DIFFERENCE IN MYOCARDIAL CHARACTERISTICS BETWEEN HYPERTROPHIC CARDIOMYOPATHY AND MYOCARDIAL HYPERTROPHY DUE TO ESSENTIAL HYPERTENSION

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To investigate the qualitative difference in myocardial hypertrophy that exists between hypertrophic cardiomyopathy (HCM) and essential hypertension (HT), we measured the mean wall thickness (MWT), the early diastolic time intervals (II\textsubscript{A}-MVO time: from the second heart sound to the point of mitral valve opening, MVO-O time: from MVO to the O point of apexcardiogram) and the MVO-O/II\textsubscript{A}-MVO ratio. The MWT in HCM and HT was measured by biventriculogram and echocardiogram, respectively.

The MWT showed no significant difference between HT (13.1 ± 3.0 mm) and non-obstructive type of HCM (14.8 ± 3.7), but the MWT in obstructive type (10.8 ± 0.24) was significantly thinner than that in HT. As the MWT increased, both II\textsubscript{A}-MVO and MVO-O time were prolonged in both groups. But the mode of prolongation was quite different. In HT, the prolongation of the II\textsubscript{A}-MVO time was almost always greater than that of the MVO-O time. In HCM, the prolongation of the latter was greater than that of the former. The MVO-O/II\textsubscript{A}-MVO ratio in HT was significantly less than that in normal subjects, but those in HCM were significantly greater.

These findings suggest that the differences in the early diastolic time intervals between HCM and HT are not due to the magnitude of the left ventricular hypertrophy, but due to myocardial characteristics.

HYPERTROPHIC cardiomyopathy (HCM) is functionally characterized by a diastolic impairment\textsuperscript{1,2} and many reports on diastolic functions of HCM have been published\textsuperscript{3–6}. Hypertensive heart disease (HT) has myocardial hypertrophy and impaired diastolic function as morphological characteristics\textsuperscript{7–10}. As Goodwin et al. reported\textsuperscript{11–13} it has been difficult to differentiate HCM, especially that of the non-obstructive type, from myocardial hypertrophy due to the hemodynamics of HT. Previously, we reported that the analysis of the early diastolic time intervals was very useful in differentiating HCM from HT\textsuperscript{14}. In short, among the early diastolic time intervals, HT was abnormal mainly in the II\textsubscript{A}-MVO time which corresponded to isovolumic relaxation time, while HCM had abnormalities not only in the II\textsubscript{A}-MVO time but also in the MVO-O time which was the phase that the left ventricular filling took place. On the

Key Words:
Myocardial hypertrophy
Early diastolic time intervals
Biventriculography
Hypertrophic cardiomyopathy
Essential hypertension

(Received June 20, 1984; accepted October 4, 1984)
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other hand, it has already been acknowledged that hearts in patients with HCM have histologically characteristic features\textsuperscript{15–19} which differ in quality and quantity from those in patients with HT and in normal subjects (N)\textsuperscript{20} But we have found no reports which clarified hemodynamically whether the difference between HCM and HT was due to the qualitative or quantitative difference of myocardial hypertrophy.

The present study was undertaken to clarify whether the differences in diastolic time intervals between HCM and HT were due to the magnitude of the left ventricular hypertrophy.

METHODS

Subjects

Seventy-nine subjects were studied and divided into the following 3 groups.

Normal subjects (N): This group comprised 22 volunteers or out-patients who had no abnormalities in physical examination, electrocardiogram, chest X-ray and echocardiogram. Subjects whose echocardiograms could not be clearly recorded were excluded from this group. The mean age was 44 ± 11 years and 15 (68\%) were men.

Essential hypertensives (HT): We selected 22 patients whose echocardiograms could be clearly recorded and did not show asymmetric septal hypertrophy\textsuperscript{21} from 48 HT who were admitted to the hospital between January 1981 and March 1983. Sixteen patients corresponded to the stage II and 6 the stage III of WHO classification\textsuperscript{22} Patients who had coronary artery disease or valvular heart disease were excluded. The mean age in this group was 48 ± 7 years and 17 (77\%) were men.

