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Atherosclerosis Prevalence within Populations of the Southeastern United States

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Abstract**—**A prevalence cohort study of atherosclerotic lesions within cadavers was performed to better understand and characterize the prevalence of atherosclerosis among Georgia residents within body donors in the Philadelphia College of Osteopathic Medicine (PCOM) - Georgia body donor program. We procured specimens from cadavers used for medical student, physical therapy student, and biomedical science student cadaveric anatomical dissection at PCOM - South Georgia and PCOM - Georgia. Tissues were prepared using hematoxylin and eosin (H&E) stain as histological slides by Colquitt Regional Medical Center Laboratory Services. One section from each of the following arteries was taken after cadaveric dissection at the site of most calcification palpated grossly (if present): left anterior descending coronary artery, left internal carotid artery, abdominal aorta, splenic artery, and hepatic artery. All specimens were graded and categorized according to the American Heart Association's Modified and Conventional Standards for Atherosclerotic Lesions using x4, x10, x40 microscopic magnification. Our study cohort included 22 cadavers, with 16 females and 6 males. The average age was 72.54 and median age was 72, with a range of 52 to 90 years old. The cause of death determination listing vascular and/or cardiovascular causes were present on 6 of the 22 death certificates. 19 of 22 (86%) cadavers had at least a single artery grading > 5. Of the cadavers with at least a single artery graded at greater than 5, only 5 of 19 (26%) cadavers had a vascular or cardiovascular cause of death reported. Malignancy was listed as a cause of death on 7 (32%) of death certificates. The average atherosclerosis grading of the common hepatic, splenic and left internal carotid arteries (2.15, 3.05, and 3.36 respectively) were lower than the left anterior descending artery and the abdominal aorta (5.16 and 5.86 respectively). This prevalence study characterizes atherosclerosis found in five medium and large systemic arteries within cadavers from the state of Georgia.

Keywords**—**Atherosclerosis, cardiovascular, histology, pathology.

I. Introduction

ATHEROSCLEROSIS is the leading cause of morbidity and mortality worldwide. In this study, we aimed to study the prevalence of atherosclerosis in Georgia. The PCOM - Georgia body donor program provides students unique access to a specific population that consists specifically of Georgia residents. This allowed a prevalence cohort study to be conducted to help characterize the atherosclerotic lesions of the cadavers as a representative subset of the population. The study denotes atherosclerotic lesions identified in five medium or large systemic arteries within cadavers from the state of Georgia.

II. Materials and Methods

Specimens were taken from cadavers used for medical student, physical therapy student, and biomedical science student anatomical dissection labs at the two separate campus locations in Moultrie and Suwannee. After cadaveric dissection, one sample from each of the following arteries: left anterior descending coronary artery, left internal carotid artery, abdominal aorta, splenic artery, and hepatic artery. If present, samples were taken from palpable or grossly visible areas of calcification [1]. The local hospital pathology lab prepared all the histological samples using a H&E stain. Using the American Heart Association's Modified and Conventional Standards for Atherosclerotic Lesions and varying microscopic magnification, every specimen was evaluated and subsequently graded and categorized accordingly [2]. Review of specimens was performed by second-year medical students, with each slide being viewed by at least two students when documenting results. Data fields documented noted the presence of the following histopathological features: foam cells, calcification, plaque, tunica intima thickening, thrombus, smooth muscle infiltration, hemorrhage, cholesterol clefts, tunica media thickening, and lipid core. An AHA classification was then made based on these documented findings. Microscopic slides were then reviewed by a pathologist to confirm documented histopathological grading. Basic statistical analyses were performed on documented findings.

III. Results

The study cohort included 22 cadavers, with 16 females and 6 males. The average age was 72.54 (72.5 for males and 72.66 for females). The cadavers ranged in age from 52 to 90 years of age with 72 years old median age. Vascular/Cardiovascular causes of death were only listed for 6/22 (< 30%) specimens for the entire cohort. Although a majority of the causes of death was not primarily vascular/cardiovascular, 19/22 (> 85%) of the specimens had at least one or more artery grading of greater than 5. Overall multisystem etiologies were listed as a cause of death on 7 of 22 (32%) of death certificates (Table I).

