CARDIAC FUNCTION OF PATIENTS WITH ESSENTIAL HYPERTENSION DURING EXERCISE AND ISOPROTERENOL INFUSION

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The left ventricular function of patients with essential hypertension was examined during exercise and isoproterenol (ISP) infusion echocardiography. Twenty-eight hypertensive patients without cardiac hypertrophy (Group NH), 20 patients with cardiac hypertrophy (Group HH), 7 patients with cardiac dilatation (Group D), and 13 normotensives (Group N), were studied during multistage exercise using a supine bicycle ergometer. In addition, 23 hypertensives (Group NH: 13 patients, Group HH: 10 patients) and 10 normotensives were studied during ISP infusion (0.005 $\mu\text{g/kg/min}$, and 0.01 $\mu\text{g/kg/min}$, respectively, for 5 min). To assess the left ventricular function, an M-mode echocardiogram was utilized at rest and during exercise and ISP infusion.

At rest, the isovolumic relaxation time (IRT) of each hypertensive group was significantly longer than that of Group N. IRT of Group HH and Group D was significantly longer than that of Group NH. Only the shortening fraction (SF) of Group D was significantly smaller than that of Group N.

During exercise the SF increased in all groups, and only the SF of Group D was significantly smaller than that of Group N at a load of 75 W as well as at rest. The SF of Group HH tended to be smaller.

There was no significant difference in peak negative dD/dt ($-dD/dt$) between any of the groups at rest; however, the $-dD/dt$ of Group HH was significantly smaller than that of Group N during ISP infusion.

We concluded that left ventricular diastolic function was disturbed in each hypertensive group at rest. Diastolic dysfunction worsened in Group HH and Group D. Only the left ventricular systolic function of Group D was already depressed at rest. Furthermore, unmanifested systolic dysfunction of the left ventricle seemed to be present in Group HH, because SF during exercise tended to be smaller and $-dD/dt$ during ISP infusion was significantly smaller than that of Group N.

LONG standing essential hypertension impairs the cardiac function by chronic pressure overload. The degree of cardiac dysfunction

accompanying essential hypertension varies because of the differences in the duration and severity of arterial hypertension and the degree of left ventricular hypertrophy.¹ It is important to assess the left ventricular function of the hypertensive heart for the treatment of essential hypertension. The evaluation of cardiac function at rest alone is not sufficient; the evaluation of

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cardiac function at loads is necessary to understand the precise pathophysiology of the hypertensive heart. In this study, we assessed the left ventricular systolic and diastolic function of hypertensive patients by dynamic exercise echocardiography and isoproterenol (ISP) infusion echocardiography.

SUBJECTS

Systemic hypertension was defined by the World Health Organization classification as at least 2 readings of systolic blood pressure over 140 mmHg or diastolic blood pressure over 90 mmHg at 2 separate visits. Cardiac hypertrophy was defined as interventricular septum thickness (IVST) at an end-diastole of over 13 mm or left ventricular posterior wall thickness (LVPWT) of over 11 mm. Cardiac dilatation was defined as left ventricular internal diameter at an end-diastole of over 57 mm.

The subjects first were examined in the supine position at rest by routine two-dimensional echocardiography. When a clear image was obtained, the subject was included in this study. Eleven subjects dropped out after dynamic exercise echocardiography and 2 subjects dropped out after ISP infusion echocardiography, because a clear image was not obtained at each load. The dynamic exercise echocardiography subjects were 55 hypertensive patients (47 men, 8 women) between 19 and 67 years old (mean 46 ± 10) and 13 normal male volunteers between 26 and 56 years old (mean 41 ± 8) without evidence of any cardiovascular or pulmonary disease by history, physical examination, electrocardiogram and chest roentgenogram (Group N). The hypertensive patients were divided into 28 patients without cardiac hypertrophy (Group NH), 20 patients with cardiac hypertrophy (Group HH), and 7 patients with cardiac dilatation (Group D). The patients in Group NH were between 28 and 62 years old (mean 46 ± 9), those in Group HH were between 29 and 67 years old (mean 48 ± 8), and those in Group D were between 19 and 55 years old (mean 41 ± 13).

