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Six-minute walk test and incremental shuttle walk test in the evaluation of functional capacity in Chagas heart disease

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Chagas heart disease (CHD) leads to a progressive functional impairment. Field tests, as the 6-min walk test (6MWT) and the incremental shuttle walk test (ISWT), may be inexpensive approaches in the evaluation of functional capacity of these patients. The present study was addressed to compare the 6MWT and the ISWT measures, and to determine the accuracy of these tests in the identification of functional impairment in patients with CHD. Thirty-five patients with CHD (47.1 ± 8.2 years, NYHA I–III) were evaluated by echocardiography, cardiopulmonary exercise test (CPET), 6MWT, and ISWT. Correlations between the CPET (peak oxygen uptake [peak VO_2] and the ratio between ventilation and the carbon dioxide production [VE/VCO_2 slope]) and the field tests (walking distances) were also performed. The receiver operating characteristic (ROC) curve was selected to identify the best distances related to identify those patients with functional impairment. There was no difference between distances walked during the 6MWT and ISWT ($P=0.694$). The Bland-Altman analysis showed good agreement between the field tests. Both 6MWT and ISWT correlated with peak VO_2 ($r=0.577$, $P<0.001$ and $r=0.587$, $P<0.001$, respectively) and ISWT correlated with VE/VCO_2 slope ($r=-0.339$, $P=0.003$). The cutoff distances of 6MWT and ISWT to identify patients with peak VO_2 less than 20 mL/kg/min were 520 m and 400 m, respectively, with no difference between the areas under ROC curves ($P=0.276$). Both the 6MWT and the ISWT demonstrated accuracy in identify functional impairment in patients with CHD, being useful tools for the risk stratification of these patients.

Keywords: Chagas disease, Exercise, Exercise test

INTRODUCTION

Chagas disease is a neglected tropical disease (World Health Organization, 2010) endemic in regions with scarce resources and with significant increase in prevalence in countries with large numbers of immigrants (Garcia et al., 2015). Chagas heart disease (CHD) is the clinical form with the worst prognosis (Dias et al., 2016; Rocha et al., 2007), defined by the presence of characteristic abnormalities of myocardial damage at electrocardiogram and/or echocardiogram, with or without left ventricular dysfunction (Andrade et al., 2011; Dias et al., 2016). The cardiac involvement leads to skeletal and cardiac muscles abnormalities (Montes de Oca et al., 2004), changes in lung function (Baião et al., 2013), inspiratory muscle weakness (Baião et al., 2013; Vieira et al., 2014), poor quality of life (Sousa et al., 2015), and reduced functional capacity (Baião et al., 2013; Mady et al., 2000), which should be regularly evaluated.

Patients with CHD may have functional impairment even in the presence of preserved left ventricular ejection fraction (LVEF) (Mady et al., 2000), and the cardiopulmonary exercise testing

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(CPET) is the gold standard in the assessment of physical function (Guazzi et al., 2008). The peak oxygen uptake (peak VO_2) and the minute ventilation-carbon dioxide production slope (VE/VCO_2 slope) can be directly measured by gas analysis and provide important clinical and prognostic information (Guazzi et al., 2008; Ritt et al., 2013). Nevertheless, the CPET is expensive and usually not available in endemic areas, limiting its applicability in clinical routine. Therefore, submaximal tests such as the 6-min walk test (6MWT) and the incremental shuttle walk test (ISWT) (Casillas et al., 2013) may be simple and inexpensive approaches to the functional assessment of patients with CHD.

The 6MWT is widely used in patients with CHD (Costa et al., 2014; Costa et al., 2017; Dourado et al., 2010). The test is easy to perform, inexpensive and well tolerated by patients (ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002). It has good reliability, moderate validity and ability to predict functional capacity in patients with heart failure (Casillas et al., 2013; Pollentier et al., 2010). However, the 6MWT is distance-limited, self-paced, and patients tend to select a comfortable speed (Morales et al., 1999), which could underestimate the functional evaluation.

Unlike the 6MWT, the ISWT is a symptom-limited test, with progressive increment of workload (Parreira et al., 2014; Singh et al., 1992). The regular increments make the test more similar to the CPET, and strong correlations are usually found between distance walked and VO_2 peak in patients with different diseases, including heart failure (Morales et al., 1999; Parreira et al., 2014) and CHD (Alves et al., 2016).

