Original Article

The Association Between the Cardio-ankle Vascular Index and Other Parameters of Vascular Structure and Function in Caucasian Adults: MARK Study

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Aim: We assessed whether there is an association between the cardio-ankle vascular index (CAVI) score and the carotid intima media thickness (IMT), the pulse wave velocity (PWV) and the central augmentation index (CAIx) that is independent of the subject's cardiovascular risk and pharmacological treatment.

Methods: The CAVI score was measured in 500 subjects using a VaSera device and the brachial ankle PWV (ba-PWV) was calculated. A carotid ultrasound was used to measure the IMT. A Mobil-O-Graph device was used to measure the carotid femoral PWV (cf-PWV) and the CAIx. The Framingham-D'Agostino and SCORE scales were used to measure the subject's cardiovascular risk.

Results: The mean value of the CAVI score was 8.59 ± 1.1 . IMT, CAIx and PWV maintained a positive association with the CAVI score ($p < 0.01$) in a multiple linear regression analysis, after adjusting for the subject's cardiovascular risk, body mass index and pharmacological treatment. The cut-off level that gave the maxima sensitivity and specificity to detect a mean IMT of > 0.90 mm was 8.95 (AUC=0.67) for the CAVI score, 8.85 (AUC=0.66) for cf-PWV and 15.10 (AUC=0.66) for ba-PWV. The cut-off to detect a maxima IMT of > 0.90 mm was 8.60 (AUC=0.62) for the CAVI score, 8.85 (AUC=0.64) for cf-PWV and 15.75 (AUC=0.70) for ba-PWV.

Conclusion: There was a positive association of the CAVI score with vascular structure and function parameters that was independent of cardiovascular risk and any medications being used by the subject. The ability of the CAVI score to predict carotid atherosclerosis is similar to that of cf-PWV and ba-PWV in Caucasian adults.

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Key words: Cardio-ankle vascular index (CAVI), Vascular structure, Vascular function, Cardiovascular risk

Introduction

The cardio-ankle vascular index (CAVI) is a new

measure of the overall stiffness of the artery from the origin of the aorta to the ankle¹, and it can be used to estimate the risk of atherosclerosis². Arterial stiffness

that is estimated using the CAVI score in healthy subjects increases linearly with aging, and the CAVI score is higher in men than in women³). In patients with risk factors such as hypertension, diabetes, hypercholesterolemia^{4, 5}, obesity⁶ and smoking⁷, the CAVI values are higher than in controls. A high CAVI score is associated with carotid and coronary atherosclerosis⁸⁻¹⁰ and is better at predicting coronary artery disease than brachial ankle pulse wave velocity (ba-PWV)^{11, 12}. Thus, the CAVI method is a useful tool for screening people with moderate to advanced levels of atherosclerosis¹³.

Evaluation of the vascular structure by measuring the carotid intima media thickness (IMT) and/or the presence of plaque is a good predictor of cardiovascular morbidity and mortality¹⁴. The vascular function evaluated with the carotid-femoral pulse wave velocity (cf-PWV) has been correlated with increased morbidity and mortality in both patients with cardiovascular disease and in healthy individuals^{15, 16}. The central augmentation index (CAIx) is an independent predictor of all-cause and cardiovascular mortality^{17, 18}.

There is much evidence supporting the relationship between the CAVI score and cardiovascular risk factors with the presence and evolution of atherosclerosis, but the great majority of studies have been done on Asian populations. The association between the CAVI score and vascular structure and function has not yet been well-studied in the Caucasian population.

Aim

The goal of this study was to assess whether the association between the CAVI score and carotid IMT, PWV and CAIx in adults is independent of the subject's cardiovascular risk and pharmacological treatment.

Methods

Study Design

This study analyzed data from 500 subjects who were included in the improving intermediate risk management (MARK) study (NCT01428934)¹⁹ which included an initial cross-sectional study and a secondary longitudinal study.

