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Chagas heart disease is associated with decreased physical activity levels: A cross-sectional analysis

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ABSTRACT

Background: Studies evaluating physical activity (PA) levels in individuals with Chagas disease (CD) are still scarce. The present study aimed to evaluate PA levels in CD individuals and examine their association with Chagas heart disease (ChHD).

Methods: We included patients with CD regularly followed in a reference center for treatment of infectious diseases. PA levels were assessed using the short version of the International Physical Activity Questionnaire (IPAQ). ChHD was determined following the Brazilian Consensus on Chagas Disease. The association between ChHD and levels of PA (total, walking, moderate, and vigorous) as a continuous variable was fitted using generalized linear models. Logistic regression models were fitted to evaluate the association between ChHD and meeting WHO's PA recommendations.

Results: Among the 361 participants included in the analysis (60.7 ± 10.7 years; 56.2 % women), 58.1 % (n = 210) complied with the WHO's PA recommendations. After adjustments for potential confounders, regression analyses revealed that ChHD without heart failure was significantly associated with reduced vigorous PA (Exp β 0.32 95 % CI 0.10 to 0.98). ChHD with heart failure had significantly lower levels of total (Exp β 0.61 95 % CI 0.44 to 0.84) and moderate (Exp β 0.59 95 % CI 0.39 to 0.89) PA. ChHD with heart failure had a lower odd of meeting the PA recommendation in comparison to those with no cardiac involvement (OR 0.48 95 % CI 0.24 to 0.97).

Conclusions: We found low levels of PA among individuals with CD. Presence of ChHD (mainly with HF) was associated with decreased levels of PA.

1. Introduction

Increased physical activity (PA) levels is an important public health strategy linked to lower risk of chronic diseases and mortality [1–3]. Despite the widely recognized benefits, low levels of PA are observed globally, mainly among individuals with chronic conditions [4–7]. A study conducted by Forechi et al. [8] including almost 15,000 participants found that individuals with chronic diseases were up to 50 % less likely to meet the PA recommendations of 150 min of moderate-to-vigorous activity per week compared to healthy individuals. In

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addition, there has been a notable decrease in total daily PA over the last decades, which is of concern as regular PA is associated with many health benefits [9]. The decrease in PA levels can be explained by the reduction in activities performed at home, reduction in occupational PA levels, change in transportation patterns in urban areas, and increase in time spent in sedentary activities due to advances in technology [10–13].

Studies investigating the PA levels of individuals with Chagas disease (CD), a parasitic infection caused by the flagellated protozoan *Trypanosoma cruzi* (*T. cruzi*), are scarce in the literature. The chronic phase of CD is characterized by a variety of clinical manifestations ranging from the absence of specific signs and/or symptoms related to the disease (indeterminate form) to involvement of organs such as heart or esophagus and/or bowel with positive *T. cruzi* serology [14]. CD can have a significant impact on increased fatigue and decreased physical functioning and exercise capacity, especially among those with Chagas heart disease (ChHD). One systematic review found that individuals with ChHD had reduced exercise tolerance compared to healthy individuals, making them less prone to engage in PA [15]. Moreover, due to changes in the epidemiological profile of the CD population with migration from rural to urban areas, many individuals modified their lifestyle, with a greater intake of inadequate foods and decreased levels of PA, which might have a detrimental effect on the prognosis for CD [16,17].

Considering the benefits of increased levels of PA on several health parameters, including in patients with ChHD [18,19], the investigation of PA levels in individuals with CD is of paramount importance for implementing comprehensive intervention strategies targeted for this population. Thus, the present study aimed to evaluate the levels of PA in patients with CD and to investigate its association with ChHD.

2. Materials and methods

2.1. Study design and data source

The present work is a secondary analysis of a cross-sectional study conducted between March 2014 and March 2017 aiming to evaluate the prevalence of comorbidities in individuals with CD. The full description and main results from the primary analysis can be found elsewhere [20].

2.2. Study population

The study population comprised patients diagnosed with CD (confirmed by positive *T. cruzi* serology using two different methods – ELISA and indirect immunofluorescence) of both sexes, >18 years old, who were regularly followed in a reference center for treatment and research of infectious diseases (INI/Fiocruz), located in the city of Rio de Janeiro, Brazil. Participants were excluded if they presented with autoimmune diseases, cancer, other infectious diseases during the data collection period, severe cognitive impairments that precluded data collection, evidence of non-chagasic heart disease, chronic use of anti-inflammatory or corticosteroids, or pregnancy.

