Original article

Relationship between cardio-ankle vascular index and coronary artery calcification in a population sample of southwestern Siberia

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Abstract: *Objective* — To examine associations between cardio-ankle vascular index (CAVI) and coronary artery calcium (CAC) score a population sample of southwestern Siberia.

Methods — From the sample of 1,620 people the final analysis included 1,316 participants 25 to 64 years of age who were enrolled in an observational cross-sectional study, Epidemiology *of Cardiovascular Diseases and Their Risk Factors in the Russian Federation* (ESSE-RF). Study participants were split among two groups: Group 1 with CAVI≥9.0 (n=128) and Group 2 with CAVI<9.0 (n=1,188). Prevalence of coronary artery calcification in both groups was analyzed via the Agatston method. We compared main demographic and clinical data between the groups, as well as CAC scores.

Results — Elevated CAVI (≥9.0) was present in 9.7% of people included in a population sample from southwestern Siberia, and coronary artery calcification was found in 33.5% of the sample. While similar rates of minimum, mild, moderate and severe CAC score were observed in the participants with elevated and normal CAVI values, CAVI as a continuous variable was statistically significantly associated with moderate and severe CAC scores (OR 1.20, 95% CI 1.06-1.37, p=0.004). CAC score values were higher in individuals at the age of ≥50 years with pathological CAVI values (116±489 vs. 75±425 in normal CAVI, p=0.035), but not in patients under the age of 50 years (64±227 and 85±475, p=0.343).

Conclusion — CAVI could possibly be used as a feasible marker before assessing the CAC score in some asymptomatic Caucasian subjects, but identifying the most appropriate methods and participants, whom it could be clearly applicable to, requires further studying.

Keywords: CAVI, coronary artery calcium score; population-based sample.

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Introduction

The social significance of reducing the risk for cardiovascular diseases (CVD), their identification and timely prevention is beyond doubt. Clinical studies assess the risk of cardiovascular events by identifying conventional risk factors. However, limited accuracy of exclusively clinical assessment has led to examining new risk markers, including coronary artery calcium (CAC) score identified using imaging techniques.

CAC score assessment is widely used in algorithms for the diagnosis of coronary artery disease (CAD). In particular, this index is proposed as the first noninvasive test in low-risk patients with suspected CAD since a zero value of the CAC score in patients with stable chest pain reliably excludes obstructive CAD [1]. European Society of Cardiology (ESC) guidelines consider CAC score assessment a likely method of elucidating the odds of obstructive CAD with an initial pretest probability within 5-15% [2]. The recent study [3] demonstrated that the use of CACS-CL (CAC score-weighted clinical likelihood) models, in addition to the new pretest probability scale, allowed increasing the share of patients classified as having a very low (<5%) clinical likelihood of CAD from 11 to 54%, thereby sparing them from further routine diagnostic testing.

For asymptomatic patients, the recommendations are less definite. On the one hand, it is known that prevalence of obstructive CAD in asymptomatic patients is comparable to the prevalence in patients with atypical angina pectoris [4]. Therefore, the wider use of CAC score in asymptomatic individuals seems quite reasonable. In the ROBINSCA trial, the CAC score classified significantly fewer people (both women and men) with intermediate and high risks of CAD, compared with the SCORE model based on orthodox risk factors [5]. Nonetheless, an increased radiation exposure in the screening assessment of the CAC index remains a major concern: therefore, the methods of reducing the radiation dose are in demand [6].

Consequently, the search for additional parameters that could be used alongside usual clinical risk factors to distinguish those asymptomatic individuals, who could benefit from the CAC score estimation, continues [7, 8]. From this standpoint, the assessment of arterial stiffness looks attractive, since this indicator is an integral marker that accumulates an impact of risk factors. Arterial stiffness is a universal marker of cardiovascular risk; accordingly, it

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was proposed for use in both screening and examination of CVD risk [9]. However, a traditional indicator of arterial stiffness – the carotid-femoral pulse wave velocity (cfPWV) – has a number of disadvantages, particularly, its dependence on the blood pressure, researcher's expertise, and lack of standardization and inconsistent convenience for patients, thereby making it difficult to use PWV for dynamic arterial stiffness assessment [9]. Accordingly, cardio-ankle vascular index (CAVI) has been proposed as a novel marker of arterial stiffness based on the stiffness parameter β, which reflects the degree of the pressure-volume ratio [10]. CAVI is free from the shortcomings of cfPWV, being independent of the blood pressure level, easy to measure (using blood pressure cuffs placed on both arms and ankles, and a microphone on the chest, without the need for sensors on the neck or groin), and not requiring as many skills from the operator [11]. CAVI was studied for 15 years, and accumulated experience was summarized in recent meta-analyses and reviews [12-14]. E.g., the association between CAVI and risk factors for CVD (arterial hypertension, diabetes mellitus, smoking, low physical activity, dyslipidemia) was confirmed [14], as well as the prognostic value of CAVI in people with a high risk of CVD [12] and in patients with CAD [15-17].

