# Association of Left Ventricular Hypertrophy and Geometry to Asymptomatic Cerebrovascular Damage in Essential Hypertension

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## Abstract

***Objectives***- The level of arterial pressure is one of the most important determinants of cardiac adaptation to hypertension and also one of the most important predictors of cardiovascular and cerebrovascular morbidity, including strokes. Multiple studies were performed on the association between left ventricular hypertrophy and preclinical brain damage in essential hypertensive patients.

***Methods***- In order to identify the relation between hypertension level, duration, age, sex and left ventricular geometry to asymptomatic brain damage, we categorized 50 essential hypertensive patients (M/20-%40; F/30–60%) using M-mode echocardiography. All the patients had been admitted in the cardiac emergency room for hypertension control According to the value of end diastolic relative wall thickness (RWT) and left ventricular mass index (LVMI), the patients were categorized into four groups: 5 patients had normal LVMI and normal RWT (normal geometry) (group 1); 7 patients had increased (RWT) and normal LVMI (concentric remodeling) (group 2); 12 patients had increased LVMI and normal RWT (eccentric hypertrophy) (group3); and 26 patients had increased LVMI and RWT (concentric hypertrophy) (group 4). Afterwards, brain MRI was performed, followed by an evaluation of lacunar lesions and leukoaraiosis in the four groups.

***Results***- The severity of leukoaraiosis was significantly greater in patients with concentric hypertrophy than in patients with normal left ventricular geometry (Chi–square 24.5, P=0.002). The number of lacunae was also significantly higher in patients with concentric left ventricular hypertrophy than in patients with normal left ventricular geometry (Chi–Square 17. 25 P=0.000).

***Conclusion***- Stepwise regression analysis confirmed that LVMI and RWT in addition to age and systolic blood pressure were independent predictors for asymptomatic cerebrovascular damage ***(Iranian Heart Journal 2004; 5(1,2):64-70).***

**Key word:** hypertension ■ left ventricular hypertrophy ■ leukoaraiosis■ lacunae.

Left ventricular size in childhood closely parallels body size, whereas in adulthood left ventricular mass is increasingly affected by the effects of obesity, hypertension, level of cardiac volume load and the level of myocardial contractility.[1] Of all of the above-mentioned factors, hypertension is the most important factor for the increase of the ventricular mass, especially ambulatory uncontrolled hypertension.[2] The heart may adapt to hypertension by developing concentric left ventricular remodeling or by retaining normal ventricular geometry.[3] A close relation between left ventricular hypertrophy and stroke has been reported in several studies,[4,5,6] because both the brain and heart are target organs of

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hypertension. However, whether left ventricular mass measurements identify asymptomatic brain damage, and whether ventricular geometry is related to asymptomatic brain damage is unknown. In the present study, we investigated the relation between asymptomatic cerebral damage evaluated by magnetic resonance imaging (MRI) and left ventricular hypertrophy of essential hypertensive patients in echocardiography with an emphasis on left ventricular geometry.

## Methods

**Subjects**: Fifty patients were enrolled in the study. They were recruited from those having been admitted to the cardiac emergency ward and the heart specialty clinic from November 1999 to February 2001 for evaluation and treatment of hypertension and having agreed to have brain magnetic resonance imaging and echocardiographic examinations. Patients with congestive heart failure, acute or previous myocardial infarction, diabetes, or a history of symptomatic cerebrovascular accident were excluded from the study. Informed consent to the procedure was obtained from each patient. All the patients received low salt diet, and approximately all of them before examination had been treated with two or three anti-hypertensive drugs. Blood pressure was measured frequently by sphygmomanometer in the hospital course or in the out-patient setting.

