THE ASSOCIATION BETWEEN ARTERIAL STIFFNESS AND CAROTID INTIMA-MEDIA THICKNESS IN PATIENTS WITH KNOWN CARDIOVASCULAR RISK FACTORS

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Abstract

Objectives. *The aim of this study was to evaluate the relationship between pulse wave velocity and carotid intima-media thickness (IMT) in patients with different cardiovascular risk factors.*

Material and methods. *This prospective study included 223 patients with at least 2 risk factors for atherosclerosis, divided based on the presence of coronary artery disease (CAD): 140 patients with angiographically documented CAD and 83 patients without CAD. The patients were compared with a control group of 74 healthy age-matched subjects (CON). We determined the following parameters: blood pressure, total cholesterol (TC), triglycerides (TG), LDL-cholesterol, HDL-cholesterol, fasting serum glucose and renal parameters: blood urea nitrogen, serum creatinine, and uric acid levels in all patients. Arterial stiffness was measured with non-invasive oscillometric Arteriograph device (Tensiomed Ltd., Budapest, Hungary) and carotid scan was performed with B-mode ultrasound.*

Results. *Patients with CAD had increased values of aortic PWV compared with patients without CAD and CON group (12.5±0.7 vs 10.9±0.6 vs 8.5±0.6 m/s, all $p<0.001$). The values of carotid IMT were significantly higher in CAD patients as compared to patients without CAD and CON group (1±0.05 versus 1.0±0.07 versus 0.7±0.08 mm, all $p<0.001$). The carotid IMT significantly correlated with aortic PWV ($r=0.787$, $p<0.001$).*

Conclusions. *Carotid IMT and aortic PWV are useful non-invasive methods for atherosclerosis detection in patients with known cardiovascular risk factors. Both determinations in the same patient will increase the clinical relevance.*

Keywords: pulse wave velocity, carotid intima-media thickness, coronary artery disease.

Introduction

Endothelial dysfunction develops from the first decade of life as a response to genetic and environmental risk factors, and seems to be the causal pathway for the initiation and progression of atherosclerosis [1]. Non-invasive measurement techniques like carotid artery B-mode ultrasound, aortic pulse wave velocity (PWV), carotid artery duplex scanning, ultrasound-based endothelial function studies and magnetic resonance imaging techniques characterize the physiologic and anatomic structural modifications in the arterial wall [2,3].

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Ultrasound is used to monitor the carotid intima-media thickness (carotid IMT) because it has a high-resolution, is noninvasive and one of the best methods for the detection of the early stages of atherosclerotic disease [4]. Due to the fact that carotid IMT provides information on the atherosclerosis extent, it can be very useful in the cardiovascular risk assessment of individual patients [5]. Until now, carotid IMT has been associated with the risk of coronary artery disease, stroke, and myocardial infarction, and it predicts the progression of coronary artery disease [6-9]. An increased IMT has been shown to be associated with the presence and extent of coronary artery disease (CAD) [10].

Aortic pulse wave velocity, a marker of atherosclerosis inversely related to distension capacity, has attracted much interest in recent years as a measure of

conduit artery stiffness [11,12]. The results of different studies showed that higher aortic PWV is a predictive marker for CV events, especially ischemic stroke [13].

The aim of this study was to evaluate the relationship between aortic PWV and carotid IMT in patients with different cardiovascular risk factors, distributed based on the presence of coronary artery disease.

Material and method

The study included 223 consecutive patients with known cardiovascular risk factors, from the Internal Medicine Department of the Victor Babes University of Medicine and Pharmacy Timisoara, which were divided based on the presence of CAD: 140 patients with angiographically proven CAD, 83 age-matched patients without CAD but having one or more conventional cardiovascular risk factors, and a control lot consisting of 74 healthy age-matched subjects. Exclusion criteria were established: cerebrovascular disease, acute myocardial infarction, unstable angina, history of coronary angioplasty or coronary bypass surgery, arrhythmia, valvular heart disorders, and heart failure (New York Heart Association criteria III–IV). Written informed consent was obtained from every enrolled patient.