Hypertrophic cardiomyopathy (HCM): Thirty-five patients with HCM whose echocardiograms could be clearly recorded were selected from 45 patients with HCM who underwent cardiac catheterization between September 1981 and March 1983. The diagnosis of HCM was made by cardiac catheterization and echocardiography. Ten patients were of the obstructive type and 25 were non-obstructive type. The diagnosis of obstructive type was made, when a patient had a pressure gradient above 20 mmHg in left ventricular outflow tract without provocation. Asymmetric septal hypertrophy was seen in 9 of 10 patients with obstructive type and 18 of 25 with non-obstructive type. Patients who had systemic hypertension, valvular heart disease and significant stenoses of coronary arteries were excluded from this group. The mean age in obstructive type was 47 ± 13 years and 7 (70\%) were men, and in non-obstructive type was 49 ± 9 years and 21 (84\%) were men.

Examinations were made under no-treatment conditions for two weeks prior to study. But examinations in hypertensive patients of stage III were carried out under medical treatment.

Early Diastolic Time Intervals

As previously reported\textsuperscript{14} the echocardiogram, apicocardio gram and phonocardiogram were recorded simultaneously. After measurement of early diastolic time intervals, one new index was calculated as follows: All measurements were averaged over five cardiac cycles.

\textit{Japanese Circulation Journal} Vol. 49, March 1985
1. The $T_{\text{IIA}}$-O time. The interval from the onset of the aortic component of the second heart sound to the O point of apexcardiogram. The $T_{\text{IIA}}$-O time was subdivided into the $T_{\text{IIA}}$-MVO time and the MVO-O time.

2. The $T_{\text{IIA}}$-MVO time. The interval from the onset of the aortic component of the second heart sound to the point of the mitral valve opening (MVO). This phase corresponds to the isovolumic relaxation time.

3. The MVO-O time. The interval from the MVO to the O point of apexcardiogram.

4. The MVO-O/$T_{\text{IIA}}$-MVO ratio.

**Cardiac Catheterization and Biventriculography**

Routine catheterization and selective coronary cine angiography were performed using the Judkins technique. Following the left ventriculography in the right anterior oblique position, the biventriculography was performed in order to measure the mean wall thickness. A 8F Cordis pigtail catheter and a 7F NIH catheter were advanced to the left and right ventricles respectively and the patients were placed in relatively shallow left anterior oblique with slight craniocaudal angulation. The two catheters were then connected to a brass block connector with Luer-Lok fittings attaching to a single pressure injector, and 40 ml of contrast medium were injected into both ventricles. The recordings were made on 35 mm cine film exposed at 60 frames per second.

**Mean Wall thickness of the Left Ventricle (MWT)**

The MWT of the patients with HCM: We know that there is a certain limitation in assessing the wall thickness in many of patients with HCM because of their disproportionate hypertrophy such as asymmetric septal hypertrophy. In this study, to avoid this inherent error as much as possible, we selected the mean wall thickness (MWT) using biventriculography as the
<table>
<thead>
<tr>
<th></th>
<th>Age</th>
<th>Heart rate</th>
<th>$II_A-O$</th>
<th>$II_A-MVO$</th>
<th>$MVO-O$</th>
<th>Mean wall thickness</th>
<th>$MVO-O/II_A-MVO$ ratio</th>
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<tr>
<td>Normal subject</td>
<td>44</td>
<td>±11</td>
<td>±9</td>
<td>±11</td>
<td>±9</td>
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<td>(n = 22, I)</td>
<td></td>
<td>±10</td>
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<td>±11</td>
<td>±14</td>
<td>±3.0</td>
<td>±0.16</td>
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<tr>
<td>Hypertension</td>
<td>48</td>
<td>±7</td>
<td>±9</td>
<td>±13</td>
<td>±14</td>
<td>13.1</td>
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<tr>
<td>(n = 22, II)</td>
<td></td>
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<td>±9</td>
<td>±13</td>
<td>±14</td>
<td>±3.0</td>
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<tr>
<td>HCM non-obstructive</td>
<td>49</td>
<td>±9</td>
<td>±8</td>
<td>±18</td>
<td>±68</td>
<td>14.8</td>
<td>1.79</td>
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<td>±18</td>
<td>±68</td>
<td>±3.7</td>
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<td>Obstructive</td>
<td>47</td>
<td>±13</td>
<td>±12</td>
<td>±13</td>
<td>±24</td>
<td>9.7</td>
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<td>(n = 10, IV)</td>
<td></td>
<td>±13</td>
<td>±12</td>
<td>±13</td>
<td>±24</td>
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<td>±0.24</td>
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<tr>
<td>II</td>
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<td>NS</td>
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<tr>
<td>IV</td>
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Values are mean ± SD.
Abbreviations: HCM = hypertrophic cardiomyopathy; $II_A$ = aortic component of the second heart sound; $O$ = O point of apexcardiogram; $MVO$ = point of mitral valve opening.
Fig. 3. Mean wall thickness in normal subjects, in patients with essential hypertensives (HT) and patients with hypertrophic cardiomyopathy (HCM).

