Original Article

Cardio-Ankle Vascular Index Is Superior to Brachial-Ankle Pulse Wave Velocity as an Index of Arterial Stiffness

Akira TAKAKI[1], Hiroshi OGAWA[2], Takatoshi WAKEYAMA[2], Takahiro IWAMI[2], Masayasu KIMURA[2], Yasuyuki HADANO[2], Susumu MATSUDA[2], Yousuke MIYAZAKI[2], Atsushi HIRATSUKA[2], and Masunori MATSUZAKI[3]

Both cardio-ankle vascular index (CAVI) and brachial-ankle pulse wave velocity (baPWV) are noninvasive methods to estimate arterial stiffness. The purpose of this study is to determine whether CAVI or baPWV is superior as an index of arterial stiffness. One hundred and thirty patients with chest pain syndrome who underwent coronary angiography (CAG) were included in this study. We obtained intima-media-thickness (IMT) and the stiffness parameter β of the carotid artery by carotid ultrasounds (CU). The peak early diastolic velocity (*E*), deceleration time of *E* (EDCT), peak atrial systolic velocity (*A*) of transmitral flow and left ventricular mass index (LVMI) were obtained by echocardiography. CAVI, baPWV, total cholesterol (T-C), low density lipoprotein cholesterol (LDL-C), high density lipoprotein cholesterol (HDL-C) and triglycerides (TG) were measured before CAG. There was a significant correlation between CAVI and baPWV (r=0.64, p<0.01). Both CAVI and baPWV were significantly correlated with age, IMT and β (age: r=0.64, p<0.01 for CAVI, and r=0.48, p<0.01 for baPWV; IMT: r=0.40, p<0.01, and r=0.31, p<0.01; β: r=0.36, p<0.01 and r=0.25, p<0.01). However, only CAVI was correlated with the parameters of left ventricular diastolic indices from echocardiography (*E*/*A*: r=0.44, p<0.01; EDCT: r=0.36, p<0.01). Additionally, LDL-C and T-C/HDL-C were also associated with only CAVI (LDL-C: r=0.26, p<0.02; T-C/HDL-C: r=0.30, p<0.01), not baPWV. Finally, only CAVI was significantly higher in the group with angina pectoris than in the normal group (9.708±1.423 *vs.* 9.102±1.412; p=0.0178). All parameters associated with atherosclerosis suggested that CAVI was superior to baPWV as a parameter of arterial stiffness. (*Hypertens Res* 2008; 31: 1347–1355)

***Key Words*: pulse wave velocity, cardio-ankle vascular index, atherosclerosis, carotid ultrasounds**

Introduction

Pulse wave velocity (PWV) obtained by non-invasive automatic devices is widely used as an indicator of arterial stiffness and a marker reflecting vascular damages (*1–3*). The measurement of PWV is useful to diagnose arteriosclerosis in any part of the body. It is a simple and reliable marker to screen the general population for effective prevention of cardiovascular disease (*4–6*). A new method for measuring PWV has been proposed in Japan. Brachial-ankle PWV (baPWV) measures the PWV in the arm and leg by applying air pressure using the volume plethysmographic method. However, baPWV has been reported to be influenced by several factors, including blood pressure (BP) and autonomic nerve function, Therefore, baPWV does not solely reflect arteriosclerosis.

On the other hand, the stiffness parameter β, an index of vascular sclerosis, is reported to be independent of BP (*7*). Initially, β of the thoracic descending aorta (TDA) was obtained by transesophageal echocardiography (TEE) (*8*).

From the [1]Takaki Medical Clinic, Shunan, Japan; [2]Division of Cardiology, Tokuyama Central Hospital, Shunan, Japan; and [3]Division of Cardiovascular Medicine, Department of Medical Bioregulation, Yamaguchi University School of Medicine, Ube, Japan.

Address for Reprints: Akira Takaki, M.D., Takaki Medical Clinic, 3198–6, Kume, Shunan 745–0801, Japan. E-mail: atakaki@cotton.ocn.ne.jp

Received November 12, 2007; Accepted in revised form March 19, 2008.

Recently, another modality was introduced for β of TDA, that is cardio-ankle vascular index (CAVI). CAVI is a new index independent of BP (*9*). The accuracy and usefulness of CAVI and its correlation with several arteriosclerotic parameters have been reported in detail (*10*). However, there has been no full comparison of the clinical usefulness of baPWV and CAVI.

In this study, we examined the difference in clinical usefulness between CAVI and baPWV as indicators of arteriosclerosis.

Methods

One hundred thirty consecutive patients (80 men and 50 women between 35 and 85 years old; mean age, 69±12 years) with chest pain syndrome who underwent coronary angiography (CAG) were enrolled in this study. The left ventricular (LV) ejection fraction (LVEF) was normal (≥60%) in all of patients. The characteristics of patients are listed in Table 1. BP and baPWV were studied using AT-form PWV/ABI (Colin, Komaki, Japan), which has been described in detail previously (*11–13*). This device simultaneously records right and left brachial and tibial arterial pressure wave forms, lead I of an electrocardiogram, and a phonocardiogram. The time difference between the brachial and ankle arterial pressure wave (ΔT) was determined by wave front velocity theory. The distance between the arm and ankle (D) was calculated based on anthropometric data for the Japanese population. Finally, the baPWV was calculated as $D/\Delta T$.

On the other hand, CAVI was measured non-invasively using a VaSera VS-1000 system (Fukuda Denshi, Tokyo, Japan). CAVI was obtained by substituting the stiffness parameter β into an equation for determining vascular elasticity and PWV. The stiffness parameter β indicates BP-independent patient-specific vascular stiffness as measured by arterial ultrasound, and is calculated by the following equation:

$$\beta = \ln (P_s/P_d) \times D/\Delta D \quad (1)$$

where P_s and P_d are the systolic BP (SBP) and diastolic BP (DBP) respectively in mmHg, D is the internal diameter of the blood vessels and ΔD is the excursion of D during a cardiac cycle.