Cardiovascular risk factors were evaluated based on a standardized interview, which included patient history, clinical examination, laboratory tests, carotid IMT and aortic PWV. We recorded the use of antihypertensive and lipid-lowering medications. All patients with CAD received appropriate medical treatment (β-blockers, aspirin, statins, and angiotensin-converting enzyme inhibitors) according to the guidelines [14]. Before enrolment in the study, 80% of the patients were on regular use of angiotensin-converting enzyme (ACE) inhibitors, 25% angiotensin receptor blockers, 40 β-blockers, 38% calcium channel blockers, 5% nitrates and 80% patients were taking diuretics. Smokers were defined as subjects who had smoked regularly for more than 1 year.

Blood was drawn from the antecubital vein in seated patients who had fasted for 12 h. The laboratory tests included total cholesterol (TC), low-density lipoprotein (LDL-cholesterol), high-density lipoprotein (HDL-cholesterol), serum glucose, serum creatinine, serum uric acid levels and blood urea nitrogen levels. LDL-cholesterol was estimated by the Friedewald equation when triglycerides were <400 mg/dl [15].

The study protocol was approved by the local ethics committee. The study was conducted according to the Declaration of Helsinki, and the written informed consent was obtained from every subject.

Assessment of aortic PWV

The simultaneous measurements of aortic PWV, and brachial blood pressure were performed within 3 to 4 minutes with the oscillometric, occlusive device, the Arteriograph (Tensiomed Ltd., Budapest, Hungary). The principle of the measurement was based on the fact that during systole, the blood volume having been ejected into the aorta generates pulse wave (early systolic peak). This pulse wave runs down and reflects from the bifurcation of aorta, creating a second wave (late systolic peak). The difference between first and reflected systolic waves (in msec) is related to the stiffness of the aorta. On the basis of those characteristics aortic PWV can be calculated. Considering TENSIOMed Arteriograph data: optimal Augmentation Index is < -30% and Aortic PWV <7 m/s. The Arteriograph measures the stiffness of the aortic wall by measuring the Pulse Wave Velocity of the aorta.

Assessment of carotid intima-media thickness

The carotid intima-media thickness was measured by high resolution B-mode ultrasound imaging using a Prosound SSD 5500; Aloka, Tokyo, Japan. A standardized imaging protocol was used for the common carotid artery IMT measurements. Carotid plaque was defined as IMT ≥1.3 mm. Each measurement was calculated by considering the average of 3 readings. Carotid thickness was defined as a focal structure that encroaches into the arterial lumen of 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 [16].

Statistical analysis

Database and processing were performed using statistical software SPSS Statistical Software Package, version 15.0 (SPSS Inc, Chicago, Illinois, USA). Mean and standard deviations for all normally distributed variables were calculated. Pearson correlation coefficients or Student's t-test were used to assess univariate relationships between carotid IMT and aortic PWV. Multiple stepwise linear regression analysis was used to further explore the independent determinants of mean IMT value. Statistical significance was defined as two-sided $p<0.05$.

Results

The clinical characteristics of the patients in this study are summarized in Table I. Diabetes, hypertension, smoking and dyslipidemia were treated as classical risk factors of cardiovascular disease. There was no significant difference in gender and presence of cardiovascular risk factors in the two groups.

We obtained statistically significant differences when we compared the mean systolic and diastolic blood pressure values between patients with CAD, without CAD and controls (all $p<0.001$).

The plasma concentrations of TC, triglycerides, LDL-cholesterol and HDL-cholesterol were significantly higher in patients with CAD than in patients without CAD ($p<0.001$) and in the control group ($p<0.001$).

The values of carotid IMT were significantly higher in CAD patients as compared to patients without CAD and CON group (1±0.05 versus 1.0±0.07 versus 0.7±0.08 mm,

Table I. Baseline characteristics of the patients (mean ± SD).

Parameters	Patients with CAD (n=140)	Patients without CAD (n=83)	CON (n=74)	*p*
Age	58.5±7.8	58.63±8.9	56.8±5.2	0.37
Sex F/M (%)	51.4/48.6	51.8/48.2	54.1/45.9	0.93
AHC+ (%)	42.9	67.5	44.6	0.001
Smokers (%)	37.1	47	35.1	0.23
SBP (mmHg)	154.9±20.9	157.8 ± 13.5	123.7± 6.3	<0.001
DBP (mmHg)	91.1±12.3	93.67±7.4	72.6±5.3	<0.001
Fasting glycemia (mg/dL)	117.1±44	98.7±12.1	90.9±8.7	<0.001
TC (mg/dL)	262±39.5	268.1±35.8	181.27±13.044	<0.001
TG (mg/dL)	168.3±79.2	147.3±49.6	111.9±27.8	<0.001
LDL-C (mg/dL)	145±26	126.3±23.8	115.6±18.5	<0.001
HDL – C (mg/dL)	35.9±4.3	40.5±7.5	46.7±6.4	<0.001
Serum creatinine (mg/dl)	0.9±0.3	0.8±0.1	0.7±0.08	<0.001
BUN (mg/dl)	37±11.4	38.3±6.9	30.1±7	0.001
Uric acid levels (mg/dl)	6.3±1.8	5.7±1.7	4.7±1.1	<0.001
Aortic PWV (m/s)	12.5±0.7	10.9±0.6	8.5±0.07	<0.001
Carotid IMT(m/s)	1±0.05	1.0±0.07	0.7±0.08	<0.001

