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**Original article**

# Carotid artery intima-media thickness is a marker for coronary artery disease

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Although cardiac mortality has declined over the past four decades, coronary artery disease (CAD) remains the leading cause of mortality worldwide. Considering the importance of CAD and effectiveness of primary prevention interventions (as are statins), is present an increasing interest in how to identify individuals with increased risk of cardiovascular incidents before they occur. Ultrasonography in B-mod of carotid arteries nowadays increasingly is using as a noninvasive and sophisticated method for evaluating the atherosclerotic load in various clinical situations. The aim of this study was to analyze the relationship between intima-media thickness of the carotid artery with the presence and extent of coronary disease. 50 patients with positive stress echocardiography are referred for coronary angiography for coronary atherosclerosis assessment. All these patients, and to 50 healthy volunteers are evaluated by B-mode ultrasound of common carotid arteries for carotid intima-media thickness (CIMT) assessment. It was shown that patients with CAD have higher values of CIMT than healthy volunteers (0.96 mm ± 0.16 mm versus 0.64 mm ± 0.0.89 mm; T-test=16.053, p<0.0001). Values of CIMT were in direct correlation with severity and extent of coronary artery disease. Values of CIMT were greater in the subgroup with three vessel disease and in the subgroup of left main coronary artery disease than they were in the subgroup with single vessel coronary artery disease and in subgroup with two vessel coronary artery disease (1.08 mm ± 0.23 mm and 1.05 mm ± 0.16 mm versus 0.87 mm ± 0.125 mm and 0.93 mm ± 0.06

mm; coefficient of correlation was r=0. 473 and this was statistically significant p<0.01). In conclusion, CIMT can be used to predict the presence and extent of coronary atherosclerosis.



## 1. Introduction

Although cardiac mortality has declined over the past four decades, coronary artery disease (CAD) remains the leading cause of mortality worldwide (World Health Organization 2012; Lloyd-Jones D et al. 2009). In the U.S., about 450 000 deaths per year are attributable to cardiovascular disease, every 25 seconds an American hit by a coronary event and every minute an American dies from such event (Lloyd-Jones D et al. 2009). Unfortunately, nearly half of all deaths occur suddenly as the initial manifestation, 150 000 of these deaths occur in patients younger than 65 years (Myerburg RJ et al. 2011). Considering the importance of CAD and effectiveness primary prevention interventions (as are statins), is present an increasing interest in how to identify individuals with increased risk of cardiovascular incidents before they occur. Ultrasonography in B-mod of carotid arteries nowadays increasingly is using as a noninvasive method for evaluating and sophisticated atherosclerotic load in various clinical situations (Thompson JB et al. 2008). It may be used for research purposes as well as for clinical purposes. Advances in ultrasonography have the potential to improve early detection of atherosclerotic vascular disease and evaluate its advancement. The measurement of the intima-media thickness of the carotid artery (CIMT) with ultrasound is simple and safe, uses no radiation, and is an inexpensive test to assess indirectly for the presence of coronary atherosclerosis (Nguyen 2009). Cardiovascular risk factors correlate well with increased CIMT, and patients with increased CIMT have higher mean values of cardiovascular risk factors than those with normal CIMT (Heiss G et al. 1991). Even more important is that: CIMT is predictive of MI and stroke (Liviakis L et al. 2010). The association between cerebral ischemia and coronary artery disease has been supported by different studies (Touboul et al., 2005), however, the association of carotid IMT with coronary artery stenosis is a matter of controversy (Adams et al., 1995). In this prospective study, the relationship between CIMT and and the presence or absence of CAD was investigated, as well and its relation to the extent of CAD.

## 2. Materials and methods

This study was conducted in the period of 06 months (1 January 2012 - June 30, 2012), in the Regional Hospital "Prim. Dr. Daut Mustafa" of Prizren, and was supported by the Ethics Committee of our institution, and were taken written consents from all participants.

In the study are included 50 patients with positive exercise stress echocardiography and 50 healthy volunteers. All of them older than 18 years old, and adjusted for age and gender. From the study are excluded all patients with prior regional wall motion abnormalities of left ventricle (prior myocardial infarction, bundle branch blocks, severe myocardial hypertrophy) and all patients with left ventricular dysfunction due to cardiac or non cardiac causes. Demographic characteristics of both groups are shown in Table 1.

