Left Ventricular Mass and Atrial Volume Determined by Cine Magnetic Resonance Imaging in Essential Hypertension

Kazuaki Mineoi, Yuji Shigematsu, Takaaki Ochi, and Kunio Hiwada

To evaluate the relationship between left atrial volume determined by cine magnetic resonance imaging and progression of left ventricular hypertrophy (LVH), left atrial volume and echocardiographic left ventricular mass (LVM) were measured in 30 hypertensive patients (15 without LVH and 15 with LVH) and 10 normotensive control subjects. We also evaluated the effects of antihypertensive therapy on the cardiac chamber volumes and LVM in hypertensive patients. The cardiac chamber volumes and LVM were indexed by body surface area. Although there were no significant differences in left ventricular chamber volumes among the three groups, both maximum and minimum left atrial volume indexes, and the LVM index were greater in hypertensive patients with LVH than in the other two groups. The LVM index was correlated with maximum left atrial volume index ($r = 0.74$, $P < .0001$), and minimum left atrial volume index ($r = 0.76$, $P < .0001$), respectively. Furthermore, in multivariate models, the LVM index was significantly correlated with maximum left atrial volume index. In hypertensive patients with LVH, both maximum and minimum left atrial volume indexes, and the LVM index significantly reduced after treatment. The percent of changes in maximum left atrial volume index after treatment was significantly correlated with the percent of changes in LVM index after treatment. In conclusion, our data indicate that LVH is an independent determinant of left atrial enlargement, and both LVH and left atrial enlargement may be reversed by some effective therapeutic interventions. Am J Hypertens 2000; 13:1103–1109 © 2000 American Journal of Hypertension, Ltd.

KEY WORDS: **Left ventricular hypertrophy, left atrial volume, hypertension, magnetic resonance imaging.**

In essential hypertension, echocardiographically determined left ventricular hypertrophy (LVH) is known to be an independent risk factor for future cardiovascular complications.[1–4] Furthermore, we have shown that LVH and structural remodeling of the left ventricle progress in parallel with hypertensive target organ damage.[5,6] Recently, Verdecchia et al[7] have confirmed that the probability of event-free survival is significantly lower in patients with large left ventricular mass (LVM) than in those with normal LVM, and it is markedly improved by the regression of LVM. On the other hand, Frohlich et al[8] have suggested that electrocardiographic evidence of a left atrial abnormality is an early sign of hypertensive heart disease. Although electrocardiographic[8] and echocardiographic[9–14] evidence of left atrial enlargement has been reported in hypertensive patients, most studies did not evaluate the relationship between left atrial enlargement and progression of LVH.

Transthoracic echocardiography is used most widely to measure LVM and cardiac chamber volumes because of its wide availability, anatomic and prognostic validation, and lack of radiation. However, this technique is

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inaccurate because it gives only an anteroposterior diameter or an area of single plane of the cardiac chambers.[15] Furthermore, when cardiac chambers contract in a uniform and symmetric pattern, a close correlation is found between echocardiographic and angiographic volume measurements.[16,17] Traditional and cine magnetic resonance imagings (Cine MRI) allow noninvasive examination and provide highly accurate and reproducible cardiac chamber volumes.[18–21]

Accordingly, the purpose of the present study was twofold: 1) to evaluate the relationship between left atrial volume determined by Cine MRI and the degree of LVH, and 2) to evaluate the effects of antihypertensive therapy on the cardiac chamber volumes and LVM in patients with essential hypertension.

METHODS

Study Population Thirty consecutive patients (11 men and 19 women) with uncomplicated essential hypertension were enrolled in the study. Patients were excluded who had preexisting cardiac disease, preexisting medical illness, such as diabetes mellitus, or M-mode echocardiograms inadequate to clearly detect the internal lines of the interventricular septum and left ventricular posterior wall. Ten age- and sex-matched normotensive subjects (4 men, 6 women) who had no history of hypertension and no evidence of cardiac disease served as controls. All subjects gave their informed consent before participation in the present study.

