Original Article

Correlation between hypertension cardiopathies and atherosclerosis in the aortic artery

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Received: 04/09/2016.
Accepted: 09/22/2017.
Published: 12/31/2017.

Suggest citation:
Moreno PPM, Ferraz MLF, Soares MH, Teixeira VPA, Helmo FR, Corrêa RRM. Correlation between hypertension cardiopathies and atherosclerosis in the aortic artery. Rev. Eletr. Enf. [Internet]. 2017 [cited __/__/__];19:a52. Available from: http://doi.org/10.5216/ree.v19.40655.

ABSTRACT

Systemic arterial hypertension is a multifactorial disease, behaving as a triggering factor for cardiovascular diseases and atherosclerosis. The objective was to describe the association of age, gender, skin color and, the atherosclerosis level in the aortic artery in hypertensive cardiopathy of autopsied individuals. We assessed 34 parts of abdominal aortic arteries of autopsied individuals with hypertensive cardiopathy (20) and without hypertensive cardiopathy (14). We collected age, gender, skin color and cause of death from the autopsy report; the quantification of the atherosclerosis intensity and the atherosclerosis level were determined using a standardized scale. In this study, the cause of death and atherosclerosis intensity had a significant association with hypertensive cardiopathy; there was a prevalence of large atheroma plaques among individuals with this entity. Thus, atherosclerosis should be investigated in individuals with hypertensive cardiopathy to prevent severe repercussions which could lead to death.

Descriptors: Atherosclerosis; Heart Diseases; Hypertension.

INTRODUCTION

Systemic arterial hypertension (SAH) is characterized by high and sustained levels of systolic and/or diastolic blood pressure. Blood pressure equal to 120/80 mmHg is considered optimum for adults. This entity is diagnosed when the systolic blood pressure is equal or higher than 140 mmHg and/or the diastolic is equal or higher than 90 mmHg, in individuals older than 18 years of age[(1)].

Because of the high prevalence rates and difficult to control, the SAH is considered an important public health issue in Brazil and the world. Consequently, we observe the increase in mortality levels caused by

diseases related to elevated blood pressure in the past 12 years, like stroke, ischemic heart disease and atherosclerosis in countries of low and medium economic development. In Brazil, cardiovascular diseases are noted among the leading causes of death in the nation, reaching registries of up to 308,466 deaths/year caused by conditions in the circulatory system[1-2].

SAH is a multi-factorial disease; its main risk factors are age, gender, ethnicity, family history, obesity, exacerbated salt ingestion, chronic use of alcoholic drinks, smoking, sedentarism and low socioeconomic level[1]. Besides the high complexity, it can be prevented and controlled by changes in eating habits and lifestyle[1,3].

Among the diseases which SAH can be associated, are noted the cardiovascular diseases (CVDs) and arteriopathies caused by vase obstruction, like the ischemic heart disease and atherosclerosis, and this association results in prevalence increase of CVDs and their complications[3]. In the SAH progression, there is the myocardiocytes lesions and hypertrophy of the left ventricle, characterizing the hypertensive cardiopathy. Consequently, the cardiac muscle is not able to keep the adequate blood flow, there is overload, hypertrophy of myocardial structures, neoformation of collagen and cyclical apoptoses, which cause severe arrhythmias until cardiorespiratory arrests[4].

Atherosclerosis is a chronic multi-factorial disease resulting from inflammatory response to the endothelial aggression, especially affecting the inner layer of medium and large caliber arteries. Cholesterol accumulation characterizes the etiopathogenesis of this entity and its esters in the inner layer of arteries resulted from the prior endothelial lesion[5]. The accumulation of interstitial oxidized lipid favors the activation of the vascular endothelium and, consequently, the recruitment and activation of monocytes in the circulation. These cells are responsible for lipid phagocytosis and synthesis of inflammatory cytokines, as the interleukins-1, which contribute for the progression of the inflammatory response, as well as, the recruitment and activation of smooth muscle cells from the medium layer for the neoformation of collagen fibers. It is possible to microscopically observe the accumulation of lipids inside the macrophages and smooth muscle cells, called foam cells, in the vascular interstitial, besides the dystrophic calcification areas. The macroscopic changes are characterized by the presence of atheroma plaques of various extension, making salience with the lumen of the vessel. Moreover, some plaques can be fibrous or even calcified depending on the intensity. In the initial lesions, the activated macrophages are responsible for the secretion of cytokines and proteolytic enzymes and, consequently, by the progression of the atherosclerotic plaque[6].

