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Cardio-Ankle Vascular Index is a Candidate Predictor of Coronary Atherosclerosis

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Background Recently, arterial stiffness parameter called cardio-ankle vascular index (CAVI) has been developed. In the current study, using coronary angiographic (CAG) findings, the usefulness of CAVI as a marker of the severity of coronary atherosclerosis was compared with that of carotid atherosclerosis parameters obtained from high-resolution B-mode ultrasonography.

Method and Result A total of 109 participants who underwent CAG were enrolled in the current study. They were divided into 4 groups according to the number of stenotic vessels on CAG; no lesion (0VD), 1-vessel (1VD), 2-vessel (2VD) and 3-vessel (3VD) groups. CAVI was significantly higher in 1VD group compared with the 0VD group ($p<0.05$), and was significantly higher in 2VD and 3VD group compared with the 1VD group. In single regression analysis, CAVI correlated positively with maximum intima-media thickness (IMT) ($p<0.01$) and plaque score ($p<0.0001$). A stepwise ordinal logistic regression analysis using mean IMT, maximum IMT, plaque score and CAVI as independent variables identified only CAVI as positively related to the severity of coronary atherosclerosis. The area under the receiver operating characteristic curve defined by CAVI was the greatest.

Conclusion CAVI might be more useful for discriminating the probability of coronary atherosclerosis than findings of carotid atherosclerosis by high-resolution B-mode ultrasonography. (*Circ J* 2008; **72:** 598 – 604)

Key Words: Arterial stiffness; Cardio-ankle vascular index; Coronary atherosclerosis; Intimal thickness; Stiffness parameter

Arteriosclerosis is a major contributor to cardiovascular disease, accounting for a high percentage of mortality and morbidity[1,2] The degree of atherosclerosis in the coronary artery is almost precisely evaluated by coronary angiography (CAG). Several non-invasive tests are known to be associated with the CAG findings. Among them, the diagnosis of carotid atherosclerosis by high-resolution B-mode ultrasonography has been reported to be an independent predictor of coronary heart disease[3,4]

The pulse wave velocity (PWV) and the stiffness parameter β evaluated by the change in diameter of the vessel wall are also used as predictors of coronary atherosclerosis[5,6] The problem of PWV in clinical use is that PWV itself essentially depends on blood pressure. Although Hasewgawa et al[7] established the aortic PWV method, which is independent on blood pressure, this method had several drawbacks, such as difficulty to find the notch of the pulse wave, requirement of some technical skill, and low reproducibility. The stiffness parameter β is based on the change of vascular diameter corresponding to arterial pressure variance[8,9] and the value does not depend on blood pressure[10] However, there are also some problems: β indicates the local property of a segment of the artery and the method requires special ultrasonic equipment.

Recently, arterial stiffness parameter called cardio-ankle vascular index (CAVI) has been developed, as a marker related arteriosclerosis including the aorta, femoral artery and tibial artery[11] CAVI is independent of blood pressure, and has adequate reproducibility for clinical use[11] Furthermore, no special technique is required for the measurement of CAVI. Several reports have shown the usefulness of CAVI for the detection of atherosclerotic diseases[11–13]

In the present study, using CAG findings, we evaluated the usefulness of CAVI as a marker of the severity of coronary atherosclerosis compared with carotid atherosclerosis parameters obtained from high-resolution B-mode ultrasonography.

Methods

Subjects

Between April 2006 and December 2006, 163 consecutive subjects underwent CAG for the evaluation, follow-up, or treatment of coronary artery disease (CAD) at Sakura Medical Center, Toho University, Japan. All subjects were examined with CAVI measurement and high-resolution B-mode ultrasonography of the carotid arteries before the CAG. As a result, 109 subjects were enrolled in the current study. These subjects were divided into 4 groups according to the severity of coronary atherosclerosis on the basis of CAG findings. The first group (0VD group) had no significant stenotic lesion. The second group (1VD group) had significant stenosis in 1 vessel. The third group (2VD group)

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Table 1 Baseline Data of the Study Population

