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Article/Artigo

Effects of an exercise program on the functional capacity of patients with chronic Chagas' heart disease, evaluated by cardiopulmonary testing

Efeitos de um programa de exercícios sobre a capacidade funcional de pacientes com cardiopatia chagásica crônica, avaliados por teste cardiopulmonar

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ABSTRACT

Introduction: Despite all efforts to restrict its transmission, Chagas' disease remains a severe public health problem in Latin America, affecting 8-12 million individuals. Chronic Chagas' heart disease, the chief factor in the high mortality rate associated with the illness, affects more than half a million Brazilians. Its evolution may result in severe heart failure associated with loss of functional capacity and quality of life, with important social and medical/labor consequences. Many studies have shown the beneficial effect of regular exercise on cardiac patients, but few of them have focused on chronic Chagas' heart disease. **Methods**: This study evaluated the effects of an exercise program on the functional capacity of patients with chronic Chagas' disease who were treated in outpatient clinics at the Evandro Chagas Institute of Clinical Research and the National Institute of Cardiology, Rio de Janeiro, Brazil. The exercises were performed 3 times a week for 1 h (30 min of aerobic activity and 30 min of resistance exercises and extension) over 6 months in 2010. Functional capacity was evaluated by comparing the direct measurement of the O_2 uptake volume (VO_2) obtained by a cardiopulmonary exercise test before and after the program ($p < 0.05$). **Results**: Eighteen patients (13 females) were followed, with minimum and maximum ages of 30 and 72 years, respectively. We observed an average increase of VO_{2peak} > 10% ($p = 0.01949$). **Conclusions**: The results suggest a statistically significant improvement in functional capacity with regular exercise of the right intensity.

Keywords: Chagas' heart disease. Exercises. Functional capacity. Cardiopulmonary exercise test. VO_2.

RESUMO

Introdução: Mesmo com todos os esforços para interrupção de sua transmissão, a doença de Chagas permanece como grave problema de saúde pública na América Latina, onde atinge entre 8 e 12 milhões de indivíduos. A cardiopatia chagásica crônica, principal responsável pela elevada morbimortalidade da doença, chega a acometer mais de meio milhão de brasileiros. Sua evolução atinge estágios graves de insuficiência cardíaca com perda de capacidade funcional e qualidade de vida, com grande impacto social e médico-trabalhista. Muitos estudos demonstram o resultado benéfico da prática regular de exercícios em cardiopatas, porém, há escassez de investigações em cardiopatia chagásica. **Métodos**: O presente estudo avaliou efeitos de um programa de exercícios sobre a capacidade funcional de dezoito pacientes (13 mulheres) com cardiopatia chagásica crônica, com idade entre 30 e 72 anos, atendidos nos ambulatórios do Instituto de Pesquisa Clínica Evandro Chagas e do Instituto Nacional de Cardiologia, na cidade do Rio de Janeiro. Os exercícios foram executados 3 vezes por semana, durante 1 hora (30 minutos de atividade aeróbica e 30 minutos de exercícios contra-resistência e alongamentos), ao longo de 6 meses, no ano de 2010. A avaliação da capacidade funcional foi realizada pela comparação da medida direta do VO_2 obtido pelo Teste de Exercício Cardiopulmonar, antes e depois do programa. Para análise estatística foram utilizados testes T de *Student* pareado e de Wilcoxon. **Resultados**: Os resultados mostram aumento médio do VO_{2pico} acima de 10%(p=0,01949). **Conclusões**: Os resultados sugerem melhora significativa da capacidade funcional com prática regular de exercícios na população amostral.

Palavras-chaves: Cardiopatia chagásica. Exercícios. Capacidade funcional. Teste de exercício cardiopulmonar. VO_2.

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INTRODUCTION

Since the discovery of Chagas' disease by Carlos Chagas in 1909, there have been significant advances in the effort to interrupt the cycle of transmission of this disease in Brazil. However, it still remains an important public health problem in Latin America, and is present from Chile and Argentina to the south of the United States[1]. In Brazil, it is the fourth highest cause of death by parasitic infection[2]. It is estimated that there are 2 million infected people in Brazil[3] and between 8-12 million in Latin America[4], with 60 million people exposed to the danger of infection[5].

Chagas' disease is an infectious parasitic illness caused by the flagellate protozoan *Trypanosoma cruzi*, whose main transmission route is by an insect vector, through infection via the fecal material of bloodsucking insects where the bite occurs[6]. Among the different forms of the evolution of Chagas' disease, chronic Chagas' heart disease (CHD) is the chief reason for the elevated rate of mortality associated with this illness and affects as many as half a million Brazilians[7]. Its evolution may result in severe stages of heart failure associated with a loss of functional capacity and quality of life, with enormous social and medical/labor consequences[8].