**Measurement of left ventricular mass index**: Echocardiographic studies were performed using HP SONOS 100 echocardiogram with 2.5-3 MHz transducer (Hewlett Packard Inc, USA) according to the recommendations of the American Society of Echocardiography.[7,8] All recordings and pictures were stored, and then LV mass was estimated by the formula from Devereux and Reichek (Penn convention)[8,9], LV mass (g)=1.04 [(LV internal dimension at diastole+ interventricular septal thickness + posterior wall thickness)$^3$ (LV internal dimension at diastole)$^3$]–13.6, and was divided by the body surface area to obtain LV mass index (LVMI). Relative wall thickness was measured at end diastole as the ratio of 2 times posterior wall thickness /LV diastolic dimension. Patients were classified as abnormal if the relative wall thickness exceeded 0.41 or LVMI exceeded 108 $g/m^2$ in women or 118 $g/m^2$ in men.[10,11] The patients were divided into the following 4 groups according to LV mass index and relative wall thickness: group 1 had normal LV geometry (normal LVMI and normal RWT) (n=5); group 2 had concentric remodeling (increased RWT and normal LVMI (n=7); group 3 had eccentric hypertrophy (increased LVMI and normal RWT) (n=12); and group 4 had concentric hypertrophy (increased LVMI and increased RWT) (n=26).

**Asymptomatic cerebrovascular damage:** Magnetic resonance imaging was performed in all the patients with a superconducting magnet with a main field strength of 1.5 T[12] (Phillips Inc, Holland). Asymptomatic lacunar infarction and leukoaraiosis were evaluated in all the patients. First, all MRI views were evaluated and reported by a radiologist (with fellowship in MRI), and then a neurologist with a knowledge of the patients' symptoms and condition reevaluated and reported all the images for further confirmation. Asymptomatic lacunar infarction and leukoaraiosis were evaluated in all the patients. A lacunae was defined as a low signal intensity area (> 0. 3cm and < 1.5 cm) on T1- weighted images which was also visible as a hyperintense lesion on T2–weighted images.[12] The number of lacunae in each patient was counted. Leukoaraiosis, deep white matter lesions, depicted on T2–weighted images was classified into 4 grades: grade l includes no abnormality or minimal periventricular signal hyperintensities in the form of caps confined exclusively to the anterior horns or rims lining the ventricle; grade 2 includes hyperintensities in both of the anterior and posterior horns of the lateral ventricles or periventricular unifocal patches; grade 3 includes multiple periventricular hyperintense punctuate lesions and their early confluence; and finally grade 4 is multiple areas of high signal intensity reaching confluence in the periventricular region.[13]

**Statistical analysis:** The difference among our groups was evaluated by ANOVA (analysis of variance) and Chi- square test. The difference in the prevalence of lacunae and the severity of leukoaraiosis was analyzed by Chi– square test. A probability of less than 0.05 was considered significant.

## Results

**Baseline characteristics:**
Table I summarizes baseline characteristics of the 4 groups. There were no significant differences in sex, body height, body weight, duration of hypertension and BMI among the patients (see Table I). Level of systolic and diastolic blood pressure had a significant difference among the 4 groups (P=0.000) Nearly all of our patients had been treated before the study with two or three of the following anti-hypertensive drugs: calcium channel blockers, beta blockers, angiotensin-converting enzyme inhibitors and diuretics. An analysis of the variance and other statistical analyses also revealed a significant relation between systolic and diastolic blood pressure with left ventricular geometric pattern, concentric hypertrophy and eccentric hypertrophy associated with greatest diastolic blood pressure compared with concentric remodeling and normal geometry (P=0.000).

