

## Macroscopic Aspects of Chronic Chagas Heart Disease in Aging

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### Summary

**Objective:** To describe the macroscopic characteristics of chronic Chagas heart disease in autopsied elderly.

**Methods:** The elderly studied were 60 or older. Twenty of them had chronic Chagas heart disease (CHD) and positive serology for the disease, and 14 had no heart disease (WHD) nor morphological changes suggestive of it and were serologically negative for Chagas disease.

**Results:** The CHD elderly had cardiac weight greater than the WHD ( $385 \pm 141.1$  vs  $306.8 \pm 62.1$ g, respectively;  $p > 0.05$ ), in addition to significantly higher heart weight-to-body weight ratio (0.71% [0.5-1.42%] vs 0.59% [0.47-0.91%]  $p < 0.05$ ). When compared, the CHD elderly presented lower fibrous thickening and/or atherosclerosis in the ascending aorta, mitral and tricuspid valves, and left and right coronaries than the WHD elderly. In the aortic and mitral valves, the lesions were significantly less severe ( $p < 0.05$ ). Left ventricular apical lesion was observed in 45% of the CHD elderly, and intracardiac thrombosis in the left ventricle was found in 10% of them.

**Conclusion:** Fibrous thickening and/or atherosclerosis were found to be less severe in the valves and arteries of the CHD elderly. Moreover, heart weight and intracardiac thrombosis frequency were lower than those detailed in the literature for non-elderly individuals.

**Key words:** Chagas cardiomyopathy; atherosclerosis; Chagas disease; aging.

### Introduction

According to the World Health Organization (WHO), thirteen million individuals are infected by the protozoan *Trypanosoma cruzi*. Around three million cases are symptomatic, and the annual incidence of new cases is one hundred thousand to two hundred thousand<sup>1</sup>. In Brazil, there is an association of epidemiological and demographic transitions<sup>2</sup>. Among the various chronic illnesses which afflict the elderly, Chagas disease in its chronic phase is found in endemic areas. Infection by *T. cruzi* in the elderly represents a public health problem due to reduction in preponderance and interruption in transmission of Chagas disease, which determines an increase in aging infected individuals<sup>3</sup>. Although chronic Chagas heart disease is the most serious lesion caused by Chagas disease, the disease is still little understood. Most infected individuals remain asymptomatic, and around 30% present cardiac and/or digestive complications in the late phase of the disease<sup>4</sup>.

In chronic Chagas heart disease described in non-elderly individuals, the macroscopic changes vary from an apparently normal heart with dilation of the right auricle to an increase in weight, global dilation associated with hypertrophy,

subendocardial fibrosis at the tip of the ventricle and papillary muscles, endocardial thickening, left ventricular apical lesion with or without intracardiac thrombosis, intracardiac thrombosis, extreme cardiomegaly with the heart weighing over 1000g, and changes in the aorta, such as supravalvular dilation and aneurysm formation<sup>5-7</sup>.

The macroscopic aspects of chronic Chagas heart disease in aging were not found in the literature. In the few studies investigating the disease in the elderly, most refer to clinical aspects<sup>8-12</sup>. Therefore, based on the increase in aging individuals with Chagas disease and on the fact that there are few pathological studies of Chagas disease in the elderly, the aim of this study was to describe the macroscopic changes of chronic Chagas heart disease in autopsied elderly.

### Methods

The elderly, whether with chronic Chagas disease or not, were selected from the reports on autopsies performed at the Teaching Hospital of the Federal University of Triângulo Mineiro (UFTM), Uberaba, Minas Gerais, from 1970 to 2000. The elderly selected were age 60 or older, and their demographic data are shown in Table 1. Among these data, causes of death were grouped into cardiovascular, infectious, neoplastic, digestive, and others, according to the description in the autopsy report of the process that could have determined the ultimate cause of death<sup>13</sup>.

Two groups were formed for the macroscopic analysis of the hearts: one consisting of fourteen elderly individuals without

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heart disease (WHD elderly) and the other consisting of 20 elderly with chronic Chagas heart disease (CHD elderly). In the CHD group, cases of emphysema; bronchitis; ischemic, hypertensive, and rheumatic heart diseases; and/or *cor pulmonale* were excluded, according to the macroscopic and microscopic morphologic characteristics. Cases with positive serology for Chagas disease, as well as those with morphologic characteristics suggestive of Chagas heart disease, were included in this group<sup>14</sup>. In the WHD group, Chagas heart disease cases and those with positive serology for Chagas disease were excluded, as well as the lesions excluded in the CHD elderly group<sup>15</sup>.

