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# Relationship between coronary artery stenosis and cardio-ankle vascular index (CAVI) in patients undergoing cardiovascular surgery

Masafumi Kanamoto [a],[*], Naoki Matsumoto [b], Tatsuya Shiga [c], Fumio Kunimoto [a], Shigeru Saito [d]

[a] Gunma University Hospital Intensive Care Unit, Japan
[b] Department of Anesthesiology, Gunma Prefectural Children's Medical Center, Japan
[c] Department of Anesthesiology, Gunma Prefectural Cardiovascular Center, Japan
[d] Department of Anesthesiology, Gunma University Hospital, Japan

## ARTICLE INFO

## ABSTRACT

*Background:* The cardio-ankle vascular index (CAVI) was developed as an indicator of arterial wall stiffness, and it is less influenced by blood pressure (BP). We investigated the relationship between the CAVI and coronary artery disease (CAD), and evaluated the effects of rapid changes in BP induced by anesthetics on CAVI.
*Materials and methods:* We measured the CAVI in 76 patients before and after the administration of anesthetics for elective cardiovascular surgery. The patients were assigned to groups with or without CAD (0VD). The CAD group was then divided into 3 subgroups based on the number of stenotic vessels (1VD, 2VD, and 3VD). We compared the CAVI between CAD and 0VD, and changes in BP during the induction of anesthesia. All data were analyzed using Stat View 5.0 software.
*Results:* Systolic BP significantly decreased from $145 \pm 21$ to $107 \pm 20$ mmHg, whereas CAVI was not altered after the administration of intravenous anesthetics. Changes in BP and in pre-anesthetic CAVI (pre-CAVI) did not correlate. The pre- and post-anesthetic values for the CAVI (post-CAVI) in the 0VD and CAD groups were $8.34 \pm 1.01$ and $8.44 \pm 1.39$, and $9.95 \pm 1.22$ and $10.12 \pm 1.56$, respectively. Both values were higher in the CAD, than in the 0VD group ($P < 0.05$).
*Conclusion:* The CAVI is independent of BP and reproducible regardless of the induction of anesthesia and is significantly higher in patients with CAD. The CAVI might be able to predict atherosclerosis and coronary artery stenosis in patients undergoing cardiovascular surgery.

## 1. Introduction

Atherosclerosis is a major contributor to cardiovascular diseases that accounts for a considerable portion of mortality and morbidity rates.[1,2] The degree of atherosclerosis in a coronary artery is usually evaluated by invasive coronary angiography (CAG). Coronary CT imaging is non-invasive, but it requires transferring patients to a specific location, and this modality is not routinely available at all institutions.

Brachial-ankle pulse wave velocity (baPWV) is a simple method of assessing early arteriosclerosis. However, blood pressure (BP) influences measured baPWV values, and complicates the interpretation of measured values among patients with unstable blood pressure.[3,4] The novel cardio-ankle vascular index (CAVI) is independent of BP because BP is adjusted based on the stiffness parameter $\beta$, which can be rapidly measured without using specialized techniques.[5–9] Reports indicate that CAVI correlates with coronary atherosclerosis,[10–12] atherosclerotic complications in patients with diabetes,[13,14] intimal thickness of the carotid artery,[15] left ventricular diastolic function,[16,17] and the degree of atherosclerosis in patients on hemodialysis.[18] However, a direct correlation between the CAVI and coronary artery stenosis in patients undergoing cardiovascular surgery has not been described, and the effects of rapid BP changes on the CAVI has not been evaluated. Blood pressure often rapidly changes in patients who undergo cardiovascular surgery, especially during peri-operative periods such as anesthesia induction.

Here, we measured the CAVI in patients undergoing elective cardiovascular surgery to determine its relationship to pre-operative coronary angiography (CAG) findings. We also determined the effects of BP changes induced by anesthetics in the

* Corresponding author. Gunma University Hospital Intensive Care Unit, Department of Anesthesiology, 3-39-15 Showamachi, Maebashishi, Gunma 371-8511, Japan.
E-mail address: kanamoto@gunma-u.ac.jp (M. Kanamoto).

operating room by measuring CAVI immediately before and 3 min after the induction of anesthesia (before tracheal intubation). Coronary artery stenosis was preoperatively evaluated in all patients.