Many studies have shown the beneficial effect of regular exercise on cardiac patients. Such an effect is a consequence, among other factors, of the increase in functional capacity by central and peripheral responses[9,10].

There is little specific scientific evidence relating to the benefit of physical exercise for patients with Chagas' disease[11]. The objective of this study was to evaluate the potential effect of an exercise program on the functional capacity of patients with chronic CHD, thus creating a basis for the practice of regular exercise as an additional medical therapy for this illness.

METHODS

Eighteen patients with chronic CHD were followed in this prospective intervention study. The patients participated in a program of exercises in the Cardiac Rehabilitation Service of the National Institute of Cardiology (INC in Portuguese). The exercises were performed 3 times a week for 1h (30 min of aerobic activity and 30 min of resistance exercises and extension) over 6 months in 2010. Functional capacity was evaluated by comparing the direct measurement of the O_2 uptake volume (VO_2) obtained by the cardiopulmonary exercise test (CPET) before and after the program.

The exercise program was structured as given below.

I) thirty minutes of aerobic exercise on an Inbrasport2000® treadmill, which was divided into the following 3 phases:

a. Five minutes of warm-up with progressive speed acceleration.

b. Twenty minutes of exertion aiming for the target cardiac frequency zone (established for each patient by the CPET – 5% above the anaerobic threshold and 10% under the maximum heartbeat or the respiratory compensation point)[12], associated with perceived exertion according to the modified Borg scale[13], and maintaining the intensity of the effort between moderate and moderate/intense. To ensure the achievement of the target cardiac frequency zone, heartbeat was measured using a Polar® cardiac monitor during the aerobic training.

c. Five minutes of cool-down until the treadmill reached a complete stop.

II) Twenty minutes of empirically programmed resistance exercise for the main muscle groups, with 2 series of 10 repetitions for each of the main muscle groups, applying a load that provided the patient with a sensation of moderate effort according to the modified Borg scale[13].

III) Ten minutes of stretching for all of the exercised muscle groups, with each position held for 20 s[14] (**Table 1**).

TABLE 1 - Resistance exercises.

Exercises	Series	Repetitions
Leg extension	2	10
Reclined rowing on pulley	2	10
Bilateral plantar flexion on step	2	20
Lateral arm raises	2	10
Standing unilateral knee flexion Reclining crucifix	22	1,010
Standing unilateral hip abduction	2	10
Triceps twist with rope on pulley	2	10
Straight abdominal	2	20
Oblique abdominal with crossed leg	2	20

The subjects consisted of men and women aged between 30-72 years and having 2 different positive results for serological tests for Chagas' disease enzyme-linked immunosorbent assay hemagglutination and indirect fluorescence and for electrocardiographic or echocardiographic characteristic alterations compatible with chronic CHD[7]; who did not engage in regular physical activity (at least 3 months earlier); and who had agreed to participate voluntarily in the study, had signed the informed consent form, and had been duly informed. In order to be included, the patients had to be regularly monitored in the Chagas' disease outpatient clinic of the Evandro Chagas Institute of Clinical Research (IPEC in Portuguese) or the INC, Rio de Janeiro, Brazil.

Patients were excluded because of the following reasons: associated angina pectoris, suspension of stress tests due to clinical or electrocardiographic evidence of myocardial ischemia; clinically evident thyroidal dysfunction; orthopedic involvement that limited treadmill use; cancer; hepatopathy; serious alcoholism; and chronic nephropathies.

The admission protocol of the Cardiac Rehabilitation Sector of the INC required the following exams prior to participation: general clinical examination, cardiopulmonary exercise test, conventional electrocardiogram, and Doppler echocardiogram.

The analysis of the potential benefits of regular exercise on functional capacity was carried out using direct measurement of the gases exhaled during the CPET. The tests were carried out in the exercise sector of the INC, utilizing the Bruce protocol[15], and applied by a single examiner. An Inbrasport® treadmill linked to a computer with the Elite® Micromed® software was used. In preparation, the patients were depilated in the thoracic region, where necessary, and rubbed with gauze and alcohol to remove any grease. Thirteen electrodes were used, corresponding to the following shunts: DI, DII, DIII, aVR, aVL, aVF, V1, V2, V3, V4, V5, V6, and MC5. The temperature of the test room was maintained at 18-22°C. Exhaled gases were analyzed by VO_{2000}® Aerosport® system, acquired breath-by breath, averaged over 20 seconds. The traditional methods of Wasserman et al.[16] were used for obtaining results for the ventilatory variables. During the test, the patients were given instructions and encouraged to reach their exhaustion point.