All participants are evaluated by B-mod ultrasound for CIMT assessment. A group of patients with positive exercise stress echocardiography are referred for coronary angiography assessment. Exercise stress echocardiography was undertaken using the testing protocol as it was recommended by EAE (European Association of Echocardiography) 2008. The test was taken as positive if there were regional kinetic abnormalities at least in two segments of the same wall of the left ventricle. B-mode ultrasonographic assessment of common carotid arteries was made using an ultrasound system equipped with high resolution linear probe of 7.5 MHz. Measurement of CIMT was made on the far wall of the common carotid artery, using a technique recommended by ASE (American Society of Echocardiography) 2008 (Fig. 1). According CIMT thickness, the group of patients with CAD is divided into two subgroups: (a) CIMT <1 mm, and (b) CIMT ≥ 1 mm.

Coronary angiography was done in different institutions, outer from our Hospital, because in our Institution coronary angiography assessment isn’t possible yet. According to the coronary angiography results, the group of patients with CAD, have divided into four subgroups: single vessel (1V), two vessels (2V), three vessels (3V) disease and disease of the left main coronary artery (LM).

### 2.1. Statistical analysis

Quantitative variables are presented as the arithmetic means ± standard deviation, the student's T-test was used for comparison between the two groups. Chi square test (X2) was applied for comparing categorical variables between two groups. Pearson's correlation coefficient (r) was used to measure linear relationship between CIMT and extent of CAD. Values of $p < 0.05$ are considered statistically significant.

**Table 1**
Demographic characteristics of study groups.

| | Patients with CAD | Control group | P values |
|---|---|---|---|
| Age (Years) | 57,3±9.7 | 56,1±7.3 | 0.49 NS* |
| Male (%) | 32 (64) | 23 (46) | 0.07 NS** |
| Hypertension (%) | 17 (34) | 9 (18) | 0.068 NS** |
| Diabetic (%) | 22 (44) | 11 (22) | 0.019 S** |
| BMI kg/m$^2$ | 28.12±2.3 | 24.6±3.1 | 0.0001 S* |
| Fasting glucose mmol/L | 6.94±1.81 | 5.733±2.29 | 0.0042 S* |
| Total Cholesterol mmol/L | 6.13±2.10 | 5.13±1.48 | 0.007 S* |
| LDL-Cholesterol mmol/L | 4.1±1.01 | 2.97±1.11 | 0.0001 S* |
| HDL-Cholesterol mmol/L | 1.05±0.29 | 1.41±0.34 | 0.0001 S* |
| Triglyceride mmol/L | 3.19±1.01 | 2.014±0.85 | 0.0001 S* |
| Smokers (%) | 31 (62) | 23 (46) | 0.108 NS** |

*Students T-test for means; **Chi square test.

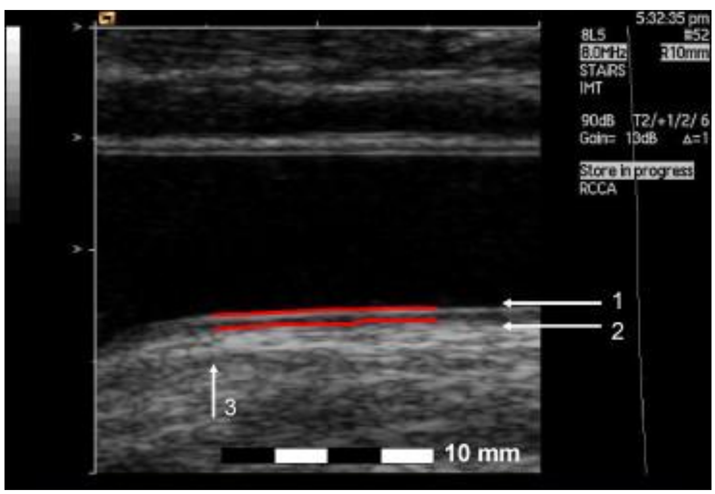


**Fig. 1.** B-mod ultrasound measurement method of CIMT.
(1) Lumen-Intima interface; (2) Media-Adventitia interface; (3) The point of transition from common carotid artery to carotid bulbs.

