

Assessment of cardiorespiratory fitness using submaximal protocol in older adults with mood disorder and Parkinson's disease

Avaliação da aptidão cardiorrespiratória por meio de protocolo submáximo em idosos com transtorno de humor e doença de Parkinson

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Abstract

Background: Evidence has shown benefits for mental health through aerobic training oriented in percentage of VO_{2max} , indicating the importance of this variable for clinical practice. **Objective:** To validate a method for estimating VO_{2max} using a submaximal protocol in elderly patients with clinically diagnosis as major depressive disorder (MDD) and Parkinson's disease (PD). **Methods:** The sample comprised 18 patients (64.22 ± 9.92 years) with MDD ($n = 7$) and with PD ($n = 11$). Three evaluations were performed: I) disease staging, II) direct measurement of VO_{2max} and III) submaximal exercise test. Linear regression was performed to verify the accuracy of estimation in VO_{2max} established in ergospirometry and the predicted VO_{2max} from the submaximal test measurement. We also analyzed the correlation between the Bland-Altman procedures. **Results:** The regression analysis showed that VO_{2max} values estimated by submaximal protocol associated with the VO_{2max} measured, both in absolute values ($R^2 = 0.65$; $SEE = 0.26$; $p < 0.001$) and the relative ($R^2 = 0.56$; $SEE = 3.70$; $p < 0.001$). The Bland-Altman plots for analysis of agreement of showed a good correlation between the two measures. **Discussion:** The VO_{2max} predicted by submaximal protocol demonstrated satisfactory criterion validity and simple execution compared to ergospirometry.

Oliveira NA, et al. / *Rev Psiq Clín.* 2013;40(3):88-92

Keywords: Exercise test, exercise, mood disorders, Parkinson's disease.

Resumo

Contexto: Evidências demonstram benefícios para a saúde mental com o treinamento aeróbico orientado em percentuais do VO_{2max} , indicando a importância dessa variável para a prática clínica. **Objetivo:** Validar um método para estimar o VO_{2max} por meio de um protocolo submáximo em idosos com diagnóstico clínico de transtorno depressivo maior (DM) e doença de Parkinson (DP). **Métodos:** A amostra foi composta por 18 pacientes ($64,22 \pm 9,92$ anos; sete pacientes com DM e 11 com DP). Foram realizadas três avaliações: I) estadiamento da doença, II) mensuração direta de VO_{2max} e III) teste de esforço submáximo. Foi realizada regressão linear para verificar a precisão de estimativa do VO_{2max} estabelecido na ergoespirometria pelo VO_{2max} predito no teste submáximo. Também foi analisada a concordância de Bland-Altman entre os procedimentos. **Resultados:** A análise de regressão mostrou que os valores de VO_{2max} estimados pelo protocolo submáximo associam-se com o VO_{2max} medido, tanto no valor absoluto ($R^2 = 0,65$; $EPE = 0,26$; $p < 0,001$) quanto no relativo ($R^2 = 0,56$; $EPE = 3,70$; $p < 0,001$). A análise de concordância de Bland-Altman mostrou boa associação entre as duas medidas. **Conclusão:** O VO_{2max} predito por meio do protocolo submáximo demonstrou satisfatória validade de critério e simples execução comparado à ergoespirometria.

Oliveira NA, et al. / *Rev Psiq Clín.* 2013;40(3):88-92

Palavras-chave: Teste de esforço, exercício, transtornos de humor, doença de Parkinson.

Introduction

Major depressive disorder (MDD) and Parkinson's disease (PD) are highly prevalent disorders representing about 7% and 1%-2% of the elderly population, respectively^{1,2}. In addition to the specific symptoms, there is also comorbidity with cardiovascular and metabolic diseases which compromise the quality of life and increase the risk of death³. MDD is associated with hypothalamic-pituitary-adrenal (HPA) axis hyperactivity, elevated cortisol levels and increased renin-angiotensin-aldosterone activation^{4,5}. These physiological changes in depressive individuals contribute to an increased risk of cardiovascular diseases, such as hypertension⁶. Moreover, the cholinergic system hyperactivity and the autonomic nervous system impairment

observed in patients with PD and depression may be associated with increased risk of cardiovascular disease^{7,8}.

