

Cardiac weight in elderly men with chronic chagas heart disease
Peso cardíaco em homens idosos com cardiopatia chagásica crônica
Peso cardíaco en hombres ancianos con cardiopatía chagásica crónica

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The aim of this study was to correlate histopathological alterations of chronic Chagas heart disease with cardiac weight in elderly men. Sixteen hearts from patients with chronic Chagas' heart disease were analyzed. The thickness of the myocardiocytes and their nuclei, the density of the mononuclear infiltrate and the nuclei of myocardiocytes and myocardial fibrosis were quantified in the left myocardium. Cardiac weight was 418.7±136.3g. Also, the cardiac weight presented a positive and significant correlation with the thickness of the cardiomyocytes and their nuclei ($rS=0.363$ and $rS=0.120$, respectively $p<0.05$) and with interstitial fibrosis ($rS=0.104$ $p<0.05$). Otherwise, no significant correlation was observed between cardiac weight and mononuclear infiltrate ($rS=-0.0118$ $p>0.05$). The density of the cardiomyocyte nuclei presented a negative and significant correlation with cardiac weight ($rS= -0.555$ $p<0.05$). Therefore, the increase of cardiac weight in chagasic elderly men was influenced by interstitial fibrosis, myocardial hypertrophy and the destruction of cardiomyocyte.

Descriptors: Aging; Chagas Cardiomyopathy; Fibrosis.

O objetivo deste estudo foi correlacionar às alterações histopatológicas da cardiopatia chagásica crônica com o peso cardíaco (Pca) em homens idosos. Foram selecionados 16 corações com alterações morfológicas e sorologia positiva (idosos cc). Quantificou-se no miocárdio esquerdo as espessuras dos miocardiócitos e seus núcleos, densidade do infiltrado mononuclear e dos núcleos de miocardiócitos e a fibrose miocárdica. O Pca nos homens idosos CC foi 418,7 ±136,3g e apresentou correlação positiva e significativa com a espessura dos miocardiócitos e de seus núcleos ($rS=0,363$ e $rS=0,120$, respectivamente $p<0,05$) e com a fibrose intersticial ($rS=0,104$ $p<0,05$). Por outro lado, verificou-se correlação negativa e não significativa entre o Pca e o infiltrado inflamatório ($rS=-0,0118$ $p>0,05$). A densidade de núcleos de miocardiócitos apresentou correlação negativa e significativa com o Pca ($rS= -0,555$ $p<0,05$). O aumento do Pca nos homens idosos cc foi influenciado pela fibrose intersticial, bem como pela hipertrofia miocárdica e destruição de miocardiócitos.

Descritores: Envelhecimento; Cardiomiopatia Chagásica; Fibrose.

El objetivo de este estudio fue correlacionar las alteraciones histopatológicas de la cardiopatía chagásica crónica con el peso cardíaco (Pca) en hombres ancianos. Fueron seleccionados 16 corazones con alteraciones morfológicas y sorología positiva (ancianos cc). Se cuantificaron en el miocardio izquierdo las espesuras de los miocardiocitos y sus núcleos, densidad del infiltrado mononuclear y de los núcleos de miocardiocitos y la fibrosis miocárdica. El Pca en los hombres ancianos CC fue 418,7 ±136,3g y presentó correlación positiva y significativa con la espesura de los miocardiocitos y de sus núcleos ($rS=0,363$ y $rS=0,120$, respectivamente $p<0,05$) y con la fibrosis intersticial ($rS=0,104$ $p<0,05$). Por otro lado, se verificó correlación negativa y no significativa entre el Pca y el infiltrado inflamatorio ($rS=-0,0118$ $p>0,05$). La densidad de núcleos de miocardiocitos presentó correlación negativa y significativa con el Pca ($rS= -0,555$ $p<0,05$). El aumento del Pca en los hombres ancianos cc fue influido por la fibrosis intersticial, así como por la hipertrofia miocárdica y destrucción de miocardiocitos.

Descritores: Envejecimiento; Cardiomiopatia Chagásica; Fibrosis.

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INTRODUCTION

In Brazil, there has been an increase in the number of elderly people and in general an increase in life expectancy^{1,2}. Among various chronic diseases that affect the elderly, Chagas heart disease is found in endemic areas as one of the most frequent morbidities, which qualifies as a public health problem.

Interrupting the vector transmission of Chagas heart disease in Brazil resulted in the increase of the number of elderly people infected by *Trypanosoma cruzi* in young people³⁻⁵, though the consequence of this infection in this group of people has received little attention^{6,7}. Chronic Chagas heart disease is one of the most serious lesions of the Chagas disease and the study of it in elderly people can contribute to the pathogenic description of the disease⁸⁻¹¹.

