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Cadaveric study of the autonomic nervous system and thoracic aortic atherosclerosis

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Abstract
Objective: The ANS is linked to atherosclerosis-induced cardiovascular events such myocardial infarction and aortic disease. Autonomic dysfunction and atherosclerosis are linked, but the mechanisms are unknown. This study examines the effect of ANS on atherosclerosis in human thoracic aorta.
Methods: The descending, aortic arch, and ascending aortas of 42 unselected adult cadavers were autopsied. Groups of ages were used. Seven grades were used by histopathology to grade tissue samples for atherosclerosis. An association between the ANS and atherosclerosis was discovered through immuno-histochemical analysis of neuron terminals on the aortic wall. Based on demographic and clinical characteristics, all data were analysed.
Results: In one or more segments, 96.2% of all participants had atherosclerosis. No aneurismal alteration. Atheromas are common independent of age or segment, and atherosclerosis increases with age; ascending aorta. A history of hypertension was statistically significant for atherosclerosis and neuron terminals in all three aortic wall segments: ascending, arch, and descending. ATHERO score was negatively correlated with neuron terminals in all three aortic segments: ascending, arch, and descending.
Conclusion: Along with clinical and animal investigations, human cadaveric studies help understand ANS pathophysiology. These data imply a relationship between autonomic dysfunction and thoracic aortic atherosclerosis, especially with hypertension. Stress-induced hypertension may be an atherosclerotic risk factor.

Keywords: Cardiovascular disease, high blood pressure, stress, the sympathetic nervous system

Introduction

The Autonomic Nervous System (ANS) is the primary system that is in charge of preserving homeostasis and controlling how the body reacts to short-term, high-stress situations. It is made up of two different parts, which are known as the Sympathetic Nervous System (SNS) and the Parasympathetic Nervous System (PNS) [1, 2]. These are two different pathways that have responses that are frequently antagonistic to one another, but they can also work together or independently to keep the functions of autonomic organs in check. Both the sympathetic nervous system and the parasympathetic nervous system provide the innervation for the cardiovascular system, which consists of the heart and the blood vessels [3-5].

In 2012, cardiovascular disease (also known as CVD) was the leading cause of death worldwide, accounting for 32 percent of the total number of deaths worldwide. Even though there are advancements in treatment procedures each year, the disease's incidence is continuously growing. The term "cardiovascular disease" refers to a group of conditions that affect both the heart and the blood arteries [6, 7]. Atherosclerotic lesions in the vasculature are the root cause of a number of cardiovascular diseases, including coronary artery disease (CAD), stroke, and peripheral artery disease (PAD). The complicated disease known as atherosclerosis is characterised by persistent inflammation of the artery wall. It most commonly affects big elastic arteries and medium-sized muscular arteries (that is, coronary arteries), and it gradually leads to deterioration of the vessel wall. Tobacco use, high blood pressure, and high cholesterol levels are the three primary contributors to the development of atherosclerosis [8-10].

These substances come from the luminal side of the arteries and affect the endothelium. Endothelial dysfunction is the pathologic process that occurs through autonomic nerve pathways in patients with hypertension.

However, the mechanisms by which this association operates are not yet completely understood. In addition, behavioural characteristics have been shown to play a role in both human and nonhuman primate research [11-13]. This has been shown to be the case. One of these elements that influences the behaviour of endothelium function from an extraluminal point of view is thought to be the Autonomic Nervous System, or ANS. In the past ten years, a great number of clinical research have pointed to a connection between altered autonomic function and cardiovascular disease (CVD) [14]. The presence of autonomic dysfunction is independently linked to an increased risk of cardiovascular events than is the case when other traditional risk factors are present. There are research that point to decreased parasympathetic activity as the primary contributor, despite the fact that the majority of these studies investigate the connection between increased activity of the sympathetic nervous system and an elevated risk of cardiovascular disease [15-17]. In addition, research indicates that psychological stress may be able to predict the occurrence of cardiovascular mortality and stroke in the future [18]. In a nutshell, the scientific community has not been able to come to a conclusion on the connection between atherosclerosis and the sympathetic nervous system. Even though there is evidence that shows an increased risk for cardiovascular mortality in the presence of sympathetic drive and that there may be a protective role for increased parasympathetic activity, the mechanisms that are responsible for mediating this relationship are still not completely understood. Through the examination of 42 human thoracic aortas that were collected through necropsy, the goal of this study is to evaluate the interaction that occurs between the ANS and the progression of atherosclerosis. If there were evidence of a potential role of both parametric and nonparametric risk factors for a nerve-driven on both inflammation and atherosclerosis, it would highlight the necessity for further exploration of this enigmatic link.