Study groups were classified according to the LVM index: 15 hypertensive patients without LVH and 15 with LVH. None of the patients had ever received any antihypertensive therapy at the time of the initial diagnostic evaluation.

Twenty hypertensive patients (10 without LVH and 10 with LVH) were treated with lisinopril (10 to 20 mg/day) or nicardipine (20 to 40 mg/day) for 24 weeks. The cardiac chamber volume measurements by Cine MRI and echocardiographic examinations were performed on the same day for all treated patients before and after treatment. Hypertension was defined as systolic blood pressure equal to or greater than 140 mm Hg or diastolic blood pressure equal to or greater than 90 mm Hg.[22] The body mass index was the weight in kilograms divided by the square of the height in meters.

Cardiac Chamber Volume Measurements by Cine MRI Cardiac chamber volume measurements were performed as previously reported,[21] using a Signa Horizon magnetic resonance imager with an 1.5 tesla superconductive magnet (GE Medical System, Milwaukee, WI). All subjects were in the resting supine position without breath-holding. A coronal image (Fig. 1A) was obtained in each subject by a spine echo technique to confirm the cardiac location. Consecutive transaxial images were acquired from the bottom to the top of the heart by electrocardiography-gated multislice spin echo technique. Cine MRI (Fig. 1B and C) was performed at each level of all transaxial slices using the rephased gradient echo technique with a repetition time of 33 msec, an echo time of 10 msec, a flip angle of 20 degrees, and a slice thickness of 10 mm. The cardiac chamber area was measured on still frames with manual tracing of endocardial surface by means of a track-ball cursor with computer software. The cardiac chamber volume was gained by summing up area in each slice multiplied by slice thickness. The following cardiac chamber volumes were indexed by body surface area: maximum and minimum left atrial volume indexes (LAVI-max and LAVI-min), left ventricular end-diastole and end-systolic volume indexes (LVEDVI and LVESVI). Left atrial emptying fraction (LAEF) and left ventricular ejection fraction (LVEF) were also calculated as follows: LAEF = (LAVI-max − LAVI-min)/LAVI-max × 100, LVEF = (LVEDVI − LVESVI)/LVEDVI × 100.

Echocardiographic Measurements Two-dimensionally guided M-mode echocardiography was performed by standard methods, as previously reported,[5,6] using an SSD-9000 echocardiograph with a 3.5-MHZ transducer (Aloka Inc., Tokyo, Japan). Left atrial dimension, left ventricular end-diastolic and end-systolic dimensions, septal and posterior wall thickness were measured according to the American Society of Echocardiography guidelines.[23] The LVM was calculated at end-diastole by using Penn convention.[24] Left ventricular midwall fractional shortening was also measured by standard methods, as previously reported.[6] Left atrial dimension, left ventricular end-diastolic and end-systolic dimensions, and the LVM were indexed by body surface area. Peak early transmitral flow velocity (E) and peak late transmitral flow velocity (A) were measured at the tips of mitral leaflets. Isovolumic relaxation time was also measured from simultaneous recordings of phonocardiogram and Doppler echocardiogram.

Definition and Statistical Analysis Upper normal limits for the LVM index were 108 and 104 g/m^2 in men and women, respectively.[5] All values are expressed as mean ± SD. The statistical evaluation was performed by one-way ANOVA with subsequent Sheffé's multiple range test. Differences in data between before and after treatment were analyzed by a paired Student's t test. Univariate correlation was analyzed using Pearson's correlation coefficient. We also performed multiple regression analyses to select appropriate independent variables producing the highest correlation with maximum left atrial volume index in hypertensive patients. Results were considered significant at the $P < .05$.

