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Research Article

Comparative Analysis of Elastic and Collagen Fibers of Coronary and Carotid Arteries in Autopsied Patients

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ABSTRACT

Introduction: Predicting cardiovascular risks is a goal pursued by authors from several research lines in an attempt to demonstrate an association between atherosclerosis in several arterial beds.

Objectives: To analyze the morphology of the carotid and coronary arteries of autopsied patients, and to assess the correlation between them.

Materials and methods: For histopathological analysis, 22 autopsy reports were evaluated and 22 sections of the Right Common Carotid Artery (RCCA), of the Left Common Carotid Artery (LCCA), of the Anterior Descending Coronary Artery (ADCA), of the Posterior Descending Coronary Artery (PDCA), and of the Circumflex Coronary Artery (Cx) were collected. Leica Qwin Plus® image software was used was used to quantify collagen and elastic fibers.

Results: Of the 22 autopsy reports analyzed, 59% of the individuals were male and had a mean age of 45 years. There was no significant difference in the percentages of elastic fibers between the carotid arteries and the different coronary arteries. There was a significant difference in the percentages of collagen fibers only for the Cx artery

Conclusion: The analyses performed show that the onset of atherogenesis is common in different arteries, thus corroborating the literature, which regards it as a systemic inflammatory process affecting several arterial beds. Therefore, studies aiming to predict atherosclerotic risks must be encouraged in order to reduce the morbidity and mortality rates associated with these diseases.

Keywords: Atherosclerosis; Carotid arteries; Coronary arteries; Autopsy

INTRODUCTION

Cardiovascular disease is one of the most relevant causes of mortality worldwide [1], accounting for one in two deaths in developed countries [2]. According to the Brazilian Society of Cardiology, it causes approximately 300 thousand deaths per year in Brazil. Arterial disease is the leading cause of mortality incidence in the population, and venous complications are less frequent. Atherosclerosis is responsible for many of the arterial cardiovascular diseases in Western countries [3]. North American estimates show that a third of the population has some sort of cardiovascular disease, which would correspond to 71.3 million inhabitants, 17 million of which have coronary disease [4-7].

Unlike other western countries, Brazil has a higher mortality rate associated with cerebrovascular diseases than with coronary diseases. According to data published by the Brazilian Society of Cardiology (SBC), the mortality rates due to cerebrovascular diseases were of 52.5% (246,322 patients) against 47.5% (222,852 patients) due to coronary diseases. Despite having similar risk factors, this statistical difference has a great impact on public Brazilian health since cerebrovascular accident is the main cause of temporary and permanent disability, thus increasing the number of costly treatments and burdening social security systems

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[8]. Furthermore, it is known that by mid-2025, Brazil will have 32 million elderly people (13% of its inhabitants). This aging population demonstrates the importance of studies and public policies supporting the treatment of chronic diseases, such as atherosclerosis [9].

At first, changes due to atherosclerosis involve mainly arteries in points of origins, bifurcations and branching. However, they may affect other sites after decades of life. After inflammation and endothelial injury, smooth muscle cells of the tunica intima are able to synthesize elastic and collagen fibers through migration by fenestrations of the internal elastic lamina. This migration occurs via chemotaxis induced by cytokines and chemokines, leading to subendothelial growth of the arterial wall [10].

Several researchers seek to interpret noninvasive atherosclerosis in patients so as to predict cardiovascular risk. Therefore, studies are performed in order to obtain screening of patients that have well-known risk factors for the development of atherosclerosis. Nevertheless, there are still controversies in the literature. In a recent study, the use of coronary computed tomography and angiography were compared, concluding that angiography proved superior to CT scanning in detecting atherosclerosis in these patients [11]. In another study, which used carotid ultrasound in pediatric patients, arterial wall thickness was shown to increase with age and with Body Mass Index (BMI) [12]. Predicting a cardiovascular risk is a study aim in several lines of research. Through the study of the carotid arteries, researchers attempt to show a correlation between carotid artery atherosclerosis and coronary artery atherosclerosis, seeking an association between them [13-18].

The mechanism of acute cardiovascular event involving coronary and carotid arteries is similar. Both the rupture and the superficial erosion of the atherosclerotic fibrous cap can cause the lipid nucleus (rich in lipids, collagen and tissue factors) to get in contact with blood components, for example, coagulation factors and platelets, hence leading to thrombosis. Regardless of the mechanism, plaque destabilization may lead to events such as acute coronary syndrome and cerebrovascular accident [19].

Cardiovascular complications that may occur in the perioperative period are a relevant concern, as they lead to an unfavorable outcome in patients, with high rates of perioperative morbidity and mortality (2%-6% for at-risk patients) [20]. Patients with coronary artery disease who are submitted to surgical stress associated with episodes of tachycardia and blood pressure changes, such as sustained hypotension and hypertension, may have a negative balance in myocardial oxygen supply and demand and, thus, have an acute coronary syndrome [21]. Furthermore, perioperative risk is higher in patients with carotid artery disease undergoing myocardial revascularization surgery, which demonstrates the importance of patient screening in order to offer better quality of care in the preoperative period and to avoid intercurrences [22].