## 2. Materials and methods

### 2.1. Subjects

All patients provided written informed consent to participate in this study, which was approved by the Ethics Committee of the Gunma Prefectural Cardiovascular Center.

Between September 2010 and March 2011, 98 patients underwent CAG before elective cardiovascular surgery at Gunma Prefectural Cardiovascular Center. We excluded 22 of them because of a low ankle-brachial index (ABI < 0.9) and chronic atrial fibrillation that could affect the CAVI.[5,10,15] The remaining 55 male and 21 female patients were included in this study.

The patients were assigned to groups according to the number of stenotic vessels identified by CAG. The ratio (%) of luminal narrowing was determined according to the American Heart Association criteria.[19] Significant stenosis was defined as narrowing of ≥75% of the vessel diameter (CAD group). The 0VD group comprised 43 patients without significant stenosis of the coronary arteries, and the 1VD, 2VD, and 3VD groups comprised 11, 12, and 10 patients with significant 1-, 2-, and 3-vessel stenosis, respectively. The elective cardiovascular procedures included coronary artery bypass grafting (on- or off-pump), valve replacement, vascular replacement (of the aortic arch or abdominal aorta), and radical surgery for congenital heart diseases (Table 1).

### 2.2. CAVI measurements

We measured the CAVI using a Vasera VS-1500 (Fukuda Denshi Co. Ltd., Tokyo, Japan). In brief, cuffs were applied to the bilateral upper arms and ankles, with the patient lying supine and the head placed in the midline position. To detect brachial and ankle pulse waves using cuffs, a low cuff pressure of 50 mmHg was applied to minimize the effect of cuff pressure on hemodynamics, and BP was measured thereafter. We applied a scale conversion for convenient comparison with PWV. We calculated CAVI as follows:

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

**Table 1**
Patients' characteristics and types of elective surgery according to coronary artery disease.

| CAD | 0VD | 1VD | 2VD | 3VD | P value |
|---|---|---|---|---|---|
| n | 43 | 11 | 12 | 10 | |
| Age (years) | 65 ± 9 | 71 ± 10 | 71 ± 5 | 66 ± 7 | 0.096 |
| Male/female | 29/14 | 10/1 | 9/3 | 7/3 | N/A |
| BMI (kg/m²) | 22.2 ± 2.9 | 23.0 ± 3.0 | 23.8 ± 2.3 | 23.5 ± 4.4 | 0.26 |
| sBP (mmHg) | 127 ± 28 | 124 ± 33 | 135 ± 31 | 118 ± 29 | 0.83 |
| dBP (mmHg) | 78 ± 19 | 77 ± 22 | 77 ± 16 | 70 ± 19 | 0.19 |
| Hypertension (%) | 22 (51) | 6 (54) | 9 (75) | 8 (80) | 0.10 |
| Diabetes mellitus (%) | 6 (14) | 1 (9) | 2 (16) | 8 (5) | 0.41 |
| Hyperlipidemia (%) | 12 (28) | 5 (45) | 8 (67) | 6 (60) | 0.08 |
| Smoking (%) | 14 (33) | 5 (45) | 4 (33) | 3 (30) | 0.73 |
| CABG (on pump) | 0 | 1 | 2 | 8 | |
| CABG (off pump) | 0 | 1 | 5 | 1 | |
| Valve surgery | 26 | 2 | 2 | 0 | |
| Vascular surgery | 13 | 8 | 4 | 1 | |
| Congenital HD | 4 | 0 | 0 | 0 | |

Values are shown as means ± SD or number of patients. P value is 0VD vs. CAD. 0VD, 1VD, 2VD, and 3VD, no, 1-, 2- and 3-vessel disease, respectively. BMI, body mass index; s/dBP, systolic/diastolic blood pressure; CABG, coronary artery bypass graft surgery; Congenital HD, congenital heart disease.

Where $Ps$ is systolic BP, $Pd$ is diastolic BP, PWV is pulse wave velocity, $\Delta P$ is $Ps-Pd$, $\rho$ is blood density, and a and b are constants. Blood pressure was obtained using an upper arm cuff.