The ISP echocardiography subjects were 23 hypertensive patients (18 men and 5 women) between 29 and 67 years old (mean 50 ± 9) and 10 normal volunteers (8 men and 2 women) between 32 and 65 years old (mean 47 ± 12). The hypertensive patients were divided into Groups NH and HH. The 13 patients in Group NH were between 29 and 59 years old (mean 45

± 8) and the 10 patients in Group HH were between 47 and 67 years old (mean 55 ± 7).

All hypertensive patients had not been treated previously or had discontinued therapy at least 2 weeks earlier.

METHODS

Echocardiograms were obtained using an electrical sector scan echocardiograph unit (Toshiba's SSH-11A) equipped with a 2.40 MHz transducer.

The subjects were studied in the supine position on dynamic exercise echocardiography using a supine bicycle ergometer (Engineering Dynamic Corporation). The subjects were fixed at shoulder level by attachments of the table that extend from the tip of the shoulders to the neck. This prevented shaking movements that would have disturbed the echocardiogram. The transducer was placed in the third or fourth left intercostal space at the left sternal edge, where the characteristic echo from the anterior cusp of the mitral valve could be identified. Then the transducer was angled to demonstrate the interventricular septum and the left ventricular posterior wall just below the tip of the mitral leaflets at the level of the chordae tendineae. Reject and attenuation controls were manipulated to achieve optimal echos. The transducer was held at the same point on the chest wall throughout the examination. To obtain the true minor dimension of the left ventricular cavity, and to standardize the technique during the examination, the left ventricle was scanned along its major axis during both rest and exercise until a satisfactory echocardiogram was obtained. As Sugishita et al. reported, observations of the transverse diameter just below the tip of anterior mitral leaflet could be a valuable marker to insure reproducibility when repeating the measurements during exercise.² The M-mode echocardiograms of the mitral valve and the aortic valve were recorded simultaneously at rest.

The subjects were studied in a slightly left decubitus position on ISP infusion echocardiography. The M-mode echocardiograms of the interventricular septum and left ventricular posterior wall were obtained in the same manner as on dynamic exercise echocardiography.

The recording of M-mode echocardiogram at rest and during each work load was done at a paper speed of 50 mm/sec by Toshiba's Line Scan Recorder Model LSR 20B (Fig. 1). The

Fig.1. M-mode echocardiogram.

Dd = left ventricular end-diastolic diameter; Ds = left ventricular end-systolic diameter; Da = left ventricular diameter at the initiation of P wave; IVST = interventricular septum thickness; LVPWT = left ventricular posterior wall thickness; IRT = isovolumic relaxation time

Fig.2. Left ventricular internal diameter and dD/dt.
dD/dt = rate of change of dimension

electrocardiogram was recorded simultaneously at rest and during each work load. Blood pressure was measured by the cuff method.

After 10 min of rest, exercise was begun at a level of 25 watts and the level increased by 25 watts every 3 min up to 75 watts. ISP infusion was begun at a dose of 0.005 $\mu\text{g}/\text{kg}/\text{min}$ for 5 min and then increased to a dose of 0.01 $\mu\text{g}/\text{kg}/\text{min}$.

We averaged the values of the following indices on the M-mode echocardiogram for 3 continuous beats at the end of the expiratory phase. Left ventricular end-diastolic internal diameter (Dd) was measured at the initiation of the QRS wave. Left ventricular end-systolic internal diameter (Ds) was defined as the narrowest left ventricular internal diameter during systole. Left ventricular

internal diameter at the initiation of P wave (Da) also was measured. Interventricular septum thickness (IVST) and left ventricular posterior wall thickness (LVPWT) were measured at the initiation of the QRS wave.

Isovolumic relaxation time (IRT) was the interval from the aortic valve closing to the mitral valve opening. Heart rate (HR) was obtained from the R-R interval of the electrocardiogram.

Left ventricular end-diastolic volume (EDV), left ventricular end-systolic volume (ESV), and left ventricular volume at the initiation of the P wave (EAV) were calculated according to the method of Teichholtz et al.³ Shortening fraction (SF), cardiac index (CI), atrial filling fraction

Fig.3. Echocardiograms at rest and during exercise.