Materials and Methods

The research was conducted at the Department of Forensic Medicine, Kamineni Institute of Medical Sciences, Narketpally, Telangana, India. Thoracic aortas that were obtained during routine autopsies of 42 deceased individuals ranging in age from 18 to 90 years. The participants' ages ranged from 18 to 90. The information contained on death certificates was used to determine the cause of death. Death certificates and medical records, if they were accessible, were searched for information about past diseases and factors that increased the risk of cardiovascular disease. There was no history of aortic aneurism or stroke in any of the people who participated in the study. Both an intention to do an autopsy and a minimum age of 18 years were requirements for participation. The consent of the deceased person's family members was obtained in the form of a letter that was signed and dated. In the areas in which a consensus could not be achieved, a third independent assessment from a Professor of the university. The research was carried out in compliance with the Declaration of Helsinki, which is a policy of the World Medical Association.

Specimen preparation

An examination of the thoracic aorta was carried out, beginning at the beginning of the ventricle and continuing all the way up to the diaphragm. After their exhumation and removal from the body, the aortas were opened longitudinally, photographed, and the interiors were macroscopically evaluated for fatty streaks, elevated lesions, plaque, and thrombus (Figure 1). Tissues from the aorta were carefully removed perpendicular to the long axis at three anatomic stations: 2.5 centimeters above the aortic valve, 1 centimeter before the branching of the brachiocephalic trunk, and 2 centimeters below the subclavian artery. All of these incisions were made parallel to the long axis. The selection of these stations was made because of rapid shifts in the direction of vessel diameter. These are areas in which the blood is likely to be disrupted by the formation of secondary and recirculation, and endothelial cells are subjected to relatively modest shear stress. According to the research that has been done, these areas are therefore regarded to be favourable locations for the development of atherosclerotic lesions.

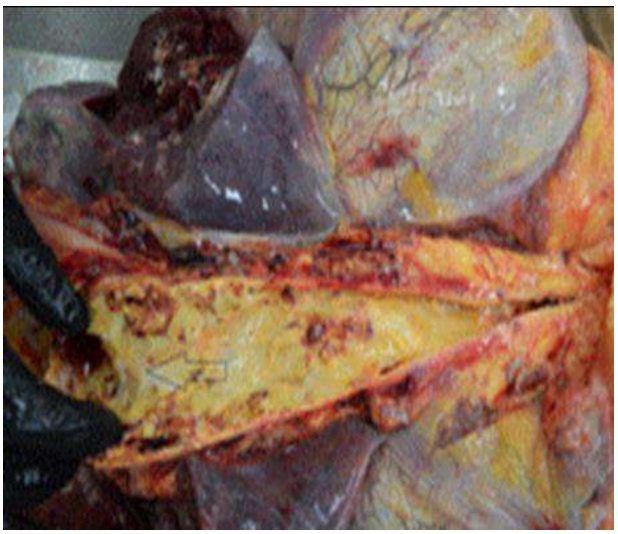

Fig 1: Anatomic sample 1 cm before brachiocephalic trunk branching.