Patients were invited to participate in the study during their regular medical appointments. Those who agreed to participate in the study were submitted to the study procedures performed in two visits within a period of no more than two months. In the first visit, patients signed the informed consent form, completed all questionnaires, and performed anthropometric measurements. On the second visit, they underwent clinical evaluation. Trained staff applied the questionnaires and performed anthropometric measurements. The same physician performed the clinical evaluation of all participants.

For this secondary analysis, sample size calculation was based on data published by Ramirez Varela et al. [21], which estimated a prevalence of physically active individuals of 72 % for the Brazilian population. Considering the population of patients with CD followed up in INI in 2013, around 1,100 patients, using a 95 % confidence interval, estimation accuracy of 5 %, and increasing the sample size by 20 % due to possible losses and refusals, a total of 310 individuals were required for the present study.

2.3. Outcome

The main outcome of the present study was PA levels, determined using the short version of the International Physical Activity Questionnaire (IPAQ-short) validated for use in the Brazilian population [22,23]. This instrument is composed of 6 questions about the duration and frequency of participation in walking, moderate, and vigorous-intensity activities over the last seven days, allowing individuals to be classified into categories according to WHO recommendations of 150 min of moderate intensity or 75 min of vigorous intensity per week, or an equivalent combination of moderate-to-vigorous intensity physical activity [24] or expressed continuously in MET x minute per week. To calculate the MET x minutes per week, the MET value of each activity (walking, moderate, and vigorous activities) was multiplied by the total minutes performed per day and then multiplied by the number of days that was performed in the previous week. MET values were assigned based on guidelines for data processing and analysis of the IPAQ [25] as follows: walking was assigned 3.3 METs, moderate activities 4.0 METs, and vigorous activities 8.0 METs.

2.4. Exposure

ChHD was determined using clinical, electrocardiographic, and echocardiographic following the Brazilian Consensus on Chagas Disease [14]. Participants were diagnosed with ChHD if they presented CD-related electrocardiographic abnormalities (2nd- and 3rd-degree right bundle-branch block, associated or not to left anterior fascicular block, frequent ventricular premature beats, polymorphous or repetitive non-sustained ventricular tachycardia, 2nd- and 3rd-degree atrioventricular block, sinus bradycardia with heart rate less than 50 bpm, sinus node dysfunction, 2nd- and 3rd-degree left bundle-branch block, atrial fibrillation, electrical inactive area, or primary ST-T wave changes). Echocardiographic alterations (segmental left ventricular wall motion abnormalities, left ventricular dilatation, or global left ventricular systolic dysfunction) and symptoms of heart failure (HF) were used to classify the ChHD into stages. For statistical analysis purposes, individuals with ChHD were categorized into ChHD without and with HF.

2.5. Covariates

Sociodemographic, clinical, and lifestyle covariates were considered to characterize the study population and to address the potential confounding for the associations between ChHD and PA levels. Age was determined by subtracting the date of interview from the date of birth. Schooling was assessed according to the number of years of formal education (<9, 9–12, and > 12 years). Race was self-reported and classified as white and non-white (black, yellow, mulatto, and indigenous). Income per capita was determined by the sum of income of individuals living in the household divided by the number of residents. Comorbidities (arterial hypertension, diabetes mellitus, dyslipidemia, and obesity) were obtained using information from medical records and anthropometric measurements during clinical evaluation. Obesity was determined if the body mass index [BMI = mass (kg)/height in square meters (m^2)] was $\geq$ 30 kg/m^2. Digestive form of CD included patients with symptoms compatible with megacolon (constipation and abdominal pain) or megaesophagus (dysphagia and regurgitation) and with complementary exams compatible with digestive form diagnosis. Smoking was categorized as current (regular use of tobacco at the time of the interview) and former/non-smoker (past occasional use/never use of tobacco). Alcohol consumption was categorized as current (any amount of alcohol intake in the last 30 days) and former/none (no alcohol consumption over the last 30 days or more). Sleep duration was determined as a continuous variable by direct question.

2.6. Statistical analysis

Statistical analysis was performed with Stata software (version 17.0). REDCap platform (Research Eletronic Data Capture) was used for data management. Exploratory analysis of the data consisted of median with interquartile range 25th-75th for continuous variables and percentage with absolute frequency for categorical variables. Cuzick (for continuous variables) and Jonckheere-Terpstra (for categorical variables) trend tests were performed to compare clinical, sociodemographic, and lifestyle characteristics stratified by ChHD. The association between ChHD and levels of PA (total, walking, moderate, and vigorous) as a continuous variable were fitted using generalized linear models with a logarithmic link function and gamma distribution due to the asymmetric and heteroscedastic nature of the residuals. The coefficients (beta) were exponentiated (Exp β) to facilitate the interpretation of the results. The association between the ChHD and levels of PA as a dichotomous categorical variable according to WHO recommendations were fitted using logistic regression models. Unadjusted and adjusted analyses were performed considering the following potential confounding variables: age, sex, race, education, arterial hypertension, diabetes mellitus, dyslipidemia, obesity, and digestive form. The statistical significance level adopted for all tests was $p \leq 0.05$.