Despite the common application of these tests in cardiac rehabilitation, no study was found that compared these measures in patients with CHD. Considering that Chagas cardiomiopathy is the most fibrosing and arrhythmogenic of known heart diseases and, consequently, with a worse prognosis (Botoni et al., 2013; Rocha et al., 2009), it is necessary to verify the performance of exercise testing in patients with Chagas cardiomyopathy. So, the present study aimed to compare the 6MWT and the ISWT measures in patients with CHD and to determine the accuracy of these field tests in the identification of functional impairment.

MATERIALS AND METHODS

This cross-sectional study was conducted at a referral center in the management of infectious and parasitic diseases. The research was carried out in accordance with the Declaration of Helsinki (World Medical Association, 2013) and was approved by the institutional ethics committee (approval number: CAAE 03993912.6.0000.5149). All the patients were informed about the objectives and agreed to voluntarily participate in the study.

Study design

The sample included CHD patients with different degrees of cardiac involvement. Eligibility criteria included the positive serology for *Trypanosoma cruzi* and the presence of arrhythmias and intraventricular and atrioventricular conduction disorders with or without left ventricular dysfunction (compatible with CHD) (Andrade et al., 2011). Patients with cardiopathy by any other causes, with comorbidities and unable to perform the exercise tests were excluded.

On the first day, the participants underwent clinical evaluation, echocardiography and CPET. The 6MWT and ISWT were performed on the following two days. A maximum interval of one week was allowed among the exercise tests. The investigators were blinded to the test results.

Echocardiographic evaluation

Echocardiography was performed according to recommendations of the American Society of Echocardiography (Lang et al., 2015) by one investigator who was blinded to the clinical evaluation of the patients. LVEF was obtained by modified Simpson rule. Early diastolic velocity (e') at the medial border of the mitral annulus was obtained and the ratio between peak mitral E and e' (E/e') was calculated.

Cardiopulmonary exercise testing

The CPET was performed on a treadmill with the metabolic analysis system MetaLyzer 3B (Cortex Medical, Leipzig, Germany). The peak VO_2 and minute ventilation-carbon dioxide production (VE/VCO_2) slope were used as the primary endpoints in functional evaluation and obtained according to current guidelines (Guazzi et al., 2016).

6-min walk test

The 6MWT was guided by American Thoracic Society guidelines (ATS Committee on Proficiency Standards for Clinical Pulmonary Function Laboratories, 2002). During the 6MWT, the volunteers had to walk at the highest possible speed, without running, in a 30-m corridor. Words of encouragement were used every minute. Two tests were applied, with 15-min interval between them and the primary endpoint was the longest 6MWT distance, expressed in meters.

Incremental shuttle walk test

The ISWT was performed using the protocol proposed by Singh et al. (1992). The test was applied in a 10-m course corridor marked out by two cones nine meters apart. The minimum speed achieved by patients on the test was controlled by signals from an audiotape previously recorded in regular intervals. The test was finished when the volunteer completed the 12 levels or could not achieve the distance target between cones within the intervals for two consecutive times. The primary endpoint was the longest ISWT distance, expressed in meters.

Statistical analysis

Statistical analyses were performed using SPSS ver. 17.0 (SPSS Inc., Chicago, IL, USA). Continuous data were expressed as mean and standard deviation and median and interquartile range, as appropriate. Categorical variables were shown as absolute number and percentage. Difference between distances walked during 6MWT and ISWT was verified by the Wilcoxon signed-rank test. Correlations were evaluated by Pearson or Spearman correlation test. The significance level was set at 5%. The agreement analysis between distances walked during submaximal field tests was verified by the Bland–Altman graph and the differences values were plotted against their mean. A ROC curve was constructed to verify the accuracy of 6MWT and ISWT in identifying those patients with peak VO_2 below 20 mL/kg/min functional impairment, defined as values according to Webber classification (Weber et al., 1982). The statistical difference between the curves was determined by chi-square using the software MedCalc version 13.1.2.0 (MedCalc Software, Ostend, Belgium).

