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Age, gender and hypertension as major risk factors in development of subclinical atherosclerosis

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ABSTRACT

Introduction: Intima-media thickness (IMT) measurement of the common carotid artery (CCA) is considered as useful indicator of carotid atherosclerosis. Early detection of atherosclerosis and its associated risk factors is important to prevent stroke and heart diseases. The aim of the present study was to investigate which risk factors are better determinants of subclinical atherosclerosis, measured by common carotid artery intima media thickness (CCA-IMT).

Methods: A total of 74 subjects were randomly selected in this cross – sectional study. Information on the patient's medical history and laboratory findings were obtained from their clinical records. Risk factors relevant to this study were age, gender, cigarette smoking status, diabetes, hypertension and dyslipidemia. Ultrasound scanning of carotid arteries was performed with a 7,5 MHz linear array transducer (GE Voluson 730 pro). The highest value of six common carotid artery measurements was taken as the final IMT. Increased CCA-IMT was defined when it was > 1 mm.

Results: Our data demonstrated higher CCA-IMT values in male patients compared with female patients. Increased CCA-IMT was the most closely related to age (P<0.001), followed by systolic blood pressure (P=0.001), diastolic blood pressure (P=0.003) and glucose blood level (P=0.048).

Conclusion: Age, gender and hypertension are the most important risk factors in development of carotid atherosclerosis. Early detection of atherosclerosis among high-risk populations is important in order to prevent stroke and heart diseases, which are leading causes of death worldwide.

Keywords: Intima-media thickness, atherosclerosis, carotid arteries, Color Doppler Sonography.

INTRODUCTION

Cardiovascular disease (CVD) remains the leading cause of death worldwide, coronary heart disease being more common than stroke in the Western countries (1). Early detection of atherosclerosis and its associated risk factors is important to prevent stroke and heart diseases.

Atherosclerosis in the carotid arteries can be easily and non-invasively detected by carotid ultrasound. Carotid ultrasound measurement is highly reliable and reproducible (2). Intima-media thickness (IMT) measurements of the common carotid artery (CCA) is considered as useful indicator of carotid atherosclerosis (1,3).

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The aim of the present study was to investigate which risk factors are better determinants of subclinical atherosclerosis, measured by common carotid artery intima media thickness (CCA-IMT).

METHODS

Study design and patients

A total of 74 subjects were randomly selected in this cross – sectional study, which was carried out on patients who underwent Color Doppler Sonography at the Clinic of Radiology, Clinical Center University of Sarajevo. All participants provided informed consent, and the study protocol was approved by the institutional Ethics Committee of the Clinical Center University of Sarajevo. Subjects younger than 18 and the ones who did not want to participate in the study were excluded.

Cardiovascular risk factors

Information on the patient's medical history and laboratory findings were obtained from their clinical records. Risk factors relevant to this study were age, gender, cigarette smoking status, diabetes, hypertension and dyslipidemia. Participants were categorized into those who never smoked, former smokers and current smokers. Subjects were classified as having diabetes mellitus if they used anti-diabetic medication or had a fasting venous blood glucose ≥ 6.1 mmol/ L (4). Patients were considered to have arterial hypertension if they had a systolic blood pressure (SBP) ≥ 140 mmHg and/or diastolic pressure (DBP) ≥ 90 mmHg, or if they were taking antihypertensive drugs (5). Dyslipidemia was defined by the values of cholesterol greater than 5.2 mmol/L and/or triglycerides greater than 1.7 mmol/L, or by usage of antilipemic medication.

Intima media thickness (IMT) measurement

Ultrasound scanning of carotid arteries was performed with a 7.5 MHz linear array transducer (GE Voluson 730 pro). All measurements were performed with subjects in a supine position. We measured IMT at the far wall of each common carotid artery. The highest value of six common carotid artery measurements was taken as the final IMT. Carotid IMT was defined as the distance from the leading edge of the first echogenic line to the leading edge of the second echogenic line on the scans, with the first line representing the lumen-intimal interface and the second line representing the collagen-containing upper layer of the adventitia (6). Increased CCA-IMT was defined when it was > 1 mm. To differentiate plaques from increased IMT, a plaque was defined as a focal structure that encroaches into the arterial lumen at least 0.5 mm or 50% of the surrounding IMT value, or demonstrates a thickness > 1.5 mm as measured from the media – adventitia interface to the intima lumen interface (7, 8). The measurement of CCA-IMT was made without knowledge of laboratory results.

Statistical analysis

Statistical analysis was performed using SPSS 20, with the Mann-Whitney test used for comparing continuous variables and the chi-square test used for categorical variables. The level of statistical significance was set at $P<0.05$.

RESULTS

The study population had a mean age of 56.20 ± 2.78 years. 36 patients (48.6%) were male and 38 patients (51.4%) were female. Of the 74 subjects, there were 34 (45.9%) with diabetes mellitus, 50 (67.6%) with dyslipidemia and 53 (71.6%) with hypertension. 31 patients (41.9%) were current smokers, 18 patients (24.3%) were former smokers and 25 patients (33.8%) were never smoking. Carotid atherosclerosis was present with a prevalence of 47.3% (35 patients) for increased CCA-IMT and 54.1% (40 patients) for carotid plaques. 55 patients (74.3%) had combination of risk factors, at least two of them. Patients had mean blood glucose level, mean plasma lipid levels and mean blood pressure values as shown in Table 1.

