Left Ventricular Regional Relaxation and Its Nonuniformity in Hypertrophic Nonobstructive Cardiomyopathy

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Background. Regional nonuniformity has been suggested to be closely related to left ventricular (LV) relaxation in diseased heart. The purpose of the present study was to assess LV global and regional relaxation in patients with nonobstructive hypertrophic cardiomyopathy (HCM).

Methods and Results. Left ventriculography was conducted simultaneously with pressure micromanometry in 10 normal control subjects and 11 patients with nonobstructive HCM. LV silhouettes in the right anterior oblique projection were divided into eight regions, and regional wall stress during isovolumic relaxation was computed for six regions from the midventricle to the apex. In HCM patients, isovolumic relaxation time (IRT) and the time constant of LV pressure decrease (Tp) were greater than in control subjects (IRT, 84±13 versus 66±6 msec; Tp, 51±8 versus 36±5 msec, respectively; p<0.01). In HCM patients, the (−)dP/dt upstroke pattern was convex-downward, and dP/dt(20/60), the ratio of dP/dt values 20 and 60 msec after peak (−)dP/dt, was less than in control subjects (1.46±0.16 versus 2.15±0.14, p<0.01). These findings suggest that there is impaired LV relaxation in HCM patients. End-systolic regional wall stress was lower, and the time constant of regional stress decrease (Tst) was prolonged for each region in HCM patients compared with control subjects. In the HCM group, Tst tended to be more prolonged in regions with increased wall thickness than in regions with normal wall thickness (60±15 versus 50±11 msec, p<0.01). The coefficient of variation for Tst values in six areas of the left ventricle was calculated in each subject and was greater in HCM patients than in control subjects (13±7% versus 7±3%, p<0.05), indicating regional nonuniformity in Tst during isovolumic relaxation in HCM patients.

Conclusions. Significant correlations existed between the coefficients of variation for Tst and Tp (r=0.80, p<0.01), IRT (r=0.79, p<0.01), and dP/dt(20/60) (r=−0.67, p<0.05) in the HCM group. Thus, regional nonuniformity is closely related to the impairment of LV relaxation in HCM. (Circulation 1991;84:1496–1504)

Left ventricular relaxation has been considered to be influenced by regional nonuniformity as well as by myocardial inactivation and loading conditions. It is well known that in coronary artery disease regional nonuniformity of left ventricular wall motion is associated with abnormal ventricular relaxation. Because both asynergy and asynchrony of ventricular wall motion contribute to regional nonuniformity, assessment of ventricular regional function appears to be important in investigating left ventricular relaxation. In patients with hypertrophic cardiomyopathy (HCM), impaired left ventricular relaxation is often observed, and regional nonuniformity has been speculated to play an important role in the relaxation abnormality. However, there are relatively few reports concerning the relation between left ventricular relaxation and regional wall dynamics in HCM. In addition, little attention has been paid to left ventricular regional wall stress in HCM.

In the present study, we conducted left ventriculography with simultaneous pressure micromanometry in normal control subjects and in patients with nonobstructive HCM to assess the nonuniformity of regional left ventricular relaxation and its relation to global left ventricular relaxation.

Methods

Subject Population

The study population comprised 10 normal control subjects and 11 patients with nonobstructive HCM.
All subjects underwent diagnostic cardiac catheterization. The 10 control subjects were catheterized for chest pain or exercise electrocardiographic abnormality and had normal cardiac hemodynamics, left ventriculogram, and coronary arteriogram. Fifteen consecutive patients with nonobstructive HCM were diagnosed by echocardiographic demonstration of hypertrophied nondilated left ventricle without evidence of left ventricular outflow tract obstruction in the absence of another cardiac or systemic disease that could produce left ventricular hypertrophy. The diagnosis was confirmed by the cardiac catheterization and angiography. Eleven of the 15 patients with nonobstructive HCM were selected for this study on the basis of the following criteria: a satisfactory left ventriculogram showing good definition of wall thickness of the entire ventricle; absence of left bundle branch block, which could produce regional asynchrony; and absence of mitral regurgitation, which could complicate analysis of isovolumic relaxation. Four patients were excluded: two patients because of unsatisfactory left ventriculograms, one because of left bundle branch block, and one because of mitral regurgitation. During cardiac catheterization, no significant intraventricular pressure gradient was detected at rest or with provocative maneuvers (Valsalva or postextrasystolic potentiation) for any of the 11 patients with HCM. All subjects were in normal sinus rhythm. Written informed consent was obtained from each subject, and no complications occurred as a result of the study.

Cardiac Catheterization and Left Ventriculography

Diagnostic cardiac catheterization was performed through the percutaneous femoral approach in each subject. All medications were withheld at least 24 hours before catheterization, except for oral premedication with 5 mg diazepam. Right heart catheterization and cardiac output measurement were conducted by the use of a 7F Swan-Ganz thermodilution catheter. Left heart catheterization was performed by the use of an 8F high-fidelity catheter-tip transducer with side holes (Millar Instruments, Houston). The micromanometer system was calibrated before insertion; during measurement, its output was adjusted to the fluid-filled pressure with zero reference at the midst level of the supine position. After aortic and left ventricular pressures were recorded, left ventriculography was performed at 60 frames/sec in the 30° right anterior oblique (RAO) projection; 35–40 ml of nonionic contrast solution was injected at a rate of 12–15 ml/sec. Left ventricular pressure was measured in the middle portion of the ventricle and recorded simultaneously with its first derivative (dP/dt) during left ventriculography on an oscillographic recorder (VR-12, Electronics for Medicine, Pleasantville, N.Y.) and a magnetic-tape data recorder with electrocardiogram and cine markers. Magnification and peripheral distortions of ventriculographic images were corrected by the use of a calibration grid positioned at the level of the left ventricle. In patients with HCM, biventriculography was also performed in the left anterior oblique projection with cranial angulation to visualize the interventricular septum and left ventricular posterior wall by using a catheter-tip transducer with side holes in the left ventricle and an 8F balloon angiographic catheter in the right ventricle. Coronary angiography was then conducted by the Judkins technique, and none of the control subjects or HCM patients had significant coronary artery stenosis of more than 50% reduction in luminal diameter. In patients with HCM, right and left ventricular endomyocardial biopsies were performed after coronary angiography.

