Correlations of pulse wave velocity with augmentation index and ambulatory arterial stiffness index in the population of patients after acute coronary syndrome

Preliminary results of the FOREVER study

Introduction Pulse wave velocity (PWV) is the most widely used measure of arterial stiffness (AS). It has a strong prognostic value in predicting cardiovascular events and all-cause mortality. PWV is considered the "gold standard" method owing to its simplicity, noninvasive nature, reproducibility, and predictive value confirmed in numerous epidemiological and clinical studies. PWV is not easily available, which limits its routine use in clinical practice.

We would like to present the data from the FOREVER study (Focus On stiffness Reduction, Endothelial function and autonomic nervous system improVement in patients after MI with or without hypErtension after cardiovascular Rehabilitation), which was launched in 2009 with the aim to evaluate the correlation between the results of two different methods of AS assessment: the augmentation index (AI) calculated by EndoPAT 2000 and the ambulatory arterial stiffness index (AASI) determined by a noncommercial software on the basis of the data from 24-hour ambulatory blood pressure monitoring (ABPM) with the reference method – PWV measurement assessed by means of the Complior device in patients after a recent troponin-positive acute coronary syndrome (ACS). An additional aim was to identify the clinical and demographic factors, which determine the values of the individual parameters of AS.

Methods The study population consisted of 32 patients aged from 38 to 78 years after recent troponin-positive ACS. The exclusion criteria were as follows: unstable coronary artery disease, indications for coronary artery bypass grafting (CABG), peripheral artery disease, uncontrolled arterial hypertension, ventricular and supraventricular arrhythmias, allergy to latex, deformities or condition after finger amputation, body mass index above 35 kg/m^2, a significant hepatic or renal failure, and an infectious disease. All patients received the same standard treatment (aspirin, clopidogrel, angiotensin-converting enzyme inhibitor, β-blocker, and statin). Nitrates were contraindicated because of the methodology of the AI. The study was approved by the Bioethics Committee of the Medical University of Lodz (RNN/24/09/KE). The examination of AS was conducted in 3 phases.

The measurement of PWV was performed in a supine position using a noninvasive device (Complior, Artech Medical, Pantin, France) with the TY-306 Fukuda pressure sensitive transducers (Fukuda, Tokyo, Japan). Transducers were placed above the area with the best palpable pulse on the carotid and femoral arteries. The distance between the sensors was measured. The system calculated PWV on the basis of about 12 to 16 records as the distance between the sensors divided by the time in which the pulse wave arrived along the aorta from the carotid artery to the femoral artery, expressed in meters per second. The device presented also the reference value and a graphic record of PWV in relation to the patient's age compared with the general population.

The AI was calculated by the EndoPAT 2000 system (Itamar Medical Ltd., Caesarea, Israel), which uses plethysmographic technology. The device recorded pulsatile volume changes in the fingers – the peripheral arterial tone (PAT) signal. The examination was performed in a supine position. The sensors were worn on the index fingers of both hands. The PAT signal was recorded for 15 minutes in total: 5 minutes of device calibration (baseline), 5 minutes after the inflation of the sphygmomanometer cuff to a pressure exceeding the patient's systolic blood pressure, and 5 minutes after the deflation of the cuff. The software allows the computer to analyze the pulse

TABLE Clinical characteristics and arterial stiffness indexes in the study group (n = 32)

Variable	Value
number of women	9
diabetes	7
smokers	17
arterial hypertension	18
STEMI	24
NSTEMI	6
age, y	58.60 ±9.34
height, m	1.69 ±0.09
weight, kg	80.73 ±15.62
BMI, kg/m^2	28.21 ±4.33
PWV, m/s	10.55 ±2.03
AI, %	24.98 ±20.12
AI@75, %	20.00 ±17.25
AASI	0.43 ±0.05
total cholesterol, mg/dl	175.21 ±56.17
LDL, mg/dl	101.00 ±46.55
HDL, mg/dl	42.86 ±11.19
TG, mg/dl	155.93 ±86.15
creatinine, m/dl	0.95 ±0.20
GFR, ml/min/1.73 m^2	97.52 ±39.38

Data are presented as number or mean ± standard deviation.

To convert the values to SI units multiply total, LDL, and HDL cholesterol by 0.0259; TG by 0.0113; creatinine by 88.4; for GFR replace 175 with 30.849 in the MDRD study abbreviated equation.