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Study Population

The study population consisted of subjects between 35 and 74 years of age who had an intermediate level of cardiovascular risk, defined as a coronary risk between five and 15% at 10 years according to the Framingham adapted risk equation²⁰, or as vascular mortality risk between 2-5% at 10 years according to the SCORE equation²¹. The exclusion criteria were terminal illness or institutionalization at the appointment time, or a personal history of atherosclerotic disease. The population sample was selected randomly from this age and risk group. Recruitment and data collection for the study were carried out from July 2011 to June 2013. A sample-size calculation indicated that the 500 patients included in the study constituted a sufficient sample for detecting a correlation coefficient of 0.125 between the CAVI score and IMT measurement in a two-sided test, with a significance level of 95% and a power of 80% (EPIDAT 4.0). The study was approved by an independent health care ethics committee at the University of Salamanca Hospital. All participants gave written informed consent according to the general recommendations of the Declaration of Helsinki²².

Measurements

Clinical data collection, anthropometric measurements and analytical parameter acquisition were performed according to previously published methods¹⁹.

Laboratory Determinations

Venous blood samples were obtained between the hours of eight and nine a.m. after the individuals had fasted and abstained from smoking, alcohol and caffeinated beverages for the previous 12 hours. The fasting plasma glucose, serum total cholesterol, high-density lipoprotein (HDL) cholesterol concentration and triglyceride concentration in the blood samples were measured using standard enzymatic automated methods. Low-density lipoprotein (LDL) cholesterol was estimated by the Friedewald equation when the direct parameter was not available. Blood samples were collected at the Alamedilla Health Center and analyzed at the Hospital of Salamanca. This was approved by the external quality assurance programs of the Spanish Society of Clinical Chemistry and Molecular Pathology.

Office Blood Pressure

Office blood pressure (BP) was calculated as the average of the last two of three measurements of systolic blood pressure (SBP) and diastolic blood pressure (DBP) made with a validated sphygmomanometer

(OMRON Model M10-IT). Measurements were made on the dominant arm of participants in the seated position after at least five minutes of rest using a cuff of appropriate size as determined by measurement of the upper-arm circumference and following the recommendations of the European Society of Hypertension²³.

Cardio-Ankle Vascular Index (CAVI) and ba-Pulse Wave Velocity

The CAVI was measured using a VaSera VS-1500® device (Fukuda Denshi). The CAVI measurement integrates cardiovascular elasticity derived from the aorta to the ankle pulse velocity through an oscillometric method, and it is used as an accurate measure of vascular stiffness that does not depend on blood pressure at the time of measurement^{1, 24}. The CAVI values were automatically calculated by substituting the stiffness parameter β in the following equation to detect the vascular elasticity: Stiffness parameter $\beta = 2\rho \times \ln/(P_s - P_d) \times \ln(P_s/P_d) \times PWV^2$, where ρ is the blood density, P_s and P_d are SBP and DBP in mm Hg, respectively, and PWV is the pulse wave velocity from the origin of the aorta to the tibial artery at the ankle through the femoral artery. The average coefficient of variation of the CAVI score is less than 5%, which is small enough for clinical use and confirms that CAVI has a favorable reproducibility²⁵. The CAVI score was measured at rest. Measurements were classified as normal (CAVI < eight), borderline (CAVI $\geq$ eight and < nine) or probable atherosclerosis (CAVI $\geq$ nine).

The ba-PWV was estimated using the following equation: $ba-PWV = (0.5934 \times \text{Height (cm)} + 14.4724) / t_{ba}$, where t_{ba} is the time difference between the time the pulse waves were transmitted to the brachium and the time the same waves were transmitted to the ankle²⁶. A ba-PWV ≥ 17.5 m/second was considered abnormal^{2, 27}. For this study, the higher obtained CAVI score and ba-PWV were considered.

cf-PWV and Central Augmentation Index (CAIx)

The cf-PWV and CAIx were estimated using an oscillometric Mobil-O-Graph (Stolberg, Germany)²⁸. The device was validated according to recommendations from the British Hypertension Society²⁹ and European Society of Hypertension³⁰. The measurements of central systolic blood pressure (cSBP) and peripheral systolic blood pressure (pSBP) were also taken on the dominant arm. Arm circumferences were measured and recorded to allow for the correct choice of cuff size (two sizes were available: 24–34 and 32–42 cm). With a conventional cuff, the determination of

the cSBP is based on an oscillometric BP measurement and uses the pulse waves assessed at the brachial artery. After the estimation of peripheral BPs, the cuff instantly reinflates, and recordings for cSBP are carried out at diastolic pressure levels for 10 seconds^{31, 32}. From the morphology of the aortic wave, CAIx was estimated using the following formula: the increase in central pressure $\times 100$ /pulse pressure. The value was adjusted to a heart rate of 75 by the Mobil-O-Graph device³². Subclinical organ damage was defined as a carotid–femoral PWV > 10 m/second^{33, 34}.