	Category of coronary angiographic findings			
	0VD group	1VD group	2VD group	3VD group
n (M/F)	26 (21/5)	35 (32/3)	30 (26/4)	18 (16/2)
Age (year, mean±SD)	58.0±11.4	60.1±8.2	67.6±7.3**	65.9±9.0*
BMI (kg/m^2)	25.1±3.6	24.8±3.7	23.3±2.3	23.3±2.8
Systolic-BP (mmHg)	132.2±17.1	130.4±16.5	135.3±20.4	138.1±19.4
Mean-BP (mmHg)	95.8±13.8	95.1±14.5	97.3±14.9	99.7±12.4
Pulse pressure (mmHg)	54.3±10.5	55.8±10.7	58.7±20.1	60.2±16.4
HbA$_{1c}$ (%)	5.77±0.91	6.57±1.92	6.60±1.28	6.23±0.98
TC (mg/dl)	198.3±63.1	192.1±33.0	183.7±29.3	172.7±53.2
TG (mg/dl)	168.6±80.1	127.4±71.3	134.6±81.5	159.7±79.4
HDL-C (mg/dl)	52.2±11.3	48.5±10.3	47.3±12.4*	39.3±11.8**
LDL-C (mg/dl)	129.1±38.6	117.2±33.7	107.0±25.2	107.5±26.5
Uric acid (mg/dl)	5.4±1.6	5.9±1.6	5.6±1.2	6.6±1.2
Incidence: n (%)				
Obesity	13 (50%)	16 (46%)	9 (31%)	5 (28%)
Hypertension	11 (42%)	23 (66%)	23 (77%)	13 (73%)
Hyperlipidemia	16 (61%)	20 (57%)	16 (53%)	10 (55%)
Diabetes mellitus	8 (31%)	11 (31%)	15 (50%)	11 (61%)
Smoking	15 (58%)	22 (62%)	17 (57%)	11 (61%)
History of CAD	0 (0%)	15 (43%)*	20 (67%)**	13 (72%)**
AP	0	8 (23%)	15 (50%)	10 (55%)
OMI	0	4 (11%)	2 (7%)	0
CABG	0	1 (3%)	3 (10%)	3 (17%)
Lipid-lowering drugs (all statins): n (%)	5 (20%)	10 (29%)	12 (40%)	7 (39%)
BP-lowering drugs: n (%)	7 (25%)	12 (35%)	13 (43%)	9 (48%)
ARB/ACEI	4 (15%)	8 (23%)	10 (33%)	6 (33%)
Ca-blocker	5 (19%)	8 (23%)	7 (23%)	4 (22%)
β-blocker	1 (4%)	3 (9%)	5 (17%)	3 (17%)

Data are presented as mean±SD or number (%) of subjects.
0VD, no lesion; 1VD, 1-vessel disease; 2VD, 2-vessel disease; 3VD, 3-vessle disease; BMI, body mass index; BP, blood pressure; HbA$_{1c}$, glycosylated hemoglobin; TC, total cholesterol; TG, triglycerides; HDL-C, high-density lipoprotein-cholesterol; LDL-C, low-density lipoprotein-cholesterol; CAD, coronary artery disease; AP, angina pectoris; OMI, old myocardial infarction; CABG, coronary artery bypass grafting; statin, HMG-CoA reductase inhibitor; ARB, angiotensin receptor antagonist; ACEI, angiotensin-converting enzyme inhibitor.
**p<0.05, **p<0.01 vs 0VD.*

had significant stenosis in 2 vessels. The fourth group (3VD group) had significant stenosis in 3 vessels. The clinical profile of the subjects is shown in Table 1. The following subjects were excluded because these conditions can affect CAVI independent of ischemic status, and were known to influence arterial stiffness: very old patients (over 80 years; n=5), had impaired renal function (serum creatinine concentration >1.5 mg/dl; n=2), chronic atrial fibrillation (n=2), valvular heart disease (moderate or severe; n=2), decreased left ventricular function (ejection fraction <50%; n=5), peripheral arterial disease defined as ankle brachial index (ABI) <0.9 (n=8) and acute coronary syndrome, including acute myocardial infarction (n=30), were excluded because these subjects were not examined with CAVI measurement in emergency cases. Details of excluded subjects are shown in Table 2. The present study was approved by the institutional review board. The purpose of this study was explained to the subjects, and consent was obtained for participation in the study and also for release of the study data.

