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Radial augmentation index associated with increase in B-type natriuretic peptide in patients with hypertension

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Abstract

Brain natriuretic peptide (BNP) level has been used as a marker of left ventricular (LV) systolic dysfunction (LVSD), even though some patients with atherosclerosis have a high BNP level irrespective of LV function. In this study, we investigate whether augmentation index (AI), which is an index of wave reflection, is involved in increasing BNP level in hypertensive patients without LVSD. Sixty treated hypertensive patients were enrolled in this study. Radial AI (r-AI) was measured in all patients. The patients were classified into tertiles on the basis of r-AI to identify the characteristics of the patients with a high r-AI.

BNP level was significantly higher in the patients classified into the highest tertile of r-AI. In echocardiography, e′, which is index of left ventricular (LV) diastolic function, decreased and LV mass index (LVMI) increased gradually with r-AI, whereas there was no difference in LV ejection fraction (LVEF). r-AI significantly correlated with LVMI ($r=0.35$, $p<0.01$) and e′ ($r=-0.30$, $p<0.05$). In univariate analysis, age, heart rate, r-AI, LVEF, e′ and LVMI were significantly correlated with BNP level, whereas multivariate analysis demonstrated that only r-AI and LVEF correlated with BNP level. In conclusion, an increase in r-AI was significantly associated with an increase in BNP level in hypertensive patients without LVSD. LV hypertrophy and diastolic dysfunction associated with increase in r-AI may be involved in increase in BNP level.

Keywords: Radial augmentation index; Brain natriuretic peptide; Left ventricular hypertrophy; Diastolic dysfunction

1. Introduction

The brain natriuretic peptide (BNP) is a member of the family of genetically distinct natriuretic peptides synthesized and released by cardiomyocytes in response to increased transmural wall stress [1]. Although BNP level has been reported to be a useful marker of left ventricular systolic dysfunction (LVSD) [2], some patients with atherosclerotic diseases such as coronary artery disease (CAD) have a high BNP level irrespective of LVSD [3,4]. This increase in BNP level occasionally confuses physicians when interpreting results; however, the underlying mechanism of this increase in BNP level in patients with atherosclerosis has not been fully elucidated.

Augmentation index (AI), which is defined as an increase in pressure from the first systolic shoulder to the peak pressure of the aortic pressure waveform expressed as a percentage of peak pressure, is one of the indexes of wave reflections [5,6]. AI is increased by cardiovascular risk

Abbreviations: BNP, brain natriuretic peptide; LVSD, left ventricular systolic dysfunction; CAD, coronary artery disease; AI, augmentation index; LV, left ventricular; r-AI, radial AI; SBP, systolic blood pressure; DBP, diastolic blood pressure; LVED, LV dimensions at end diastole; LVES, LV dimensions at end systole; LVEF, left ventricular ejection fraction; LAD, left atrium dimension; DcT, deceleration time of E-wave; TDI, tissue doppler imaging; e′, early diastolic velocity.

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factors such as age, smoking and hypertension, and was found to be an independent marker of coronary artery disease [7].

Increase in BNP level is caused by LV diastolic dysfunction independently of LV systolic function [8]. Recently, some investigators have demonstrated that an increase AI may result in left ventricular (LV) diastolic dysfunction [9] as well as LV hypertrophy [10,11]. Thus, there is a possibility that an increase in AI may be involved in increasing BNP level irrespective of LVSD. To date, central aortic augmentation has been evaluated noninvasively by mathematically transforming the radial artery pulse waveform to the aortic pulse waveform [6]. Recently, similar information on central pressure wave reflection can be obtained directly from radial pulse as radial AI (r-AI) without the need for a transfer function [11–13]. In this study, we measured r-AI in patients with hypertension without LVSD and investigated the influence of r-AI on BNP level.

2. Methods

Sixty treated hypertensive patients were enrolled in this study from the Okayama University Hospital. r-AI was measured in all the patients. Serum BNP level was also measured. We then classified the patients into tertiles on the basis of r-AI to identify the characteristics of the patients with a high r-AI.

