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Arterial stiffness parameters: How do they differ?

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ABSTRACT

Background: Carotid-femoral pulse wave velocity (PWV), as a parameter of aortic stiffness, is an established marker of cardiovascular risk. There has been increasing use of arterial stiffness parameters combining aortic and muscular stiffness or a parameter derived from PWV – the stiffness index beta (BETA = ln(*systolic/diastolic pressure*) × 2 *blood viscosity/pulse pressure* × PWV^2). The aim of this study was to compare different arterial stiffness parameters in a general population random sample.

Methods and results: In 809 individuals from the Czech post-MONICA study (aged 54 ± 13.5 years, 47% men), we compared the association of carotid-femoral PWV (cfPWV), carotid-ankle PWV (caPWV), and BETA with cardiovascular risk factors, parameters of subclinical organ damage, and presence of manifest cardiovascular disease.

Both cfPWV and caPWV were similarly associated with blood pressure and glucose level, while cfPWV was more strongly associated with age, cholesterol level and glomerular filtration rate whereas caPWV with Sokolow-Lyon index. BETA derived from cfPWV and caPWV was less dependent on blood pressure, while it showed a closer association with coronary heart disease presence, as compared to cfPWV and caPWV.

Conclusions: Addition of lower extremity to aortic stiffness has an effect on the association with cardiovascular risk factors while having no effect on the association with manifest cardiovascular disease. Beta transformation of PWV decreases its dependence on blood pressure and may increase its power in cardiovascular risk prediction.

1. Introduction

Pulse wave velocity (PWV) measured between the carotid and femoral arteries (cfPWV) as a measure of aortic stiffness has been shown to be an independent predictive factor for all-cause and cardiovascular morbidity and mortality in patients with various levels of cardiovascular risk [1]. In contrast, stiffness of other arterial territories has a smaller or no ability to predict cardiovascular outcomes [2–6]. Indeed, carotid stiffness has been shown to predict cardiovascular events in patients with end-stage renal disease [2] and after renal transplantation [3], while in a large cohort of patients with manifest cardiovascular disease, carotid stiffness was not an independent risk factor for vascular events [4]. Brachial and femoro-tibial PWV were not predictors of cardiovascular mortality in patients with end-stage renal disease [5]. Furthermore, only carotid-femoral PWV was independently associated with coronary artery calcification, carotid and femoral plaques in men with and without coronary artery disease, whereas carotid-radial and femoro-tibial PWV were not [6].

Difference in predictive value of these arterial territories may be explained by different histological structure and different effect of aging and risk factors on these structures. In elastic arteries, aging and risk factors lead to fragmentation and alteration of the elastic fiber network responsible for buffering function. On the other hand, in the muscular arteries these risk factors lead to changes in the extracellular matrix involving mainly collagen fibers, and to hypertrophy of vascular smooth muscle cells and the arterial wall, acting in the opposite direction on arterial stiffness [7,8].

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While the parameter commonly used in Europe and USA is the carotid-femoral PWV (measured between carotid and femoral artery), in Japan and other East Asian countries, arterial stiffness has been measured between the brachial artery and ankle—the so called brachial-ankle PWV index (baPWV). This arterial stiffness parameter reflects the properties of peripheral muscular arteries, but it has been shown to be more influenced by aortic stiffness [9,10]. The effect of addition of muscular arterial stiffness to aortic stiffness on the association with cardiovascular risk factors, parameters of subclinical organ damage and in cardiovascular risk prediction has not been fully evaluated. To date, there has been only one large-scale study comparing baPWV and cfPWV [11]. In this cross-sectional study, brachial-ankle pulse wave velocity was shown to exhibit an extent of associations with cardiovascular disease risk factors and clinical events similar to that of cfPWV.

Recently, a new parameter of regional arterial stiffness derived from the arterial stiffness parameter BETA, called cardio-ankle vascular index (CAVI) has been proposed. BETA can be calculated from PWV using the equation $\mathrm{BETA} = ln(SBP/DBP) \times 2\varsigma/PP \times PWV^2$ [12], where the (ln) denotes natural logarithm, (SBP) systolic blood pressure, (DBP) diastolic blood pressure, (PP) pulse pressure, (ς) blood viscosity and (PWV) pulse wave velocity. In order to match BETA and PWV, CAVI was introduced using scale conversion constants from BETA ($\mathrm{CAVI} = a[ln(SBP/DBP) \times 2\varsigma/PP \times PWV^2] + b$) [13]. The proposed advantage of this new stiffness parameter over PWV is its independence from blood pressure [14]. CAVI is suggested to better reflect structural changes of the arterial wall independently of distending blood pressure. However, the predictive role of this new arterial stiffness parameter has never been tested against PWV.

The purpose of our study was (1) to assess the effect of addition of muscular arterial stiffness to aortic stiffness on association with cardiovascular risk factors and subclinical organ damage as compared to aortic stiffness alone and (2) to compare the new stiffness parameter BETA of the carotid-femoral and carotid-ankle regions with the carotid-femoral and carotid-ankle PWV, respectively.

