Clinical utility of digital volume pulse analysis in prediction of cardiovascular risk and the presence of angiographic coronary artery disease

Konstantinos Vakalis, Aris Bechlioulis, Katerina K. Naka, Konstantinos Pappas, Christos S. Katsouras, Lampros K. Michalis*

Department of Cardiology and Michaelidion Cardiac Center, University of Ioannina, Ioannina, 45110, Greece

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Abstract  Background: Stiffness Index (SI), assessed by finger photoplethysmography (digital volume pulse analysis), has been suggested as a simple and easy measure of arterial stiffness. However, its potential association with cardiovascular risk and coronary artery disease (CAD) has been little studied. The aims of the study were to investigate the relation of SI with classical risk factors and established arterial stiffness indices and its ability to predict cardiovascular risk and the presence of angiographic CAD.

Methods: We enrolled 126 consecutive patients (mean age 61 years, 74% males) with suspected stable CAD undergoing diagnostic coronary angiography. Cardiovascular risk was assessed using Framingham risk score (FRS) and the European Heart score. Carotid-femoral (PWVcf) and carotid-radial (PWVcr) pulse wave velocity and augmentation index, using applanation tonometry, and SI using finger photoplethysmography, were measured in all patients.

Results: SI was positively correlated with PWVcr (p < 0.017) but not with PWVcf. Increased SI (R^2 0.19, p < 0.001) was independently associated with higher diastolic blood pressure and male gender. Increased SI and PWVcf were associated with higher FRS and Heart score (p < 0.05 for all), while only higher PWVcf was associated with the presence of angiographic CAD (p = 0.007).

Conclusions: SI, easily derived using finger photoplethysmography, was related to classical risk factors and peripheral arterial rather than aortic stiffness. SI and PWVcf were the only vascular indices associated with cardiovascular risk, but only PWVcf was related to the presence of angiographic CAD.
Introduction

Cardiovascular disease (CVD) is one of the most common causes of mortality and morbidity in the western world. Atherosclerosis is the leading cause of CVD and the identification of individuals at high CVD risk has been an important priority of modern medicine. The assessment of CVD risk in clinical practice is currently based on the calculation of "risk scores" such as the Framingham Risk Score (FRS) and the European Heart Score, that take into consideration the presence of various established cardiovascular risk factors i.e., age, gender, smoking, blood pressure, lipids and diabetes status. However, in several occasions the estimated risk may be misleading leading to the search of novel markers that could refine risk stratification. Indices of subclinical atherosclerosis have been suggested to improve prediction of cardiovascular events.

Increased arterial stiffness is thought to occur early in the atherosclerotic process and established measures of arterial stiffness, such as aortic pulse wave velocity (PWV) and augmentation index (AIx), have been shown to be associated with cardiovascular prognosis in several studies and large meta-analyses. Increased carotid-femoral PWV (PWVcf) have also been associated with the presence of coronary atherosclerosis in patients undergoing coronary angiography. Digital volume pulse (DVP) analysis using finger photoplethysmography is a non-invasive method for evaluating arterial stiffness with high reproducibility and low inter-observer variability. Stiffness index (SI), derived by contour analysis of the digital pulse, is considered to be a measure of arterial stiffness and has been previously associated with aortic PWV. However, very few data exists associating this index to cardiovascular risk scores, while its usefulness for risk stratification and the prediction of the presence of coronary atherosclerosis, especially in comparison to established arterial stiffness indices, has not been previously studied.

The aims of the present study were to investigate the association of SI with i) classical risk factors, ii) established arterial stiffness indices such as PWV and AIx derived by arterial tonometry and iii) cardiovascular risk (as assessed by FRS and Heart Score) and the presence of significant angiographic coronary artery disease (CAD), in high risk patients with suspected stable CAD undergoing diagnostic coronary angiography.

Methods

Study patients and design

One hundred thirty seven consecutive subjects referred for diagnostic coronary angiography due to suspected stable coronary atherosclerosis. Further research is needed to clarify the value of this useful index of arterial stiffness in risk stratification.

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lipoprotein (HDL) cholesterol and diabetes. Accordingly, the European Heart Score predicts 10-year risk for developing a fatal cardiovascular event; a risk score of < 1%, 1—<5%, 5—10% and ≥10% indicates low, intermediate, high and very high risk respectively. Risk factors included in the Heart Score are age, gender, smoking, systolic blood pressure, total and HDL cholesterol. Patients with diabetes are considered to be at high risk according to the European Society of Cardiology guidelines on cardiovascular prevention.24

**Coronary angiography**

Coronary angiography was performed according to the standard Judkins technique. Significant CAD was defined as ≥50% stenosis in the internal diameter of at least one coronary artery (≥30% for the left main coronary artery). All coronary angiograms were visually assessed by two experienced angiographers and a consensus was reached. Reviewers were blinded to the results of coronary angiography and other findings.

