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Relationship between blood pressure and left ventricular mass in male patients with essential hypertension

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Summary

We performed retrospective study of the relationship between the severity and duration of hypertension and echocardiographically-detected left ventricular hypertrophy (echo-LVH) in patients with untreated essential hypertension. The subjects consisted of 92 untreated essential hypertensives who were observed for more than 5 years from the onset of diastolic hypertension (≧95 mmHg), and whose left ventricular (LV) mass index was measured at the end of the observation period. On the basis of the frequency of diastolic hypertension during the observation period, the population was categorized in 3 groups. In Group I (32 cases), diastolic hypertension was observed in more than 80% of blood pressures obtained throughout the entire observation period. In Group II (38 cases), diastolic hypertension was observed in 33 to 80% of the observation period. In Group III (22 cases), diastolic hypertension was observed in less than 33% of the observation period. The average diastolic blood pressure during the entire observation period in each group were 101.0, 96.0, and 90.7 mmHg in groups I, II, and III, respectively. The LV mass index was significantly higher in groups I (114.6 g/m^2) and II (105.3 g/m^2) than in group III (90.7 g/m^2) ($p<0.01$). The prevalence of echo-LVH (more than

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121 g/m²) was 34.4%, 18.4%, and 4.8% in groups I, II, and III, respectively. The average diastolic blood pressure in patients with echo-LVH (99.3±5.1 mmHg) was significantly higher than in patients without echo-LVH (95.7±4.7 mmHg).

We concluded that the degree and duration of diastolic pressure elevation are closely correlated to the LV mass index.

Key words
Essential hypertension   Echocardiography   Left ventricular mass   Left ventricular hypertrophy

Introduction

The development of left ventricular (LV) hypertrophy in hypertension results from long-standing high blood pressure (BP). Longitudinal observation of BP is required to elucidate the relationship between the development of LV hypertrophy and the BP. Echocardiographic technique for measuring the LV mass has been used in numerous studies over the past several years to assess the development of LV hypertrophy in hypertension.[1~7] However, all reported studies were conducted by comparing the relationship between the LV mass and the BP, both of which were recorded cross-sectionally or during 24-hour ambulation.[8~16]

The present study evaluated the relationship between the BP and echocardiographically-detected LV hypertrophy (echo-LVH) in men with mild and untreated essential hypertension, whose BP was periodically recorded for more than 5 years. Specifically, the effect of higher diastolic blood pressure (DBP) on LV hypertrophy was investigated.

Materials and methods

Subjects

We studied 92 male employees with untreated essential hypertension. Each subject had received a long-term follow-up examination for hypertension as part of a periodic health examination since the first detection of 150/90 mmHg or higher BP. The subjects fulfilled the following criteria: 1) no medical history of antihypertensive therapy; 2) followed for more than 5 years after diastolic hypertension (DBP≧95 mmHg) was detected; 3) male subjects with essential hypertension.

All subjects with evidence of cardiac diseases other than essential hypertension were excluded from the study based on results of the medical history, physical examination, urinalysis, blood cell counts, serum electrolytes, creatinine and blood urea nitrogen (BUN), fasting blood glucose, ECG and echocardiography.

The average of the BPs recorded one to 4 times each year was used as the BP of that year. BP was measured using a mercury sphygmomanometer while the subject was seated with his left arm at his heart level.

Hypertensive groups: Ninety-two hypertensive male patients were categorized in 3 groups on the basis of the frequency of diastolic hypertension (DBP≧95 mmHg) during the entire observation period. Group I included 32 patients whose DBP was ≧95 mmHg over 80% of the BP records during the study period. Group II included 38 patients whose DBP was ≧95 mmHg in 33% to 80% of the BP records during the follow-up period. Group III included 22 patients whose DBP was ≧95 mmHg in less than 33% of the BP records during the follow-up period (**Table 1**).