**Table I. Baseline characteristics in four groups**

| | Normal geometry | Concentric remodeling | Eccentric Hypertrophy | Concentric Hypertrophy | Overall P Value |
|---|---|---|---|---|---|
| Number (M/F) | 5(3/2) | 7(2/5) | 12(6/6) | 26(9/17) | |
| Age | 61+/-15 | 64+/-11 | 64+/-8 | 65+/-11 | 0.5 |
| Body Height (cm) | 160+/-10 | 161+-9 | 159+/-8 | 163+/-9 | 0.5 |
| Body Weight (Kg) | 60+/-8 | 59+/-10 | 61+/-9 | 58+/-10 | 0.42 |
| BMI (Kg/m2 ) | 25+/-3.2 | 24+/-2.9 | 26+/-8 | 25+/-31 | 0.3 |
| Duration of hypertension (y) | 4.6+/_0.5 | 7.5+/-4.7 | 8.3+/-8 | 7.1+/4.4 | 0.3 |
| Systolic blood pressure (mmhg) | 158+/-10 | 169+/-15 | 175+/-15 | 178+/-41 | 0-33 |
| Diastolic blood pressure (mmhg) | 91+/-5 | 98+/2-5 | 97+/-4 | 105+/-8 | 0.001 |
| LV mass index | 101 +/3.6 | 95+/-4.4 | 178+/-43 | 207+/-63 | 0.000 |
| Relation wall Thickness | 38+/-2 | 50+/-7 | 34+/-3 | 54+/-9 | 0.000 |

Also, systolic blood pressure in concentric and eccentric hypertrophy was greater than normal geometry and concentric remodeling with a meaningful correlation (p=0.003). Moreover, LVMI was significantly related to systolic and diastolic blood pressure (P= 0.001, P= 0.004, Figs.1, 2).