2.7. Ethical aspects

All participants received information about the goals and procedures of the study and agreed to participate by signing an informed consent form. The study was approved by the Institutional Review Board of the Evandro Chagas National Institute of Infectious Disease (CAAE: 58273916.0.000.5262) on December 09, 2013.

3. Results

Among the 361 participants included in the analysis (60.7 ± 10.7 years; 56.2 % women), 58.1 % (n = 210) complied with the WHO's PA recommendations 150 min of moderate intensity or 75 min of vigorous intensity per week, or an equivalent combination of moderate-to-vigorous intensity physical activity.

The characteristics of patients stratified by ChHD are presented in Table 1.. Overall, patients with ChHD with HF showed a lower number of comorbidities, including a lower percentage of diabetes mellitus, dyslipidemia, and obesity, presented a lower total and moderate PA levels, and were less likely to comply with the WHO's PA recommendations.

The association between ChHD with PA levels are demonstrated in Table 2.. Compared to those with no cardiac involvement, ChHD without HF was significantly associated with a reduction of vigorous PA in both unadjusted (Exp β 0.40 95 %CI 0.16 to 0.98) and adjusted (Exp β 0.32 95 %CI 0.10 to 0.98) analyses. Moreover, individuals with ChHD with HF had significantly lower levels of total (Exp β 0.60 95 %CI 0.44 to 0.82), moderate (Exp β 0.54 95 %CI 0.37 to 0.80), and vigorous PA (Exp β 0.21 95 %CI 0.06 to 0.73) in the unadjusted analysis. After adjusting for potential confounding variables, the associations remained significant for total (Exp β 0.61 95 %CI 0.44 to 0.84) and moderate PA (Exp β 0.59 95 %CI 0.39 to 0.89).

Table 3 presents the association between ChHD with compliance with the WHO's PA recommendations. Those with ChHD with HF had a lower odd of meeting the PA recommendation in comparison to those with no cardiac involvement in both unadjusted (OR 0.51 95 %CI 0.26 to 0.98) and adjusted (OR 0.48 95 %CI 0.24 to 0.97) analyses.

4. Discussion

The present study demonstrated a low compliance with WHO's PA recommendations in a sample of urban patients regularly followed in a reference center for treatment and research of CD. Moreover, ChHD appears to be related to lower PA levels, especially among those with HF, being associated with a decreased level of total and moderate PA.

The lower prevalence of physically active individuals in our study in comparison to overall estimates for the Brazilian population at the same period (72 %) can be explained by factors related to individuals' health condition [21]. CD can limit exercise capacity [15], affect emotional and psychological state, and lead to symptoms such as depression, anxiety, and lack of motivation [26]. Additionally, individuals with CD often need to dedicate considerable time and energy to manage their health condition, including medical appointments, treatments, medications, and self-care, which can result in a perception of lacking time and stamina to engage in PA. In certain cases, patients with CD may have substantial concerns about the possibility of worsening their health condition when performing PA [27], discouraging PA practice.

Table 1
The characteristics of patients stratified by ChHD.