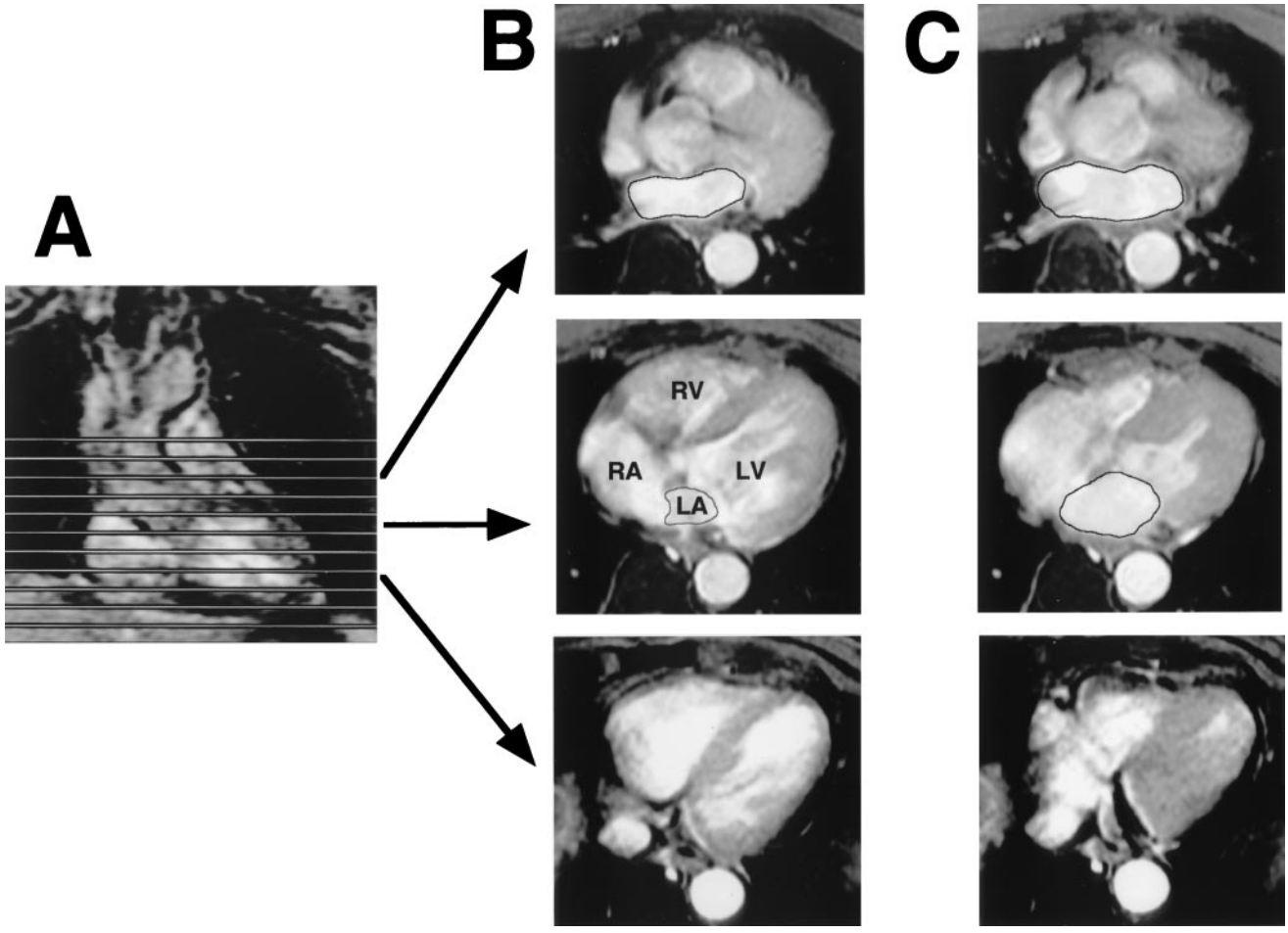

FIG. 1. *The process of magnetic resonance imaging (MRI).* **A)** *Coronal MRI was obtained for cardiac location. Consecutive transaxial electrocardiography gated multislice spin echo imagings were acquired.* **B)** *(end-diastolic) and* **(C)** *(end-systolic): Cine MRI was performed at each level of all these transaxial spin echo imagings involving the heart. RA = right atrium; LA = left atrium; RV = right ventricle; LV = left ventricle.*

RESULTS

Clinical Profiles and Echocardiographic Data Table 1 shows the clinical characteristics and echocardiographic data of the study subjects. There were no significant differences in age, sex, and heart rate among the three groups. The body mass index was slightly, but significantly, higher in hypertensive patients with LVH than in controls.

