

## CAROTID INTIMA MEDIA THICKNESS IS IN A RELATION TO RISK FACTORS FOR CORONARY ARTERY DISEASE

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*Introduction.* Carotid intima-media thickness (CIMT) is a double line pattern measured from the lumen-intima to media-adventitia interface. Measuring CIMT with B-mode ultrasound can detect early arterial wall changes. We aimed to measure CIMT in manifested atherosclerotic disease and find a relation to present risk factors.

*Material and methods.* This cross sectional study included a population of 657 patients, with documented coronary artery disease (CAD), 66,1% were men (469 pts), 33,9% were women (241 pts). The mean age of patients was 64,72 years (55,6–73,8). The measurement of CIMT (maximal and mean) was performed with B-mode ultrasound, on longitudinal view, on multiple plaque-free segments at the level of common carotid artery, on the far wall, on both sides. Multivariate regression analysis was done to estimate independent factors for CIMT, when risk factors, age, and sex included in analysis.

*Results.* The mean value of maximal CIMT was 0,96 mm (0,52–1,4), mean value of mean CIMT was 0,88 mm (range 0,61–1,15) and mean systolic blood pressure of 133,21 mm Hg (108,03–158,39) was found. Increased CIMT was found in 75,7% of patients (502 pts). Smoking was found as an independent risk factor for increased CIMT with odds ratio (OR) 4,7 (95% CI; 0,67–5,32) and diabetes mellitus with OR 1,6 (95% CI; 0,47–2,16).

*Conclusion.* Diabetes and smoking are independently related to increased CIMT. These are preliminary results of National survey on 657 pts with coronary artery disease.

**Key words:** survey, carotid intima-media thickness, B-mode ultrasound, risk factors, coronary artery disease.

### INTRODUCTION

Coronary artery disease (CAD) is the leading cause of cardiovascular mortality and among all other diseases [1, 2]. Diabetes is one of a common risk factors associated with CAD. Other factors include, hypercholesteraemia, arterial hypertension, obesity, and smoking [3].

Carotid artery disease (CARD), shares same risk factors as those with CAD [4]. CIMT is a powerful predictor of future coronary events as the meta-analysis of 8 observational studies performed by Lorenz, et al. [5].

We aimed to measure CIMT and find the relation to present risk factors in patients with manifested coronary artery disease.

### MATERIAL AND METHODS

#### STUDY DESIGN

We performed cross-sectional study that included 657 patients. Inclusion criteria for the study was previously confirmed coronary artery disease (CAD) with coronary angiography. The study was performed at University Clinic of Cardiology, Vascular Lab, Skopje, R.N. Macedonia. The data were collected for a period of 24 months, with signed informed consent by patients.

#### RISK FACTORS

For each patient were collected the following data:

age, gender and risk factors such as arterial hypertension (defined as systolic blood pressure (SBP) >140 mm Hg or antihypertensive treatment), hyperlipidemia (LDL cholesterol  $\geq 2,8$  mmol/L; HDL  $\leq 1,03$  mmol/L; tryglicerides  $\geq 1,7$  mmol/L), diabetes, treated by oral hypoglycemic agents or insulin therapy, smoking – including current tobacco users and obesity (defined as BMI  $\geq 30$  kg/m<sup>2</sup>).

### CAROTID ULTRASOUND

The examination of the common carotid artery (CCA) was performed with B-mode ultrasound using a linear probe (7,5–10 MHz), with probe positioned strictly perpendicular to the vessel wall, with angle between the probe and vessel wall smaller than 60°, on longitudinal view. The measurements were performed manually, measuring values of maximal IMT, at least 3 values, the highest was taken as a target value and mean IMT, as a mean value of all measured IMT value, on both sides (Fig.). The measurements were performed at far wall, that is the recommended one for IMT measurements because it represents the true biological thickness of the vessel wall, whereas the measurements at the near wall are not so exact because the echogenicity of the adventitial layer is masking the adventitial-medial boundary. If there was no clear boundary of intima-media complex at the

far wall, the near wall CIMT value was noticed. The measurements were done at multiple plaque free segments, at least 5 mm below the end of CCA, with clear intimal and medial layers demarcated, at length of at least 10 mm straight arterial segment. The optimal diameter of the wall was measured at end-diastole, when the artery has the smallest diameter, because at systole the CIMT is thinning. As an increased CIMT was taken the value of 0,9 mm.

The measurements were done following the recommendations of Mannheim Carotid Intima-Media Thickness and Plaque Consensus [6].

### STATISTICAL ANALYSIS

Multivariate logistic regression analysis was used with SPSS 23 for Windows, to estimate the relation between smoking, diabetes, hyperlipidemia, arterial hypertension, obesity diabetes and sex with increased CIMT. The mode was age adjusted.

### RESULTS

From the total number of 657 patients, 66,1% were men (469 pts), 33,9% were women (241 pts). They were aged between 55–73 years, with mean age of 64,72 years. Increased CIMT had 75,7% (502) of patients. The mean value of maximal CIMT was 0,96 mm (0,52–1,4 mm), the mean value of mean CIMT was 0,88 mm (0,61–1,15 mm). Mean SBP was 133,21 mm Hg (108,03–158,39 mm Hg) (Table 1). Most of the patients in the survey were smokers and have arterial hypertension (Table 2).