A = Echocardiogram of a 33-year-old man (Group N); B = Echocardiogram of a 54-year-old woman (Group NH); C = Echocardiogram of a 50-year-old man (Group HH); D = Echocardiogram of a 31-year-old man (Group D)

(AFF), total peripheral vascular resistance (TPR), and left ventricular mass (LVM) were calculated according to the following formulae⁴;

$$SF = (Dd - Ds) / Dd$$

$$CI (l/min/m^2) = (EDV - ESV) \times HR / BSA$$

$$AFF (\%) = [(EDV - EAV) / (EDV - ESV)] \times 100$$

$$TPR (dyne/sec/cm^{-5}) = MBP \times 79.92 / (EDV - ESV) \times HR$$

$$LVM (g) = 1.04 \times [(Dd + IVST + LVPWT)^3 - Dd^3] - 14$$

(BSA = body surface area,
MBP = mean blood pressure)

Peak negative dD/dt ($-dD/dt$) was obtained according to the method of Gibson et al⁵ using an electronic computer (Kontron's Cardio 80) (Fig. 2).

STATISTICS

The results were expressed as mean $\pm$ standard deviation. Statistical analysis was done by Student's 't' test. A p value less than 0.05 was considered to indicate statistical significance. When the relationship between variables was considered to be continuous, a linear regression analysis was performed.

RESULTS

Figure 3 shows the resting and dynamic exercise echocardiograms for all groups. The endocardial echo of the interventricular septum and the left ventricular posterior wall can be seen clearly. Of the subjects in whom a clear echocardiogram could be obtained at rest, a clear exercise echocardiogram was obtained in 86%.

TABLE I BLOOD PRESSURE, HEART RATE AND M-MODE ECHOCARDIOGRAPHIC DATA AT REST ON EXERCISE ECHOCARDIOGRAPHY IN NORMOTENSIVE SUBJECTS AND HYPERTENSIVE PATIENTS

Group	Blood pressure (mmHg)	Heart rate (beats/min)	Dd (cm)	Ds (cm)	IVST (cm)	LVPWT (cm)
Group N	123 ± 11 / 78 ± 7	66 ± 14	4.9 ± 0.4	3.1 ± 0.4	1.0 ± 0.2	0.8 ± 0.1
Group NH	158 ± 14 / 101 ± 12***	67 ± 10	5.0 ± 0.3	3.2 ± 0.4	1.0 ± 0.2	0.8 ± 0.1
Group HH	175 ± 24 / 110 ± 13***	69 ± 8	4.7 ± 0.5	3.1 ± 0.6	1.7 ± 0.4****	1.2 ± 0.2****
Group D	162 ± 26 / 107 ± 14***	72 ± 7	6.2 ± 0.6****	5.0 ± 0.9***	1.3 ± 0.3***	1.3 ± 0.2****

There is no significant difference in heart rate between any of the groups. Dd and Ds of Group D are significantly increased only compared with those of Group N. IVST and LVPWT of Group HH and Group D are significantly increased compared with those of Group N.

Group N = normotensive subjects; Group NH = patients with hypertension without cardiac hypertrophy; Group HH = patients with hypertension accompanied by cardiac hypertrophy; Group D = patients with hypertension accompanied by cardiac dilatation; Dd = left ventricular end-diastolic diameter; Ds = left ventricular end-systolic diameter; IVST = interventricular septum thickness; LVPWT = left ventricular posterior wall thickness.

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.005$; **** $p < 0.001$ vs Group N

TABLE II IRT, AFF, CI AND TPR AT REST

Group	IRT (sec)	AFF (%)	CI (l/min/m ²)	TPR (dyne/sec/cm ⁻⁵)
Group N	0.05 ± 0.01	25.0 ± 11.0	2.81 ± 0.64	1602 ± 274
Group NH	0.07 ± 0.01**	29.4 ± 10.1	3.05 ± 0.61	1967 ± 475*
Group HH	0.09 ± 0.02†***	40.4 ± 11.0***	2.51 ± 0.57	2650 ± 868*
Group D	0.11 ± 0.02†***	37.4 ± 11.4*	3.10 ± 1.03	2012 ± 695

IRT was significantly longer in all hypertensive groups than in Group N. AFF of Group HH and Group D was significantly greater than that of Group N. There was no significant difference in CI between each hypertensive group and Group N, but CI of Group HH tended to be smaller. TPR of Group NH and Group HH was significantly greater than that of Group N. TPR of Group D tended to be greater than that of Group N.