Of the primary sites identified and graded, the two sites with the highest consistent grading were the left anterior descending at 5.16 and the abdominal aorta at 5.86. The other sample sites such as the common hepatic, splenic, and left internal carotid were graded at 2.15, 3.05, and 3.36 respectively (Table II).

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Conventional AHA Classification	Modified AHA classification for imaging techniques
Type I: initial lesion with foam cells Type II: fatty streak with multiple foam cell layers	Type I/II: near-normal wall thickness, no calcification
Type III: preatheroma with extracellular lipid pools	Type III: diffuse intimal thickening or small eccentric plaque, no calcification
Type IV: atheroma with confluent extracellular lipid core Type V: fibroatheroma	Type IV/V: plaque with lipid or necrotic core surrounded by fibrous tissue with possible calcification
Type VI: complex plaque with possible surface defect, haemorrhage or thrombus	Type VI: complex plaque with possible surface defect, haemorrhage or thrombus
Type VII: calcified plaque	Type VII: calcified plaque
Type VIII: fibrotic plaque without lipid core	Type VIII: fibrotic plaque without lipid core and with possible small calcification

Fig. 1 AHA classification for atherosclerosis grading [2]

TABLE I
STUDY CAUSE OF DEATH BY SYSTEM

Multisystem	7
Respiratory	5
Cardiovascular	4
Neurologic	3
Hematologic	1
Renal	1
Metastasis	1

TABLE II
GRADING OF ATHEROSCLEROSIS BY VASCULAR SITE

	N	Avg Grade	Grade Range	Ca %	Plaque %	Cholesterol %
L Carotid A	22	3.36	0-7	32%	32%	18%
L Coronary A	22	5.16	1-7	55%	77%	59%
Splenic A	22	3.05	0-7	23%	27%	14%
Common Hepatic A	20	2.15	1-7	10%	5%	5%
Abdominal Aorta	22	5.86	1-7	77%	68%	68%

Atherosclerosis grading compared between sexes provided striking data as females had a higher grading of atherosclerosis within a subset of the arteries sampled (Tables III, IV).

TABLE III
GRADING OF FEMALE ATHEROSCLEROSIS BY VASCULAR SITE

	N	Avg Grade	Grade Range	Ca %	Plaque %	Cholesterol %
L Carotid A	16	2.88	0-7	13%	25%	19%
L Coronary A	16	4.84	1-7	50%	75%	63%
Splenic A	16	3.44	1-7	31%	25%	13%
Common Hepatic A	14	2.21	1-7	14%	7%	7%
Abdominal Aorta	16	5.50	1-7	75%	75%	63%

TABLE IV
GRADING OF MALE ATHEROSCLEROSIS BY VASCULAR SITE

	N	Avg Grade	Grade Range	Ca %	Plaque %	Cholesterol %
L Carotid A	6	4.67	1-7	67%	50%	17%
L Coronary A	6	6.00	5-7	67%	83%	50%
Splenic A	6	2.00	0-5	0%	33%	17%
Common Hepatic A	6	2.00	1-2	0%	0%	0%
Abdominal Aorta	6	6.83	6-7	83%	50%	83%

In the left internal carotid artery, abdominal aorta, and left anterior descending artery, the male specimens had higher average grading of atherosclerosis, which is not surprising. However, in the splenic artery and the common hepatic artery, the female specimens had higher average grading compared to the male specimens (Tables III, IV).