Multivariate regression analysis of CIMT and independent risk factors showed that smoking and diabetes are independent risk factors that had influence to increasing CIMT. Smoking has the most significant relative risk, with OR 4,7 (95% CI; 0,67–5,32) and diabetes with OR 1,6 (95% CI; 0,47–2,16).

### DISCUSSION

CIMT is a marker of atherosclerotic process not only in carotid arteries, but in coronary arteries, the aorta and lower limb arteries too. The measurement of CIMT should be done routinely for discovering generalized atherosclerosis in every asymptomatic adult at moderate risk for CVD according to SCORE or hypertensive patients for discovering asymptomatic organ damage [7, 8].

In studies analyzing the relation between blood pressure and CIMT, the Multi-Ethnic Study of Atherosclerosis (MESA) with 6606 patients included, multivariate regression models of CIMT and Framingham Risk Factors showed that all risk factors, except smoking were significantly associated with increased CIMT. From

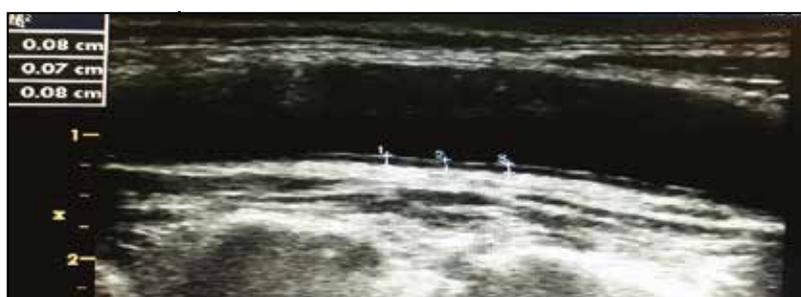


Fig. Measurement of intima-media complex at the level of common carotid artery- far wall

all risk factors associated, systolic blood pressure had the most significant correlation coefficient with mean far wall IMT ( $B=0.161$   $p<0.001$ ) [9].

In the analysis of Wang, et al. of 14 cohorts with 59 025 patients included, where clustering of two, three or four risk factors, concluded that CIMT did increase with the number of risk factors present. Compared to those with no risk factors, those with one risk factor had a higher common CIMT-mean difference 0,026 mm (95% CI; 0,022–0,030). For those with two, three or four risk factors, the increase in common CIMT was 0,052 mm (95% CI; 0,048–0,056), 0,074 mm (95% CI; 0,069–0,079) and 0,114 mm (95% CI; 0,103–0,124), respectively. In the clusters where the elevated systolic blood pressure was present, contributed most to the extent of atherosclerosis [10].

In studies analyzing the association between diabetes mellitus and CIMT, two studies performed from Bosevski, et al. at showed that hyperglycemia (measured as fasting blood glucose or HbA<sub>1c</sub>) was independent risk factor for increased CIMT in patients with type 2 diabetes mellitus [11, 12]. In IRAS study the data showed that patients with type 2 diabetes mellitus are with higher value of CIMT versus non-diabetics. In general population the progression of CIMT is 0,05–0,07 mm/annually, while in type 2 diabetic patients population

	Mean value	Range
Mean of the Max IMT	0,96 mm	0,52–1,4 mm
Mean of the Mean IMT	0,88 mm	0,61–1,15 mm
Mean SBP	133,21 mm Hg	108,03–158,39 mm Hg

Risk factors	Pts (Percentage)
Arterial Hypertension	183 (27,8)
Hyperlipidemia	151 (22,9)
Smoking	204 (31)
Diabetes	223 (33,9)
Obesity	151 (22,9)

the progression of CIMT is twice as rapidly – 0,1 mm/annually [13].

Smoking has been proved as a major risk factor for atherosclerosis. The newest cohort study performed by Kiriya, et al. with 1209 patients, presented at ESC Congress 2019, showed that the value of CIMT didn't differ between smokers and non-smokers, but the rate of increased value of CIMT was higher in smokers over 60 years old [14]. In ARIC population based cohort study, with 12 953 patients included, the strong relationship between active smoking and increased CIMT was proved, but interesting fact was that also passive smoking exposure is related to greater IMT [15]. We did not include a passive smoking in our survey.

In the cross-sectional study Chi, et al., with 1044 patients included, was shown that SBP in a combination with smoking, fasting blood glucose and ageing were significant factors for carotid atherosclerosis in patients with essential hypertension. Smoking was with significant OR: 4,072 (95% CI; 1,466–11,310), similar with the results from our study [16].

We presented a preliminary results from National survey on Screening for Carotid artery disease. We can conclude that diabetes and smoking are independently related to increased CIMT. The measurement of CIMT should be done routinely for discovering generalized atherosclerosis and stopping its progression with appropriate treatment (such as antihypertensive drugs, antidiabetics).

*Conflict of interest: none declared.*

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