

## Original Article

# Association of Cardio-Ankle Vascular Index with Brain Natriuretic Peptide Levels in Hypertension

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**Aims:** Plasma brain natriuretic peptide (BNP) is an established marker of cardiovascular events in individuals without heart failure. Although the cardio-ankle vascular index (CAVI) is clinically used as a parameter of arterial stiffness, its usefulness for predicting cardiovascular events has not been fully examined. This study aimed to evaluate the association among CAVIs, plasma BNP levels and left ventricular (LV) hypertrophy and dysfunction in hypertensive patients.

**Methods:** We enrolled 136 hypertensive patients ( $69 \pm 10$  years) who had been taking antihypertensive medications for at least one year. Echocardiography was performed to evaluate LV hypertrophy and function. Plasma BNP levels and CAVIs were also measured simultaneously.

**Results:** CAVI was correlated with plasma BNP ( $r=0.245$ ,  $p=0.004$ ). Multiple linear regression analysis revealed three independent determinants of CAVI: age ( $\beta=0.568$ ,  $p<0.001$ ), diameter of ascending aorta ( $\beta=0.289$ ,  $p<0.001$ ), and diabetes ( $\beta=0.207$ ,  $p=0.003$ ). In addition, multiple linear regression analysis revealed two independent determinants of the plasma BNP level: left atrial diameter ( $\beta=0.334$ ,  $p<0.001$ ) and CAVI ( $\beta=0.256$ ,  $p=0.002$ ).

**Conclusion:** The present study indicates that increased CAVI is independently associated with elevated plasma BNP produced by increased LV afterload, that is, arterial stiffness, in hypertensive patients. Moreover, the present study raises the possibility that CAVI may be as useful as the plasma BNP level for predicting the risk of cardiovascular events in hypertensive patients.

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**Key words;** Cardio-ankle vascular index, Plasma brain natriuretic peptide, Hypertension, Echocardiography

## Introduction

Brain natriuretic peptide (BNP) is secreted from cardiomyocytes in response to arterial or ventricular wall stretch<sup>1</sup>. Clinical investigations of BNP have fo-

cused on its use in diagnosing heart failure and left ventricular hypertrophy and dysfunction<sup>2, 3</sup>; however, the Framingham Heart Study<sup>4</sup> demonstrated that plasma BNP levels predicted the risk of death and cardiovascular events in a community-based sample of individuals without heart failure. Thus, BNP has recently been well used in antihypertensive treatment to assess hypertensive target organ damage<sup>5</sup> and risk stratification<sup>6</sup> in patients without heart failure. Several studies<sup>7, 8</sup> have demonstrated that antihypertensive treatment decreased plasma BNP levels and could be

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used as a biochemical marker of effective blood pressure control.

In 2006, a new arterial wall stiffness parameter, the cardio-ankle vascular index (CAVI), was proposed<sup>9)</sup>. Its clinical significance for diabetes mellitus<sup>10)</sup>, carotid arteriosclerosis, hypertension<sup>11)</sup>, coronary artery disease<sup>12)</sup> and renal disease<sup>13)</sup> have already been reported, suggesting that CAVI is increased in arteriosclerotic diseases. Several studies<sup>14, 15)</sup> have reported that elevated CAVI was associated with left ventricular (LV) diastolic dysfunction in patients with arteriosclerosis-related disease, including hypertension, diabetes, and dyslipidemia. Plasma BNP levels are well known to be increased in patients with LV diastolic dysfunction<sup>16)</sup>; therefore, increased CAVI may be associated with elevated plasma BNP in hypertensive or diabetic patients, who are at risk of LV diastolic dysfunction; however, there are no data regarding the association between CAVI and plasma BNP level in these patients. Moreover, the clinical usefulness of CAVI in predicting cardiovascular events has not been fully examined. In the present study, we investigated the association of CAVI with the plasma BNP level, an established marker of cardiovascular events, in hypertensive patients without cardiovascular disease. In addition, we assessed LV hypertrophy and dysfunction using echocardiography, and examined the association of LV hypertrophy and dysfunction with CAVI and the plasma BNP level.