Table 2 Details of Excluded Subjects

	n
Impaired renal function	2
Chronic atrial fibrillation	2
Valvular heart disease (moderate or severe)	2
Very old patients (over 80 years)	5
Left ventricular dysfunction (ejection fraction <50%)	5
Peripheral arterial diseases (ABI <0.9)	8
Acute coronary symdrom	30
Unstable AP	7
Acute myocardial imfarction	23

Date are number of subject.
ABI, ankle brachial index.

Measurement of Body Weight and Blood Pressure

Body weight and blood pressure were measured in the morning after 12 h of fasting. Blood pressure was measured at least twice in a sitting position.

Assay of Glycosylated Hemoglobin (HbA$_{1c}$), Serum Lipids and Uremic Acid

Blood samples were collected in the morning after 12 h of fasting. Serum was separated within 1 h, and samples were used for the measurements of the following chemical parameters. HbA$_{1c}$, including stable and unstable fractions, was measured by high pressure liquid chromatography with the Hi-Auto A$_{1c}$ kit (Kyoto Daiichi Kagaku, Kyoto, Japan). Data of the stable type were used in the present analysis. Total cholesterol (TC), triglyceride (TG), low-density lipoprotein-cholesterol (LDL-C), uric acid (UA) and serum creatinine were measured with an automatic analyzer (Hitachi 7150 available from Hitachi, Tokyo, Japan). High-density lipoprotein-cholesterol (HDL-C) was measured by the selective inhibition method (Daiichi Pure Chemicals, Tokyo, Japan)[14]

Examination of Coronary Risk Factors

Patients were examined for coronary risk factors including age, smoking, hypertension, hyperuricemia, diabetes mellitus, hypercholesterolemia, high LDL-C, hypertriglyceridemia, low HDL-C, obesity and a history of CAD. Smoking was recorded as positive in the case of current or a past history of cigarette smoking. Hypertension was defined as a history of hypertension (systolic pressure ≥140 mmHg or diastolic pressure ≥90 mmHg). Hyperlipidemia was defined as a history of high TC (≥220 mg/dl), high LDL-C (≥140 mg/dl) and/or high TG (≥150 mg/dl). A history of CAD was defined as documentation of medication and history of myocardial infarction, angina pectoris, and/or previous coronary intervention confirmed by reviewing the medical records. Obesity was defined as body mass index (BMI) ≥25.

Measurement of CAVI

CAVI was measured with a VaSera CAVI instrument (Fukuda Denshi Co Ltd, Tokyo) by the methods described previously![11] Briefly, cuffs were applied to bilateral upper arms and ankles, with the subject lying supine and the head held in midline position. After resting for 10 min, the examinations were performed. To detect the brachial and ankle pulse waves with cuffs, a low cuff pressure from 30 to 50 mmHg was used to ensure minimal effect of cuff pressure on hemodynamics. Furthermore, blood pressure was measured thereafter. Finally, for the convenience of comparison with the PWV, scale conversion was performed. CAVI was calculated by the following formula:

$$\mathrm{CAVI} = a\{(2\rho/\Delta P) \times \ln(Ps/Pd)PWV^2\} + b,$$

where Ps is systolic blood pressure, Pd is diastolic blood pressure, PWV is pulse wave velocity, ΔP is Ps– Pd, ρ is blood density, and a and b are constants.