	No cardiac involvement (n = 110)	ChHD without HF (n = 195)	ChHD with HF (n = 56)	p-value for trend
Age in years (median; 25–75 % IQR)	59.0; 52.0–66.0	64.0; 58.0–69.0	60.5; 52.0–65.0	0.142
Women (%; n)	54.5; 60	59.4; 116	48.2; 27	0.751
White vs *non-white* (%; n)	28.1; 31	17.9; 35	26.7; 15	0.376
Scholling (%; n)				
< 9 years	63.6; 70	67.2; 131	75.0; 42	0.167
9–12 years	18.2; 20	19.5; 38	16.1; 9	0.872
> 12 years	18.2; 20	13.3; 26	8.9; 5	0.092
Residents per domicile (median; 25–75 % IQR)	2.0; 2.0–4.0	3.0; 2.0–3.0	3.0; 2.0–3.5	0.813
Income per capita (median; 25–75 % IQR)	785.0; 550.0–1000.0	750.0; 428.5–1120.0	700.0; 436.6–900.0	0.156
Sleep hours (median; 25–75 % IQR)	7.0; 6.0–8.0	6.0; 5.0–8.0	7.0; 5.0–8.0	0.958
Number of comorbidities (median; 25–75 % IQR)	2.0; 1.0–3.0	2.0; 1.0–2.0	1.0; 0.0–2.0	**< 0.001**
Arterial Hypertension (%; n)	61.8; 68	78.4; 153	39.2; 22	0.210
Diabetes Mellitus (%; n)	27.2; 30	19.4; 38	17.8; 10	0.098
Dyslipidemia (%; n)	60.0; 66	54.7; 107	35.7; 20	**0.008**
Obesity (%; n)	30.0; 33	27.6; 54	10.7; 6	**0.023**
Previous use of Benzonidazole (%; n)	9.0; 10	7.6; 15	12.5; 7	0.668
Current smoking (%; n)	45.4; 50	48.7; 95	42.8; 24	0.955
Current alcohol intake (%; n)	44.5; 49	37.4; 73	37.5; 21	0.263
Total PA MET.min/week (median; 25–75 % IQR)	1711.5; 792.0–3870.0	1440.0; 660.0–3306.0	1344.5; 577.0–2272.0	**0.017**
Walking MET.min/week (median; 25–75 % IQR)	585.7; 198.0–990.0	594.0; 148.5–990.0	552.7; 214.5–957.0	0.760
Moderate PA MET.min/week (median; 25–75 % IQR)	840.0; 240.0–1920.0	720.0; 60.0–1680.0	410.0; 0.0–970.0	**0.009**
Vigorous PA MET.min/week (median; 25–75 % IQR)	0.0; 0.0–0.0	0.0; 0.0–0.0	0.0; 0.0–0.0	0.898
Meeting PA Recommendations (%; n)	64.5; 71	57.4; 112	48.2; 27	**0.044**

*Cuzick's test for trends in continuous variables / Jonckheere-Terpstra test for trends in categorical variables.
ChHD: Chagas heart disease; HF: Heart failure.

Table 2
Association between ChHD with walking, moderate, vigorous and total PA levels (MET.min/week).

Variables	Total PA		Walking		Moderate PA		Vigorous PA	
	Exponentiated Beta Coeficient (95 % CI)		Exponentiated Beta Coeficient (95 %CI)		Exponentiated Beta Coeficient (95 % CI)		Exponentiated Beta Coeficient (95 % CI)	
	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted	Unadjusted	Adjusted
No cardiac involvement	Reference	Reference	Reference	Reference	Reference	Reference	Reference	Reference
ChHD without HF	0.83 (0.66–1.04)	0.94 (0.75–1.19)	0.99 (0.75–1.31)	1.03 (0.78–1.36)	0.86 (0.65–1.15)	0.99 (0.74–1.34)	**0.40 (0.16–0.98)**	**0.32 (0.10–0.98)**
ChHD with HF	**0.60 (0.44–0.82)**	**0.61 (0.44–0.84)**	0.90 (0.61–1.32)	0.84 (0.57–1.24)	**0.54 (0.37–0.80)**	**0.59 (0.39–0.89)**	**0.21 (0.06–0.73)**	0.42 (0.08–2.24)

ChHD: Chagas heart disease; HF: Heart failure.

Table 3
Association between ChHD with meeting WHO PA recommendation.

Variables	Meeting WHO PA recommendation	
	OR (95 %CI)	
	Unadjusted	Adjusted
No cardiac involvement	Reference	Reference
ChHD without HF	0.74 (0.45–1.20)	0.82 (0.49–1.38)
ChHD with HF	**0.51 (0.26–0.98)**	**0.48 (0.24–0.97)**

ChHD: Chagas heart disease; HF: Heart failure.

Moreover, low socioeconomic and educational levels, characteristics of the population with CD, are usually associated with lower levels of PA [28,29].

Other studies have reported low levels of PA in individuals with CD. In a study conducted by Jackson et al. [16] assessing the self-reported PA levels of 137 immigrants with CD living in Switzerland, only 37.2 % were classified as physically active. Similarly, Soares et al. [30] also reported low levels of PA measured by the short version of the IPAQ, with only 19 % of individuals being classified as regularly active. In the study conducted by Geraix et al. [31], 17 % of the subjects were considered physically active as engaging in leisure PA for at least 30 min on $\geq$ 4 days of the week. One potential explanation for the higher levels of PA observed in our study compared to others could be that the patients included in our study may have received information about the importance of adopting healthy lifestyle habits, including PA, as part of their routine medical appointments. In addition, reference health centers often provide exercise-based rehabilitation programs, as is the case with INI/Fiocruz. Finally, the social support provided by health centers is also another important factor, where individuals can interact with others who are living in similar situations, share experiences, and exchange mutual support. This encouraging and supportive environment can stimulate the practice of PA [32,33].