Pulse wave velocity was obtained by dividing the estimated vascular length by the time required for the pulse wave to propagate from the aortic valve to the ankle and measured using upper arm and ankle cuffs. We determined scale conversion constants (a, b) to match the CAVI with the aortic PWV method established by Hasegawa and coworkers.[20] The scale conversion constants allowed the conversion of massive amounts of extant PWV data into CAVI. All these measurements and calculation systems were assembled in the hardware, and values were automatically calculated by the Vasera.

### 2.3. Anesthetic management

After measuring the first CAVI value, anesthesia was induced with propofol (1–2 mg/kg) or midazolam (0.1–0.15 mg/kg) and fentanyl (4–6 μg/kg) or remifentanil (0.5 μg/kg/min). Rocuronium (0.8 mg/kg) was then administered, and the patients were mask-ventilated with 100% oxygen. A second CAVI value was measured 3 min later and immediately before endotracheal intubation.

### 2.4. Statistical analysis

All data are expressed as mean ± standard deviation (SD). The sample size was calculated before starting the study based on the notion that an increase of 1 in the CAVI is important. The power of the sample size to detect a 20% difference between 0VD and CAD with a 5% probability of a type II error was 80%. Systolic BP and the CAVI were compared before and after the induction of anesthesia using a paired t-test. Patients' characteristics and pre/post-anesthesia CAVI values in the 0VD and CAD group were compared using an unpaired t-test. A one-way ANOVA and Fisher's test were used for multiple comparisons in 0VD, 1VD, 2VD, and 3VD CAVI values. Values of $P < 0.05$ were considered to indicate statistical significance in all comparisons. All data were analyzed using Stat View 5.0 software (Abacus Concepts Inc., Berkeley, CA, USA).
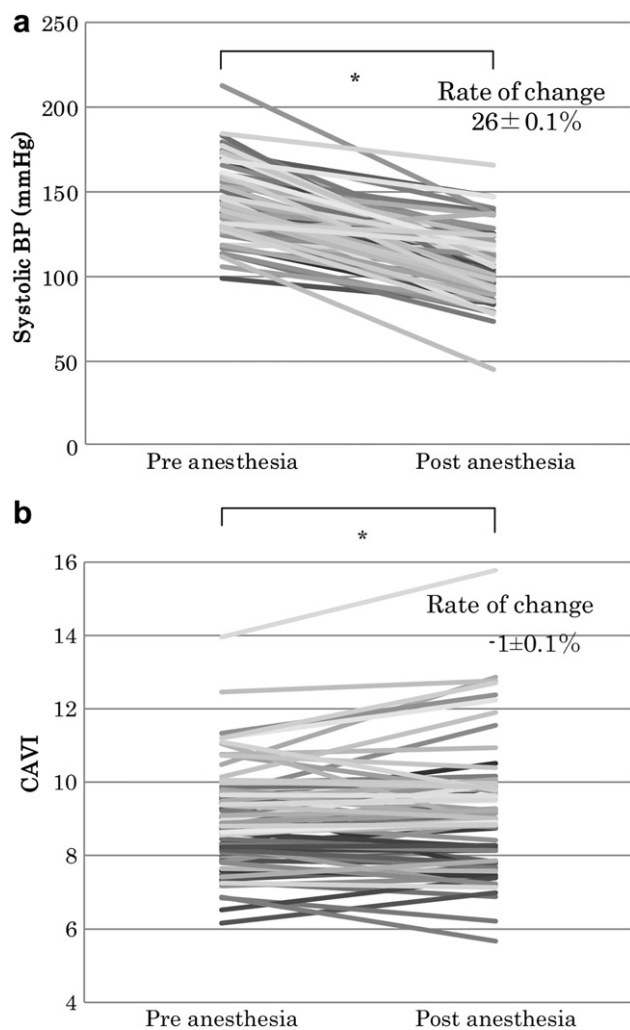
## 3. Results

Table 1 shows the clinical characteristics of the 76 patients. Systolic and diastolic BP before the induction of anesthesia, body mass index, and ratios of complications (hypertension, diabetes mellitus, and hyperlipidemia) did not significantly differ between the 0VD and CAD groups.

Systolic BP significantly decreased from 145 ± 21 to 107 ± 20 mmHg with a rate of change of 26 ± 0.1% (Fig. 1a), whereas the CAVI did not change after the induction of anesthesia (Fig. 1b). The change in BP did not correlate with pre-CAVI values (Fig. 2).