Among elderly people with cardiopathic Chagas, body weight, ischemia, cardiac insufficiency, the increase of the thickness of the left ventricle and atrial fibrillation are factors related to changes in cardiac weight^{12,13}. The increase of cardiac weight in the elderly with chronic cardiopathic Chagas was described in research¹⁴, though the causes of the variation of cardiac weight during the process of aging were not found in other investigations. As such, based on the importance of cardiac weight as an indicator of cardiac diseases, the objective of this study was to relate histopathological changes of chronic Chagas heart disease with cardiac weight in elderly males.

METHOD

Samples

Male patients, 60 years of age or more, suffering from chronic Chagas heart disease, selected from autopsy reports performed in the General Pathology course of the Clinical Hospital of the Federal University of Triângulo Mineiro (CH/FUTM), Uberaba, Minas Gerais. The study was approved by the Research Ethics Committee of the university, protocol n. 0181. For the analysis of the hearts, sections containing cardiac fragments of 16 elderly males with chronic Chagas heart

disease (idoso cc) were selected, with positive serology and morphological characteristics compatible with the disease¹⁴. Cases of emphysema, bronchitis, ischemia, hypertension, cardiac or rheumatic Chagas disease and pulmonary diseases were excluded, according to the morphological presentation¹⁴. Age, sex, cardiac weight, body weight and height were obtained from the autopsy reports. The nutritional state was evaluated by the body mass index (BMI). The relationship between cardiac weight and body weight was considered according to the previous study¹⁴.

Morphological Analyses

The hearts were previously stored in formaldehyde at 3.7% and analyzed in front trim. The thickness of the left ventricle wall was measured in the middle point of the longitudinal diameter without considering the endocardium and the epicardium¹⁵. The morphometry was performed by means of digital caliper (Digimes Stainless Steel) and the measurement of the thickness was taken as the average expressed in millimeters (mm).

The density of myocardiocytes with lipofuscin, the nuclei of myocardiocytes, mononuclear inflammatory infiltrate, as well as the thicknesses of myocardiocytes and their nuclei were analyzed in blades colored with Eosin Haematoxylin, using the program "AxionVision 3.1 Carl Zeiss". The images were obtained using the 40x lens and the quantification was performed in a microscopic field of 0.0409mm². To obtain the densities, in each random microscopic field, all of the myocardiocytes were marked with lipofuscin, their nuclei and the cells of the inflammatory infiltrate. The thicknesses of the myocardiocytes and of their nuclei were obtained in the midpoint of their respective nuclei.

The quantification of the myocardial fibrosis was performed on blades colored with picosirius, under polarized light, with the 10x lens, using the system of automatic image analysis "KS 300 - Carl Zeiss". The fibrosis was measured in interstitial areas, with the subendocardial and epicardial regions being excluded, similar to the

quantification performed in the other study¹⁶. The interstitial region was considered an area of fibrosis around and in between the myocytes, with the exclusion of vessels and micro-scars. The number of evaluated fields for each variable was defined according to the calculation of the accumulated average¹⁷.

Statistical Analysis

The variables were analyzed with respect to distribution and variance. The correlations were made via the Spearman test (rS). The

results were deemed statistically significant when $p < 0.05$.

RESULTS

The average age of the individuals was 67.6 years (± 5.55), with a cardiac weight of 418.7g (± 136.3) and the relationship between cardiac weight and body weight varied from 0.5 to 1.41%. The values of the morphometric parameters evaluated in elderly men with chronic Chagas heart disease are presented in Table 1.

Table 1. Number of fields used for morphometry and values of the morphological parameters evaluated in elderly men with chronic Chagas heart disease. Uberaba, MG, Brazil, 2017.

Morphological parameters	Number of fields	Median (Min and Max)
Total fibrosis (%)	80	4,67 (0,32-18,64)
Interstitial fibrosis (%)	80	2,67 (0,15-14,29)
Density of the nucleus of myocytes (cells/mm ²)	42	155,38 (59,91-431,70)
Density of myocytes with lipofuscin (cells/mm ²)	60	154,57 (111,26-561,48)
Density of mononuclear infiltrate (cells/mm ²)	70	90,33 (27,72-290,08)
Thickness of myocyte (μm)	35	19,20 (9,80-29,20)
Thickness of nucleus of myocyte (μm)	20	5,78 (4,11- 8,21)

The correlations between cardiac weight and morphological changes of myocardial in individuals evaluated are presented in Table 2.