Thus, to quantify the thickness of the atheroma plaque is an important instrument to stratify the cardiovascular risk for acute myocardial infarction and stroke, for example, among individuals with hypertensive cardiopathy[7]. Also, research points the increased risk for cardiovascular diseases and atherosclerosis in a ten-year period due to complications from aging, associated to SAH in this population[8]. The literature is lacking studies describing the macroscopic atherosclerosis characteristics concomitant to hypertension cardiopathy in autopsied individuals[9].

Therefore, the objective of the study was to describe the association of age, gender, skin color and

atherosclerosis level in the aortic artery with the occurrence of hypertensive cardiopathy among autopsied individuals in the Hospital de Clínicas da Universidade Federal do Triângulo Mineiro (HC-UFTM).

METHODS

An exploratory and descriptive study, where we retrospectively assessed 797 autopsy reports from 1984 to 2014 in the HC-UFTM. Initially, we excluded 567 cases due to age less than 18 years, incomplete autopsy reports, the cause of death differently from cardiopathy (ex: dilated myocardiopathy, rheumatic cardiopathy, valve cardiopathy) and absence of aorta in the organ bank. Thus, we obtained 230 cases. From those, we selected 20 segments of abdominal aorta of hypertensive cardiopathy cases, and 14 segments of abdominal aorta of cases without hypertensive cardiopathy and other diagnoses that could interfere in the blood pressure, as auto-immune diseases and nephropathies. We excluded cases with damaged aortas and, therefore, that harmed the macroscopic atherosclerosis assessment, totalizing the exclusion of 196 cases. Thus, we assessed 34 artery segments of abdominal aortas of autopsied individuals with and without hypertensive cardiopathy (Figure 1).