## Methods

### Subjects and Protocol

The study subjects were 136 hypertensive outpatients (82 male, 54 female; mean age  $69 \pm 10$  years, range 31-87 years) at Kagawa University Hospital who were diagnosed with hypertension. They had been taking antihypertensive medications for at least one year. Hypertension was defined as systolic blood pressure  $\geq 140$  mmHg and/or diastolic blood pressure  $\geq 90$  mmHg. Patients on hemodialysis or with a history of heart failure or ischemic heart disease were excluded. Patients with renal impairment, defined by clinically abnormal serum creatinine  $>2.0$  mg/dL, were also excluded. None of the subjects had a history of any atherosclerotic cardiovascular disease or stroke. Patients with left ventricular asynergy or valvular heart disease were excluded. Blood pressure was determined using the conventional cuff method at the time of the echocardiographic examination. Echocardiographic examinations were performed to assess cardiac structural changes and cardiac function. Before echocardiographic examination, blood analysis and measurement

of CAVI were performed. Relationships among clinical characteristics, including blood pressure and laboratory data, plasma BNP level, CAVI, and echocardiographic parameters were analyzed. This protocol was approved by the Ethics Committee of Kagawa University. Informed consent was obtained from all participants.

### Blood Analysis

Blood was sampled in the morning after a 12-hour overnight fast. Plasma total cholesterol, triglyceride, high-density lipoprotein cholesterol (HDL-C), and brain natriuretic peptide (BNP) were measured by standard laboratory techniques.

### Measurement of CAVI

CAVI was recorded using a VaseraVS-1000 vascular screening system (Fukuda Densi, Tokyo, Japan) with the patient resting in a supine position. The principal underlying CAVI has been described previously<sup>9)</sup>. ECG electrodes were placed on both wrists, a microphone for detecting heart sounds was placed on the sternum, and cuffs were wrapped around both arms and both ankles. Blood pressure was measured after detecting the pulse.

CAVI is determined by the following equation:

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

where Ps and Pd are systolic and diastolic blood pressure, PWV is pulse wave velocity from the origin of the aorta to the junction of the tibial artery with the femoral artery,  $\Delta P$  is  $Ps - Pd$ ,  $\rho$  is blood density, and a and b are constants. After automatic measurements, the obtained data were analyzed using VSS-10 software (Fukuda Densi), and the values of right and left CAVI were calculated. The averages of the right and left CAVIs were used for analysis. The average coefficient of variation of CAVI in our laboratory was 3.9%, which was sufficiently low for clinical usage and indicated that CAVI had good reproducibility.

### Echocardiographic Examination

Two-dimensional and M-mode echocardiography were performed using the Vivid Seven System (GE; Horten, Norway). We first measured the following left ventricular structural parameters by M-mode echocardiography: ventricular septal thickness (VS) at the chordae tendineae level, left ventricular end-diastolic diameter (LVDd), left ventricular end-systolic diameter (LVDs), and left ventricular posterior wall (PW) thickness at the chordae tendineae level, the end-systolic diameter of the left atrium (LAD), the diameter of the ascending aorta (AO), and the maximum inferior vena cava diameter. The left ventricular

mass was calculated according to the American Society of Echocardiography convention<sup>17)</sup> using the following formula: left ventricular mass =  $0.80 [1.04 \times (PW + VS + LVDd)^3 - (LVDd)^3] + 0.6$ . The left ventricular mass index (LVMI) was calculated as the left ventricular mass divided by the body surface area. The left ventricular ejection fraction (LVEF) was estimated by Teichholz's method<sup>18)</sup> and was used as a parameter of left ventricular systolic function.