CAD patients have higher CAVI values, as highlighted in the review [14]. Previous studies showed that an increase in CAVI was associated with the severity of coronary artery calcification [18-21]. However, these data were from Asian populations and cannot be reliably extrapolated onto other ethnic groups. This constituted the background for our research, the objective of which was to determine the associations between CAVI and CAC score in a population-based sample in Russia.

Material and Methods

Patient population

This study was carried out in 2013 as a part of a multicenter observational epidemiological study, ESSE-RF (Epidemiology of Cardiovascular Diseases and their Risk Factors in Russian Federation Regions) [22], in Kemerovo Oblast (the southwestern part of Siberia). The object of the ESSE-RF study was a random sample of local Caucasian male and female residents 25 to 64 years of age. The standard protocol of the ESSE-RF was expanded with an additional measurement of CAVI. Cardiac computed tomography (CT) was also used in all patients to quantify the CAC score. The study protocol was approved by the local Ethics Committee of the Research Institute for Complex Issues of Cardiovascular Disease. The research was performed in compliance with the Declaration of Helsinki. Patients were included in the study after they provided written informed consent.

The study design is presented in *Figure* 1. From the sample of 1,620 people, 25 subjects did not undergo CAVI, 159 patients with the ankle-brachial index (ABI) <0.9 and 120 patients with CAD were excluded from further analysis. The remaining 1,316 study participants were distributed among two groups: Group 1 consisted of patients with CAVI ≥9.0 (n=128), whereas Group 2 included patients with CAVI <9.0 (n=1,188).

Demographic and clinical characteristics

The demographic characteristics, age, gender, education, marital status, risk factors and clinical characteristics were assessed by means of ESSE-RF questionnaires. The ESSE-RF questionnaires were developed based on international surveys and consisted of 12 subsets. They were described in more detail earlier [23, 24].

Instrumental and laboratory examinations

The following parameters were measured in all study participants: blood pressure (BP), heart rate, anthropometry (height; weight; waist and hip circumferences – WC and HC), total cholesterol, high- and low-density lipoprotein cholesterols (HDL-C and LDL-C), triglycerides, glucose, uric acid and creatinine. Fasting blood samples were collected from the cubital vein. Blood serum was obtained by low-speed centrifugation at 900 g for 20 min at a temperature of +4 °C. Concentrations of total cholesterol, HDL-C and LDL-C, triglycerides, glucose, creatinine and uric acid were measured in all participants sensu the study protocol. The blood serum concentrations were determined on the Abbot Architect c8000 biochemical analyzer (USA) using Abbot Diagnostic test kits (USA).

Measuring CAVI

Arterial stiffness was measured with VaSera VS-1000 device (Fukuda Denshi Company Ltd, Tokyo, Japan). CAVI was computed on 1,595 (99.1%) study participants for the right and left lower limbs. The patient was resting in a supine position. Cuffs were placed approximately 2 cm above the antecubital fossa on the arms and 2 cm above the medial malleolus on the legs. Elbows and heels were elevated on special pillows to stabilize the pulse wave. The fixed cuffs did not touch the surface of the couch. Electrocardiogram (ECG) electrodes were placed a few centimeters above the wrist on each forearm. A small microphone was taped onto the chest. The procedure took no more than 10-15 minutes. The highest CAVI value was used for further calculations. Additionally, ABI values for each ankle were automatically measured sensu the 2005 ACC/AHA guidelines.

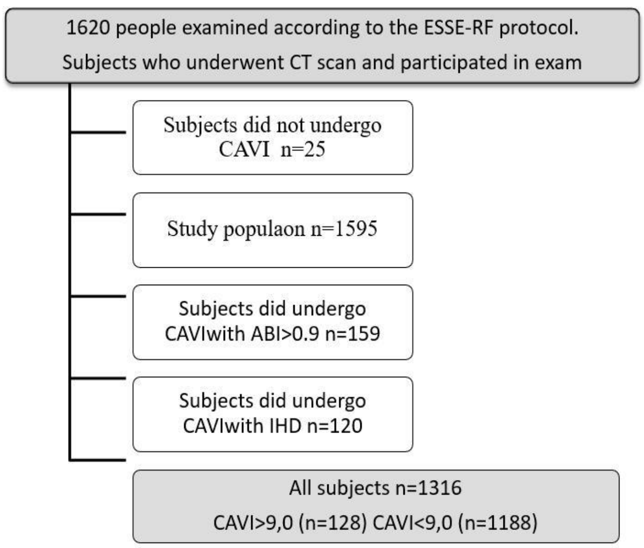

Figure 1. Flowchart of patient selection.