**Measurement of vascular indices**

All measurements were performed following an overnight fast (subjects were also asked to refrain from smoking and caffeine use for at least 6 h) and before the administration of scheduled medications. Measurements were taking place in a quiet, temperature controlled room (≈22 °C) after a brief period of rest by a single operator who was blinded to the results of coronary angiography and other findings.

**Pulse wave velocity and central augmentation index**

Assessment of PWVcf, carotid-radial (PWVcr) and Alx was performed in the supine position non-invasively with the commercially available Sphygmocor system (Version 7.01, At Cor Medical, Sydney, Australia) using applanation tonometry as previously described15,25,26 by a single operator who was blinded to the results of coronary angiography and other findings. Pressure waveforms were recorded from the right radial artery (SI) and simultaneously recorded electrocardiogram as reference frame. PWV was calculated as distance/transit time and was used to identify independent predictors of vascular indices; variables whose univariate associations with cardiovascular risk estimates and the presence of significant CAD. The Area Under the Curve (AUC) of regression models were calculated and their predictive accuracy was compared using the methodology described by Hannley and McNeil (c-statistic).17 p values were always two-sided and a value of p < 0.05 was considered significant. The SPSS statistical software package (version 15.0 for Windows, SPSS Inc. Chicago, IL, USA) was used.
Results

Table 1 shows the characteristics and cardiovascular profile of the 126 subjects included in the final analysis. Of these patients, 74% were males, 36% were currently smoking, 38% had type 2 diabetes, 75% had hypertension and 86% had hypercholesterolemia. According to the FRS and European Heart score, 37% and 25% of our population respectively was classified as high or very high risk for future CAD events (FRS > 20%) or cardiovascular death (Heart score > 5%) in the next 10 years. Presence of significant angiographic CAD was found in 41% of our patients.

Univariate associations of various vascular indices with cardiovascular risk factors are shown in Table 2. In multivariate analysis, 1) SI ($R^2 0.19, p < 0.001$) was independently associated with diastolic blood pressure ($B 0.08, p < 0.001$) and male gender ($B 1.17, p = 0.004$), 2) PWVcf ($R^2 0.29, p < 0.001$) was independently associated with age ($B 0.07, p < 0.001$) and systolic blood pressure ($B 0.03, p = 0.004$), 3) PWVcr ($R^2 0.19, p < 0.001$) was independently associated with diastolic blood pressure ($B 0.03, p = 0.001$) and male gender ($B 0.44, p = 0.033$) and 4) Alx ($R^2 0.34, p < 0.001$) was independently associated with height ($B -0.24, p = 0.016$), male gender ($B -5.47, p = 0.007$), systolic blood pressure ($B 0.12, p = 0.003$) and waist circumference ($B -0.14, p = 0.04$).

SI was positively correlated with PWVcr ($r 0.212, p = 0.017$), while a trend for a significant association with Alx ($r 0.163, p = 0.069$) was also found. SI did not correlate with PWVcf ($p = NS$). PWVcf was positively correlated with PWVcr ($r 0.280, p = 0.002$) and Alx ($r 0.188, p = 0.036$) while PWVcr was also positively correlated with Alx ($r 0.197, p = 0.028$).

Associations of vascular indices with cardiovascular risk estimates and the presence of CAD are shown in Table 3. Increased SI and PWVcf were associated with higher estimated risk for CAD events (OR 1.59, 95% CI 1.08, 2.35, $p = 0.020$ and OR 1.68, 95% CI 1.14, 2.47, $p = 0.009$ per 1 SD increase for SI and PWVcf respectively) as assessed by FRS and with higher estimated risk for cardiovascular mortality (OR 1.61, 95% CI 1.07, 2.43, $p = 0.023$ and OR 1.78, 95% CI 1.18, 2.69, $p = 0.006$ per 1 SD increase for SI and PWVcf respectively) as assessed by Heart score. The accuracy of SI and PWVcf for identifying high risk individuals according to FRS (AUC 0.658 vs 0.624 respectively for SI and PWVcf) and Heart score (AUC 0.662 vs 0.654 respectively for SI and PWVcf) did not differ significantly ($p > 0.05$ for both comparisons). Presence of angiographic CAD was associated only with increased PWVcf (OR 1.72, 95% CI 1.16, 2.54, $p = 0.007$ per 1 SD increase); none of the other vascular indices was associated with the presence of CAD.

Discussion

Stiffness Index, assessed by DVP analysis using photoplethysmography, has been previously suggested as a measure of arterial stiffness. It's simple, easy and rapid acquisition in the finger would make it a very appealing tool in the evaluation of cardiovascular risk via the assessment of arterial stiffness. However, the use of SI in clinical practice is very limited compared to other indices of arterial stiffness. Applanation tonometry has been widely used for several decades to derive PWVcf and PWVcr, indices of aortic and peripheral arterial stiffness, and Alx, a more complex index determined both by the aortic stiffness and the reflections of the pulse wave from the peripheral circulation. PWVcf and Alx have been extensively studied in relation to cardiovascular risk factors and independently associated with cardiovascular prognosis. In the present study, increased SI was associated with higher blood pressure (especially diastolic blood pressure) and male gender. The association of blood pressure (systolic, diastolic or mean blood pressure) with SI has been previously reported and depicts the major effect of blood pressure on arterial stiffness indices. This effect was also confirmed by our results; an independent association of PWVcf and Alx was found with systolic blood pressure, while PWVcr was associated with diastolic blood pressure. Higher SI in male patients may be attributed to higher stature compared to women since height is the nominator in the formula used to calculate SI, while males were also found to have higher PWV in peripheral muscular arteries (PWVcr). Interestingly, in contrast to previous studies,
SI was not related to age. However, our population consisted mostly of patients >50 years old (90%), while previous studies included healthier and younger patients and increasing SI with aging was more prominent in age groups <55 years old.  