Hypertension was diagnosed in patients who had a history of medical treatment, a systolic blood pressure (SBP) $\geq$140 mmHg or a diastolic blood pressure (DBP) $\geq$90 mmHg. Patients with atrial fibrillation or peripheral artery disease, defined as having an ankle-brachial pressure index <0.9 in either leg, were excluded from this study. Informed consent was obtained from all patients.

2.1. Echocardiography

Two-dimensional and M-mode resting echocardiographic recordings were obtained using commercially available instruments. LV dimensions at end diastole (LVED) and end systole (LVES) were measured at the papillary muscle level from the parasternal short-axis view, and LVED and LVES were used to calculate left ventricular ejection fraction (LVEF). Left atrium dimension (LAD) was measured at the end systole on the basis of an M-mode recording at the level of the aortic root. Mitral inflow was assessed by pulsed-wave doppler echocardiography from the apical four-chamber view. On the basis of the mitral inflow profile, E- and A-wave velocities, the deceleration time of E-wave (DcT) and E/A ratio were measured. Tissue doppler imaging (TDI) of the mitral annulus was obtained from the apical four-chamber view as previously described [14]. A sample volume was placed sequentially at the lateral and septal mitral annulus, and early diastolic velocity (e′) was measured. We used average value of e′ measured at septal and lateral site. The ratio of mitral velocity to the early diastolic velocity of the medial mitral annulus (E/e′) was also calculated.

2.2. Hemodynamic analysis

SBP, DBP and heart rate were measured in the right upper arm using an oscillometric method after 5 min of rest in a sitting position. Immediately after measuring BP, the left radial arterial waveform was recorded by the tonometric method using a newly developed automatic waveform analyzer, described previously (HEM-9000AI; Omron Healthcare Co., Ltd., Kyoto, Japan) [11,13]. r-AI was calculated using the following equation: (second peak systolic BP − diastolic BP) / (first peak BP − DBP) * 100 (%).

2.3. Laboratory measurements

Blood samples were obtained during a fasting state. The serum lipid profiles comprising total cholesterol, triglyceride and LDL cholesterol were estimated by an enzymatic method. Plasma BNP level was measured with a commercially available specific immunoradiometric assay kit for human BNP (Shionoria BNP kit, Osaka, Japan) [15].

Table 1
Patient characteristics

	Radial augmentation index, %				
	All	1-tertile (47–84) (n=20)	2-tertile (85–93) (n=20)	3-tertile (94–116) (n=20)	p
Age (years)	66±11	62±4	67±10	69±7	0.40
Male sex (%)	68	90	70	50	<0.05
Height (cm)	160±8	163±8	160±9	156±8	0.06
Weight (kg)	61±10	63±10	61±11	58±8	0.35
BMI (kg/m^2)	24±3	23±2	24±3	24±3	0.93
CAD (%)	32	30	30	35	0.93
Coronary risk factor					
Dyslipidemia (%)	57	50	60	60	0.76
Diabetes (%)	21	20	30	15	0.50
Medication					
β-blockers (%)	35	15	35	55	<0.05
ACEIs or ARBs (%)	42	30	52	45	0.34
Calcium channel blockers (%)	37	50	36	25	0.26
Statins (%)	44	40	47	45	0.89
TC (mg/dl)	202±32	202±24	203±37	200±35	0.85
LDL-C (mg/dl)	107±28	105±23	109±32	107±28	0.93
TG (mg/dl)	158±88	168±97	174±83	133±84	0.13
HbA1c (%)	5.8±0.9	5.9±1.0	5.7±0.7	5.7±0.9	0.26
Creatinine (mg/dl)	0.9±0.3	0.8±0.2	1.0±0.4	0.8±0.2	0.36
BUN (mg/dl)	18.1±6.7	17.0±5.2	18.1±9.1	19.0±4.8	0.20
BNP (pg/ml)	44±40	26±34	38±34	66±42	<0.01

Values are expressed as numbers with the percentages in parentheses or mean±SD. BMI, body mass index; CAD, coronary artery disease; ACEs, angiotensin converting enzyme inhibitor; ARBs, angiotensin receptor blocker; TC, total cholesterol; LDL-C, LDL cholesterol; TG, triglyceride; BNP, brain natriuretic peptide.