Legend: CAD=coronary artery disease; AHC+ = family history of coronary artery disease, SBP=systolic blood pressure; DBP=diastolic blood pressure, CT=Total cholesterol; TG=triglycerides; LDL-C=LDL-cholesterol; HDL-C=HDL-cholesterol; BUN=Blood urea nitrogen, PWV=pulse wave velocity.

p<0.001) (Figure 1 and Figure 2).

The patients with CAD had increased values of aortic PWV compared with patients without CAD and CON group (12.5±0.7 vs 10.9±0.6 vs 8.5±0.6 m/s, all p<0.001) (Figure 1 and Figure 2).

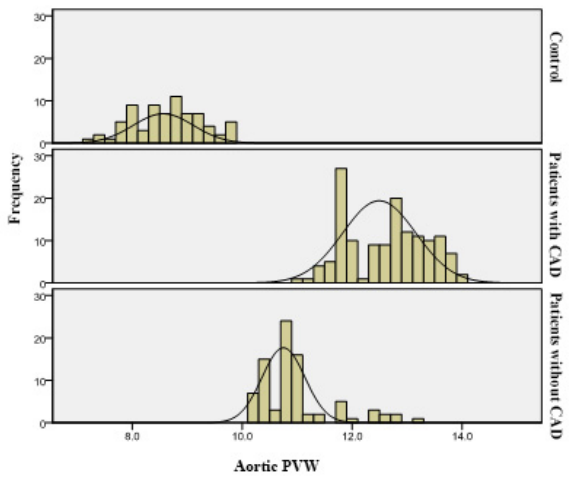

Figure 1. The histograms of aortic PWV in the studied groups.

Multiple stepwise linear regression analysis, with mean carotid IMT as the dependent variable showed that aortic PWV, total cholesterol and systolic blood pressure were significant independent determinants of mean IMT value.

For patients without CAD a significant week correlation between aortic PWV and carotid IMT was obtained (r=0.246, p=0.037) (Figure 3).

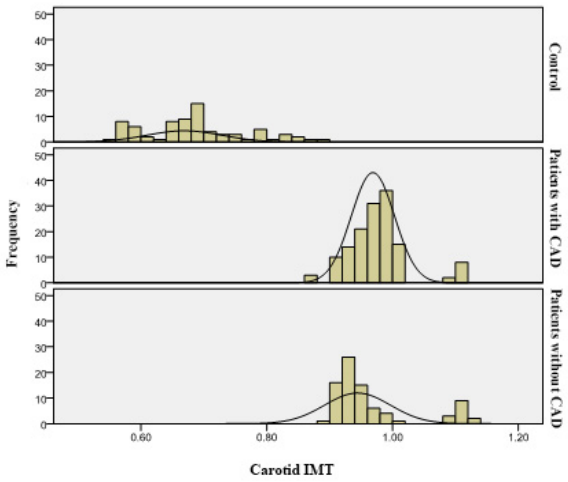

Figure 2. The histograms of carotid IMT in the studied groups.

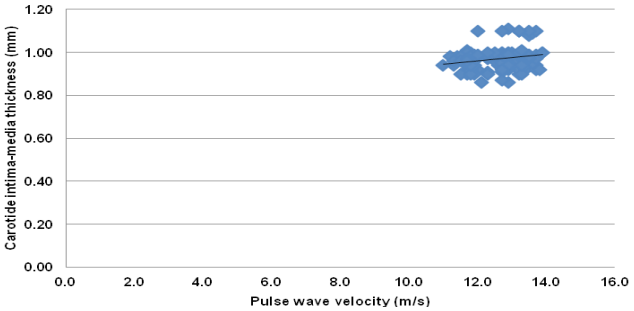

Figure 3. Correlation between carotid IMT and aortic PWV in patients without CAD.