Bramwell-Hill's formula expresses the relationship between the volume elastic modulus and PWV as follows:

$$PWV^2 = \Delta P/\rho \times V/\Delta V \quad (2)$$

where ΔP is the pulse pressure, ρ is the blood density, V is the volume of the blood vessel, and ΔV is the change of V.

From Eq. (2), the following formula is derived:

$$V/\Delta V = D/\Delta D/2 = 2\rho/\Delta P \times PWV^2 \quad (3)$$

where D is the diameter of the blood vessels and ΔD is the change of D.

When we substitute Eq. (3) for Eq. (1), we obtain the stiffness parameter β as $\beta = CAVI = \ln (P_s/P_d) \times 2\rho/\Delta P \times PWV^2$.

Table 1. Anthropometricts in All Participatants

Number of subjects	Men: 80, women: 50
Age (years)	69±12
SBP (mmHg)	137±31
DBP (mmHg)	79±13
T-C (mg/dL)	203±39
TG (mg/dL)	140±114
HDL-C (mg/dL)	52±17
LDL-C (mg/dL)	124±36
Treated hypertension (*n*)	68
Diabetes mellitus (*n*)	27
Smoking (*n*)	36
Stroke (*n*)	11
PAF (*n*)	10
AP (*n*)	86

SBP, systolic blood pressure; DBP, diastolic blood pressure; T-C, total cholesterol; TG, triglyceride; HDL-C, high density lipoprotein cholesterol; LDL-C, low density lipoprotein cholesterol; PAF, paroxysmal atrial fibrillation; AP, angina pectoris.

CAVI was measured as follows. PWV was obtained by dividing the vascular length (L) by the time (T) required for the pulse wave to propagate from the aortic valve to the ankle, as shown in Fig. 1. T is difficult to obtain, because the starting time of the blood stream from the aortic valve is difficult to identify from the valve's opening sound. Therefore, T is obtained by summing t_b and t_{ba} in place of t_b' and t_{ba}, because t_b' and t_b are theoretically equal (t_{ba}: the time between the rise of the brachial pulse wave and rise of the ankle pulse wave; t_b: the time between the aortic valve's closing sound and the notch of the brachial pulse wave; t_b': the time between the aortic valve's opening sound and the rise of the brachial pulse wave).

To detect the brachial and ankle pulse waves with cuffs, the pressure of the cuffs is kept low at 30 mmHg to 50 mmHg to ensure a minimal effect of cuff pressure on the hemodynamics (*14*). baPWV and CAVI were measured at about the same time with the subject lying in a supine position after resting for at least 5 min.

After the measurement of baPWV and CAVI, we performed carotid ultrasounds (CU) and an echocardiogram (UCG). The intima-media-thickness (IMT), the plaque score (PS) calculated by sum of IMT≥1.1 mm and β of carotid artery were obtained by CU. CU was performed using a SSD 4000 ultrasound machine (Aloka Co. Ltd, Tokyo, Japan) with a 7.5 MHz transducer. The IMT was evaluated as the distance between the lumen-intimal interface and the medial-adventitial interface, and was measured using two calipers on the frozen frame of a suitable longitudinal image. The upper limit of normal for the IMT was defined as 1.0 mm. To assess the severity of atherosclerosis, we used the PS, which was calculated by summing all plaque thickness in both carotid

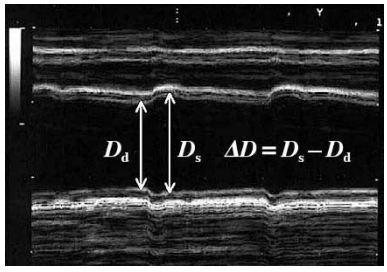

Fig. 1. *Dimensional change of the carotid artery by US. Stiffness parameter* $\beta = [\ln (P_s/P_d)] \times D_d/(D_s - D_d)$. *$P_s$, peak systolic blood pressure; P_d, peak diastolic blood pressure; D_d, minimum dimension of carotid artery; D_s, maximum dimension of carotid artery.*

systems (*15–17*).

We used the max IMT and average β of both common carotid arteries in this study. The measurement of β in the carotid artery was done at a point without plaque (*18*). We measured the minimum dimension (D_d) and maximum dimension (D_s) of the carotid artery, then calculated the systolic dimensional change ($\Delta D = D_s - D_d$) on the M-mode echogram. The leading edge of near gain in the carotid artery is inside IMT. β was calculated as $\ln (P_s/P_d) \times (D_d/\Delta D)$ and used to express the stiffness of the carotid arterial wall (Fig. 1).

We next performed UCG. All Doppler profiles were recorded in apical 4-chamberview. The peak velocities of early (*E*) and late (*A*) mitral inflow and the deceleration time of the E wave (EDCT) were measured using pulse-wave Doppler with the sample volume at the tip of the mitral valve leaflets. We also recorded the M-mode of the left ventricle (LV). The thickness of the LV posterior wall (LVPW) and interventricular septum (IVS), and the LV diastolic dimension (LVDd) were obtained by the M-mode of LV. The mass of the LV (LVM) was calculated as $1.04 \times [(\text{LVPW} + \text{IVS} + \text{LVDd})^3 - \text{LVDd}^3] - 13.6$. The index of LVM (LVMI) was calculated by LVM/body surface area.

All participants gave written informed consent for the two studies, which were approved by the committee and conducted in accordance with the Declaration of Helsinki (2000) of the World Medical Association. Both studies were approved by the Ethics Committee of Tokuyama Central Hospital.