Table 1. Baseline characteristics in groups with pathological and normal CAVI values

Parameters	*CAVI ≥9.0 (n=128)*	*CAVI <9.0 (n=1,188)*	*p-value*
Male, n (%)	57 (44.53)	512 (43.1)	0.75
Age, years	57.0 (53.5; 61.0)	46.0 (35.0; 54.0)	<0.001
CVD family history, n, (%)	81 (63.28)	721 (60.69)	0.56
Smoking, n (%)	34 (26.56)	363 (30.56)	0.34
Smoking history, years	39.5 (28.0; 43.5)	24.0 (16.0; 34.0)	<0.001
Physical inactivity, n (%)	34 (26.56)	433 (36.45)	0.026
Disability, n (%)	7 (5.47)	51 (4.29)	0.53
Working people, n (%)	74 (57.81)	943 (79.44)	<0.001
Height, cm	166.9 (160.2; 172.5)	167.5 (160.0; 175.5)	0.21
Weight, kg	80.25 (69.35; 90.7)	76.7 (65.0; 89.4)	0.1
BMI, kg / m^2	28.57 (24.42; 33.01)	27.04 (23.48; 31.6)	0.013
Waist circumference, cm	97.5 (86.0; 106.5)	91.0 (81.0; 102.0)	<0,001
Hip circumference, cm	105.95 (98.5; 112.0)	103.0 (96.0; 110.0)	0.002
Total cholesterol, µmol/L	5.2 (4.48; 6.13)	5.03 (4.34; 5.83)	0.033
HDL cholesterol, µmol/L	1.66 (1.41; 1.91)	1.64 (1.4; 1.94)	0.88
LDL cholesterol, µmol/L	3.65 (3.02; 4.35)	3.35 (2.71; 4.06)	0.006
Triglycerides, µmol/L	1.19 (0.87; 1.66)	1.05 (0.75; 1.5)	0.008
Glucose, µmol/L	5.1 (4.56; 5.65)	4.86 (4.5; 5.34)	0.004
Creatinine, µmol/L	71.15 (62.45; 77.85)	69.6 (64.0; 77.4)	0.97
Uric acid, µmol/L	0.31 (0.26; 0.36)	0.29 (0.24; 0.35)	0.15
Stroke, n (%)	9 (7.03)	15 (1.26)	<0.001
Diabetes, n (%)	7 (5.47)	33 (2.78)	0.09
Bronchial asthma, n (%)	5 (3.91)	43 (3.62)	0.86
Renal disease, n (%)	41 (32.03)	285 (23.99)	0.045
Malignancy, n (%)	5 (3.91)	44 (3.7)	0.9
Hypertension, n (%)	72 (56.25)	310 (26.09)	<0.001

Values are presented as median (interquartile range) or a number (percentage), unless stated otherwise. CAVI, cardio-ankle vascular index; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Table 2. Correlation analysis for CAVI vs. other factors

Parameters	*All subjects, n=1,316*	
	r	p-value
Age	0.534	<0.000001
Male	-0.103	0.000079
Physical activity	-0.090	0.000977
Smoking	0.008	0.804820
Smoking history	0.513	<0.000001
Diabetes	0.117	0.000007
Hypertension	0.266	<0.000001
Waist	0.1109	0.000022
BMI	0.028	0.278264
Total cholesterol	0.187	<0.000001
Triglycerides	0.099	0.000163
Glucose	0.161	<0.000001
CAC score	0.003	0.882947

CAVI, cardio-ankle vascular index; BMI, body mass index; CAC, coronary artery calcium.

CT imaging and CAC analysis

The imaging was performed on a Somatom Sensation 64 multi-slice detector-row CT scanner (Siemens, Germany). The evaluation protocol for CAC included a low-dose, step-by-step scan of the heart area [25]. The data set was analyzed using the Leonardo multimodal workstation software (Siemens, Germany) via the Agatston method [26]. Calcium deposits were registered with maximum calcification density of over 130 Hounsfield units (HU). Calcium score was calculated in each patient. The CAC scores were categorized as follows: 0 – no calcification; 1-10 – minimum calcification; 11-100 – mild calcification; 101-400 – moderate calcification; >400 – severe calcification. In addition to estimating the CAC score, we calculated the volume of calcinates (mm^3).

Statistical analysis

Statistical analysis was performed using STATISTICA 8.0 software. Qualitative values were presented in absolute numbers (n) and percentages (%), comparisons between the groups were performed using $\chi 2$ tests. The normality of distribution was verified via Kolmogorov-Smirnov test. Quantitative variables were presented as medians with lower and upper quartiles (ME [LQ, UQ]) for distributions other than normal, and as mean ± SD in normal distribution. Bivariate correlation analyses with Spearman correlations were employed to evaluate associations between CAVI and other variables. The Wald-Wolfowitz runs test was used to compare two independent groups (subjects with CAVI ≥9.0 vs. subjects with CAVI <9.0). Nonlinear logistic regression with the odds ratio (OR) was applied to determine any possible relationships of CAVI with the severity of coronary artery calcification. Confidence interval (CI) was established at 95%. Differences were considered statistically significant at p<0.05.