There were no significant differences in left atrial dimension index, left ventricular end-diastolic and end-systolic dimension indexes among the three groups. The interventricular septal thickness, the posterior wall thickness, and the LVM index were significantly greater in hypertensive patients with LVH than in the other two groups. The E/A ratio was smaller in hypertensive patients than in controls. The isovolumic relaxation time was the greatest in hypertensive patients with LVH, followed by those without LVH.

Cine MRI Measurements As shown in Table 2, there were no significant differences in left ventricular end-diastolic volume index, end-systolic volume index, and left ventricular ejection fraction among the three groups. Both maximum and minimum left atrial volume indexes were greater in hypertensive patients with LVH than in the other two groups. As shown in Figure 2, the LVM index was correlated with maximum left atrial volume index ($r = 0.74$, $P < .0001$), and minimum left atrial volume index ($r = 0.76$, $P < .0001$), respectively. In addition, maximum left atrial volume index was significantly correlated with isovolumic relaxation time ($r = 0.49$,$P < .02$), midwall fractional shortening ($r = 0.48$,$P < .02$), and systolic blood pressure ($r = 0.45$,$P < .05$). In multivariate models, the LVM index was significantly correlated with maximum left atrial volume index (Table 3).

Effects of Antihypertensive Therapy As shown in Table 4, systolic and diastolic blood pressures were

TABLE 1. CLINICAL PROFILES AND ECHOCARDIOGRAPHIC DATA

Characteristic	Normotensive Control Subjects (n = 10)	EH Without LVH (n = 15)	EH With LVH (n = 15)
Men/women	4/6	4/11	7/8
Age (yr)	56 ± 8	57 ± 9	56 ± 8
Body mass index (kg/m^2)	21.1 ± 2.1	24.4 ± 3.1	25.4 ± 2.5*
Systolic blood pressure (mm Hg)	119 ± 11	158 ± 16‡	161 ± 12‡
Diastolic blood pressure (mm Hg)	68 ± 10	95 ± 8‡	97 ± 11‡
Heart rate (beats/min)	63 ± 5	72 ± 10	67 ± 8
Left atrial dimension index (mm/m^2)	20.2 ± 1.9	19.0 ± 2.5	19.9 ± 1.5
LVDd index (mm/m^2)	31.8 ± 1.7	30.3 ± 3.3	29.6 ± 3.3
LVDs index (mm/m^2)	19.1 ± 1.7	18.2 ± 2.6	17.4 ± 2.7
Midwall fractional shortening (%)	20.8 ± 1.9	19.7 ± 2.1	17.3 ± 1.8‡§
LVM index (g/m^2)	82.9 ± 12.9	90.9 ± 15.4	133.6 ± 24.2‡‖
E/A ratio	1.4 ± 0.4	0.8 ± 0.2†	0.9 ± 0.2†
Isovolumic relaxation time (msec)	73.3 ± 8.8	86.1 ± 9.0†	98.6 ± 12.5†§

EH = essential hypertension; LVH = left ventricular hypertrophy; LVDd and LVDs = left ventricular end-diastolic and end-systolic dimension; LVM = left ventricular mass.

Values are mean ± SD.