Statistical Analysis

Statistical analysis was performed using StatView version 5.0 (Abacus Concepts, Calabasus, USA). Quantitative data are expressed as the mean value±SD. Multivariate analysis of the associations was performed using the standard linear regression technique. Significance was established at $p<0.05$.

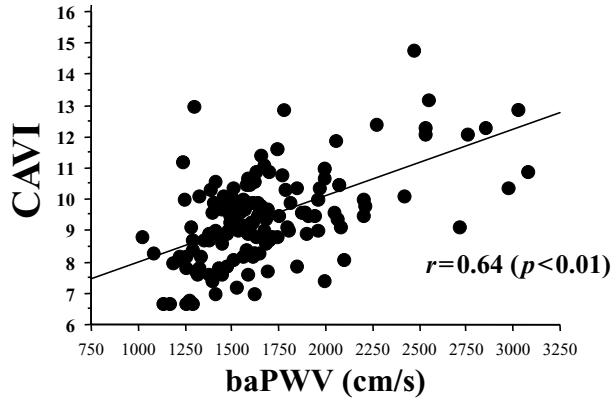

Fig. 2. *There was a good correlation between CAVI and baPWV.*

Results

Relationship between CAVI and baPWV in Patients with Chest Pain Syndrome

The mean values of CAVI and baPWV were 9.404±1.552 and 1,676±389 cm/s, respectively. Figure 2 depicts the relationship between CAVI and baPWV. A good correlation was observed between CAVI and baPWV ($r=0.64$, $p<0.01$). Both CAVI and baPWV were correlated with age ($r=0.64$, $p<0.01$ and $r=0.48$, $p<0.01$).

Relation of CAVI and baPWV to BP

CAVI was not correlated with SBP or DBP. However, both SBP and DBP were significantly correlated to baPWV (SBP: $r=0.47$, $p<0.01$; DBP: $r=0.22$, $p<0.02$; Fig. 3).

Relation of CAVI and baPWV to Parameters from CU

There were significant correlations between CAVI and IMT ($r=0.40$, $p<0.01$), and CAVI and β ($r=0.36$, $p<0.01$). On the other hands, there was a lesser but still significant association between baPWV and IMT ($r=0.31$, $p<0.01$) or β ($r=0.25$, $p<0.01$) (Fig. 4).

Relation of CAVI and baPWV to Parameters from UCG

CAVI, but not baPWV, was correlated to parameters of LV diastolic property from echocardiography (*E*/*A*: $r=0.44$, $p<0.01$; EDCT: $r=0.38$ $p<0.01$). Neither CAVI nor baPWV was significantly correlated to LVMI (Fig. 5).