Blood pressure is obtained by the cuff of the upper arm. PWV is obtained by dividing the vascular length by the time for which the pulse wave is propagated from the aortic valve to the ankle. It is measured by cuffs of upper arms and ankles. To be compatible with the aortic PWV method established by Hasegawa and coworkers[7], scale conversion constants (a, b) are determined so as to match CAVI with the aortic PWV method. By scale conversion constants, massive previous data of PWV could be converted to CAVI. All these measurements and calculation system were equipped together and automatically calculated in the VaSera. The average coefficient of variation of CAVI is less than 5%, which is small enough for clinical usage and indicates that CAVI has good reproducibility![14]

Angiographycal Study

Selective CAG was performed using a trans-femoral approach or trans-radial approach. Two experienced angiographers reviewed all coronary angiograms. The severity of coronary stenosis was assessed in the worst view projection. The percentage of luminal narrowing was recorded according to the American Heart Association criteria![15] Significant stenosis was defined as narrowing of 75% or more of the vessel diameter. The severity of CAD was based on the number of stenotic coronary vessels. Angiographers who evaluated the CAG for stenosis were blinded to all clinical data of the subjects.

Measurement of Intimal Wall Thickness of Carotid Artery

Duplex carotid ultrasonography was performed with the linear-array 7.5-MHz transducers (EUB-525, Hitachi, Inc, Tokyo, Japan; SSA-260A, Toshiba, Inc, Tokyo, Japan). Intima-media thickness (IMT) was measured as reported previously![16] Briefly, a region of approximately 1.5 cm proximal to the flow divider in the common carotid artery was identified, and far-wall IMT was evaluated as the distance between the luminal-intimal interface and the medial-adventitial interface. When an optimal image was obtained, it was frozen in the end-diastolic phase to minimize variability during the cardiac cycle. IMT was measured twice bilaterally from 4 contiguous sites approximately 5 mm and 10 mm proximal to the dilatation of the common carotid artery. The highest IMT value (max IMT) and the mean IMT were used.

Plaque score was calculated as reported previously![17] Briefly, plaques (localized increases in IMT ≥1.1 mm) were detected by cross-sectional and longitudinal scanning of bilateral common and internal carotid arteries. Plaque score was computed by summing up the maximum thickness (in mm) of each plaque located in bilateral carotid arteries.

All measurements of common carotid artery IMT were performed as a part of the routine clinical work-up by the same technician, and all evaluations were done by the same clinician. They were blinded to all clinical data of the subjects.

Statistical Analysis

Comparison between groups was performed using Student's t-test. Data were subjected to one-way ANOVA with Dunnett's multiple comparison of means. Mean IMT, MaxIMT, Plasque score, and CAVI adjusted for age was calculated per groups using analyses of covariant. The relationship between CAVI and various clinical parameters was analyzed using simple regression analysis. To select significant risk factors associated with the severity of coronary atherosclerosis, multivariate analysis was performed using ordinal logistic regressions analysis with stepwise forward selection method. Sensitivity and specificity with respect to the severity of coronary atherosclerosis were analyzed using a conventional receiver-operating-characteristic (ROC) curve. In all comparisons, values of p less than 0.05 were considered statistically significant. Statistical analysis was performed with SPSS 11.01.1 Statistical Package for Windows.

Results

Comparison of Clinical Characteristics Between Groups

The clinical characteristics of the 4 groups are shown in Table 1. Age was significantly higher in 2VD and 3VD groups than in the 0VD group. The proportion of patients who had a history of ischemic heart disease increased significantly with an increase in number of stenotic vessels. HDL-C tended to decrease with an increase in number of stenotic vessels, with significant differences in the 2VD and 3VD groups. Other characteristics did not differ significantly between groups.

Relationship Between CAG Findings and CAVI or Carotid Atherosclerosis

Mean IMT did not differ significantly between the 4 groups (Fig 1A). Max IMT and plaque score were significantly greater in 1VD, 2VD and 3VD groups compared with the 0VD group, but were not significantly different between 1VD, 2VD and 3VD groups (Figs 1B,C). CAVI