Low cardiorespiratory fitness^{9,10} is one of the factors contributing to the all cause risk of death including cardiovascular disease. Maximum values of metabolic equivalent (MET) above 6 MET for women and 8 MET for men are associated with a 15% reduced risk of death⁹. With aging, it is expected to occur a decrease of the maximum volume of oxygen uptake (VO_{2max}): 10%¹¹ and 5%¹² per decade in sedentary and active individuals, respectively. On the other hand, aerobic exercise contributes to the reduction of the decline of VO_{2max} ¹³. In addition to the favorable responses in cardiovascular health, there is also a decrease in depressive symptoms and functional decline, as well as improvement in cognitive functions, which are potentially

efficient in the treatment of mental illness¹⁴. However, the prescription of aerobic exercise intensity is essential to the efficiency and safety of the training program, especially considering the high prevalence of cardiovascular disease in this population.

To determine VO_{2max} , ergospirometry is a direct method considered the "gold standard", also enabling the identification of ventilation thresholds. This measure has high reliability of VO_{2max} in Alzheimer's disease patients ($r = 0.94$, $p < 0.001$)¹⁵ and PD ($r = 0.90$)¹⁶, being used for diagnosis, prognosis and therapeutics, especially for prescribing aerobic training. However, its applicability in rehabilitation and physical activity centers becomes difficult due to their high financial and operational cost.

Besides the low cardiorespiratory fitness resulting from the physical inactivity and specific symptoms of MDD and PD diseases, behavioral and motor changes also difficult the maximal tests implementation in these patients. Loss of pleasure and energy are depressive symptoms common in MDD and can difficult the performance of a maximal exercise test. On the other hand, some PD symptoms, such as tremor, rigidity, bradykinesia and postural instability may difficult the implementation of the test due to problems in motor skills. Moreover, in more advanced stages of MD and PD diseases these symptoms may worsen. Because of that, the target intensity in maximum tests is rarely reached by these patients. Thus, sometimes it is necessary and recommended the use of metabolic equations suggested by the American College of Sports Medicine (ACSM) for the oxygen uptake estimation, including VO_{2max} ¹⁷.

Predictive methods of VO_{2max} through submaximal protocols have good reliability¹⁸ and may be a simple and low cost alternative in clinical interventions for exercise prescription. Recently, Santos *et al.*¹⁸ found good reproducibility of a submaximal treadmill protocol for obtaining the predicted VO_{2max} ($r = 0.89$) for both maximum heart rate (HR_{max}) estimated by age (220-age)¹⁹ and the frequency peak heart (HR_{peak}) ($r = 0.83$). Further to the advantages of submaximal protocol, the method allows the individualization of the increments by stage, being able to adapt the initial loads and intensity settings during the procedure, as the speed and inclination to reach the steady state in the intensity at 70% of heart rate reserve (HR_{res}). However, it is not yet established the validity of this procedure, particularly in elderly patients with mental disorders.

This study is meant to bridge the gap to obtain reliable parameters for the prescription of aerobic training in elderly diagnosed with MDD and PD. Moreover, there are not predictive protocols designed for this population. The aim of this study is to establish the criterion validity of a protocol of VO_{2max} prediction based on HR_{res} to be used in MDD and PD patients.

Methods

Subject

This study is part of a larger project regarding the effect of exercise training on the mental health of seniors and obtained approval from the research ethics committee of the Institute of Psychiatry, Universidade Federal do Rio de Janeiro (n° 70Liv2-09). MDD patients were diagnosed according to Diagnostic and Statistical Manual of Mental Disorders (DSM-IV) criteria and the study performed at the Center for Alzheimer's Disease and Related Disorders, Institute of Psychiatry, Universidade Federal do Rio de Janeiro (CDA-IPUB-UFRJ). Screening of patients with PD was performed at the Institute of Neurology Deolindo Couto (INDC/UFRJ).

Inclusion criteria for MDD were age between 60 and 80 years and mild to moderate depressive symptoms assessed by the Hamilton Depression Scale (HAM-D) validated for Portuguese²⁰. Inclusion criteria for PD were age between 45 and 70 years, diagnosis of idiopathic Parkinson's disease, stage 1 to 3 in Hoehn-Yahr²¹. Exclusion criteria common to all patients were illiteracy, stroke, associated neurodegenerative diseases, Parkinsonism, mental comorbidities, use of other treatments such as electroconvulsive therapy, psychotherapy, and clinical decompensate diseases. Other exclusion criteria were cardiac

history of acute myocardial infarction and ischemia, symptoms of coronary artery disease (angina), ventricular extrasystole, patients who were taking beta-blocker medications. Of the 31 patients enrolled, 13 were excluded (nine showed no eligibility criteria for the study and four did not attend all visits). The sample consisted of 18 patients who read and signed an Informed Consent Form.

