Left Ventricular Geometry and Cardiac Function in Mild to Moderate Essential Hypertension

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To elucidate left ventricular (LV) cardiac structure and function in patients with mild to moderate essential hypertension, we studied the relationship between LV geometry and function. We evaluated LV diastolic and systolic functions by M-mode echocardiography in 91 age-matched normotensive control subjects (NT) and 124 patients with essential hypertension. Hypertensive patients were divided into two groups based on the WHO stage classification: WHO I (n=76) and WHO II (n=48). Patients in WHO I and WHO II were further categorized according to the relative wall thickness as normal left ventricle (n=47), concentric remodeling (n=29), concentric hypertrophy (n=25), and eccentric hypertrophy (n=23). LV diastolic function was significantly decreased in the hypertensive groups compared to NT. There was no significant difference in LV systolic performance among NT, WHO I and WHO II. LV contractility was significantly increased in WHO I compared to NT. In respect to ventricular geometric pattern, LV diastolic function was significantly decreased in both the concentric hypertrophy and eccentric hypertrophy groups. LV systolic dysfunction was noted only in the eccentric hypertrophy group. In conclusion, patients with concentric remodeling had normal systolic and diastolic functions. LV diastolic function was impaired in both the concentric and eccentric hypertrophy groups due to an increase in LVMi. Moreover, LV systolic impairment was noted in the eccentric hypertrophy group due to an inappropriate compensation to LV systolic load. (Hypertens Res 1995; 18: 151-157)

Key Words: hypertension, echocardiography, systolic function, diastolic function, ventricular geometric adaptation

Untreated hypertension leads to cardiovascular complications. It is generally recognized that left ventricular hypertrophy (LVH) due to hypertension is an adaptive response to increased afterload (1-3) and finally leads to hypertensive heart failure (4-6). Recently, Koren et al. (7) have demonstrated that echocardiographically determined LV geometry is strongly associated with major cardiovascular events. It is therefore important to know the pathophysiology of LVH and the LV geometric pattern. LV diastolic dysfunction, which represents the first functional impairment of the heart in essential hypertension, can be detected even in the absence of demonstrable LVH (8-12). On the other hand, echocardiographic studies have established that LV systolic performance in hypertensive patients with LVH is maintained within the normal range (9). However, the role of LVH and LV geometric pattern in the development of hypertension in patients is not fully understood.

The aim of this study is to elucidate the relationship between LV geometric pattern and LV cardiac function in patients with mild to moderate essential hypertension.

Subjects and Methods

A total of 124 essential hypertensive patients with satisfactory echocardiograms were selected from 164 consecutive, essential hypertensive patients who were admitted to our hospital between January 1984 and January 1993. Twenty-five patients were excluded because the M-mode echocardiograms were not adequate to detect clear internal lines of the interventricular septum and LV posterior wall. Fifteen patients who had coronary artery disease, valvular disease, asymmetric septal hypertrophy or bundle branch block were also excluded. Ninety-one age-matched normotensive control subjects (NT) with SBP < 140 mmHg and DBP < 90 mmHg on repeated measurements, and no abnormalities on routine physical and laboratory examinations were enrolled in this study. Blood pressure was measured after five minutes' rest in the sitting position using a standard mercury sphygmomanometer (phase V, diastolic) on at least three separate visits to our outpatient clinic in two months. The mean of these three readings was taken as the patient's blood pressure. Essential hypertensive patients were
defined as having SBP > 160 mmHg and/or DBP > 90 mmHg; secondary hypertension was ruled out by routine physical and laboratory examinations. The hypertensive patients were classified according to the WHO stage classification (13). (1) WHO I (n = 76): essential hypertensive patients without LVH. LVH was defined as left ventricular mass index (LVMi) equal to or greater than 119 g/m² in men and 110 g/m² in women, based on the upper 95% confidence limit of NT. (2) WHO II (n=48): essential hypertensive patients with LVH.

Pattern of Left Ventricular Geometry
To further evaluate the significance of LVH and LV cardiac function, LV geometric patterns in WHO I and WHO II were determined according to sex-specific relative wall thickness. Upper normal limits for relative wall thickness were 44% in men and 42% in women, based on the upper 95% confidence limit of NT. Patients with WHO I were considered to have concentric remodeling if relative wall thickness was higher than 44% in men or 42% in women. Patients with WHO II were considered to have concentric hypertrophy if relative wall thickness was higher than 44% in men or 42% in women or eccentric hypertrophy if relative wall thickness was normal.