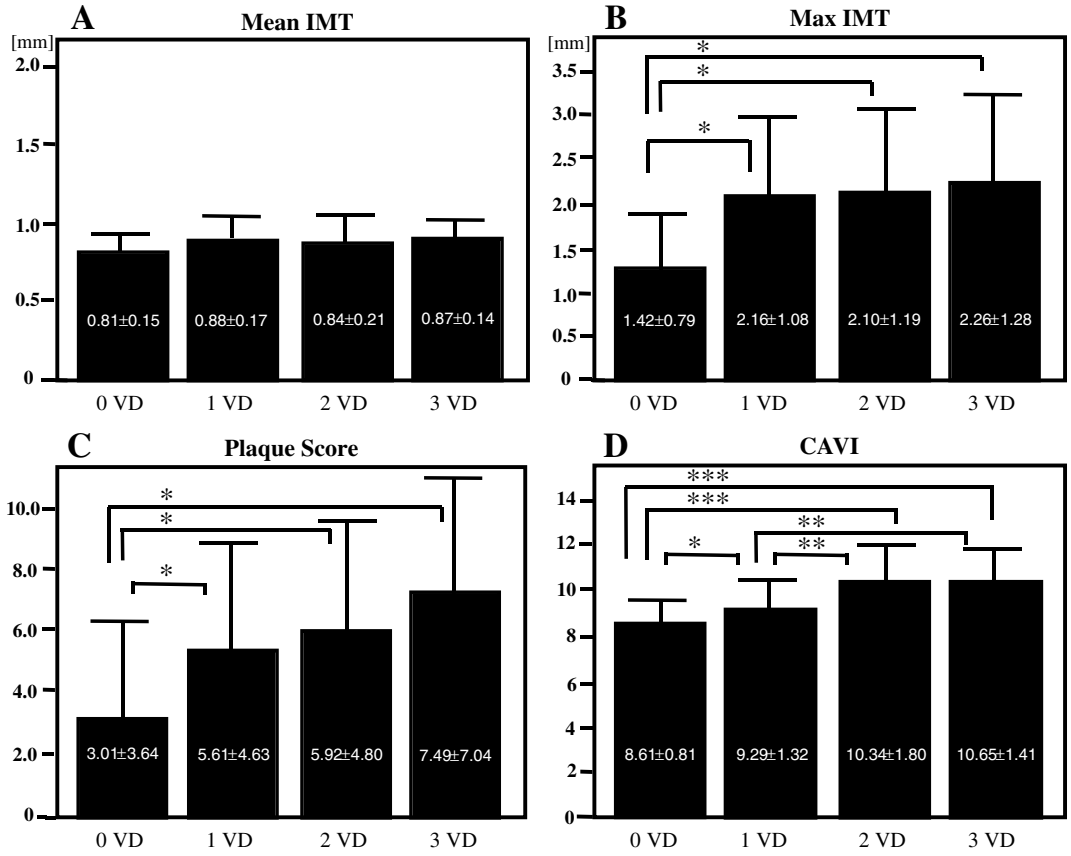

Fig 1. Relationship between coronary angiographic findings and cardio-ankle vascular index (CAVI) or carotid atherosclerosis parameters obtained from B-mode ultrasonography. Graph A, B, C and D show mean intima-media thickness (IMT), max IMT, plaque score and CAVI, respectively. 0VD, no lesion; 1VD, 1-vessel disease; 2VD, 2-vesel disease; 3VD, 3-vessel disease. Data are shown as mean ± SD, adjusted for age. *p<0.05, **p<0.01, ***p<0.001.

was significantly higher in 1VD group compared with the 0VD group (p<0.05), and was significantly higher in 2VD or 3VD group compared with the 1VD group (Fig 1D).

Correlation Between CAVI and Clinical Parameters

To clarify the correlation between CAVI and various clinical parameters, simple regression analyses were performed as the dependent variable (Table 3). Age, systolic blood pressure, pulse pressure, max IMT, and plaque score correlated positively with CAVI. However, no significant correlation was observed between CAVI and mean IMT, BMI, TC, TG, HDL-C, LDL-C, or UA.

Ordinal Logistic Regression Analysis With Stepwise Forward Selection Method of the Association Between Variables and CAD Findings

Results of the stepwise multiple ordinal logistic regression analysis of the relationship between coronary risk factors and CAG findings are summarized in Table 3. CAVI, HbA_{1c} and a history of CAD were positively related to the severity of coronary atherosclerosis (Table 4). Age, mean IMT, max IMT and plaque score were not significantly related.

