Clinical and Experimental Health Sciences

Correlation Between the Level of Atherosclerosis and Pathological Features of Coronary Artery Disease: A Study of 100 Autopsy Cases

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Received: 31.05.2022 **Accepted:** 25.12.2022

ABSTRACT

Objective: Atherosclerosis is a generalized, chronic disease of large and medium-sized muscular elastic arteries. Relation between intensity of atherosclerosis and coronary artery disease, and risk factors of atherosclerosis could not been revealed completely by autopsy studies. We aimed to renew this shortage of knowledge with our autopsy study prospectively.

Methods: One hundred cases were autopsied within 48 h after death. Atherosclerotic risk factor data were collected including age, gender, height, weight, smoking and any chronic coronary artery disease. Atherosclerosis severity was evaluated macroscopically by examining the inner surfaces of the vascular lumens and revealed with postmortem pathological findings of coronary artery disease.

Results: The mean age was 42 ± 22 years. Seventy-four percent of cases were male, while 26% were female. Smoking duration ranged from 1 to 50 years with a mean duration of 17 ± 12 years. Existence of atherosclerosis in main vessels were also in correlation with age, duration of smoking and BMI (Body Mass Index) ($p<.05$.) significantly. Existence of coronary artery disease at autopsy were in correlation with existence of atherosclerosis in thoracic aorta, abdominal aorta and subclavian artery significantly ($p<.05$.), but not in correlation with those in carotid artery ($p>.05$.).

Conclusion: Atherosclerosis in main arteries except those in carotid artery was a good indicator of coronary artery disease.

Keywords: Atherosclerosis, Coronary Artery Disease, Forensic Pathology, Autopsy.

1. INTRODUCTION

Atherosclerosis is a generalized, chronic disease of large and medium-sized muscular elastic arteries. Plaque growth results in a reduction in lumen size and encroachment on the media. Thus, myocardial infarction, stroke, peripheral vascular disease and aneurism in aorta occurs (1). Coronary artery disease known as atherosclerotic heart disease is the largest contributor of cardiovascular diseases and maintain as a predominant cause of death worldwide. Many atherosclerotic factors such as hyperlipidemia, smoking, BMI, ageing, family cardiac diseases had been shown to be risk factors for coronary artery disease. Every vascular system has different cellular reactions to atherosclerotic risk factors (2). The correlated findings of atherosclerosis of the vascular system with the coronary artery disease will be a guide for the evaluation of obscure cardiovascular deaths at autopsy. The aim of the current study was to explore correlation between coronary artery disease and atherosclerosis in main arteries.

2. METHODS

2.1. Cases

The institutional ethics committee approved by Ethics Committee of Forensic Council of Turkey, numbered 237/2009 ATK in 2009, and informed consent was obtained from the relatives of each case. The subjects were prospective random cases in the East Black Sea Region Morgue of the Council of Forensic Medicine in where autopsied within 48 h after death. Atherosclerotic risk factor data were collected including age, gender, height, weight (BMI= weight/height) during autopsy and cigarette usage and information related to any chronic family disease or any evidence of clinical atherosclerotic disease (coronary artery disease, myocardial infarction, ischemic cerebral infarct, and peripheral vascular disease) from relatives of cases before autopsy.