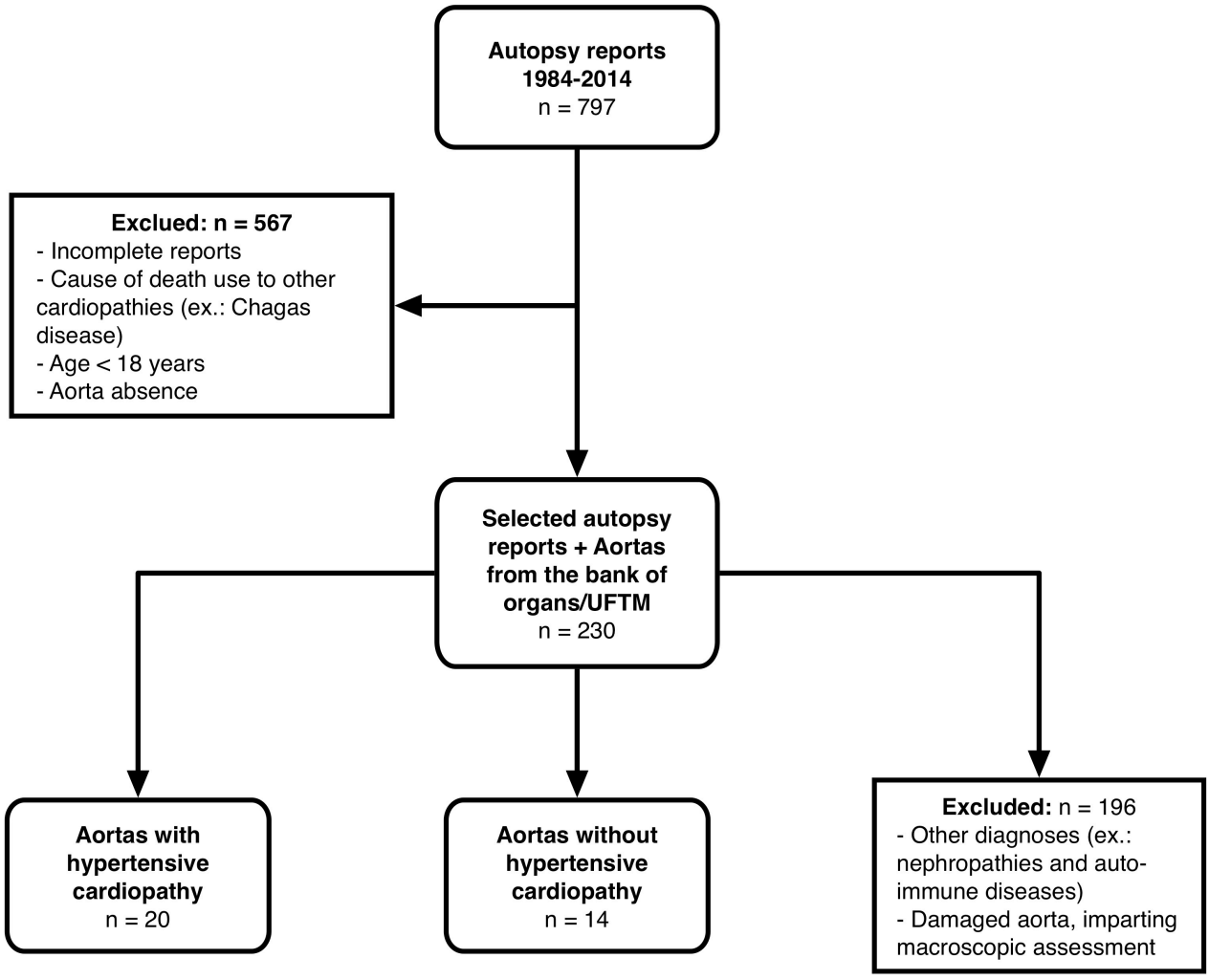

Figure 1: Triage of autopsy reports and aortic arteries with and without hypertensive cardiopathy during 1984-2014.

The design of groups was established according to literature data[2] as:

- Hypertensive Cardiopathy (HC): individuals who developed atherosclerosis in large vessels, with SAH diagnosis and cardiac lesions resulting from SAH; understanding that hypertensive cardiopathies are a result from prolonged SAH cases, followed of myocardiocytes lesions and later hypertrophy of the left ventricle.
- Without Hypertensive Cardiopathy (WHC): individuals without SAH history, but because of other comorbidities that will not be explored in the present study (Diabetes Mellitus or dyslipidemias, for example), had also developed atherosclerosis in large vessels.

In the autopsy report, we collected information referring to age (years), gender (male/female), skin color (white/non-white) and, the cause of death (classified according to the most prevalent entities: cardiopathy, infection, inflammation, and neoplasia).

Three observers assessed the segments to quantify the atherosclerosis of each segment of the abdominal artery. Each observer analyzed the impairment of the aortic artery segments (presence of lipid stretch, quantity of lipid plaques, plaque extension, presence of collagen, hemorrhage or calcifications and, atherosclerotic plaque integrity) and subjectively registered the point in a non-millimetric scale from 0.0 cm to 12.0 cm. After, with the help of a millimetric rule, the observer measured the distance of 0.0 cm until the point marked in the scale. After quantifying the atherosclerosis intensity, the three observers consensually standardized the atherosclerosis level according to intensity using the mean:

1. discrete: from 0.1 to 4.0cm;
2. moderate: 4.1 to 7.0cm;
3. accentuate: 7.1 to 12.0cm[9].

We created an electronic Microsoft Excel® spreadsheet with all collected data, and we conducted statistical analysis using the GraphPad Prism® version 5.0 software. After, we tested the quantitative variables to verify if they presented normal distribution, using the Kolmogorov-Smirnov test. We analyzed the qualitative variables gender and color using the Fisher's Exact test, while we used the Chi-Square ($\chi 2$) for the various causes of death and atherosclerosis level. We expressed all results as absolute and percentage (%) values. We expressed the quantitative variable age (years) as the mean ± standard deviation (X ± SD), and we compared the means using the Student's t-test. We expressed the atherosclerosis intensity (cm) as median and minimum and maximum values (Med – Min-Max), and we analyzed them using the Mann-Whitney (T) test. We considered statistically significant the differences lower than 5% ($p<0.05$).

