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ORIGINAL ARTICLE

Peak oxygen uptake during the incremental shuttle walk test in a predominantly female population with Chagas heart disease

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ABSTRACT

BACKGROUND: Chagas heart disease (CHD) patients may have a reduced functional capacity (FC). Field tests, as the Incremental Shuttle Walk Test (ISWT), can estimate peak oxygen uptake (VO_2 peak). However, the relationship between the ISWT and the Cardiopulmonary Exercise Testing (CPET), the gold standard in the assessment of FC, is not well established in CHD patients.
AIM: This study aimed to evaluate the FC of CHD patients by ISWT with direct measurement of VO_2 peak and to compare these findings with data obtained from CPET. A secondary goal was to derive a regression equation to calculate the VO_2 peak by ISWT.
DESIGN: Cross-sectional and correlative study.
SETTING:Research laboratory setting.
POPULATION: Thirty-two CHD patients (58.8±9.0 years, 81.3% women) participated in this study.
METHODS: Eligible patients underwent clinical evaluation, echocardiography, CPET by ramp protocol and ISWT according to current guidelines.
RESULTS: The distance walked in ISWT showed a positive correlation with VO_2 peak from CPET and ISWT (r=0.456, P=0.009 and r=0.869, P<0.001, respectively). In the agreement analysis, the values of the differences between VO_2 peak from CPET and ISWT showed absence of bias (mean bias ±95% CI and mean -1.29±5.09 mL.kg.min). Based in real values of VO_2 obtained from ISWT, one equation including sex, functional class and distance walked was provided to predict the VO_2 values in this test.
CONCLUSION: This study showed the good correlation between distance walked in ISWT and VO_2 peak directly measured in both tests, and additionally, provided an equation to calculate a predictive VO_2 peak by ISWT, suggesting a good alternative to evaluate the FC of CHD patients, especially in locations where sophisticated testing is not available.
CLINICAL REHABILITATION IMPACT: The results confirm the possibility of using the ISWT for the evaluation of the FC in patients with CHD, especially in locations where sophisticated testing is not available.

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Key words: Chagas cardiomyopathy - Functional residual capacity - Exercise test.

Chagas disease is a parasitic illness first reported in 1909 and remains until today as a major public health problem in Latin America.[1] The cardiac clinical form is especially important because its evolution could result in severe stages of heart failure associated with progressive reduction in functional capacity (FC) and quality of life, with high social, medical and labor consequences.[2, 3] Chagas heart disease (CHD) is an acquired inflammatory disease characterized by chronic fibrosing myocarditis and progressive impairment of cardiac contractile function that result in a poor prognosis.[4]

Thus, the assessment of FC is an important part of the physical exam. The cardiopulmonary exercise testing (CPET), the gold standard in the analysis of FC, improved understanding of the relationship between performance, FC and physiological parameters, providing reliable and high reproducibility variables in the evaluation of exercise capacity.[5] However, the test is expensive and not well tolerated by some patients,[6, 7] which limits its applicability in clinical routine.[8] On the other hand, field tests like the Incremental Shuttle Walk Test (ISWT) and the Six-Minute Walk Test (6MWT) are simple, easier to administer, have lower costs, are better tolerated by patients [6] and were already applied in the Chagasic population,[9, 10] including to detect changes in FC after aerobic training.[11]

Regarding the methodological differences between CPET and 6MWT, the ISW has been used and presents more similar procedures to those of CPET.[12] The ISWT is a symptom-limited test and the load (determined by speed) has stages with standardized increments.[13] Previous studies demonstrated a good correlation between the distance walked in ISWT and VO_2 peak in heart failure patients [14, 15] and accuracy in identifying functional impairment in CHD patients.[16] However, no other study performed the direct measurement of VO_2 in patients with CHD during field tests.

This study aimed to evaluate the FC of CHD patients by ISWT with direct measurement of VO_2 and validate comparing it with data from CPET. A secondary goal was to derive the regression equation to calculation of oxygen uptake in ISWT.

Materials and methods

This cross-sectional study was approved by the institutional review board of Federal University of the Jequitinhonha and Mucuri Valleys and all patients gave their written informed consent before participating in study.