Assessment of Vascular Structure by Carotid IMT

In order to assess the carotid IMT before starting the study, a carotid ultrasound was performed by two investigators trained for this purpose. The reliability of such recordings was evaluated before the study using the intra-class correlation coefficient, which showed values of 0.97 (95% CI: 0.94 to 0.99) for intra-observer agreement on repeated measurements in 20 subjects, and 0.90 (95% CI: 0.74 to 0.96) for inter-observer agreement. According to the Bland-Altman analysis, the mean difference for inter-observer agreement (95% limits of agreement) was 0.01 (–0.03 to 0.06). A Sonosite Micromax ultrasound device paired with a 5–10 MHz multi-frequency, high-resolution linear transducer with the Sonocal software program was used for performing automatic measurements of IMT in order to optimize reproducibility. Measurements of the common carotid artery were made after the examination of a 10 mm longitudinal section at a distance of one cm from the bifurcation. Measurements were obtained from the proximal and distal wall, and from the lateral, anterior and posterior projections following an axis perpendicular to the artery to discriminate two lines: one for the intima-blood interface and the other for the media-adventitious interface. A total of six measurements were obtained from the right carotid, with another six measurements from the left carotid, using average values (average maxima IMT) automatically calculated by the software package³⁵. The measurements were obtained with the subject lying down, with the head extended and turned slightly opposite to the examined carotid artery. The average IMT was considered abnormal if the value was greater than 0.90 mm, if there were atherosclerotic plaques with a diameter of 1.5 mm, or if there was a focal increase of 0.5 mm or 50% of the adjacent IMT³⁴.

Cardiovascular Risk Assessment

The risk of cardiovascular morbidity and mortality was estimated using the published risk equation

Table 1. Baseline demographic and clinical characteristics of patients (*n* = 500)

	Mean/Median/Number <i>n</i>	SD/IQR/ (%)
Age (years)	60.3	8.4
Women, <i>n</i> (%)	228	45.6
Smoking, <i>n</i> (%)	117	23.4
Body mass index (kg/m ²)	27.8	25.3-30.3
Waist circumference (cm)	97.4	10.6
Obesity, <i>n</i> (%)	140	27.8
Office SBP (mm Hg)	134	17
Office DBP (mm Hg)	81	11
Heart Rate (beats/minute)	69	63-77
Hypertension, <i>n</i> (%)	401	80.2
Antihypertensive Drugs, <i>n</i> (%)	266	53.2
Fasting glucose (mg/dL)	89	82.0-99.0
HA1c (%)	5.7	5.4-6.0
Diabetes, <i>n</i> (%)	138	27.6
Antidiabeticdrugs, <i>n</i> (%)	82	16.4
Total cholesterol (mg/dL)	216.2	38.5
Triglycerides (mg/dL)	108.6	81.8-149.8
HDL-cholesterol (mg/dL)	53.5	44.8-63.9
LDL-cholesterol (mg/dL)	135.5	34.3
Dyslipidemian, <i>n</i> (%)	418	83.8
Lipid lowering drugs, <i>n</i> (%)	185	37.0
IMT average mean (mm)	0.74	0.09
IMT average mean > 0.90 mm, <i>n</i> (%)	75	15.0
IMT average máxima (mm)	0.90	0.12
IMT average máxima > 0.90 mm, <i>n</i> (%)	221	44.2
IMT average máxima > 1.00 mm, <i>n</i> (%)	88	17.7
IMT average máxima > 1.10 mm, <i>n</i> (%)	27	5.4
CAIx (%)	26.7	13.8
cf-PWV (m/second)	8.6	1.3
cf-PWV > 10 m/second, <i>n</i> (%)	74	15
ba-PWV (m/second)	14.2	12.7-16.2
ba-PWV > 17.5 m/second, <i>n</i> (%)	65	13.1
CAVI score	8.59	1.10
CAVI ≥ 9, <i>n</i> (%)	155	31.3
CVR Framingham-D'Agostino	20.1	13.3
SCORE scale	3.4	3.2

Values are means (standard deviations (SD) for normally distributed, continuous data and medians (interquartile range (IQR)) for asymmetrically distributed, continuous data and number and proportions for categorical data.