ROC Curve for the Presence of CAD

The ROC curves of CAVI, mean IMT, plaque score and max IMT were examined. The ROC curves show the fraction of true-positive results (sensitivity) and false-positive results (1-sensitivity) for various cutoff levels of each parameter. The cutoff levels that gave the maximal sensitivity and specificity for CAVI, plaque score, max IMT and mean IMT were 8.8, 3.7, 1.7 mm and 1.0 mm, respectively. The ROC curves of the 4 parameters at these optimal cutoff levels are shown in Fig 2. At the respective cutoff levels, the sensitivities for CAVI, plaque score, max IMT and mean IMT were 82%, 69%, 65% and 31%, respectively, and the specificities were 76%, 85%, 80% and 90%, respectively (Table 5).

Table 3 Correlation Between CAVI and Various Clinical Parameters Analyzed by Simple Linear Regression Analysis

	r	*p value*
CAVI		
vs Age	*0.454*	*<0.0001*
vs BMI	*–0.179*	*NS*
vs Systolic-BP	*0.219*	*<0.05*
vs Mean-BP	*0.182*	*NS*
vs Pulse pressure	*0.258*	*<0.01*
vs Mean IMT	*0.181*	*NS*
vs Max IMT	*0.276*	*<0.01*
vs Plaque score	*0.406*	*<0.0001*
vs TC	*0.019*	*NS*
vs TG	*–0.063*	*NS*
vs HDL-C	*–0.169*	*NS*
vs LDL-C	*0.127*	*NS*
vs Uric acid	*0.065*	*NS*

CAVI, cardio-ankle vascular index; IMT, intima-media thickness. Other abbreviations see in Table 1.

Table 4 Ordinal Logistic Regression Model on Number of Vessels

Independent variable	*Regression coefficient*	*Standard error*	*t-value*	*p value*
CAVI	*–0.646*	*0.1738*	*12.50*	*<0.0001*
History of CAD [0:(–), 1:(+)]	*1.0093*	*0.2676*	*14.22*	*<0.0001*
HbA1c	*–0.3414*	*0.1616*	*4.46*	*0.0288*
Age	*0.0013*	*0.0283*	*0.00*	*0.9641*
Final model				
CAVI	*–0.6117*	*0.1578*	*15.05*	*<0.0001*
History of CAD [0:(–), 1:(+)]	*1.0062*	*0.2627*	*14.67*	*<0.0001*
HbA1c	*–0.340*	*0.1612*	*4.47*	*0.0344*

Not accepted variables (p<0.1) were age, BMI, mean IMT, max IMT, plaque score, hypertension [0:(–), 1:(+)], hyperlipidemia [0:(–), 1:(+)], diabetes smoking, TC, TG, LDL-C, uric acid, HbA1c.
Abbreviations see in Tables 1,3.

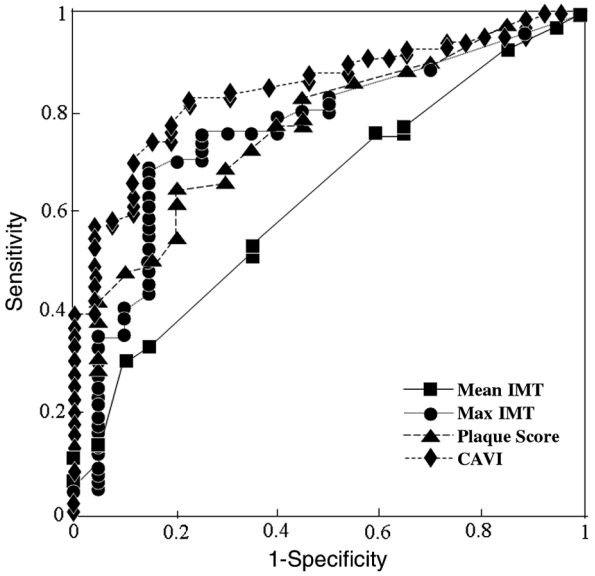

Fig 2. Usefulness of mean intima-media thickness (IMT), max IMT, plaque score and cardio-ankle vascular index (CAVI) for discriminating the probability for coronary atherosclerosis. Curves represent receiver-operating-characteristic (ROC) curves for discriminating the probability for coronary atherosclerosis. Each curve is defined by mean IMT (■), max IMT (●), plaque score (▲) or CAVI (◆). The ROC area defined by CAVI is the greatest among these 4 parameters.