Experimental design

The patients made three visits in the morning with an interval of up to two weeks between assessments. For PD patients it was taken into consideration the "on-off" and "wearing-off" phenomena, which are fluctuations of motor skills due to the use of levodopa. To avoid impairment of motor skills, patients were assessed during "on" period. Patients were submitted to a cognitive evaluation and motor skills assessment (for PD). Both disorders were staged using the Hamilton Depression Scale (HAM-D)²⁰, the Hoehn-Yahr²¹ and the motor domain of the Unified Scale for Assessment of Parkinson's disease (UPDRS III), all validated for the Portuguese.

Next, the volunteers underwent direct measurement of VO_{2max} through the maximum test protocol (ergospirometry) supervised by a cardiologist. On the third visit VO_{2max} was estimated using the submaximal protocol^{18,22}. Patients were instructed to eat light meals, drink water, did not ingest alcohol and did not smoke on the test day. Furthermore, they were instructed not to perform intense effort over the past 48 hours before assessments. Before starting the test, patients were instructed on the scale of perceived exertion [Borg Scale (6-20)]²³, and the safety procedures to the test on a treadmill. Weight and height were measured using a mechanical platform scale (Welmy 110, Welmy Industry and Commerce Ltda., SP, Brazil).

Maximal exercise test with gas analysis: The direct measurement through the maximal test with gas analysis was performed at the Medicine Exercise Clinic (MEDSPORT), in a room with a temperature of 23°C and relative humidity of 55%. Heart rate was monitored through derivation D2 on electrocardiograph (ECG Digital Elite, Micromed Biotechnology Ltda., DF, Brazil) and blood pressure was measured by a mercury sphygmomanometer (Diagnostix™, American Diagnostic Corporation®, USA).

The Treadmill Ramp Test Protocol²⁴ (ATL Millennium Super, Ltda Inbramed®, RS, Brazil) was chosen because it considers the biological individuality of patients. This protocol consisted of continuous and gradual increased stages according to the adaptation to the treadmill each patient. Tests used exclusively walking, in which the doctor set the speed and inclination to be achieved by the patient and the computerized system (VO2000, Medical Graphics®, 13° PC Ergo software version 3.3, RS, Brazil) calculated the rate at which the power was increased during testing. The cardiorespiratory variables VO_2 , respiratory exchange ratio (R), carbon dioxide production (VCO_2) and pulmonary ventilation (VE) were measured using a gas analyzer coupled to the computerized system, with samples every 10 seconds.

Systems analysis of O_2 and CO_2 were calibrated according to manufacturer's specification before each test. The peak oxygen consumption (VO_{2peak}) was considered as highest value obtained at the end of the effort. To consider this test as maximum effort some criteria were observed, such as to reach a plateau in oxygen uptake, perceived exertion above 17 (Borg scale 6-20) and mainly, volitional fatigue. Furthermore, the evaluators were alerted to the criteria for interruption with diagnostic purposes suggested by ACSM¹⁷.

Submaximal protocol: The testing was performed at the Institute of Neurology Deolindo Couto. Vital signs were measured after 10 min rest in the supine position in a quiet and refrigerated room. During the tests we monitored and recorded heart rate by frequency meters every 20 s (model FS3™, Polar®, Finland), the subjective feeling of exertion by the Borg scale (6-20)²³ and blood pressure was measured and recorded every 2 min through the device (DuraShock, Welch Allyn, Tycos®, SC, Brazil).

To determine the HR_{res} we used the equation $(HR_{max} - HR_{res}) \times \text{intensity} + HR_{res}$, in which HR_{max} = maximum heart rate estimated by equation $(220 - \text{age})^{19}$, HR_{res} = resting heart rate measured after 10 min of rest the patient in the supine position and intensity = intensity that the patient should reach during the test (65% of HR_{res}), and keep the steady-state (70% of HR_{res}).

The submaximal protocol consisted of an initial 3-min warm-up on treadmill (JOG model 500, Technogym The Wellness Company®, Italy), in which the initial rate varied according to the adaptation to the treadmill between patients. The increased metabolic ratio for each stage was equivalent to 1 MET and provided by manipulating the speed and inclination on the treadmill. The objective was to reach the intensity corresponding to approximately 65% of HR_{res} . Once achieved, this exercise intensity was maintained for six minutes featuring a steady-state²⁵. By the end of this phase, it was expected that the HR was stabilized at approximately 70% of HR_{res} . The criteria for interruption of both tests followed the recommendations of ACSM¹⁷.