### 3. Results

In the control group the mean CIMT was 0.64 ± 0. 09 mm, while in the group of patients with CAD the mean CIMT was 0.96 ± 0.16 mm, which is found to be statistically significant ($p < 0.0001$) (Fig. 2).

The mean CIMT value was higher in the group of patients with single vessel CAD than it was in the control group (0.87 mm ±0.125 mm versus 0.64 mm ± 0.09 mm, $p < 0.0001$). The mean CIMT thickness was higher in subgroups with three vessel disease and disease of the left main coronary artery than the mean CIMT thickness in subgroups with a single and two vessel disease (1.08 mm ± 0.23 mm and 1.05 mm ± 0.16 mm versus 0.87 mm ± 0.125 mm and 0.93 mm ± 0.06 mm; r = 0.473, p<0.01) (Figure 3).

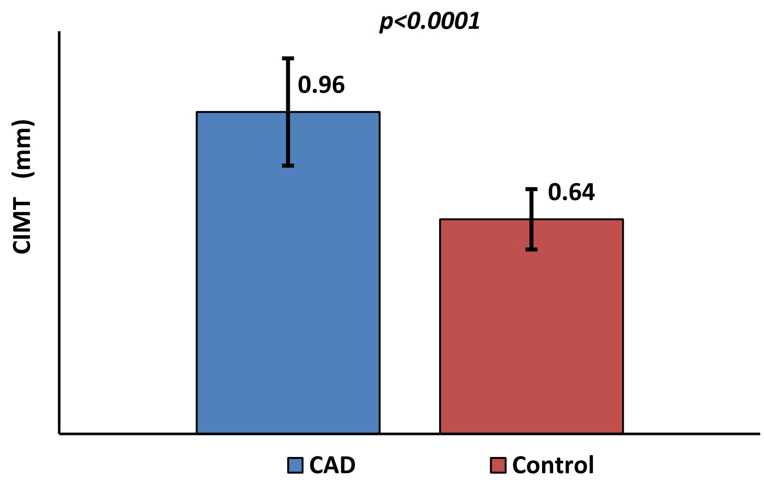


**Fig. 2.** Values of mean CIMT in study groups.

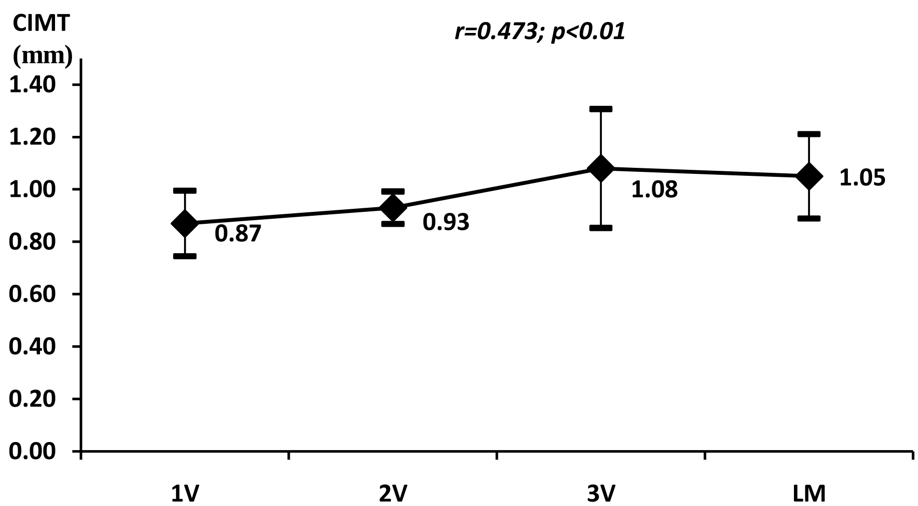


**Fig 3.** The mean CIMT thickness according to coronary angiography data.

The largest number of patients with CIMT > 1mm belongs to the subgroup with three vessel disease and to the subgroup of left main CAD, while the largest number of patients with CIMT <1 mm belongs to a subgroup with single and two vessel disease and it was found to be statistically significant (p <0.005) (Fig. 4).