Results

Baseline characteristics

The demographic and clinical characteristic of participants vs. CAVI value range (≥9.0 or <9.0) are summarized in *Table* 1. Baselines characteristic, according to another cutoff value of CAVI (≥ 8.0 or < 8.0) are presented in Appendix 1. These cutoff values of CAVI were identified from previous review [14]; they correspond to pathological values, or intermediate and pathological values, respectively. Participants with higher CAVI values (≥9.0) were older (58±8.3 vs. 47.0±11.4, p<0.001), and had higher values of WC, HC and body mass index (BMI), total cholesterol (p=0.012), triglycerides (p<0.001), LDL-C (p=0.009), uric acid (p<0.001) and glucose (p<0.001). Also, smoking history was longer in this group, compared with participants with normal CAVI (p<0.001). Participants with elevated CAVI reported a higher prevalence of diabetes mellitus (p=0.0048) and arterial hypertension (p<0.001). They were subjected to antihypertensive therapy more frequently (p<0.001). Also, participants with pathological CAVI had higher systolic and diastolic blood pressure (p<0.001).

Coronary artery calcification was detected by CT in 33.5% of study participants. CAC scores in groups with different CAVI value ranges exhibited no statistically significant differences, regardless of the cutoff values (*Table* 1, *Appendix* 1, *Figure* 2) on any of the minimum, mild, moderate or severe CAC score levels (*Figure* 3).

Correlation analysis with CAVI

As shown in *Table* 2, we examined the correlations of various variables with CAVI as a continuous variable. Age (r=0.534, p<0.05), male gender (r=0.103, p<0.05), presence of arterial hypertension (r=0.266, p<0.05) and diabetes mellitus (r=0.117, p<0.05), low level of physical activity (r=0.091, p<0.05), duration of smoking history (r=0.514, p<0.05), waist size (r=0.111, p<0.05), glucose (r=0.162, p<0.05), cholesterol (r=0.187, p<0.05) and triglyceride (r=0.099, p<0.05) levels revealed significant correlations with CAVI. However, the CAC score (r=0.003, p>0.05) or presence of severe coronary calcification (r=0.037, p>0.05) did not exhibit statistically significant trends.

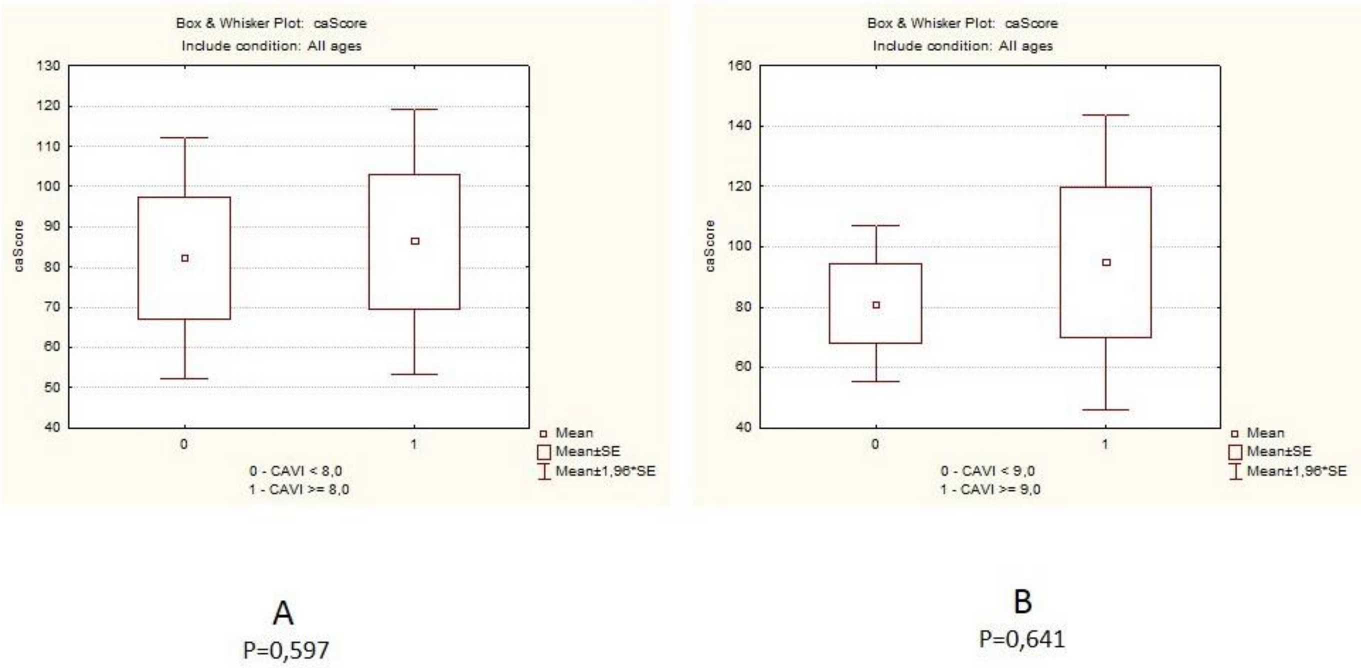

Figure 2. CAC score in groups with different CAVI values in all subjects. A – groups with CAVI<8.0 vs. CAVI≥8.0; B – groups with CAVI<9.0 versus CAVI≥9.0.