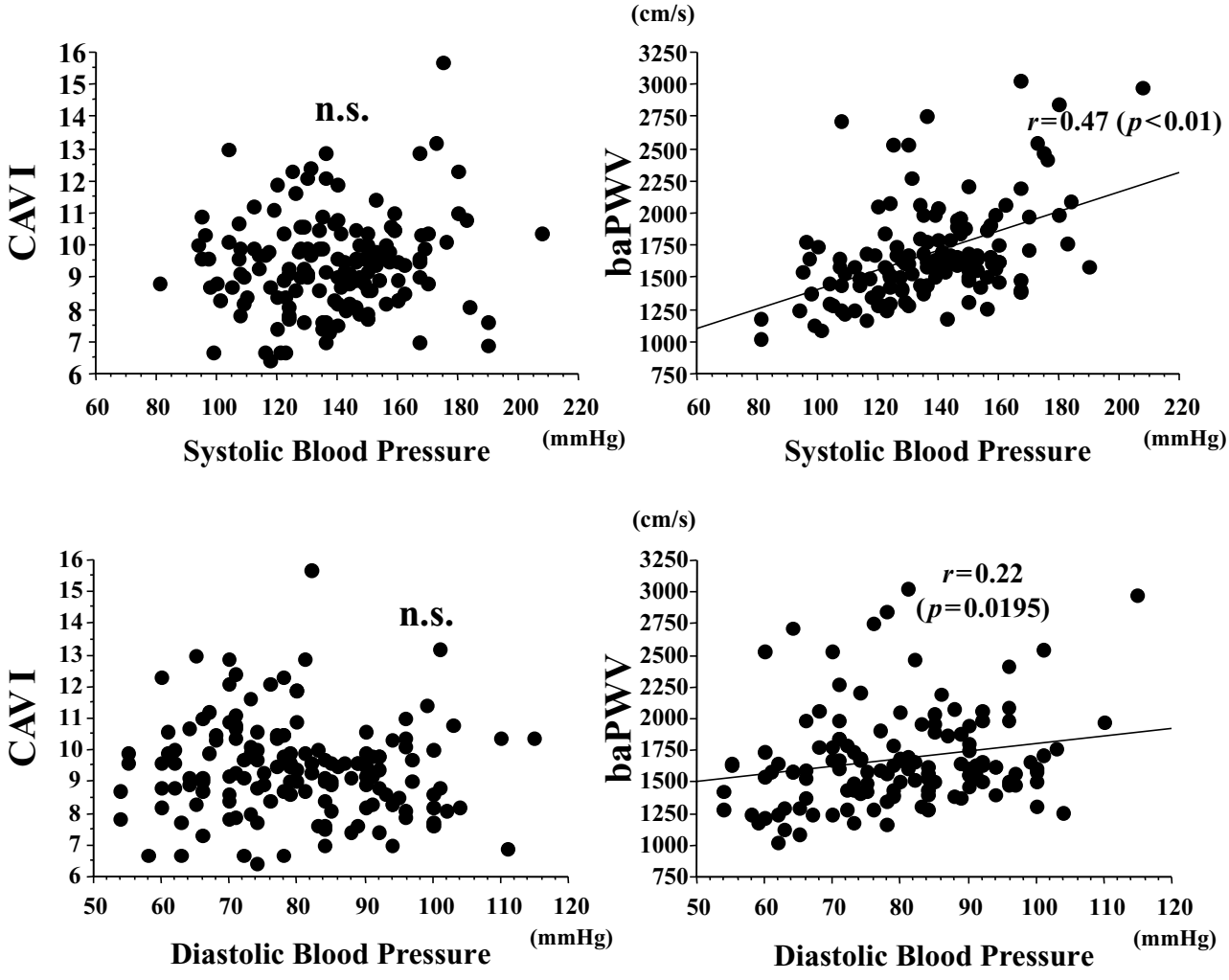

Fig. 3. *baPWV, but not CAVI, was well correlated with systolic blood pressure (SBP: upper) and poorly correlated with diastolic blood pressure (DBP: lower).*

Relation of baPWV and CAVI to Parameters of Serum Lipids

Low density lipoprotein cholesterol (LDL-C) and total cholesterol (T-C)/high density lipoprotein cholesterol (HDL-C) were significantly associated with CAVI (LDL-C: $r=0.26$, $p=0.0195$; T-C/HDL: $r=0.30$, $p<0.01$). However, baPWV was not significantly correlated to serum lipids such as T-C, LDL-C, triglycerides (TG), and HDL-C (Fig. 6).

Relationship between baPWV or CAVI and Coronary Artery Disease with Chest Pain Syndrome

Eighty-six of the 130 patients (66%) had angina pectoris (AP group) and were admitted due to significant coronary arterial stenosis (more than 75% stenosis) as determined by CAG. These patients were further divided into three subgroups by the stenotic ratio of the coronary artery. Those with ratios of 75%, 75–90%, and over 90% were included in the low (L), medium (M), and high (H) stenotic ratio groups, respectively. The sclerotic score of L, M, and H was given 1, 3, or 5 points, respectively. Moreover, we scored total sclerotic score (TSS) by summing up the sclerotic score of the all stenotic lesions from No. 1 to No. 15. We classified coronary artery (No. 1–No. 15) by according to the classification of American Heart Association. The CAVI of the AP group was significantly higher than that of the normal coronary group with chest pain syndrome (9.708 ± 1.423 *vs.* 9.102 ± 1.412: $p=0.0178$) (Fig. 7). Age was not significantly different between the AP and normal coronary group (68 ± 12 *vs.* 69 ± 13 years). CAVI was not significantly different between one-vessel disease and multi-vessel disease (9.482 ± 2.135 *vs.* 9.705 ± 2.804: $p=0.12$). However, there was poor correlation between CAVI and TSS. baPWV was not significantly different between the