SBP: Systolic Blood Pressure. DBP: Diastolic Blood Pressure. HDL: High Density Lipoprotein. LDL: Low Density Lipoprotein. IMT: Intima-media thickness. CAIx: Central Augmentation Index. cf-PWV: carotid femoral Pulse Wave Velocity. ba-PWV: brachial ankle Pulse Wave Velocity. CAVI: Cardio-Ankle Vascular Index. CVR: Cardiovascular Risk. SCORE: Systematic Coronary Risk Evaluation.

(D'Agostino scale) based on the Framingham study³⁶). Risk factors for morbidity and mortality used by the D'Agostino scale include age, total cholesterol, HDL cholesterol and SBP as quantitative variables, as well as sex, drug treatment for hypertension, smoking and a history of diabetes mellitus as dichotomous variables.

Cardiovascular mortality risk was estimated using the Systematic Coronary Risk Evaluation (SCORE) scale²¹), including age, total cholesterol and SBP as quantitative variables, along with sex and smoking as dichotomous variables. With a history of diabetes mellitus, the risk increased three fold in men and five fold

Table 2. Values of vascular structure and function parameters grouped by CAVI value

Value of CAVI	≤ 8 (normal) 34.8%	Between 8-9 (borderline) 33.9%	≥ 9 (atherosclerosis probable) 31.3%	<i>p</i> -value
Age (year) **¥	53.9 ± 7.9	60.6 ± 6.8	65.5 ± 6.6	< 0.001
IMT average mean (mm) #¥	0.71 ± 0.09	0.73 ± 0.09	0.77 ± 0.10	< 0.001
IMT average maxima (mm) #¥	0.88 ± 0.11	0.89 ± 0.10	0.95 ± 0.12	< 0.001
CAIx (%) **	23.76 ± 14.49	28.02 ± 14.17	28.71 ± 12.14	0.002
cf-PWV (m/second) **¥	7.75 ± 1.12	8.70 ± 13.13	9.50 ± 1.08	< 0.001
ba-PWV (m/second) **¥	12.45 ± 1.38	14.22 ± 1.50	16.64 ± 2.28	< 0.001
CVR Framingham-D'Agostino **¥	15.44 ± 10.37	20.49 ± 13.20	25.06 ± 14.40	< 0.001
SCORE scale **¥	1.85 ± 1.99	3.42 ± 2.69	5.34 ± 3.80	< 0.001

IMT: Intima-media thickness. CAlx: Central Augmentation Index. cf-PWV: carotid femoral Pulse Wave Velocity. ba-PWV: brachial ankle Pulse Wave Velocity. CAVI: Cardio-Ankle Vascular Index. CVR: Cardiovascular Risk. SCORE: Systematic Coronary Risk Evaluation.

The *p*-values were determined by ANOVA test: **p* < 0.05 between normal and borderline; #*p* < 0.05 between normal and atherosclerosis; ¥*p* < 0.05 between borderline and atherosclerosis.

in women.

Anthropometric Measurements

Body weight was determined on two occasions using a homologated electronic scale (Seca 770) following calibration (precision ± 0.1 kg), with the patient wearing light clothing and no shoes. Height was measured with a portable system (Seca 222), recording the average of two readings. Body mass index (BMI) was calculated as weight (kg) divided by height squared (m²). Finally, waist circumference was measured using a flexible graduated measuring tape with the patient in the standing position without clothing. The individuals performing the measurements were blinded to the clinical data of the patient. All assessments were made within a period of 10 days.