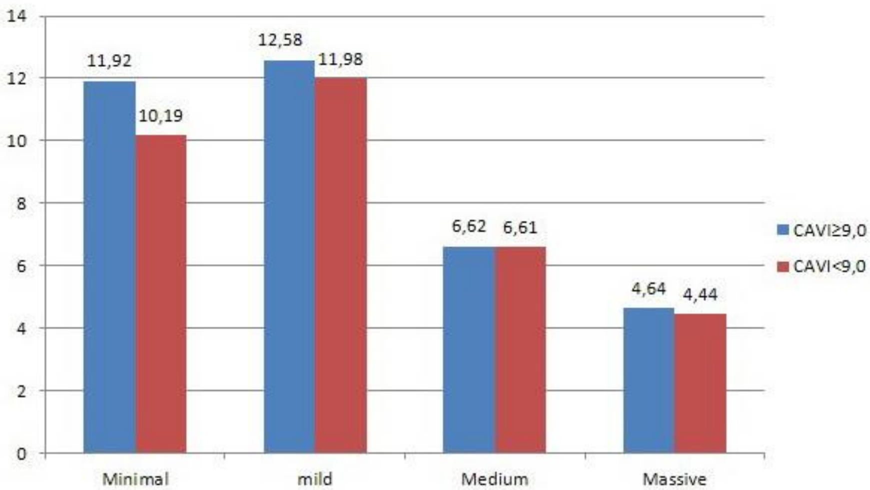

Figure 3. The degree of coronary arteries calcification (Agatston score) in participants with CAVI ≥9.0 vs. CAVI <9.0 (p>0.05 in all cases).

Univariate logistic regression analysis: CAVI vs. CAC score

As demonstrated in *Table* 3, CAVI as a continuous variable was associated significantly with CAC score ≥100 (OR 1.20, 95% CI 1.06-1.37, p=0.004) and CAC score of 100-399 (OR 1.28, 95% CI 1.11-1.48, p=0.0007). CAC index minimum values were detected less frequently with growing CAVI (OR 0.78, 95% CI 0.66-0.93, p=0.005). We could not detect such dependences when evaluating CAVI relationships above the cutoff values. Only at CAVI values of over 8.0, an association with a rarer detection of a moderate CAC score was noted (OR 0.46, 95% CI 0.23-0.93, p=0.030).

Association of CAVI with CAC score vs. age

We additionally evaluated the effect of the patient age on the relationship between CAVI and CAC score. Higher CAC score was not observed in the general studied cohort with CAVI more than 9.0 (*Figure* 2B), however, CAC score was significantly higher among participants ≥50 years of age with pathological CAVI values, compared with participants with normal CAVI (116±489 vs. 75±425, p=0.035, *Figure* 4B). On the contrary, there was a tendency in people with pathological CAVI under 50 years of age towards lower values of CAC score (64±227 and 85±475, p=0.343, *Figure* 5B). At CAVI cutoff value of 8.0, age had no effect on the relationship between CAVI and CAC score (*Figures* 2A, 4A, 5A).

When conducting correlation analyses separately in these age groups, we noted similar associations of CAVI with studied factors (*Appendix* 2). At the same time, negative correlation of CAVI with minimum CAC score was found only among patients under 50 years of age (*Appendix* 2).