The primary result of the study used the comparison of the maximum values of O_2 consumption at the peak of exertion (VO_{2peak}), pre- and post-training. Other variables of the CPET were studied as secondary results. The first of them was VO_2 in the first ventilatory threshold, also known as the lactate threshold or anaerobic threshold (VO_2AT). Another variable evaluated as a secondary result was the O_2 pulse, which analyzes the relationship of VO_2 with the heartbeat (VO_2/beat) during exercise and permits an estimate of systolic volume (SV). The third variable evaluated as a secondary result was the ventilatory equivalent of CO_2 or the VE/VCO_2 slope, which represents the quantity of air that needs to be ventilated for 1 min to eliminate 1 L of CO_2[7].

The data were entered into an Excel® spreadsheet, always by the same typist. For the database, a standard comma separated value file was used. For statistical analysis, the program R 2.10 was used with Students' paired t-test and the Wilcoxon test. The level of statistical significance was set at a value of $p < 0.05$. According to the sample calculation, 12 patients were the minimum necessary to guarantee a power of 80% and confidence of 95%, considering an improvement of 10% in the primary results.

Exploratory data analysis utilized the descriptions of the relative and absolute frequencies of the categorical variables and the description of the summary measurements of the quantitative variables (i.e., VO_{2peak}, VO_2AT, and VO_2/beat), such as average, median, standard deviation, and interquartile range (IQR). Where statistically significant difference occurred, these were compared to the values of the median and IQR.

Ethical considerations

For this study, the recommendations of the World Health Organization, the Helsinki Statement of Rights, and the National

Commission on Research Ethics (CONEP in Portuguese) Resolution 196/96 were respected. The entire study process was explained to the patients, and their authorization was registered in an informed consent form. This study was approved by the ethics committees of the INC and IPEC under numbers 0237/26.05.2009 and P 065/2010, respectively.

RESULTS

We selected 54 patients. Of this total, 18 concluded the program, exceeding the value of the sample calculation. Before the study began, 30 patients were excluded due to their inability to join the exercise program (lack of time/availability and/or distance of residence) or associated comorbidities. The study was initiated with 24 patients; however, 6 did not finish the program: 1 had severe pneumonia, 1 had a transitory ischemic accident, 1 had lumbago related to work activities, 1 had acute peripheral vascular disease (none of them were related to exercise), and 2 dropped out.

Of the 18 patients that finished the study, 13 (72.2%) were women. Their functional class was I/II according to the New York Heart Association, and their mean ejection fraction was 54%. **Table 2** shows the general characteristics of the subjects with regard to age (years), body mass index in kg/m^2, and medications in use during the training period.

TABLE 2 - General features.

	30-72	**56.67 (mean) ± 9.46 (SD)**	
Age (years)	**15.60-37.60**	**26.24 (mean) ± 4.46 (SD)**	
BMI	**Drugs**	**n**	**%**
Using:	Diuretic	15	83.0
	ACEI	12	66.5
	antihypertensive	10	55.5
	beta-blocker	10	55.5
	Statin	9	50.0
	ARB	8	44.5
	OHG	6	33.5
	Digitalis	3	17.0
	anti-arrhythmic	2	11.0
	CCB	2	11.0
	ASA	2	11.0
	fibrate	1	5.5
	warfarin	1	5.5
	other	11	61.0

BMI: body mass index; **SD:** standard-deviation; **ACEI:** angiotensin-converter enzyme inhibitor; **ARB:** angiotensin-receptor blocker; **OHG:** oral hypoglycemic; **CCB:** calcium channel blocker; **ASA:** acetylsalicylic acid; **other:** drugs not used for cardiovascular control.

Regarding the primary result, the pre-conditioning VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$) varied between 9.32 and 33.43, with an average of 21.81, median of 21.11, and interquartile range of 18.69-26.94. The post-conditioning VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$) varied between 12.45 and 37.93, with an average of 24.24, median of 24.48, and interquartile range of 18.36-29.15. The average increase in VO_{2peak} was equivalent to 11.14% ($p = 0.019$). The variation can be seen in **Figure 1**.

