# Influence of blood pressure on cardio-ankle vascular index (CAVI) examined based on percentage change during general anesthesia

Barkhwa Kim, Koji Takada, Syunichi Oka and Toru Misaki

Cardio-ankle vascular index (CAVI) and brachial-ankle pulse wave velocity (baPWV) are non-invasive methods for estimating arterial distensibility. The purpose of this study is to evaluate whether CAVI as an index of true arterial stiffness is superior to baPWV based on the percentage change in hemodynamics under general anesthesia. CAVI (segment from heart to ankle), k-CAVI (heart to knee) and baPWV (brachial to ankle) in 30 oral surgery patients were measured to compare the decreased blood pressure (BP) after 10 min of tracheal intubation during general anesthesia with the control BP (after 5 min of rest). General anesthesia was performed under endotracheal intubation through intravenous injection of propofol, fentanyl and vecuronium or rocuronium. In both the elderly ( $\geq$  65 years) and middle-aged (<65 years) groups, CAVI and k-CAVI did not change during general anesthesia, whereas baPWV and systolic BP (SBP) showed a statistically significant decrease. Thus, the changes in CAVI ( $\Delta$ CAVI) and k-CAVI ( $\Delta$ k-CAVI) showed no significant correlations with those of SBP ( $\Delta$ SBP), whereas the changes in baPWV ( $\Delta$ baPWV) were significantly correlated with  $\Delta$ SBP.  $\Delta$ CAVI and  $\Delta$ k-CAVI showed no significant differences between the two groups, whereas  $\Delta$ baPWV and  $\Delta$ SBP in the elderly group was much higher than that in the middle-aged group. Measurement of CAVI was not affected by the decrease in BP during general anesthesia. In contrast, baPWV was significantly influenced by changes in BP. These findings suggest that CAVI is a useful index of true arterial stiffness and is superior to baPWV. *Hypertension Research* (2011) **34**, 779–783; doi:10.1038/hr.2011.31; published online 7 April 2011

Keywords: arterial stiffness; blood pressure; brachial-ankle pulse wave velocity; cardio-ankle vascular index; general anesthesia

# INTRODUCTION

It has been clarified that arteriosclerosis progresses before the onset of cardiac disease and sclerosis of the aorta precedes sclerosis of the cerebral artery or coronary artery. To predict a cardiovascular event, quantitative diagnosis of arteriosclerosis is of paramount importance. A simple quantitative method for early diagnosis of arteriosclerosis is required to prevent hemodynamic complications during general anesthesia for oral surgery patients with arteriosclerotic disease. Arterial distensibility is attracting attention as an index for assessing early-stage arteriosclerosis, as it is an independent predictor of all-cause and cardiovascular mortality, fatal and nonfatal coronary events, and fatal strokes in patients with essential hypertension.<sup>1,2</sup>

Arterial distensibility can be evaluated by measuring the pulse wave velocity (PWV) between two sites in the arterial tree.<sup>3,4</sup> In particular, brachial-ankle PWV (baPWV), which is a simple non-invasive method of assessing arterial distensibility, has been widely used in Japan.<sup>5–8</sup> BaPWV is closely related to risk factors and organ damage associated with cardiovascular disease.<sup>9–11</sup> This method is calculated from the brachial-ankle distance and brachial-ankle pulse wave spread

time via a very simple mechanism that can easily be used for measurement without special techniques. However, the problem with the clinical use of baPWV is that the index itself is closely dependent on blood pressure (BP) levels.<sup>12–14</sup> If the parameter includes functional factors such as BP, it is difficult to evaluate arterial stiffness. To assess so-called 'true arterial stiffness' by this simple method, compensation for BP is essential.

To overcome this disadvantage, a novel diagnostic parameter known as the cardio-ankle vascular index (CAVI) has been developed in Japan.<sup>15</sup> CAVI is also correlated with coronary stenosis, diabetes mellitus and metabolic syndrome.<sup>6,16–20</sup> This parameter is reported to be independent of BP levels.<sup>4,12,13,15</sup> However, these reports examined the relationship between BP and the parameter for a single measurement at one time point, and it has not been fully clarified whether these parameters are affected in the same patients by short-term changes in hemodynamics, such as those occurring during general anesthesia.

The aim of the present study is to investigate the actual influence of BP changes on CAVI and baPWV examined based on percentage change before and after general anesthesia in oral surgery patients.