* P < .05; † P < .01; ‡ P < .001 versus normotensive control subjects; § P < .01; ‖ P < .001 versus EH without LVH.

significantly decreased after treatment. However, heart rate showed no significant difference between before and after treatment. In hypertensive patients with LVH, although there were no significant differences in left ventricular volume index and left ventricular ejection fraction, both maximum and minimum left atrial volume indexes significantly reduced after treatment. The LVM index and the isovolumic relaxation time were also significantly decreased in hypertensive patients with LVH after treatment. In hypertensive patients without LVH, although the isovolumic relaxation time was significantly decreased, the cardiac chamber volumes, the LVM index, and the E/A ratio showed no significant differences between before and after treatment. In addition, as shown in Fig. 3, the changes in maximum left atrial volume index after treatment was significantly correlated with the changes in LVM index after treatment in hypertensive patients.

TABLE 2. THE CARDIAC CHAMBER VOLUMES MEASURED BY CINE MRI

Characteristic	Normotensive Control Subjects (n = 10)	EH Without LVH (n = 15)	EH With LVH (n = 15)
LAVI-max (mL/m^2)	32.7 ± 6.0	34.0 ± 4.8	41.7 ± 6.8*†
LAVI-min (mL/m^2)	14.2 ± 3.7	13.7 ± 2.3	19.4 ± 4.4*†
LAEF (%)	56.9 ± 6.0	57.8 ± 6.3	53.5 ± 5.2
LVEDVI (mL/m^2)	72.0 ± 10.2	68.6 ± 11.0	73.1 ± 9.3
LVESVI (mL/m^2)	20.2 ± 2.9	19.8 ± 4.2	21.8 ± 4.1
LVEF (%)	71.9 ± 1.8	71.2 ± 3.5	70.4 ± 2.3

MRI = magnetic resonance imaging; LAVI = left atrial volume index; LAEF = left atrial emptying fraction; LVEDVI = left end-diastolic volume index; LVESVI = left ventricular end-systolic volume index; LVEF = left ventricular ejection fraction.

Values are mean ± SD.

* P < .01 versus normotensive control subjects; † P < .01 versus EH without LVH.

DISCUSSION

Multivariate linear regression models of the present study indicate that the degree of LVH was the most potent determinant of left atrial volume in patients with essential hypertension. In addition, both maximum and minimum left atrial volume indexes, and the LVM index significantly reduced after antihypertensive therapy. The changes in maximum left atrial volume index after treatment was significantly correlated with the changes in the LVM index after treatment.

Electrocardiographic[8] or echocardiographic[9–14] evidence of left atrial enlargement has been reported in hypertensive patients. The Framingham Heart Study[12] demonstrated statistically significant effects of systolic and pulse pressures on left atrial size. However, in the Framingham Heart Study,[12] inclusion of LVM in these multivariate models eliminated or attenuated the associations of the pressure variables with left atrial size. The present study provided the evidence that systolic blood pressure was weakly (r = 0.45), but significantly correlated with maximum left atrial volume index in