The following macroscopic characteristics were evaluated: fibrous thickening and atherosclerosis in the ascending aorta, in the pulmonary trunk, and in the aortic, pulmonary, mitral, and tricuspid valves; epicarditis; the shape of the heart; endocardial fibroelastosis; left ventricular apical lesion; and endocardial thrombosis<sup>16</sup>. The severity of the processes was classified semiquantitatively according to predominance in the structure analyzed as follows: absent, mild when up to 25% of the structure was affected, moderate when 26% to 50% of the structure was affected, and severe when over 51% of the structure was affected. Cardiac weight was obtained from the autopsy reports, and the heart weight-to-body weight ratio (HW/BW) was calculated with the weight in grams multiplied by 100. The HW/BW normality pattern was considered as less than or equal to 0.5%<sup>17</sup>.

Statistical analysis was performed using the *SigmaStat 2.03 program*. Comparison of two groups with normal distribution and homogenous variance was performed using the *Student's t-test* and, when this was not the case, the *Mann Whitney test* to compare two groups, or the *Kruskal-Wallis*, followed by the *Dunn test*, to compare more than two groups. The

significance level was set at 5% ( $p < 0.05$ ). This research project was approved by the Ethics Committee of the UFTM, file No. 357.

## Results

The cardiac weight of the CHD elderly was greater than that of the WHD elderly ( $385 \pm 141.1$  vs  $306.8 \pm 62.1$ g, respectively;  $p > 0.05$ ), and their HW/BW ratio was significantly higher than that of the CHD elderly (0.71% [0.5-1.42%] vs. 0.59% [0.47-0.91%],  $p < 0.05$ ). The CHD elderly, when compared to the WHD elderly, presented less fibrous thickening and/or atherosclerosis in the ascending aorta segment (Figure 1), mitral and tricuspid valves, and left and right coronaries (Figure 2), but the difference was not statistically significant ( $p > 0.05$ ). On the other hand, atherosclerosis in the aortic valve (Figure 1) and fibrous thickening in the mitral valve (Figure 3) were significantly less severe in the CHD elderly ( $p < 0.05$ ) (Table 2). Global cardiac dilation, however, was significantly more severe in the CHD elderly ( $p < 0.05$ ) (Table 2). All other macroscopic changes are shown in Table 2.

In the CHD elderly, left ventricular apical lesion was detected in 45% ( $n = 9$ ) and intracardiac thrombosis in the left ventricle in 10% ( $n = 2$ ), all of which were associated with left ventricular apical lesion. In these cases of intracardiac thrombosis, cardiac weight was 520 g and 850 g. Cardiac weight of the CHD elderly with left ventricular apical lesion was greater than in those without the lesion ( $431.1 \pm 186.6$  vs  $347.3 \pm 80.4$ g, respectively;  $p > 0.05$ ).

## Discussion

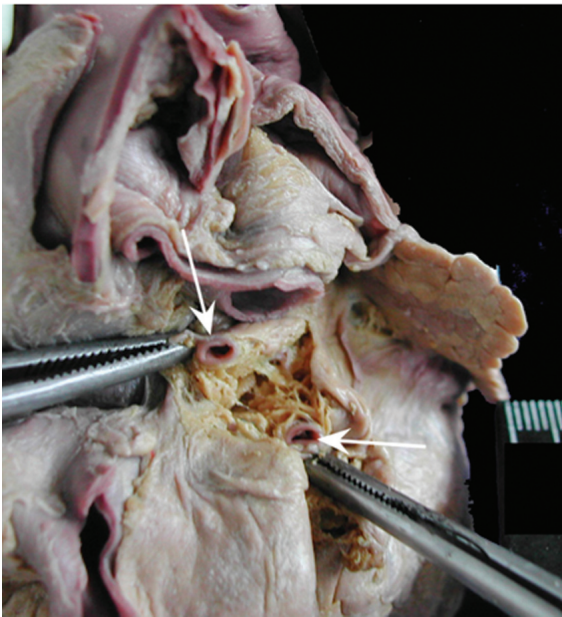
According to a literary review, this appears to be the first description of macroscopic characteristics of chronic Chagas heart disease in aging. In general, in the macroscopic cardiac evaluation, the CHD elderly presented less severe fibrous thickening and/or atherosclerosis in the valves and arteries evaluated than the WHD elderly. Moreover, cardiac weight and intracardiac thrombosis frequency were lower than that described in the literature for non-elderly individuals<sup>18-20</sup>.