Department of Dental Anesthesiology, Nihon University School of Dentistry, Tokyo, Japan

Correspondence: Dr B Kim, Department of Dental Anesthesiology, Nihon University School of Dentistry, 1-8-13 Kanda-Surugadai, Chiyoda-ku, Tokyo 101-8310, Japan. E-mail: kim@dent.nihon-u.ac.jp npg

Received 13 October 2010; revised 21 January 2011; accepted 30 January 2011; published online 7 April 2011

# METHODS

## Measurement of CAVI and baPWV

The purpose of this study was explained to the subjects, and consent was obtained for participation in the study and for release of the study data. The study was conducted in accordance with the Declaration of Helsinki.

CAVI and baPWV were measured non-invasively using the VaSera VS-1000 vascular screening system (Fukuda Denshi, Tokyo, Japan).<sup>21</sup> CAVI is clinically used as an index reflecting the distensibility of arteries from the aortic valve to the ankle<sup>22,23</sup> or knee (Figure 1). The principles underlying the CAVI<sup>13,15,22,23</sup> and baPWV<sup>8,9</sup> measurement methods have been described previously. CAVI is calculated based on the changes in vascular diameter at each beat and PWV.<sup>13,15,22,23</sup> Examination can be easily and non-invasively completed in a short period of time by measuring BP at four limbs, phonocardiogram and ECG. To detect the brachial and ankle pulse waves with cuffs, the pressure of the cuffs is kept low at 50 mm Hg to minimize the effects of cuff pressure on hemodynamics.<sup>21</sup>

CAVI was measured at the following segments: CAVI (heart to ankle) and k-CAVI (heart to knee). Baseline CAVI, k-CAVI and baPWV values were measured between 1600 and 1800 hours, around the same time of hospitalization before surgery. All measurements were conducted in a room kept at a constant temperature with the subject resting in a supine position after resting for 5 min. Ankle-brachial pressure index (ABPI) was also measured at the same time as the distensibility parameters. ABPI represents the ratio of systolic pressure in the ankle over that in the brachium, and is used for the diagnosis of obstructive arteriosclerosis. In this study, subjects with an ABPI <0.9 in the preoperative period were excluded due to suspected obstructive arteriosclerosis or to rule out possible inaccuracies in measured values.<sup>6</sup>

#### General anesthesia

With no premedication, general anesthesia was induced intravenously with fentanyl  $2 \ \mu g \ kg^{-1}$  and propofol  $2 \ mg \ kg^{-1}$  serially at a rate of  $10-6 \ mg \ kg^{-1}$  per h, followed by vecuronium 0.14 mg kg<sup>-1</sup> or rocuronium 0.9 mg kg<sup>-1</sup> to facilitate endotracheal intubation. General anesthesia was maintained with oxygen (FiO<sub>2</sub>: 0.4), nitrous oxide and propofol (4–8 mg kg<sup>-1</sup> per h). Depth of anesthesia was



Figure 1 Measurement of arterial distensibility parameters.

evaluated with a bispectral index (BIS) monitor (model A-2000, Aspect Medical System, Natick, MA, USA) and was controlled such that BIS values were maintained in a range from 40 to  $60^{.24,25}$  Respiration rate and ventilation volume were controlled at 12–14 breaths per min and 8–10 ml kg<sup>-1</sup>, respectively, such that the partial pressure of end-expiratory carbon dioxide was in the range of 30–35 mm Hg. Left brachial BP, heart rate (HR), arterial oxygen saturation and end-tidal CO<sub>2</sub> concentration as an anesthetic monitor were measured using a monitoring system (model BP608, Nippon Colin, Tokyo, Japan).

Values for CAVI, k-CAVI, baPWV and BP on the right side, as well as HR, were recorded using VaSera at 10 min after intubation by propofol induction of anesthesia.