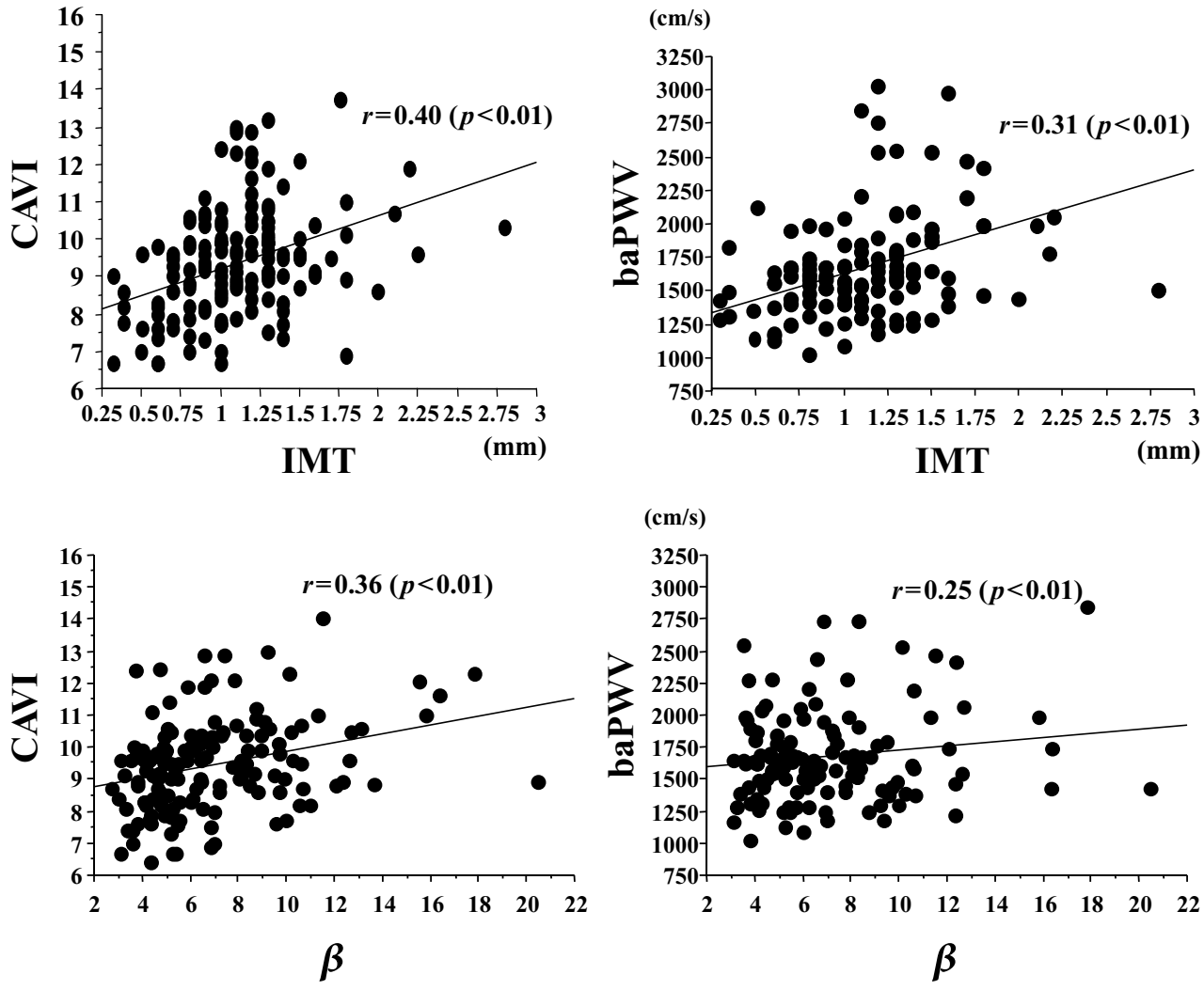

Fig. 4. *Both CAVI and baPWV were significantly correlated with IMT (upper) and β (lower).*

AP group and normal coronary group (1,674±426 *vs.* 1,645±347 cm/s) (Fig. 8).

Discussion

Both CAVI and baPWV are noninvasive methods for to estimating arterial stiffness, and in the present study both were shown to be significantly correlated with age (r=0.64, p<0.01 for CAVI, r=0.48, p<0.01 for baPWV). These parameters were also significantly correlated with each other in this study (r=0.64, p<0.01). However, the difference in clinical usefulness between CAVI and baPWV has not been fully discussed before. Therefore, in this study, we investigated the differences in efficacy between CAVI and baPWV as indicators of arterial stiffness.

PWV is a useful approach for diagnosing arteriosclerosis in any part of the body. It has been reported that baPWV is a predictor of prognosis of the patients with cardiovascular disease and a marker of severity of atherosclerotic vascular damage. A high baPWV could be a quantitative risk for microalbuminuria in patients with essential hypertension. A 200 cm/s increase in baPWV has been shown to increase the risk of microalbuminuria by about 19% (*19*). However, PWV is strongly influenced by BP and is increased by obesity, high fasting glucose level, and metabolic syndrome (*20*).

CAVI is a new index of arterial stiffness that is independent of BP. It has been reported that CAVI is associated with age and SBP but not with DBP in dialysis patients and type 2 diabetes patients, respectively (*14*, *21*). CAVI was not related to SBP and DBP in this study. However, both SBP and DBP significantly correlated to baPWV (SBP: r=0.47, p<0.01; DBP: r=0.22, p<0.02). These findings suggested that CAVI was superior to baPWV as an index of arterial stiffness.

CU-detected IMT and PS of the carotid artery have been shown to be markers of arteriosclerosis for the whole body. In particular, it has been reported that a thickened IMT of the