* = p < 0.05, *** = p < 0.001

Fig. 4. Relationship between the mean wall thickness (MWT), the II₄-MVO (closed mark) and the MVO-O time (open mark) in patients with essential hypertension (square) and in normal subjects (circle). In accordance with the increment of the wall thickness, the duration of both phases increased and the prolongation of the II₄-MVO time was greater than that of the MVO-O time. 'a' and 'b' represent the regression curves between the MWT and the MVO-O time, and between the MWT and the II₄-MVO time, respectively.

Biventriculography was performed in 17 patients with non-obstructive cardiomyopathy and 6 with obstructive cardiomyopathy, and the measurement of the MWT was made in 15 patients with non-obstructive type and 4 patients with obstructive type whose biventriculograms were clearly obtained. The MWT in this group was calculated from the biventriculography using a modification of Redwood’s method as:

\[ \text{MWT} = \frac{A}{L} \]

where A = area of the left ventricular wall shown by biventriculogram, L = length linked the middle point between the inner line and the outer line of the left ventricular wall (Fig. 1). The measurement of the wall thickness was made from end-diastolic frame of the cine angiograms and corrected for error due to magnification. The area of the left ventricular wall was determined by planimetry.

The MWT of N and HT: The MWT in N and HT was measured using the echocardiographic method, because hypertensive patients who have asymmetric septal hypertrophy were not included in this study.

The MWT of these groups was calculated using the M-mode echocardiography as:

\[ \text{MWT} = \text{IVS} + \text{PW} / 2 \]

where IVS = end-diastolic thickness of the interventricular septum, and PW = end-diastolic thickness of the posterior left ventricular wall. Echocardiographic recordings for
Fig. 5. Relationship between the mean wall thickness (MWT), and the IIₐ-MVO time (closed mark) and the MVO-O time (open mark) in patients with hypertrophic obstructive cardiomyopathy (triangle) and hypertrophic non-obstructive cardiomyopathy (rhombus). To the increment of the MWT, quite different from hypertensives, the prolongation of the MVO-O time was almost always greater than that of the IIₐ-MVO time in hypertrophic cardiomyopathy.

measuring the wall thickness were obtained with the ultrasound beam passing through the left ventricle just caudal to the tips of the mitral leaflets at the R wave of a simultaneously recorded electrocardiogram. The wall thickness measurements were taken from leading edge to leading edge according to the criteria of the American Society of Echocardiography.

Comparison of angiographic and echocardiographic measurements: In order to determine whether these two different methods are similar, we compared the left ventricular posterior wall thickness measured by angiographic method with that by M-mode echocardiography in 66 subjects. Figure 2 showed the relationship between the wall thickness of the posterior wall measured by these two methods. A high correlation between these two different methods indicates that they are sufficiently comparable to each other as already reported by other investigators. In addition, Yoshioka et al. reported that interventricular septal thickness at end-diastole obtained by M-mode echocardiographic method was also closely correlated with that by angiographic method in patients without ventricular hypertrophy and in hypertensive patients. The wall thickness measured by echocardiographic method showed a slightly smaller value compared with that measured by the angiographic methods in patients with HCM. This was most likely due to the fact that the method using the M-mode echocardiogram usually measured the position at the thinnest portion of the left ventricular posterior wall in many patients with HCM.

Statistical analysis: All data are expressed as mean ± SD. Comparison of the data between groups was made using the Mann-Whitney U test because the data were not normally distributed. Statistical significance was defined as p < 0.05.

RESULTS

The results are summarized in Table I.