IRT = isovolumic relaxation time; AFF = atrial filling fraction; CI = cardiac index; TPR = total peripheral vascular resistance.

* $p < 0.01$; ** $p < 0.005$; *** $p < 0.001$ vs Group N

† $p < 0.001$ vs Group NH

A. Dynamic bicycle exercise

I. At rest

(1) Systolic blood pressure (SBP), diastolic blood pressure (DBP) and heart rate (HR)

SBP and DBP of all hypertensive groups were higher than those of Group N. There was no significant difference in HR between any of the groups (Table I).

(2) Left ventricular internal dimension and left ventricular wall thickness

Only the Dd and Ds of Group D were significantly larger than those of Group N.

IVST and LVPWT were increased significantly more in Group HH and Group D than in Group N (Table I).

(3) Shortening fraction

SF was 0.37 ± 0.04 in Group N, 0.36 ± 0.05 in Group NH, 0.33 ± 0.07 in Group HH, and 0.20 ± 0.07 in Group D. Only the SF of Group D was significantly smaller than that of Group N.

(4) Isovolumic relaxation time and atrial filling fraction

IRT was significantly longer in all hypertensive groups than in Group N. The IRT of Group HH and Group D was significantly longer than that of Group NH. The AFF of Group HH and Group D was significantly greater than that of Group N, but there was no significant difference in AFF between Group N and Group NH (Table II).

(5) Cardiac index

There was no significant difference in CI

Fig.4. Serial changes in blood pressure and heart rate at rest and during exercise. Blood pressure of all hypertensive groups is higher than that of Group N during exercise. There is no significant difference in heart rate between any of the groups during exercise. BP = blood pressure; SBP = systolic blood pressure; DBP = diastolic blood pressure; HR = heart rate

between each hypertensive group and Group N, but the CI of Group HH tended to be smaller (Table II).

(6) Total peripheral vascular resistance

The TPR of Group NH and Group HH was significantly greater than that of Group N. The TPR of Group D tended to be greater than that of Group N (Table II).

II. Exercise

(1) Blood pressure and heart rate

Blood pressure of all groups increased during exercise. The SBP at a load of 75W was 156 ± 17 mmHg in Group N, 187 ± 20 mmHg in Group NH, 209 ± 30 mmHg in Group HH, and 196 ± 34 mmHg in Group D. DBP was 84 ± 8 mmHg in Group N, 110 ± 14 mmHg in Group NH, 117 ± 19 mmHg in Group HH, and 112 ± 15 mmHg in Group D at a load of 75W. HR increased in all groups during exercise and there was no significant difference in HR at a load of 75W between

any of the groups (Fig. 4).

(2) Left ventricular internal dimension

Dd was 4.8 ± 0.4 cm in Group N, 4.9 ± 0.4 cm in Group NH, 4.6 ± 0.5 cm in Group HH and 6.4 ± 0.7 cm in Group D at a load of 75W. The Dd decreased in Group N and Group NH, was unchanged in Group HH, and increased in Group D at a load of 75W when compared with the values at rest.

Ds was 2.6 ± 0.4 cm in Group N, 2.7 ± 0.4 cm in Group NH, 2.6 ± 0.6 cm in Group HH, and 4.9 ± 0.9 cm in Group D at a load of 75W. Although the Ds decreased at a load of 75W when compared with that at rest in Group N, Group NH and Group HH, it was unchanged in Group D (Fig. 5).

(3) Shortening fraction

SF increased in all groups during exercise and became 0.45 ± 0.06 in Group N, 0.44 ± 0.04 in Group NH, 0.42 ± 0.09 in Group HH, and $0.24 \pm$

Fig.5. Comparison between Dd and Ds at rest and those at a load of 75 W.

Dd of Group D is only increased at a load of 75 W as opposed to at rest. There is no significant difference in Ds of Group D at rest and at a load of 75 W.

Fig.6. Serial changes of SF at rest and during exercise.

SF of Group D is decreased more than that of Group N during exercise.

SF = shortening fraction

0.06 in Group D at a load of 75 W. Only the SF of Group D was significantly smaller; the SF of Group HH tended to be smaller than that of Group N (Fig. 6).