Methods
M-mode echocardiography was performed using a SSD-870 echocardiograph (Aloka Co., Ltd., Tokyo, Japan) with a 3.5 MHz transducer. Recordings were carried out at a paper speed of 100 mm/s. Echocardiographic measurements of the patients with WHO I and WHO II were performed after their anti-hypertensive medication was stopped for at least 2 weeks if they had been administered antihypertensive drugs in the outpatient clinic. LV end-diastolic dimension, end-systolic dimension, interventricular septal thickness, and LV posterior wall thickness were measured according to the recommendations of the Penn convention (14). The left ventricular mass was then estimated by the formula of Devereux and Reichek (14), and was divided by the body surface area to derive the LVMi. End-systolic wall stress was calculated by the methods of Wilson et al. (15) using the equation: end-systolic wall stress = 0.334 × SBP × LVESD/Ts × (1 + Ts/LVESD), where LVESD = LV end-systolic dimension, and Ts = LV posterior wall end-systolic thickness. The value of end-systolic wall stress/LV end-systolic volume index was used as an index of LV contractility (16). LV end-systolic volume was estimated with Teichholtz's formula (17), and was divided by the body surface area to derive the LV end-systolic volume index. Ejection fraction and fractional shortening were calculated using standard methods. The peak shortening rate and peak lengthening rate were calculated from the peak rate of change of LV dimension in systole normalized by the instantaneous systolic dimension, and the peak rate of change of LV dimension in diastole normalized by the instantaneous diastolic dimension, respectively. All recordings were coded and read by two independent investigators. All measurements were carried out over at least three cardiac cycles and averaged with the aid of a computer interfaced with a graphic analyzer (model Cardio 500, Kontron Electronik, Eching, Germany). Blood samples for measurements of plasma renin activity, plasma aldosterone concentration, and plasma noradrenaline and adrenaline levels were obtained from the brachial vein after the subjects remained in supine position for 30 min after an overnight fasting. These neurohumoral factors were measured in patients with WHO I (n=72) and WHO II (n=41). Plasma renin activity and aldosterone concentration were measured by using radioimmunoassay kits, Renin RIABEADS (Dinabot Co. Ltd., Tokyo, Japan) and Aldosterone RIAKIT II (Dinabot Co. Ltd.,), as described previously (18). Plasma catecholamines were measured by high performance liquid chromatography with electrochemical detection (19).

Statistics
Values in the text and tables are expressed as means ± SD. Statistical analysis was performed by analysis of variance followed by Tukey's multiple range test. Pearson correlation coefficients were calculated to evaluate the relation between variables. The statistical significance was defined as p < 0.05.

Results
WHO Stage Classification and Cardiac Function
Clinical characteristics and echocardiographic data of NT and hypertensive patients are shown in Table 1. Among the NT and hypertensive groups, there were no significant differences in sex, height, and heart rate. Among the hypertensive groups, SBP and mean BP were significantly higher in WHO II than in WHO I. LV end-diastolic dimension was significantly smaller in WHO I than in NT. Both interventricular septal thickness and LV posterior wall thickness were significantly greater in WHO II than in WHO I. LV end-diastolic dimension, and mean BP were significantly higher in WHO II than in WHO I. Among the hypertensive groups, these thicknesses were significantly greater in WHO II than in WHO I. Similar findings were obtained for LVMi. End-systolic wall stress was significantly greater in the hypertensive groups than in NT, but there was no significant difference between WHO I and WHO II.

There were no significant differences among NT, WHO I and WHO II in ejection fraction and fractional shortening. End-systolic wall stress/LV end-systolic volume index was significantly increased in WHO I compared to NT. This parameter was significantly lower in WHO II than in WHO I (Fig. 1). Figure 2 shows the relationships between peak shortening rate or peak lengthening rate and LVMi. There was no significant relationship between peak shortening rate and LVMi, whereas a significant relationship between peak shortening rate and LVMi was obtained for the hypertensive groups (r = 0.25, p < 0.01). Peak lengthening rate was significantly decreased in the hypertensive groups compared to NT (3.08 ± 0.77 s⁻¹ vs. 3.80 ± 0.81 s⁻¹, p < 0.01).
Among the hypertensive groups, peak lengthening rate was significantly lower in WHO II than in WHO I (2.79 ± 0.73 s⁻¹ vs. 3.27 ± 0.73 s⁻¹, p < 0.01). There was a significant inverse relationship between peak lengthening rate and LVMi (Fig. 2).

