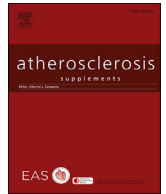




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Large artery stiffness according to different assessment methods in adult population of St.Petersburg

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A B S T R A C T

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Objective: The aim of the present study was to assess the prevalence of increased arterial stiffness by different diagnostic methods and its association with cardiovascular risk in Russian population-based cohort.

Design and methods: In terms of Russian epidemiological study ESSE-RF a random selection of 452 apparently healthy Saint-Petersburg inhabitants aged 25–65 years was performed. Fasting lipids, glucose and blood pressure measurements were performed. We used 3 diagnostic methods of arterial stiffness assessment: pulse wave velocity by applanation tonometry (SphygmoCor - PWV-S) and pulse wave velocity by volumetric sphygmography (VaSera - PWV-V), and cardio-ankle vascular index (CAVI) by VaSera.

Results: 341 (75,4%) had normal parameters of arterial stiffness assessed by all methods. Spearman's coefficient of correlation and "kappa" coefficient for PWV-S and CAVI were 0,74 and 0,04, for PWV-S and PWV-V - 0,10 and 0,06, for CAVI and PWV-V - 0,28 and 0,03, respectively. There was a significant correlation between cardiovascular risk (defined by SCORE) and PWV-S ($r = 0,38$, $p < 0,001$) and a non-significant trend of increasing CAVI along with cardiovascular risk ($r = 0,35$, $p = 0,14$).

Conclusions: Different methods of arterial stiffness assessment showed a weak correlation with each other. Carotid-femoral pulse wave velocity detected by applanation tonometry is associated with high cardiovascular risk score and might be considered as better additional risk marker for cardiovascular risk stratification.

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1. Introduction

Increased arterial stiffness is considered to be one of the possible early markers of arteriosclerosis and is defined as a surrogate end point for cardiovascular disease. According to Expert consensus on the measurement of aortic stiffness in daily practice 2012 [1], the measurement of carotid-femoral pulse wave velocity (PWV) is recommended as a gold standard for assessing arterial stiffness. Data from Framingham prospective study showed, that increased carotid-femoral PWV was associated with 48% risk elevation of first cardiovascular event and improved by 0,7% the predictive value of traditional risk model in European population

[2]. A lot of alternative methods for PWV measurement exist which include assessment of peripheral arteries function as well. The major disadvantage of all methods based on applanation tonometry is blood pressure dependency [3]. Another limitation for wide clinical implication is time-consuming and demand to be performed by trained personnel.

One of the new noninvasive methods is assessment of cardio-ankle vascular index (CAVI), which is positioned as a blood pressure independent marker and is measured by another technique based on volumetric sphygmography [4]. Large epidemiological Japan study revealed correlation between CAVI and traditional risk factors, such as hypercholesterinemia, left ventricular hypertrophy and diabetes mellitus [5]. During the last decade several data about prognostic value of CAVI were published [6], but large prospective studies which examine relation of CAVI to cardiovascular risk are still in progress. Previous attempts to compare the above

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mentioned methods were inconclusive because of small sample size, specific ethnic cohorts of patients or groups with the certain comorbidity [7–9]. The aim of our study was to assess the prevalence of increased arterial stiffness by different diagnostic methods and its association with general cardiovascular risk score in St. Petersburg population-based cohort.

2. Methods

2.1. Participants

This study was based on the data from ESSE-RF study, design described earlier in details [10]. In brief, ESSE-RF is a cross-sectional study in 13 Russian regions to investigate prevalence of risk factors and to evaluate contribution of traditional and new risk factors into morbidity and cardiovascular mortality in the population of Russian Federation. The study was conducted in compliance with current Good Clinical Practice standards and in accordance with the principles set forth under the Declaration of Helsinki (1989). Institutional review board approval of the study protocol was obtained before the initiation of study's participant enrollment. All participants entering the program agreed to and signed informed consent.

Among the participants of Saint-Petersburg population-based sample of ESSE-RF study (1600 Saint-Petersburg inhabitants aged 25–64 years old) 500 patients were selected as a random sample for arterial stiffness assessment.

2.2. Study design

All subjects were invited in the out-patient department of the Almazov Centre during morning hours (from 8 to 11 a.m.) after overnight fasting. Upon arrival, blood tests were performed and medical history was registered. All subjects were interviewed by standard questionnaire including information about social and demographic characteristics of participants, behavior customs (i.e. smoking status) and previous cardiovascular diseases, concomitant medication. Current smoking was defined as having smoked a cigarette in the last 30 days.