The pre- (pre-CAVI) and post- (post-CAVI) anesthesia values for CAVI were 8.34 ± 1.01 and 8.44 ± 1.39 in the 0VD group, 9.95 ± 1.22 and 10.12 ± 1.56 in the CAD group (Fig. 3a and b), and 10.27 ± 1.46 and 10.75 ± 2.01, 9.56 ± 0.98 and 9.56 ± 0.98, and 10.07 ± 1.19 and 10.1 ± 1.44 in the 1-, 2- and 3VD groups, respectively (Fig. 4a and b). These values were significantly higher in all three groups with CAD than with 0VD ($P < 0.05$).

## 4. Discussion

The CAVI has recently served as a parameter of atherosclerosis in various diseases since not only can it be measured rapidly and non-invasively, but it is also independent of BP and quite reproducible.[5–9] Some studies have indicated that CAVI could be a useful predictor of coronary atherosclerosis in individuals with risk factors for

Fig. 2. Relationship between systolic BP reduction and CAVI. Degree of reduction in systolic BP and CAVI do not significantly correlate ($R = 0.17$, $P = 0.13$). The degree of BP reduction (rate of change (%)) is calculated; $(1 -$ post-anesthesia BP/pre-anesthesia BP$) \times 100$.

Fig. 1. (a) Comparison of systolic blood pressure (sBP) between pre- and post-anesthesia. Systolic BP significantly decreased after administering intravenous anesthetics. Systolic BP: pre vs. post-anesthesia: $145 \pm 21$ vs. $107 \pm 20$ mmHg. *$P < 0.01$. Rate of change (%) was calculated as: $(1 -$ post-anesthesia BP/pre-anesthesia BP$) \times 100$. (b) Comparison of CAVI between pre- and post-anesthesia. CAVI did not significantly change after administering intravenous anesthetics. CAVI pre vs. post-anesthesia; $9.04 \pm 1.36$ vs. $9.16 \pm 1.68$. *$P = 0.61$. Rate of change (%) was calculated as: $(1 -$ post-anesthesia CAVI/pre-anesthesia CAVI$) \times 100$.

cardiovascular disease, and indicate the severity of coronary atherosclerosis. Nakamura et al reported that the CAVI increases with an increasing number of stenosed vessels and established a CAVI cutoff of 8.91 for the presence of coronary stenosis.[10] Izuhara et al similarly found that CAVI is independently associated with the severity of coronary atherosclerosis.[15] Horinaka et al and Miyoshi et al found other evidence that the CAVI is a good predictor of coronary artery disease.[11,12] Sairaku et al reported that the CAVI is higher in patients with acute coronary disease than in those with stable angina pectoris.[21]

The presence and extent of coronary artery disease is usually determined by coronary angiography, although it is invasive and associated with an increased risk of complication. Coronary artery computed tomography (coronary CT) is non-invasive, and it can detect coronary atherosclerosis with high sensitivity. However, these methods require specialized devices and operators, as well as a large space. Consequently, these modalities are not routinely available at all institutions. The extent of atherosclerosis has been estimated using PWV, but this can be influenced by blood pressure,
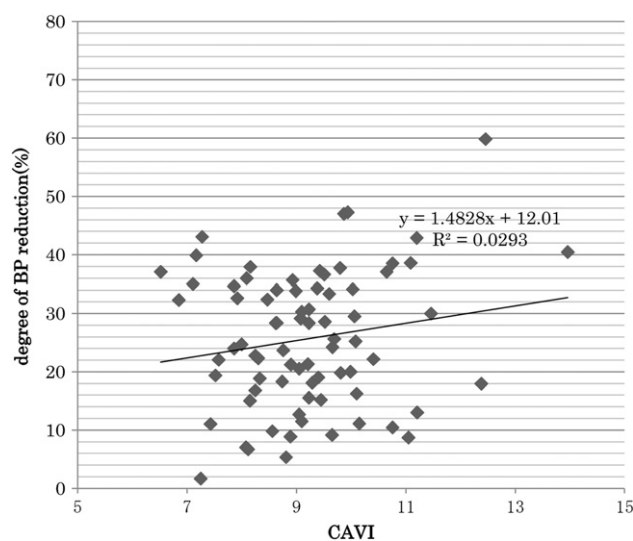
and it is not very reproducible.[3,4] Because it is independent of BP, highly reproducible, easy to apply, and does not require special techniques, the potential of CAVI as a novel parameter of atherosclerosis has recently become recognized.