Study design

Thirty-two CHD patients were selected from a primary care health center in an endemic area. The inclusion criteria were: diagnosis for CHD confirmed by at least two of the three available tests (indirect immunofluorescence, indirect hemagglutination and/or ELISA);[17] being clinically stable to allow the full implementation of the assessment protocol; and the presence of typical echocardiographic [18] and/or electrocardiographic abnormalities of CHD, such as right bundle branch block, left anterior hemiblock, partial atrioventricular block and ventricular extrasystoles.[19] So, the definition of CHD is based on the presence of ECG abnormalities and symptoms of heart failure and the echocardiographic evaluation was mainly to measure left ventricular systolic function to define the stages of the disease.[20] Criteria for exclusion were: cardiac disease of any other etiology; use of cardiac pacemaker; pulmonary, pleural or kidney disease; musculoskeletal abnormalities or the inability to perform the exercise tests.

Patients were submitted to a clinical evaluation by a cardiologist who included a structured anamnesis protocol with anthropometric data (weight, height, Body Mass Index), a 12-lead electrocardiogram at rest in standing position and a transthoracic echocardiography realized with a portable ultrasound Sonosite MicroMaxx® (Bothell, WA, USA). The echocardiography was performed according to the recommendations of the American Society of Echocardiography [21] and left ventricular ejection fraction (LVEF) was obtained by Simpson's rule.

Blood pressure (BP) and heart rate (HR) were evaluated at rest, on peak of the effort and at recovery phase from CPET and ISWT. The BP was monitored using the BD® sphygmomanometer and stethoscope Littmann® Cardiology and the HR was evaluated using the continuous recording from electrocardiogram during the CPET and by transmitter's Polar® (model S810i, Finland) associated with the receiver of HR signal of ambulatory gas analyzer kit in ISWT. All volunteers were submitted to CPET and ISWT with direct measurement of VO_2. The exercise tests were performed with one week intervals, firstly applying the CPET.

CPET

This test was applied in a ergospirometry room in a local hospital using the gas analyzer VO2000 Med Graphics® (St. Paul, MN, USA) and treadmill model ATL® Inbrasport (Porto Alegre, RS, Brazil). Using the software Heart Ware Ergo MET® (BRA), test data was recorded breath by breath and VO_2 peak was the highest value recorded at the moment of interruption of the test. Twelve-lead electrocardiograms continuously recorded the rhythms as HR. The modified Bruce Protocol [22] was used and for this study only the VO_2 peak, BP and HR were considered. The assessment of BP was performed at the final thirty-second mark of each phase of the protocol.

TABLE I.—*Characteristics of the study population (N.=32)*

Variables	Values
Age (years)	58.8±9.0
Female sex, N.(%)	26 (81.3)
Weight (kg)	65.0±18.4
Height (m)	1.6±0.1
BMI (Kg/m²)	27.2±4.5
Resting hemodynamics	
HR (bpm)	70.0±11.0
SBP (mmHg)	137.5 (117.5-140.0)
DBP (mmHg)	80.0 (77.5-80.0)
Echocardiographic data	
LVSD (mm)	33.0±8.7
LVDD (mm)	49.8±6.4
LVEF (%)	62.4±13.4
Functional Class – NYHA, N. (%)	
I	19 (59.4)
II	13 (40.6)
Drugs, N. (%)	
Antihypertensive	
Diuretics	20 (62.5)
Angiotensin-convertingenzymeinhibitors	14 (43.8)
Angiotensin II receptor blockers	8 (25.0)
Calciumchannelblockers	5 (15.6)
Non-cardioselective beta blockers	5 (15.6)
Cardioselective beta blockers	3 (9.4)
Antiplateletagents	14 (43.8)
Antiarrhythmics	5 (15.6)
Cardiotonics	1 (3.1)
Antianginalagents	3 (9.4)
Antilipemic	12 (37.5)

The values are presented as mean and standard deviation (M±SD), median (MD) and interquartile range (25-75%) or absolute number (percentage).
BMI: Body Mass Index; HR: heart rate; SBP: systolic blood pressure; DBP: diastolic blood pressure, LVSd: left ventricular end-systolic diameter; LVDd: left ventricular end-diastolic diameter; LVEF: left ventricular ejection fraction; NYHA: New York Heart Association.

Test termination criteria consisted of the patient's inability to maintain the imposed workload (inability to maintain speed consistently on the treadmill or the development of significant exercise-induced chest pain, dyspnea or ECG abnormalities).