Statistical Analysis

Continuous variables were expressed as the mean ± standard deviation for normally distributed continuous data, as the median (interquartile range) for asymmetrically distributed continuous data and as the frequency distribution for categorical data. The statistical normality was tested using the Kolmogorov-Smirnov test. A Pearson correlation was used to analyze the relationship between normally distributed continuous data. The difference of means between more than two categories of variables for normally distributed continuous data was subjected to an ANOVA using the Tukey method in post hoc contrasts with alpha less than 0.05. We performed multiple linear regression analyses with the CAVI score as the independent variable. The mean IMT, CAlx, cf-PWV and ba-PWV were the dependent variables. We adjusted for BMI, antihypertensive drugs, lipid-lowering drugs, antidia-

betic drugs and whether the Framingham-D'Agostino cardiovascular risk (model 1) or SCORE scale was used (model 2). Sensitivity and specificity with respect to the mean IMTs of >0.90 mm, and maxima IMTs of >0.90 mm, >1.00 mm and >1.10 mm were analyzed using a conventional receiver-operating-characteristic (ROC) curve. The data were analyzed using the Statistical Package for the Social Sciences version 20.0 software program (SPSS, Chicago, IL, USA). A value of *p* < 0.05 was considered statistically significant.

Results

A total of 500 patients were enrolled. **Table 1** shows the characteristics of cardiovascular risk factors, cardiovascular risk estimated with scales and the values of the parameters used for vascular structure and function. The mean CAVI value was 8.59 ± 1.10, and 31.3% of the subjects had a CAVI score greater than nine. The mean age was 60.30 ± 8.40 years, and 45.60% of the subjects were women.

Table 2 shows the values of age, mean IMT, cf-PWV, ba-PWV, CAlx and cardiovascular risk (Framingham-D'Agostino and SCORE) according to CAVI values (≤ eight, between eight and nine and ≥ nine). The values of all analyzed parameters directly increase with the increasing cut-off point of the CAVI score.

The average mean IMT and average maxima IMT showed positive correlation with the CAVI, ba-PWV, cf-PWV and CVR (*p* < 0.01). All analyzed parameters of vascular function and cardiovascular risk showed positive correlation with the CAVI score (*p* < 0.01) (**Table 3**).

In multiple linear regression analysis, the vascular

Table 3. Bivariate correlations of the CAVI score with vascular structure and function and RCV

	CAVI	IMT average mean (mm)	IMT average maxima (mm)
CAVI	---	0.291 **	0.282 **
CAIx	0.122 **	0.011	0.007
cf-PWV (m/second)	0.559 **	0.426 **	0.396 **
ba-PWV (m/second)	0.777 **	0.308 **	0.300 **
CVR Framingham-D'Agostino	0.300 **	0.429 **	0.415 **
CVR SCORE scale	0.458 **	0.440 **	0.428 **

IMT: Intima-media thickness. CAIx: Central Augmentation Index. cf-PWV: carotid femoral Pulse Wave Velocity. ba-PWV: brachial ankle Pulse Wave Velocity. CAVI: Cardio-Ankle Vascular Index. CVR: Cardiovascular Risk. SCORE: Systematic Coronary Risk Evaluation.

The *p*-values were determined by Pearson correlation. **p* < 0.05; ***p* < 0.01.

Table 4. Regression analysis with vascular structure and function parameters as the dependent variables and the mean CAVI score as the independent variable

	β	95% CI	<i>p</i> -value
Dependent variable: IMT average mean			
1. CAVI	2.392	1.344-3.441	< 0.001
2. CAVI	1.508	0.492-2.524	0.004
Dependent variable: IMT average maxima			
1. CAVI	2.027	1.082-2.973	< 0.001
2. CAVI	1.409	0.424-2.395	0.005
Dependent variable: CAIx			
1. CAVI	1.200	0.500-1.800	< 0.001
2. CAVI	0.800	0.200-1.400	0.011
Dependent variable: cf-PWV			
1. CAVI	0.440	0.374-0.505	< 0.001
2. CAVI	0.406	0.335-0.487	< 0.001
Dependent variable: ba-PWV			
1. CAVI	0.295	0.273-0.318	< 0.001
2. CAVI	0.291	0.259-0.304	< 0.001

Dependent variable: IMT: Intima-media thickness. CAIx: Central Augmentation Index. cf-PWV: carotid femoral Pulse Wave Velocity. ba-PWV: brachial ankle Pulse Wave Velocity.

Independent variable: CAVI: Cardio-Ankle Vascular Index.