Regarding the applanation tonometry derived indices, our results are in accordance with previous studies. The main determinants of PWVcf were age and systolic blood pressure, while AIx was associated with systolic blood pressure and gender as discussed above; these associations have not been previously reported.

In the current study, SI was found to be associated with peripheral arterial stiffness of the upper limb (PWVcr), while there was a trend for a significant association with AIx. SI was not related to aortic stiffness (PWVcf), although previous studies have reported a modest correlation of SI with PWVcf ($r = 0.54-0.65$).  


| Table 2: Univariate and multivariate associations of vascular indices with cardiovascular risk factors. |
|---|---|---|---|---|---|
| | Univariate analysis | | Multivariate analysis | | |
| | Correlation coefficient (r) | p value | B coefficient (95% CI) | p value |
| SI, m/sec | Diastolic blood pressure, mmHg | 0.368 | <0.001 | 0.08 (0.05, 0.12) | <0.001 |
| | Systolic blood pressure, mmHg | 0.239 | 0.007 | | |
| | Male gender, yes/no | 0.211 | 0.018 | 1.17 (0.38, 1.96) | 0.004 |
| | Smoking, yes/no | 0.191 | 0.032 | | |
| PWVcf, m/sec | Systolic blood pressure, mmHg | 0.355 | <0.001 | 0.03 (0.01, 0.05) | 0.004 |
| | Heart rate, beats/min | 0.350 | <0.001 | | |
| | Age, years | 0.337 | <0.001 | 0.07 (0.03, 0.10) | <0.001 |
| | Hypertension, yes/no | 0.275 | 0.002 | | |
| | Glucose, mg/dl* | 0.156 | 0.082 | | |
| | Diabetes, yes/no | 0.153 | 0.087 | | |
| | LDL cholesterol, mg/dL | -0.151 | 0.090 | | |
| AIX, % | Height, cm | -0.490 | <0.001 | -0.24 (-0.44, -0.05) | <0.016 |
| | Male gender, yes/no | -0.460 | <0.001 | -5.47 (-9.45, -1.50) | 0.007 |
| | HDL cholesterol, mg/dL | 0.327 | <0.001 | | |
| | Age, years | 0.258 | 0.004 | | |
| | Systolic blood pressure, mmHg | 0.224 | 0.012 | 0.12 (0.04, 0.20) | 0.003 |
| | Waist circumference, cm | -0.225 | 0.013 | -0.14 (-0.26, -0.01) | 0.04 |
| | Diastolic blood pressure, mmHg | 0.202 | 0.024 | | |
| | Smoking, yes/no | -0.173 | 0.054 | | |
| | Heart rate, beats/min | 0.172 | 0.055 | | |
| PWVcr, m/sec | Diastolic blood pressure, mmHg | 0.336 | <0.001 | 0.03 (0.02, 0.05) | 0.001 |
| | Heart rate, beats/min | 0.286 | 0.001 | | |
| | Systolic blood pressure, mmHg | 0.227 | 0.01 | | |
| | Age, years | -0.192 | 0.031 | | |
| | Male gender, yes/no | 0.168 | 0.060 | 0.44 (0.04, 0.85) | 0.033 |

*Natural logarithm used in analysis. Only variables with a $p < 0.1$ in the univariate analysis are shown.

AIX = augmentation index, CI confidence interval; PWVcf = pulse wave velocity carotid-femoral; PWVcr = pulse wave velocity carotid-radial; SI stiffness index.
with the presence of significant angiographic CAD in our population, an association reported by other studies, further supporting the established value of aortic stiffness in the prediction of cardiovascular risk. These findings indicate that SI, an easily measured and highly reproducible vascular index, could prove to be helpful in the prediction of cardiovascular risk, but larger studies are needed to investigate its potential prognostic role.

In conclusion, the digital volume pulse analysis-derived SI was found to be related to peripheral arterial rather than aortic stiffness suggesting that SI may not be an appropriate index for the evaluation of aortic stiffness, at least in older high risk patients. Both SI and PWVcf were found to have a similar accuracy in the discrimination of patients at high cardiovascular risk, but only PWVcf was associated with the presence of significant angiographic CAD in our population. More research is needed to define the role of this potential useful index of arterial stiffness in the prediction of cardiovascular risk.

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Conflict of interest

None of the authors has any conflict of interest related to this article.

References


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