DOI: 10.33808/clinexphealthsci.1123538

2.2. Vascular Pathology

The large-artery specimens examined including the common carotid artery, subclavian artery and aorta subdivided into the thoracic and abdominal aorta. After en bloc extirpation of the cervical, mediastinal, abdominal, retroperitoneal, and pelvic organs at autopsy, the large arteries were cut open and fixed in 10% formalin solution. The severity of atherosclerosis was evaluated macroscopically by examining the inner vessel surfaces, which were evaluated on cut sections (right common carotid artery from the bifurcation of the brachiocephalic artery to the bifurcation of the external and internal carotid artery; right subclavian artery from the bifurcation of the brachiocephalic artery to the exit point from the right clavicle as the axial artery; thoracic aorta from the aortic arch beneath the first costal artery exit or at the level of the ligamentum arteriosum to the entry of the aortic hiatus in the diaphragm; abdominal aorta from the exit of the aortic hiatus in the diaphragm to the aortic bifurcation at the pelvis). Atherosclerosis severity was evaluated macroscopically by examining the inner surfaces of the vascular lumens and calculated with stereological method (3). The term “atheroma” was used in a broad sense and included fatty streaks, fibrous plaques, complicated lesions, and calcification. One pathologist with extensive experience in the visual grading procedures evaluated the raised lesions. The degree of atherosclerosis in the sections was graded as follows: 0, no evidence of atherosclerosis, i.e., normal and consistent thickness and diameter of the vessel without intimal or medial thickening; 1, minimal changes and/or fatty streaks causing slight increases in vessel thickness, usually without affecting the lumen; 2, fibrous or atheromatous plaques, thickening of the intima, between the endothelial cell layer and the internal elastic; 3, advanced atherosclerotic plaques with fibrous deposition or complicated plaques with necrosis, ulceration, thrombosis, or hemorrhage; and 4, calcified plaques causing vessel wall stiffness. To compare atherosclerosis in these four vessels with other variable data, grade 0 and 1 was used for the absence of atherosclerosis, while grades 2, 3, and 4 accounted for the presence of atherosclerosis. The sum of all vascular luminal areas also was manually measured macroscopically and ratio of atherosclerotic area to total vascular area was calculated for each vessel on two-dimensional images with stereological method (3). All data including atherosclerotic area in all vascular area represented in numeric data as percentile. During the macroscopic and microscopic examination at autopsy, obstruction in more than 70% of the coronary arteries was due mainly to coronary atherosclerosis and hemorrhage and/or scarring in cardiac tissue also supported with microscopic examination but was also identified as acute and/or chronic myocardial infarction.

2.3. Statistical Analysis

All data were evaluated using the SPSS 25.0 program (SPSS, Inc., Chicago, IL, USA). The group data comparison was conducted with the Mann-Whitney U and chi-square tests. Correlations among numerical data were identified with Spearman’s correlation test. A p level of <0.05 was accepted as statistically significant.

3. RESULTS

Four hundred vessel samples (thoracic aorta, abdominal aorta, right common carotid, and right subclavian artery from each of 100 cases) were evaluated. The mean age was 42 ± 22 years. Presence of atherosclerosis in each artery of the cases in relation to their age was shown in Table 1.Seventy-four percent of cases were male, while 26% were female. The smoking status of the cases was unknown (35%), nonsmoking (37%), and smoking (28%). Smoking duration ranged from 1 to 50 years with a mean duration of 17 ± 12 years. 31% of cases were found to have findings of coronary artery disease macroscopically and/or microscopically (Figure 1-4). Results of atherosclerosis in main vessels of cases with and without coronary artery disease and/or myocardial infarction wereshown in Table 2. Results of statistical correlation in between atherosclerosis in main vessels and age, gender, duration of smoking, BMI, anamnesis of family coronary artery disease were shown in Table 3.

Results of statistical correlation with and without coronary artery disease and/or myocardial infarction,with age, gender, duration of smoking, BMI, anamnesis of family coronary artery disease were shown in Table 4.

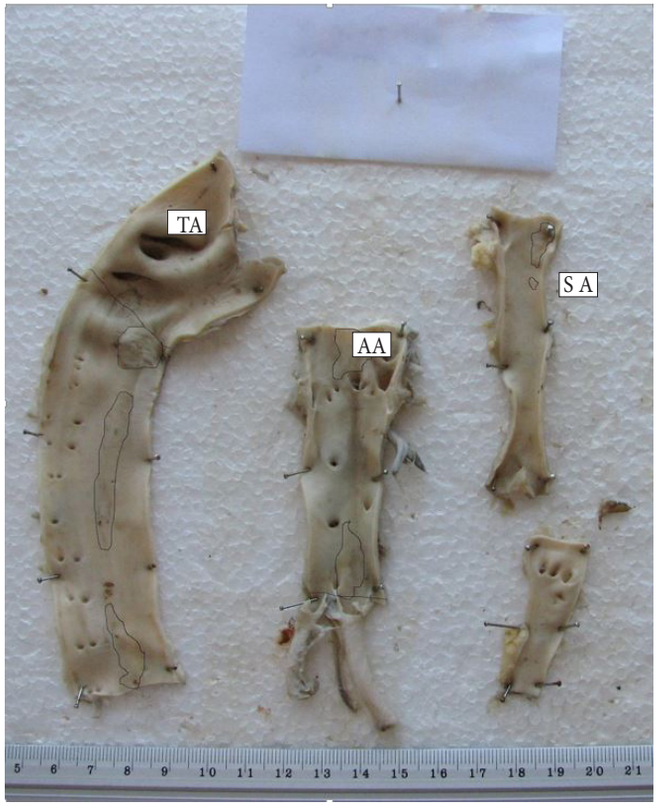

Figure 1*.Minimal changes and/or fatty streaks in arterial lumen TA: Thorasic Aorta, AA: Abdominal Aorta, SA: Subclavian Artery, CA: Carotid Artery*