#### Evaluation

Subjects were 30 patients (15 males and 15 females) scheduled to undergo oral surgery for a maximum of 3 h. A strong correlation between age and distensibility parameters (that is, CAVI and baPWV) had already been shown in all 30 patients during the preoperative period<sup>19–21</sup> (Figure 2). Therefore, the influence of BP changes on CAVI and baPWV was evaluated separately in the elderly ( $\geq$ 65 years) and middle-aged (<65 years) groups to eliminate the effects of age (age-dependence).<sup>6</sup>

The influence of hemodynamic changes on CAVI, k-CAVI and baPWV from the preoperative resting period to the stage during general anesthesia was evaluated. All parameters (CAVI, k-CAVI, baPWV, ABPI, BP and HR) during general anesthesia 10 min after endotracheal intubation following administration of anesthetic agents (2nd measurement) were compared with baseline data taken before surgery (first measurement). Correlations between the percentage changes in CAVI ( $\Delta$ CAVI=(2nd CAVI—1st CAVI)/1st CAVI), k-CAVI ( $\Delta$ k-CAVI=(2nd k-CAVI—1st k-CAVI)/1st k-CAVI) or baPWV ( $\Delta$ baPWV=(2nd baPWV—1st baPWV)/1st baPWV) and decreases in systolic BP ( $\Delta$ SBP=(2nd SBP—1st SBP)/1st SBP) were examined.

#### Statistical analysis

Quantitative data are expressed as mean values  $\pm$  s.d. Statistical analysis included unpaired *t*-test, paired *t*-test and simple regression analysis. Comparisons between two groups were performed by unpaired *t*-test and intra-group comparisons were performed by paired *t*-test. Associations between  $\Delta$ SBP and  $\Delta$ distensibility parameters were assessed by Pearson's correlation coefficient. A *P*-value <0.05 was considered to indicate statistical significance.

#### RESULTS

Table 1 summarizes the clinical characteristics of the subjects. Among the subjects, 14 cases (46.7%) took no anti-hypertensive agents, 12 cases (40.0%) took a calcium antagonist, and nine cases (30.0%) took an angiotensin converting enzyme inhibitor or angiotensin receptor blocker. Oral surgery in the subjects consisted of cystectomy in 18 cases (60.0%), tumorectomy in 11 cases (36.7%) and sagittal split mandibular ramus osteotomy in one case (3.3%).

Figure 3 shows the relationship between preoperative SBP and arterial distensibility parameters. In both groups, baPWV was strongly correlated with SBP, but CAVI and k-CAVI were not significantly correlated at the preoperative stage.



Figure 2 Relationship between age and preoperative arterial distensibility parameters in all subjects (n=30).

Table 2 shows the comparison between the elderly and middle-aged groups with regard to parameter values at the preoperative stage and during anesthesia, as well as the percentage change ( $\Delta$ ). On intragroup analysis, SBP decreased significantly from the preoperative stage to during general anesthesia in both groups (elderly group, P < 0.001; middle-aged group, P=0.003; unpaired t-test). Mean baPWV during general anesthesia showed a significant decrease (P<0.001 in the elderly group, and P=0.006 in the middle-aged group; paired t-test). In contrast, mean CAVI was only significantly different (P=0.025; paired t-test) in the middle-aged group, and k-CAVI in both groups and CAVI in the elderly group showed no significant differences. ABPI decreased significantly after general anesthesia (elderly group, P < 0.002; middle aged group, P < 0.009; paired *t*-test); that is, ankle SBP decreased to a greater degree than brachial SBP under general anesthesia. Although HR decreased significantly only in the elderly group (P=0.020, paired t-test) from the preoperative stage to general anesthesia, there were no significant correlations between  $\Delta$ CAVI and  $\Delta$ HR.

On analysis between the two groups, CAVI, k-CAVI and baPWV in the elderly group were significantly higher than those in the middleaged group at the preoperative period and during anesthesia.  $\Delta$ CAVI

# Table 1 Patient characteristics

	Elderly	Middle-aged	Р
Age (years)	73.1±5.5	$54.9 \pm 4.6$	< 0.001
Gender (male:female)	8:9	7:6	
Height (cm)	$156.4 \pm 7.6$	163.6±11.2	NS
Body weight (kg)	55.7±8.9	$64.0 \pm 14.6$	NS
Body mass index	22.8±3.5	23.5±2.9	NS
Hypertension	9	7	NS
Diabetes	1	1	NS
Hyperlipidemia	2	2	NS

Abbreviation: NS, non-significant.

or  $\Delta$ k-CAVI did not show any significant differences between the two groups, although  $\Delta$ baPWV in the elderly group was much higher than in the middle-aged group.