Atherosclerosis in the aortic valve and fibrous thickening in the mitral valve were significantly less severe in CHD elderly than in the WHD. In another study no difference was noted in the frequency of myocardial infarction and coronary atherosclerosis in non-elderly individuals with or without chronic Chagas disease. Morphological findings of the artery disease were also similar in both groups<sup>21</sup>. Modulation in inflammatory response probably occurs<sup>22</sup> in chronic Chagas heart disease in the elderly, which could lead to the development of less severe atherosclerotic lesions. Therefore, it is possible that inflammatory modulation in Chagas heart disease enables the modulation of common pathways for the development of heart disease and atherosclerosis, which would indirectly inhibit the progression of the atherosclerotic lesions.

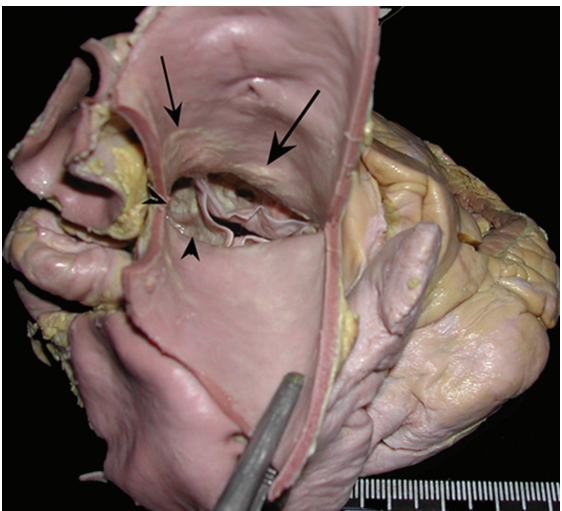
Global heart dilation was significantly more frequent in CHD elderly; severe chronic epicarditis and endocardial fibroelastosis were also predominant in the CHD elderly, yet

**Table 1 - Demographic characteristics of autopsied elderly with chronic Chagas heart disease (CC elderly) and without heart disease (WHD elderly)**

Demographic characteristics	CHD elderly (n = 20)	WHD elderly (n = 14)
Age (median-years)	67 (60 - 101)	72.5 (60 - 92)
Body Mass Index (kg/m <sup>2</sup> )	18.5 ± 4	20.8 ± 4.4
<b>Gender % (n)</b>		
Male	80 (16)	50 (7)
Female	20 (4)	50 (7)
<b>Race % (n)</b>		
White	60 (12)	78.6 (11)
Non-white	40 (8)	21.4 (3)
<b>Death causes % (n)</b>		
Cardiovascular	20 (4)	7.1 (1)
Infectious	50 (10)	71.5 (10)
Neoplastic	25 (5)	21.4 (3)
Other	5 (1)	-



**Fig. 1** - Left coronary with mild atherosclerotic plaque (arrow) in an elderly patient with chronic Chagas heart disease.



**Fig. 2** - Mild atherosclerotic plaques in the ascending aorta (arrow) and in the aortic valve (arrow head) in an elderly patient with chronic Chagas heart disease.

there was no statistical difference in proportions. Cardiac dilation in Chagas heart disease found in the elderly is a characteristic of the disease, as already described in the non-elderly<sup>16,23</sup>. On the other hand, the other macroscopic changes described previously were also found in the WHD elderly. Yet, although these changes were not specific, they increased in intensity in Chagas heart disease. Ventricular dilation and reduction in myocardial compliance are also related to the destruction of cardiomyocytes associated with fibrosis<sup>24</sup>. This



**Fig. 3** - Mitral valve with mild fibrous thickening (arrow) in an elderly patient with chronic Chagas heart disease.

fact may have contributed to the cardiac dilation found in the CHD elderly.

Left ventricular apical lesion and intracardiac thrombosis in the left ventricle associated with apical lesion were found only in the CHD elderly. This fact is in accordance with the literature, which describes left ventricular apical lesion as a lesion typical of Chagas heart disease and is considered one of the most important macroscopic changes for the diagnosis of the heart disease, which in turn can lead to intracardiac thrombus formation<sup>25</sup>.

