fim, não houve diferença nos valores de VO2 estimados e obtidos para o GJ (22,6±5,5 vs. 23,1±8,7mL/kg/min, respectivamente). A fórmula de predição superestimou os valores de VO2 para idosos e pacientes com IC crônica. Porém, no GJ os valores de VO2 se mostraram semelhantes para a fórmula de predição e o obtido durante o CPX em cicloergômetro.

INTRODUCTION

The cardiopulmonary exercise testing (CPX) is a noninvasive method for assessing the integrity of cardiovascular, respiratory, muscular, peripheral, neurophysiological, humoral, and hematological changes in the human body during physical exercise. CPX is also useful in determining functional capacity by providing the two most common functional limitation indexes: the peak oxygen consumption (VO2peak) – the peak VO2 attained at maximum-effort – or maximal oxygen consumption (VO2max) – VO2 plateau at maximum exhaustion; and the ventilatory anaerobic threshold (VAT) at submaximal or maximal exercise. VO2peak and VAT during exercise may function as a prognostic marker and determine individuals’ functional capacity. However, the standard evaluation method may fail in identifying VAT in chronic heart failure (HF) patients (approximately 10% of the cases), as it would imply a worse prognosis. These markers may also contribute to exercises prescription.

Despite being the gold standard measure for determining functional capacity, VO2max or VO2peak, and VAT, the CPX requires a very expensive equipment, a team with at least three well-trained researchers, and a specialized laboratory for its proper operation. Thus, few places have all the necessary technological apparatus for conducting CPX and are specialized in this exam, such as professional soccer clubs and the research labs of few universities.

Functional capacity is indirectly evaluated using prediction equations with correction for the anthropometric characteristics and the executed workload. Our results corroborate those reported by Almeida et al. Prediction equations enable us to estimate VO2 at VAT and at the peak exercise, so that it is important to discuss the advantages of this method when compared with the CPX. Prediction equations are more affordable, practical, and fast in determining VO2. The literature is incipient regarding the similarity between results obtained by prediction (indirect) and by the gold standard in a cycle ergometer (direct). Such similarity would add value to
the use of the indirect method for obtaining VO\(_2\) at VAT and peak exercise, or even validate the similarity between the estimated and obtained VO\(_2\). In this context, this study aims to evaluate whether VO\(_2\) values at VAT and peak exercise estimated by prediction equations are similar to those established by the gold standard in a cycle ergometer for healthy young and older adults and chronic HF patients.

**METHODOLOGY**

Healthy young and older male adults, and patients with chronic heart failure (HF) were evaluated. Groups formed by older adults and chronic HF patients were selected by convenience sampling. All participants agreed to participate in this research. The cardiopulmonary exercise testing (CPX) was performed on cycle ergometer using a ramp protocol.

**Study design and subjects**

This is an observational cross-sectional study conducted with male participants who met the following inclusion criteria: 1) young group (YG) – aged 19-36 years and considered healthy according to clinical evaluation; 2) older group (OG) – aged 60-91 years and considered healthy according to clinical evaluation; and 3) chronic HF group (HFG) – presenting a history of stable chronic HF caused by left ventricular systolic dysfunction during the last 6 months (left ventricular ejection fraction <45%), clinical stability in the last 3 months, and no history of angina or coexistence of pulmonary disease.

Chronic HF patients with clinical or functional evidence of chronic obstructive pulmonary disease (FEV\(_1\)/FVC <70\%)\(^{14}\), exercise-induced asthma, significant angina or arrhythmias, and myocardial infarction in the past 6 months, as well as those who joined a cardiac rehabilitation program in the past year were excluded. As for the YG and OG, volunteers with a history of cardiovascular, respiratory, muscular, orthopedic, neurological, metabolic, and immunologic disease, or with clinical or functional evidence of chronic obstructive pulmonary disease (FEV\(_1\)/FVC <70\%)\(^{14}\) were excluded.

All volunteers underwent clinical evaluation, biochemical exams, and electrocardiography. Pulmonary function testing (spirometry) was performed using the Vitalograph® spirometer (Hand-Held 2021 instrument, Ennis, Ireland) to measure the forced vital capacity (FVC) to determine the forced expiratory volume (FEV\(_1\)) and FEV\(_1\)/FVC ratio\(^{15}\). We employed values reported by Knudson et al.\(^{16}\) as reference for conditions and technical procedures, expressed in body temperature pressure standard (BTPS). Acceptability and reproducibility criteria were defined according to the American Thoracic Society (1995) recommendations. HF was assessed according to the New York Heart Association (NYHA) classification. All patients with chronic HF were optimized with beta-blocker therapy. This work was approved by the Ethics Committee of the Federal University of São Carlos, SP, Brazil (protocol 238/06) and the Federal University of Rio de Janeiro, Rio de Janeiro, RJ, Brazil (protocol CAAE 47813415.8.0000.5257). All volunteers agreed to participate by signing the informed consent form, and subjects' privacy and data confidentiality were fully guaranteed during all stages of the study.