Figure 4 depicts the relationship between  $\Delta$ SBP and  $\Delta$ distensibility parameters.  $\Delta$ CAVI and  $\Delta$ k-CAVI did not show any significant correlations with  $\Delta$ SBP ( $\Delta$ CAVI: P=0.327, r=0.253 in the elderly group, P=0.608, r=0.157 in the middle-aged group;  $\Delta$ k-CAVI: P=0.983, r=0.005 in the elderly group, P=0.252, r=0.406 in the middle-aged group), whereas  $\Delta$ baPWV showed a significant decrease

# Table 2 Comparison of arterial distensibility and hemodynamic parameters between elderly and middle-aged groups

	Baseline	Dur-anesthesia	Change rate (∆)
Elderly (≥65 years)	group		
CAVI (r)	$9.30 \pm 1.00^{\ddagger \ddagger}$	$8.95 \pm 1.23^{\ddagger \ddagger}$	$-3.8\pm8.2$
k-CAVI (r)	$9.08 \pm 1.22^{\ddagger \ddagger}$	$8.79 \pm 1.39^{\ddagger \ddagger}$	$-3.2\pm7.6$
baPWV (r)	$17.44 \pm 2.85^{\ddagger\ddagger}$	$13.59 \pm 2.14^{\dagger\dagger,\ddagger\ddagger}$	$-21.2 \pm 11.1^{\ddagger\ddagger}$
SBP (mm Hg)	$138.2 \pm 13.3^{\ddagger \ddagger}$	$102.5 \pm 17.5^{\dagger\dagger}$	$-25.4\pm13.3^{\ddagger\ddagger}$
DBP (mm Hg)	83.7±9.4	$64.8 \pm 13.4^{\dagger}$	$-22.4 \pm 14.4$
HR (bt per min)	66.1±11.2	59.6±9.8	$-8.9 \pm 13.0$
ABI (r)	$1.18\pm0.06$	$1.11\pm0.06^{\dagger\dagger}$	$-5.5\pm6.1$
Middle-aged (<65 y	ears) group		
CAVI (r)	$6.94 \pm 0.70$	$6.43 \pm 1.12^{\dagger}$	$-7.6 \pm 10.6$
k-CAVI (r)	$6.90 \pm 0.81$	6.58±1.01	$-4.2 \pm 13.4$
baPWV (r)	$11.92 \pm 0.89$	$10.77 \pm 1.68^{\dagger\dagger}$	$-9.8 \pm 10.7$
SBP (mm Hg)	$124.5 \pm 9.9$	$109.9 \pm 16.1^{\dagger\dagger}$	$-11.7 \pm 11.8$
DBP (mm Hg)	80.9±8.9	70.77±16.5	$-12.9 \pm 16.1$
HR (bt per min)	$65.1 \pm 10.5$	59.0±10.3	$-8.2 \pm 16.8$
ABI (r)	$1.18\pm0.09$	$1.11\pm0.11^{\dagger\dagger}$	$-6.3 \pm 8.0$

Abbreviations: ABI, ankle-brachial pressure index; baPWV, brachial-ankle pulse wave velocity; CAVI, cardio-ankle vascular index; DBP, diastolic blood pressure; HR, heart rate; SBP, systolic blood pressure.

<sup>†</sup>P<0.05; <sup>††</sup>P<0.01 comparison between baseline and during anesthesia. <sup>‡</sup>P<0.05; <sup>‡†</sup>P<0.01 comparison between two groups.



Figure 3 Relationship between pre-SBP and arterial distensibility parameters.



Figure 4 Relationship between  $\Delta$ SBP and  $\Delta$ arterial distensibility parameters.

in parallel with  $\Delta$ SBP (*P*=0.009, *r*=0.614 in the elderly group, *P*=0.015, *r*=0.657 in the middle-aged group).

and CAVI decreased slightly, but not significantly, during general anesthesia.

#### DISCUSSION

In this study, CAVI showed no relationship with SBP at the preoperative stage. In addition, baPWV changed significantly in parallel with percentage changes in BP under general anesthesia, whereas CAVI and k-CAVI did not significantly change. General anesthesia is unlikely to improve arteriosclerosis itself, and thus, CAVI and k-CAVI are apparently less influenced by short-term changes in BP. Because of its independence from BP, CAVI may be a more sensitive and purer indicator of arterial wall stiffness than baPWV. This makes CAVI useful for serial evaluation of arterial stiffness within the same patient. Yambe et al.<sup>26</sup> reported that baPWV was positively correlated with both intima-media thickness and plaque score in hypertensive patients, whereas Masugata et al.27 reported that baPWV was associated with plaque score in type 2 diabetes, and Okura et al.4 found that CAVI was related to intima-media thickness, but not to plaque score.<sup>4</sup> Thus, CAVI was confirmed to be an index of arteriosclerosis rather than atherosclerosis, as CAVI had no correlation with plaque score in hypertensive patients.