The body weight was obtained in light clothing and without shoes by medical scales VEM-150–“Massa-K” (Russia), height was measured by medical stadiometer (Russia). The body mass index (BMI) was calculated according to Quetelet formula. $BMI \geq 30 \text{ kg/m}^2$ was classified as obesity.

Peripheral brachial blood pressure was recorded on the right arm three times after 5 min rest by an automated sphygmomanometer (OMRON M3 Expert, Japan) with mean BP calculation. Hypertension was defined as a systolic blood pressure of at least 140 mm Hg, diastolic blood pressure of at least 90 mm Hg, or use of medication prescribed for hypertension. Electrocardiography was performed on device PADSy («Medset Medizintechnik GmbH», Germany). Patients with atrial fibrillation (permanent or paroxysmal) according to ECG signs didn't undergo arterial stiffness measurements and were excluded from data analysis ($n = 7$).

2.3. Blood tests

Biospecimen collection was performed by the qualified personnel using the standard venopuncture technique. Fasting blood lipids (total cholesterol, low-density lipoprotein cholesterol (LDL), high-density lipoprotein cholesterol (HDL), triglycerides (TG)), serum creatinine and plasma glucose were detected by Abbot Architect c8000 (USA) with «Abbot Diagnostic» kits (USA). Glomerular filtration rate (GFR) calculation was performed by CKD-EPI formula [11]. Patients with $GFR < 60 \text{ ml/min/1.73 m}^2$ ($n = 3$)

were excluded from data analysis. Patients with glucose level 5,6 - 6,9 mmol/l were referred to impaired fasting glycaemia group. Diabetes mellitus was defined as glucose level $\geq 7,0 \text{ mmol/l}$, or use of medication prescribed for diabetes. Groups of patients with high level of TG ($> 1,7 \text{ mmol/l}$), LDL ($> 3,0 \text{ mmol/l}$) and low level of HDL ($< 1,0 \text{ mmol/l}$ in men and $< 1,2 \text{ mmol/l}$ in women) were formed according to use of lipid-lowering therapy.

2.4. Instrumental investigation

After acclimatization in supine position (standardized conditions, quiet atmosphere, temperature maintained at 24°C) arterial stiffness measurement was performed, comprising determination of PWV by SphygmoCor (Atcor, Australia - PWV-S) and then CAVI, PWV by VaSera (Fukuda, Japan - PWV-V) within 10 min of each other on the same bed without changing supine position. Caffeine and smoking were not allowed within 3 h before measurements.

2.5. Arterial stiffness measurement by SphygmoCor

The carotid-femoral distance was measured according to a formula, recommended by Expert Consensus (2012): (common carotid artery - common femoral artery) $\times 0,8$ [1]. A special pencil sized tonometer was placed on the carotid artery to capture steady pulse waveforms for at least 10 s. Then the tonometer was placed on the femoral artery and pulse waveforms were captured for at least 10 s. Then, according to patient data, such as height, weight, brachial blood pressure before the procedure, the software automatically calculated the PWV-S, using the mean time difference (ΔT) among the R-wave and the pressure wave and the arterial path length between the two recording sites: $[PWV-S = \text{distance (meters)}/\text{time (seconds)}]$. The current cut-off value for PWV-S, proposed in 2012, was 10 m/s [1].

2.6. Arterial stiffness measurement by VaSera

ECG electrodes placed on both wrists and a phonocardiogram electrode placed at the right sternal border in the 2nd intercostal space. 4 cuffs with sensors at all four limbs to generate plethysmograms were applied to both upper arms and ankles. The two amorphous probes were placed at projection of common carotid and femoral artery pulsation. PWV was obtained by dividing the vascular length by the time taken for the pulse wave to propagate from the aortic valve to the ankle. These measurements and calculation system were automatically done using the VaSera VS-1000. The cut-off value for PWV-V was also adopted as 10 m/s.

To be compatible with the aortic PWV method established by Hasegawa et al. scale conversion constants were determined to match CAVI with the aortic PWV method. The mean value of CAVI was calculated as arithmetic mean of right CAVI and left CAVI. The reference value of CAVI was $< 9,0$ [12].

2.7. Cardiovascular risk assessment

10-year risk of fatal and non-fatal cardiovascular events was calculated by the SCORE algorithm [13]. According to the results all patients were divided into low ($\leq 1\%$), intermediate (1–5%), high (5–10%) and very high ($> 10\%$) risk groups. 38 patients from 500 participants had previous cardiovascular events (ischemic heart disease – 27, myocardial infarction – 17, stroke – 25 patients) were excluded from the data analysis.

2.8. Data analysis

Statistical analysis was performed by SPSS Statistics 17.0 (USA).

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