The aim of this study was to evaluate the initial development of atherosclerosis in different coronary and carotid arterial beds of autopsied patients, demonstrating similar amounts of elastic and collagen fibers in their intima and media layers.

MATERIALS AND METHODS

This study was approved by the Human Research Ethics Committee of the Federal University of the Triângulo Mineiro (UFTM) under protocol number 1638.

We evaluated 22 complete autopsy reports collected by the Department of General Pathology of the Clinical Hospital of the Federal University of the Triângulo Mineiro (HC/UFTM), in Uberaba, Minas Gerais state, Brazil, regardless of the cause of death or underlying diseases. Moreover, 22 sections of the following arteries were collected: Right Carotid Artery (RCA), Left Carotid Artery (LCA), Anterior Descending Coronary Arteries (ADCA), Posterior Descending Coronary Arteries (PDCA), and Circumflex Coronary Arteries (Cx). The carotid and coronary sections collected were fixed in 10% formaldehyde. Subsequently, the sections were histologically processed, dehydrated in high-concentration alcohols (70-100%), diaphanized in xylol, and embedded in paraffin. 4 µm thick serial sections were mounted on slides. The sections were placed on glass slides with poly-L-lysine® and processed for histochemistry. Quantification of the percentage of elastic and collagen fibers was performed by Verhoeff's stain and Picrosirius stain, respectively.

For quantification of elastic and collagen fibers, morphometry of the intima and media layers was performed using the Leica Qwin Plus® software with a 20x objective (620x final magnification). Collagen fibers were analyzed under polarized light with a birefringent appearance and reddish color. The area consisting of elastic fibers is observed as a darkened stain area in the scanned image. The number of fields analyzed for the stains (Picrosirius and Verheoff) was established by the mean cumulative test [23], with the slides divided into four quadrants subsequently divided into ten fields, totaling forty fields per slide.

A Microsoft Excel® spreadsheet was used for statistical analysis. The data were analyzed using the Graphpad Prism 5.0 software. Normal distribution of the quantitative variables was assessed by the Shapiro-Wilk test. Continuous variables with normal distribution were expressed as mean and standard deviation ($x \pm SD$), and the variables with non-normal distribution were expressed as median, minimum and maximum (med, min-max). The variables with normal distribution and homogeneous variance were analyzed by Student's t-test; otherwise, the Mann-Whitney test (U) was used. The results were considered statistically significant when the probability of error was less than 5% ($p<0.05$).

RESULTS

The autopsied patients selected for the study had a median age of 45 years, ranging from 25 to 74 years.

Verhoeff's stain was used for quantification of elastic fibers per field (%) so that the medians of the right carotid (6.195%) and left carotid (5.89%) arteries were also obtained. The medians of the anterior descending coronary artery, posterior descending coronary artery and circumflex artery comprised 5.595%, 5.870% and 5.735% of the analyzed area, respectively (Table 1).

Table 1: Percentage of elastic fibers in different arterial beds of autopsied patients in the HC-UFTM and the association of the percentage of elastic fibers between the right and left carotid arteries and the different coronary arteries of autopsied patients, with no significant difference between all the arterial beds analyzed.

Arterial bed	Median (%)	(Min – Max) (%)
Right Carotid	6.195	2.2 – 16.57
Left Carotid	5.89	2.66 – 15.81
Cx coronary artery	5.735	2.12 – 13.19
ADCA	5.595	1.15 – 14.46

PDCA	5.87	0.98 – 12.56
	55	55
Right carotid		
Anterior descending	U=183	p=0.169
Posterior descending	U=199	p=0.318
Circumflex	U=187	p=0.200
	55	55
Left carotid		
Anterior descending	U=126	p=0.716
Posterior descending	U=232	p=0.823
Circumflex	U=221	p=0.603

min: minimum; max: maximum; U: Mann-Whitney test

Table 1 shows the relationship between the right and left carotid arteries and the coronary arteries concerning the measurement of elastic fibers per imaging field (%), which showed no significant difference between all the arterial beds analyzed.

Picrosirius red staining was performed to quantify collagen fibers per field (%), and the medians of the right carotid (2.895%) and left carotid (2.805%) arteries were obtained. The medians of the anterior descending coronary artery, posterior descending coronary artery and circumflex artery comprised 3.085%, 3.270% and 1.9% of the analyzed area, respectively (Table 2).

Table 2: Percentage of collagen fibres in different arterial beds of autopsied patients in the HC/UFTM and the association of collagen fibres between the right and left carotid arteries and the different coronary arteries of autopsied patients, showing a significant difference between the right and left carotid arteries and the circumflex artery.