In our study, ChHD (mainly with HF) was associated with decreased levels of PA. The presence of chronic conditions and lower health are usually associated with low levels of PA. Supporting this finding, Stojanovic, Babulal, and Head [29] reinforce that physical health plays an important role in the ability and willingness to engage in PA, in which low physical well-being is associated with lack of motivation to exercise, leading to a constant feeling of reduced stamina and fatigue that can decrease even more the PA levels. Another factor to consider is that poor physical health can lead to a self-efficacy reduction, in which individuals with health problems may doubt their abilities to engage in PA. Moreover, metabolic aspects may also contribute to decreased PA levels in patients with ChHD. A cross-sectional study conducted by Montes de Oca et al. [34] assessed the metabolic and structural characteristics of peripheral muscles in patients with CD and their relationship with maximal functional performance in exercise. According to the classification adopted in their study, they studied 11 patients with stage II (characterized by ECG abnormalities and segmental motility alteration of the heart without congestive HF), 8 patients with stage III (characterized by ventricular dilatation, abnormal ECG findings, autonomic dysfunction, congestive HF, and/or marked arrhythmia), and 11 healthy volunteers. The findings indicated that patients with more advanced cardiac disease (stage III) have reduced oxidative capacity and, therefore, reduced exercise tolerance, which can potentially lead to a decrease in PA levels. Additionally, Silva et al. [35] suggest that ChHD and factors related to disease severity can lead to a significant reduction in functional capacity. In another study, Costa et al. [36] observed that patients with ChHD have lower levels of PA and functional capacity compared to healthy individuals. Additionally, a significant association was found between the decrease in PA levels and the reduction of functional capacity. Such findings may be one of the reasons explaining low levels of total PA in individuals with ChHD with HF, as these patients have reduced functional capacity, and then being more limited to perform daily living activities, compared to those without HF symptoms [15].

5. Limitations

The present study has some limitations. Our sample consisted of patients who are regularly followed in a reference healthcare center, which may limit the generalizability of the results to the overall population with CD. Moreover, the cross-sectional design limits the establishment of causal relationships and temporal sequence of events. Therefore, the results should be interpreted with caution. Additionally, PA measurement was based on self-reported data, which may have introduced recall bias and/or measurement error, driving our results to the null hypothesis [37]. However, the IPAQ questionnaire is the most common method used to evaluate PA levels, presenting acceptable measurements properties to estimate PA levels in different populations [38], although not previously validated for patients with CD.

6. Conclusion

Our study found low levels of PA among individuals with CD, with ChHD (mainly with HF) being associated with decreased levels of PA. Interventions strategies targeting to improve PA levels in patients with CD are warranted. Despite the potential benefits of increased PA levels on the health parameters of individuals with CD, especially those with ChHD, studies with a large sample size and comprehensive evaluation of long-term efficacy and optimal dosing of PA remain scarce in the literature. By addressing the barriers and specific challenges associated with ChHD, healthcare professionals can play a crucial role in promoting a more active lifestyle, ultimately improving their overall health outcomes.

CRediT authorship contribution statement

Leonardo Gonçalves Ribeiro: Writing – review & editing, Conceptualization, Formal analysis, Investigation, Writing – original draft. **Tatiana Rehder Gonçalves:** Writing – review & editing, Writing –

original draft, Methodology, Investigation, Formal analysis. **Vitor Barreto Paravidino:** Formal analysis, Investigation, Writing – original draft, Writing – review & editing. **Henrique Silveira Costa:** Writing – review & editing, Investigation, Writing – original draft. **Luiz Fernando Rodrigues Junior:** Investigation, Writing – original draft, Writing – review & editing. **Flavia Mazzoli-Rocha:** Investigation, Writing – original draft, Writing – review & editing. **Gilberto Marcelo Sperandio da Silva:** Investigation, Writing – original draft, Writing – review & editing. **Fernanda de Souza Nogueira Sardinha Mendes:** Investigation, Writing – original draft, Writing – review & editing. **Roberto Magalhães Saraiva:** Conceptualization, Formal analysis, Investigation, Supervision, Writing – original draft, Writing – review & editing. **Alejandro Marcel Hasslocher-Moreno:** Conceptualization, Formal analysis, Investigation, Writing – original draft, Writing – review & editing. **Mauro Felippe Felix Mediano:** .

Declaration of competing interest

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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