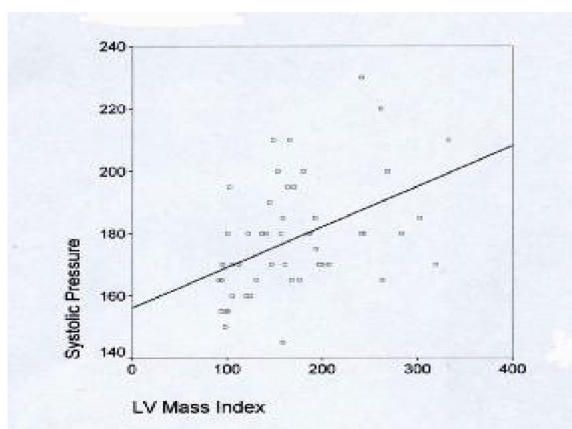


**Fig 1.** Relation of LV MI to SBP

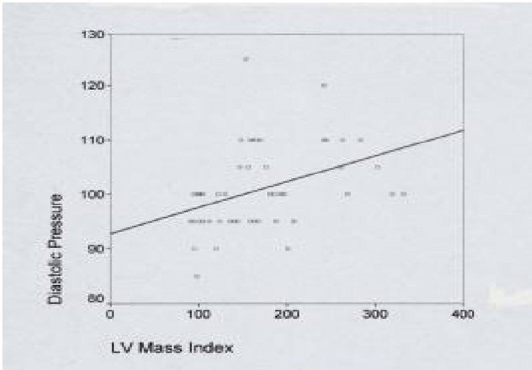


**Fig. 2.** Relation of LV MI to DBP

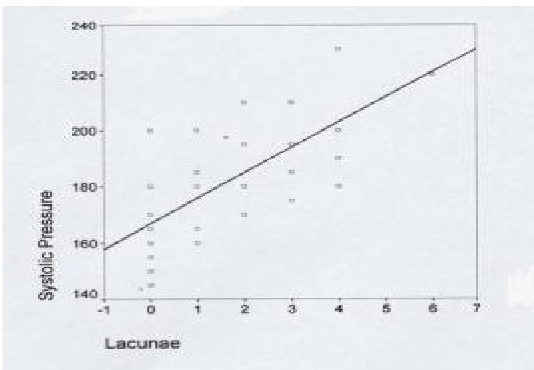


**Fig. 3**. Relation of Lacunae to SBP

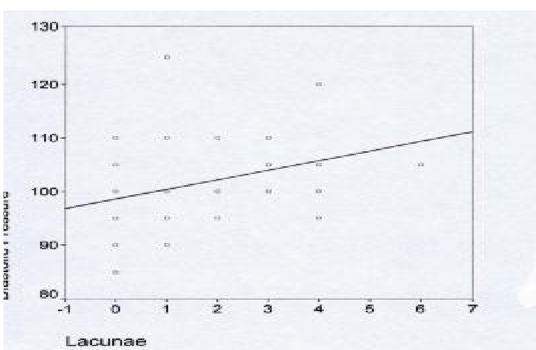


**Fig. 4.** Relation of Lacunae to DBP

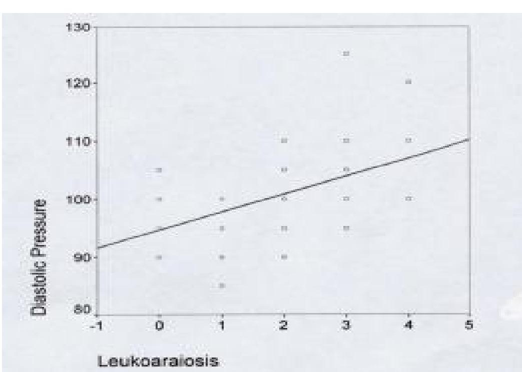


**Fig. 5**. Relation of Leukoaraiosis to DBP

## Prevalence and severity of asymptomatic cerebrovascular damages:

In our study the number of lacunae was significantly increased in patients with left ventricular hypertrophy and high left ventricular mass (of 26 pts, 21 pts (77%) had lacunae) and 5 pts (21%) did not have lacunae compared to patients with a normal LV mass (of 5 pts, no one had lacunae) P=0.009, see Table III. The severity of leukoaraiosis was also significantly increased in patients with high left ventricular mass (of 26 pts, 23 pts (88%) had significant leukoaraiosis) relative to normal LV mass (of 5 pts, only one patient had leukoaraiosis), P=0.002 see Table II.

**Table II. Geometry- Leukoaraiosis cros-stabulation**

| Geometry | Leukoaraiosis 0-1 | Leukoaraiosis II-IV | Total |
|---|---|---|---|
| Nnormal Left Ventricle Count<br>% Within Geometry<br>% Within Leukoaraiosis<br>% of Total | 4<br>80.0%<br>23.5%<br>8.0% | 1<br>20.0%<br>3.0%<br>2.0% | 5<br>100.0%<br>10.0%<br>10.0% |
| Eccentric hypertrophy Count<br>%within geometry<br>%Within leukoaraiosis<br>% of Total | 5<br>41/7%<br>29.4%<br>10.0%. | 7<br>58.3%<br>21.2%<br>14.o% | 12<br>100.0%<br>24.0%<br>24.0% |
| Concentric remodeling Count<br>% Within Geometry<br>% Within Leukoaraiosis<br>% 0f Total | 5<br>71.4%<br>29.4%<br>10.0% | 2<br>28.65<br>6.1%<br>4.0% | 26<br>100.0%<br>14.%<br>14 ./0% |
| Concentric hypertrophy Count<br>%Withi Geometry<br>% Within Leukoaraiosis<br>% of Total | 3<br>11.5%<br>17.6%<br>6.0% | 23<br>88.5%<br>69.7%<br>46.0% | 26<br>100.0%<br>52/0%<br>52.0% |
| Total Count<br>%within Geometry<br>% Within Leukoaraiosis<br>% of Total | 17<br>34.0%<br>100.0%<br>34.0% | 33<br>66.0%<br>100%<br>34.0% | 50<br>100.0%<br>100.0%<br>100.0% |

**P=0.002**

**Table III. Geometry- Lacunae Cross- tabulation**

| Geometry | Lacunae No | Lacunae yes | Total |
|---|---|---|---|
| **Normal Left Ventricle** | | | |
| **Count** | 5 | | 5 |
| **% Within Lacunae** | 21. 7% | | 10.0% |
| **% of Total** | 10.0% | | 10.0% |
| **Eccentric Hypertropy** | | | |
| **Count** | 8 | 4 | 12 |
| **% Within Lacunae** | 34.8% | 14.8% | 24/0% |
| **%Of Total** | 16.0% | 8.0% | 24.0% |
| **Concentic Remodeling** | | | |
| **Count** | 5 | 2 | 27 |
| **% Within Lacunae** | 21.7% | 7.4% | 14.0% |
| **%Of Total** | 10.0% | 4.0% | 14.0% |
| **Concentric Hypertrophy** | | | |
| **Count** | 5 | 21 | 26 |
| **%Within Lacunae** | 21.7% | 77.8% | 52.0% |
| **% Of Total** | 10.0% | 42.0% | 52.0% |