We measured CAVI in patients before and after the induction of anesthesia for elective cardiovascular surgery to determine whether CAVI is independent of changes in BP induced by anesthetics, and to define the relationship between the CAVI and coronary artery stenosis. Changes in BP induced by anesthetics did not influence CAVI in the present study, and the CAVI was significantly higher in patients with coronary artery disease. To our knowledge, this is the first study to measure CAVI before and after the induction of anesthesia in the operating theater and to determine the effects of acute changes of BP on CAVI.

We found that CAVI was consistently independent of BP in all patients examined. The decrease in blood pressure after the administration of anesthetics is thought to be considerable in patients with a high CAVI (that is, with advanced atherosclerosis.) However, the present study found no statistically significant correlation. Anesthesia induction provoked similar BP changes in patients with and without CAD. Patients with CAD are generally thought to have more atherosclerosis and hypertension than healthy individuals. However, our patients were scheduled for elective surgery, and their pre-operative BP was carefully managed. This pre-operative background might explain the minor difference in BP values.

Although the CAVI significantly increased in patients with coronary artery disease, it was not related to the severity of CAD as reported.[10,15] This might be because of the limited number of patients with multiple coronary stenosis who elected to undergo surgery in the present study. A larger-scale study of patients with more severe disease might be able to detect a correlation between CAVI and the number of diseased coronary arteries. The present results suggest that coronary stenosis can exist at least in one branch when patients have a high CAVI.

In addition, this study has several limitations. Firstly, we excluded patients with ABI < 0.9 because their CAVI was considered inaccurate. However, CAD is closely related to peripheral arterial disease, and a low ABI is an independent marker of an additive risk for CAD.[22] Therefore, ABI might predict coronary atherosclerosis,
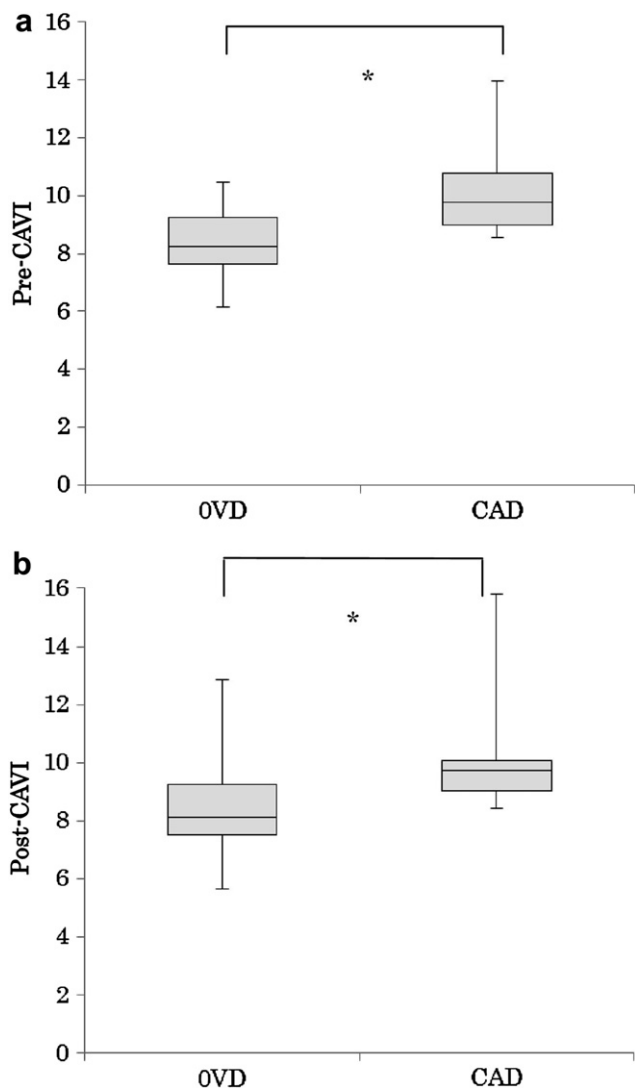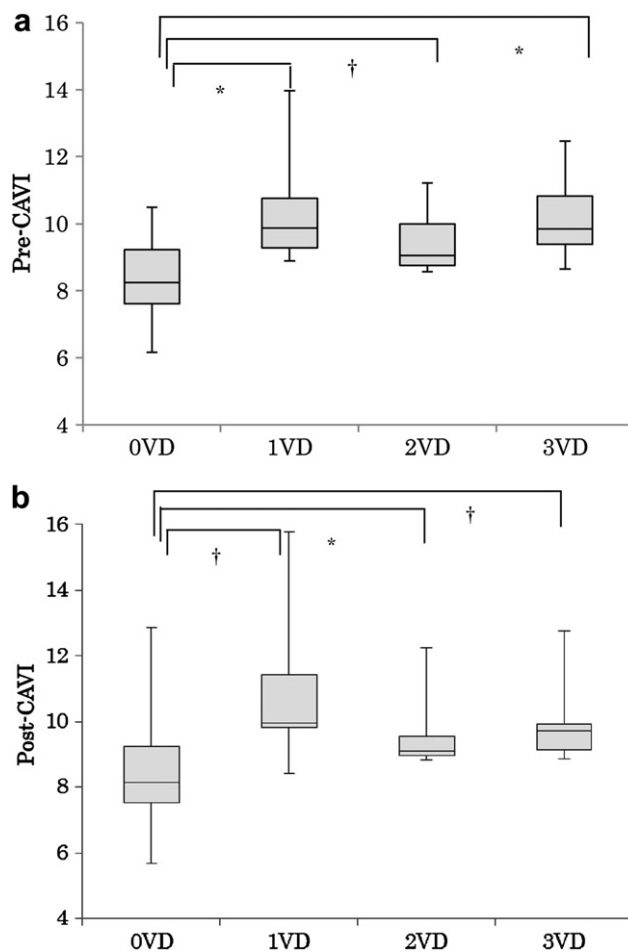
**Fig. 3.** (a) CAVI before induction of anesthesia (pre-CAVI) in 0VD vs. CAD. Pre-CAVI is significantly higher in CAD than in 0VD (*$P < 0.01$). (b) CAVI after induction of anesthesia (post-CAVI) in 0VD vs. CAD. Post-CAVI is significantly higher in CAD than in 0VD (*$P < 0.01$).