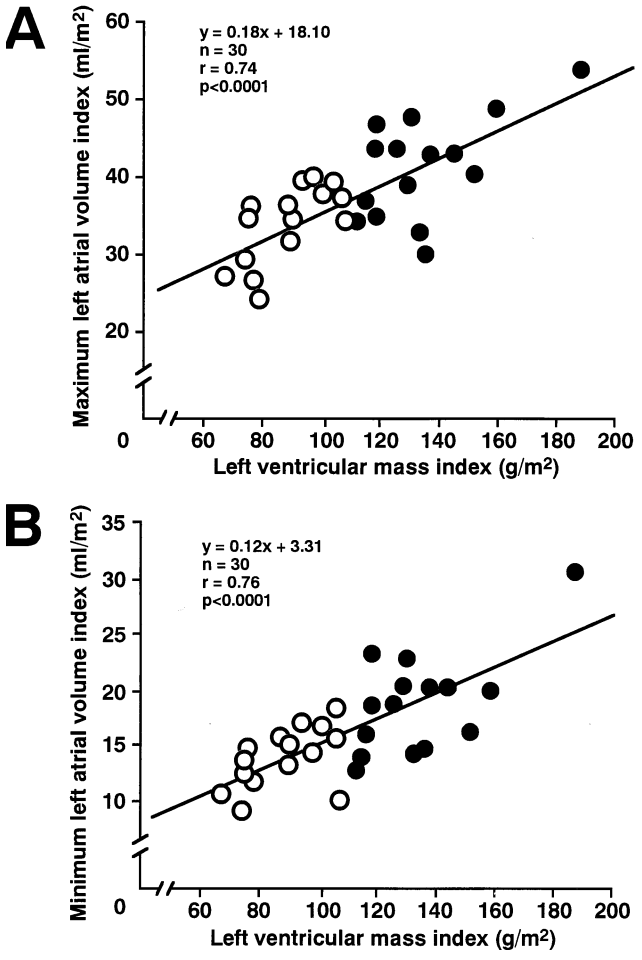

FIG. 2. *Relationships between the left ventricular mass index and maximum left atrial volume index* **(A)**, *and minimum left atrial volume index* **(B)**. *Open circles and closed circles show hypertensive patients without left ventricular hypertrophy (LVH) and with LVH, respectively. There was a significant positive relationship between the variables.*

hypertensive patients. However, as in the Framingham Heart Study,[12] adjustment of LVM index negated the significant correlation between maximum left atrial volume index and systolic blood pressure. Thus, it is possible that the correlation between systolic pressure with left atrial size may be mediated through the more clearly defined correlation between hypertension and LVH.

TABLE 3. MULTIPLE REGRESSION ANALYSIS OF INDEPENDENT VARIABLES FOR MAXIMUM LEFT ATRIAL VOLUME INDEX

Independent Variable	Standard Coefficient (β)	Standard Error	*P*
Systolic blood pressure	0.061	0.053	0.705
Left ventricular mass index	0.501	0.048	0.018
Isovolumic relaxation time	0.197	0.095	0.344

The maximum left atrial volume index: adjusted $R^2 = 0.461$, $P < .01$.

The influence of left ventricular diastolic function on left atrium has been investigated in hypertensive patients.[10,25] In the previous studies, we reported that left ventricular diastolic dysfunction in hypertension was more severely damaged in isovolumic phase than in rapid filling phase[26] and that prolongation of isovolumic relaxation time was observed even in hypertensive patients without LVH.[27] Thus, we measured isovolumic relaxation time as an index of left ventricular diastolic dysfunction. In the present study, we confirmed prolongation of isovolumic relaxation time in hypertensive patients without LVH. Furthermore, there was a good positive correlation between maximum left atrial volume index and isovolumic relaxation time in hypertensive patients. However, inclusion of LVM index in multivariate models eliminated the correlation between maximum left atrial volume index and isovolumic relaxation time. This finding suggests that left atrial enlargement is mainly dependent on the degree of LVH.

Transthoracic echocardiography is used most widely to measure the cardiac chamber volumes and provides anatomic and functional information in hypertensive patients. However, several factors may limit the echocardiographic acquisition. Transthoracic echocardiography only gives an anteroposterior diameter or an area of single plane of the cardiac chambers, greatly simplifying the possible cardiac chamber configuration and thus making volume estimation unreliable.[15] On the other hand, Cine MRI depicts the blood flow as high intensity without contrast material and can provide highly accurate and reproducible cardiac chamber volumes.[21] In addition, because Cine MRI is tomographic, cardiac chamber volume measurements are independent of chamber orientation. In fact, our data showed that left atrial volume determined by Cine MRI in hypertensive patients with LVH were greater than those in normotensive control subjects and hypertensive patients without LVH, although there was no significant difference in echocardiographic left atrial dimension.