Adjusted by: Model 1: Framingham-D'Agostino scale. Body mass index. Antihypertensive drugs. Lipid lowering drugs and antidiabetic drugs. or Model 2: SCORE scale. Body mass index. Antihypertensive drugs. Lipid lowering drugs and antidiabetic drugs.

structure and function parameters maintained a positive association with the CAVI score (*p* < 0.01) after adjusting for BMI, antihypertensive drugs, lipid-lowering drugs, antidiabetic drugs, and the use of the Framingham-D'Agostino (model 1) or SCORE scales (model 2) (**Table 4**).

The cut-offs that demonstrated better sensitivity and specificity for detection of a subclinical organic lesion defined by a mean carotid IMT of >0.90 mm were 8.95 with an area under the curve (AUC) of 0.67 for the CAVI score, 8.85 with an AUC of 0.66 for cf-

PWV and 15.10 with an AUC of 0.66 for ba-PWV. To detect a maxima IMT of >0.90 mm, the cut-offs were 8.75 with an AUC of 0.62 for the CAVI score, 8.85 with an AUC of 0.64 for cf-PWV and 15.75 with an AUC of 0.70 for ba-PWV. The respective cut-off levels, specificities, sensitivities and the areas under the curve are shown in **Fig. 1**.

The cut-offs that demonstrated better sensitivity and specificity for detection of a subclinical organic lesion defined by a carotid maxima IMT >1.10 mm were 8.74 with an AUC of 0.64 for the CAVI score,

Cut-Off Values and AUC of the Receiver-Operating-Characteristic for the Presence of: a: IMT mean > 0.90 mm; b: IMT maxima > 0.90 mm

Presence of carotid atherosclerosis IMT max > 0.90 mm						Presence of carotid atherosclerosis IMT max > 0.90 mm					
	Cut-off value	Sensitivity	Specificity	AUC (CI 95)	p Value		Cut-off value	Sensitivity	Specificity	AUC (CI 95)	p Value
CAVI	8.95	70%	64%	0.67 (0.57-0.77)	<0.01	CAVI	8.75	60%	59%	0.62 (0.57-0.67)	<0.01
cf-PWV	8.85	70%	60%	0.66 (0.55-0.77)	<0.01	cf-PWV	8.85	60%	62%	0.64 (0.59-0.69)	<0.01
ba-PWV	15.10	60%	60%	0.66 (0.55-0.78)	<0.01	ba-PWV	15.75	62%	70%	0.70 (0.66-0.75)	<0.01

AUC, area under the curve. IMT: Intima-media thickness. CAVI: Cardio-Ankle Vascular Index. cf-PWV: carotid femoral Pulse Wave Velocity. ba-PWV: brachial ankle Pulse Wave Velocity.

Fig. 1. The usefulness of the mean cardio-ankle vascular index (CAVI) score, carotid femoral pulse wave velocity (cf-PWV) and brachial ankle pulse wave velocity (ba-PWV) for discriminating the probability for a mean and maxima intima media thickness (IMT) of > 0.90 mm. Curves represent receiver-operating-characteristic (ROC) curves for discriminating the probability of carotid atherosclerosis. Each curve is defined by the mean CAVI score, cf-PWV and ba-PWV.

8.85 with an AUC of 0.66 for cf-PWV and 14.48 with an AUC of 0.59 for ba-PWV. For detection of a maxima IMT of > 1.00 mm, the cut-offs were 8.56 with an AUC of 0.58 for the CAVI score, 8.85 with an AUC of 0.67 for cf-PWV and 14.04 with an AUC of 0.61 for ba-PWV. The respective cut-off levels, sensitivities, specificities and the areas under the curve are shown in Fig. 2.

Discussion

The present study is the first report on the relationships between the CAVI score and various parameters used to assess vascular structure and function in Caucasian adults. The results show that the CAVI score was positively correlated with vascular structure and function, independent of the subject's cardiovascular risk and drug treatment. The cut-offs that are

more sensitive and specific in view of predicting carotid atherosclerosis with a mean IMT of > 0.90 mm are 8.95 for the CAVI score, 8.85 m/second for cf-PWV and 15.10 m/second for ba-PWV.