**Fig. 4.** (a) CAVI before induction of anesthesia (pre-CAVI) and number of CAD (*$P < 0.01$, †$P < 0.05$). Pre-CAVI and number of CAD are not significantly related (1- vs. 2- and 3VD, $P = 0.17$ and $P = 0.72$, respectively; 2- vs. 3VD, $P = 0.28$). (b) CAVI after induction of anesthesia (post-CAVI) and number of CAD (*$P < 0.01$, †$P < 0.05$). Post-CAVI and number of CAD are not significantly related (1- vs. 2- and 3VD $P = 0.08$ and $P = 0.41$, respectively; 2- vs. 3VD, $P = 0.30$).

especially when the value is low. Measuring both the CAVI and the ABI in patients with CAD might be valuable where possible, since measurements of these two parameters are reliable, and they seem to be mutually compensational; that is, earlier atherosclerosis is detected by CAVI, whereas ABI detects established and advanced atherosclerosis. Secondly, we also excluded patients with atrial fibrillation. However, patients with CAD might have atrial fibrillation. Another study of such patients might provide more extensive information about the association between atherosclerosis and CAD.

The present study demonstrated that CAVI could indicate coronary artery stenosis in patients with heart disease. Applying this finding to patients without heart disease might be presumptuous. However, if coronary artery stenosis can be indicated by the CAVI in patients with coronary risk factors such as hypertension, diabetes, hyperlipidemia, and a smoking habit, physicians could prepare more effective intra- and post-operative management strategies to prevent the onset of serious cardiovascular events.

We concluded that the CAVI could predict atherosclerosis and coronary artery stenosis in patients undergoing cardiovascular surgery, and that it was reproducibly independent of BP regardless of the effects of anesthetics.

## Conflicts of interest

All authors have none to declare.

## Acknowledgment

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