BaPWV has been developed as a more convenient assessment of arterial distensibility. However, the problem with the clinical use of baPWV is that the index itself is closely dependent on BP.<sup>4</sup> In addition to morphological or pathophysiological changes, environmental and psychological factors may increase BP and affect baPWV measurement. Therefore, baPWV is less useful as a functional stiffness parameter, as assessment of so-called 'true arterial stiffness' requires compensation for BP.<sup>13</sup>

The present results also confirmed a preoperative relationship between SBP and distensibility parameters, in agreement with several other papers.<sup>16</sup> The serial effects of short-term changes in BP on CAVI in the same patient have not been reported previously, although it has been reported that CAVI has a much lower correlation with BP than baPWV, but this was based on single measurements in patients.<sup>6</sup> As shown in Table 2, BP and baPWV decreased significantly, Propofol has a sedative effect and a direct vasodilator action on vessel smooth muscle.<sup>28,29</sup> The vascular distensibility of the muscular vessels is affected by sympathetic nerve activity. It is very likely that the influence of anesthesia, whereby the vascular smooth muscle of the muscular vessels relaxes and expands, is reflected in baPWV, as ABPI decreased uniformly despite being measured at 10 min after tracheal intubation under general anesthesia (that is, ankle SBP decreased to a greater degree than brachial SBP). As baPWV is affected by BP and sympathetic tonus, the decrease in baPWV paralleled that in BP due to the vasodilator effects of propofol. In contrast, the relationships between  $\Delta$ SBP and  $\Delta$ CAVI or  $\Delta$ k-CAVI during general anesthesia did not show significant parallels. CAVI may only be affected by sympathetic tonus, and thus CAVI varied slightly in this study.

Very recently, Shirai *et al.*<sup>30</sup> suggested that CAVI was not affected by BP at the time of measurement, but was affected by changes in the contractility of smooth muscle cells after administration of  $\beta$ -1 and  $\alpha$ -1 adrenergic receptor blockers. They concluded that CAVI may be composed of both organic stiffness and functional stiffness factors based on smooth muscle contraction. Thus, the slight decrease in CAVI by anesthesia in this study cannot be ignored, and may be consistent with the effects of an  $\alpha$ -1 adrenergic blocking vasodilator.

In addition, there have been no reports on the utility of k-CAVI as an arterial stiffness parameter. The segments measured in both CAVI and baPWV include elastic and muscular vessels (aorta and femoraltibial arteries), but those measured in k-CAVI include only elastic vessels, other than the tibial arteries (aorta to knee). As shown in Figure 4,  $\Delta$ CAVI or  $\Delta$ k-CAVI during general anesthesia was not seen as parallel shifts with  $\Delta$ SBP. In particular, the correlation coefficient between  $\Delta$ SBP and  $\Delta$ k-CAVI in the elderly group was much lower than that between  $\Delta$ SBP and  $\Delta$ CAVI, despite showing no significant correlations. This may be because the segments measured in k-CAVI exclude the muscular tibial arteries, and thus k-CAVI may also be useful as an index of vessel stiffness. Arterial distensibility includes organic arterial sclerosis and a functional factor, which is controlled for BP (cardiac output) and constriction of vascular smooth muscle. Thus, CAVI and k-CAVI are slightly affected by changes in autonomic nervous function and muscular factors in peripheral vessels. This suggests that CAVI can be readily applied to the clinical evaluation of both organic arteriosclerosis and functional stiffness, including the vasoconstriction of smooth muscle.

There have been several reports on increases in arterial distensibility parameters being strongly correlated with aging. As vascular elasticity is greatly influenced by aging, it is necessary to remove the influence of physiological aging to evaluate the risk of blood vessel distensibility in patients with arteriosclerotic disease. In this study, both CAVI and baPWV were correlated with age, and thus distensibility parameters were evaluated separately in the elderly and middle-aged groups.

#### **Study limitations**

Our study had several limitations. First, it was difficult to clearly confirm the utility of CAVI in this study because of the small number of subjects. Further studies with larger numbers of subjects, particularly arteriosclerosis patients showing high CAVI values, are necessary. Second, the data in this study lacked objectivity; thus, comparative studies using objective measurements (for example, adrenalin concentration and HR variability (HRV) at the time of the CAVI measurement) are needed.