In hypertensive patients, LVH develops because of increased afterload, and as a result, systolic function of the left ventricle is maintained.[28,29] However, left ventricular midwall systolic function is commonly depressed in hypertensive patients with normal ejection fraction and increased ventricular wall thicknesses.[30,31] In the present study, patients with greater LVM index had larger left atrial volume indexes and more depressed midwall systolic function. The left atrial emptying fraction did not differ among hypertensive patients with LVH, without LVH, and normotensive control subjects and remained unchanged after treatment. In addition, with the successful treatment of

TABLE 4. EFFECTS OF ANTIHYPERTENSIVE THERAPY

Characteristic	EH Without LVH (n = 10)		EH With LVH (n = 10)	
	Before	After	Before	After
Systolic blood pressure (mm Hg)	155 ± 13	139 ± 19†	166 ± 9	135 ± 11†
Diastolic blood pressure (mm Hg)	98 ± 8	81 ± 7†	102 ± 9	81 ± 10†
Cine MRI measurements				
LAVI-max (mL/m^2)	33.3 ± 3.4	32.4 ± 3.4	41.4 ± 4.7	38.0 ± 3.8†
LAVI-min (mL/m^2)	13.2 ± 2.6	13.3 ± 2.7	19.3 ± 3.6	17.4 ± 3.8†
LAEF (%)	58.5 ± 5.9	59.0 ± 5.5	53.6 ± 5.3	54.6 ± 6.0
LVEDVI (mL/m^2)	71.7 ± 9.2	70.8 ± 8.6	70.0 ± 6.1	69.7 ± 5.8
LVESVI (mL/m^2)	20.5 ± 3.4	19.5 ± 3.6	20.8 ± 3.3	20.5 ± 2.3
LVEF (%)	71.4 ± 2.7	73.0 ± 2.4	70.4 ± 2.5	70.5 ± 2.4
Echocardiographic measurements				
LVM index (g/m^2)	91.4 ± 17.4	90.8 ± 17.7	124.7 ± 26.6	111.4 ± 23.0*
E/A ratio	0.85 ± 0.12	0.95 ± 0.05	0.82 ± 0.20	0.96 ± 0.11
Isovolumic relaxation time (msec)	89.5 ± 5.9	79.8 ± 7.2*	99.3 ± 9.8	91.3 ± 5.9*

Abbreviations as in Tables 1 and 2.

Values are mean ± SD.

* P < .05; † P < .01 versus before.

arterial hypertension, the LVM index and left atrial volume indexes were significantly reduced in hypertensive patients with LVH. The changes in maximum left atrial volume index after treatment was significantly correlated with the changes in LVM index after treatment. These finding also suggest the clear correlation between left atrial volume and the degree of LVH.

Finally, our data provide the evidence that LVH is an independent determinant of left atrial enlargement, and both LVH and left atrial enlargement may be reversed by some effective therapeutic interventions.

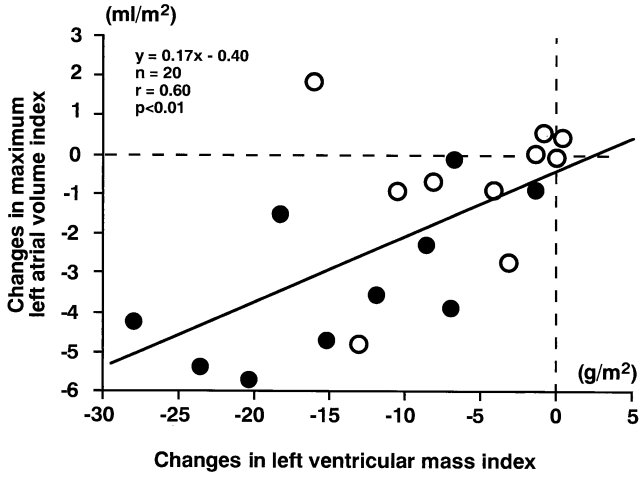

FIG. 3. *Relationship between changes in left ventricular mass index after treatment and changes in maximum left atrial volume index. Open circles and closed circles show hypertensive patients without left ventricular hypertrophy (LVH) and with LVH, respectively. There was a good positive relationship between the variables.*

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