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The Cardio-Ankle Vascular Index and Carotid Ultrasound Data Reflect Different Concepts of Vascular Damage

Suzuki *et al.* recently reported the effects of conventional cardiovascular risk factors on the arterial stiffness and carotid atherosclerosis in young patients¹⁾. The authors selected the cardio-ankle vascular index (CAVI) and carotid ultrasound data as markers of arterial stiffness and carotid atherosclerosis, and concluded that there was a positive relationship between conventional cardiovascular risk factors and physiological arteriosclerosis markers. We fundamentally agree with their analytical procedure, but the arterial stiffness and carotid atherosclerosis are different concepts²⁾, and carotid plaques and the intima-media thickness (IMT) also represent different aspects of vascular damage³⁾.

The arterial stiffness is a fundamental pathological change in cardiovascular disease (CVD), and is an important risk factor for the development of CVD^{4, 5)}. The pulse wave velocity (PWV) has been measured to estimate the severity of atherosclerosis⁶⁾, and the CAVI was developed by improving on the PWV method for assessing the arterial stiffness⁷⁾. Kangas *et al.* reported the advantages of measuring the PWV in patients with metabolic syndrome, even in the absence of hypertension⁸⁾, and the CAVI has been applied clinically for monitoring the severity of atherosclerosis⁹⁾.

We herein present findings demonstrating the ability of an increased CAVI value to predict the changes in the carotid plaque size or carotid IMT.

A total of 134 men, aged 31 to 86 years old (mean $\pm$ standard deviation, 64.1 ± 10.8), underwent intensive health checkups between April 2013 and

March 2014. The subjects receiving treatment for hypertension, diabetes mellitus and/or dyslipidemia were included in this study. Informed consent was obtained from all of the participants. This study was conducted with the approval of the Institutional Review Board of Sano City Hospital, Tochigi Prefecture, Japan (November 21, 2013).

After each subject had rested in the sitting position for at least 5 min, the brachial systolic and diastolic blood pressures were measured using an automated blood pressure measurement device (UM-101; A & D Company, Ltd., Tokyo). The body mass index (BMI) was calculated as the weight (in kilograms) divided by height (in meters) squared. The waist circumference (WC) was measured midway between the iliac crest and the 12th rib.

Carotid ultrasound detection was performed with a color Doppler ultrasound diagnostic apparatus (Aplio SSA-700A, Toshiba Corporation, Tokyo) by a trained technician. The maximal IMT was adopted for the analysis. The carotid artery plaque size was also determined, and the total plaque score was calculated.

The CAVI, an index of arterial stiffness, was measured non-invasively (VaSera VS-1500AE, Fukuda Denshi, Japan). The mean CAVI values obtained on the right and left sides for each participant were used for the analysis.

All tests were two-sided, and $p < 0.05$ was set as the statistical significance level. All analyses were performed using the SPSS 21 statistical software package (SPSS Inc. Japan). The results are expressed as the

Table 1. The characteristics of the subjects (mean and standard deviation) stratified by the presence/absence of plaque and an intima-media thickness of ≥ 1 mm

Variables	Plaque		IMT	
	+ $n = 101$	- $n = 33$	≥ 1 mm $n = 43$	< 1 mm $n = 91$
Age	65.8, 10.1**	58.7, 11.3	71.1, 7.2***	60.7, 10.7
BMI	23.9, 2.7	24.3, 3.7	24.1, 2.6	24.0, 3.1
WC	85.3, 7.6	84.3, 9.0	86.2, 6.7	84.5, 8.4
SBP	124.4, 13.9*	118.2, 13.5	127.1, 12.9*	120.9, 14.1
DBP	74.2, 9.7	73.7, 8.8	73.2, 9.3	74.5, 9.6
CAVI	8.6, 1.1***	7.7, 0.96	9.0, 1.1***	8.1, 1.1

SD; Standard deviation, BMI; Body mass index, WC; waist circumference, SBP; Systolic blood pressure, DBP; Diastolic blood pressure, CAVI; Cardio-ankle vascular index

Student's *t*-test was used for the analysis. * $p < 0.05$, ** $p < 0.01$, *** $p < 0.001$

Table 2. The results of a multiple logistic regression analysis performed to identify the predictors of the total plaque score (a) or an IMT ≥ 1 mm (b) with adjustments for the age, body mass index, systolic blood pressure and CAVI

Variables	OR of (a) (95% CI)	OR of (b) (95% CI)
Age (one unit increase)	1.02 (0.97-1.08)	1.1 (1.06-1.2)***
BMI (one unit increase)	1.03 (0.88-1.2)	1.2 (1.01-1.4)*
SBP (one unit increase)	1.01 (0.97-1.05)	1.01 (0.98-1.05)
CAVI (one unit increase)	1.9 (1.01-3.4)*	1.4 (0.84-2.2)

Abbreviations: OR; odds ratio, CI; confidence interval
All other abbreviations are listed in Table 1.