Table 1. *Presence of atherosclerosis (Ath) in each artery of the cases in relation to their age.*

Artery (n) / Age (Years)	Thoracic Aorta	Abdominal Aorta	Subclavian Artery	Carotid Aorta
0-10				
Existence of Ath	0	0	0	0
Lack of Ath	8	8	8	8
11-20				
Existence of Ath	1	4	0	1
Lack of Ath	8	5	9	8
21-30				
Existence of Ath	3	8	1	3
Lack of Ath	9	4	11	9
31-40				
Existence of Ath	10	13	10	5
Lack of Ath	7	4	9	12
41-49				
Existence of Ath	9	10	7	5
Lack of Ath	5	4	7	9
51-60				
Existence of Ath	12	14	7	8
Lack of Ath	4	2	9	8
61-70				
Existence of Ath	10	10	6	6
Lack of Ath	1	1	5	5
71-80				
Existence of Ath	9	9	5	5
Lack of Ath	0	0	4	4
81-90				
Existence of Ath	2	3	2	2
Lack of Ath	1	0	1	1
> 90				
Existence of Ath	1	1	0	0
Lack of Ath	0	0	1	1
Totally	100	100	100	100

Table 2. *Presence of atherosclerosis in main arteries were compared to microscopic findings of cases with and without coronary artery disease and/or myocardial infarction.*

	Existence of coronary artery disease and/or myocardial infarction (n)	Lack of coronary artery disease and/or myocardial infarction (n)	p
Carotid artery	10	25	NS
Subclavian artery	18	20	0.02.
Toracic aorta	26	31	<.001.
Abdominal aorta	28	44	<.001.

NS: Nonspecific statistically; P<.05. is significant

Figure 2*.Fibrous or atheromatous plaques in arterial lumen, TA: Thorasic Aorta, AA: Abdominal Aorta, SA: Subclavian Artery, CA: Carotid Artery*

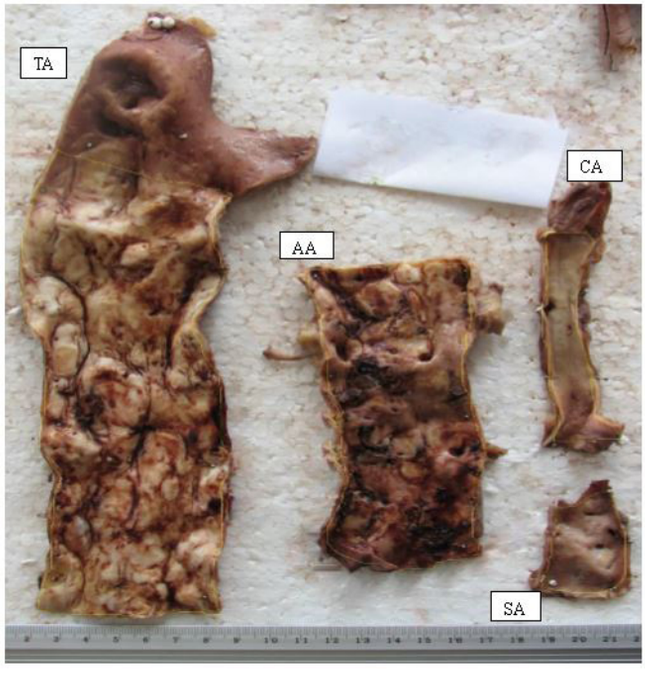

Figure 3. *Complicated plaques in arterial lumen TA: Thorasic Aorta, AA: Abdominal Aorta, SA: Subclavian Artery, CA: Carotid Artery*