**Experimental protocols**

The recruited volunteers underwent the following steps:

**Physical evaluation**

All volunteers underwent a detailed physical examination that collected personal data, anthropometric data, vitals, and nutritional status (body mass index-BMI).

**Maximum or symptom-limited cardiopulmonary exercise test**

The CPX was performed on cycle ergometer (Inbramed, Porto Alegre, Brazil) using a ramp protocol. Patients initially got a 3-minute rest, sitting on the cycle ergometer; then, they started the 3-minute warm-up with a pedal load ranging from 1W (applied to OG and HFG) to 15W (applied to YG). The physical exercise protocol initiated after this stage, adding 10 to 25W load every minute until physical exhaustion – when the volunteer was unable to keep cycling under the imposed load. Volunteers were instructed to maintain a 60-70rpm cadence throughout the CPX\(^{17}\).

An evaluator was responsible for controlling load distribution using the ergometer. After completion, participants underwent a 3-minute post-test recovery period at 25W load, followed by a 2-minute rest, where they remained seated on the cycle. The BORG scale was collected every 3 minutes until load interruption, and ventilatory and metabolic variables and heart
Peripheral oxygen saturation (SpO₂ – Onyx 9500®) and ECG electrocardiogram (Wincardio USB) in different leads – MC5, DII, DIII, aVR, aVL and aVF, and V1 to V6 – were continuously monitored throughout the experimental procedure. A team of physiotherapist and physician researchers conducted the tests, attentive to signs and symptoms of inadequate response to exercise. Ventilatory and metabolic variables were obtained using a computerized ergospirometric system (VO2000 – Portable Medical Graphics Corporation®).

Tidal volume was obtained using a high-flow pitot tube pneumotachometer connected to the VO2000® system and coupled to a face mask properly adjusted to the volunteer’s face size, avoiding air leakage. After placing the mask, the volunteer was instructed not to communicate verbally, using only hand gestures to inform perceived exertion according to the modified Borg rating scale (CR-10) every 3 minutes, or to signal protocol interruption. The test was initiated when participants’ respiratory quotient (R) was 0.8. The equipment provides real-time values of VO₂, VCO₂, pulmonary ventilation (LV), HR and SpO₂, O₂ ventilatory equivalents (VE/VO₂), VCO₂ ventilatory equivalents (VE/VCO₂), metabolic variables, respiratory exchange ratio (RER), fractions at end-tidal O₂ expiration (FETO₂), partial fractions (FETCO₂), tidal volume (VC) and respiratory rate (RR), were also calculated. The test was interrupted when participants were unable to maintain the cadence of 60-70 rpm; presented profuse sweating, complex arrhythmias, angina, pallor, maximum HR, systolic blood pressure (SBP) >220mmHg, peripheral desaturation less than 90%, dizziness, and cyanosis.

Using the prediction equation

After analyzing CPX scores, the data were tabulated in Microsoft Office Excel® for Windows XP® (USA) and grouped so that we could apply Astrand’s prediction equation¹⁹ for VAT and VO₂, considering:

\[
\text{VO}_2 \text{mL/kg.min}^{-1} = (\text{workload-watts} \times 12) + 300 / \text{body mass (kg)}
\]

Then, VO₂ values at VAT and peak were compared between the two models to verify similarity.

Statistical analysis

The SigmaPlot statistical software (version 11.0 for Windows/2008) was used for data processing. The Shapiro-Wilk and Levene’s tests were used to verify data normality and homogeneity of variances. The two-way repeated measures analyses of variance (two-way ANOVA) and Holm-Sidak post-hoc were used to compare YG, OG, and HFG regarding the obtained and estimated VO₂. All measures were expressed as mean ± standard deviation (SD). The significance level was 5% (p <0.05).

RESULTS

All volunteers underwent the cardiopulmonary exercise testing (CPX) on cycle ergometer to determine oxygen consumption (VO₂) at the ventilatory anaerobic threshold (VAT) and at exercise peak. Then, we estimated VO₂ for the same moments using a prediction equation. No volunteer was excluded from the survey after data collection, as described in Figure 1.

Figure 1. Flowchart describing patients selection at each stage of the study
Table 1 shows the demographic and anthropometric data of the study volunteers. We found volunteers in the older group (OG) to present similar weight and height, without indication of obesity according to the body mass index (BMI). Left ventricular ejection fraction (LVEF) in the heart failure group (HFG) was classified as moderate to severe according to the New York Heart Association (NYHA) in classes II and III.