We next measured the parameters of LV diastolic function by recording the conventional transmitral flow velocity using pulsed Doppler echocardiography<sup>19, 20)</sup>. The conventional transmitral flow velocity was recorded from the apical transducer position with the sample volume situated between the mitral leaflet tips. The peak velocity of early transmitral flow velocity (E velocity) and the peak velocity of late transmitral flow velocity (A velocity) were recorded, and the ratio of E to A (E/A ratio) was calculated.

Furthermore, pulsed wave tissue Doppler echocardiography (TDE) was performed by activating the TDE function in the same machine. Mitral annular velocities were recorded from the apical window. Sample volumes were located at the septal site of the mitral annulus. Peak early diastolic mitral annular velocities (E') were measured over three cardiac cycles, and the results were averaged<sup>21, 22)</sup>. This parameter obtained from TDE was also analyzed as a parameter of LV diastolic function. Furthermore, the ratio of E velocity to E' velocity (E/E') was calculated and was used as a parameter of LV preload, which reflects LV diastolic function<sup>21, 22)</sup>.

### Statistical Analysis

Data are expressed as the means  $\pm$  SD. Statistical analysis was performed using the SPSS software package (SPSS, Chicago, IL). Linear regression analysis was performed to evaluate the association between CAVI, BNP and other variables. Stepwise multiple regression analysis was performed to identify the independent determinants of CAVI and the plasma BNP level.  $P < 0.05$  was considered significant.

## Results

### Clinical and Echocardiographic Characteristics of Subjects

The clinical and echocardiographic parameters of the subjects are summarized in **Table 1**. The percentage (75 %) of subjects prescribed angiotensin II receptor blockers or angiotensin-converting enzyme inhibitors (ARB/ACEI) was highest among those who were also taking antihypertensive drugs. Mean values of sys-

**Table 1.** Clinical and echocardiographic characteristics of the patients

Number (male/female)	136 (82/54)
Age (years)	69.2 $\pm$ 9.7
BMI (kg/m <sup>2</sup> )	23.0 $\pm$ 3.6
Diabetes mellitus (n (%))	24 (18)
Dyslipidemia (n (%))	44 (32)
Statin (n (%))	34 (25)
Antihypertensive drugs	
ARB/ACEI (n (%))	102 (75)
CCB (n (%))	85 (63)
$\beta$ -blockers (n (%))	33 (24)
Diuretics (n (%))	41 (30)
Systolic BP (mmHg)	135 $\pm$ 19
Diastolic BP (mmHg)	81 $\pm$ 10
Heart rate (beats/min)	65 $\pm$ 10
Total cholesterol (mg/dL)	192 $\pm$ 30
HDL cholesterol (mg/dL)	50 $\pm$ 13
Triglycerides (mg/dL)	117 $\pm$ 61
BNP (pg/mL)	36.9 $\pm$ 29.4
CAVI	9.4 $\pm$ 1.3
Echocardiographic structural parameters	
LV end-diastolic diameter (mm)	46.5 $\pm$ 5.8
LV end-diastolic diameter (mm)	27.1 $\pm$ 4.5
LVMI (g/m <sup>2</sup> )	115 $\pm$ 34
LAD (mm)	37.1 $\pm$ 5.8
AO (mm)	32.1 $\pm$ 3.8
Echocardiographic functional parameters	
LVEF (%)	72 $\pm$ 7
E (cm/s)	55 $\pm$ 14
A (cm/s)	72 $\pm$ 16
E/A	0.79 $\pm$ 0.22
E' (cm/s)	5.5 $\pm$ 1.8
E/E'	10.7 $\pm$ 3.6

BMI, body mass index; ARB, angiotensin II receptor blockers; ACEI, angiotensin-converting enzyme inhibitors; CCB, calcium channel blockers; BP, blood pressure; HDL, high-density lipoprotein; BNP, brain natriuretic peptide; CAVI, cardio-ankle vascular index; LV, left ventricular; LVMI, left ventricular mass index; LAD, left atrial diameter; AO, diameter of ascending aorta; LVEF, left ventricular ejection fraction; E, peak early diastolic transmitral flow; A, peak late diastolic transmitral flow; E/A, the ratio of E to A; E', peak early diastolic annular velocity; E/E', the ratio of E to E'.