Normotensive group: Sixty-five apparently healthy males comprised an age- and sex-matched control group, who had had routine physical checkups at our hospital and had normal BPs (<140/90 mmHg) and normal ECGs.

Echocardiographic methods

M-mode echocardiography was performed with a commercially available ultrasonoscope (Toshiba SSH-60A) using a 3.75 MHz transducer, and images were recorded with a polaroid camera or multi-format camera. Patients were examined in the supine or in the left lateral

Table 1. Classification according to the incidence of diastolic hypertension

Groups*	Incidence of diastolic hypertension	n	Age (years)	Observation period (years)
I	More than 80%	32	43.3±7.1	8.5±3.3
II	33% to 80%	38	45.9±7.5	10.6±5.2
III	Less than 33%	22	41.9±8.0	9.3±4.4
Control**		65	44.6±6.2	

* see text for details, ** normotensive (less than 140/90 mmHg) and normal ECG group.

decubitus position (within 45°). End-diastolic measurements of the interventricular septal thickness (IVST), left ventricular internal dimension (LVIDd) and posterior wall thickness (PWT) were made according to the recommendations of the American Society of Echocardiography (**Fig. 1**).[17] The LV mass and LV mass index were calculated using the following formula according to Devereux and Reicheck.[3,5,18]

$$\text{LV mass} = 1.04\ \{(\text{IVST}+\text{LVIDd}+\text{PWT})^3 - \text{LVIDd}^3\} - 13.6\ (\text{g})$$

$$\text{LV mass index} = \text{LV mass}/\text{BSA}\ (\text{g/m}^2)$$

Statistical methods

Statistical analysis of the continuous variables was performed using Wilcoxon's non-parametric and unpaired test. Discrete variables were compared by a chi-square test. Values in the text and tables were presented as means±standard deviations (SD). Probability (p) values less than 0.05 were considered statistically significant.

Results

Comparison of blood pressures

The mean value of the systolic blood pres-

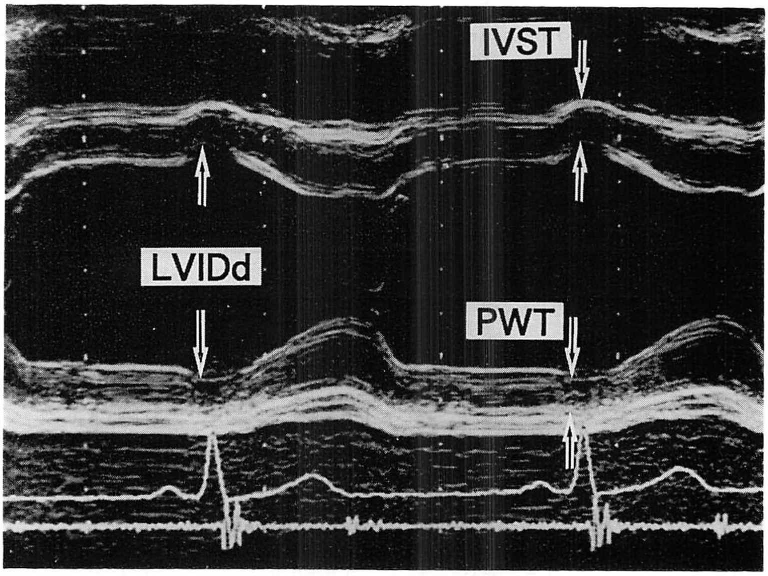

Fig. 1. M-mode echocardiographic measurements.

Measurements were made at the onset of an R wave on the ECG, using standard leading-edge to leading-edge method according to the American Society of Echocardiography.[17]

LVIDd=end-diastolic LV internal dimension; IVST=interventricular septal thickness; PWT=posterior wall thickness.

sures (SBP) during the entire observation period was 151.6±9.5 mmHg in group I, 150.2±9.1 mmHg in group II, and 147.9±12.6 mmHg in group III. No significant difference was observed among the groups. The mean value of the DBP during this time was 101.0±3.3 mmHg in group I, 96.0±3.0 mmHg in group II, and 90.7±3.1 mmHg in group III. As shown in **Fig. 2**, significant differences in DBP were observed among the 3 groups. However, the values in the control group were 114.6±10.9 mmHg for SBP and 72.1±9.0 mmHg for DBP.