Left ventricular apical lesion was found in 45% of CHD elderly cases and intracardiac thrombosis in 10% of the cases, all of which were associated with left ventricular apical lesion. These frequencies were lower than in another study which describes left ventricular apical lesion in 53.2% of the cases, in which 49.5% also presented cardiac thrombosis<sup>18</sup>. Other authors reported 73% of intracardiac thrombosis in severe Chagas heart disease in non-elderly individuals. Left ventricular apical lesion was described in 68% of the cases, 48% of which were significantly associated with apical thrombosis<sup>19</sup>. Moreover, in large left ventricular apical lesions, besides the risk of thrombosis, there is also the danger of arrhythmia and changes in heart function<sup>18</sup>.

The lesser frequency of left ventricular apical lesion and intracardiac thrombosis in CHD elderly shows that, in the elderly studied, Chagas heart disease is characterized by milder forms that allow functional adaptation of the heart to lesions in the organ, thus enabling survival. Cardiac weight was greater in the individuals that had left ventricular apical

Table 2 - Macroscopic cardiac evaluation of autopsied elderly with chronic Chagas heart disease (CHD elderly) and without heart disease (WHD)

Macroscopic alterations	CHD elderly (n = 20) % (n)				WHD elderly (n = 14) % (n)				p
	Absent	Mild	Moderate	Severe	Absent	Mild	Moderate	Severe	
Fibrous thickening									
Ascending aorta	-	40 (8)	55 (11)	5 (1)	-	42.8 (6)	14.4 (2)	42.8 (6)	>0.05
Tricuspid valve	15 (3)	65 (13)	10 (2)	10 (2)	-	42.9 (6)	50 (7)	7.1 (1)	>0.05
Mitral valve	-	45 (9)*	30 (6)	25 (5)	-	7.1 (1)	42.9 (6)	50 (7)	<0.05*
<b>Atherosclerosis</b>									
Ascending aorta	-	40 (8)	50 (10)	10 (2)	-	21.4 (3)	57.2 (8)	21.4 (3)	>0.05
Aortic valve	50 (10)*	15 (3)	35 (7)	-	-	14.3 (2)	64.3 (9)	21.4 (3)	<0.05*
Mitral valve	25 (5)	25 (5)	45 (9)	5 (1)	7.1 (1)	35.7 (5)	57.2 (8)	-	>0.05
Right coronary	60 (12)	10 (2)	5 (1)	25 (5)	50 (7)	7.1 (1)	7.1 (1)	35.8 (5)	>0.05
Left coronary	30 (6)	20 (4)	10 (2)	40 (8)	7.1 (1)	35.8 (5)	7.1 (1)	50 (7)	>0.05
Global heart dilation	-	25 (5)	35 (7)	40 (8)*	50 (7)	14.3 (2)	28.6 (4)	7.1 (1)	<0.05*
Chronic epicarditis	5 (1)	30 (6)	20 (4)	45 (9)	28.6 (4)	28.6 (4)	21.4 (3)	21.4 (3)	>0.05
Endocardial fibroelastosis	5 (1)	75 (15)	5 (1)	15 (3)	28.6 (4)	57.1 (8)	14.3 (2)	-	>0.05

lesion and intracardiac thrombosis, probably due to the more severe myocardial lesions in these cases as described by other authors<sup>19</sup>.

Cardiac weight in the CHD elderly ( $385 \pm 141.1$ g) was lower than that found in literature, where the cardiac weight of non-elderly individuals varies from  $415 \pm 136.8$  g to  $568.49 \pm 133.79$  g<sup>17,20,23</sup>. Likewise, the median HW/BW ratio in the CHD elderly (0.71% [0.5-1.42%]) was less than the average found in the literature for non-elderly individuals ( $1.1 \pm 0.22\%$ )<sup>17</sup>. Cardiac weight in the CHD elderly lower than that described in the literature shows that although heart enlargement also occurs in the elderly, it seems to be less marked, probably due to less severe myocardial lesions during aging.

Macroscopic lesions in CHD elderly were qualitatively similar to those described in the literature for non-elderly individuals, but less severe. The study of chronic Chagas heart disease may also contribute toward a greater understanding of other lesions, such as atherosclerosis. These mechanisms may

be involved in the modulations that produce the characteristics peculiar to Chagas heart disease in the elderly. Therefore, less severe fibrous thickening and/or atherosclerosis in the valves and arteries of CHD elderly were found. In addition, cardiac weight and intracardiac thrombosis frequency were lower than described in non-elderly individuals.

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## Potential Conflict of Interest

No potential conflict of interest relevant to this article was reported.

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