Left Ventricular Dysfunction Assessed by Cardiac Time Interval Analysis Among Different Geometric Patterns in Untreated Hypertension

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Background: Left ventricular (LV) hypertrophy is a powerful independent predictor of morbidity and mortality in hypertensive patients. Abnormal LV geometric patterns are also associated with hypertensive complications, and concentric hypertrophy is associated with the highest mortality in hypertensive patients. However, the relationship between geometric patterns and cardiac dysfunction is not fully established. We hypothesized that the Tei index, which is a measure of global cardiac function, is a feasible parameter for estimating cardiac dysfunction among the different LV geometric patterns in hypertensive patients.

Methods and Results: We enrolled 60 consecutive patients with untreated essential hypertension. Subjects were divided into 4 groups: normal geometry, concentric remodeling, eccentric hypertrophy and concentric hypertrophy. We measured ejection fraction, mitral E/A ratio, Tei index, ejection time, and isovolumic contraction and relaxation times. There were significant correlations between LV mass index and systolic blood pressure ($P<0.01$), ejection fraction ($P<0.05$), mitral E/A ratio ($P<0.05$) and Tei index ($P<0.0001$). In multiple regression analysis, only the Tei index independently correlated with LV mass index ($P<0.01$). Concentric hypertrophy significantly increased the Tei index compared with the other 3 groups.

Conclusions: The Tei index provides a better marker for LV dysfunction by hypertensive hypertrophy than conventional parameters. LV function in concentric hypertrophy was most impaired among all the geometric patterns in untreated hypertensive patients. (*Circ J* 2012; **76**: 1409–1414)

Key Words: Echocardiography; Hypertension; Left ventricular function; Left ventricular hypertrophy

Essential hypertension is a major risk factor for cardiovascular disease. In hypertensive patients, pressure and/or volume overload leads to left ventricular (LV) hypertrophy, which is a powerful independent predictor of morbidity and mortality.¹ Hypertensive LV hypertrophy causes heart failure, especially diastolic heart failure, which is heart failure with a normal LV ejection fraction (LVEF) because of LV diastolic dysfunction. However, several studies have reported that patients with diastolic heart failure have not only diastolic dysfunction but also systolic dysfunction, when parameters other than LVEF were used to evaluate systolic function.^{2–5} Therefore, global cardiac function including systolic and diastolic LV function should be evaluated by non-conventional functional parameters such as the Tei index. The Tei index,

combining systolic and diastolic functional parameters, may be a better and simpler parameter to estimate LV global function than conventional indices of purely systolic or diastolic function in hypertensive patients.

Based on LV mass and relative wall thickness, patients with essential hypertension can be classified into 4 different LV geometric patterns: normal, concentric remodeling, concentric hypertrophy and eccentric hypertrophy.^{6–8} Previous studies have reported that abnormal LV geometric patterns are associated with a greater risk of hypertensive complications, and patients with concentric LV hypertrophy have the highest mortality and cardiovascular event rate.^{7,9} The relation between these 4 different LV geometric patterns and LV function has not been elucidated. Therefore, we aimed to investigate the correlation

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Table 1. Patients' Characteristics (n=60)

Age (years)	50±14
Gender (M/F)	30/30
BMI (kg/m ²)	25±4
Body surface area (m ²)	1.65±0.19
Heart rate (beats/min)	68±11
Systolic BP (mmHg)	164±19
Diastolic BP (mmHg)	98±16
Stage 1 hypertension (%)	32
Stage 2 hypertension (%)	33
Stage 3 hypertension (%)	35
Dyslipidemia (n, %)	18 (30%)
Total cholesterol (mg/dl)	203±33
Triglycerides (mg/dl)	112±56
HDL-cholesterol (mg/dl)	62±22
Diabetes mellitus (n, %)	18 (30%)
Fasting plasma glucose (mg/dl)	106±25
HbA _{1c} (%)	5.2±1.2
Creatinine (mg/dl)	0.7±0.2

Values are mean±SD.

BMI, body mass index; BP, blood pressure.

Table 2. Echocardiographic Measurements (n=60)

LV diastolic dimension (mm)	49±5
Interventricular septum thickness (mm)	11±3
LV posterior wall thickness (mm)	10±2
Relative wall thickness	0.40±0.10
LV mass (g)	182±61
LV mass index (g/m ²)	110±35
LVEF (%)	69±9
Mitral E/A ratio	1.0±0.3
Mitral E deceleration time (ms)	207±52
LV Tei index	0.44±0.13
ICT (ms)	33±20
IRT (ms)	95±24
ET (ms)	296±28

Values are mean±SD.