tolic (135  $\pm$  19 mmHg) and diastolic (81  $\pm$  10 mmHg) blood pressure were not high because the blood pressure of the participants was well controlled. The mean BNP level (36.9  $\pm$  29.4 pg/mL) was slightly elevated in response to increased LV afterload due to hypertension. The mean LVEF was 72  $\pm$  7%; all patients had normal systolic function (LVEF  $\geq$  55%). The elevated mean LVMI (115  $\pm$  34 g/m<sup>2</sup>) indicated the presence of LV hypertrophy in the subjects. In addition, a de-

**Table 2.** Correlations between clinical and echocardiographic parameters and CAVI

	Univariate		Multivariate	
	<i>r</i>	<i>p</i> value	$\beta$	<i>p</i> value
Age	0.250	0.004	0.568	<0.001
BMI	-0.370	<0.001	-	NS
Diabetes mellitus	0.022	NS	0.207	0.003
Dyslipidemia	-0.089	NS	-	NS
Antihypertensive drugs				
ARB/ACEI	-0.162	NS	-	NS
CCB	0.063	NS	-	NS
$\beta$ -blockers	0.078	NS	-	NS
Diuretics	-0.073	NS	-	NS
Systolic BP	0.197	0.021	-	NS
Diastolic BP	0.046	NS	-	NS
Heart rate	-0.034	NS	-	NS
Total cholesterol	-0.158	NS	-	NS
HDL cholesterol	-0.040	NS	-	NS
Triglycerides	-0.040	NS	-	NS
BNP	0.245	0.004	-	NS
Echocardiographic LV structural parameters				
LV end-diastolic diameter	-0.144	NS	-	NS
LV end-systolic diameter	-0.058	NS	-	NS
LVMI	0.132	NS	-	NS
LAD	-0.055	NS	-	NS
AO	0.348	<0.001	0.289	<0.001
Echocardiographic LV functional parameters				
LVEF	-0.075	NS	-	NS
E	-0.209	0.014	-	NS
A	0.156	NS	-	NS
E/A	-0.350	<0.001	-	NS
E'	-0.432	<0.001	-	NS
E/E'	0.221	0.009	-	NS

CAVI, cardio-ankle vascular index; BMI, body mass index; ARB, angiotensin II receptor blockers; ACEI, angiotensin-converting enzyme inhibitors; CCB, calcium channel blockers; BP, blood pressure; HDL, high-density lipoprotein; BNP, brain natriuretic peptide; LV, left ventricular; LVMI, left ventricular mass index; LAD, left atrial diameter; AO, diameter of ascending aorta; LVEF, left ventricular ejection fraction; E, peak early diastolic transmitral flow; A, peak late diastolic transmitral flow; E/A, the ratio of E to A; E', peak early diastolic annular velocity; E/E', the ratio of E to E'; NS, not significant.

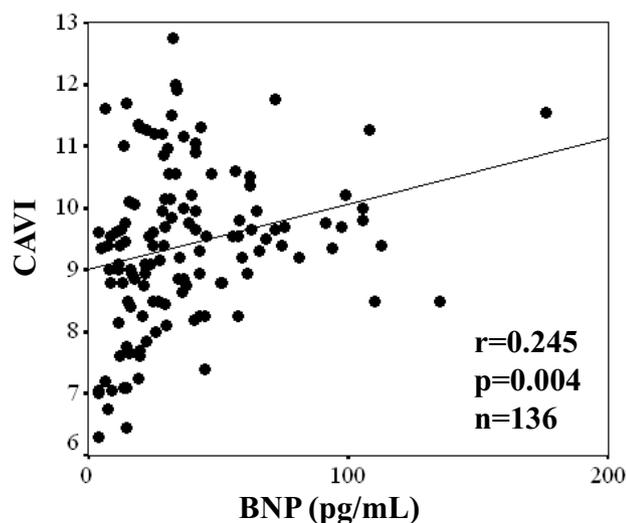
creased mean E/A ( $0.79 \pm 0.22$ ) and E' ( $5.5 \pm 1.8$  cm/s) indicated LV diastolic dysfunction accompanying LV hypertrophy. An increased mean E/E' ( $10.7 \pm 3.6$ ) suggested a hypertension-induced increase in left atrial pressure, which is a parameter of LV diastolic dysfunction<sup>21, 22</sup>.