Table 2. Correlation between cardiac weight of elderly men with chronic Chagas heart disease and morphological parameters. Uberaba, MG, Brazil, 2017.

Morphological parameters	rS	p
Thickness of myocyte	0,363	< 0,001*
Thickness of nucleus of myocyte	0,120	0,0150*
Interstitial fibrosis	0,104	< 0,001*
Total fibrosis	0,094	< 0,001*
Density of mononuclear infiltrate	-0,0118	0,961
Thickness of left ventricle wall	0,199	0,449
Thickness of nucleus of myocyte	-0,555	0,0247*
Density of myocytes with lipofuscin	-0,639	0,007*

Cardiac weight of the elderly presented a positive correlation, though not significant, with age (rS=0.290, $p > 0.05$) and BMI (rS=0.286, $p > 0.05$). In addition, the correlation of cardiac weight with the thickness of myocytes and their nuclei,

total fibrosis and interstitial fibrosis was positive and significant ($p < 0.05$).

On the other hand, there was a negative and significant correlation between the nucleus and the density of myocytes with lipofuscin. Further, a

negative and insignificant correlation was observed between cardiac weight and mononuclear inflammatory infiltrate ($p > 0.05$)

DISCUSSION

In this study, the weight of hearts of elderly men increased significantly with the increase of myocardial fibrosis, but there was no correlation with the density of mononuclear inflammatory infiltrate.

Perivascular inflammation together with diffuse fibrosis, are processes that accompany the development of chronic Chagas heart disease¹⁸⁻²⁰. However, it could be possible that with aging there is a decrease in mononuclear inflammatory infiltrate, whereas fibrosis remains, likely because of the inefficient degradation of collagen during myocardial remodeling.

With age there occurs a significant decrease in the intensity of mononuclear inflammatory infiltrate, once the decrease of parasitism seems to coincide with a more discrete inflammatory response²¹. In other studies with patients suffering from Chagas disease^{21, 22}, the increase in cardiac weight was associated with the intensity of inflammation and fibrosis.

Hypertrophy associated with chronic Chagas heart disease was proportional to the inflammatory process, and especially to fibrosis²². Serious myocarditis is associated with fibrosis and the most important characteristic of the disease is the accumulation of collagen around the myocardiocytes²¹. In fact, the inflammatory process participates in the development of lesions, which results in the increase in cardiac weight in the advanced stage of the disease. The reduction of inflammatory infiltrate in the elderly can be associated with the decrease of the immune system response and a reduction of antigenic stimulation by parasitism²¹.

The cardiac weight found in elderly men, 418.7g ($\pm 136,3g$) was similar to the weight interval from 415g ($\pm 136,8$) to 487.2g ($\pm 129,1$) related in another study²¹, which was less than that of another study²³ that had a weight average of 508.2g ($\pm 110,7$).

As reported in yet another study²⁴ it is possible that the increase in cardiac weight only occurs beginning at a certain age.

There was a positive correlation observed between cardiac weight and hypertrophy of myocardiocytes, evaluated by the thickness and their nuclei in elderly men, as was observed in another study²³. On the other hand, chronic coronary disease in the elderly people can exacerbate the decrease in the density of the nuclei of myocardiocytes, which occurs in individuals without cardiopathy.

Another study²⁵ described some cardiac parameters associated with normal aging and concluded that, in addition to a significant decrease in the density of myocardiocyte nuclei, there were isolated areas of fibrosis in the endomyocardium. Beyond this, the same study²⁵ verified that with age, there was a reduction in the number of myocardiocyte nuclei per volume unit, in both ventricles.

CONCLUSION

The increase in cardiac weight in elderly men can be influenced by interstitial fibrosis, hypertrophy and destruction of myocardiocytes.

The autopsy sample provides a wealth of information about the morphological characterization of lesions. However, one of the limitations encountered in this type of study is the lack of clinical data that makes it impossible to determine relationships between the development of lesions and clinical outcome.

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CONTRIBUTIONS

Flávia Aparecida Oliveira took part in the conception of the study, data collection and writing. **Joana Estela Rezende Vilela, Larissa Oliveira Queiroz** and **Douglas Montielle Silva Nascimento** took part in data collection and writing. **Vicente de Paula Antunes Teixeira** took part in data collection, writing and review criticism. **Eliza Carla Barroso Duarte** and **Liliana Borges Menezes** took part in data collection and writing. **Juliana Reis Machado** participated in the conception of the study, its writing and critical review. **Eliza Carla Barroso Duarte** and **Liliana Borges Menezes** took part in the critical review. **Marlene Antônia Reis** took part in the conception of the study, its writing and its critical review.

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