**P=0.000**

The severity of leukoaraiosis was significantly related to diastolic and systolic blood pressure (P=0.000, P=0.000, Figs. 5, 6). The number of lacunae in all the patients was also related to systolic and diastolic blood pressure (p=0.000, p=0.014, Figs. 3, 4). The prevalence of lacunae and the severity of leukoaraiosis had a significant relation to RWT (P=006, P=0.008). The prevalence of lacunae and the severity of leukoaraiosis were significantly increased in concentric and eccentric hypertrophy compared to normal left ventricular geometry and concentric remodeling of left ventricle (Of 7 pts, only 2 pts had leukoaraiosis and lacunae), (P= 0.000, P=0.002, see Fig 5). Stepwise regression analysis revealed that LV mass index, relative wall thickness, diastolic blood pressure and systolic blood pressure were significantly related to asymptomatic cerebrovascular damage (Figs. 3-5). In our study, there was no significant relationship between leukoaraiosis and lacunae with the age of the patients (P=0. 574), sex of the patients (P=0.079) and the duration of hypertension (P=0.569). A possible cause for this dissociation is the small size of the study group.

These findings indicate that LV geometric pattern can predict the presence and severity of asymptomatic cerebrovascular damage independent of age or duration of high blood pressure in hypertensive patients.

## Discussion

In the present study, we reported that hypertension was one of the most important determinants of LV mass and that not only LVH but also geometric configuration of the LV was significantly related to the presence as well as the severity of asymptomatic cerebrovascular damage, including leukoaraiosis and lacunae. On the other hand, LV morphologic changes are very frequent among hypertensive patients and only one quarter of hypertensive patients were free of morphological alteration.[13] In our study, the duration of hypertension, age and sex of the patients had no impact on cerebrovascular damage of hypertension. The presence and severity of lacunae was highest in the group with concentric hypertrophy, and LV mass index was also greatest in this group. Asymptomatic cerebrovascular damage is associated with cognitive dysfunction,[15] depression of mood,[16] and impairment of blood pressure regulation[17], suggesting the possible presence of functional abnormalities in these patients, even though they were neurologically normal. One of the other impacts of LV hypertrophy and change of LV morphology on the cerebrovascular system is the elevation of brain natriuretic peptide (BNP). Plasma BNP levels in concentric hypertrophy and eccentric hypertrophy were higher than those in the normal LV geometry and concentric remodeling groups.[14] In their prospective study, Kobayashie et al. recently showed that asymptomatic cerebral infarction, namely lacunar infarction, was associated with a higher incidence of future strokes.[19] These findings indicate that asymptomatic cerebrovascular damage can be used as a surrogate end point of hypertension. Lacunae[20] as well as leukoaraiosis[21] are closely related to the reduced capacity of the cerebral circulation. These findings indicate the need for more clinical attention to blood pressure control and preservation of cerebral circulation in patients with LV hypertrophy, especially those with concentric hypertrophy. Furthermore, serial echocardiography is mandatory for the prevention of serious cerebrovascular accidents in all hypertensive patients. The treatment of hypertension in order to promote LVH regression may also provide a better prognosis for hypertensive patients.[22] It is likely that the patients in the present study were more severely hypertensive and had failed to take their drugs regularly because hospital admission provides better blood pressure control. This may account for the high prevalence of left ventricular and cerebrovascular abnormalities in the studied population. However, our study groups were very small and better results are achieved with more patients. Stepwise regression analysis revealed that higher relative wall thickness was an independent predictor for leukoaraiosis and lacunae.

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