**4. Discussion**

For detection of atherosclerosis are widely in use non-invasive and invasive methods. Measurement of CIMT is recommended by the AHA (American Heart Association) 2000 as the most useful method for identification of atherosclerosis. The CIMT thickness has consistently shown that it is accompanied by cardiovascular risk factors and the incidence and prevalence of CAD (Nambi et al. 2012). The test is safe, but the opportunities to obtain accurate and reproducible measurements are disturbing. Of all the segments that are used for CIMT thickness measurements, common carotid artery is easy for examination and has higher reproducibility; therefore it was recommended to be used as a segment for measurement of CIMT thickness (Roman MJ, et al. 2006).

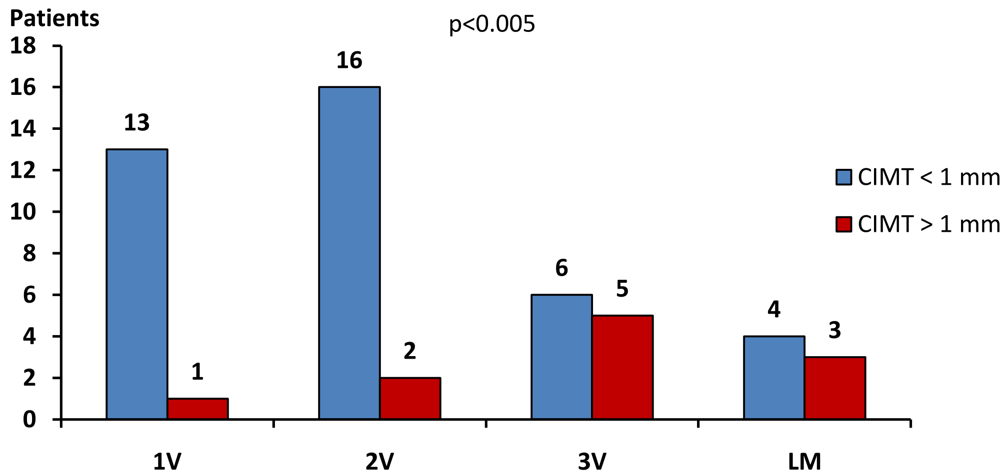


**Fig. 4.** Patients with CAD according to CIMT value and to coronary angiography data.

There are several prospective epidemiological studies that support the direct correlation between CIMT and risk from myocardial infarction and stroke in patients without a history of cardiovascular disease (Chambless LE, et al. 1997; O'Leary DH, et al. 1999). In a study by Demircan S et al. 2005 it was found that CIMT of patients with acute coronary syndrome was significantly higher compared to patients with stable chest angina. The most important finding of our study was the direct correlation between CIMT of common carotid arteries with atherosclerosis in coronary arteries. The difference in CIMT thickness between the group of healthy volunteers and groups of patients with coronary artery disease was statistically significant even after adjusting for age and gender. In other words, the increase in CIMT thickness of the carotid arteries is sufficient to predict changes in coronary arteries. And other authors have also shown similar results (Chambless LE et al. 2000). Using the value of CIMT ≥ 1 mm in common carotid arteries, as it was suggested in the ARIC study (Chambless LE et al., 1997), as a border for coronary atherosclerosis may underestimate the issue. Our results showed that only 11 (22%) patients with CAD have CIMT values higher than 1 mm. Our results support recommendations of SHAPE II (Screening for Heart Attack Prevention and Education) to set ≥ 50th percentile of CIMT thickness as a burden for atherosclerosis presence (Morteza Naghavi et all., 2006). The largest number of our patients is in moderate to high risk group according to CIMT values. The small sample possibly may reflect the final outcome, so multicentric studies with larger samples are needed in this area. Coronary angiography examinations are done in different centers, because of our public institutions such examination are not routine yet, and this may have an impact on the results of this study. Interpretation of results from the coronary angiography only by visual analysis has certain subjectivity, and that was why we did not determine the load border of atherosclerosis in coronary arteries.

## 5. Conclusion

Measurement of CIMT thickness in common carotid arteries is feasible for clinical purposes. The results from this study have shown that increase of CIMT thickness is associated with the presence and extension of coronary artery disease. By measuring CIMT thickness can be possible to identify patients at high risk for CAD even they are asymptomatic. This can help clinicians from a primary health care to build strategies for prevention of CAD according to individual risk score.

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