Statistical analysis

The statistical programme SPSS for Mac OS was used to perform the analysis on the data. The results of the studies performed on the continuous variables are shown as the mean accompanied by the standard deviation. The analysis of variance (ANOVA) was used to examine the data between each segment as well as the data between the number of segments with atherosclerotic change and age. If the p values were lower than.05, the differences were considered to be statistically significant. The Pearson correlation coefficient was calculated, and multiple regression analyses were carried out in order to establish the nature of the connection that exists between the ATHERO score and the presence of neuron terminals.

Results

With the exception of hypertension, there were no discernible differences in the clinical features between the age groups. Smoking, coronary artery disease, diabetes, and hypertension were the clinical features that showed no statistical significance between the two age groups. There were 21 participants in each group, with men being the predominant gender in both groups. The demographic information and the causes of death are listed in Table 1.

Table 1: Information on demographics and the causes of death

Cause of death	N (%) N=42	Age in years (mean)	M/F
MI	15	63.1	14/2
Accident	14	56.1	12/4
Cancer	09	64.2	7/5
COPD	04	66	3/2

On the other hand, in the current study, eight participants aged 65 years had a history of hypertension that was positive, and there was a substantial positive link. In addition, both the prevalence and severity of aortic atheromas were found to be highly influenced by age, with a strong positive association existing between all three segments of the aorta and the two age groups. Figure 1 demonstrates that the existence of atheromas was prevalent in all of the participants, independent of age or segment, and that the severity of atherosclerosis increased with the subjects' advancing years. Table 2 displays the clinical characteristics of the cases that were investigated by autopsy.

Table 2: The clinical characteristics of the instances that were autopsied

		N=42	N %
Gender	Male	30	71.42%
	Female	12	28.57%
Smoking	Yes	25	59.52%
	No	17	40.47%
Hypertension	Yes	30	71.42%
	No	12	28.57%
CAD	Yes	24	57.14%
	No	18	42.85%
Diabetes	Yes	10	23.80%
	No	32	76.19%
Hypercholesterolemia	Yes	10	23.80%
	No	32	76.19%

Discussion

Atherosclerosis is an inflammatory process that occurs in arteries that are big and medium in size. It is characterised by a progressive thickening of the intima of the vessel wall, which ultimately results in the vessel wall becoming more rigid. Atherosclerosis is the most frequent pathologic condition in human beings that leads to cardiovascular disease (CVD). Atherosclerotic changes of an arterial wall in humans do not occur randomly, and they do not occur everywhere in the arterial tree. Rather, they occur preferentially at certain sites, such as the inner wall of curved segments and the outer wall of bifurcations of relatively large arteries. This has been demonstrated by a great number of studies (i.e., thoracic aorta). Aorta disorders are therefore varied, and they are related with many biological systems within the aortic wall, as well as the contact those biological systems have with blood [19, 20].

The incidence of aortic disorders varies at different points along the aorta, such as the abdominal aorta, the ascending aorta, the aortic arch, and the descending aorta. According to the findings of a study conducted by Anderson *et al*., the risk of developing an atherosclerotic aneurysm in the abdominal aorta is at least three times higher than the risk of developing one in the descending aortic arch. In contrast, 65% of aortic dissections happen in the ascending aorta, 20% in the descending aorta, 10% in the aortic arch, and just 5% in the abdominal aorta. These percentages are based on the location of the affected part of the aorta. Differences in the biological architecture of the aorta, in particular the perfusion system of the aortic wall, are thought to be the root cause of this phenomenon. Although the preferred sites of examination, as described in the Methods section, were prone to the accumulation of aneurismal changes or dissection, the current study did not find any evidence of aneurysms in the thoracic aorta [21].

This was the case despite the fact that the aneurysms were expected to be found there. Despite this, it was discovered that atherosclerosis is prevalent in all of the participants, regardless of their ages. It is well established that the development of occurs throughout the course of a person's entire life and begins at a very young age. Both the prevalence and severity of aortic were greatly influenced by age in the study that was conducted by Allison *et al*. [22, 23].