ISWT

The ISWT was performed using the protocol proposed by Singh *et al.*[13] The test was applied in a local hospital using a 10-meter course corridor marked out by two cones nine meters apart to reduce the need for sudden changes in the direction. The minimum speed achieved by patients on the test was controlled by signals from an audiotape previously recorded in regular intervals. Thus, for each one of 12 levels of the test, a reduction of the time between signal sound intervals was imposed.

Using the ambulatory gas analyzer kit VO2000 Med Graphics® (St. Paul, MN, USA), the direct measure of oxygen uptake was obtained by setting the machine for measure the VO_2 for each 30 seconds. Data was transferred to Aerograph® program for further analysis. The VO_2 peak was the highest value recorded on last level attained by the individual.

The test was finished when the volunteer completed the 12 levels or could not complete the distance target between cones within the intervals for two consecutive times.

Statistical analysis

G Power software, version 3.1.0, was used to determine the sample size as 29 individuals to detect the least

TABLE II.—*Comparison of hemodynamic variables and VO2 peak between Incremental Shuttle Walk Test and Cardiopulmonary Exercise Testing.*

	CPET	ISWT	P value
SBP rest (mmHg)	137.5 (117.5-140.0)	130.0 (128.8-140.0)	0.135
DBP rest (mmHg)	80.0 (77.5-80.0)	90.0 (79.5-93.5)	<0.001*
HR rest (bpm)	69.8±11.4	72.7±15.7	0.315
SBP max (mmHg)	175.8±23.9	176.9±26.6	0.838
HR max (bpm)	136.3±24.5	149.5±30.4	0.060
VO_2 peak (mL.kg.min)	21.0±5.3	22.3±5.5	0.160
Distance walked	-	503.4±177.2	-

The values are presented as mean and standard deviation (M±SD) or median (MD) and interquartile range (25-75%).
CPET: cardiopulmonary exercise testing; ISWT: Incremental Shuttle Walk Test; SBP: systolic blood pressure; DBP: diastolic blood pressure; HR: heart; VO_2 peak: peak oxygen uptake.
*P value <0.05.

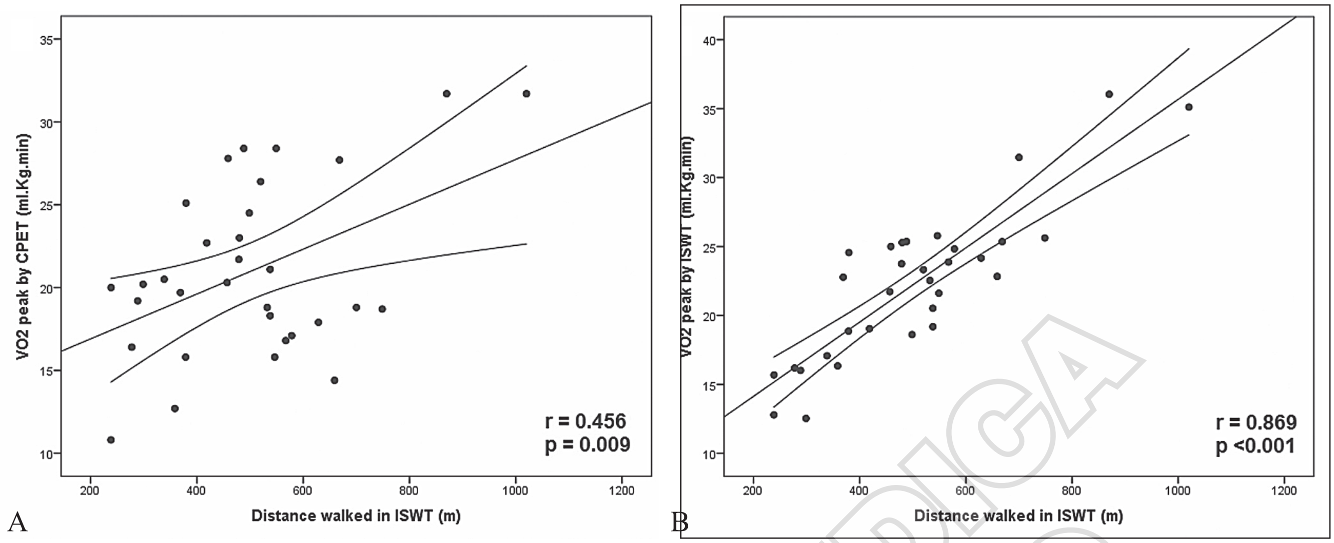

Figure 1.—Correlation between (A) distance walked in ISWT and VO_2 peak by CPET and (B) distance walked in ISWT and VO_2 peak by ISWT.

r value of 0.5 between VO_2 peak from ISWT and CPET, with an alpha error of 0.05 and statistical power of 80%.