Echocardiographic measurements

Table 2 and **Fig. 3** show echocardiographic measurements in each group. The measurements obtained from the 65 healthy males in the control group were used as normal values for the echocardiographic measurements (**Table 2**).

There were no significant differences in the LVIDd index among these groups. The IVST

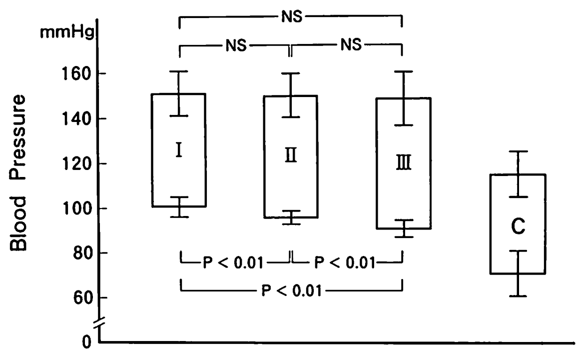

Fig. 2. Mean values of blood pressure during the entire observation period in groups I, II and III and the normotensive group (C).

No significant difference was found in systolic blood pressure, but significant differences were observed in diastolic blood pressures.

NS=not significant.

Table 2. Echocardiographic measurements

		Group I	Group II	Group III	Control
n		32	38	22	65
LVIDd	(mm)	49.9±4.3	47.8±8.4	45.8±9.7	48.9±3.7
LVIDdI	(mm/m²)	28.4±3.0	27.4±4.8	28.1±2.1	28.6±2.3
LVIDs	(mm)	31.5±4.7	31.2±4.2	31.5±4.6	31.5±4.1
LVIDsI	(mm/m²)	17.8±2.6	18.0±2.7	18.4±2.6	18.9±3.5
IVST	(mm)	9.8±2.1**‡	9.1±1.4*	8.5±1.3	8.3±0.9
IVSTI	(mm/m²)	5.5±1.4**†	5.3±0.9*	5.0±0.9	4.8±0.6
PWT	(mm)	9.4±1.3**‡	9.3±1.4**‡	8.3±0.8	8.2±0.7
PWTI	(mm/m²)	5.4±0.9**	5.4±0.9**	4.9±0.5	4.8±0.5

* $p<0.05$, ** $p<0.01$, vs control.

† $p<0.05$, ‡ $p<0.01$, vs group III.

LVIDdI=LVIDd index ; LVIDsI=LVIDs index ; IVSTI=IVST index ; PWTI=PWT index. Other abbreviations as in Fig. 1.

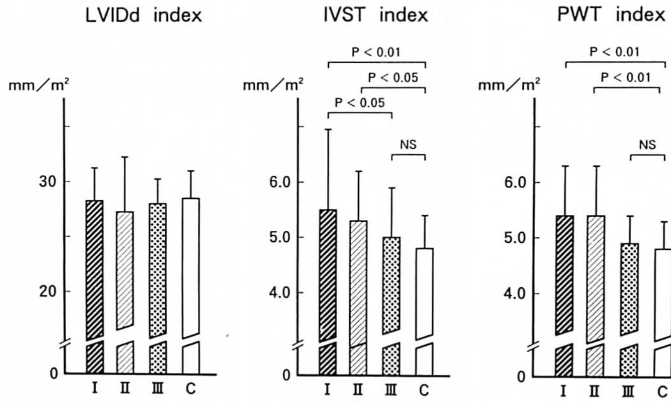

Fig. 3. Echocardiographic measurements in groups I, II and III and the normotensive group (C).

There was no significant difference in LVIDd index. IVST index and PWT index were significantly greater in groups I and II compared with the control group.