#### Association between CAVI and Other Variables

Linear regression analysis was performed to examine the relationship between CAVI and other variables in all subjects (Table 2). The CAVI correlated with age ( $r=0.250$ ,  $p=0.004$ ), BMI ( $r=-0.370$ ,  $p<$

$0.001$ ), systolic blood pressure ( $r=0.197$ ,  $p=0.021$ ), BNP ( $r=0.245$ ,  $p=0.004$ ), diameter of ascending aorta ( $r=0.348$ ,  $p<0.001$ ), E ( $r=-0.209$ ,  $p=0.014$ ), E/A ( $r=-0.350$ ,  $p<0.001$ ), E' ( $r=-0.432$ ,  $p<0.001$ ), and E/E' ( $r=0.221$ ,  $p=0.009$ ). The correlation between CAVI and BNP ( $r=0.245$ ,  $p=0.004$ ) is depicted in Fig. 1.

Stepwise multiple regression analysis was performed to identify which clinical and echocardiographic parameters were independently associated with CAVI. Stepwise multiple regression analysis was performed for all parameters in Table 2. This analysis



**Fig. 1.** Relationship between BNP and CAVI

BNP was correlated with CAVI ( $r=0.245$ ,  $p=0.004$ ).  
BNP, brain natriuretic peptide; CAVI, cardio-ankle vascular index

indicated that age ( $\beta$  coefficient=0.568,  $p<0.001$ ), diameter of ascending aorta ( $\beta$  coefficient=0.289,  $p<0.001$ ) and diabetes ( $\beta$  coefficient=0.207,  $p=0.003$ ) were independently associated with CAVI (**Table 2**).

#### Association between BNP and Other Variables

Linear regression analysis was performed to examine the relationship between BNP and other variables in all subjects (**Table 3**). The BNP was correlated with age ( $r=0.277$ ,  $p=0.001$ ), CAVI ( $r=0.245$ ,  $p=0.004$ ), left atrial diameter ( $r=0.319$ ,  $p<0.004$ ), E ( $r=-0.179$ ,  $p=0.037$ ), E/A ( $r=-0.253$ ,  $p=0.003$ ), E' ( $r=-0.316$ ,  $p<0.001$ ), and E/E' ( $r=0.202$ ,  $p=0.018$ ).

Stepwise multiple regression analysis was performed to identify which clinical and echocardiographic parameters were independently associated with BNP. Stepwise multiple regression analysis was performed for all parameters in **Table 3**. This analysis indicated that left atrial diameter ( $\beta$  coefficient=0.334,  $p<0.001$ ) and CAVI ( $\beta$  coefficient=0.256,  $p=0.002$ ) were independently associated with BNP (**Table 3**).

#### Discussion

This study presents data regarding the relationships between CAVI and the plasma BNP level, an established marker of cardiovascular events, in treated hypertensive patients who had been receiving antihypertensive drugs for at least one year. The data led us to the following conclusions. First, increased CAVI is

associated with elevated plasma BNP. Second, independent determinants of CAVI are age, diameter of the ascending aorta, and diabetes. Finally, independent determinants of the plasma BNP level are left atrial diameter and CAVI.

