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Prediction of peak oxygen pulse (O_2P_{peak}) without exercise testing in older adults

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ABSTRACT

Peak oxygen pulse has been considered a surrogate of cardiovascular function and an independent predictor of all cause mortality. However, O_2P_{peak} depends on maximal volitional effort which may limit its utility in older subjects. The aim of this study was to develop a model to estimate O_2P_{peak} without exercise in an elderly sample. This cross-sectional study enrolled 67 community-dwelling older adults (69.4 ± 7.1 years; 41 men) for the non-exercise model development and 30 community-dwelling older adults (67.7 ± 6.4 years; $n = 30$; 17 men) for cross-validation. The non-exercise model was derived through hierarchical regression model and cross-validated by means of PRESS statistics and comparison against an independent sample. Classification accuracy of the model for tertiles of estimated and actual O_2P_{peak} was tested by gamma (γ) nonparametric correlation. The following prediction equation was generated: −3.416 + 0.137 × weight (kg) + 1.226 × Veterans Specific Activity Questionnaire (VSAQ) (metabolic equivalents, METs) + 1.987 × gender (0 = women, 1 = men) − 2.045 × β-Blockers use (0 = no, 1 = yes) - − 0.044 × resting heart rate (HR) ($R^2 = 0.83$; standard error of estimate (SEE) = 1.68 mL beat^{-1}). Correlation in cross-validation group was 0.80 ($P < 0.001$). A high probability was observed for the model to rank the values in the same tertile in validation and cross-validation groups ($\gamma = 0.98$; $\gamma = 0.92$, respectively, $P < 0.05$). In conclusion, O_2P_{peak} can be estimated with reasonable precision without exercise testing, providing an alternative for elder subjects not capable to perform maximal effort.

1. Introduction

Peak oxygen uptake (VO_{2peak}) is one of the most important variables obtained during CPX (Oliveira, Myers, Araújo, Arena, et al., 2009), both in clinical and research settings. However, directly measured VO_{2peak} is not always feasible due to either pragmatic or financial reasons, or because the technical expertise required is not available. Therefore, several methods have been proposed to estimate VO_{2peak} with and without exercise testing (Maranhao Neto, Lourenco, & Farinatti, 2004). In addition, interest has arisen in recent years in the clinical and prognostic value of other CPX variables, such as the minute ventilation carbon dioxide production (VE/VCO2) slope (Arena, Myers, & Guazzi, 2008, Arena, Myers, Hsu, Peberdy, et al., 2007), the oxygen uptake efficiency slope (OUES) (Arena et al., 2008), and O_2P_{peak} (Cohen-Solal et al., 1997; Laukkanen, Kurl, Salonen, Lakka, & Rauramaa, 2006; Oliveira, Myers, Araújo, Abella, et al., 2009; Oliveira, Myers, Araújo, Arena, et al., 2009).

The O_2P_{peak}, defined by dividing VO_{2peak} by peak HR, has been considered a surrogate for stroke volume (Oliveira, Myers, & Araujo, 2011), and has been shown to be an independent predictor of all-cause mortality in healthy subjects and in patients with cardiovascular disease (Oliveira, Myers, Araújo, Abella, et al., 2009). Although readily available from CPX, O_2P_{peak} depends on maximal volitional effort, which may be limited in older subjects due to limited functional capabilities, orthopedic problems, and a high prevalence of frailty in this population (Church et al., 2008). Non-exercise prediction models may therefore be useful alternatives in order to estimate O_2P_{peak}. Such models can be developed by means of regression-based equations that usually include variables that are readily available, such as anthropometric measures, demographic characteristics, and daily activity habits (Maranhao Neto & Farinatti, 2003; Maranhao Neto et al., 2004). However, the

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available models are limited to the estimation of VO_{2peak} (Maranhao Neto & Farinatti, 2003).

While many efforts have been made to estimate VO_{2peak} from non-exercise variables, to our knowledge there are no equations that have been developed to estimate O_2P_{peak}, especially in older adults. The present study was therefore designed to develop a non-exercise prediction model for O_2P_{peak} and test its validity in a sample of older individuals.

2. Materials and methods

2.1. Subjects

The initial sample consisted of 143 subjects admitted to the Elderly Care Center of the Third Age Open University (UnATI-UERJ) between March 2004 and September 2007. To be included in the study patients were required to be asymptomatic, have stable disease, and show no abnormalities on their resting electrocardiogram within the previous six months. Patients underwent clinical exams to detail their medical history and completed a brief questionnaire providing demographic information, which was used to determine whether they appropriate for a maximal CPX. Subjects with valvular disease, lung disease, anemia, and those who exhibited O_2 desaturation during exercise (more than 4% at maximal effort) were excluded from the study. In addition, all exercise tests terminated early for clinical reasons were not considered maximal and were excluded from the study.

A total of 97 subjects (58 men) were considered eligible for the analysis. The sample was randomly assigned into two groups: validation (to develop the model) and cross-validation (to validate the model in an independent data set). The experimental protocol was approved by institutional Ethical Committee, and all participants provided written informed consent prior to study enrollment, in accordance with the Declaration of Helsinki.