LV, left ventricular; LVEF, left ventricular ejection fraction; ICT, isovolumic contraction time; IRT, isovolumic relaxation time; ET, ejection time.

between LV mass and LV function and the effect of LV geometry on the severity of LV dysfunction in patients with untreated essential hypertension.

Methods

Subjects

We enrolled 60 consecutive patients with untreated essential hypertension and without heart failure symptoms (mean age, 50±14; 50% male). Blood pressure (BP) was measured at the office with a calibrated mercury sphygmomanometer after a 5-min rest while seated on 2 different occasions. Hypertension was defined as systolic BP ≥140 mmHg or diastolic BP ≥90 mmHg. Stage 1 hypertension was defined as systolic BP of 140–159 mmHg or diastolic BP of 90–99 mmHg, stage 2 hypertension was defined as systolic BP of 160–179 mmHg or diastolic BP of 100–109 mmHg, and stage 3 hypertension was defined as systolic BP ≥180 mmHg, diastolic BP ≥110 mmHg.¹⁰

Figure 1. Measurement of the Tei index with Doppler echocardiography. ECG, electrocardiogram; ET, ejection time; ICT, isovolumic contraction time; IRT, isovolumic relaxation time; LV, left ventricular; "a", the time interval from the cessation to the onset of mitral inflow; "b", the time interval from the onset to the cessation of aortic flow; "c", the time interval between the peak of the QRS complex in the ECG and the onset of mitral inflow; "d", the time interval between the peak of the QRS and the cessation of LV ejection flow.

Patients were excluded if they had secondary hypertension, ischemic heart disease, atrial fibrillation, congenital heart disease, or other organic heart disease such as significant valvular disease. The patients' characteristics are summarized in **Table 1**. This protocol was approved by the Institutional Committee of Kagoshima University Hospital, and written informed consent was given by all patients.

Echocardiography and Cardiac Time Interval Analysis

Standard 2-dimensional and Doppler echocardiography were performed using a commercially available echocardiographic machine (ATL HDI 5000) with a 2.0–3.5-MHz transducer. Interventricular septal thickness (IVS), posterior wall thickness (PWT) and LV internal dimension (LVID) were measured at end-diastole according to established standards of the American Society of Echocardiography (ASE).¹¹ LVEF was obtained using a modified biplane Simpson's method from the apical 2- and 4-chamber views. LV mass was calculated according to the ASE-recommended formula:¹¹

$$\text{LV mass (g)} = 0.8 \times \{1.04[(\text{IVS} + \text{LVID} + \text{PWT})^3 - (\text{LVID})^3]\} + 0.6$$

LV mass was divided by body surface area to obtain the LV mass index (LVMI). Relative wall thickness (RWT) was also calculated using the formula:

$$\text{RWT} = (2 \times \text{PWT}) / \text{LVID}$$

The LV geometry in each subject was classified into 1 of 4 patterns based on LVMI and RWT: (1) normal when LVMI was ≤115 g/m² for men and ≤95 g/m² for women, and RWT was ≤0.42; (2) concentric remodeling when LVMI was ≤115 g/m² for men and ≤95 g/m² for women, and RWT was >0.42; (3)

	Table 3. Correlations Between LV Mass Index and Other Study Variables			
	Single regression analysis		Multiple regression analysis	
	r value	Univariate P value	Multivariate P value	Coefficient
Age (years)	0.10	NS	NA	NA
BMI (kg/m ²)	0.03	NS	NA	NA
Systolic BP (mm Hg)	0.34	<0.01	NS	0.181
Diastolic BP (mmHg)	0.16	NS	NA	NA
LVEF (%)	−0.33	<0.05	NS	−0.131
Mitral E/A ratio	−0.30	<0.05	NS	−0.101
Mitral E deceleration time (ms)	0.22	NS	NA	NA
LV Tei index	0.50	<0.0001	<0.05	0.346

NS, not significant; NA, not available. Other abbreviations see in Tables 1,2.

concentric hypertrophy when LVMI was >115 g/m² for men and >95 g/m² for women, and RWT was >0.42; and (4) eccentric hypertrophy when LVMI was >115 g/m² for men and >95 g/m² for women, and RWT was <0.42.^{6,7}

Pulsed Doppler recordings of mitral flow velocities were obtained from the apical 4-chamber view by placing the sample volume between the tips of the mitral leaflets, and LV outflow velocities were obtained by placing the sample volume in the outflow tract below the aortic valve leaflets. Peak early (E) and late diastolic (A) transmitral filling flow velocities, E/A ratio and deceleration time (DcT) of the E wave were measured.