For CAD patients we also obtained a significant and medium correlation between aortic PWV and carotid IMT (r=0.513, p=0.009) (Figure 4).

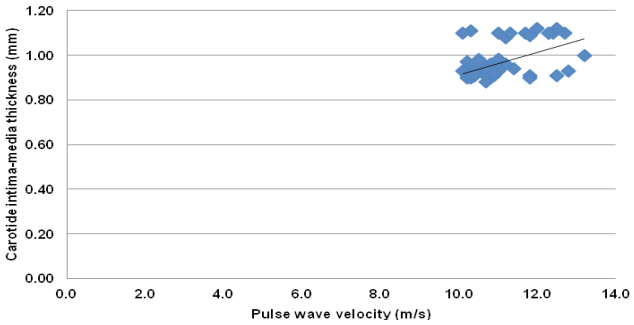

Figure 4. Correlation between carotid IMT and aortic PWV in CAD patients.

A significant correlation between aortic PWV and carotid IMT was obtained in all studied groups (r=0.787, p<0.001) (Figure 5).

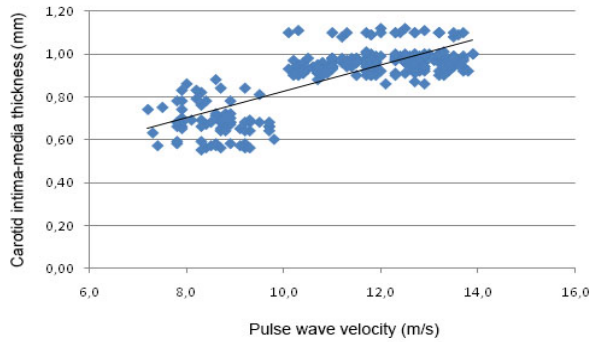

Figure 5. Correlation between aortic PWV and carotid IMT in all studied groups.

Discussion

Increased vascular stiffness is important in hypertension and its complications, including atherosclerosis, suggesting that therapy should also be directed at vascular stiffness [17]. Furthermore, it has already been established that systolic blood pressure determines a mechanical stimulus to the arterial wall remodeling through an excessive collagen production, leading to changes in the viscoelastic properties of the aorta and branches [18]. Although the carotid ultrasonography is a gold standard of the detection of asymptomatic atherosclerosis, the correlation between aortic PWV and the presence of preclinical carotid plaques was poorly investigated. In this study, we showed that aortic PWV was independently associated with carotid IMT in patients with known cardiovascular risk factors, even after controlling of age and gender. Our results are in concordance with previous trials that studied the clinical significance of carotid IMT and aortic PWV in patients with and without coronary artery disease [19,20]. Different reports also showed an excellent correlation between enhanced arterial stiffness, aortic PWV and endothelial dysfunction as assessed by reduced brachial artery flow-mediated dilation [20]. Laurent *et al.* reported a direct relationship between aortic stiffness and cardiovascular and all-cause mortality in hypertensive patients without kidney disease [21].

Similar with the results of our study, the Rotterdam Study, conducted in >3000 elderly subjects aged 60 to 101 years, showed that arterial stiffness was strongly associated with atherosclerosis at various sites in the vascular tree [22].

The mean and maximum carotid IMT and aortic were all significantly higher in coronary artery disease patients as compared to patients without coronary artery disease in a study that included sixty-four patients with angiographically documented coronary artery disease and 84 age-matched individuals without coronary artery disease [23]. These results were in concordance with the results of our study.

On the contrary, other studies have shown no significant correlation between arterial stiffness and atherosclerosis or the association has been demonstrated only in calcified plaques [24,25].

We consider that the relative impact of the various risk factors on the arterial wall requires further evaluation. Furthermore, the number of studies that followed the association between carotid IMT and aortic PWV in patients with different cardiovascular risk factors was relatively small.

Limitations of the study

We are aware of the limitations of this study, which refer to the relatively small number of the participants. The correlation between aortic PWV and carotid IMT was not further evaluated after adjustment for age and arterial tension values, the main factors that influence aortic PWV.

Conclusions

Carotid IMT and aortic PWV are useful non-invasive methods for atherosclerosis detection in patients with different cardiovascular risk factors. Both determinations in the same patient will increase the clinical relevance.

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