Data in this study showed that 62.9% of male patients and 37.1% of female patients had increased CCA-IMT; the difference was statistically significant (P=0.035). Increased CCA-IMT was found in 37.1% patients who are current smokers, 28.6% patients who are former smokers and 34.3% patients who were never smoking; the difference was not statistically significant (P=0.652). In patients with history of hypertension 85.7% had increased CCA-IMT compared with 14.3% in normotensive patients; the difference was statistically significant (P=0.019). In patients with history of diabetes, the

TABLE 1. Baseline characteristics of the study population

Variables	Minimum	Maximum	Mean	Std.Dev.
Age (years)	19.00	75.00	56.2027	11.99998
CCA-IMT (mm)	0.50	1.40	0.9284	0.22787
GUK (mmol/L)	3.70	18.70	6.3765	2.45300
Holesterol (mmol/L)	2.80	9.97	5.2619	1.36254
Trigliceridi (mmol/L)	0.51	4.67	1.9634	0.91296
Systolic blood pressure (mmHg)	100.00	220.00	140.0000	22.08328
Diastolic blood pressure (mmHg)	60.00	120.00	87.3649	10.73411

TABLE 2. Correlation coefficient between CCA-IMT values and quantified variables of the study population

Variables	Pearson correlation coefficient with CCA-IMT	P-value
Age (years)	0.606	< 0.001
Systolic blood pressure (mmHg)	0.387	0.001
Diastolic blood pressure (mmHg)	0.409	< 0.001
Glucose blood level (mmol/L)	0.146	0.215
Cholesterol (mmol/L)	0.000	0.997
Triglyceride (mmol/L)	-0.137	0.243

prevalence of increased CCA-IMT was 51.4% compared with 48.6% in non-diabetic patients; the difference was not statistically significant (P=0.484). In patients with history of dyslipidemia 62.9% had increased CCA-IMT compared with 37.1% in non-dyslipidemic patients; the difference was not statistically significant (P=0.463).

Increased CCA-IMT was the most closely related to age (P<0.001), followed by systolic blood pressure (P=0.001), diastolic blood pressure (P=0.003) and glucose blood level (P=0.048), but was not statistically associated with total triglyceride (P=0.914) and cholesterol (P=0.486) blood level.

Significant correlation was also found between CCA-IMT values and age (P<0.001), systolic blood pressure (P=0.001) and diastolic blood pressure (P<0.001),but not with glucose blood level (P=0.215), triglyceride (P=0.243) and cholesterol (P=0.997), Pearson correlation coefficient and P-value showed in Table 2.

DISCUSSION

The results of our above mentioned study indicate that age, gender and hypertension are the most important risk factors in development of carotid atherosclerosis.

Other studies also observed that hypertension influences the carotid IMT (6,9) and find it the most prominent risk factor for thicker IMT and for the development of carotid stenosis (9,10). Mechanisms by which hypertension predisposes to atherosclerosis may include endothelial dysfunction, hyperinsulinemia, hemodynamic stress, and multiple metabolic alterations. Impaired production of endothelium derived relaxing factors and increased activity of endothelium-derived contractile substances have been demonstrated in hypertensive patients, preceding overt atherosclerotic disease. In addition, enhanced smooth muscle cell proliferation with intimal wall thickening and proteoglycan accumulation accelerates atherosclerosis. Hypertension increases the wall shear stress and barotrauma to the arterial intima. Increased flow velocity and wall shear stress are considered to be the important factors that caused hypertension-induced intima-media hypertrophy and thickness (10).

Cross-sectional analyses suggest that age is related to carotid wall thickening in all carotid beds, and carotid wall IMT is greater in men than in women 27 (2,10), because atherosclerosis develops in men at an earlier stage (1).

Our study also showed that increased CCA- IMT was related to glucose blood level, but not with history of diabetes mellitus. Various literature findings support the idea that glucose is a risk factor for atherosclerosis, but possibly of minor importance than traditional CVD risk factors. Stern et al. developed a model for the prediction of cardiovascular diseases which included age, sex, and ethnicity, lipids, blood pressure, BMI, family history and smoking as traditional CVD risk factors. Accordingly, Meigs et al. found that fasting glucose was not an independent risk factor for CVD (11).

Surprisingly we did not find statistically significant correlation of increased CCA-IMT with smoking and dyslipidemia. Johnson et al. conducted study on 795 subjects and also observed that smoking status did not independently predict carotid IMT, but found a significant increasing trend between pack-years of smoking and carotid atherosclerosis (12). We should have also taken into account cumulative smoking exposure, such as pack-years, and duration of smoking habit to properly evaluate the effects of cigarette smoking on carotid atherosclerosis. Liang et al reported a significant dose-dependent relationship between pack-years and CCA-IMT with the risk of carotid plaque. Further, Baldassarre et al found that carotid IMT was positively related to pack-years in former and current smokers (12).

Dyslipidemia is one of the important risk factors for atherosclerosis. Even though many studies detected the increase of IMT in patients with dyslipidemia (13, 14), there are still some that find no significant correlation between carotid IMT and dyslipidemia (15, 16).

Limitations of this study were its cross-sectional nature and a relatively small sample size.

CONCLUSION

Carotid sonography is recommended as a screening tool for future cardiovascular events among high-risk populations, especially for patients with hypertension, which we proved to be the most important risk factor for carotid atherosclerosis. Blood pressure measurement also should be performed routinely for every adult in clinical practice. Appropriate antihypertensive therapy should be used in order to lower blood pressure and to prevent hypertensive complications such as carotid atherosclerosis.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

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