Arterial bed	Median (%)	(Min – Max) (%)
Right Carotid	2.895	0.09 – 7.7
Left Carotid	2.805	0.51 – 9.56
Cx coronary artery	1.9	0.1 – 14.79
ADCA	3.085	0.07 – 19.15
PDCA	3.27	0.1 – 18.48
Right carotid		
Anterior descending	U=193	p=0.25
Posterior descending	U=192	p=0.245
Circumflex	t=2.197	p=0.033*
Left carotid		
Anterior descending	U=198	p=0.307
Posterior descending	U=177	p=0.13
Circumflex	t=2.212	p=0.032*

Min: minimum; max: maximum; U: Mann-Whitney test; t: Student's t-test

Table 2 shows an association between both the right and left carotid arteries with each coronary artery (anterior descending, posterior descending and circumflex arteries) regarding the percentage measurement of collagen fibers, which showed a significant difference between the right and left carotid arteries and the circumflex artery ($p<0.05$).

DISCUSSION

Non-communicable chronic diseases have become a worldwide concern. Atherosclerotic disease, as well as other cardiovascular diseases, is associated with high morbidity and mortality rates, especially among the elderly. Nonetheless, the increased incidence of these diseases in young people is noteworthy, since arterial endothelial changes can begin even in the neonatal period [24,25]. This change in the profile of patients represents a major impact on public and private health. Understanding of the pathophysiology, progression, risk factors, and clinical features associated with the disease is paramount to a better preventive approach [26].

Several studies addressing factors associated with systemic atherogenesis are published every year. The correlation between coronary artery lesions and carotid artery lesions is well known. Autopsy studies have shown coexistence of lesions in both arterial beds. A morphometric study of autopsied patients demonstrated that patients with chronic kidney disease are at increased risk of carotid, coronary, cerebral and iliac atherosclerosis [27]. This can be confirmed by another in vivo study in which more than 50% of patients with chronic kidney disease had coronary stenosis [28,29]. In another autopsy study, 75% of patients had severe atherosclerotic lesions in the coronary, carotid and iliac arteries [30].

In our study, analysis of elastic fibers showed that there was no significant difference between all the arterial beds, which demonstrates a similar neoformation of elastic fibers, with coronary and carotid involvement. Elastic fibers form approximately half of the extracellular matrix; they are the most prevalent protein in the arterial wall. Secreted by smooth muscle cells, elastic fibers play a key role in reducing arterial wall tension in hemodynamic changes, before collagen fibers are involved [31]. This can be seen in our study, as the percentage of elastic fibers was higher than that of collagen fibers. Quantitative and/or qualitative changes in the production of elastic fibers result in the breakdown of arterial wall homeostasis, thus reducing the defense against existing cholesterol esters and increasing atherosclerotic plaque formation [32].

It could be noticed that there was no significant difference in collagen fibers between RC and LC arteries and AD and PD coronary arteries; the percentage of collagen fibers was similar in these arterial beds. These findings corroborate the literature, which regards atherogenesis as a chronic systemic disorder in which inflammation and plaque formation may occur simultaneously in several arterial beds of the human body. In the present study, there was a significant difference only between the RC and LC arteries and the Cx artery, and collagen fibers increased more in the carotid arteries. This can be explained by the decrease in the diameter of the Cx artery in comparison with the other coronary arteries, with reduced turbulence in blood flow, when there is decreased lesion formation in the arterial intima [26].

In a study of chest pain patients, diagnosed with acute coronary syndrome, the ADCA was compromised in 44%-56% of the cases, followed by right coronary artery involvement (27%-39%) and Cx artery involvement (17%). That demonstrates the major clinical importance of ADCA in coronary artery disease [33].

The increased production of collagen fibers may trigger arterial stenosis, whereas a deficient production may qualitatively and/or quantitatively cause risk of plaque rupture [32]. As this imbalance is deleterious to patients in both cases, complications such as acute myocardial infarction and stroke may be eventually triggered [20]. In a study of patients undergoing bypass/coronary grafting surgery due to ischemic heart disease, a significant accumulation of lipids was observed in the collagen fiber layer, which led the authors to associate the presence of an unstable atherosclerotic plaque with the increase and destructuring of collagen fibers in the arterial wall [34].

In a study of postoperative patients undergoing carotid endarterectomy due to chronic atherosclerosis, it was observed that 30% of the patients had concomitant coronary disease, with a mortality rate of 0.3% in 30 days and acute coronary syndrome as cause of death [35]. In another study, the authors suggest an association of carotid and coronary disease in up to 72% of the patients [36]. The medical team providing assistance to clinical and surgical patients must know about the coexistence of these diseases so as to seek alternatives and provide follow-up care and preoperative preparation to reduce associated morbidities.

CONCLUSION

Our study demonstrated that the histological analysis of different arterial beds of autopsied patients has a similar percentage of elastic and collagen fibers in the carotid and coronary arteries. It suggests that both beds are susceptible to the initial phase of atherogenesis, which, associated with risk factors, may lead to complications of advanced plaque formation over time with aging. It is known that, through screening studies and therapeutic interventions, it is possible to change the course of the disease, reaching stagnation of lesion progression as well as plaque stabilization, which shows that the identification of the risk factors associated with atherogenesis is crucial to reducing cardiovascular complications in these patients.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

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