Doppler time intervals were also measured from the mitral

inflow and LV outflow velocities. The interval “a” was taken from the cessation to the onset of mitral inflow and this was equal to the sum of isovolumic contraction time (ICT), ejection time (ET) and isovolumic relaxation time (IRT) (Figure 1). The interval “b” was taken from the onset to the cessation of aortic flow and this was the LV ET. Thus, the sum of ICT and IRT was obtained by subtracting interval “b” from “a”. The Tei index, combining systolic and diastolic function, was defined as the sum of ICT and IRT divided by ET: (a−b)/b. We also measured the interval “c” between the peak of the QRS complex and the onset of mitral inflow, and the interval “d” between the peak of the QRS complex and the cessation of LV outflow. Therefore, IRT=c−d, and ICT=(a−b)−(c−d). Data

Table 4. Correlations Between LV Mass Index and Cardiac Time Intervals

	r value	Univariate P value	Multivariate P value	Standardized regression coefficient
ICT (ms)	0.54	<0.0001	<0.0001	0.518
IRT (ms)	0.30	<0.05	<0.05	0.247
ET (ms)	−0.08	NS	NA	NA

Abbreviations see in Tables 1–3.

Table 5. Comparisons of Clinical Characteristics Among Geometric Patterns

	Normal (n=22)	Concentric remodeling (n=9)	Eccentric hypertrophy (n=12)	Concentric hypertrophy (n=17)	P value
Age (years)	48±13	46±13	53±17	54±15	NS
Gender (M/F)	10/12	5/4	7/5	8/9	NS
BMI (kg/m ²)	24±4	26±5	23±3	25±3	NS
Heart rate (beats/min)	71±10	72±12	65±8	65±10	NS
Systolic BP (mmHg)	161±22	159±14	165±17	171±19	NS
Diastolic BP (mmHg)	97±17	100±10	98±14	100±19	NS
Dyslipidemia (n, %)	7 (32%)	3 (33%)	2 (17%)	6 (35%)	NS
Diabetes mellitus (n, %)	7 (32%)	2 (22%)	3 (25%)	6 (35%)	NS

Abbreviations see in Tables 1,3.

were obtained from 3 consecutive cardiac cycles and averaged. All echocardiographic measurements were performed by a single experienced cardiologist blinded to all of the other clinical and demographic data.

Statistical Analysis

The results are expressed as the means±SD. The relationship between LVMI and the other continuous study variables was analyzed with simple linear regression analysis. Multiple stepwise linear regression analysis was performed to determine which variables were independent predictors of LVMI. A 1-way analysis of variance (ANOVA) with Fisher's PLSD post hoc analysis was used to determine if there were differences among the 4 groups. All statistical analyses were performed with Statview version 5.0 (SAS Institute, Cary, NC, USA). A P-value <0.05 was considered significant.

Results

Patients' Characteristics

The characteristics of the patients with untreated hypertension are summarized in **Table 1**. The population consisted of 60 middle-aged patients with an equal number of males and females; 24 patients (40%) were obese, as defined by a BMI ≥25 kg/m².

Echocardiographic Measurements

The echocardiography data are summarized in **Table 2**: 22 patients had a normal LV geometric pattern and 9 had a concentric remodeling pattern; 29 (48%) had LV hypertrophy, defined as a LVMI was >115 g/m² for men and >95 g/m² for women; 12 patients had eccentric hypertrophy and 17 had concentric hypertrophy.

Association Between LVMI and Other Variables

The results of a linear regression analysis between LVMI and all of the other variables are shown in **Table 3**. Systolic BP, LVEF, mitral E/A ratio and LV Tei index were significantly

correlated with LVMI (**Figure 2**). Only LV Tei index was independently correlated with LVMI in the multiple regression analysis (**Table 3**).

Association of LVMI With Components of the Tei Index

LV Tei index correlated well with LVMI as shown in **Table 3** and **Figure 2**. The Tei index consists of ICT, ET and IRT. Therefore, we examined which components of the Tei index were independently correlated with LVMI (**Table 4**). Multiple regression analysis showed that both ICT and IRT were independently correlated with LVMI, whereas there was no correlation between ET and LVMI. Furthermore, the correlation between ICT and LVMI was stronger than the correlation between IRT and LVMI (P<0.0001 vs. P<0.05, respectively).