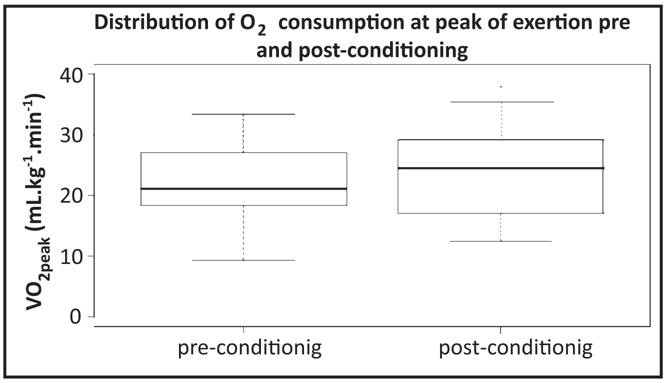

FIGURE 1 - O_2 uptake at exertion peak - VO_{2peak} ($mL \cdot kg^{-1} \cdot min^{-1}$).

Regarding the secondary results, the pre-conditioning O_2 pulse ($mL.beat^{-1}$) varied between 4.80 and 19.80, with an average of 10.76, median of 10.65, and interquartile range of 6.90-13.30. The post-conditioning O_2 pulse ($mL.beat^{-1}$) varied between 6.00 and 18.30, with an average of 11.85, median of 11.30, and interquartile range of 9.07-1.67. The average increase of O_2 pulse was equivalent to 10.18% ($p = 0.044$). The variation can be seen in **Figure 2**.

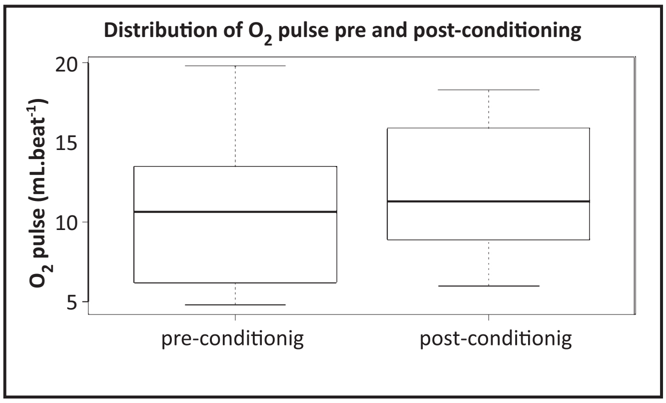

FIGURE 2 - O_2 pulse - VO_2/beat ($mL.beat^{-1}$).

The pre-conditioning VO_2AT ($mL.kg^{-1}.min^{-1}$) varied between 5.24 and 19.04, with an average of 14.73, median of 15.74, and interquartile range of 11.21-18.52. The post-conditioning VO_2AT ($mL.kg^{-1}.min^{-1}$) varied between 11.32 and 25.00, with an average of 17.49, median of 17.75, and interquartile range of 13.31-21.33. The average increase of VO_2AT was equivalent to 18.74% ($p = 0.016$). The variation can be seen in **Figure 3**.

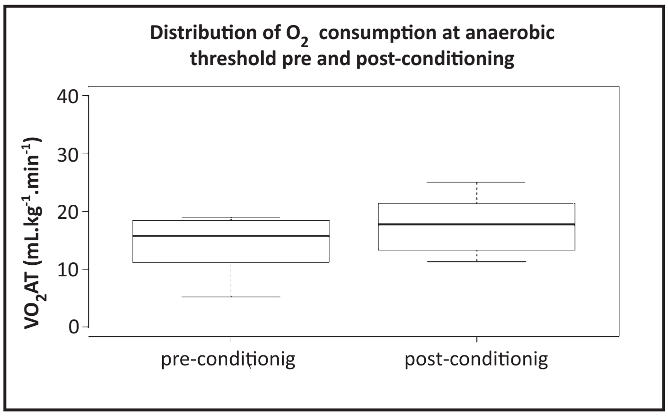

FIGURE 3 - Anaerobic threshold - VO_2AT ($mL.kg^{-1}.min^{-1}$).

The pre-conditioning VE/VCO_2 slope varied between 17.40 and 30.60, with an average of 24.15 and median of 24.27. The post-conditioning VE/VCO_2 slope varied between 19.40 and 32.40, with an average of 24.95 and median of 24.69. The average increase of VE/VCO_2 was equivalent to 1.73% ($p = 0.582$), a value not considered significant.

DISCUSSION

The objective of this study was to evaluate the potential effect of an exercise program on the functional capacity of patients with chronic CHD, thus creating a basis for the practice of regular exercise as an additional medical therapy for this disease. In the literature reviewed, only 1 study correlated the effects of regular physical training with CHD[18].

As previously mentioned, many studies have shown the beneficial effect of regular exercise on cardiac patients. Regular exercise generates cardiovascular, metabolic, and ventilatory modifications, both acute and chronic, in response to increased physiological demands[19]. Such modifications provoke an increase in functional capacity with central and peripheral responses[10].