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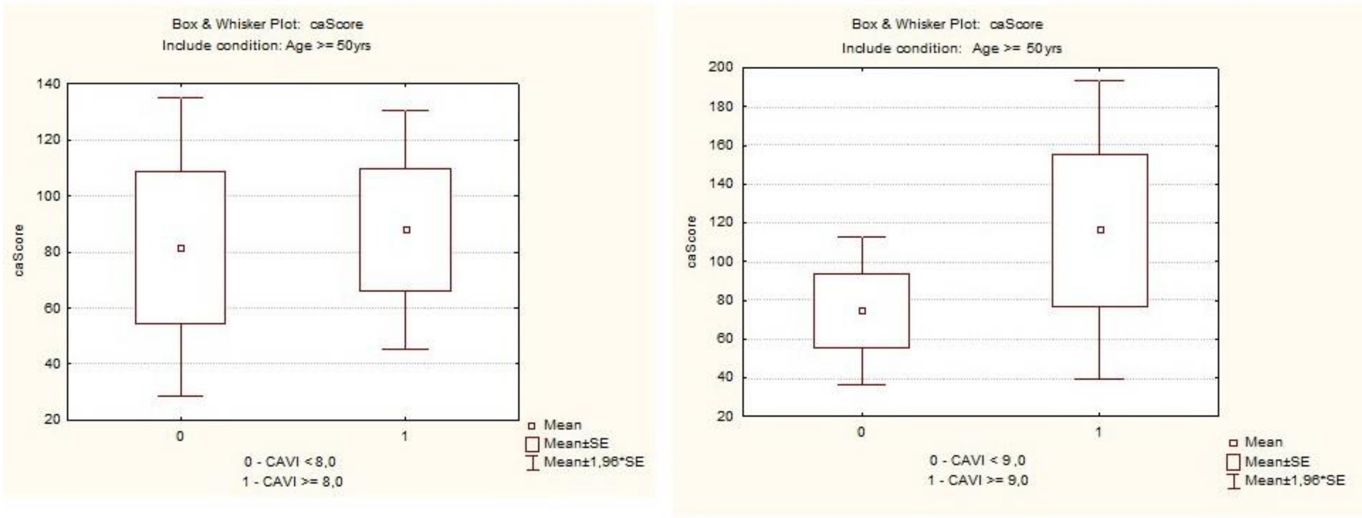
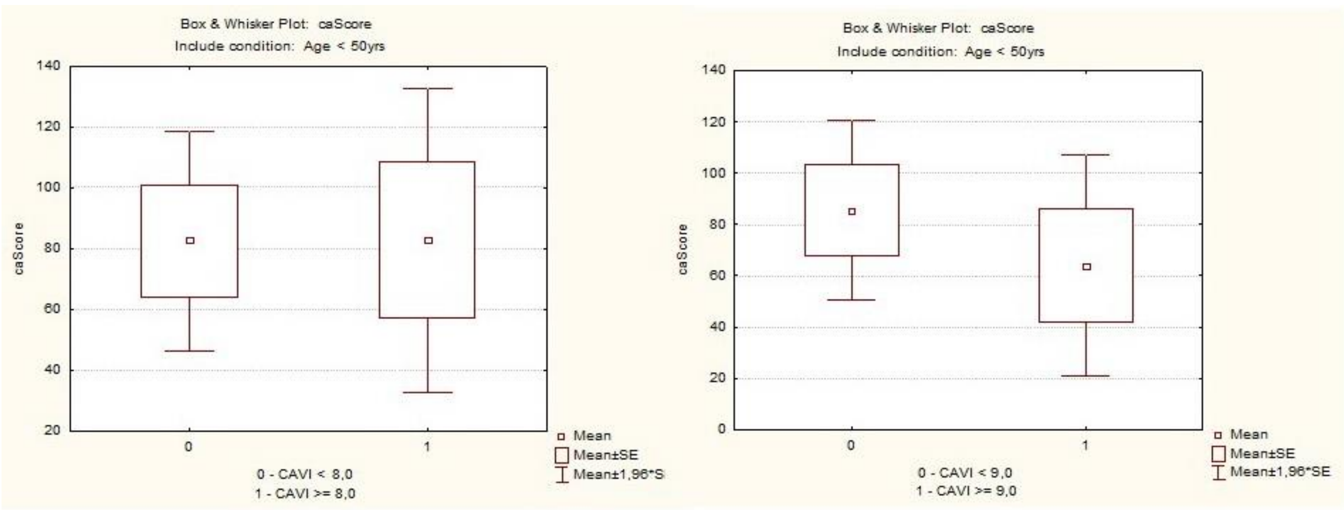


A
P=0,489

B
P=0,035

Figure 4. CAC score in groups with different CAVI values in subjects ≥50 years of age. A – groups with CAVI<8.0 vs. CAVI≥8.0; B – groups with CAVI<9.0 versus CAVI≥9.0.



A
P=0,795

B
P=0,343

Figure 5. CAC score in groups with different CAVI values in subjects <50 years of age. A – groups with CAVI<8.0 vs. CAVI≥8.0; B – groups with CAVI<9.0 versus CAVI≥9.0.

Discussion

We did not find a relationship between CAVI and CAC index when examining a population sample from southwestern Siberia. This was somewhat unexpected, since such dependence was previously observed in Asian countries [18-21]. Nevertheless, the CAC index values were higher in individuals with pathological CAVI values at the age of ≥50 years, but not in those under 50 years of age. Investigating the reason for such differences – whether it is the influence of geographic and ethnic factors or something else – requires analyzing previous publications.

Early studies of the kind examined patients with carbohydrate metabolic disorders. For example, examination of patients with diabetes and prediabetes revealed a relationship between elevated CAVI values and CAC score [19]. However, the correlation between CAVI and CAC score (r=0.167) was significantly weaker in this cohort than the correlation between CAVI and age (r=0.609) [19]. Mineoka Y et al. [18] demonstrated a more convincing correlation between CAVI and CAC in patients with type 2 diabetes mellitus, similar in strength to the relationship between CAVI and age. In addition, the relationship between CAVI and CAC was more pronounced in patients receiving insulin, in patients with poor glycemic control, and in presence of diabetic retinopathy and nephropathy. Why was it possible to identify the association between ABI and CAC index in patients with carbohydrate metabolism disorders, but not in our population sample? A possible explanation is the effect of diabetes mellitus on condition of peripheral arteries. A decrease in ABI below 0.9 leads to an equivalent decline in CAVI values; therefore, CAVI is not analyzed in such patients. However, it is precisely in the patients with ABI reduction to under 0.9, in whom significant calcification of the coronary arteries is noted more frequently [27]. Moreover, the patients with diabetes characteristically develop medial peripheral arterial calcification [28], and in such cases, ABI values obtained via volume plethysmography could be falsely elevated. In arterial calcification, ABI values greater than 1.3-1.4 are considered abnormal [29, 30]. Accordingly, some diabetic patients who developed peripheral atherosclerosis (and consequently have a greater CAC score) have an ABI exceeding 0.9. Therefore, they are not excluded from the CAVI analysis, increasing the association between CAVI and CAC score in diabetic patients.