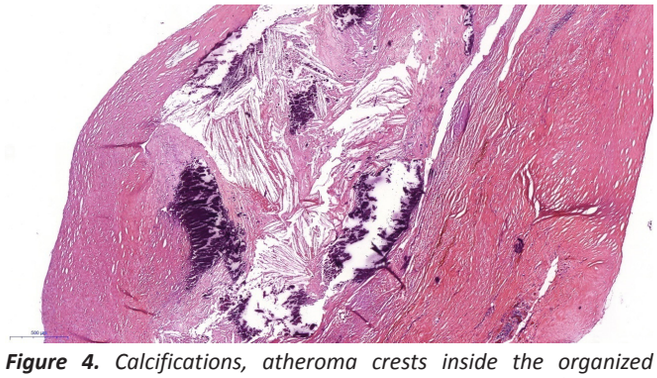

Figure 4. *Calcifications, atheroma crests inside the organized atheroma plaque has been shown in longitudinal section of coronary artery (3.5 X H&E).*

Table 3. *Correlation in between existence of atherosclerosis in main arteries and age, gender, duration of smoking, BMI, anamnesis of family coronary artery disease.*

	Existence of atherosclerosis in carotid artery	Existence of atherosclerosis in subclavian artery	Existence of atherosclerosis in thoracic aorta	Existence of atherosclerosis in abdominal aorta
Age	p<.001.	p<.001.	p<.001.	p<.001.
Gender (F/M)	NS	NS	NS	NS
Smoking (Year)	p=.006.	p=.015.	p=.009.	p=.036.
BMI	p<.001.	p=.023.	p=.001.	p<.001.
Family cardiac disease	NS	NS	NS	NS

NS=Non-significant; P<.05. is significant

Table 4. *Characteristics of cases with and without coronary artery disease and/or myocardial infarction. NS: Nonspecific statistically.*

	Existence of coronary artery disease and/or myocardial infarction	Lack of coronary artery disease and/or myocardial infarction	p
Age	61 ± 15	34 ± 20	<.001.
Gender (F/M)	7/24	19/50	NS
Smoking (year)	29 ± 12	12 ± 9	.002
BMI	27.16 ± 3.31	25.85 ± 5.42	NS
Family coronary artery disease	57%	24%	.023

NS=Non-significant. P<.05. is significant

4. DISCUSSION

Autopsy studies assess more valuable information about atherosclerotic lesions than that of clinical studies. Macroscopic and microscopic examination of a vessel on a postmortem specimen allows for exact lumen area measurements (4-6). In the current study, atherosclerosis in main vessels except carotid artery was found to be a significant marker of the coronary artery disease. Coronary atherosclerosis is generally less severe than aortic atherosclerosis but parallels the process in the aorta and explains the low incidence of coronary artery disease despite severe aortic atherosclerosis. Of all vessels, the aorta (both abdominal and thoracic) was the most affected by atherosclerotic plaques in relation with coronary artery disease (7-11). Complicated and calcified plaques were most clearly discovered on the intimal surfaces of the aorta at the sametime with fibrous plaques in other vessels (8). We also noticed that cases without raised atherosclerotic plaques in the aorta did not have coronary artery disease. Assessing plaques may be a more useful predictor of risk in cases without known coronary artery disease.

In our study, significant atherosclerotic disease in the carotid arteries did not predict significant coronary artery disease (12, 13). Some clinical and autopsy studies have shown that atherosclerotic disease of carotid artery was directly correlated with the degree of coronary artery disease which was unlikely in the current study (7, 14).

In our study, the subclavian atherosclerotic stenosis was positively associated with other markers of atherosclerosis and coronary artery disease (15,16) contrary to study which has stated that subclavian artery atherosclerosis was infrequent and especially combination of it with coronary artery disease was even rare (17). Engelhorn et al have stated that the right subclavian artery atherosclerosis could be considered to be as a risk factor for the assessment of cardiovascular risk by CCA-IMT(Common Carotid Intimal Medial Thickness) (18). Gongora – Riveraet et all. stated that coronary atherosclerosis and myocardial infarction were highly prevalent in patients died from a stroke due to atherosclerosis in the carotid and cerebral arteries (19). In literature, although the carotid artery bifurcation lesions are associated with the development of a positive coronary artery calcification after taking into account cardiovascular risk factors, body mass index and ethnicity, the absence of carotid artery plaque, does not exclude the possibilty that a coronary artery disease (20). In other study, the coexistence of carotid or intracranial atherosclerosis with coronary artery disease was confirmed in about 16% of patients (21). The exact correspondence between the carotid artery and the coronary artery is unclear, with some contradictory study results (11). More research is needed to identify the full extent of all risk factors for severe stenosis and cardio – or cerebral vascular events, among which, inflammatory biomarkers such as CRP, ESR, cytokines and also prior vascular events are likely to play a key role (22). Also, There is a concept that atherosclerosis affects both carotid and coronary systems, although not always in identical phenotypic manner (23, 24). We assume that autopsy studies find out more valuable and evident data about vessels compared to studies with imaging techniques (25).