Table 1. Characteristics of the sample (n = 35)

Variable	Value
Characterization of the sample	
Age (yr)	47.1 ± 8.2
Male sex	23 (66)
Body mass index (kg/m^2)	26.5 ± 4.6
NYHA functional class	
I	20 (57)
II	09 (26)
III	06 (17)
Echocardiographic variable	
LVEF (%)	59.0 (41.0–64.0)
LVDD (mm)	55.7 ± 11.5
E/e' ratio	12.2 ± 4.2
Functional variable	
Peak VO_2 (mL/kg/min)	26.3 ± 8.1
VE/VCO_2 slope	31.9 ± 4.2
6MWT distance (m)	571.0 ± 81.7
ISWT distance (m)	437.9 (329.0–658.2)
ISWT level reached	
Level 5–8	23 (66)
Level 9–11	5 (14)
Level 12	7 (20)

Values presented as mean ± standard deviation, number (%), or median (interquartile range).
NYHA, New York Heart Association functional class; LVEF, left ventricular ejection fraction; LVDd, left ventricular end-diastolic diameter; E/e' ratio, ratio of the early diastolic transmitral flow velocity to early diastolic mitral annular velocity; peak VO_2, peak oxygen uptake; VE/VCO_2, minute ventilation-carbon dioxide production; 6MWT, 6-min walk test; ISWT, incremental shuttle walk test.

RESULTS

Patients with CHD (n = 35) were evaluated and the characteristics of the sample are shown in Table 1.

No significant difference was found between the distances traveled ($P = 0.694$). The agreement between the distances walked during field tests is demonstrated in the Bland–Altman diagram (Fig. 1). Only one pair (2.8%) lies outside the limits of agreement.

As shown in Fig. 2, significant correlation of peak VO_2 was observed both with the 6MWT distance ($r = 0.577$, $P < 0.001$) and with the ISWT distance ($r = 0.587$, $P < 0.001$). The VE/VCO_2 slope correlated only with ISWT distance ($r = -0.339$, $P = 0.003$).

The area under the ROC curve showed that the distance walked during the 6MWT and the ISWT can identify patients with functional impairment (area under the curve [AUC], 0.77; 95% confidence interval [CI], 0.61–0.93 and AUC, 0.87; 95% CI, 0.75–0.99, respectively). The optimal cut point value for 6MWT

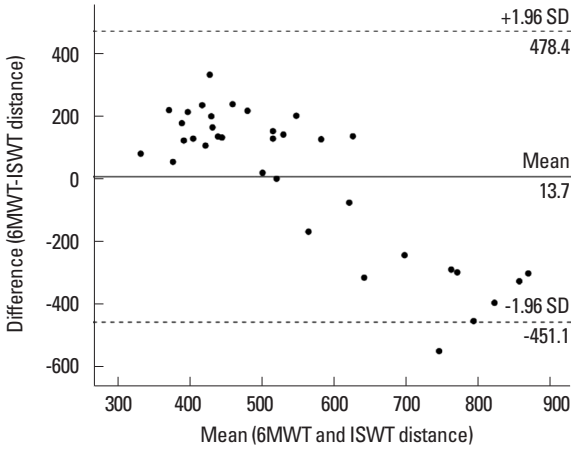

Fig. 1. Bland-Altman diagram showing the agreement between the distances walked by the 6MWT and ISWT. 6MWT, 6-min walk test; ISWT, incremental shuttle walk test; SD, standard devation.