Previous studies<sup>23, 24</sup>) demonstrated that aortic stiffness as assessed by brachial-ankle pulse wave velocity (baPWV) was associated with the plasma BNP level. Our data demonstrated for the first time that aortic stiffness as assessed by CAVI was also associated with the plasma BNP level. As CAVI is influenced by pulse wave velocity (PWV), CAVI is correlated with PWV to some degree; however, CAVI is different from PWV, especially in patients with increased arterial stiffness<sup>25</sup>). Therefore, the present study confirms the feasibility of using CAVI to assess arterial stiffness by comparing it to the plasma BNP level. As CAVI is a newly developed parameter of arterial stiffness, there are few prospective studies estimating the clinical usefulness of CAVI in assessing the risk of cardiovascular events. While the plasma BNP level is an established marker of the risk of cardiovascular events<sup>4</sup>), CAVI may be as useful as the plasma BNP level in predicting the risk of cardiovascular events in hypertensive patients.

One of the merits of CAVI is that it is less influenced by blood pressure than baPWV<sup>9, 26</sup>). Of course, blood pressure was not selected in the present study as an independent determinant of CAVI by multiple regression analysis even if systolic blood pressure showed a weak correlation ( $r=0.197$ ,  $p=0.021$ ) with CAVI by linear regression analysis (**Table 2**). Our data also demonstrated that CAVI, but not blood pressure was an independent determinant of plasma BNP (**Table 3**). As the plasma BNP level reflects hypertension-induced cardiac damage, including left ventricular (LV) hypertrophy<sup>27</sup>) and diastolic dysfunction<sup>28</sup>), our data indicate that hypertension-induced cardiac damage should be estimated not by blood pressure but by arterial stiffness, as assessed by CAVI.

In the present study, age and diabetes were independent determinants of CAVI (**Table 2**). This is in agreement with previous studies<sup>9, 10</sup>); however, our data can add new information on the characteristics of CAVI by showing a significant association between CAVI and the diameter of the ascending aorta (**Table 2**). In the present study, the diameter of the ascending aorta was selected as an independent determinant of CAVI. Previous studies<sup>29, 30</sup>) reported that dilation of the ascending aorta reflected the effects of hypertension and atherosclerosis. Other previous studies<sup>31, 32</sup>) have demonstrated that dilation of the ascending aorta could be a useful marker of target organ damage, in-

**Table 3.** Correlations between clinical and echocardiographic parameters and BNP

	Univariate		Multivariate	
	<i>r</i>	<i>p</i> value	$\beta$	<i>p</i> value
Age	0.277	0.001	-	NS
BMI	-0.026	NS	-	NS
Diabetes mellitus	-0.024	NS	-	NS
Dyslipidemia	0.032	NS	-	NS
Antihypertensive drugs				
ARB/ACEI	-0.106	NS	-	NS
CCB	0.074	NS	-	NS
$\beta$ -blockers	0.088	NS	-	NS
Diuretics	0.086	NS	-	NS
Systolic BP	0.061	NS	-	NS
Diastolic BP	-0.057	NS	-	NS
Heart rate	-0.141	NS	-	NS
Total cholesterol	-0.012	NS	-	NS
HDL cholesterol	0.013	NS	-	NS
Triglycerides	-0.052	NS	-	NS
CAVI	0.245	0.004	0.256	0.002
Echocardiographic LV structural parameters				
LV end-diastolic diameter	0.008	NS	-	NS
LV end-systolic diameter	-0.025	NS	-	NS
LVMI	0.150	NS	-	NS
LAD	0.319	<0.001	0.334	<0.001
AO	0.075	NS	-	NS
Echocardiographic LV functional parameters				
LVEF	-0.004	NS	-	NS
E	-0.179	0.037	-	NS
A	0.087	NS	-	NS
E/A	-0.253	0.003	-	NS
E'	-0.316	<0.001	-	NS
E/E'	0.202	0.018	-	NS