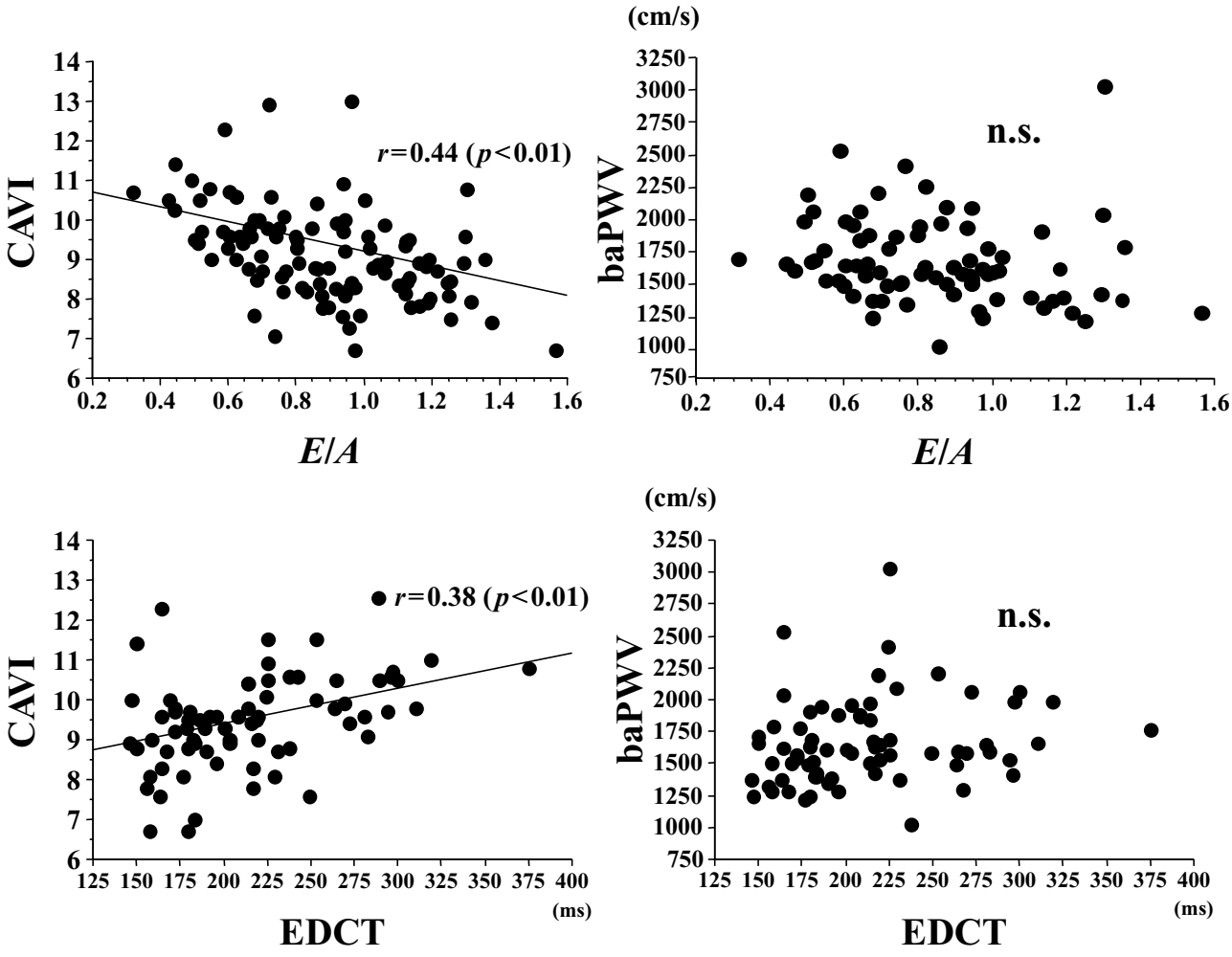

Fig. 5. *Not baPWV but CAVI has significant correlation to E/A (upper) and EDCT (lower).*

carotid artery is a good indicator of severe symptomatic coronary artery disease (*22*). PS is related to the progression of coronary artery disease. The stiffness index β, which represents the mechanical properties of the arterial wall, is calculated from the relationship between systemic BP and the diameter of the artery. Hirai *et al*. reported that the importance of carotid aortic distensibility (β) as a prognostic indicator of the extent of the coronary artery disease (*18*).

Several studies have demonstrated that arterial stiffness as assessed by PWV correlates well with IMT and PS detected by CU. However, the correlation is not close (*23*). Therefore in this study, we compared CAVI and baPWV with two parameters of arteriosclerosis such as IMT and β. We observed significant correlations between CAVI and IMT (r=0.40, p<0.01), and between CAVI and β (r=0.36, p<0.01). On the other hands, baPWV had poor correlation to IMT (r=0.31, p<0.01) and β (r=0.25, p<0.01). These parameters suggested that CAVI was superior to baPWV as a marker of arterial stiffness.

Generally, LV diastolic dysfunction is characterized by decreases in *E* velocity, prolongation of the deceleration time of *E*, and increases in *A* velocity. High BP for a long time induced LV hypertrophy (LVH) and diastolic dysfunction. baPWV is influenced by BP. We therefore hypothesized that there might be a good correlation between baPWV (but not CAVI) and LV diastolic function. However, the actual result showed the opposite. One reason for this may have been that many patients in this study did not have very severe hypertension or LVH. In addition, echocardiographic diastolic parameters such as *E/A* and EDCT are influenced by age. Both CAVI and baPWV were correlated with age in this study (r=0.64, p<0.01 for CAVI and r=0.48, p<0.01 for baPWV; Fig. 3). This may have been another reason that CAVI was correlated with LV diastolic function.

LDL-C is also a major risk factor for coronary artery disease and the National Cholesterol Education Program (NCEP) recommends that patients with ischemic heart disease receive drug therapy to lower their LDL-C. CAVI was