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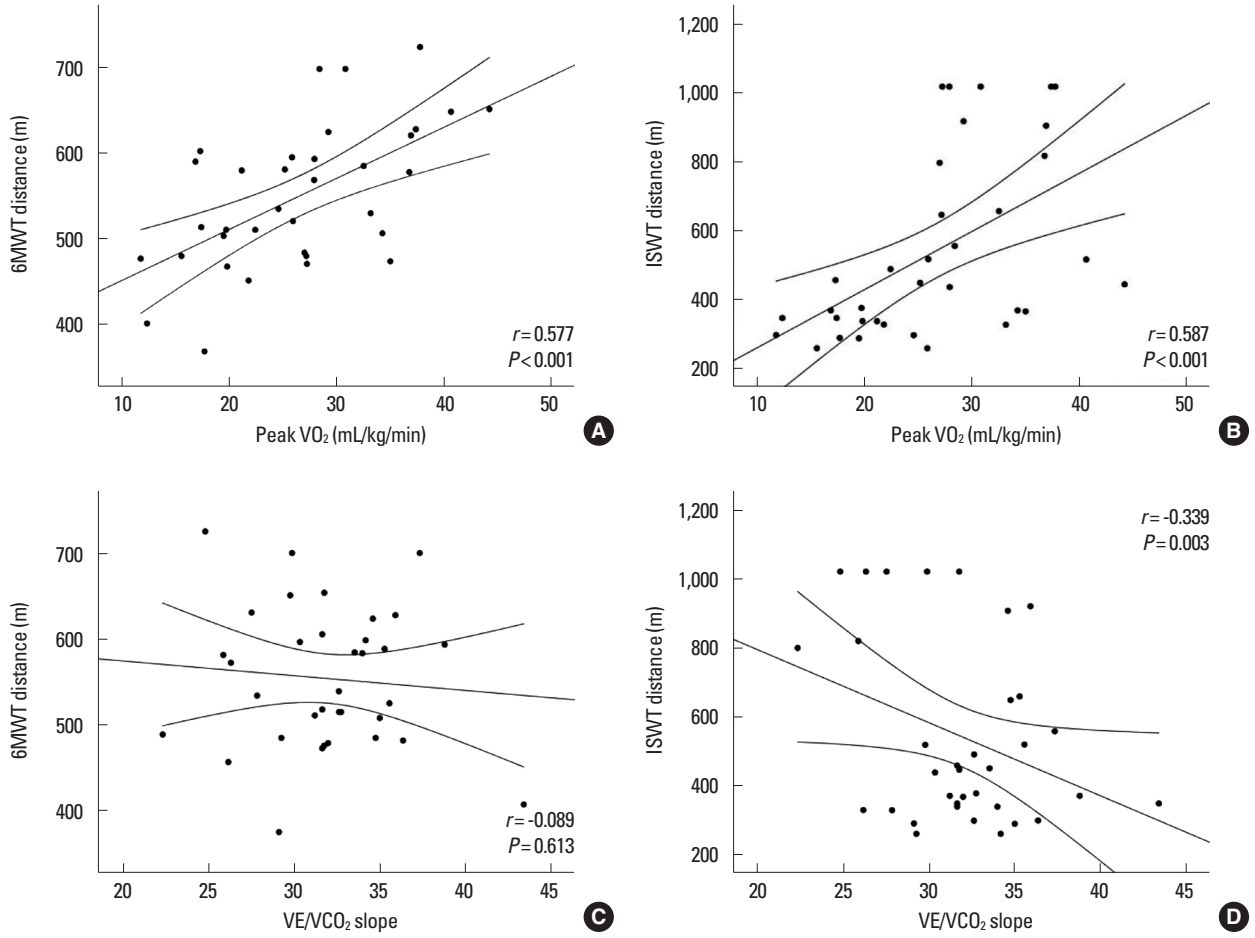

Fig. 2. Correlation of peak VO_2 and 6MWT distance (A); peak VO_2 and ISWT distance (B); VE/VCO_2 slope and 6MWT distance (C); VE/VCO_2 slope and ISWT distance (D). VO_2, oxygen uptake; 6MWT, 6-min walk test; ISWT, incremental shuttle walk test; VE/VCO_2, minute ventilation-carbon dioxide production.

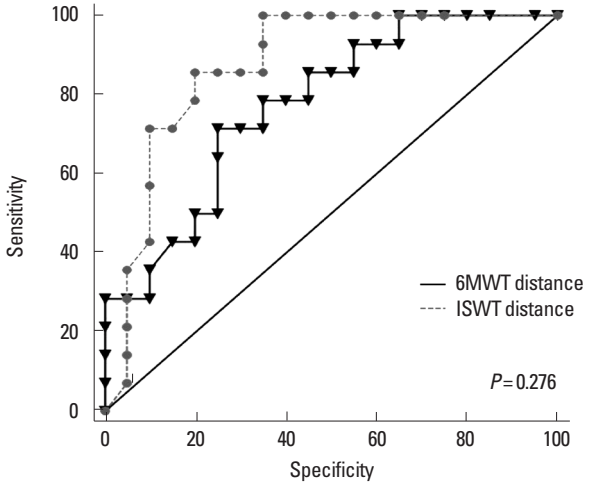

Fig. 3. Area under the receiver operating characteristic curve demonstrating the accuracy of the distances walked during the 6MWT and ISWT in identifying patients with functional impairment (peak VO_2 <20 mL/kg/min). 6MWT, 6-min walk test; ISWT, incremental shuttle walk test; VO_2, oxygen uptake.

and ISWT to identify functional impairment was a distance less than 520 m and 400 m, respectively. The sensibility and specificity for this cutoff value were, respectively, 75% and 71% for 6MWT distance and 80% and 86% for ISWT distance. As shown in Fig. 3, there was no significant difference between the areas under the curves ($P = 0.276$).