## CONCLUSION

Our findings suggest that propofol-induced general anesthesia induces no changes in CAVI, but leads to decreases in baPWV, due to the different characteristics of the arterial distensibility parameters. CAVI is a simple quantitative method for reliably assessing arterial stiffness and is less influenced by short-term changes in BP occurring under general anesthesia. CAVI may thus be more closely linked with true arterial stiffness than baPWV.

# **CONFLICT OF INTEREST**

The authors declare no conflict of interest.

- Blacher J, Asmar R, Djane S, London GM, Safar ME. Aortic pulse wave velocity as a marker of cardiovascular risk in hypertensive patients. *Hypertension* 1999; 33: 1111–1117.
- 2 Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, Ducimetiere P, Benetos A. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension* 2001; **37**: 1236–1241.
- 3 Mattace-Raso FU, van der Cammen TJ, Hofman A, van Popele NM, Bos ML, Schalekamp MA, Asmar R, Reneman RS, Hoeks AP, Breteler MM, Witteman JC. Arterial stiffness and risk of coronary heart disease and stroke. The Rotterdam Study. *Circulation* 2006; **113**: 657–663.
- 4 Okura T, Watanabe S, Kurata M, Manabe S, Koresawa M, Irita J, Enomoto D, Miyoshi K, Fukuoka T, Higaki J. Relationship between cardio-ankle vascular index (CAVI) and carotid atherosclerosis in patients with essential hypertension. *Hypertens Res* 2007; 30: 335–340.
- 5 Nakamura U, Iwase M, Nohara S, Kanai H, Ichikawa K, Iida M. Usefulness of brachialankle pulse wave velocity measurement: correlation with abdominal aortic calcification. *Hypertens Res* 2003; 26: 163–167.
- 6 Ibata J, Sasaki H, Kakimoto T, Matsuno S, Nakatani M, Kobayashi M, Tatsumi K, Nakano Y, Wakasaki H, Furuta H, Nishi M, Nanjo K. Cardio-ankle vascular index measures arterial wall stiffness independent of blood pressure. *Diabetes Res Clin Pract* 2008; 80: 265–270.