Abbreviations: AI – augmentation index, AI@75 – corrected augmentation index, AASI – ambulatory arterial stiffness index, BMI – body mass index, GFR – glomerular filtration rate, HDL – high-density lipoproteins, LDL – low-density lipoproteins, MDRD – Modification of Diet in Renal Disease, NSTEMI – non-ST-elevation myocardial infarction, PWV – pulse wave velocity, SD – standard deviation, STEMI – ST-elevation myocardial infarction, TG – triglycerides

wave and to determine the AI as an amplitude of the reflected wave, expressed as a percentage of the pulse pressure.

The AASI was calculated using a noncommercial software developed at the Department of Microelectronics and Computer Science, Lodz University of Technology, as one minus the slope of regression of diastolic blood pressure relative to systolic blood pressure from ABPM. The ABPM device, based on the oscillometric method, recorded blood pressure every 15 minutes during the day and every half an hour during the night.

A statistical analysis was made using the Statistics Toolbox software, Matlab (R2010a, MathWorks, Natick, Massachusetts, United States) . The Kolmogorov–Smirnov test was used to check whether the distribution of the studied parameters was normal. To check the relation between the studied parameters, we determined the Pearson's correlation coefficient (r), and a P-value of less than 0.05 was considered statistically significant. To verify the relationship between the measured parameters when other relevant random variables were removed, partial correlation parameters were calculated in 2 stages. Sex was excluded from the analysis because of the small representation of women in the study group (n = 9).

Results The study included 32 patients (23 men, 9 women) aged from 38 to78 years. The characteristics of the study population are shown in the **TABLE**.

We observed a significant linear relationship between PWV and the AASI (r = 0.51, P = 0.01). There was no correlation between PWV and the AI (r = 0.17, P = 0.25) and no significant correlation between the AASI and AI (r = 0.40, P >0.05).

All parameters of AS correlated positively with the patients' age: PWV (r = 0.46, P = 0.003), AASI (r = 0.69, P = 0.0004), and AI (r = 0.33, P =.04). We observed a strong inverse correlation between the AI and patients' height (r = –0.47, P = 0.0009) and weight (r = –0.44, P = 0.002). Therefore, patients' age, height, and weight were included in a multivariate analysis. We confirmed the correlation between PWV and age and between the AASI and age after the elimination of the effect of height and weight (r = 0.41, P = 0.02 and r = 0.69, P <0.001, respectively). After eliminating the effect of height and weight, there was no correlation between the AI and age (r = 0.07, P = 0.70). The linear correlation between the parameters of AS adjusted for age, regarded as an important determinant of AS, did not affect the statistical significance of the correlation between the AASI and PWV (r = 0.48, P = 0.03).

Discussion In our study, we attempted to assess the correlation between the results of 2 different methods of AS measurement and compare them with the reference method (PWV), and we obtained a significant correlation only for the AASI. The AASI is a relatively new and controversial parameter of AS assessment. The pioneering study of this parameter by Li et al.[1] showed a positive correlation with PWV (r = 0.51, P <0.0001) in a group of 166 healthy volunteers.[1] A large study by Bastos et al.[2] conducted on 1200 patients with hypertension not only yielded a significant correlation of the 2 parameters (r = 0.31, P <0.001), but also confirmed the predictive value of the AASI for cardiovascular events and stroke during a 15.2-year follow-up. A positive correlation between the AASI and PWV was also confirmed in recent studies by Xu et al.[3] and Gómez-Marcos et al.[4]

A recently published meta-analysis by Kollias et al.[5] demonstrated the predictive value of the AASI for future cardiovascular events, particularly stroke and its association with PWV (r = 0.03) from 9 studies in adults. In our study, we obtained a positive linear relationship between PWV and the AASI (r = 0.51, P = 0.01), which remained significant after the elimination of the definite effect of age on both variables (r = 0.48, P = 0.03).

We did not observe a correlation between PWV measured by Complior and the AI calculated by EndoPAT 2000. It might have been caused by the PAT signal, which is used to assess the AI and which can be strongly affected by numerous factors, including the resistance of the peripheral arteries, the activity of the autonomic nervous system, hormones, endogenous mediators, and the use of drugs that do not affect PWV.

In summary, in the population of patients with a recent myocardial infarction, we have observed a correlation between PWV, which is the reference marker of AS, and the AASI. The main factor that determined those variables was the patients' age. However, the linear correlation between PWV and the AASI remained significant also when it was adjusted for age. We believe that in patients with ACS, the assessment of risk factors such as AS is important for secondary prevention of cardiovascular events. The AASI might be a useful, cheap, and widely available method that could be considered for screening purposes. However, our population was too small to draw firm conclusions and the issue requires further research.

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