Correspondence

Prediction of peak oxygen uptake in patients with Chagas heart disease: Value of the Six-minute Walk Test

Henrique Silveira Costa, PhD a,⁎, Márcia Maria Oliveira Lima, PhD b, Maria Clara Noman Alencar, PhD a, Giovane Rodrigo Sousa, PhD a, Pedro Henrique Scheidt Figueiredo, MSc b, Maria Carmo Pereira Nunes, PhD a, Antônio Luiz Ribeiro, PhD a, Manoel Otávio Costa Rocha, PhD a

a Postgraduate Course of Infectious Diseases and Tropical Medicine, Department of Internal Medicine, Medical School and Hospital das Clinicas of the Universidade Federal de Minas Gerais (UFMG), Belo Horizonte, Brazil
b Healthy and Biological Sciences Faculty, Physical Therapy School, Universidade Federal dos Vales do Jequitinhonha e Mucuri (UFVJM), Diamantina, Brazil

Available online 13 November 2016
Accepted 10 November 2016
Received in revised form 8 November 2016
Received 3 July 2016
Article history:

Article info

Contents lists available at ScienceDirect
International Journal of Cardiology
journal homepage: www.elsevier.com/locate/ijcard

Chagas disease, an infection caused by the protozoan Trypanosoma cruzi, affects about 10 million people worldwide and another 100 million are at risk of becoming infected [1]. In recent decades, changes in the epidemiological profile of Chagas disease has been observed leading to urbanization and globalization of the infection with increasing prevalence in North America and Europe [2]. Heart disease is the most severe clinical form of the Chagas disease [3] leading to exercise intolerance, especially in advanced stages of the disease.

In clinical practice, peak oxygen uptake (VO2peak) is considered the best index of functional capacity (FC), exercise tolerance and cardiopulmonary function [4]. However, maximal exercise testing may not be available in endemic areas for Chagas disease, where usually have poor infrastructure and limited technological resources. An alternative approach is the Six-minute Walk Test (6MWT), a simple, inexpensive and effective tool in assessing FC in cardiac patients [5]. In patients with Chagas heart disease (CHD), the 6MWT was associated with echocardiographic variables [6], demonstrated the effectiveness of exercise-based intervention [7] and correlated with VO2peak [8]. However, compared to the VO2peak, the distance walked during the test provides limited information about the functional status of the patient and a model that predicts VO2peak based on 6MWT is needed in the accurate assessment of FC.

Thus, the present study was designed to derive a regression equation that can determine the VO2peak by 6MWT and clinical variables in CHD patients and to compare the predicted values by the regression equation with observed VO2peak.

This cross-sectional study was conducted at the Referral Outpatient Center for Chagas Disease at the Hospital das Clinicas of the Universidade Federal de Minas Gerais (UFMG), Brazil. The research was carried out in accordance with the Declaration of Helsinki and was approved by institutional ethics committee. All the patients gave their written informed consent prior participating in the study.

Criteria for inclusion were the serological diagnosis of Chagas disease, clinical, electrocardiographic or echocardiographic findings compatible with CHD and stable clinical condition. Exclusion criteria were the presence of systemic or heart disease by any other causes, associated co-morbidities and the inability to perform exercise testing.

The sample comprised patients with a wide spectrum of CHD presenting different degrees of cardiac involvement. The previously selected patients underwent clinical evaluation, echocardiography, maximal treadmill exercise test and 6MWT by current guidelines.

Data were analyzed with SPSS version 17.0 (SPSS Inc., Chicago, IL, USA). Continuous variables were described as mean ± SD. Uni and multivariate linear regression analysis were performed to determine the factors that were associated with VO2peak. The significance level of 0.05 was considered statistically significant. The agreement analysis between observed and predicted VO2peak was verified by Bland-Altman method and the differences values were plotted against their mean.

A total of 81 CHD patients (48.6 ± 8.1 years; 63% males, NYHA I-III), were evaluated. Demographic characteristics, echocardiographic and functional variables in the overall study population are shown in Table 1.

In the final multivariable model, gender, NYHA functional class, 6MWT distance, age and body mass index remained as independent predictors of VO2peak (Table 2). The predicted VO2peak is represented by the model: VO2peak = 53.43 + (1.35 x gender; coded 0 for female and 1 for male) – (5.59 x NYHA) + (0.01 x 6MWT distance) – (0.29 x age) – (0.035 x BMI); r2 = 0.61, p < 0.001.