Table 1. Anthropometric data and clinical characteristics of the study population

| Variables       | YG (n=18) | OG (n=14) | HFG (n=24) |
|-----------------|-----------|-----------|------------|
| Age (years)     | 27.1±6.0  | 61.4±6.3  | 53.1±13.6  |
| Height (cm)     | 170.1±0.1 | 171.0±0.1 | 169.0±7.0  |
| Weight (kg)     | 76.2±11.0 | 75.0±6.3  | 76.3±12.8  |
| BMI (kg/m²)     | 24.9±3.2  | 24.3±3.0  | 26.5±3.8   |
| FEVE            | 30.0±7.8  |           |            |
| Functional status |           |           | 30.0±7.8   |
| NYHA II/III     |           |           | 9/15       |
| CPX             |           |           |            |
| VO₂ AT (L/min)  | 1.8±0.6   | 1.0±0.2   | 0.65±0.19  |
| VO₂ AT (mL/kg/min) | 23.1±8.8   | 13.1±2.2 | 8.7±2.5   |
| VO₂ peak (mL/min) | 2.9±0.9    | 1.7±0.3  | 1.1±0.3   |
| VO₂ peak (mL/kg/min) | 37.1±11.9    | 21.8±3.4 | 15.1±4.1  |
| VE (L/min)      | 32.1±9.9  | 30.3±6.3  | 51.7±12.9  |
| Spirometry      |           |           |            |
| VEF1 (% estimated) | 98.6±8.0  | 99.6±9.4  | 80.3±8.6   |
| VEF1/FVC        | 96.7±5.4  | 94.4±5.8  | 82.0±4.2   |
| FVC (% estimated) | 99.0±8.8  |           |            |
| Medications (n) |           |           |            |
| Diuretics       |           |           | 14         |
| Digitalis       |           |           | 9          |
| β-blockers      |           |           | 24         |
| Inhibitor-ECA   |           |           | 15         |

Values expressed as mean ± SD. BMI: body mass index; NYHA: New York Heart Association; CPX: cardiopulmonary exercise testing; VO₂AT: oxygen consumption at ventilatory anaerobic threshold; VO₂peak: oxygen consumption at exercise peak; FEV1: forced expiratory volume in the first second; FVC: forced vital capacity; YG: young group; OG: older group; HFG: heart failure group.

After follow-up and evaluation of the volunteers, we found no statistical difference between values estimated by the prediction equation and obtained by CPX regarding VO₂ at VAT and exercise peak in the YG. However, the prediction equation overestimated VO₂ values for the OG and HFG (Figures 2 and 3).

DISCUSSION

Our main findings suggest that the prediction equation proposed by Cooper et al.,19 for cycle ergometer successfully obtained oxygen consumption (VO₂) at ventilatory anaerobic threshold (VAT) and exercise peak when applied to a young population, showing no significant statistical difference when compared to the gold standard (CPX). However, the same does not apply for older adults and chronic heart failure (HF) patients evaluated in this study.

In 2015, Costa et al.20 analyzed the level of agreement between oxygen consumption rate at no-load CPX and VO₂ peak in an incremental cycle ergometer protocol within two groups: the GS – formed by apparently
expressed through a mathematical model; this model is or more variables are somehow related, which must be verified whether two variables affect other variables. That is, it verifies how a variable behavior influences the behavior of another); and c) stepwise regression (modified forward selection, whereby all variables are previously tested for their partial F-statistics at each step. A variable added to the model in the previous step may be redundant due to its relationship with other variables, and it is excluded when its partial F-statistic is less than F_out. Age, BMI, velocity, slope, and exercise duration were used as independent variables. The VO_2max equation was developed based on the regression analysis using the regression model (mL/kg/min)=58,443−(0.21×age)−(0.632×BMI)−(68,639×slope)+(1579×time). The values estimated by these regression models were not significantly different from those obtained (p<0.05). The VO_2max estimated by the ACSM’s equation for runners overestimated the values obtained by the direct method (14.6% with p<0.05). Thus, the authors concluded that the ACSM’s equation for runners using the Bruce protocol fails in accurately predicting VO_2max in athletes aged 18–37 years, where only the regression models were moderately correlated with the VO_2max values obtained by ergospirometry. Almeida et al. assessed the validity of the equation proposed by Cureton et al. (VO_2peak=−8.41+0.34*2+0.21(age×gender)−0.84(BMI)+108.94) for estimating the VO_2max of young Brazilians at a timed 1600-meter race, and suggest a prediction equation specific for this population. This study comprised 30 physically active male volunteers (23±3.1 years, 74.8±5.8kg, 1.78±0.05m, 49.8±6.5mL.kg−¹.min−¹) who underwent a maximal treadmill incremental test and a 1.600-meter race – different from those exercises used in our study. The individuals were divided into two groups: G1) for developing a prediction equation for VO_2max specific for young Brazilians; and G2) for analyzing the validities of both equations. The results showed statistically significant differences between VO_2max value directly obtained in the CPX (50.1±7.1mL.kg−¹.min−¹) and values estimated by the equation proposed by Cureton et al. (44.2±6.5mL.kg−¹.min−¹), with a low correlation between them (r=0.21). The VO_2max and running speed obtained in G1 lead to the following prediction equation: VO_2max=0.177*1.600Vm(m.min−¹)+8,101. When this new equation was applied to G2 participants, the estimated VO_2max (50.1±7.2mL.kg−¹.min−¹) was the same as that obtained by the gold standard (50.1±7.1mL.kg−¹.min−¹), with a high correlation between them (r=0.81). The authors concluded that...
the equation proposed by Cureton et al.23 (based on the results of a North American sample) underestimated the VO_{2}\text{max} of physically active young Brazilians. The equation proposed in our study validly estimated the VO_{2}\text{max} for the 1600-m performance test considering the studied population. However, the VO_{2}\text{VAT} and VO_{2}\text{peak} of healthy sedentary young people obtained from the direct method was not significantly different from those estimated by the prediction equation proposed by Cooper and Store19 considering the same population.