Figure 3 shows the relationship between end-systolic wall stress/LV end-systolic volume index and LVMi in hypertensive patients. There was a significant inverse relationship between end-systolic wall stress/LV end-systolic volume index and LVMi. With respect to neurohumoral factors, LVMi was not correlated with plasma renin activity (r=0.01, n =113), plasma aldosterone concentration (r=0.21), or plasma noradrenaline or adrenaline levels (r = 0.11, r=0.01, respectively).

Ventricular Geometric Pattern and Cardiac Function
Table 2 shows the clinical backgrounds and echocardiographic findings associated with different ventricular geometric patterns in 124 hypertensive patients. Of the 76 hypertensive patients with WHO I, 47 had a normal relative wall thickness (normal left ventricle) and 29 had an increased relative wall thickness (concentric remodeling). Of the 48 hypertensive patients with WHO II, relative wall thickness was normal in 23 patients (eccentric...
hypertrophy) and increased in 25 patients (concentric hypertrophy). There were no significant differences among the four different geometric patterns in sex, height, weight, body surface area, or heart rate. SBP was significantly higher in the eccentric hypertrophy and concentric hypertrophy groups than in the normal left ventricle group. Both LV end-diastolic dimension and LV end-systolic dimension were significantly smaller in the concentric remodeling group than in the normal left ventricle group. Both interventricular septal thickness and LV posterior wall thickness were significantly greater in the concentric remodeling group than in the normal left ventricle group. Among patients with increased LVMi, both interventricular septal thickness and LV posterior wall thickness were significantly greater in the concentric remodeling group than in the eccentric hypertrophy group. However, there was no significant difference in LVMi between the eccentric hypertrophy and concentric hypertrophy groups. End-systolic wall stress was significantly smaller in the concentric remodeling and concentric hypertrophy groups than in the normal left ventricle group. There was no significant difference in end-systolic wall stress between the normal left ventricle and eccentric hypertrophy groups, but end-systolic wall stress was significantly greater in the eccentric hypertrophy group than in NT.

There were no significant differences in either ejection fraction or fractional shortening among the four different geometric patterns. Figure 4 graphically shows the relations of peak shortening rate and peak lengthening rate to the four different patterns of left ventricular geometry. Peak shortening rate was significantly decreased in the eccentric hypertrophy group (2.26 ± 0.44 s⁻¹) compared to the normal left ventricle and concentric remodeling groups (2.71 ± 0.52 s⁻¹, p < 0.01 and 2.72 ± 0.55 s⁻¹, p < 0.05, respectively). Peak lengthening rate was significantly decreased in the eccentric hypertrophy and concentric hypertrophy groups (2.79 ± 0.86 s⁻¹, p < 0.05 and 2.79 ± 0.58 s⁻¹, p < 0.05, respectively) compared to the normal left ventricle group (3.34 ± 0.60 s⁻¹). However, there was no significant difference in peak lengthening rate between the concentric hypertrophy and eccentric hypertrophy groups.

Discussion

In this study, we examined the pattern of ventricular geometric adaptation to systemic hypertension and the relation to LV cardiac function in mild to moderate essential hypertensive patients.

Progression of Hypertension

The present study demonstrated that LV diastolic function was impaired in the early stage of hypertension. Our results confirmed the findings by Fouad et al. (8) and Bonaduce et al. (11), who described LV diastolic dysfunction in hypertensive patients without LVH. However, in the present study LVMi in WHO I, which was defined as no LVH, was significantly increased compared to NT. In addition, we showed an inverse relationship between LVMi and LV diastolic function in NT and hypertensive patients. This suggests that LV diastolic dysfunction in WHO I in the present study may
be partly associated with increased LVMi. There are several possible explanations for the diastolic dysfunction in LVH: 1) a decrease in coronary flow reserve, 2) accumulation of collagen in the myocardial interstitium, and 3) impaired calcium handling associated with increased LVMi. Thus, LV diastolic function is impaired in the early stage of hypertension and deteriorates as the stage of hypertension progresses.