Evaluation of asymptomatic participants [20] showed a relationship between CAVI and the presence of a pronounced CAC score (≥300) in a univariate logistic regression analysis. However, this relationship was no longer observed in multivariate analysis (corrected for gender, age, arterial hypertension, diabetes mellitus, and dyslipidemia). In our study, we were unable to detect statistically significant correlation between CAVI and CAC index for the entire population sample, only finding such association in people over 50 years old. Similar data were obtained in a study by Park et al. [20], in which CAVI was positively associated with severe coronary calcification in patients over 50 years old and inversely associated with subjects under 50 years of age. Since the share of younger patients (up to 50 years old) was quite large in our study, amounting to 55% of all participants, this could influence the association of CAVI with CAC score, leveling off this relationship for the entire sample.

Table 3. Univariate logistic regression (relation of CAC to CAVI)

Parameters	*OR (95% CI)*	*p-value*
Model 1. Minimum and average CAC (from 0 to 99)		
CAVI max	0.90 (0.8-1.02)	0.092
CAVI≥8.0	1.19 (0.78-1.2)	0.427
CAVI≥9.0	1.22 (0.69-1.82)	0.776
Model 2. Moderate and severe CAC (100 and above)		
CAVI max	1.20 (1.06-1.37)	0.004
CAVI≥8.0	0.68 (0.3923-1.14)	0.137
CAVI≥9.0	0.78 (0.36-1.67)	0.517
Model 3. Minimum CAC (0-9)		
CAVI max	0.78 (0.662-0.93)	0.004
CAVI≥8.0	1.76 (0.98-3.17)	0.059
CAVI≥9.0	1.45 (0.69-3.04)	0.327
Model 4. Average CAC (10-99)		
CAVI max	1.03 (0.90-1.17)	0.678
CAVI≥8.0	0.84 (0.51-1.40)	0.509
CAVI≥9.0	0.99 (0.87-1.14)	0.981
Model 5. Moderate CAC (100-399)		
CAVI max	1.28 (1.11-1.48)	0.0007
CAVI≥8.0	0.46 (0.23-0.93)	0.029
CAVI≥9.0	0.79 (0.29-2.22)	0.665
Model 6. Severe CAC (400 or more)		
CAVI max	1.01 (0.79-1.29)	0.946
CAVI≥8.0	1.29 (0.58-2.93)	0.527
CAVI≥9.0	0.84 (0.28-2.55)	0.764

CAVI, cardio-ankle vascular index; CAC, coronary artery calcium score.

Based on the results of our study, we propose the following. To begin with, since CAVI is easy to measure (the procedure does not require special training and provides high reproducibility) [31], such studies could be useful in routine clinical practice as a follow-up method. Also, further examination of CAVI association with CAC score in asymptomatic participants is advisable in patients of older age groups (with a minimum age of 45-50 years); in younger people, such association was neither identified in our research nor in previous studies. Finally, taking into account not only people with pathological CAVI values, but with ABI below 0.9 is reasonable while selecting a group for subsequent CAC score assessment. A simultaneous assessment of both CAVI and ABI values was proposed before, as these measurements are complementary; that is, early atherosclerosis is detected by CAVI, while ABI detects established and advanced atherosclerosis [32] and decreases the probability of missing patients who are likely to have higher CAC index values due to impossibility of determining CAVI. Finally, according to our data, the cutoff CAC score ≥9.0 should be used, which is higher than the CAVI threshold in previous studies (≥8.0) [19,20] but fully corresponds to the criteria of pathological CAVI proposed in a recent review [14]. CAVI ≥9.0 was also able to predict future cardiovascular events in patients with diabetes mellitus, along with a high CAC score [21]. However, whether it is possible to identify such pattern in asymptomatic participants, remains uncertain and requires further research.

There are various limitations to our study. First, it was cross-sectional in nature; therefore, it is unclear whether CAVI could affect the progression of CAC score; hence, future studies should assess these associations prospectively. Second, since the study was conducted at a single center, the possibilities for extrapolation of our findings are quite limited. Third, CAVI cutoff value of 9.0 could be not applicable to other population albeit it is proposed as optimal in a recent review [14]; while these values are suggested for Asian patients, we had to focus on them as there are no similar recommendations for Russian patients yet.