Index=divided by BSA. Abbreviations are as in Fig. 1.

index was significantly greater in group I than in group III ($p<0.05$), and greater in groups I and II compared with the control group ($p<0.01$, $p<0.05$, respectively). The PWT index of group II was significantly greater than that of group III and also greater in groups I and II compared with the control group.

LV mass index

The LV mass index was $114.6\pm23.8\ g/m^2$ in group I, $105.3\pm22.1\ g/m^2$ in group II, $90.7\pm16.1\ g/m^2$ in group III and $91.5\pm14.3\ g/m^2$ in the control group as depicted in **Fig. 4.** The LV mass index was significantly greater in groups I and II than in group III and the control group. The LV mass index was slightly greater in group I than in group II, but this difference was not statistically significant.

Left ventricular hypertrophy detected by echocardiography (Echo-LVH)

The tentative cutoff value of the LV mass index which we used for recognizing left ventricular hypertrophy was the mean plus double standard deviation of the LV mass index in the control group, 121 g/m^2 among men. Echo-LVH was observed more frequently in group I than in group III and more in groups I and II compared with the control group (**Table 3**). As shown in **Table 3**, the prevalence of echo-LVH

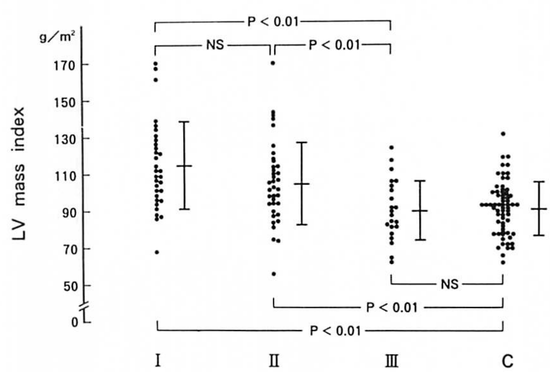

Fig. 4. LV mass index in groups I, II and III and normotensive group (C).

LV mass index was significantly greater in groups I and II compared with group III and the control group.

NS=not significant.

was greater in group I than in group II, but this difference was not statistically significant. The prevalence of echo-LVH was 20.7% in all hypertensives.

Relationship between LV mass index and blood pressure

A significant positive correlation was observed between the LV mass index and the

Table 3. Prevalence of echo-LVH in each group

	LV mass index $\geqq 121\ g/m^2$
Group I	34.4% (11/32)**†
Group II	18.4% (7/38)*
Group III	4.5% (1/22)
Total (I, II, III)	20.7% (19/92)
Control	1.5% (1/65)

* $p<0.05$, ** $p<0.01$, vs control.
† $p<0.05$, vs group III.

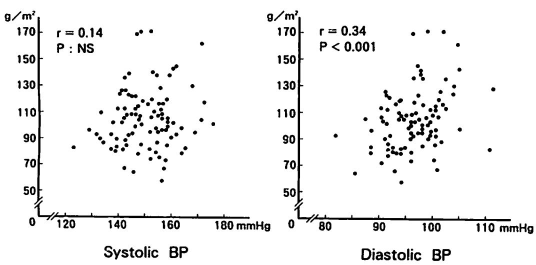

Fig. 5. Correlation between LV mass index and blood pressure.

There was no significant correlation between average systolic blood pressure (Systolic BP) and LV mass. A significant positive correlation was observed between average diastolic blood pressure (Diastolic BP) and LV mass.

NS = not significant.

average DBP during the entire observation period ($p<0.001$, $r=0.32$). However, there was no significant correlation between the LV mass index and the average SBP during this period (**Fig. 5**).