Discussion

Recently, arterial stiffness parameter called CAVI that reflect arteriosclerosis has been developed as a non-invasive and easy technique for the diagnosis of atherosclerosis. Shirai et al have reported that CAVI is independent of blood pressure and has adequate reproducibility for clinical use, and that CAVI is high in patients with hemodialysis![11] Kubozono et al have shown that CAVI is associated with coronary risk factors. These reports suggest that CAVI is related to coronary atherosclerosis![13] However, the relationship between CAVI and coronary atherosclerosis has not been documented. In the present study, we found that the magnitude of CAVI might be associated with the severity of coronary atherosclerosis. These results indicate that high risk group of coronary atherosclerosis might be differentiated by CAVI.

CAVI is also known to correlate positively with age![13] In fact, in the present study, CAVI correlated positively with age. However, after adjustment for age in a result of analyses of covariant, the higher values of CAVI in 1VD, 2VD and 3VD compared with 0VD were unrelated to age. Therefore, results of the stepwise ordinal logistic regression analysis showed no significant correlation between age and CAG findings despite a significant correlation between CAVI and CAG findings. The diagnosis of carotid atherosclerosis by high-resolution B-mode ultrasonography has also been reported to be an independent predictor of coronary heart disease;[3,4] and this method has become popular as a routine test. Carotid atherosclerosis detected by this method is mainly evaluated by mean IMT, max IMT or plaque score. In this study, we compared CAVI and the above carotid atherosclerosis parameters to examine which is the important indicator for the severity of coronary atherosclerosis. Max IMT, plaque score and CAVI showed a significant correlation with severity of coronary atherosclerosis (Fig 1), but no significant correlation was observed between mean IMT and severity of coronary atherosclerosis. By stepwise ordinal logistic regression analysis, however, only CAVI among these factors was associated with severity of coronary atherosclerosis (Table 4). These results indicate that CAVI might indicate the severity of coronary atherosclerosis. It is reported that atherosclerotic change of aorta precede coronary atherosclerosis, and carotid atherosclerosis follows coronary atherosclerosis![18,19] These reports might explain the reason why CAVI is a more important indicator for discriminating the probability of coronary atherosclerosis than findings of carotid atherosclerosis, because CAVI mainly reflects the atherosclerotic change of aorta. Actually, patients with high max IMT and plaque score frequently had a history of CAD (data not shown). Therefore, max IMT and plaque score might be more useful as predictors for secondary prevention of CAD rather

Table 5 Cut-Off Values and AUC of the Receiver-Operating-Characteristic for the Presence of CAD

	Cut-off value	*Sensitivity*	*Specificity*	*AUC (SE)*	*p value*
CAVI	*8.81*	*83.90%*	*70%*	*0.775 (0.069)*	*0.001*
Plaque score	*2.95*	*74.20%*	*70%*	*0.741 (0.073)*	*0.004*
Max IMT	*1.35*	*74.20%*	*65%*	*0.759 (0.071)*	*0.003*

AUC, area under the curve. Other abbreviations see in Tables 1,3.