* $p < 0.05$, *** $p < 0.001$

means and SDs. After calculating the Spearman's correlation coefficients among the CAVI, IMT and total plaque score, a multiple logistic regression analysis was performed to analyze the associations between the ultrasound markers of carotid atherosclerosis and the CAVI, after controlling for the age, body mass index and systolic blood pressure.

The characteristics of the study participants are presented in **Table 1**. The demographic and clinical characteristics of the subjects with and without ultrasound evidence of carotid atherosclerosis are shown. Significant differences were observed regarding the age, systolic blood pressure and CAVI between the two groups.

The Spearman's correlation coefficients between the CAVI and the IMT and total plaque score were 0.435 ($p < 0.001$) and 0.47 ($p < 0.001$), respectively. In addition, the Spearman's correlation coefficient between the IMT and total plaque score was 0.598 ($p < 0.001$).

A multiple logistic regression analysis was conducted to determine the correlations between the CAVI and ultrasound data after adjustments for the age, BMI and systolic blood pressure (**Table 2**). A significant association of the CAVI with the existence of a plaque was recognized. However, this disappeared when IMT ≥ 1 mm was adopted as a dependent variable.

In summary, a logistic regression analysis showed that the predictive ability of the CAVI differs for each ultrasound marker of carotid atherosclerosis, although the CAVI, IMT and total plaque score were significantly correlated. The former result partly relates to the content of **Fig. 1** published by Suzuki *et al.*⁽¹⁾.

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We declare that there are no conflicts of interest associated with this study.

References

- 1) Suzuki J, Kurosu T, Kon T, Tomaru T: Impact of cardiovascular risk factors on progression of arteriosclerosis in younger patients: evaluation by carotid duplex ultrasonography and cardio-ankle vascular index (CAVI). *J Atheroscler Thromb*, 2014; 21: 554-562
- 2) Koivisto T, Virtanen M, Hutri-Kähönen N, Lehtimäki T, Jula A, Juonala M, Moilanen L, Aatola H, Hyttinen J, Viikari JS, Raitakari OT, Kähönen M: Arterial pulse wave velocity in relation to carotid intima-media thickness, brachial flow-mediated dilation and carotid artery distensibility: the Cardiovascular Risk in Young Finns Study and the Health 2000 Survey. *Atherosclerosis*, 2012; 220: 387-393
- 3) Zureik M, Temmar M, Adamopoulos C, Bureau JM, Courbon D, Thomas F, Bean K, Touboul PJ, Ducimetiere P, Benetos A: Carotid plaques, but not common carotid intima-media thickness, are independently associated with aortic stiffness. *J Hypertens*, 2002; 20: 85-93
- 4) Adji A, O'Rourke MF, Namasivayam M: Arterial stiffness, its assessment, prognostic value, and implications for treatment. *Am J Hypertens*, 2011; 24: 5-17
- 5) Cavalcante JL, Lima JA, Redheuil A, Al-Mallah MH: Aortic stiffness: current understanding and future directions. *J Am Coll Cardiol*, 2011; 57: 1511-1522
- 6) Cecelja M, Chowienzyk P: Dissociation of aortic pulse wave velocity with risk factors for cardiovascular disease other than hypertension: a systematic review. *Hypertension*, 2009; 54: 1328-1336
- 7) Shirai K, Utino J, Otsuka K, Takata M: A novel blood pressure-independent arterial wall stiffness parameter; cardio-ankle vascular index (CAVI). *J Atheroscler Thromb*, 2006; 13: 101-107
- 8) Kangas P, Tikkaoski AJ, Tahvanainen AM, Leskinen MH, Viitala JM, Kähönen M, Kööbi T, Niemelä OJ, Mustonen JT, Pörsti IH: Metabolic syndrome may be associated with increased arterial stiffness even in the

absence of hypertension: a study in 84 cases and 82 controls. *Metabolism*, 2013; 62: 1114-1122

- 9) Nakamura K, Tomaru T, Yamamura S, Miyashita Y, Shirai K, Noike H: Cardio-ankle vascular index is a candidate predictor of coronary atherosclerosis. *Circ J*, 2008; 72: 598-604

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