The prevalence of calcification was 16% in people under the age of 50 years old, and it increased to 93% in people over the age of 70 years old. It has also been reported that the development of atherosclerosis grows significantly with age up to an age of around 65, regardless of the sex and ethnic background of the individuals who participated in the investigations. In addition to this, 61.5% of all participants had an ATHERO Score of 4-6 in the ascending aorta, 78.9% of all subjects had an ATHERO Score of 4-6 in the aortic arch, and 86.5% of all subjects had an ATHERO Score of 4-6 in the descending aorta [23, 24].

Atherosclerotic disease of the aortic arch is an independent risk factor for recurrent vascular events, according to findings from pathology, transesophageal echocardiography (TEE), and, more recently, scanning and magnetic resonance imaging studies. These studies were conducted more recently. Atherosclerosis of the horacic aorta is another significant indication for widespread atherosclerosis (coronary, carotid, and peripheral arterial disease, including aneurysms). Hypertension, smoking, and high cholesterol are three of the risk factors for cardiovascular disease that have been linked to significant plaques in the thoracic aorta. Because of the development of methodological approaches that allow direct assessment of systemic and regional sympathetic cardiovascular drive in humans, the role of the Sympathetic Nervous System (SNS) in the pathogenesis of Hypertension (HT) has undergone a remarkable transformation over the past fifty years. HT is a condition that is characterised by elevated blood pressure. A close connection between the endothelium and the ANS is implied by the connections that have been found between endothelial dysfunction and ANS imbalance. When someone has hypertension, their autonomic cardiovascular control is disturbed, which results in a decrease in the parasympathetic tone and an increase in the sympathetic impulses to the heart and peripheral veins. The most important aspects of neural blood pressure regulation are the output of the heart and the resistance of the systemic vasculature [22, 24].

According to Gamboa *et al*., the interaction that exists between the autonomic nervous system (ANS) and vascular function may contribute to the pathogenic process that occurs in the setting of pathologic disorders such as hypertension. Studies conducted on patients with hypertension and high sympathetic tone have shown that the increased risk of coronary artery disease cannot be fully attributed to the elevation in blood pressure alone. These studies also suggest that there may be additional links

between ANS modulation and CVD, one of which is inflammation. It is thought that inflammation may offer a mechanistic link between some of the classic risk factors, such as hypertension, and the advancement of atherosclerosis. The idea of inflammation is important to atherosclerosis, and it is thought that this may be the case. Previous research has found an association between autonomic dysfunction and both atherosclerosis and cardiovascular disease (CVD). Surprisingly, only a small number of studies have investigated whether or not autonomic dysfunction is directly associated with cardiovascular disease (CVD) or whether or not hypertension could act as a mediator in this association. Furthermore, to the best of our knowledge, these studies have never used thoracic aortic atherosclerosis as the primary endpoint. According to the findings of the current research, hypertension is a significant risk factor that is clearly linked to the development of atherosclerotic lesions as well as ANS in all three sections of the thoracic aorta. The possibility exists that this finding is attributable to hypertension brought on by stress. Mental stress is a potent stimulant for activity in the central sympathetic nervous system. According to the findings of Ghiadoni and colleagues, acute mental stress can generate transitory endothelial dysfunction, which can last for up to four hours and is accompanied by increases in blood pressure, heart rate, and salivary cortisol [25-27].

Conclusions

In conclusion, our findings lend credence to the hypothesis that there is a major two-way association between autonomic dysfunction and the existence of atherosclerosis in the human thoracic aorta in people of all ages, particularly in situations in which hypertension is present. Therefore, it is plausible that hypertension brought on by stress can be considered to be a potential risk factor in the development of atherosclerosis. Therefore, research on a large scale are required to confirm the relationship between the ANS and the development of atherosclerosis in people, as this connection has not yet been conclusively shown.

Conflict of Interest: None
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