Data were analyzed with statistical package SPSS® 17.0 (SPSS Inc., Chicago, IL, USA). The values are presented in mean and standard deviation (M±SD) or median and interquartile range (MD±25-75%) in accordance with the distribution by the Kolmogorov-Smirnov Test. The paired student t test or Wilcoxon test was used to compare means, as appropriate. The Pearson's correlation test was performed to verify correlations between exercise tests and Bland-Altman diagram was used to measure the agreement between VO_2 peak by CPET and ISWT.

To define an equation to predict the VO_2 peak in ISWT, a matrix interpolating age (cutoff point of ≤60 years), functional class and sex was built using R Core Team software. The model adjusted was generalized estimating equations (GEE) that modeled the mean oxygen uptake according to other variables considered.

The level of significance was set at 0.05 for all analyzes.

Results

The study population comprised 32 patients, 81.3% women and six patients (18.8%) with an abnormal left ventricular ejection fraction (LVEF<55%). Population characteristics are presented in Table I.

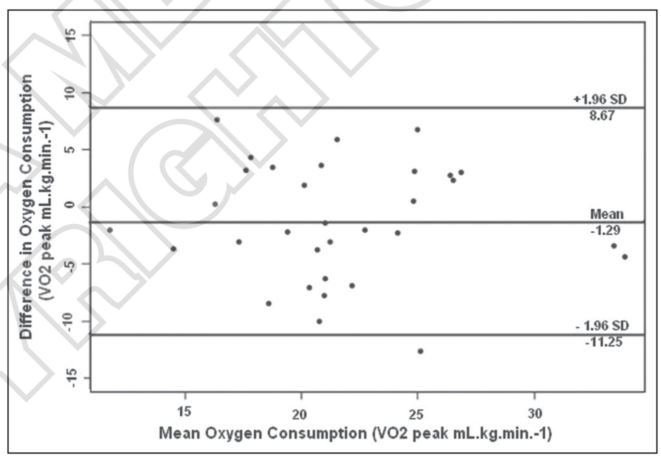

Figure 2.—A Bland-Altman diagram showing the agreement between VO_2 peak values in cardiopulmonary exercise testing (CPET) and Incremental Shuttle Walk Test (ISWT). Mean bias ±95% CI and mean -1.29±5.09 mL.kg.min.

The comparison between FC and hemodynamic variables at rest and stress is shown in Table II. Only diastolic blood pressure (DBP) at rest was different between tests. The hemodynamic response to effort was similar in both tests.

A positive correlation was observed between VO_2 peak in CPET and distance walked in ISWT (r=0.456, P=0.009; Figure 1A) even as VO_2 peak and distance walked in ISWT (r=0.869, P<0.001; Figure 1B).

The Bland-Altman analysis showed a strong agree-

TABLE III.—*Estimated values of the coefficients of equation to predict of VO2 peak.*

Variable	Descriptor Variable		Coefficient	Confidence Interval	P value
β0	Constant	-	12.21	10.78/13.62	<0.001*
β1	Distance	-	0.03	0.02/0.03	<0.001*
β2	Sex	Female	1.76	-0.19/3.71	0.07
		Male	0	-	-
β3	Functional Class (NYHA)	Asymptomatic (NYHA I)	0	-	-
		Symptomatic (NYHA≥II)	-2.61	-4.43/-0.78	<0.001*
β4	Interaction term distance *vs.* sex	Female	-0.01	-0.01/-0.00	<0.001*
		Male	0	-	-

NYHA: New York Heart Association.
*P<0.05.