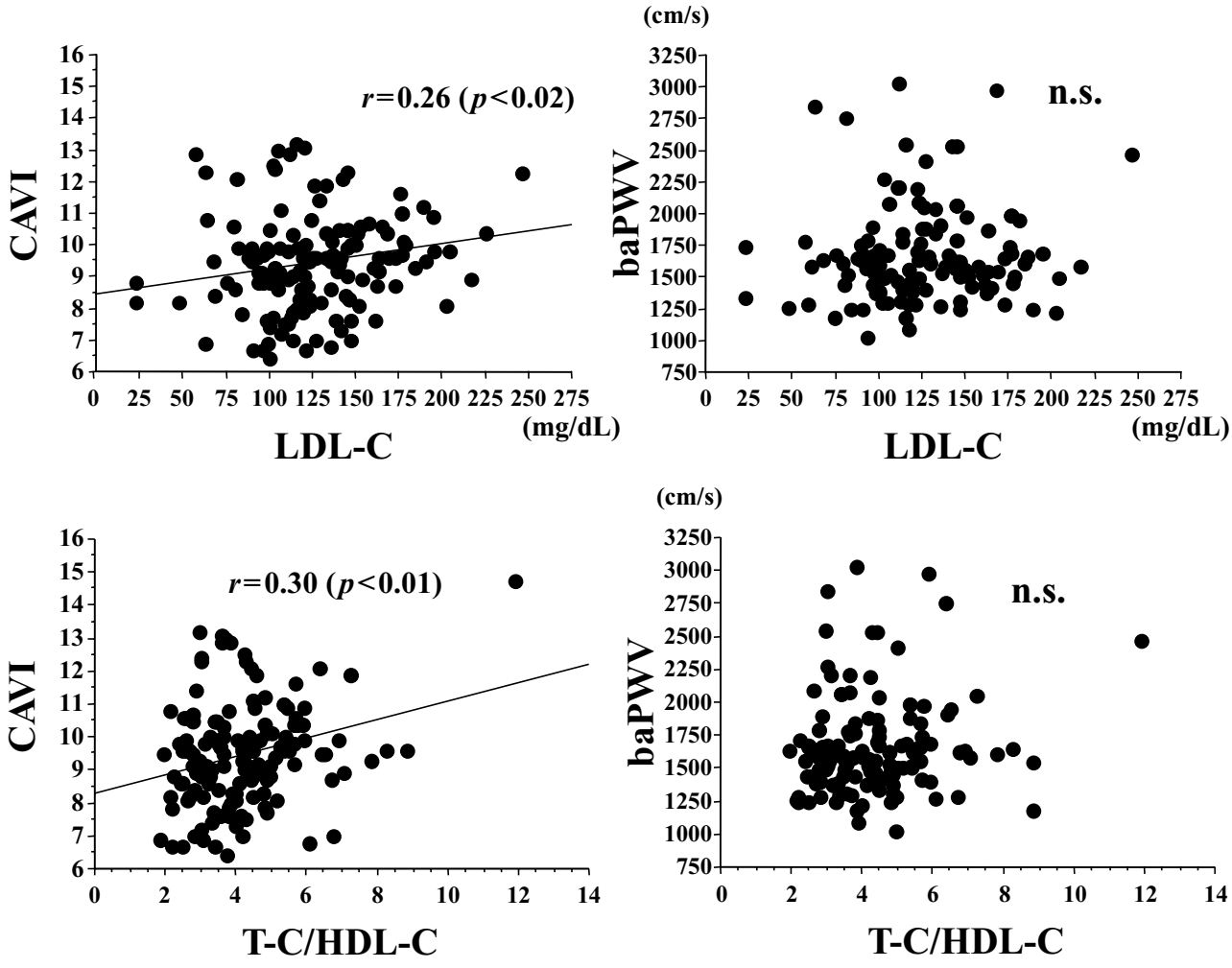

Fig. 6. *Not baPWV but CAVI has a poor correlation to LDL-C (upper) and T-C/HDL-C (lower).*

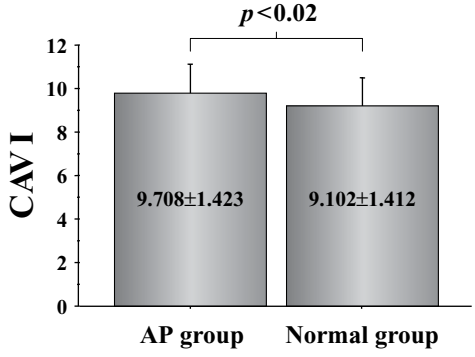

Fig. 7. *The CAVI of the group with significant coronary arterial stenosis (AP group) was significantly higher than that of the normal coronary group.*

correlated with LDL-cholesterol and T-C/HDL-C in this study. A possible reason for this was that 39 patients (30% of all subjects) were taking statins. The clinical benefit of the statins for the primary and secondary prevention of cardiovascular complications of advanced atherosclerosis, especially coronary artery disease, is being tested in several large clinical trials (*24*). By lowering T-C and LDL-C, CAVI might also be decreased.

Shirai *et al*. reported that CAVI in patients undergoing percutaneous transluminal coronary angioplasty or in patients showing ischemic changes in their electrocardiogram was higher than that in patients without arteriosclerotic disease (*14*). Similarly, another investigator proposed that aortic-femoral PWV was feasible and useful for detection of atherosclerotic coronary disease (*25*). Our data suggested that 86 patients with significant coronary arterial disease had a higher value of CAVI than the normal group (9.708±1.423 *vs*. 9.102±1.412, $p=0.0178$). However, we could not distinguish patients with intact coronary arteries from patients with significant coronary stenosis by baPWV. The mean value of baPWV in our study was 1,676±389 cm/s. This value was not

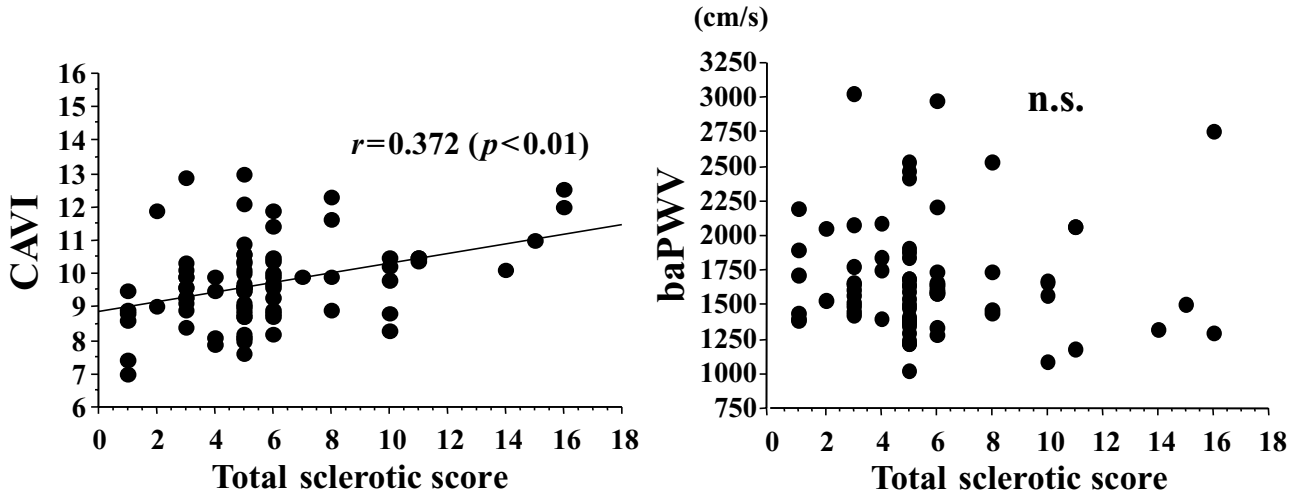

Fig. 8. *CAVI, but not baPWV, was significantly correlated with the total sclerotic score.*

particularly high. In this study, 80% of 86 patients had single-vessel disease. If multi-vessel disease had been more predominant in this study, baPWV might have distinguished patients with intact coronary from patients with significant coronary stenosis. This is, because arteriosclerosis of the coronary artery is influenced by many factors, such as age, lipids, diabetes mellitus (DM), hypertension, smoking and so on.