The VO_2 was obtained by equation: $VO_2 = [0.1 (\text{speed}) + 1.8 (\text{speed}) (\text{inclination}/100) + 3.5]$, in which the speed is given in m/min. Finally, VO_{2max} was predicted by the equation: $VO_{2max} = [(VO_2 - 3.5) / 3.5 HR_{res} + 3.5]$, in which the VO_{2max} is expressed in $\text{mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$.

Statistical analysis

We applied the Shapiro-Wilk and Levene tests to test the distribution and data variance, respectively. A linear regression was performed to verify the accuracy of the estimate in VO_{2max} established in cardiopulmonary exercise testing by VO_{2max} predicted in submaximal test. The accuracy of prediction was established by the coefficient of determination and adjusted by the standard error of the estimate (SEE). Moreover, to verify the correlation between measured VO_{2max} and estimated VO_{2max} it was used the reliability analysis Bland-Altman.

The software used for data analysis was the Statistical Package for the Social Sciences version 19 (SPSS® Inc., Chicago, IL, USA) and a value $p \leq 0.05$ was accepted as indicating statistical significance.

Results

The sample consisted of 18 patients, 11 with PD and seven with MDD. Patients had a mean age of 64.2 (SD = 9.92) years and mean schooling of 9.5 (SD = 4.13) years. The average weight and height of all patients was 67 (62.5 to 72.3) kg and 1.63 (SD = 0.09) meters, respectively. Among the patients, 11 were taking antiparkinsonian medications (61.1%), seven were taking selective serotonin reuptake inhibitors (38.9%) and eight were taking antihypertensive medications (44.4%). There was a normal distribution and homogeneity for age, education, mini mental state examination (MMSE), height, body mass index, number of medications, HAM-D score and UPDRS. Regarding symptoms of the disease, depressive patients had mild symptoms of depression assessed by HAM-D (11 ± 6). PD patients had a median score of 2.5 (2.0-3.0) on Hoehn Yahr Scale and 31.8 (SD = 10.5) points in the evaluation of motor symptoms by UPDRS III. All patients had adequate adaptation in both protocols investigated and no complications were observed.

All patients showed mean absolute VO_{2max} of $1.6 \pm 0.4 \text{ L} \cdot \text{min}^{-1}$ (measured directly) and $1.9 \pm 0.4 \text{ L} \cdot \text{min}^{-1}$ (indirect measure). The VO_{2max} values were made relative to the body mass of $23.8 \pm 3.8 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (direct measure) $27.5 \pm 5.5 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$ (indirect measurement). Regression analysis showed that the VO_{2max} values estimated by submaximal protocol are associated with VO_{2max} measured both in absolute value ($R^2 = 0.65$, $F(1,16) = 29.78$; $SEE = 0.26$; $p < 0.001$) and the relative ($R^2 = 0.56$, $F(1,16) = 20.76$, $SEE = 3.70$, $p < 0.001$). The Bland-Altman concordance analysis presented BIAS -3.70 ± 3.63 (mean, SD) (95% CI, -10.82, 3.41) for the relative VO_{2max} and BIAS -0.25 ± 0.25 (95% CI, -0.74, 0.25) for the absolute VO_{2max} , showing a good agreement between the two methods (Figure 1).

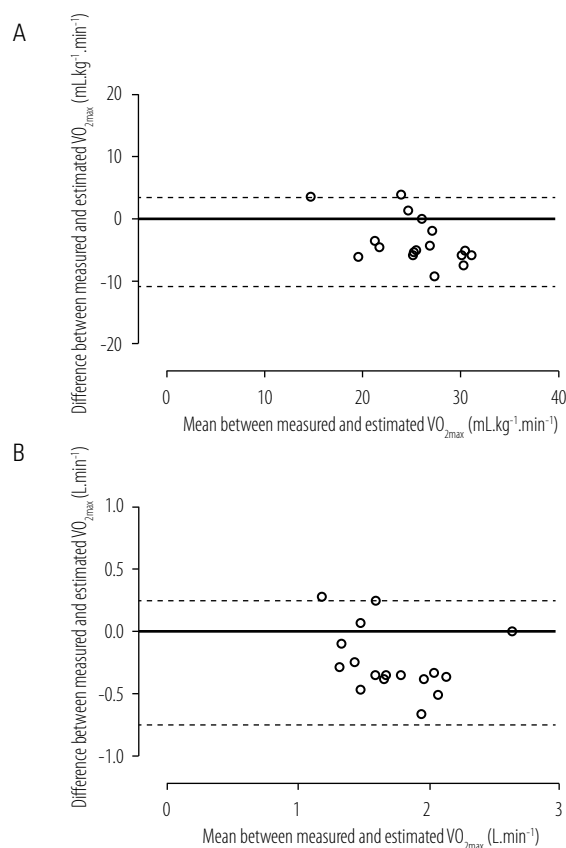


Figure 1. Bland-Altman Plot between relative VO_{2max} (A) and absolute VO_{2max} (B) in maximal and submaximal protocols.