The Ethics in Research Committee of the UFTM approved the study (CAAE: 48022015.0.0000.5154).

RESULTS

We assessed 34 samples of aortic arteries of autopsied adults during 1984 to 2014. From those, 59% (20) had hypertensive cardiopathy and mean age of 61.45 ± 12.14 years, while 41% (14) did not have it and were 60.50 ± 14.85 years old.

In the HC group, 15% (3) were females, and 85% (17) were males.; 40% (8) were non-white and 60%

(12) were white. While 7% (1) in the WHC group were females, and 93% (13) were males; 36% (5) of the sample was non-white, and 64% (9) were white.

The mean age (t = 0.2049; p = 0.838); gender (p = 0.627) and color (p = 1.000) were not significantly associated among the assessed groups.

The cause of death presented a significant association with the presence of hypertensive cardiopathy (X^2 = 8.711, *p* = 0.033). In the HC group, 60.0% (13) deaths were due to cardiopathies and 20.0% (4) caused by infections; while in the WHC group, this proportion was 35.7% (5) and 7.1% (1), respectively. There was no death caused by neoplasia in the first group, this entity affected 28.6% (4) among those without hypertensive cardiopathy (Figure 2).

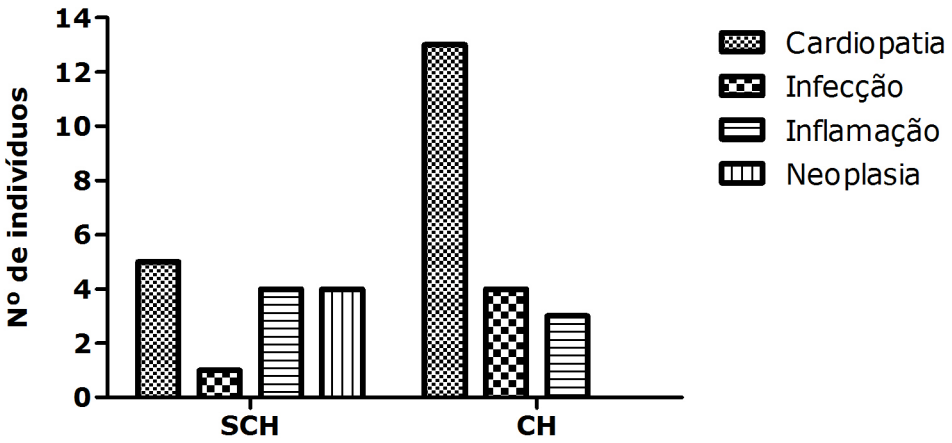

Figure 2: Death causes according to the presence of hypertensive cardiopathy in autopsies conducted in Hospital de Clínicas da Universidade Federal do Triângulo Mineiro during 1984-2014 .

Similarly, we also observed a significant association between the atherosclerosis intensity and the presence of hypertensive cardiopathy (X^2 = 9.166; p = 0.010). Considering that 75% (15) of the HC group was classified as accentuated, while in the WHC group, this proportion was 29% (4) (Table 1).

Table 1: Atherosclerosis intensity according to the presence of hypertensive cardiopathy in autopsies conducted in Hospital de Clínicas da Universidade Federal do Triângulo Mineiro de Uberaba, MG, Brazil, during 1984-2014 (p = 0.010).

Atherosclerosis	WHC - % (n)	HC - % (n)
Discrete	42 (6)	5 (1)
Moderate	29 (4)	20 (4)
Accentuated	29 (4)	75 (15)
Total	**100 (14)**	**100 (20)**

WHC: without hypertensive cardiopathy. HC: hypertensive cardiopathy.

Atheroma plaques of large extension were more frenquent among individuals with hypertensive cardiopathy (T = 63.00; p = 0.007) (Figure 3).