Early diastolic time intervals: The duration of each early diastolic time interval in N was significantly shorter than that in HT and both types of HCM. The duration of the IIₐ-O time was by far the longest in non-obstructive type of HCM, but showed no significant difference between HT and obstructive type. As for the IIₐ-MVO and MVO-O time, it was characteristic of most of the patients with HCM that the prolongation of the MVO-O time was more prominent than that of the IIₐ-MVO time. On the other hand, it was characteristic of HT that the prolongation of the
II$_A$-MVO time was more prominent than that of the MVO-O time.

Mean wall thickness: Mean wall thickness (MWT) in each patient is shown in Fig. 3. As a matter of course, the MWT in HT and HCM was significantly greater than that of N. The MWT in non-obstructive type of HCM showed no significant difference compared with that in HT. On the other hand, the MWT in obstructive type of HCM was significantly less than that of HT.

Relationship between the early diastolic time intervals and the MWT: Fig. 4 showed the relationship between the MWT and the II$_A$-MVO time (closed marks) and MVO-O time (open marks) in patients with HT (square) and N (circle). Both the II$_A$-MVO and MVO-O time were prolonged as the MWT increased, and the magnitude of the II$_A$-MVO time was almost always greater than that of the MVO-O time. Figure 5 showed the same relationship in 19 patients with HCM. Triangle and rhombus represented the obstructive type and non-obstructive type respectively. As seen in HT and N, both phases were also prolonged in HCM as the MWT became greater. However, quite different from HT and N, the magnitude of the II$_A$-MVO time was almost always less than that of the MVO-O time.

MVO-O/II$_A$-MVO ratio: The MVO-O/II$_A$-MVO ratio in each patient is shown in Fig. 6. This ratio in HT was significantly less than that of N. However, quite different from HT the ratio in HCM was significantly greater than that of N. This new parameter clearly separated the non-obstructive type of HCM from HT.

**DISCUSSION**

HCM is one of the representative diseases characterized morphologically by myocardial hypertrophy. However, studies concerning the relationship between the severity of the myocardial hypertrophy and the cardiac functions have been rarely reported probably because the myocardial hypertrophy of HCM was difficult to quantitate as mentioned in the method's section. In this study, we selected the biventriculogram to quantitate the magnitude of the myocardial hypertrophy of HCM as did Redwood et al.$^{23}$ At present, we believe this method is the best considering the characteristic mode of myocardial hypertrophy of HCM as disproportionate ventricular septal hypertrophy compared with the posterobasal left ventricular free wall.$^{35,21,30}$ However, this method might include an error in overestimating the wall thickness. But this possibility does not negate the differences in the early diastolic time intervals between HCM and HT, because there was no significant difference in the MWT between two diseases in spite of a little overestimation of the wall thickness in HCM.

As to the effect of heart rate on the early diastolic time intervals, Alves reported$^{31}$ that the II$_A$-MVO time and the MVO-O time remained almost constant over different RR intervals. In our study, the II$_A$-O time in both HCM and HT was greater than that in N. Concerning the hemodynamic significance of the O point of apexcardiogram, some reported that the O point corresponded approximately to the nadir of the left ventricular pressure.$^{32-34}$ Lorell et al. reported$^{35}$ that in HCM the recording of the left ventricular pressure showed a continuous decrease of pressure into the middle diastole and this finding suggested the presence of a prolonged left ventricular relaxation phase. Therefore, the prolongation of the II$_A$-O time means that it takes more time to reach its nadir in HCM and that seems to be one of the indicators reflecting an impaired diastolic relaxation.

The II$_A$-O time was subdivided into the II$_A$-MVO time and the MVO-O time. The former corresponds to isovolumic relaxation time and the latter represents the phase that the left ventricular filling takes place.$^{34}$

The II$_A$-MVO time in HCM and HT was significantly greater than that in N, but there was no difference between the non-obstructive type of HCM and HT. There have been some reports concerning the prolongation of the isovolumic relaxation time in patients with various heart disease including HCM and HT.$^{7-10,36}$ Isovolumic relaxation time depends upon three factors, the aortic pressure, the rate of pressure fall of the left ventricle and the height of left atrial pressure.$^8$ An increased wall thickness, which is a common morphological characteristics of HCM and HT, may affect the rate of pressure fall and this may be the main factor responsible for the prolongation of the isovolumic relaxation time. This explanation was also suggested by the fact that the II$_A$-MVO time in obstructive type, whose MWT was thinner than those in non-obstructive type and HT, was significantly less than those in these two groups. Anyhow, this phase was not essential in differentiating HCM from HT.