Differences of LV Dysfunction Among LV Geometric Patterns

We analyzed the differences of LV Tei index and its components in the 4 different LV geometric patterns. There were no significant differences in clinical characteristics among geometric patterns (**Table 5**). LV Tei index and ICT in the group with concentric hypertrophy were significantly greater than in the other 3 groups (**Figures 3A,B**). The IRT value in the group with concentric hypertrophy was significantly greater than that in the groups with normal geometry and concentric remodeling (**Figure 3D**). There were no significant differences in ET among the 4 groups (**Figure 3C**).

Discussion

We examined the correlation between LV mass and LV function by echocardiography in patients with untreated hypertension. The main findings of the present study are: (1) LV Tei index independently correlated with LVMI, and (2) ICT in concentric hypertrophy was significantly greater compared with all other geometric patterns. Our study is the first to demonstrate that LV Tei index correlated with LVMI and LV geometry in patients with untreated hypertension.

Although there are many studies that have examined LV

Figure 3. Differences in the left ventricular (LV) Tei index and its components in the 4 LV geometric patterns. ICT, isovolumic contraction time; IRT, isovolumic relaxation time. *P<0.05, **P<0.01, ***P<0.001.

function in patients with hypertension, most of the subjects had already received antihypertensive therapy. Lowering BP may decrease LV mass and modify LV function. Moreover, antihypertensive drugs, such as calcium-channel blockers, β -blockers, angiotensin-converting enzyme inhibitors, or angiotensin-receptor blockers, should attenuate LV dysfunction. Because none of the subjects in this study had been treated for hypertension, we could eliminate the confounding effects of antihypertensive therapy on the relation between LV function and mass.

Tei Index in Hypertension

The Tei index has been proposed as a measure of global LV function, combining LV systolic and diastolic functions.¹² Compared with other conventional parameters of LV function, there is a stronger association between the Tei index and prognosis in various cardiac diseases, which strongly suggests that the Tei index is a more sensitive marker of global LV dysfunction.^{13–16} A modified Tei index, which is calculated using tissue Doppler rather than standard Doppler, has also been proposed. Both the Tei index and the modified Tei index have been used in previous studies to evaluate LV function in hypertensive patients.^{17–20} The modified Tei index was shown to be increased in hypertensive patients before the development of overt hypertrophy, and the increment was more pronounced after the development of hypertrophy.¹⁷ These results are consistent with the results of our study. Gur et al showed a relationship between the modified Tei index and aortic distensibility in patients with essential hypertension.¹⁸ A large European clinical trial (SILVHIA study) showed that LV Tei index decreased after antihypertensive treatment in hypertensive pa-

tients with LV hypertrophy.¹⁹ However, they did not examine the correlation of Tei index with LVMI or how the various LV geometric patterns influenced the Tei index.

ICT and IRT in Hypertension

We demonstrated that LVMI significantly correlated with LV Tei index, and also with IRT and ICT, which are 2 components of the Tei index. Importantly, ICT had the strongest correlation with LVMI among the 3 components of the Tei index. This finding suggests that hypertensive LV remodeling has a great effect on intrinsic systolic dysfunction, reflected by a prolonged ICT, even in hypertensive patients with normal LVEF. We should note that a normal EF does not necessarily mean normal systolic function, and ICT is a sensitive parameter for evaluating intrinsic systolic function in patients with essential hypertension. LV systolic dysfunction, expressed by ICT, has been reported to play an important role in the development of diastolic heart failure in patients with hypertension.²¹

LV Geometric Patterns in Hypertension

We precisely analyzed LV functional parameters in hypertensive patients after classifying them into 4 different LV geometric patterns. A previous study reported that hypertensive patients with concentric hypertrophy had the highest mortality and cardiovascular event rate, followed by those with eccentric hypertrophy.⁷ These findings are consistent with our finding that LV Tei index and ICT were the highest in concentric hypertrophy. These results suggest that global LV dysfunction, including systolic and diastolic LV dysfunction, is associated with a worse prognosis in patients with concentric hypertrophy.

Study Limitations

First, because most of the patients in this study were in the early phase of hypertension with mild LV dysfunction, there were few patients with heart failure. Further research is needed to determine which LV geometric pattern in hypertension is most likely to progress to heart failure. Second, the study population was small and the study was performed at a single hospital. A multicenter study to confirm these results with a larger number of patients is also required.

Conclusions

The Tei index provides a better marker for LV dysfunction due to hypertensive hypertrophy than the conventional parameters. LV function was most impaired in patients showing concentric hypertrophy among all the geometric patterns in untreated hypertensive patients.

Disclosures

None.

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