A multivessel approach in patients with a single clinical manifestation of atherosclerosis is needed as atherosclerosis is a systemic disease and the clinical manifestation of it is associated with multiple factors like etnicity, diet, body mass index (21). Age, smoking and BMI were also found to be as

risk factors for atherosclerosis in vessels (26-28). Older age was a risk for both raised atherosclerotic lesions in the four vessels and coronary artery disease. The atherosclerotic process began in childhood and develops inconspicuously for many decades before cardiovascular complications such as coronary artery disease, myocardial infarction occur in middle and late age (5,14).

Some studies have reported no discernible differences in atherosclerosis before the age of 30, by which time virtually all individuals display some degree of intimal disease (15). Raised lesions were also not commonly determined in our cases before the age of 30 (29). However, autopsy studies have shown that the first atherosclerotic lesions actually begin to develop in the abdominal aorta, similar to our findings (15, 11). We did not detect any differences in atherosclerotic lesions of vessels and coronary artery disease between females and males due to the small number of females (n = 24) in the study.

Age, smoking and family coronary artery disease were risk factors for coronary artery disease (30,31).

In our study, smoking increased the incidence of coronary artery disease because of its vessel constrictive and ischemic effects, and also a significant correlation existed between smoking and raised atherosclerosis in the four vessels (27, 28, 32). Nakashima et al. suggested that a correlation have not existed between smoking and coronary artery disease (31). A large series autopsy case study is needed to predict the effects of smoking on atherosclerosis.

We found that the raised plaques in the four vessels increased arithmetically by surface extent when the weight to height ratio increased due to an increased fatty diet (15, 27, 28,). However, an increase in the weight to height ratio was not correlated with the incidence of coronary artery disease.

Reliable information about chronic family disease (any cardiac disease and/or diabetes mellitus) could not be obtained from the relatives of all cases before autopsy. When reliable information was obtained, a strong relationship existed between family coronary artery disease and coronary artery disease.

Atherosclerosis in aort and subclavian artery was found to be as risk factor for the assessment of coronary artery disease with association of well defined risk factors such as age, smoking, family coronary disease at our autopsy study. Age, smoking and BMI were also formatives for atherosclerosis in the main arteries.

5. CONCLUSION

Atherosclerosis in aorta and subclavian artery was found to be a risk factor for the assessment of coronary artery disease in our autopsy study. Age, smoking and BMI were also formatives for atherosclerosis in the main arteries.

Limitations

Female cases (n=24) were small in number because of randomized sectional study. So, we could not evaluate statistically correlation of gender with other data. Medical record data and smoking status of some cases couldn't be obtained completely from their relatives. Their record data had been shown as unknown. The evaluation of vessel lumens and cardiac tissue both macroscopically and microscopically had been performed by the same pathology specialist.

Acknowledgements: *We thank Prof. Dr. İsmail Birincioğlu, for their valuable contributions in gathering data of this study. This article is dedicated to the cherished memory of Prof.Dr.İsmail Birincioğlu passed away in 03, 16, 2022 at the age of 61.*
Funding: *The author(s) received no financial support for the research.*
Conflicts of interest: *The authors declare that they have no conflict of interest.*
Ethics Committee Approval: *This study was approved by Ethics Committee of Forensic Council of Turkey, (Approval date: 15/05/2009 and number: 237/2009)*
Peer-review: *Externally peer-reviewed.*
Author Contributions:
Research idea: NTY
Design of the study: NTY
Acquisition of data for the study: NTY, HCK
Analysis of data for the study: NTY, HCK, SE
Interpretation of data for the study: NTY, SE
Drafting the manuscript: NTY
Revising it critically for important intellectual content: SE, NTY
Final approval of the version to be published: NTY, HCK, SE

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How to cite this article: Turan Yurtsever N, Ekemen S, Ketenci HÇ. Correlation Between the Level of Atherosclerosis and Pathological Features of Coronary Artery Disease: A Study of 100 Autopsy Cases. Clin Exp Health Sci 2023; 13: 571-576. DOI: 10.33808/clinexphealthsci.1123538