Cardiac weight in elderly men with chronic chagas heart disease

Peso cardíaco em homens idosos com cardiopatia chagásica crônica

Peso cardiaco 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 myocardioocytes and their nuclei, the density of the mononuclear infiltrate and the nuclei of myocardioocytes 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 cardiomycocytes 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=0.118 p>0.05). The density of the cardiomycocyte 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 cardiomycocyte.

Descriptors: Aging; Chagas Cardiomyopathy; Fibrosis.

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O objetivo deste estudo foi correlacionar as alterações histopatológicas da cardiopatia chagásica crônica com o peso cardáico (Pca) em homens idosos. Foram selecionados 16 corações com alterações morfológicas e sorológia positiva (idosos cc). Quantificou-se no miocárdio esquerdo as espessuras dos miocardíocitos e seus núcleos, densidade do infiltrado mononuclear e dos núcleos de miocardíocitos e a fibrose miocárica. O Pca nos homens idosos CC foi 418,7 ±136,3g e apresentou correlação positiva e significativa com a espessura dos miocardíocitos 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 miocondríocitos 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 miocondríocitos.

Descritores: Envelhecimento; Cardiomiopatia Chagásica; Fibrose.

O objetivo deste estudo foi correlacionar as alterações 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 quantificaron en el miocardio izquierdo las espesuras de los miocardíocitos y sus núcleos, densidad del infiltrado mononuclear y de los núcleos de miocardíocitos y la fibrosis miocárica. El Pca en los hombres ancianos CC fue 418,7 ±136,3g y presentó correlación positiva y significativa con la espesura de los miocardíocitos y de sus núcleos (rS=0,363 y rS=0,120, respectivamente p<0,05) y con la fibrose 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 miocardíocitos presentó correlación negativa y significativa con el Pca (rS= -0,555 p<0,05). El aumento del Pca en los hombres ancianos cc fue influenciado por la fibrosis intersticial, así como por la hipertrofia miocárdica y destrucción de miocardíocitos.

Descritores: Envejecimiento; Cardiomiopatía Chagásica; Fibrosis.
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 people\(^3\)-\(^5\), 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 disease\(^8\)-\(^11\).

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 research\(^14\), 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 disease\(^14\). Cases of emphysema, bronchitis, ischemia, hypertension, cardiac or rheumatic Chagas disease and pulmonary diseases were excluded, according to the morphological presentation\(^14\). 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 study\(^14\).

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 epicardium\(^15\). The morphometry was performed by means of digital caliper (Digimess 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 0.0409mm\(^2\). 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 picrosirius, 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 study\textsuperscript{16}. The interstitial region was considered an area of fibrosis around and in between the myocardiocytes, 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 average\textsuperscript{17}.

\textbf{Statistical Analysis}

The variables were analyzed with respect to distribution and variance. The correlations were made via the Spearman test (r\textsubscript{S}). The results were deemed statistically significant when \(p<0.05\).

\textbf{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.

\begin{table}[h]
\centering
\caption{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.}
\begin{tabular}{llll}
\hline
\textbf{Morphological parameters} & \textbf{Number of fields} & \textbf{Median (Min and Max)} \\
\hline
Total fibrosis (%) & 80 & 4,67 (0,32-18,64) \\
Interstitial fibrosis (%) & 80 & 2,67 (0,15-14,29) \\
Density of the nucleus of myocardiocytes (cells/mm\textsuperscript{2}) & 42 & 155,38 (59,91-431,70) \\
Density of myocardiocytes with lipofuscin (cells/mm\textsuperscript{2}) & 60 & 154,57 (111,26-561,48) \\
Density of mononuclear infiltrate (cells/mm\textsuperscript{2}) & 70 & 90,33 (27,72-290,08) \\
Thickness of myocardiocyte (µm) & 35 & 19,20 (9,80-29,20) \\
Thickness of nucleus of myocardiocyte (µm) & 20 & 5,78 (4,11-8,21) \\
\hline
\end{tabular}
\end{table}

The correlations between cardiac weight of elderly men with chronic Chagas heart disease and morphological parameters are presented in Table 2.

\begin{table}[h]
\centering
\caption{Correlation between cardiac weight of elderly men with chronic Chagas heart disease and morphological parameters. Uberaba, MG, Brazil, 2017.}
\begin{tabular}{lll}
\hline
\textbf{Morphological parameters} & \textbf{\textit{r}}\textsubscript{S} & \textbf{\textit{p}} \\
\hline
Thickness of myocardiocyte & 0,363 & <0,001* \\
Thickness of nucleus of myocardiocyte & 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 myocardiocyte & -0,555 & 0,0247* \\
Density of myocardiocytes with lipofuscin & -0,639 & 0,007* \\
\hline
\end{tabular}
\end{table}

Cardiac weight of the elderly presented a positive correlation, though not significant, with age (\textit{r}\textsubscript{S}=0.290, \(p>0.05\)) and BMI (\textit{r}\textsubscript{S}=0.286, \(p>0.05\)). In addition, the correlation of cardiac weight with the thickness of myocardiocytes 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 myocardiocytes 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 disease^{18-20}. 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 response^{21}. 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 fibrosis^{22}. Serious myocarditis is associated with fibrosis and the most important characteristic of the disease is the accumulation of collagen around the myocardiocytes^{21}. 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 parasitism^{21}.

The cardiac weight found in elderly men, 418.7g (±136,3g) was similar to the weight interval from 415g (± 136,8) to 487.2g (±129,1) related in another study^{21}, which was less than that of another study^{23} that had a weight average of 508.2g (±110,7). As reported in yet another study^{24} 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 study^{23}. 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 study^{25} 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 study^{25} 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.

**REFERENCES**


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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