DISCUSSION

To the best of our knowledge, this is the first study that compared the 6MWT and ISWT distance and CPET variables in CHD patients with mild cardiac involvement. The main findings are (a) the good agreement between the 6MWT and ISWT distance, (b) the significant correlations between the 6MWT and ISWT distance and peak VO_2 as well as between ISWT distance and VE/VCO_2, and (c) the good accuracy of both field tests in the identification of patients with functional impairment.

Morales et al. (1999) analyzed the association between the 6MWT and the ISWT with peak VO_2 (CPET) in 46 patients (53±10 years, NYHA 2.8±0.7). They found that the correlation between the ISWT and peak VO_2 was stronger ($r=0.83$, $P<0.001$) than the 6MWT ($r=0.69$, $P<0.001$). However, the present study found that the correlation between 6MWT and ISWT distance with peak VO_2 were similar.

Another study (Pulz et al., 2008) verified the association between the 6MWT and ISWT distances and peak VO_2 in heart failure patients (n=63, 51.3±10.2 years, NYHA II–IV), with 25% of the sample being composed by patients with CHD. The authors verified both the 6MWT and ISWT had strong correlations with peak VO_2 ($r=0.76$ and $r=0.79$, respectively). They also found significant difference between the distances traveled during the submaximal field tests ($P<0.001$), unlike the present study.

Most of patients in the present study were in NYHA functional class I and with preserved LVEF, which can partially explain the differences. We believe that field tests can underestimate the maximal functional capacity in patients with mild cardiac impairment. During the 6MWT, patients tend to select a comfortable speed, even if they can walk faster. In the ISWT, many of the patients with good functional capacity can reach the maximum level of the test (level 12), which occurred in the present study with 20% of the sample. However, patients rarely reached the maximum level of the CPET. Therefore, it appears that both field tests can be applied in the evaluation of functional capacity in CHD patients with good correlation with peak VO_2, regardless of the degree of cardiac involvement. However, we recommend caution with this statement as a result of the small sample evaluated.

Our results also demonstrated that ISWT distance correlated weakly with VE/VCO_2 slope. This may have clinical relevance, since VE/VCO_2 slope is the only variable assessed by CPET considered an independent predictor of survival in CHD patients (Ritt et al., 2013). Indeed, survival data are not available in the present study, which is a limitation for the analysis of predictive validity, and the prognostic value of ISWT distance should be investigated in longitudinal studies.

Additionally, the present study verified that both field tests have good accuracy in the identification of CHD patients with functional impairment, without significant difference between the areas under the ROC curve. The cutoff points of distance walked with good sensitivity and specificity in identifying patients with functional impairment may be useful in the risk stratification of patients and in the adoption of preventive management based on physical exercise. Previous studies (Morales et al., 1999; Pulz et al., 2008) also reported the effectiveness of 6MWT and ISWT in identifying patients with heart failure and severely reduced peak VO_2, showing cutoff values of 380 for ISWT and 490 for 6MWT (Pulz et al., 2008) or 450 for both (Morales et al., 1999).

These results have important clinical meaning in the setting of CHD, since the endemic areas are generally poor, and the maximal exercise test may not be available. Furthermore, emerging studies have shown that exercise training can be beneficial to patients with Chagas disease (Fialho et al., 2012; Lima et al., 2010; Mediano et al., 2016) and field tests can also aid in risk stratification, which is very important for directing patients to cardiac rehabilitation (Bocchi et al., 2012). Therefore, both 6MWT and ISWT may be helpful in the functional evaluation and risk management of patients with CHD.

In conclusion, the 6MWT and the ISWT provide similar measures for assessment of the functional capacity in patients with mild CHD. Both field tests, inexpensive and easy-to-perform, can identify patients with functional impairment and have potential value for the assessment of patients with CHD in resource-limited areas.

CONFLICT OF INTEREST

No potential conflict of interest relevant to this article was reported.

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