Myers et al. considered functional capacity a strong predictor of mortality in cardiac patients and normal individuals, more so than other pre-established risk factors[20]. In heart failure, functional capacity is considered an important predictive marker. In this context, functional capacity can be represented by the consumption of O_2 during exercise[17].

The maximum consumption of O_2 (VO_{2max}) has been considered the best indicator of human capacity to sustain prolonged exertion. However, faced with the technical difficulties of measurement in cardiac patients or individuals with poor conditioning, it must be said that the highest measurement of O_2 consumption attained during exercise (VO_{2peak}) would be an objective indicator of functional capacity, especially when associated with the measurement of anaerobic metabolism through records of ventilatory variables obtained in the CPET[21]. In addition, VO_{2peak} is an important predictor, as much for deaths by cardiac events as for deaths due to other diseases. In this way, even a small gain in aerobic conditioning can improve not only functional capacity but also life expectancy[20].

The value of the primary post-conditioning measure (VO_{2peak}) had a comparative average increase that was statistically significant[22] (11.14%, $p = 0.01949$). As this measurement is extremely dependent on the collaboration of the patient in really making the maximum effort, other variables were studied as secondary measures so that important information could be obtained, even from sub-maximum effort, because during the CPET, the patients were stimulated to achieve their maximum effort, but not all of them felt comfortable doing so.

Considering the secondary measures, the study of VO_2AT is relevant because it corresponds to the moment at which the accumulation of plasma lactate occurs with subsequent buffering by bicarbonate, resulting in the elevation of CO_2 output[17].

Concerning O_2 pulse (VO_2/beat), VO_2 is well known to be directly proportional to sistolic volume (SV) versus the arteriovenous O_2 content difference ($C_{(A-V)}O_2$). In the absence of illness such as anemia, hemoglobinopathy, hypoxic pulmonary disease and cardiomyopathy due to shunting, we can consider that $C_{(A-V)}O_2$ rises exaggeratedly without significant deviation and that VO_2 becomes dependent on the cardiac output (i.e., $VO_2 = SV \times HB$). As such, we can infer that the O_2 pulse (VO_2/HB) = SV[13].

In heart disease patients with alterations in pulmonary diffusion and perfusion, e.g., pulmonary hypertension, edema or interstitial pulmonary fibrosis, elevated anaerobic metabolism, and central hyperventilation, the value of the VE/VCO_2 slope may be increased due to alterations in chemoreceptors and ergoreceptors. It is a value that varies with the moment at which it is measured, and for this reason, the analysis continues throughout the entire exertion period by using linear regression or slope[17]. A VE/VCO_2 slope value of up to 30 is considered normal, while a value more than 36 is related to a worse prognosis[13].

In the present sample, the value of the VE/VCO_2 slope was found to be within the normal range, and therefore did not suffer alterations that could be considered significant. The remaining secondary results evaluated had statistically significant alterations in terms of the improvement of functional capacity and physical conditioning[22].

The elevated number of women (72.2%) found in this sample may be related to the fact that they may have more available time to commit. Considering that the wide age range used in this study could influence its results, if we exclude the youngest (30 years) and oldest (72 years) patients, the remaining patients are aged between 44-62 years, with a mean of 56.67 years and a median of 58.50 years, which minimizes this possible influence.

In a review of the literature, just 1 similar study was found. The study by Lima et al. correlated the effect of regular physical training with CHD[18]. The article was published in the European Journal of Heart Failure in June 2010 and reported the improvement of functional capacity in patients with Chagas' cardiomyopathy undergoing a 12-week exercise program. This single-blind, randomized study compared 21 cases and 19 control subjects.

In the present study, there was no control group, which is a limitation; nevertheless, the results are in accordance with the findings of the group from Minas Gerais[18]. In the study performed by Lima et al., the exercise program was executed over a 3-month period, which is half the duration of the present study. Besides, in the study of Lima et al., VO_2 was measured indirectly (inferred or approximate value) through a standard exercise test. In the present study, a more precise measurement system was used, i.e., the cardiopulmonary exercise test, in which VO_2 was measured directly via the exhaled gases.

In conclusion, during the course of the exercise program there was neither an improvement nor worsening of cardiac symptoms. The results suggest that regular exercise was beneficial to the sample studied, in terms of the improvement of physical conditioning and functional capacity. This study may provide a basis for the prescription of exercise in the treatment of chronic CHD in association with medical therapy.

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CONFLICT OF INTEREST

The authors declare that there is no conflict of interest.

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