2.2. Procedures

Anthropometric measurements included weight and height. Self-rated fitness was evaluated using a Brazilian Portuguese version of the VSAQ, which has been cross-culturally validated (Maranhao Neto, Ponce de Leon, & Farinatti, 2008). The VSAQ is a widely-used tool consisting of a 13-item list of activities in progressive order that estimates exercise capacity expressed in METs (Maranhao Neto, Ponce de Leon, & Farinatti, 2011; Myers, Do, Herbert, Ribisl, & Froelicher, 1994). Participants indicated the activities on the scale that would typically cause fatigue, shortness of breath, chest discomfort, or otherwise cause them to stop exercising. The VSAQ was administered by interview in a standard fashion according to recommendations published elsewhere (Maranhao Neto et al., 2008).

All subjects (validation and cross-validation groups) performed a clinically supervised maximal exercise testing on an electromagnetic cycle ergometer (Cateye™ EC-1600, Cat Eye, Tokyo, Japan) using an individualized ramp protocol. Subjects underwent a familiarization trial to get accustomed to the procedures on the day prior to the exercise test. Individualized treadmill work rate increment was set such that the test duration was targeted to last between 8 and 12 min.

Gas exchange data were acquired every 10 seconds by the VO2000 metabolic analyzer (Medical Graphics™, St. Paul, MN, USA). VO_{2peak} was defined as the highest value obtained within 10-s intervals during the test. HR was measured at rest in a sitting position and continuously during CPX by ECG (Elite Ergo PC 3.2.1.5; Micromed™, Sao Paulo, Brazil). Peak HR was also considered the highest value obtained using 10-s intervals during CPX. Blood pressure was measured manually at rest and at every minute during exercise using a sphygmomanometer WelchAlln (Tycos™, Arden, New York, USA). O_2P_{peak} was calculated by dividing VO_{2peak} by HR_{peak} and expressed in milliliters per beat. It is noteworthy that for all patients VO_{2peak} and HR_{peak} were achieved at the same 10-s interval. The Borg CR-10 perceived exertion scale was used to estimate the degree of exertion every minute (Borg, 1998).

Subjects were verbally encouraged to exercise to volitional fatigue. Standard clinical criteria were used to terminate the test (American College of Sports Medicine – ACSM, 2010). These included moderate to severe angina, abnormal ST depression (>2.0 mm horizontal), sustained drop in systolic blood pressure, or serious rhythm disturbances. The CPX was considered as maximal if the subjects satisfied at least three of four criteria: (a) maximum voluntary exhaustion defined by attaining score of 10 on the Borg CR-10 scale or when the cadence could not be maintained at a minimum of 50 rpm; (b) 90% of the predicted HR_{max} [220 − age] or presence of a HR plateau (ΔHR between two consecutive work rates $\leq$4 beats min^{-1}); (c) presence of VO_2 plateau (ΔVO_2 between two consecutive work rates of less than 2.1 mL kg^{-1} min^{-1}); (d) maximal respiratory exchange ratio (RER_{max}) > 1.10 (Howley, Bassett, & Welch, 1995).

2.3. Statistical analyses

Data normality was confirmed by univariate analysis. Differences between the Validation and Cross-Validation Groups were tested by the Student t and chi-square tests. Body mass, self-related fitness (VSAQ Score), gender, beta-blocker usage, resting HR, and age were entered respectively into the first, second, third, fourth, five and six blocks of the hierarchical linear regression procedure to develop a model to predict O_2P_{max}.

The coefficient of determination (R^2) and the SEE were calculated and the prediction equation generated was then cross-validated for an independent sample, using the Pearson correlation between the estimated and actual O_2P_{peak}. Differences between predicted and measured O_2P_{peak} were also tested by Students t-tests. In order to detect the classification accuracy of the model, the estimated and actual O_2P_{peak} were ranked in tertiles and compared by the γ nonparametric correlation of Goodman and Kruskal in both groups (validation and cross-validation). Two-tailed statistical significance for all analyses was accepted as $P \leq 0.05$. All calculations were performed using the Stata version 10.1 software (Statacorp™, College Station, TX, USA).

3. Results

Table 1 presents descriptive statistics as well as values for cardiorespiratory variables at rest and maximal exercise for both the validation and cross-validation groups. These groups differed only in resting systolic blood pressure ($P = 0.03$).

The five selected variables were significantly associated ($P < 0.01$) O_2P_{peak} after the linear regression procedure. Body weight, self-related fitness (VSAQ Score), gender, β-blocker use, and RHR accounted for 48%, 25%, 5%, 1.7% and 2.5% of the O_2Ppeak variance, respectively. The following prediction equation was generated: O_2Ppeak = −3.416 + 0.137 × body weight (kg) + 1.226 × VSAQ Score (METs) + 1.987 × gender (0 = women, 1 = men) − 2.045 × β-Blockers use (0 = no, 1 = yes) − 0.044 × RHR (bpm) [SEE = 1.67 mL $beat^{-1}$]. Based on the R^2 value, the obtained model explained 83% of the variability in O_2P_{peak}. No significant differences were detected between estimated and actual O_2P_{peak}. Fig. 1 illustrates the results for the comparison between estimated and actual values in both validation and cross-validation groups, indicating that the model was appropriate to estimate O_2P_{peak} in senior subjects.