(4) Cardiac index

CI increased in all groups during exercise and became 5.14 ± 1.08 l/min/m² in Group N, 5.74 ± 0.95 l/min/m² in Group NH, 4.69 ± 0.87 l/min/m² in Group HH, and 6.19 ± 1.6 l/min/m² in Group D at a load of 75 W. Although there was no significant difference in CI between each hypertensive group and Group N, the CI of Group HH tended to be smaller than that of Group N.

(5) Total peripheral vascular resistance

TPR decreased in all groups during exercise and became 1021 ± 169 dyne/sec/cm⁻⁵ in Group N, 1173 ± 204 dyne/sec/cm⁻⁵ in Group NH, 1556 ± 416 dyne/sec/cm⁻⁵ in Group HH, and 1081 ± 275 dyne/sec/cm⁻⁵ in Group D at a load of 75 W.

Fig. 7. Echocardiogram at rest and during ISP infusion.

A = Echocardiogram of a 54-year-old woman (Group N); B = Echocardiogram of a 43-year-old man (Group NH); C = Echocardiogram of a 50-year-old man (Group HH)

TABLE III BLOOD PRESSURE, HEART RATE AND M-MODE ECHOCARDIOGRAPHIC DATA AT REST ON ISOPROTERENOL INFUSION ECHOCARDIOGRAPHY IN NORMOTENSIVE SUBJECTS AND HYPERTENSIVE PATIENTS

Group	Blood pressure (mmHg)	Heart rate (beats/min)	Dd (cm)	Ds (cm)	IVST (cm)	LVPWT (cm)
Group N	125 ± 13 / 75 ± 10	67 ± 13	4.8 ± 0.4	3.0 ± 0.4	0.9 ± 0.2	0.8 ± 0.1
Group NH	159 ± 26 / 99 ± 13****	72 ± 12	4.6 ± 0.4	3.0 ± 0.4	1.0 ± 0.1	0.8 ± 0.1
Group HH	165 ± 18 / 105 ± 11****	69 ± 7	4.4 ± 0.6	3.0 ± 0.6	1.7 ± 0.4****	1.1 ± 0.3***

IVST and LVPWT of Group HH are significantly increased compared with those of Group N. There is no significant difference in heart rate, Dd and Ds between any of the groups.

*** $p < 0.005$; **** $p < 0.001$ vs Group N

B. Isoproterenol infusion

Figure 7 shows the resting and ISP infusion echocardiograms for all groups. Of the subjects in whom a clear echocardiogram could be obtained at rest, a clear ISP infusion echocardiogram was obtained in 94%.

(1) Blood pressure, heart rate, left ventricular internal dimension, and left ventricular wall thickness at rest

At rest the SBP and DBP of Group NH and

Group HH were significantly higher than those of Group N, but there was no significant difference in SBP and DBP between Group NH and Group HH. There was no significant difference in HR between any of the groups. There was no significant difference in Dd or Ds between any of the groups. Only the IVST and LVPWT of Group HH were significantly thicker than those of Group N (Table III).

(2) Mean blood pressure

Fig. 8. Serial changes of MBP and heart rate at rest and during isoproterenol infusion. MBP of all groups decreases similarly during isoproterenol infusion. There is no significant difference in heart rate during isoproterenol infusion between any of the groups. MBP = mean blood pressure

Fig. 9. Serial changes of peak negative dD/dt at rest and during isoproterenol infusion. There is no significant difference in peak negative dD/dt at rest between all groups. Peak negative dD/dt of Group HH is decreased more than those of Group N and Group NH during isoproterenol infusion. $-dD/dt$ = peak negative dD/dt

MBP decreased in all groups during ISP infusion (Fig. 8) and there was no significant difference in the reduction rate of MBP during ISP infusion between any of the groups.

(3) Heart rate

There was no significant difference in HR between any of the groups during ISP infusion or at rest (Fig. 8).

(4) Total peripheral vascular resistance

TPR of all groups decreased during ISP infusion and there was no significant difference in the reduction rate of TPR during ISP infusion between any of the groups.

(5) Peak negative dD/dt

There was no significant difference in $-dD/dt$ at rest between any of the groups, but the $-dD/dt$ of Group HH was significantly smaller than that of Group N or Group NH during ISP infusion.