As for the MVO-O time, Alvaes reported that in this phase, the rate of relaxation of the left ventricle was greater than the rate of blood filling, and the O point of apexcardiogram was the turning point where the rate of filling and the rate of relaxation were in equilibrium, and he named this phase active suction period. Different from the II A-MVO time, the duration of the MVO-O time does not depend upon the aortic pressure, but seems to strongly depend upon the rate of pressure fall of the left ventricle. Therefore, the prolongation of the MVO-O time may mean the impairment of the rate of left ventricular relaxation. This phase in HT was slightly greater than that in N. On the other hand, that in HCM was not only greater by far than that in N but also greater than that in HT. Furthermore, the duration of the MVO-O time in even obstructive type whose II A-MVO time was shorter than that in HT was greater than that in HT. These findings show that the prolongation of the MVO-O time is an essential abnormality in HCM but not in HT. The duration of the MVO-O time may mainly correlate with the extent of the distribution of the myocardial cellular abnormalities. Because, the prominent prolongation of this phase was seen only in HCM groups, and both the prolongation of this phase and the degree of the MWT in obstructive type were less than those in non-obstructive type. These observations are compatible with the following histological findings: Firstly, myocardial cellular abnormalities exist in patients with HCM but were rarely found in patients with HT. Secondly, the distribution of the cellular abnormalities was limited to the ventricular septum in the obstructive type, but it was not only in the ventricular septum but also in the ventricular free walls in non-obstructive type. This phase appears to be indispensable to differentiate HCM from HT.

We examined the relationship between the degree of the wall thickness, and the duration of the II A-MVO and MVO-O time. As shown in Fig. 4 and Fig. 5, the duration of these two phases in patients with HCM and HT prolonged, as the MWT increased. However, the relationship of the prolongation in diastolic intervals to the increase of the MWT was quite different in these two diseases. In HT, the prolongation in the II A-MVO time was greater than that in the MVO-O time. But in HCM, inversely, the prolongation of the latter was greater than that of the former. Considering that the MWT showed no difference between HCM and HT, this finding suggests a qualitative difference between HCM and HT. The II A-MVO time in both groups showed the limit of the prolongation or a tendency to shorten when the wall thickness was over about 15 mm. This was most likely due to the elevation of the left atrial pressure. On the other hand, the MVO-O time in HCM did not show this tendency.

As already mentioned, HT had abnormality mainly in the II A-MVO time, but HCM had not only in the II A-MVO time but also in the MVO-O time. Taking this into considerations, we devised the MVO-O/II A-MVO ratio as a new indicator for the differentiation of HCM and HT. The mean ratio in both types of HCM were significantly greater than that in HT and especially as shown in Fig. 6, this ratio could provide a clear separation of patients with non-obstructive type of HCM from HT. In addition, ratios in HCM and HT showed quite a different attitude in comparison with that in N. The ratio in HT was significantly less than that in N, but on the contrary, that in HCM was greater than that in N. If the difference in this ratio between N and HT is due to the quantitative difference of myocardial hypertrophy between two groups, the difference between HCM and HT is not a matter of degree in myocardial hypertrophy, but a matter of myocardial characteristics in two diseases.

REFERENCES


7. NIMURA Y, MATSUO H, MOCHIZUKI S, AOY K, WADA O, ABE H: Analysis of a cardiac cycle of the left side of the heart in cases of left ventricular overloading or change with the ultrasonic Doppler method. Am Heart J 75: 49, 1968

8. LEWIS BS, LEWIS N, SAPOZNIKOV D, GOTS-MAN MS: Isovolumic relaxation time in man. Am

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9. CHEN W, GIBSON D: Relation of isovolumic relaxation to left ventricular wall movement in man. Br Heart J 42; 51, 1979


15. TEARE D: Asymmetrical hypertrophy of the heart in young adults. Br Heart J 20: 1, 1958


27. SJOGEN AL, HYTONEN I, FRICK MH: Ultrasonic measurements of left ventricular wall thickness. Chest 57: 37, 1970


34. VENCO A, GIBSON DG, BROWN DJ: Relation between apex cardiogram and changes in left ventricular pressure and dimension. Br Heart J 39: 117, 1977


Japanese Circulation Journal Vol. 49, March 1985