Conclusion

Elevated CAVI (≥9.0) was present in 9.7% of study participants included in a population sample from southwestern Siberia, and coronary artery calcification was discovered in 33.5% of the sample. While similar rates of minimum, mild, moderate and severe CAC scores were detected in participants with elevated and normal CAVI values, CAVI as a continuous variable was statistically significantly associated with moderate and severe CAC scores (OR 1.20, 95% CI 1.06-1.37, p=0.004). CAC score values were higher in patients ≥50 years of age with pathological CAVI values, but not in people under the age of 50 years. CAVI could probably be used as a feasible marker before assessing the CAC score in some asymptomatic Caucasian subjects, but identifying the most appropriate methods and participants, whom it could be clearly applicable to, requires further research.

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Conflict of interest

The authors declare no conflicts of interest. Funding providers had no role in designing the study; collection, analyses, or interpretation of data; writing the manuscript and the decision to publish the results.

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Appendix 1. Baseline characteristics according to CAVI (intermediate and pathological values vs. normal values)

Parameters	CAVI ≥8.0 (n=330)	CAVI <8.0 (n=986)	p
Male, n (%)	154 (46.53)	416 (42.15)	0.16
Age, years	57.0 (50.0; 60.0)	43.0 (34.0; 52.0)	<0.001
Family history of CVD, n (%)	215 (64.95)	588 (59.57)	0.082
Smoking, n (%)	87 (26.28)	312 (31.61)	0.067
Smoking history, years	36.0 (28.0; 42.0)	22.0 (15.0; 31.0)	<0.001
Physical inactivity, n (%)	98 (29.61)	370 (37.49)	0.009
Disability, n (%)	19 (5.47)	39 (3.95)	0.16
Working people, n (%)	198 (59.8)	795 (80.56)	<0.001
Height, cm; Me	166.8 (160.8; 173.0)	167.8 (160.5; 175.0)	0.069
Weight, kg; Me	78.95 (68.0; 89.4)	76.3 (64.1; 89.6)	0.03
BMI, kg/m^2	28.09 (24.99; 32.38)	26.79 (23.07; 31.48)	0.0005
Waist circumference, cm	95.5 (86.0; 105.0)	90.0 (80.0; 101.0)	<0.001
Hip circumference, cm	104.0 (98.0; 111.0)	102.0 (95.0; 110.0)	0.0011
Total cholesterol, µmol/L	5.34 (4.67; 6.09)	4.97 (4.27; 5.74)	<0.001
HDL cholesterol, µmol/L	1.63 (1.4; 1.92)	1.65 (1.4; 1.94)	0.89
LDL cholesterol, µmol/L	3.65 (3.02; 4.34)	3.28 (2.63; 3.99)	<0.001
Triglycerides, µmol / L	1.18 (0.86; 1.68)	1.01 (0.73; 1.47)	<0.001
Glucose, µmol/L	5.06 (4.6; 5.67)	4.84 (4.46; 5.27)	<0.001
Creatinine, µmol/L	71.45 (63.4; 77.8)	69.3 (63.8; 77.2)	0.17
Uric acid, µmol/L	0.31 (0.26; 0.35)	0.29 (0.24; 0.35)	0.01
Stroke, n (%)	12 (3.63)	12 (1.22)	0.0045
Diabetes, n (%)	19 (5.74)	21 (2.13)	<0.001
Bronchial asthma, n (%)	17 (5.14)	31 (3.14)	0.093
Renal disease, n (%)	95 (28.7)	231 (23.4)	0.053
Malignancy, n (%)	15 (4.53)	34 (3.44)	0.36
Hypertension, n (%)	171 (51.66)	211 (21.38)	<0.001

Values are presented as median (interquartile range) or a number (percentage), unless stated otherwise. CAVI, cardio-ankle vascular index; BMI, body mass index; HDL, high-density lipoprotein; LDL, low-density lipoprotein.

Appendix 2. Correlation analysis of CAVI with CAC in different age groups

Parameters	*Subjects 50 years of age and older (n=546)*		*Subjects under 50 years of age (n=770)*	
	r	p	r	p
Age	0.279	<0.000001	0.257	<0.000001
Male	-0.222	<0.000001	-0.161	0.000004
Physical activity	-0.049	0.230026	-0.023	0.532097
Smoking	0.111	0.008470	0.076	0.177363
Smoking history	0.237	0.000066	0.264	<0.000001
Diabetes	0.026	0.504333	0.023	0.496651
Hypertension	0.186	0.000002	0.109	0.001671
Waist	-0.003	0.923457	-0.028	0.412396
BMI	-0.150	0.000134	-0.090	0.009989
Total cholesterol	-0.021	0.595208	0.115	0.000983
Triglycerides	0.007	0.842296	0.033	0.333536
Glucose	0.061	0.122080	0.103	0.003185
CAC Score	0.001	0.976473	-0.010	0.754711

CAVI, cardio-ankle vascular index; CAC, coronary artery calcium.