(At the rate of $0.005 \mu\text{g/kg/min}$: Group N, $3.43 \pm 0.69 \text{ cm/sec}$; Group NH, $3.15 \pm 0.61 \text{ cm/sec}$; Group HH, $2.49 \pm 0.48 \text{ cm/sec}$. At the rate of $0.01 \mu\text{g/kg/min}$: Group N, $4.04 \pm 0.86 \text{ cm/sec}$; Group NH, $3.98 \pm 0.75 \text{ cm/sec}$; Group HH, $2.80 \pm 0.48 \text{ cm/sec}$) (Fig. 9).

(6) Correlation of peak negative dD/dt with left ventricular mass and mean blood pressure

Fig.10. Correlation of peak negative dD/dt with LVM and MBP after isoproterenol infusion ($0.005 \mu\text{g}/\text{mg}/\text{min}$) in Group NH and Group HH.

Peak negative dD/dt is inversely related to LVM, but it is not related to MBP.

$-dD/dt$ = peak negative dD/dt ; LVM = left ventricular mass; MBP = mean blood pressure

As we observed the difference in $-dD/dt$ between Group NH and Group HH during ISP infusion, we studied the correlation of $-dD/dt$ with LVM and MBP in all hypertensive patients. $-dD/dt$ was inversely related to LVM ($0.005 \mu\text{g}/\text{kg}/\text{min}$: $r = -0.64$ $p < 0.01$, $0.01 \mu\text{g}/\text{kg}/\text{min}$: $r = -0.68$ $p < 0.001$), but was not related to MBP (Fig. 10).

DISCUSSION

There are several variations in the hypertensive heart. In the hypertrophied group, cardiac hypertrophy compensates for chronic arterial hypertension and normalizes wall stress. In the dilated group, wall stress is increased by dilatation of the left ventricular cavity. It is necessary, therefore, to evaluate the cardiac function of subgroups classified by the hypertrophy and dilatation of the left ventricle in order to understand the clinical course and severity of the condition in the hypertensive heart.⁶

Exercise is a physiologic load and so we could estimate left ventricular reserve by dynamic exercise echocardiography. However, there are several problems with the evaluation of cardiac function; that is, blood pressure increases and TPR decreases considerably during exercise. On the other hand, ISP infusion echocardiography is suitable for the evaluation of left ventricular function, because ISP acts on the heart selec-

tively, to some extent. So, we could evaluate cardiac function in hypertensives in detail using these methods.

When we study the hypertensive heart, it is important to exclude patients with hypertrophic cardiomyopathy or dilated cardiomyopathy. Therefore, we excluded above-mentioned diseases according to the WHO/ISFC report.⁷

The cardiovascular hemodynamics of patients with essential hypertension have been studied for many years.⁸ However, the assessment of cardiac function in hypertensives has produced conflicting results because of differences in study subjects and methods.⁹⁻¹³

Frohlich et al.⁹ showed that the left ventricular systolic function in hypertensive patients with only left atrial overload on the electrocardiogram was impaired. Karliner et al.¹⁴ and Toshima et al.¹⁰ suggested that the left ventricular systolic function was normal, not only in non-hypertrophied hypertensives but also in hypertrophied hypertensives whose wall stress was normalized by hypertrophy.

We studied cardiac function in patients with essential hypertension during exercise and ISP infusion. In this study, the left ventricular systolic function of Group D at rest was impaired because only the SF of this group was smaller than that of Group N. Otherwise, the SF of Group HH was within the normal range, as was that of Group NH, but it tended to be smaller

than that of Group N. These results were in agreement with the reports of Karliner et al. and Toshima et al.. The CI of Group NH and Group HH was maintained at normal by the normal left ventricular systolic function. The CI of Group D also was normal because left ventricular dilatation compensated for cardiac dysfunction. The left ventricular diastolic function at rest of each hypertensive group showed a significantly longer isovolumic relaxation time (IRT) than that of Group N. The IRT of Group HH and Group D was significantly more prolonged than that of Group NH. This indicates that the left ventricular early diastolic function is already damaged in the hypertensive heart at the stage of non-hypertrophy, and left ventricular hypertrophy or dilatation worsens left ventricular diastolic dysfunction. It appeared that increased AFF compensated for the severely damaged left ventricular early diastolic function in Group HH and Group D.