Consistent with the results of this study, there are several reports showing that the CAVI score is positively correlated with the carotid IMT and cf-PWV in hypertensive patients^{9, 37, 38}, in type 2 diabetes mellitus patients³⁹, in coronary artery disease patients^{5, 8}, and in the general population⁴⁰. These results suggest that the CAVI score is a useful clinical marker for evaluating atherosclerosis. Kadota *et al.* suggested the use of the CAVI score as a screening tool for atherosclerosis based on their findings in a general population study of 1014 adults⁴⁰. They showed a strong, significant association of the CAVI score with carotid IMT.

Similarly, we found an association between the

Cut-Off Values and AUC of the Receiver-Operating-Characteristic for the Presence of IMT maxima >1.10mm and IMT maxima >1.0mm

Presence of carotid atherosclerosis IMT max > 1.10 mm						Presence of carotid atherosclerosis IMT max > 1.0 mm					
	Cutt-off value	Sensitivity	Specificity	AUC (CI 95)	p Value		Cutt-off value	Sensitivity	Specificity	AUC (CI 95)	p Value
CAVI	8.74	60%	57%	0.64 (0.54-0.73)	0.021	CAVI	8.56	55%	50%	0.58 (0.51-0.65)	0.016
cf-PWV	8.85	72%	60%	0.66 (0.55-0.77)	<0.01	cf-PWV	8.85	66%	63%	0.67(0.60-0.73)	<0.01
ba-PWV	14.48	60%	56%	0.59 (0.49-0.69)	0.142	ba-PWV	14.04	64%	51%	0.61(0.57-0.68)	<0.01

AUC, area under the curve. IMT: Intima-media thickness. CAVI: Cardio-Ankle Vascular Index. cf-PWV: carotid femoral Pulse Wave Velocity. ba-PWV: brachial ankle Pulse Wave Velocity.

Fig. 2. The usefulness of the mean cardio-ankle vascular index (CAVI) score, carotid femoral pulse wave velocity (cf-PWV) and brachial ankle pulse wave velocity (ba-PWV) for discriminating the probability for a maxima intima media thickness (IMT) of >1.10 mm. and >1.00 mm. Curves represent receiver-operating-characteristic (ROC) curves for discriminating the probability of carotid atherosclerosis. Each curve is defined by the mean CAVI score, cf-PWV and ba-PWV.

CAVI score and PWV. Atherosclerosis has been estimated using the cf-PWV¹⁵⁾, but this can be influenced by BP, and it is not very reproducible^{1, 24)}. Because the CAVI score is independent of BP, highly reproducible, easy to apply and does not require special techniques, the potential of the CAVI score as a novel parameter of atherosclerosis has recently been recognized²⁾. Izuara *et al.* suggested that the CAVI score reflects systemic arterial sclerosis, including carotid atherosclerosis as well as coronary atherosclerosis, and that the CAVI score might be more useful for discriminating the probability of coronary atherosclerosis than the finding of carotid atherosclerosis by high-resolution cf-PWV.⁸ Another study also showed that the CAVI score might be more useful for discriminating the probability of coronary atherosclerosis than findings of carotid atherosclerosis¹⁰⁾.

Assessment of CAIx is a simple approach to

quantify the role of wave reflection in determining an elevation of the central BP value^{6, 41)}. The relationship between CAIx and the CAVI score opens new lines of research. This study determined the cut-off values of the CAVI score, cf-PWV and ba-PWV for predicting mean or maxima IMTs of >0.90 mm. CAVI values were found to be similar to those described by other authors⁴²⁾ or recommended in clinical practice guidelines in the case of cf-PWV. These results suggest that the CAVI score predicts carotid atherosclerosis in Caucasian adult patients, and may be helpful in clinical practice in this patient group.

Limitations

The main limitation associated with this study was the source of the data for the cross-sectional study, which prevented us from establishing a temporal rela-

tionship between the CAVI score and the different parameters that assess vascular function and structure during one week. However, this is the first study to examine the relationship between the CAVI score and different vascular structure and function parameters in adults.

Conclusion

The CAVI score shows a positive association with vascular structure and function parameters independent of the subject's cardiovascular risk and drug treatment, and the ability of the CAVI score to predict carotid atherosclerosis is similar to that of cf-PWV and ba-PWV in Caucasian adults. Therefore, like other parameters, the CAVI method could be a useful tool to screen people for atherosclerosis.

Conflict of Interests

The authors declare that they have no conflicts of interest.

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