TABLE IV.—*Equation to predict the peak oxygen uptake in mL.kg.min.*

General equation: $\beta0 + \beta1_{(distance)}$ x distance walked + $\beta2_{(sex)} + \beta3_{(Functional\ Class)} + \beta4_{(distance\ vs.\ sex)}$

Sex	NYHA	Deduction of the equation for sex and NYHA	Final Equation
Female	Asymptomatic	(β0+β2)+(β1+β4) x distance walked	13.97+0.02 x distance walked
	Symptomatic	(β0+β2+β3)+(β1+β4) x distance walked	11.36+0.02 x distance walked
Male	Asymptomatic	β0+β1 x distance walked	12.21+0.03 x distance walked
	Symptomatic	(β0+β3)+β1 x distance walked	9.60+0.03 x distance walked

NYHA: New York Heart Association.

ment by absence of bias between different methods to evaluate the VO_2 peak. The mean bias was close to zero and the 95% CI of the difference was similarly narrow (-1.29±5.09 mL.kg.min; Figure 2).

The model GEE was used to define the equation of prediction of the VO_2 peak in ISWT. The variable age was not included since it was not related to the mean VO_2 peak; the sex (female) variable had an interaction with the distance walked that was included in the final model. The estimated values of the coefficients equations are presented in Table III.

The general equation and their derivations according sex and functional class are presented in Table IV. The observed curves and predicted lines to oxygen uptake according with proposed model for this population are shown in Figure 3.

Discussion

The present study shows that the ISWT is a valid alternative method in assessing FC in a group of patients with CHD. The main findings of this study are: 1) the correlation between distance walked in ISWT and VO_2 peak directly measured in both tests (ISWT and CPET); and 2) the agreement analysis that showed an absence of bias between VO_2 peak values obtained from two methods. Additionally, we provide an equation to calculate a predictive VO_2 peak by ISWT. These results have important clinical meaning in the setting of Chagas disease, since endemic areas are generally poor, have few resources and the maximal exercise test may not be available.

The present study has some important differences in relation to previously published studies about the ISWT.[7, 14-16] These studies showed a stronger correlation between the distance walked in ISWT and VO_2 obtained in CPET. Pulz *et al.*[7] evaluated 63 patients with heart failure and found a strong correlation between these variables (r=0.79, P<0.001). Similarly, Morales *et al.*[14] studied 46 clinically stable patients with heart failure and found a close correlation (r=0.83, P<0.001). Lewis *et al.*[15] evaluated 25 patients with heart failure and also observed a strong correlation (r=0.730, P<0.001). In the present study, the correlation between these variables was more modest. This difference may be explained based on different characteristics of study population, since they evaluated the FC by ISWT of cardiac patients due to many etiologies.[7, 14] In our study, the majority of patients had normal left ventricular ejection fraction (81.3%) and were patients exclusively with CHD.

