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Original article

Factors influencing left atrial volume in treated hypertension

Yuan Chen (MD)[a,b], Hirotomo Sato (MD)[a], Nobuhide Watanabe (MD)[a], Tomoko Adachi (MD)[a], Nobuhiro Kodani (MD)[a], Masatake Sato (MD, PhD)[a], Nobuyuki Takahashi (MD, PhD)[a], Jun Kitamura (MD, PhD)[a], Hidetoshi Sato (MD, PhD)[a], Kazuto Yamaguchi[a], Hiroyuki Yoshitomi (MD)[a], Kazuaki Tanabe (MD, PhD, FJCC)[a,*]

[a] *Division of Cardiology, Department of Internal Medicine, Shimane University Faulty of Medicine, Izumo, Japan*
[b] *Department of Cardiology, Second Hospital Affiliated Ningxia Medicine University, China*

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ABSTRACT

Background: Left atrial (LA) enlargement has been documented to occur in hypertension (HT), and has been an index for evaluating the diastolic function of the left ventricle. Enlargement of the LA is one of the vital factors that induce heart failure and atrial fibrillation (AF) in patients with HT.
Methods and subjects: 130 treated hypertensive patients were enrolled. All recruits participated in an echocardiogram, electrocardiogram, a routine blood examination including brain natriuretic peptide (BNP), and physical examinations.
Results: Left ventricular mass (LVM) indexed to height$^{2.7}$ had a significant positive correlation with left atrial volume index (LAVI) ($p < 0.0001$), as well as natural logarithm BNP ($p < 0.001$). Blood pressure levels were not associated with LAVI, neither body mass index nor age. LAVI had a positive correlation with factors involving the left ventricle volume, LVM, and right ventricle systolic pressure (RVSP) ($r = 0.687$, $p < 0.0001$). The parameters of LV diastolic function were positively but weakly associated with LA size. In the subgroup of LAVI, the evidence of paroxysmal atrial fibrillation (PAF): LAVI < 32 ml/m^2 had no PAF, whereas the incidence of PAF was 7.5%, 11.4%, and 15.2%, respectively in the LAVI > 32 ml/m^2 group. Of anti-hypertension drugs, angiotensin-converting enzyme inhibitors and angiotensin receptor blockers had a tendency to reduce LAVI; however, there was no statistical significance within the groups.
Conclusions: Left ventricular volume and mass are independent factors affecting LAVI in treated HT. The incidence of PAF is associated with LA size. In patients with treated HT, LA size may be a useful surrogate marker for monitoring the effectiveness of medical therapy and occurrence of AF.

Introduction

Left atrial (LA) enlargement often occurs in patients with hypertension (HT) [1,2]. HT results in left ventricular (LV) hypertrophy and reduces LV diastolic function. LA volume is less influenced by acute hemodynamic changes and reflects sub-acute or chronic diastolic function. The increase in LA size and function occur in parallel with the degree of LV diastolic dysfunction. It has been established that LA volume is a sensitive marker for the severity of LV diastolic dysfunction [3,4]. Moreover, the occurrence of paroxysmal atrial fibrillation (PAF) in hypertensive subjects is associated with LA enlargement [5], and the risk of developing AF is increased by 1.5 times in patients with HT [5,6]. The Framingham study revealed that a 5 mm increase in LA dimension produced a 39% increase in the incidence of AF [7]. AF is a major risk factor for stroke and mortality. Therefore, it is crucial to identify patients who have PAF in order to prevent subsequent thromboembolic complications, especially in patients with HT. It is of importance to assess the factors that affect LA volumes and the risk of AF in patients with HT. Although the effect of HT on LA was extensively studied, few studies have addressed this in detail with relation to treated HT, particularly in a population with well-controlled blood pressure (BP). Accordingly, we performed a study of patients with HT and well-controlled BP who had a comprehensive assessment of echocardiography, especially for LA volume and its relative factors.

Methods

Subjects

This was a retrospective cross-sectional study, which randomly selected adult patients with HT history who underwent a transthoracic echocardiogram for any indication at our institution from

* Corresponding author at: 89-1 Enya-cho, Izumo, 693-8501, Japan. Tel.: +81 853 20 2249; fax: +81 853 20 2201.
E-mail address: kaz@med.shimane-u.ac.jp (K. Tanabe).

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January to December 2008. This study protocol was approved by the Ethical Committee of Shimane University.

Subjects consisted of 873 patients with HT from admission to the clinic in the Cardiology Department of Shimane University Hospital. The data were corroborated from hospital records with their treating physician. Patients who had previously documented significant valvular disease (more than mild valvular regurgitation or stenosis), myocardial infarction, LV ejection fraction of <50%, and a history of AF, previous cardiac surgery, or implanted devices, and incomplete data were excluded. Of the 873 patients recruited, 743 of the patients were excluded based on the above exclusion criteria. The final HT population analyzed consisted of 130 patients with sinus rhythm and well-controlled BP (<140/90 mmHg) [8]. Mean age was 69.6 ± 10.1 years old, and the proportion of females was 39.2% (51/130). BP was checked, at the same day of the echocardiographic examination, and electrocardiogram and/or ambulatory electrocardiographic recording, routine blood samples including brain natriuretic peptide (BNP) were performed within one week. The normal value of BNP is <20 pg/ml, whereas >40 pg/ml is defined as abnormal.