BNP, brain natriuretic peptide; BMI, body mass index; ARB, angiotensin II receptor blockers; ACEI, angiotensin-converting enzyme inhibitors; CCB, calcium channel blockers; BP, blood pressure; HDL, high-density lipoprotein; CAVI, cardio-ankle vascular index; LV, left ventricular; LVMI, left ventricular mass index; LAD, left atrial diameter; AO, diameter of ascending aorta; LVEF, left ventricular ejection fraction; E, peak early diastolic transmitral flow; A, peak late diastolic transmitral flow; E/A, the ratio of E to A; E', peak early diastolic annular velocity; E/E', the ratio of E to E'; NS, not significant.

cluding left ventricular hypertrophy, carotid atherosclerosis and microalbuminuria in hypertensive patients. Our data support these previous studies and prove the feasibility of CAVI in assessing atherosclerosis.

In the present study, some patients had relatively high levels of BNP (>100 pg/mL) (**Fig. 1**). Patients with a history of heart failure or heart failure per se were excluded from the present study; however, patients with relatively high levels of BNP (>100 pg/mL) in the present study may be at risk of developing heart failure in the future. A BNP cut-off value of 100 pg/

mL has been shown to be useful for estimating cardiac risk in primary care<sup>33</sup>). The present study demonstrated that BNP 100 pg/mL was equal to CAVI 10.1 using simple linear regression analysis (**Fig. 1**); therefore, CAVI may be as useful as the plasma BNP level in predicting the risk of cardiovascular events in hypertensive patients.

The most striking result in our analysis was that CAVI and left atrial diameter were independent determinants of the plasma BNP level (**Table 3**). CAVI is a parameter of arterial stiffness, which reflects LV afterload<sup>34</sup>). Left atrial diameter is increased in response to

elevated atrial pressure, which reflects LV preload<sup>35</sup>). Therefore, our data indicate that LV afterload (CAVI) and preload (left atrial diameter) are associated with the plasma BNP level, which reflects cardiac organ damage in hypertensive patients. The associations among plasma BNP and CAVI and left atrial diameter underlie the increase in LV afterload and preload in hypertensive patients. We cannot determine the precise mechanisms of these associations. One possible explanation is that hypertension-induced afterload elevation produces LV hypertrophy and diastolic dysfunction, which lead to increased LV preload; however, LVMI as a parameter of LV hypertrophy was not associated with plasma BNP in the present study (**Table 3**). As the participants in this study were hypertensive patients who had been treated for at least one year, the treatment may have improved their LV hypertrophy. Our data suggest that left atrial diameter and CAVI rather than LVMI may be useful for assessing cardiac organ damage in treated hypertensive patients.

The present study has several limitations. First, it lacks a control group to determine whether the relationship between CAVI and BNP is specific to hypertensive patients. Second, we have no data to determine whether pharmacological interventions, including antihypertensive agents and statins, have beneficial effects on arterial stiffness and BNP levels because the present study was cross-sectional. A previous study<sup>36</sup> demonstrated that long-term angiotensin II receptor blocker (ARB) treatment had a more beneficial effect on arterial stiffness than long-term calcium-channel blocker (CCB) treatment. Follow-up studies regarding the relationship between CAVI and BNP levels are needed in healthy subjects, untreated hypertensive patients, and treated hypertensive patients. Third, the present study included 24 (18 %) diabetic patients with hypertension (**Table 1**). Diabetes mellitus was independently associated with CAVI (**Table 2**). The relationship between CAVI and BNP may be influenced by the presence of diabetes. Further studies including a large number of diabetic patients with hypertension are needed to elucidate the influence of diabetes. Finally, it was surprising that CAVI was inversely correlated with BMI in simple linear regression analysis (**Table 2**); however, multiple linear regression analysis demonstrated that BMI was not selected as an independent determinant of CAVI. Further studies are needed to determine the relationship between CAVI and BMI.

In conclusion, increased CAVI is independently associated with elevated BNP, which is produced by increased LV afterload, that is, arterial stiffness in hy-

pertensive patients. CAVI may be as useful as the plasma BNP level for predicting the risk of cardiovascular events in hypertensive patients.

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