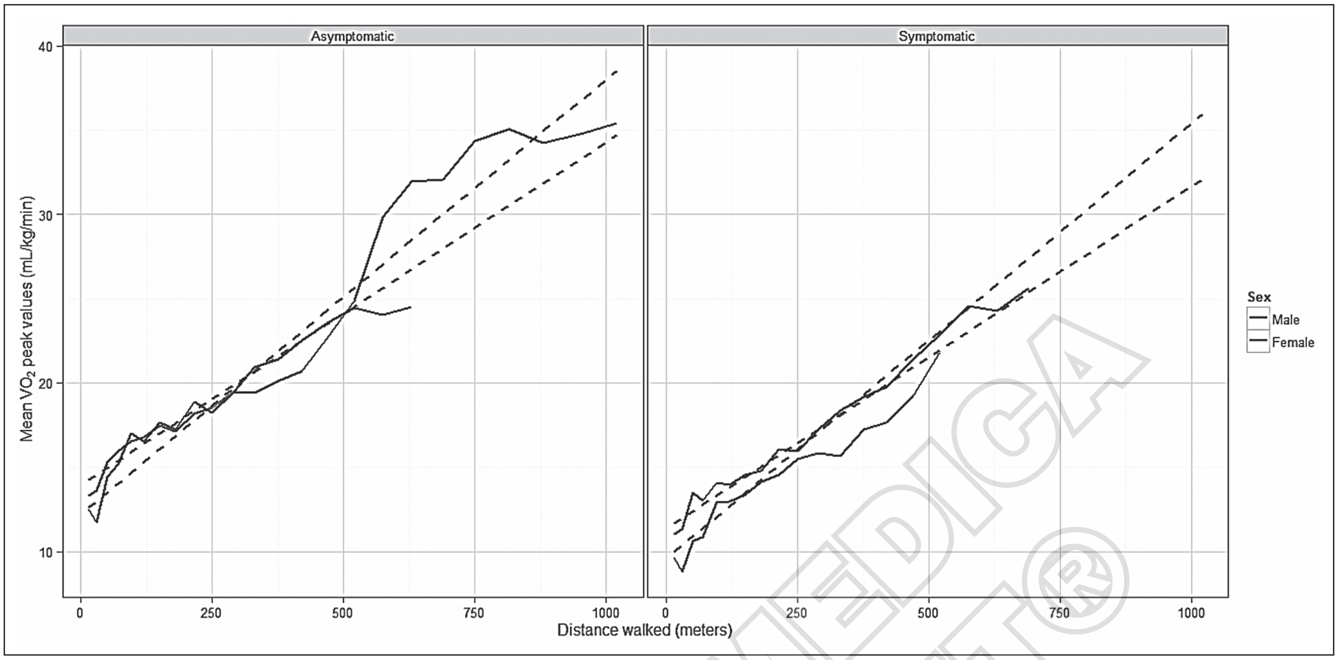

Figure 3.—Mean of peak oxygen uptake (VO_2 peak) according to sex and functional class (asymptomatic and symptomatic): observed curves (continuous lines) and predicted lines (traced).

In an innovative way, our study evaluated the FC by direct measurement of VO_2 peak during the ISWT. We observed a strong correlation between distance walked and VO_2 peak in ISWT (r=0.869, P<0.001), showing that the distance walked is a representative parameter to assess the FC when CPET is not available. The direct measure of VO_2 by expired gas analysis is the best way to assess the FC but this method is expensive and not available in many health centers.

Another important result of our study was the good agreement observed between VO_2peak values in ISWT and CPET. In addition to demonstrating a linear relationship between distance walked and VO_2 peak in ISWT, our study showed that VO_2 peak values in ISWT are close to these values in CPET. Since the ISWT is a test with incremental and progressive characteristics similar to CPET, the physiological overload imposed by both tests may be similar. This was confirmed when we observed that BP and HR values on effort were similar. In this context, with agreement analysis between the values of VO_2 peak in CPET and ISWT, it was possible to elucidate the ability of this field test to assess the FC with more accurate measure.

The importance of searching for tests to evaluate the FC is based on the fact that VO_2 is a significant index of prognosis and survival in CHD patients [23] and the assessment of FC is necessary to follow the progress of the disease. In this setting, simple and inexpensive methods to detect functional impairment as field tests are important tools in the clinical routine.

Currently, no studies were found that evaluated the FC by VO_2 directly measured during the ISWT in CHD patients. Previous studies assessed this variable during the ISWT in patients with chronic obstructive pulmonary disease [24] showing good correlation between VO_2 peak and distance walked in ISWT (r=0.86, P<0.001).

As the VO_2 peak is an important parameter to assess the changes of FC, to prescribe training intensities [25, 26] and to stratify FC, some studies propose equations to estimate this variable. Recently, a study [16] showed the ability of distance walked in ISWT in predicting a VO_2 peak value of at least 25.0 mL.kg.min. We proposed one equation to calculate the predicted VO_2 peak in ISWT, stratified by sex and functional class (NYHA I and NYHA≥II), that can be clinically useful, with values of the β0 coefficient based on real oxygen uptake measured during the ISWT. Age did not achieve a statistical significance in the multivariate model and was not included in the equation. Due to the interaction between sex and the walked distance, males had greater slope of the lines for both functional classes, although they have lower baseline values.

Morales *et al.*[14] proposed 3 equations to calculate the predicted VO_2 peak in ISWT based on a multivariate model. None of these equations were derived from real values of VO_2 peak stratified for levels or fractions of the distance walked during the ISWT, which leads us to believe that our equation can more accurately predict the VO_2 peak in this test. Also, variables that depended on previous exams and that were poorly accessible were not included in our equation.

Our study has some limitations, such as the disproportion between males and females as well as among individuals with preserved and reduced LVEF. Future studies should consider evaluating patients underrepresented in our study, such as males and those with ventricular dysfunction.

Conclusions

The values of VO_2 peak obtained during ISWT showed agreement with those from CPET and with the distance walked at ISWT and the distance walked in ISWT showed correlation with VO_2 peak obtained in CPET. Furthermore, based on real values of oxygen uptake during ISWT, we provided an equation for predicting the VO_2 peak with potential clinical value. These findings confirm the possibility of using the ISWT for the evaluation of the FC in patients with Chagas heart disease, especially in locations where sophisticated testing is not available.

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