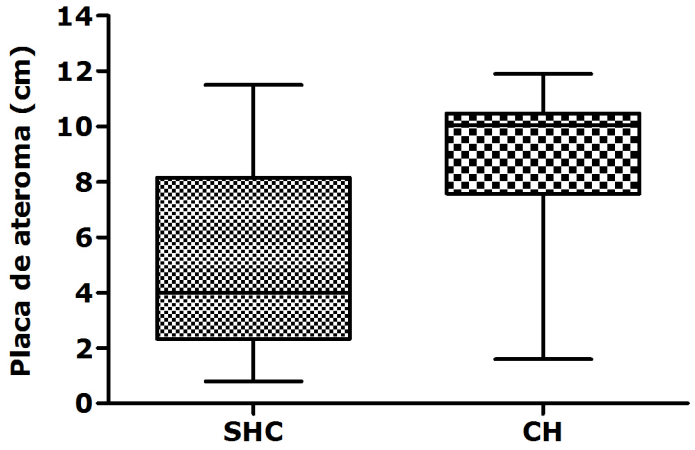

Figure 3: Extension of atheroma plaque according to the presence of hypertensive cardiopathies in autopsies conducted in Hospital de Clínicas da Universidade Federal do Triângulo Mineiro during 1984-2014.

DISCUSSION

In this study, the age did not influence among individuals with hypertensive cardiopathy. However, literature data points the SAH prevalence and cardiac insufficiency, for example, in 60%[1] and e 70%[10] of individuals in the age group above 60 years. Also, studies aiming to assess the epidemiology and the cardiovascular risk for cardiac insufficiency and SAH points to an age mean between 61 and 63.2[8] years, respectively, therefore demonstrating that findings from our study agree with the literature.

Regarding gender and skin color, both also did not influence the group with hypertensive cardiopathy in this study. However, both factors seemed to be relevant for its incidence, once studies highlight the prevalence of hospitalizations in Brazil due to hypertensive cardiopathy[11] and of hypertension[12] among men. In contrast, starting at 70 years of age, women have a higher hypertension incidence, accompanied or not of left ventricular hypertrophy [4]. The literature also emphasized that non-white ethnicity is more likely to develop SAH, but in countries like Brazil where there is intense miscegenation[4,11], this influence might not be perceptible among people with HC.

Cardiopathies and infections were the leading causes of death in the hypertensive cardiopathy group, with a significant association between variables. Cardiovascular diseases are responsible for 20% of death in individuals older than 30 years in Brazil, followed by neoplasia, respiratory diseases and external causes[2]. According to studies that followed hypertensive patients for up to 15 years, between 45%(13) and 60%[14] of deaths were associated to cardiovascular diseases, like coronary artery disease[13,15] and cardiac insufficiency[15]. The literature also reinforces factors like obesity, diabetes mellitus, dyslipidemia[2,15], cerebral-vascular conditions and kidney failure[13], for example, favoring the increase of death risk for these individuals.

Infections, like pneumonia and sepsis, are responsible for many deaths in hypertensive cardiopathy. Studies point that among hypertensive elderly with previous cardiac insufficiency, the proportion of deaths due to infections can reach 37%[13,16]. A recent literature review[17] emphasized the presence of chronic

cardiac disease favoring an increment 3.3 times of community pneumonia, and up to 9.9 times invasive pneumococcal disease according to age and other factors associated to diabetes mellitus, smoking, chronic bronchitis, and asthma, confirming the results found in the present study.

When we investigated the presence of atherosclerosis and hypertensive cardiopathy, we found strong association, once 75% of individuals presented accentuated atherosclerosis in the aortic artery. A study assessed the morphological characteristics of atherosclerosis in autopsied individuals reported a significant correlation between the level of atherosclerosis and the presence of cardiovascular disease[9].