Discussion

This study aimed to investigate the use of an indirect method for predicting VO_{2max} based on HR_{res} and VO_{2res} through a submaximal protocol in patients with highly prevalent mental and neurodegenerative diseases in the elderly population, specifically the MDD and PD. The results showed good correlation between directly VO_{2max} measured and VO_{2max} provided by the proposed submaximal protocol, with standard error of the estimate of $0.26 \text{ L} \cdot \text{min}^{-1}$ and $3.70 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$. All patients were able to perform the tests without any adverse response or impairment during or after the evaluations, highlighting the ease of application and safety of the protocol.

According to Bland-Altman analysis, we observed a difference between direct and indirect measurement, assuming that there is a slight overestimation in indirect measurement. However, the values of SEE were similar to those found in the literature²². Through the mean VO_{2max} obtained by direct measurement ($23.7 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$) and the indirect measurement ($27.4 \text{ mL} \cdot \text{kg}^{-1} \cdot \text{min}^{-1}$), it was possible to calculate the mean METs (6.8 to 7.8 METs, respectively). It is believed that individuals with maximal aerobic capacity of 7.9 METs or more have lower mortality rates and less cardiovascular disease⁹. These data indicate the suitability of the method to cardiorespiratory evaluation in MDD and PD patients, since they are at greater risk for cardiac events^{3,6}. In addition, psychiatric disorders are prevalent in cardiac patients who participate in a supervised exercise program, even without functional impairment and multiple comorbidities²⁶.

For greater safety, we recommend consideration of the standard error of estimate reported and demonstrated by the present study. Our data corroborate a previous data in a study which used a cycle ergometer through a submaximal protocol ramp with sedentary individuals which found high reproducibility ($r = 0.85$, $p < 0.001$) and

validity ($r = 0.75$, $p < 0.001$)²⁷. The development of these methods or indirect tests aims at helping the cardiovascular evaluation and direction for the prescription of exercise training.

The adhesion to exercise program and training effectiveness also depends on factors related to prescription, such as the intensity of the effort. Too light or too high intensity seems to be associated with a worse affective response and possibly lower adherence to an exercise program, especially in sedentary individuals²⁸. Furthermore, studies have shown an ideal intensity for a better benefit on motor, cognitive, and behavioral skills. According to the “inverted U” theory²⁹, moderate intensities promote the best response, requiring strict control of this variable in patients with mental disorders³⁰.

According to ACSM guidelines for elderly population³¹, it is recommended to practice 150 minutes per week of physical activity, and the frequency with aerobic activity at least three times per week, intensity at 40 to 60% of HR_{res} , 11-13 in Borg scale, lasting at least 20 min. Studies that have investigated the effect of aerobic exercise in the treatment of MDD in elderly have used VO_{2max} relative for the prescription of training intensity^{32,33}. It has already been demonstrated that aerobic exercise performed two to three times a week during 30 min, with 60% VO_{2max} (12 to 14 on the Borg scale) were effective for the additional treatment in MDD^{32,33}. Such evidence supports the importance of determining VO_{2max} to prescribe aerobic training.

This study presents some limitations which should be considered, for example, the small number of patients and medication used by the PD patients, since they reduce the HR. In particular, this aspect may explain the slight overestimation of VO_{2max} observed. Future studies are needed to replicate these analyzes separately for each population taking into consideration the type of medication used. Furthermore, it is suggested that future studies compare the prediction equations HR_{max} proposed by Fox *et al.*¹⁹ and Tanaka *et al.*³⁴. Although the present study used only MDD and PD patients, it is expected that the method for predicting VO_{2max} from a submaximal protocol can be used by patients with other mental disorders. Thus, future research should replicate this method with specific populations.

Conclusion

VO_{2max} predicted by submaximal protocol demonstrated satisfactory validity criterion and simple implementation when compared to ergospirometry. Exercise prescription for older adults with MDD and PD can be adequately performed based on physiological variables obtained by this protocol, which should consider the accuracy reported by this study. This recommendation suggests safer and more effective aerobic training.

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