On the other hands, there was a poor correlation between CAVI and TSS. Generally, age, lipids and DM are major coronary risk factors. In our study, these factors showed a greater association with CAVI than with baPWV. This may have been one reason that CAVI, but not baPWV, was poorly correlated with TSS.

In summary, our data suggested that CAVI reflected arteriosclerosis and was superior to baPWV as an index of arterial stiffness.

References

1. Cohn JN: Vascular wall function as a risk marker for cardiovascular disease. *J Hypertens* 1999; **17** (Suppl 5): S41–S44.
2. Lehmann ED: Clinical value of aortic pulse-wave velocity measurement. *Lancet* 1999; **354**: 528–529.
3. Asmar R, Benetos A, Topouchian J, *et al*: Assessment of arterial distensibility by automatic pulse wave velocity measurement: validation and clinical application studies. *Hyertension* 1995; **26**: 485–490.
4. Yamashina A, Tomiyama H, Arai T, *et al*: Brachial-ankle pulse wave velocity as marker of atherosclerotic vascular damage and cardiovascular risk. *Hypertens Res* 2003; **26**: 615–622.
5. Munakata M, Ito N, Nunonaka T, Yoshinaga K: Utility of automated brachial ankle pulse wave velocity measurements in hypertensive patients. *Am J Hypertens* 2003; **16**: 653–657.
6. Imanishi R, Seto S, Toda G, *et al*: High brachial-ankle pulse wave velocity is an independent predictor of the presense of coronary artery disease in men. *Hypertens Res* 2004; **27**: 71–78.
7. Hayashi K, Sato M, Handa H, *et al*: Biomechanical study of the constitutive laws of vascular wall. *Exp Mechanics* 1974; **14**: 440–444.
8. Tomochika Y, Tanaka N, Ono S, *et al*: Assessment by transesophageal echocardiography of atherosclerosis of the descending thoracic aorta in patients with hypercholesterolemia. *Am J Cardiol* 1999; **83**: 703–709.
9. Yambe T, Yoshizawa M, Saijo Y, *et al*: Brachio-ankle pulse wave velocity and cardio-ankle vascular index (CAVI). *Biomed Pharmacother* 2004; **58**: S95–S98.
10. Takaki A, Ogawa H, Wakeyama T, *et al*: Cardio-ankle vascular index is a new noninvasive parameter as arterial stiffness. *Circ J* 2007; **71**: 1710–1714.
11. Yamashina A, Tomiyama H, Takeda K, *et al*: Validity, reproducibility, and clinical significance of noninvasive brachial-ankle pulse wave velocity measurement. *Hypertens Res* 2002; **25**: 359–364.
12. Matsui Y, Kario K, Ishikawa J, *et al*: Reproducibility of arterial stiffness indices (pulse wave velocity and augmentation index) simultaneously assessed by automated pulse wave analysis and their associated risk factors in essential hypertension. *Hypertens Res* 2004; **27**: 851–857.
13. Munakata M, Ito N, Nunonaka T, *et al*: Utility of automated brachial ankle pulse wave velocity measurements in hypertensive patients. *Am J Hypertens* 2003; **16**: 653–657.
14. Shirai K, Otsuka K, Takata M: A novel blood pressure–independent arterial wall stifness parameter; cardio-ankle vascular index (CAVI). *J Atheroscler Thromb* 2006; **13**: 101–107.
15. O'Leary DH, Polka JF, Kronmal RA, *et al*: Carotid-artey intima and media thickness as a risk factor for myocardial infarction and stroke in older adults. *N Engl J Med* 1999; **340**: 14–22.
16. Geroulakos G, O'Gorman DJ, Kalokiki E, *et al*: The carotid

intima-media thickness as a marker of the presence of severe symptomatic coronary artery disease. *Eur Heart J* 1994; **15**: 781–785.
17. Tanaka H, Nishino M, Ishida M, *et al*: Progression of carotid atherosclerosis in Japanese patients with coronary artery disease. *Stroke* 1992; **23**: 946–951.
18. Hirai T, Sasayama S, Kawasaki T, *et al*: Stiffness of systemic arteries in patients with myocardial infarction. *Circulation* 1989; **80**: 78–86.
19. Munakata M, Nunokawa T, Yoshinaga K, *et al*, J-TOPP Study Group: Brachial-ankle pulse wave velocity is an independent risk factor for microalbuminuria in patients with essential hypertension—a Japanese Trial on the Prognostic Implication of Pulse Wave Velocity (J-TOPP). *Hypertens Res* 2006; **29**: 515–521.
20. Nakanishi N, Shiraishi T, Wada M: Brachial-ankle wave velocity and metabolic syndrome in a Japanese population: the Minoh study. *Hypertens Res* 2005; **28**: 125–131.
21. Wakabayashi I, Matsuda H: Effects of age on the relationship between cardio-ankle vascular index and atherosclerotic progression in patients withtype 2 diabetes mellitus. *Jpn J Geriat* 2006; **43**: 217–221.
22. Geroulakos G, O'Gorman DJ, Kalokiki E, *et al*: The carotid intima-media thickness as a marker of the presence of severe symptomatic coronary artery disease. *Eur Heart J* 1994; **15**: 781–785.
23. Yambe M, Tomiyama H, Hirayama Y, *et al*: Arterial stiffening as a possible risk factor for both atherosclerosis and diastolic heart failure. *Hypertens Res* 2004; **27**: 625–631.
24. Grotta JC, Yatsu FM, Pettigrew LC, *et al*: Prediction of carotid stenosis progression by lipid and hematologic measurements. *Neurology* 1989; **39**: 1325–1331.
25. Park SM, Seo HS, Lim HE, *et al*: Assesment of arterial stffiness index as a clinical parameter for atherosclerotic coronary artery disease. *Circ J* 2005; **69**: 1218–1222.