2. Methods

2.1. Study population

The Czech post-MONICA study is a population survey studying trends and determinants of cardiovascular risk factors in a random sample of the Czech population. Methods of the Czech post-MONICA study have been described elsewhere [15]. Our study included patients aged over 25 years resident in Pilsen district. The response rate in this district was 68%. A total of 834 individuals had complete data on carotid-femoral, femoral-ankle PWV and parameters of subclinical organ damage. Based on previous reports [16–18] that lower extremity peripheral arterial disease artificially decreases lower extremity arterial stiffness, we excluded 25 subjects with an ankle-brachial index (ABI) below 1.0. This left us with 809 patients. The study was approved by the local ethics committee of the Institute for Clinical and Experimental Medicine and Thomayer Hospital, Prague, Czech Republic, and was in accordance with the Declaration of Helsinki. All participants provided informed consent.

2.2. Laboratory analysis

All laboratory analyses were performed centrally in the Institute for Clinical and Experimental Medicine, Prague, Czech Republic. Lipid analyses were performed in the Lipid Laboratory of the Institute for Clinical and Experimental Medicine using a fully automated enzymatic method (Cobas MIRA S analyzer) with enzymatic kits by the same manufacturer. Glycemia and serum creatinine were also determined by enzymatic methods, and urinary albumin excretion in the first morning spot using immunoturbidimetry.

2.3. Definition of risk factors, target organ damage and manifest cardio-renal disease

Hypertension was defined as SBP $\geq$140 mm Hg, diastolic blood pressure DBP $\geq$90 mm Hg, or current use of antihypertensive medication. Diabetes was defined as fasting plasma glucose $\geq$7.0 mmol/l or use of oral antidiabetic drugs and/or insulin. Dyslipidemia was defined as any of the following: total cholesterol $\geq$5 mmol/l, LDL cholesterol $\geq$3 mmol/l, triglycerides $\geq$1.7 mmol/l, HDL-cholesterol $<$1 mmol/l in men and $<$1.2 mmol/l in women or use of lipid-lowering drugs. Chronic kidney disease (CKD) was defined as estimated glomerular filtration rate (eGFR) below 60 ml/min/1.73 m^2. Estimated glomerular filtration rate was determined by the simplified CKD-EPI formula as described by Levey [19]. Microalbuminuria was defined as an albumin/creatinine ratio $\geq$1.9 mg/mmol in men and $\geq$2.8 mg/mmol in women. Resting ECG was acquired by a MAC 5500 device (GE Healthcare, Waukesha, WI, USA) and digitally processed by purpose-written software. ECGs with complete left or right bundle branch block, atrial fibrillation, and paced rhythm or from individuals with a myocardial infarction history were excluded from further analysis. The Sokolow-Lyon index [$SV_1 + RV_{5/6}$] was calculated. A Sokolow-Lyon voltage over 35 mm was considered an ECG sign of left ventricular hypertrophy. The association of arterial stiffness indices with parameters of subclinical organ damage was analyzed only in individuals without a history of cardiovascular events. Coronary artery disease was defined as a history of myocardial infarction or revascularization (coronary artery bypass grafting or percutaneous coronary intervention). We estimated the ten-year risk of fatal cardiovascular disease in individuals between 40 and 65 years of age without manifest cardiovascular disease and diabetes using equation developed by the SCORE project [20] with country-specific coefficients.

2.4. Measurement of large artery properties

Large artery properties were measured using the SphygmoCor device (AtCor Medical Ltd, West Ryde, New South Wales, Australia) in the recumbent position as described previously [21]. Carotid-femoral (cfPWV) and femoral-ankle (faPWV) pulse wave velocity were assessed separately according to recommendations [22]. Consecutive registrations of the pulse waves are ECG-gated and thus the time shift (Δt) between the foot of wave at the first and second sites can be calculated. The distance between the two sites was measured on the body surface. To determine cfPWV, we measured the distance from the jugular fossa to the pulsation of the femoral artery in the groin and subtracted the distance from the jugular fossa to carotid pulsation to obtain the traveled distance (D). The distance between the femoral artery and dorsal pedal/posterior tibial artery was measured to calculate faPWV. PWV was calculated as D (meters)/Δt (seconds). Carotid-ankle PWV (caPWV) was calculated as the sum of carotid-femoral and femoral-ankle traveled distance divided by the sum of carotid-femoral and femoral-ankle time shift. Stiffness index Beta derived from cfPWV and caPWV (cfBETA and caBETA) was calculated by the equation $ln(SBP/DBP) \times 2\varsigma/PP \times PWV^2$, where PWV is cfPWV and caPWV, respectively.

2.5. Statistical analysis

Descriptive statistics is given as mean and standard deviation (SD), or as frequency and percent. The association of scale