Standard transthoracic echocardiographic study

Echocardiograms were performed according to established clinical practice using 3 commercially available instruments, using harmonic 2.5–5 MHz variable frequency phased-array transducers. LA and LV diameter by M-mode was measured in the parasternal long-axis view [9]. LV wall thickness was measured by M-mode using American Society of Echocardiography (ASE) criteria [10]. Relative wall thickness was measured as 2× posterior wall thickness in diastole divided by LV diastolic dimension, as an index of the LV geometric pattern [11,12]. LV end-diastolic and end-systolic volumes were determined from the apical 4- and 2-chamber views using the biplane method of discs [10]. LA volumes were measured at ventricular systole just before the mitral valve opening. All volumes were calculated from the apical 4- and 2-chamber zoomed views using the biplane method of discs [13,14]. LA volumes were indexed to body surface area (BSA). LA enlargement was defined as $\geq$32 ml/m^2.

LV diastolic function was determined using standard echocardiographic parameters including peak E velocity, peak A velocity, E/A ratio, and the deceleration time. The early diastolic velocity (Ea) and late diastolic velocity (Aa) of mitral annulus were measured by Doppler tissue imaging, by placing the sample volume at the septal annulus, recording at a sweep speed of 100 mm/s and measured as an average of 3 beats.

Left ventricular mass

The ASE-recommended area-length method was used to determine LV mass (LVM) [10]. LVM was indexed to allometric height$^{2.7}$ [15,16]. According to values from the Strong Heart Study [16], LVM subgroups were: group 1, normal LVM in women was classified as $\leq$44 g/m$^{2.7}$ and in men was $\leq$49 g/m$^{2.7}$, group 2, mildly increased LVM in women was 45–50 g/m$^{2.7}$ and in men 50–56 g/m$^{2.7}$, group 3, moderately increased LVM in women was 51–56 g/m$^{2.7}$ and in men 57–63 g/m$^{2.7}$, and group 4, severely increased LVM in women was $\geq$57 g/m$^{2.7}$ and in men $\geq$64 g/m$^{2.7}$.

Statistical analysis

All values are expressed as mean ± SD. Plasma concentrations of BNP did not follow a Gaussian distribution and then were transformed with a natural logarithm preceding statistical analysis. Linear regression was used to examine the correlation between the clinical factors and LA size. Subgroups of different drugs were analyzed using one-way ANOVA. The correlation between 2 variables was assessed by the Pearson rank correlation coefficient. Univariate and multivariate regression analysis was used to examine independent predictors of an increased LA size. Data were analyzed using SPSS version 11.5 (SPSS Inc., Chicago, IL, USA) and Graphpad Prism 5.0 (Graphpad, La Jolla, CA, USA), $p < 0.05$ was considered statistically significant.

Table 1
Clinical characteristics of the hypertensive population (n = 130).

Arrhythmias, %	22.3
Atrial enlargement, %	83.0
DM, %	44.6
Hyperlipidemia, %	54.6
Current smoker, %	31.5
LV diastolic function	
Restricted filling pattern, %	3.0
Pseudonormal filling pattern, %	36.2
Medication	
AECI or ARBs, %	18.5
Calcium antagonists, %	25.4
Both, %	44.6
Others, %	15.4

DM, diabetes mellitus; LV, left ventricular; ACEI, angiotensin-converting enzyme inhibitors; ARBs, angiotensin receptor antagonist; Others, β-blockers or diuretics; Both, ACEI and/or ARBs and calcium antagonists.

Results

Clinical characteristics of the HT group are given in Table 1. In our study, 80% of the population was on $\leq$3 antihypertensive medications, and their BP was well controlled (systolic BP, 135.2 ± 18.5 mmHg, diastolic BP, 73.9 ± 13.2 mmHg). The mean values for clinical and echocardiographic parameters for the patients are listed in Tables 1–4.

LA volume and factors influencing LA enlargement

Defining LA enlargement as the mean ± SD as calculated from the LA volume indexed to BSA in this study, LA enlargement was found in 83% of the hypertensive population in our study, 55.4% was severe LA enlargement ($\geq$40 ml/m^2).

Table 2
Relationship of left atrial volume index to age, blood pressure, left ventricular mass, and parameters of left ventricular function (univariate regression analysis).

Variable	Left atrial volume index		
	r	*B*	*p*
Age	0.076	0.117	NS
Gender	0.068	2.182	NS
Body mass index	0.061	−0.264	NS
Systolic blood pressure	0.071	0.061	NS
Diastolic blood pressure	0.107	−0.128	NS
Anti-hypertensive agents	0.091	0.085	NS
LV ejection fraction	0.125	−0.265	NS
LV mass	0.392	0.117	<0.0001
LV mass indexed height$^{2.7}$	0.513	0.564	<0.0001
LV relative wall thickness	0.085	−15.28	NS
Inter-ventricular septal thickness	0.230	1.915	0.008
LV posterior wall thickness	0.150	1.488	NS
LV end-diastolic diameter	0.351	1.065	<0.0001
LV end-systolic diameter	0.303	0.914	<0.0001
LV end-diastolic volume	0.480	0.360	<0.0001
LV end-systolic volume	0.340	0.456	0.0001
Peak E wave velocity	0.169	0.102	NS
E wave deceleration time	0.072	−0.018	NS
Peak A wave velocity	0.024	0.018	NS
A wave duration	0.163	0.022	NS
E/A ratio	0.200	11.240	0.023
RVSP	0.372	1.048	<0.0001

LV, left ventricular; RVSP, right ventricular systolic pressure.