Dyslipidemia favors the SAH severity; once there is a positive association between the increase of serum levels of triglycerides, low-density lipoprotein, very low-density lipoprotein and apolipoprotein B100, and the increment in blood pressure and risk of cardiopathies in hypertensive individuals[18]. The continuous deposit of cholesterol in the inner layer triggers the endothelial activation, the recruitment of monocytes and smooth muscle cells, the synthesis of inflammatory mediators and the neoformation of collagen, for example. Consequently, the atherosclerosis progression is related to the loss of the endothelial function and the reduction of elasticity caused by organization compromise, function, and signaling between the components of the aortic artery[19].

Individuals with SAH have ticker aortic artery due to atherosclerosis[7,19] and, consequently, lower vessel distensibility, when compared to the non-hypertensive; highlighting that increased blood pressure favors not only the fat deposits but also the progressive stiffness[5,7] and aortic endothelial dysfunction[5] in the hypertensive cardiopathy.

Atherosclerosis severity presents strong correlation with the increased risk of cardiovascular and non-cardiovascular diseases[19]. A study shows that complicated atherosclerosis (severe atheroma plaques, the presence of ruptures, ulcerations, and thrombi), associated to SAH, diabetes mellitus, dyslipidemia, and smoking, for example, favors the incidence of coronary artery disease[6]. The plaque thickness between 2.1 and 3.0, 3.1 and 4.0, 4.1 and 5.0 and, > 5.0 mm, represent a risk of 57%, 60%, 81% and 86%, respectively, for the occurrence of this condition[20]. Similarly, individuals with atherosclerosis, hypertensive, with an ankle-brachial index ≤ 0.9 and older than 70 years, have an increased risk for peripheral artery disease[21].

In contrast, in the absence of hypertensive cardiopathy, atherosclerotic lesions are more discrete. The literature highlights that aging and the presence of other comorbidities are important factors in the progression of atherosclerosis in individuals without SAH. The atherosclerosis intensity reaches 53% of these individuals discretely and, 19% in a moderate way. Among elderly, especially, there is a prevalence of atherosclerosis about seven times higher in comparison to young adults[22].

We observed the prevalence of large atheroma plaques among individuals with hypertensive cardiopathy, in comparison to those without it. About 60% of individuals with coronary artery disease[23] or hypertrophy of the left ventricle associated to SAH[23-24], diabetes mellitus[23], and dyslipidemia[25], for example, presented higher incidence of complex plaques in the descendent aorta (thoracic and abdominal segments); extension and volume up to three times larger among those with hypertensive cardiopathy[23-24],

when compared to normotensives.

The literature points minimal mean thickness for the atheroma plaque starting in 3mm[20,25], and maximum ≥ 7mm[25] about the mean inner thickness of the aortic artery. Besides, it is estimated that approximately 35% and 42% of individuals with atherosclerosis have the significant presence of ulcerations and calcifications[25], respectively.

Thus, we perceive that atherosclerosis extension and complexity are dependent on SAH time, advanced age, increased blood pressure and intense blood flow, which is responsible for the endothelial vessel lesion.

CONCLUSION

In this study, the gender and color did not have an association between the atherosclerosis presence and hypertensive cardiopathy. However, it was observed that most individuals with hypertensive cardiopathy had accentuated atherosclerosis and more extensive atheroma plaques, being cardiopathies and infections the leading causes of death in this group.

Atherosclerosis is a complex disease; it can be associated with different entities. Dyslipidemia, for example, increases the severity of atherosclerosis, SAH, and the risk of cardiopathies in hypertensives. These individuals have thicker aortic artery, extensive, ulcerated and calcified atheroma plaques and, predisposition to a higher risk of death.

Thus, atherosclerosis should be considered when assessing individuals with hypertensive cardiopathy aiming to prevent severe repercussions, which could lead to death.

Funding

The study which originated this work had financial support of the agencies:

- National Council of Technological and Scientific Development (CNPq) [process number: 470029/20110];
- Coordination for the Improvement of Higher Education Personnel (CAPES) [process number: PNPD-02604/094];
- Foundation of Reseach Support of Minas Gerais State (FAPEMIG) [process number: CDS-APQ-02135-14];
- Teaching and Research Foundation of Uberaba (FUNEPU) [process number: CDS-922/2009].

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