Lima and Abatti24 aimed to create a method capable of estimating the maximum VO_{2} during physical activity using basic physiological data (weight, BMI, height, age, HR, and walking distance). For that, they used a study sample composed of 30 male young adults, apparently healthy, whose mean age was 23.4 years (+3.18 years), mean height 1.78m (+0.06m), and mean weight 72.12kg (+7.55kg). Absolute oxygen absorption per unit of time, HF at each moment of the test, and anthropometric data were collected, and VO_{2}\text{max} (L/min) values were plotted according to weight, BMI, age, and HR at various speeds. The factors that most influenced VO_{2}\text{max} were body weight (0.48) and BMI (0.42), although relatively distant from the unit, indicating a weak correlation. Considering that, the authors analyzed other parameters with higher correlation coefficients, and calculated the HRs for different speeds and different individuals for the absolute oxygen absorption per unit of time, reaching a mean linear correlation of r=0.91. Such coefficient indicates that an equation relating HR and VO_{2}\text{max} can be obtained for the various running speeds. Following Jackson et al.25, who employed BMI for creating a model capable of determining VO_{2}\text{max}, which was later modified by DF de Lima, who introduced BMI for estimating VO_{2}\text{max} (VO_{2}\text{max} (l/min)=(-0.02595age)+3.948), being a most precise and accurate prediction equation for representing this study group. Alternative methods for predicting VO_{2}\text{max}, independent from physical exercises, have been widely tested and proved to be highly reliable.

Studies employing methods similar from ours to assess healthy older adults and chronic HF patients are still scarce in the literature. In our study, the prediction equation proposed by Cooper et al.19 was unable to estimate VO_{2}\text{VAT} and VO_{2}\text{peak} values for these populations, which may be justified by the fact that this equation considers only anthropometric values and load, regardless of individuals’ health and age. A single predictive model will unlikely be able to properly measure the peak VO_{2} in all aspects, especially regarding the multiple indications and applications that it must necessarily attend. Our model aims not to be presented as the best, but rather as a simple, practical, and efficient alternative for reaching its goal.

Our study has some limitations: 1) Although data was collected at every breath, the gas analyzer supplied the data only every three breaths; 2) Patients with chronic HF were treated with beta-blockers and 3) The limited number of participants.

**CONCLUSION**

The prediction equation used in our study reached values similar to those obtained by the direct method performed in a cycle ergometer for VO_{2} at VAT and VO_{2} at exercise peak when applied in the YG. However, the prediction equation overestimated the values when compared to those obtained by CPX (gold standard) for the older group and for patients with chronic HF.

**Clinical application**

Considering the economic and technological obstacles for determining functional capacity, we inferred that mathematics would be a plausible way of overcoming these barriers. Therefore, we applied simple prediction equations that require more accessible variables and are much cheaper than the gold standard, besides being fast and applicable in a larger number of people, saving time and avoiding possible limitations pertinent to CPX administration in a cycle ergometer. This prediction equation may provide resources and open new horizons for researchers and clinicians.

**ACKNOWLEDGMENTS**

The authors would like to thank the Conselho Nacional de Desenvolvimento Científico e Tecnológico (CNPq) and the Fundação Carlos Chagas de Apoio à Pesquisa do Estado do Rio de Janeiro (FAPERJ) for funding this research from the Research Group in Cardiorespiratory Evaluated and Rehabilitation (GECARE).

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