than for primary prevention. Other studies reported artrial stiffness was significantly higher and vascular endothelial function was significantly lower in severely obese children with insulin resistance than in controls, conversely IMT did not change?[20,21] This result might indicate that impairment of nitric oxide-dependent vascular relaxation, endothelial dysfunction is already present in severely obese children and is related to indices of insulin resistance, arterial stiffness and vascular endothelial dysfunction might be an early step in the development of atherosclerosis than increased IMT. This result might also explain the reason why CAVI reflects coronary atherosclerosis than findings of carotid atherosclerosis. Furthermore, ROC analysis of mean IMT, max IMT, plaque score and CAVI showed that the area under the ROC defined by CAVI was the greatest among the 3 scores. From these findings, CAVI might be more useful for discriminating the probability for coronary atherosclerosis than findings of carotid atherosclerosis by high-resolution B-mode ultrasonography. However, several studies have shown an strong association between increased IMT and CAD?[3,4] as well as between increase arterial stifness including stiffness parameter β and PWV[6,22] previously. Therefore, it is difficult to clarify which of IMT and CAVI has superiority as clinical atherosclerosis makers.

In the Rotterdam study, artrial stiffness was strongly associated with common carotid IMT, plaques in the carotid artery and in the aorta, adjusted for age?[23] We think also that both are related closely, and are important as makers of stages of atherosclerosis. In fact, in the present study, max IMT and plaque score correlated positively with CAVI. This result might suggest that CAVI reflects systemic arterial sclerosis including carotid atherosclerosis as well as coronary atherosclerosis.

However, our study has some limitations. First, subjects in this study were very few compared to previous data of IMT?[3,4] and no prospective study was reported about CAVI. To confirm our theory, further large-scale and prospective study are required. Second, we did not evaluate the relationship with CAVI and metabolic syndrome at an early stage of atherosclerosis and risk of cardiovascular disease. Recent reports show that metabolic syndrome could produce atherosclerotic stenosis of the coronary arteries independent of promotion of the development of coronary atherosclerosis via an increase of arterial stiffness?[24] Metabolic syndrome has a strong relationship with increased IMT and arterial stiffness, and these methods can be used as a surrogate marker for high cardiovascular disease risk?[25] Influence of metabolic syndrome on our results should be examined in future. Third, in the present study, subjects with ABI <0.9 were excluded, because CAVI of these subjects showed inaccurate data. However, CAD is closely linked to peripheral arterial disease?[26] and it is reported that a low ABI is an independent marker for an additive risk of CAD?[27] Therefore, to predict coronary atherosclerosis, ABI should be used, especially in subjects with ABI <0.9.

In this study, the difference of a history of CAD might influence on our results. We analyzed subjects without a history of CAD, and obtained almost the same results. These results were statistically not significant, because subjects were too few to analyze statistically (data not shown). Furthermore, by ordinal logistic regression analysis, CAVI was associated with severity of coronary atherosclerosis. From these findings, we speculate that the difference of a history of CAD hardly influence our results. However, further studies by subjects without a history of CAD are required.

Among non-invasive methods, the imaging studies using multidetector-row computed tomography and nuclear medicine have good sensitivity for the detection of coronary atherosclerosis. However, these methods need special devices, a large amount of space and special technician. Consequently, few institutions are able to perform these tests routinely. Although CAVI might show lower sensitivity for diagnosing coronary atherosclerosis than diagnostic imaging, CAVI is a simple method that requires no special technique. It is possible that if a CAVI device is available, almost all institutions can measure CAVI. Accordingly, CAVI might be useful for the screening of coronary atherosclerosis.

CAD is a common cause of sudden death, partially as a result of the lack of a simple and reliable non-invasive diagnostic method of atherosclerosis, which can be used routinely in clinical settings. Therefore, an atherosclerotic marker is needed in common practice.

These results demonstrate that CAVI might be useful as a routine test for the detection of CAD and the evaluation of atherosclerosis at medical examination and the use with a practicing physician, a large-scale prospective study to evaluate CAVI is warranted. We expect that this non-invasive examination can contribute to atherosclerotic diagnosis and treatment as surrogate marker in future.

Conclusions

This study has shown that CAVI, a parameter of arterial stiffness, is significantly and strongly associated with the presence and severity of coronary atherosclerosis than carotid atherosclerosis parameters. Thus, CAVI might be a useful predictor of coronary atherosclerosis in subjects with a risk factor for cardiovascular disease, and might indicate the severity of coronary atherosclerosis. To confirm our theory, further large-scale and prospective study are required.

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