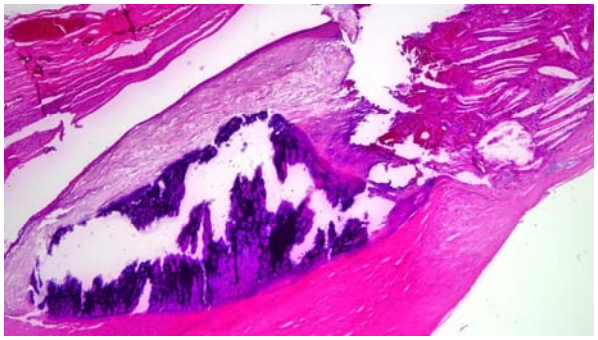

Fig. 2 Abdominal aorta with calcification and cholesterol clefts

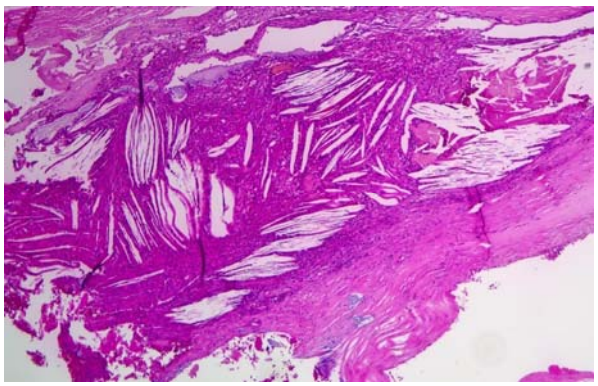

Fig. 3 Abdominal aorta with cholesterol clefts on H&E stain

IV. DISCUSSION

The study of atherosclerosis has become increasingly important within the context of chronic diseases within the United States. The advances in western medicine and public health over the past century led to an increase in life expectancy which is naturally tied with an increase in the burden of chronic diseases within the United States [3]. The global burden of atherosclerosis has increased even while the age-adjusted mortality rate has decreased in recent years [4]. Atherosclerosis remains a healthcare and public health salient issue with a variety of outcomes surrounding it that need better understanding.

The pathogenesis of atherosclerosis has been studied in great detail to understand the potential avoidable causes of this chronic disease. The current theory is that atherosclerosis is a chronic inflammatory response to endothelial injury [5]. Robbins' describes the sequence of events that leads to atherosclerosis: endothelial injury and dysfunction, accumulation of lipoproteins, platelet adhesion, monocyte migration, foam cell differentiation, smooth muscle cell

recruitment, and smooth muscle cell and extracellular matrix production [5]. The morphological changes seen in the vascular wall vary over time. Fatty streaks, which are minimally raised lesions within the vascular wall do not cause disruption of blood flow, an early sign of atherosclerosis seen grossly [5]. Microscopically, these streaks contain foam cells, which are macrophages that contain lipids. Clinically relevant atherosclerotic plaques then arise from these fatty streaks, which can lead to disturbances in blood flow. Atherosclerotic plaques can become organized with a layer of fibrous tissue that results in partial occlusion of the vessel and can rupture which can lead to thrombosis [6]. These varying morphological forms of atherosclerosis lead to a variety of clinical manifestations. Risk factors of atherosclerosis can impact the severity and amplitude of the disease.

Risk factors associated with atherosclerosis are classified as modifiable or non-modifiable. Modifiable risk factors are hyperlipidemia, hypertension, cigarette smoking, diabetes, and inflammation [5]. Non-modifiable risk factors are genetic abnormalities, family history, increasing age, and male gender [5]. A 2003 study describes some risk factors as having increased impact on certain vascular sites, while others only predict severity of atherosclerosis [7]. This study is unable to comment on a number of these risk factors due to the fact that study specimens were taken from cadavers with blinded medical records except for the cause of death. However, as the anatomical sex is known, a comparison of the grading of atherosclerosis by site between the two sex was able to be completed. In this study, it was found that males on average had higher grading of atherosclerosis than females in the left internal carotid artery, the left anterior descending artery, and the abdominal aorta (Tables III, IV). However, the females on average had higher grading of atherosclerosis than males in the splenic artery and the common hepatic artery (Tables III, IV).

Throughout the study, the modified classification system developed by the Committee on Grading Lesions of the Council on Arteriosclerosis with the American Heart Association was utilized to grade the vascular lesions based on specific guidelines and tissue samples' observed characteristics (Fig. 1). Within this grading system, type I/II lesions are stated to have little to no thickening of the arterial walls with the absence of calcification [8]. Type III lesions maintain the absence of calcification but present with diffuse intimal thickening or even a small eccentric plaque and type IV/V lesions display a clear plaque with either a lipid or necrotic core surrounded by fibrous tissue and possibly calcification [8]. Type VI lesions show a complex plaque with potentially surface defects, hemorrhage, or thrombus present, while type VII lesions are very specific for calcification predominately throughout the plaque [8]. Type VIII lesions must have a fibrotic plaque without a lipid core and with possible small calcification but predominantly fibrous tissue changes [8]. There were lesions present of the various grades throughout our entire sample population including those with no noticeable morphological changes in which they were graded 0 (Figs. 2-5).