Characteristics of subgroups with and without echo-LVH

All patients in groups I, II and III were categorized in 2 subgroups; one group with echo-LVH (more than 121 g/m²); the other group without echo-LVH (less than 121 g/m²) (**Table 4**). Patients with echo-LVH did not differ significantly from patients without echo-LVH with respect to age, length of observation period, average SBP during the entire observation period and the voltage of SV_1 plus $RV_{5,6}$

Table 4. Characteristics of the subgroups with and without echo-LVH

	LV mass index $<121\ g/m^2$	$\geqq 121\ g/m^2$
Age (years)	43.6±7.9	46.1±7.1
Duration (years)	9.5±4.7	9.7±3.8
SBP (mmHg)	149.9±10.4	151.4±9.6
DBP (mmHg)**	95.7±4.7	99.3±5.1
$SV_1+RV_{5,6}$ (mm)	33.5±9.0	35.9±6.4
n	73	19

** $p<0.01$.

SBP = systolic blood pressure; DBP = diastolic blood pressure.

on electrocardiography. However, the average DBP was significantly higher in patients with echo-LVH than in those without echo-LVH ($p<0.01$; 99.3±5.1 vs 95.7±4.7 mmHg).

Electrocardiographic findings

The voltage of SV_1 plus $RV_{5,6}$ on ECG was 33.1±8.1 mm in group I, 35.2±9.8 mm in group II, 33.4±6.9 mm in group III and 29.5 ±6.2 mm in the control group. There were no significant differences between these groups (**Fig. 6**).

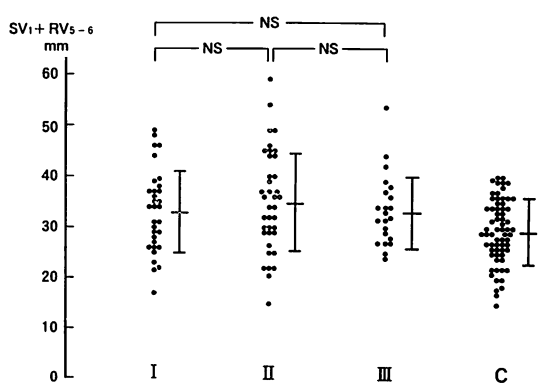

Fig. 6. Voltage of $SV_1+RV_{5,6}$ on electrocardiogram in groups I, II and III and the normotensive group (C).

There was no significant difference between the groups.

NS = not significant.

Discussion

An echocardiographic method for measuring LV mass is reportedly more sensitive and accurate than electrocardiography for the identification of hypertensive LV hypertrophy.[2,3,19,20] Age- and sex-matched healthy normal subjects were utilized as controls in the present study, because the LV mass is influenced by body surface area, age and sex. The tentative cutoff value we proposed for recognizing LV hypertrophy in apparently normal male Japanese subjects was $\geqq 121$ g/m^2, which was somewhat less than the values reported by Devereux et al. ($\geqq 111$ g/m^2 in women, $\geqq 135$ g/m^2 in men).[11,18] The prevalence of LV hypertrophy defined with the identical cutoff for LV mass (>120 g/m^2) reportedly ranges from 23 to 48% in hypertensive patients and from 0 to 10% in normal subjects.[9,21,22] These observations were made for small number of patients with mild to moderately severe essential hypertension who were evaluated in a referral center. Hammond et al. reported that using the same echocardiographic criteria, the prevalence of LV hypertrophy was lower, 12% among patients with borderline hypertension, and 20% among employed patients[10] with relatively mild, uncomplicated sustained hypertension. In the present study, the prevalence of LV hypertrophy was 20.7% in employed male patients with mild to moderate untreated hypertension. This is consistent with the data reported by Hammond et al.[10]

Older ages and longer duration of the hypertensive state may be associated with a greater prevalence and greater severity of hypertensive cardiac hypertrophy. However, most studies have shown a relatively poor correlation between BP and LV hypertrophy.[9,23~25] In addition, cross-sectional studies of large clinical or unselected patient populations with systemic hypertension, the SBP was only weakly related to echocardiographic LV mass, with correlation coefficients of 0.24 to 0.45.[9,23~25] Ever weaker correlation was observed between DBP and LV mass in these studies.[9,23~25] An average 24-hour SBP was reported to be correlated most closely with LV mass.[8,14] Ren et al. reported a substantially closer correlation between LV mass and maximum systolic arterial pressure during treadmill exercise testing than between LV mass and BP at rest prior to exercise.[26] Furthermore, the Framingham data recently reported by Levy et al. showed that LV mass increased with age commensurate with the elevation of the SBP, which was within the normal range.[27] The reason for the dissociation between blood pressure levels and LV hypertrophy has not been fully clarified.