With respect to LV systolic function, hypertensive patients in WHO I and WHO II showed normal systolic pump performance in terms of variables such as ejection fraction and fractional shortening. However, hypertensive patients without LVH tended to have increased left ventricular contractility, as indicated by end-systolic wall stress/LV end-systolic volume index. This finding is in agreement with other studies on LV systolic function in patients with mild essential hypertension, and suggests an enhanced contractile state in the early stages of hypertension (3, 9, 20, 21). Although LV systolic function in WHO II was similar to that in NT, it was significantly decreased in WHO II compared to WHO I, and an inverse relationship between LV systolic function and LVMi was found when the hypertensive group was considered as a whole. Thus, LVH associated with hypertension seems to be always accompanied by a decrease in myocardial contractility. Takahashi et al. (22) reported that in hypertensive patients with advanced LVH the myocardial contractility was depressed. This finding is in agreement with previous studies in humans and animals, which showed an impairment of myocardial contractility in LVH (23, 24).

Left Ventricular Geometry and Cardiac Function
Since the ratio of relative wall thickness to chamber radius provides prognostic information in patients with valvular heart disease (25) and primary myocardial disease (26), this parameter is often used to gauge whether assessment of LVH is appropriate or not regarding the prevailing hemodynamic conditions. Ganau et al. (27) described four patterns of LV geometry assessed by the relation between relative wall thickness and LVMi in patients with hypertension. Recently, Koren et al. (7)
demonstrated that LV geometry was strongly associated with cardiovascular prognosis in essential hypertensive patients. In assessing the role of LVH in the development of hypertensive heart failure in patients with hypertension, it is important to know the pattern of geometric adaptation to systemic hypertension and LV cardiac function. Cardiac structure and function in the normal left ventricle group are similar to those in NT, but end-systolic wall stress in the normal left ventricle group was significantly increased compared to that in NT. Although end-systolic wall stress is considered to be a hemodynamic trigger for LVH (1, 3, 5, 6), the initial geometric pattern by which the heart adapts to end-systolic wall stress is unclear. It is generally recognized that the heart adapts to increased wall stress by adding contractile elements in parallel with the thickening of the left ventricular wall. Moreover, the myocardial oxygen requirement is reduced for a given pressure either by an increase in LV wall thickness or a decrease in LV volume. The process from an almost normal LV structure to distinct LVH is unknown. However, our results taken together with reported papers support the hypothesis that the concentric remodeling pattern must be regarded as an initially adaptive structural change. LV systolic function in the concentric remodeling group was almost normal, but LV diastolic function was decreased, compared with that in NT. This observation suggests that increased myocardial collagen content associated with an increase in LVMi is responsible for the increased myocardial stiffness.

In addition, increased relative wall thickness itself can influence the diastolic performance of the left ventricle independent of increased LVM (28). The concentric hypertrophy group showed increased relative wall thickness and LVMi with a normal LV end-diastolic dimension. This group exhibited a similar end-systolic wall stress compared with the concentric remodeling group. An increase in LVMi is associated with an increase in LV end-diastolic dimension in order to maintain end-systolic wall stress. Considering that LVH develops as an adaptive process allowing the heart to normalize end-systolic wall stress and LV systolic function, a concentric hypertrophy pattern is considered to originate from a concentric remodeling pattern. Indeed, the concentric hypertrophy group had a normal LV systolic function. On the other hand, LV diastolic function in the concentric hypertrophy group was significantly decreased compared with that of the normal left ventricle group. In the group with eccentric hypertrophy, ejection fraction and fractional shortening were normal despite a high end-systolic wall stress. These findings agree with the report by Ganau et al. (27) who showed that fractional shortening was normal in this group. On the other hand, the eccentric hypertrophy group has been shown to be associated with a depressed ventricular functional response to stress (29). In the present study, both systolic and diastolic functions assessed by the speed of shortening or lengthening of the left ventricle, in the eccentric hypertrophy group were impaired compared with those in the normal left ventricle group. It has been considered that an eccentric hypertrophy pattern is a morphological adaptive response to volume overload (1, 2, 5, 6). In addition, our previous study (30) demonstrated that the development of hypertension was associated with a state of volume retention. Hemodynamically, the LV end-diastolic dimension in this group was increased to maintain systolic pump performance via the Frank-starling mechanism. On the other hand, hypertensive heart disease has conceptually been assimilated with other forms of pressure overload such as aortic stenosis, in which LV dilatation represents a transition toward LV heart failure. Thus, the eccentric hypertrophy group showed a high end-systolic wall stress, indicating an inadequate adaptation to systemic hypertension. Therefore, the eccentric hypertrophy group is associated most strongly with a predisposition to hypertensive heart failure.

References

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