- 7 Kubo T, Miyata M, Minagoe S, Setoyama S, Maruyama I, Tei C. A simple oscillometric technique for determining new indices of arterial distensibility. *Hypertens Res* 2002; 25: 351–358.
- 8 Yamashina A, Tomiyama H, Takeda K, Tsuda H, Arai T, Hirose K, Koji Y, Hori S, Yamamoto Y. Validity, reproducibility, and clinical significance of noninvasive brachialankle pulse wave velocity measurement. *Hypertens Res* 2002; 25: 359–364.
- 9 Yamashina A, Tomiyama H, Arai T, Hirose K, Koji Y, Hirayama Y, Yamamoto Y, Hori S. Brachial-ankle pulse wave velocity as a marker of atherosclerotic vascular damage and cardiovascular risk. *Hypertens Res* 2003; 26: 615–622.
- 10 Munakata M, Ito N, Nunokawa T, Yoshinaga K. Utility of automated brachial ankle pulse wave velocity measurements in hypertensive patients. *Am J Hypertens* 2003; 16: 653–657.
- 11 Imanishi R, Seto S, Toda G, Yoshida M, Ohtsuru A, Koide Y, Baba T, Yano K. High brachial-ankle pulse wave velocity is an independent predictor of the presence of coronary artery disease in men. *Hypertens Res* 2004; 27: 71–78.
- 12 Matsui Y, Kario K, Ishikawa J, Eguchi K, Hoshide S, Shimada K. 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 hypertensive patients. *Hypertens Res* 2004; 27: 851–857.
- 13 Yambe T, Yoshizawa M, Saijo Y, Yamaguchi T, Shibata M, Konno S, Nitta S, Kuwayama T. Brachio-ankle pulse wave velocity and cardio-ankle vascular index (CAVI). *Biomed Pharmacother* 2004; **58**: S95–S98.
- 14 Yambe T, Meng X, Hou X, Wang Q, Sekine K, Shiraishi Y, Watanabe M, Yamaguchi T, Shibata M, Kuwayama T, Maruyama M, Konno S, Nitta S. Cardio-ankle vascular index (CAVI) for the monitoring of atherosclerosis after heart transplantation. *Biomed Pharmacother* 2005; **59**: S177–S179.
- 15 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.
- 16 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.
- 17 Wakabayashi I, Masuda H. Association of acute-phase reactants with arterial stiffness in patients with type 2 diabetes mellitus. *Clin Chim Acta* 2006; 365: 230–235.
- 18 Satoh N, Shimatsu A, Kato Y, Araki R, Koyama K, Okajima T, Tanabe M, Oishi M, Kotani K, Ogawa Y. Evaluation of cardio-vascular index, a new indicator of arterial stiffness independent of blood pressure, in obesity and metabolic syndrome. *Hypertens Res* 2008; **31**: 1921–1930.
- 19 Takenaka T, Hoshi H, Kato N, Kobayashi K, Takane H, Shoda J, Suzuki H. Cardio-ankle vascular index to screen cardiovascular diseases in patients with end-stage renal diseases. J Atheroscler Thromb 2008; 15: 339–344.
- 20 Noike H, Nakamura K, Sugiyama Y, Iizuka T, Shimizu K, Takahashi M, Hirano K, Suzuki M, Mikamo H, Nakagami T, Shirai K. Changes in cardio-ankle vascular index in smoking cessation. J Atheroscler Thromb 2010; 17: 517–525.
- 21 Kadota K, Takamura N, Aoyagi K, Yamasaki H, Usa T, Nakazato M, Maeda T, Wada M, Nakashima K, Abe K, Takeshima F, Ozono Y. Availability of cardio-ankle vascular index (CAVI) as a screening tool for atherosclerosis. *Circ J* 2008; **72**: 304–308.
- 22 Masugata H, Senda S, Okuyama H, Murao K, Inukai M, Hosomi N, Yukiiri K, Nishiyama A, Kohno M, Goda F. Comparison of central blood pressure and cardio-ankle vascular index for association with cardiac function in treated hypertensive patients. *Hypertension Res* 2009; **32**: 1136–1142.
- 23 Takaki A, Ogawa H, Wakeyama T, Iwami T, Kimura M, Hadano Y, Matsuda S, Miyazaki Y, Hiratsuka A, Matsuzaki M. Cardio-ankle vascular index is superior to brachial-ankle pulse wave velocity as an index of arterial stiffness. *Hypertens Res* 2008; **31**: 1347–1355.
- 24 Lysakowski C, Elia N, Czarnetzki C, Dumont L, Haller G, Combescure C, Tramer MR. Bispectral and spectral entropy indices at propofol-induced loss of consciousness in young and elderly patients. *Br J Anaesth* 2009; **103**: 387–393.
- 25 Gurses E, Sungurtekin H, Tomatir E, Dogan H. Assessing propofol induction of anesthesia dose using bispectral index analysis. *Anesth Analg* 2004; 98: 128–131.
- 26 Yambe M, Tomiyama H, Hirayama Y, Gulniza Z, Takata Y, Koji Y, Motobe K, Yamashina A. Arterial stiffening as a possible risk factor for both atherosclerosis and diastolic heart failure. *Hypertens Res* 2004; 27: 625–631.
- 27 Masugata H, Senda S, Yoshikawa K, Yoshihara Y, Daikuhara H, Ayada Y, Matsushita H, Nakamura H, Taoka T, Kohno M. Relationships between echocardiographic findings, pulse wave velocity, and carotid atherosclerosis in type 2 diabetic patients. *Hypertens Res* 2005; **28**: 965–971.
- 28 Robinson BJ, Ebert TJ, O'Brien TJ, Colinco MD, Muzi M. Mechanisms whereby propofol mediates peripheral vasodilation in humans. Sympathoinhibition or direct vascular relaxation? *Anesthesiology* 1997; 86: 64–72.
- 29 Klockgether-Radke AP, Frerichs A, Kettler D, Hellige G. Propofol and thiopental attenuate the contractile response to vasoconstrictors in human and porcine coronary artery segments. *Eur J Anaesthesiol* 2000; **17**: 485–490.
- 30 Shirai K, Song M, Suzuki J, Kurosu T, Oyama T, Nagayama D, Miyashita Y, Yamamura S, Takahashi M. Contradictory effects of β1- and α1- adrenergic receptor blockers on cardio-ankle vascular stiffness index (CAVI) -CAVI is independent of blood pressure. J Atheroscler Thromb 2011; 18: 49–55.