The dynamic exercise test was performed because the cardiac function of hypertensives during exercise might be different from that at rest. There is no agreement as to the changes in left ventricular internal diameter and left ventricular volume during exercise.¹⁵⁻²⁰ In the present study, both left ventricular end-diastolic internal diameter and left ventricular end-systolic internal diameter decreased, and the degree of decrease was greater in the latter in Group N. In Group NH and Group HH, left ventricular end-systolic internal diameter decreased more than left ventricular end-diastolic internal diameter. These results were in agreement with the reports of Braunwald et al. and Kitamura et al.. On the other hand, in Group D, left ventricular end-systolic internal diameter did not decrease during exercise, and left ventricular end-diastolic internal diameter increased. It therefore appeared that the Frank-Starling effect existed during exercise in Group D, as was reported by Asai.¹⁶

The SF of all groups increased during exercise. The SF of Group D was smaller than that of Group N during exercise, and so the damaged left ventricular systolic function of Group D was evident during exercise. The left ventricular systolic function was not impaired in Group NH, but it tended to be impaired in Group HH because the SF of Group HH tended to be smaller than that of Group N at a load of 75W.

The CI of Group HH tended to be smaller than that of Group N during exercise, but there was no significant difference in CI between other

hypertensive groups and Group N. In Group D, CI remained normal in spite of the severe damage in cardiac function. This seemed to be due to left ventricular dilatation and the Frank-Starling effect during exercise.

Aside from Group D, which had damaged cardiac function, our findings on the cardiac function of other hypertensive groups during exercise were not in agreement with the other reports. Strauer et al.²¹ claim that cardiac hypertrophy does not cause cardiac dysfunction during exercise. However, Kitamura et al.¹⁵ showed that decreased CI during severe exercise meant left ventricular systolic dysfunction in Group HH. During moderate exercise, our study showed that left ventricular systolic function seemed to be maintained normally not only in Group NH but also in Group HH. It was questionable whether left ventricular systolic function in Group HH remained normal or not during severe exercise because SF and CI tended to be smaller in Group HH than in Group N at a load of 75W.

As above, only left ventricular systolic function of Group D was impaired at rest, and the left ventricular systolic function of Group HH might be impaired during severe exercise. Therefore, isoproterenol infusion echocardiography was done in Group NH and Group HH to evaluate cardiac function in detail. Group D was excluded from this study because of evident left ventricular systolic dysfunction.

When we studied the cardiac function during ISP infusion, it was necessary to consider the effect of ISP on HR and afterload. In our study, there was no significant difference in changes of blood pressure and TPR during ISP infusion between any of the groups, and there was also no significant difference in HR at rest or during ISP infusion between any of the groups. Therefore, it was possible to compare the cardiac function between normotensive controls and hypertensive patients even allowing for the influence of afterload.

During ISP infusion there was no significant difference in $-dD/dt$ between Group N and Group NH. Although there was no difference in blood pressure between Group NH and Group HH, there was a significant difference in $-dD/dt$ between the two groups during ISP infusion. The reduced response for ISP in Group HH did not seem to be due to increased blood pressure, but the increased LVM seemed to cause the decreased $-dD/dt$, because $-dD/dt$ was not related

to mean blood pressure but was related inversely to LVM.

Ayobe et al.²² showed that there was a reduced response for ISP and the reduction of receptor numbers together with the increased LVM in renal hypertensive rats. Ginsburg et al.²³ observed reduced response to ISP in the papillary muscle of failing hearts. Recently Volpe et al.²⁴ reported that LVM was related to a dose of ISP which increased HR 25 beats in hypertensive patients.

Our present study corresponded to these reports. Latent left ventricular systolic dysfunction due to increased LVM was suggested in Group HH by the reduction of increase rate of $-dD/dt$ during ISP infusion. Sugishita et al.²⁵ showed that there was an increased response to ISP in hypertrophied hearts. The difference between our data and Sugishita's report may be due to the differences in subjects and the dose of ISP.

Left ventricular systolic function was not impaired in Group NH, because there was no significant difference in $-dD/dt$ between Group N and Group NH at rest and during ISP infusion.

We concluded that left ventricular diastolic function was impaired in each hypertensive group at rest. Only left ventricular systolic function of Group D was already impaired at rest. Furthermore, latent left ventricular systolic dysfunction seemed to exist in Group HH because SF during exercise tended to be smaller, and $-dD/dt$ during ISP infusion was significantly smaller, than that of Group N.

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