For LV hypertrophy to develop, it seems necessary that BP remain continuously elevated for an extended period. Both BP and duration of hypertensive state are regarded as determinants of the hypertensive LV hypertrophy. Therefore, longitudinal studies of BP is necessary to evaluate the relationship between BP and LV hypertrophy. Thus, we studied the relationships between LV mass and the BP on the basis of longitudinal observations of the "casual" BP. The present study demonstrated that the LV mass index was significantly greater in groups I and II as compared with group III and the control group, and a significantly positive correlation was observed between LV mass and the average DBP. Thus, the group with the greatest frequency of diastolic hypertension exhibited the greatest level of LV mass index and the greatest prevalence of echo-LVH.

However, in the present study, there was no significant correlation between LV mass and average SBP. In addition, the mean value of SBP did not differ significantly among the groups. These characteristics of SBP could result from the fact that SBP varies much more compared with DBP, and the higher the levels of SBP, the greater the variability, as Littler et al. demonstrated.[28]

In conclusion, DBP appears to be an important correlate of LV hypertrophy on the grounds that there was a significant correlation between DBP and echo-LVH.

Clinical implications are that patients with DBP exceeding 100 mmHg for an extended period should be treated to prevent the development of LV hypertrophy. The average DBP in patients with echo-LVH was 99.3 mmHg, in our study. However, LV hypertrophy was also observed, even in patients with mild hypertension with average DBP from 90 to 95 mmHg over long terms. This indicates the need for vigorous examinations, including echocardiography. In addition, echo-LVH, was not observed in some patients with high DBP levels. This dissociation between BP levels and LV mass may have resulted from BP variability or from other sources such as genetic factors.[29~32]

Conclusion

The degree and duration of diastolic hypertension as obtained from casual BP measurements correlated closely with the LV mass index and LV hypertrophy. Echocardiographically, the LV mass index was considered useful in detecting LV hypertrophy in hypertensive patients.

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要　　約

本態性高血圧症男性例における血圧と左室心筋重量との関係

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長期にわたり血圧の観察を行い得た未治療の本態性高血圧症患者で，心エコー図による左室心筋重量係数（LVMI）を測定し，高血圧の程度および持続期間と左室肥大との関連について retrospective に検討した．対象は拡張期高血圧(95 mmHg 以上）発症より5年以上観察ができ，観察期間終了時に心エコー図による LVMI の測定を行い得た未治療の本態性高血圧症，92 例の男性である．全観察期間中に拡張期高血圧を示す割合により以下3群に分類した．I 群は全観察期間中の 80% 以上に拡張期高血圧を認めた 32 例，II 群は 33% 以上，80% 未満で拡張期高血圧を認めた 38 例，III 群は 33% 未満でのみ拡張期高血圧を認めた 22 例で，各群の全観察期間における拡張期血圧の平均は I 群 101.0, II 群 96.0, III 群 90.7 mmHg であった．LVMI は I 群，II 群が III 群より高値を示し，I 群 114.6, II 群 105.3, III 群 90.7 g/m² であった．LVMI が 121 g/m² 以上の左室肥大例は I 群 34.4%，II 群 18.4%，III 群 4.8% であった．左室肥大例の拡張期血圧は 99.3±5.1 mmHg で，左室肥大のない症例の 95.7±4.7 mmHg と比較すると有意な差を認めた．随時血圧における拡張期高血圧の程度およびその持続期間は，左室心筋重量による左室肥大と密接に関連していると考えられた．

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