Evaluation of disease presence in different vascular beds can inform healthcare professionals of site-specific risk factors with targeted lifestyle and pharmaceutical interventions. VanderLaan et al. describe atherosclerotic disease burden in right coronary arteries with minimal disease evidence in the abdominal aorta in young patients with elevated HbA_1c levels, while patients who smoked had lesions in the abdominal aorta and no effect on the right coronary artery [9]. As was seen in this project, the severity of disease seen in one vascular site may not correlate with the same severity of disease in another vascular site within the same individual. Females within the study had a greater prevalence and severity of atherosclerosis in the splenic artery and common hepatic artery compared to males. This dichotomy of atherosclerosis warrants further study as a 2020 study indicated the dichotomy between male and female is well documented, but more data are needed [10].

As is seen in all research projects, this research has a few limitations that should be known. Lack of a history of associated risk factors was a major limitation of our study. Also, tissue collection for this project took place months after original dissection, which resulted in less ideal collection conditions. In a few cases, folding of the tissue specimen during processing resulted in unclear microscopic slides for review (Fig. 4).

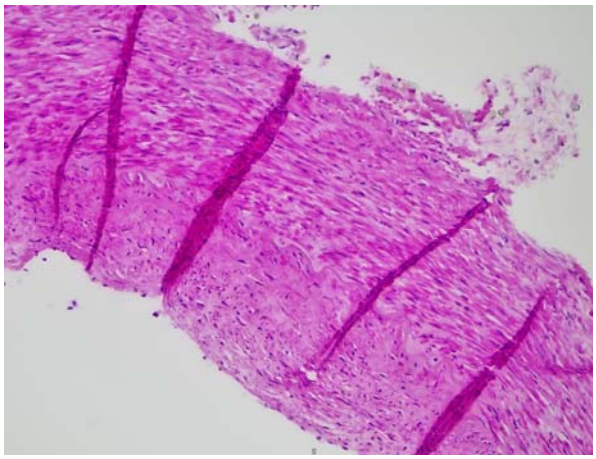

Fig. 4 Example of section limitation with folding of tissue while processing on H&E stain

The preparation of a few slides resulted in us not being able to determine if there was a fibrotic core present as the specimen on the slide was not held together (Fig. 5). A few histological slides had staining artifacts related to how the slide was prepared. Lastly, we were unable to obtain common hepatic artery specimens in two cadavers due to lack of usable artery after the completion of dissection for academic purposes. Thus, instead of having 22 specimens for the common hepatic artery, the study only contained 20 (Table II).

Originally, this project was designed to include cerebrovascular sites in addition to the five sites that were included in the study. By including cerebral vascular sites in a future study, the ability to understand potential correlations between severity in certain systemic sites that may present with earlier clinical manifestations and locations within the brain may enable clinicians to better understand the full breadth of atherosclerosis within their patients. Additionally, this project will aim to continue to collect specimens at the PCOM-South

Georgia and PCOM-Georgia sites as a means of validating the results within this paper and ensuring a good sample size with more generalizable results to the residents and populations of the southeastern United States.

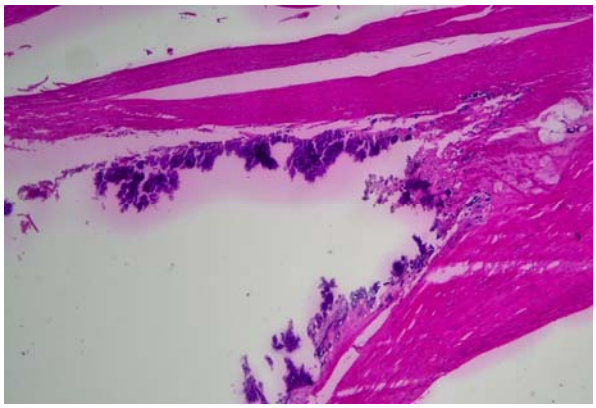

Fig. 5 Example of specimen processing resulted lack of fibrotic core determination

V. Conclusion

Atherosclerosis is a chronic disease that will continue to have lasting impacts on the health of Americans. More studies reviewing the prevalence of atherosclerosis in systemic vasculature will enable clinicians to better understand potential correlations of atherosclerosis within their patient populations. Differences seen between each sex within each of the five sites sampled in this study provide a basis for these future studies to better understand atherosclerotic differences between males and females.

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