Table 1.
A strong correlation between observed and predicted VO2peak was verified ($r = 0.81, p < 0.001$) and there was no significant difference between the values ($p = 0.223$). The agreement analysis showed that only five pairs (6.1%) of VO2peak lied outside the range of the limits of agreement and the mean bias was close to zero ($mean = -0.64 \pm 4.68$ mL.kg.min) (FIG. 1).

The present study is the first that derived a model to predict VO2peak in CHD patients based on the 6MWT distance and clinical variables. The predicted VO2peak by the equation VO2peak = 53.43 + (1.35 x gender) – (5.59 x NYHA) + (0.01 x 6MWT distance) – (0.29 x age) – (0.035 x BMI) showed a strong correlation with observed VO2peak ($r = 0.81; p < 0.001$), without difference between these values ($p = 0.223$) and with $r = 0.61$.

The 6MWT distance explained only 28% of the variance in VO2peak but the addition of age, gender, body mass index and NYHA functional class to the regression model using 6MWT distance substantially improves the ability to predict VO2peak as demonstrated by an explained variance of 61%.

The prediction of VO2peak by simple and easily measured clinical parameters as the 6MWT and clinical data can assist in more accurate evaluation of FC in areas where the maximal exercise test is usually not available, enabling monitoring the functional status of CHD patients as well as their risk stratification based on functional impairment.

**Table 1**

<table>
<thead>
<tr>
<th>Variables</th>
<th>Mean ± SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>48.6 ± 8.1</td>
</tr>
<tr>
<td>Male gender (%)</td>
<td>51 (63%)</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>25.4 ± 4.3</td>
</tr>
<tr>
<td>NYHA functional class</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>46 (56.8%)</td>
</tr>
<tr>
<td>II</td>
<td>29 (35.8%)</td>
</tr>
<tr>
<td>III</td>
<td>6 (7.4%)</td>
</tr>
<tr>
<td>6MWT distance (m)</td>
<td>535.7 ± 82.7</td>
</tr>
<tr>
<td>VO2peak (mL.kg.min)</td>
<td>28.1 ± 7.5</td>
</tr>
<tr>
<td>METs</td>
<td>7.9 ± 2.1</td>
</tr>
<tr>
<td>SBP achieved</td>
<td>79.5 ± 13.0</td>
</tr>
<tr>
<td>LVEF (%)</td>
<td>43.7 ± 13.7</td>
</tr>
<tr>
<td>LVDD (mm)</td>
<td>603 ± 9.4</td>
</tr>
<tr>
<td>LVsd (mm)</td>
<td>508 ± 6.6</td>
</tr>
<tr>
<td>E/e ratio</td>
<td>10.9 ± 4.3</td>
</tr>
</tbody>
</table>

Data presented as mean and standard deviation or number (percentage). BMI = body mass index; NYHA = New York Heart Association functional class; 6MWT = six-minute walk test; VO2peak = peak oxygen uptake; METs = metabolic equivalent task; SBP = systolic blood pressure; LVDd = left ventricular end-diastolic diameter; LVsd = left ventricular end-systolic diameter; E/e ratio = ratio of the early diastolic transmitral flow velocity to early diastolic mitral annular velocity.

Furthermore, the etiological treatment in CHD, although mandatory, is still controversial [9]. In the meantime, exercise training under supervision is one of the key points of the non-pharmacological treatment of patients with CHD [10] and methods for evaluating FC in these patients should be investigated.

In the agreement analysis, the mean bias between the observed and predicted VO2peak was close to zero, but the limits of agreement (±1.96 SD) was 9.17 mL.kg.min. However, the clinical course of CHD is diverse [11] and heterogeneous results in the assessment of VO2peak are expected.

Echocardiographic variables were not used in the model. Firstly, the main objective of the present study was to derive a regression model that could be easily applied without sophisticated equipment. Secondly, left ventricular ejection fraction, one of the most important prognostic factors in Chagas disease [3], had no significant correlation with VO2peak in CHD patients [12].

Study limitations include the evaluation of exercise capacity was performed by conventional treadmill exercise testing and not by Cardiopulmonary Exercise Testing. However, it has been established that the indirect assessment of the VO2peak is highly correlated with the direct measurement [13].

We concluded that peak oxygen uptake can be easily predicted by 6MWT and clinical data in Chagas heart disease patients. The model has a good performance to predict VO2peak without additional information and has potential value in the assessment of functional capacity in these patients in resource-limited areas. To validate the model, a study using the proposed equation in an endemic area population is in progress.

**Conflict of interest**

The authors report no relationships that could be construed as a conflict of interest.

**References**