Hemodynamic Measurement

End diastole was determined as the beginning of the increase of left ventricular pressure where dP/dt became zero, and end systole was determined as the time of 20 msec preceding left ventricular peak (−)dP/dt. As indexes of left ventricular relaxation, isovolumic relaxation time (IRT), peak (−)dP/dt, time constant for isovolumic pressure decrease (Tp), and dP/dt(20/60) were determined. IRT was determined as the interval between end systole (20 msec before peak (−)dP/dt) and mitral valve opening. Mitral valve opening was confirmed by the appearance of a nonopacified blood jet through the mitral valve on the left ventriculogram. Time constant Tp was calculated during isovolumic relaxation as the negative reciprocal of the slope of the regression line between the elapsed time from end systole and the natural logarithm of left ventricular pressure. The mean value of the correlation coefficient for this regression was 0.993 in control subjects and 0.990 in HCM patients. dP/dt(20/60) was the ratio of (−)dP/dt values at 20 msec to values at 60 msec after peak (−)dP/dt. This index decreases as the (−)dP/dt upstroke pattern assumes a convex-downward contour, which is considered to indicate impairment of early-to-middle left ventricular relaxation.

Regional Wall Stress and Time Constant

Left ventricular silhouettes consisting of endocardial and epicardial contours in the RAO projection were digitized frame by frame during the isovolumic relaxation period. Ectopic and postectopic beats were excluded from analysis. None of the patients showed prominent protrusion of papillary muscle shadows that may obscure the endocardial contour and thus results in overestimation of wall motion and thickness, and none of them had marked right ventricular hypertrophy or pericardial effusion that might obscure the epicardial contour. Intraobserver and interobserver differences for ventriculographic data acquisition were both less than 5% with respect to the digitized areas, indicating good reproducibility of measurements.

The details of the method with which to estimate regional wall stress were previously described. The left ventricular silhouette was divided into eight regions by one long axis joining the midpoint of the aortic valve plane to the left ventricular apex, which was assumed to
TABLE 1. Hemodynamic and Volumetric Parameters

<table>
<thead>
<tr>
<th>Group</th>
<th>Age (years)</th>
<th>HR (beats/min)</th>
<th>PSP (mm Hg)</th>
<th>EDP (mm Hg)</th>
<th>CI (l/min)</th>
<th>EDVI (ml)</th>
<th>ESVI (ml)</th>
<th>EF (%)</th>
<th>IRT (msec)</th>
<th>Peak (−)dP/dt (mm Hg/sec)</th>
<th>Tp (msec)</th>
<th>dP/dt(20/60)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n=10)</td>
<td>51±8</td>
<td>71±10</td>
<td>127±15</td>
<td>7±2</td>
<td>3.3±0.6</td>
<td>73±12</td>
<td>26±5</td>
<td>63±4</td>
<td>66±6</td>
<td>1,755±202</td>
<td>36±5</td>
<td>2.15±0.14</td>
</tr>
<tr>
<td>HCM (n=11)</td>
<td>54±14</td>
<td>68±18</td>
<td>123±15</td>
<td>13±6*</td>
<td>3.0±0.4</td>
<td>66±10</td>
<td>23±6</td>
<td>66±6</td>
<td>84±13†</td>
<td>1,114±165†</td>
<td>51±8†</td>
<td>1.46±0.16†</td>
</tr>
</tbody>
</table>

HR, heart rate; PSP, left ventricular peak systolic pressure; EDP, left ventricular end-diastolic pressure; CI, cardiac index; EDVI, left ventricular end-diastolic volume index; ESVI, left ventricular end-systolic volume index; EF, ejection fraction; IRT, isovolumic relaxation time; Tp, time constant for isovolumic left ventricular pressure decrease; dP/dt(20/60), ratio of dP/dt at 20 and 60 msec after peak (−)dP/dt; HCM, hypertrophic cardiomyopathy.

*p<0.05 vs. control subject.
†p<0.01 vs. control subject.

be an axis of symmetry of the left ventricle, and by three perpendicular short axes at equal intervals. These eight regions were termed regions 1–8 in a clockwise direction from the anterobasal to the inferoposterior portion. Because region 1 is adjacent to the aortic valve and region 8 includes the mitral valve ring, these two most basal regions were excluded from analysis. In the other six regions, regional wall stress was estimated by the modified Janz’s formula5,19,20 for each frame of the left ventriculogram. Regional wall stress was calculated by multiplying left ventricular pressure by the ratio of cavity area to wall area.

Regional fractional shortening was evaluated by the area method, and percent area change during systole was calculated as (end-diastolic area minus end-systolic area) multiplied by 100 and divided by end-diastolic area.20 In addition, to evaluate timing of regional contraction, the time interval from end diastole to minimum regional area (t-area\textsubscript{min}) was obtained for each region of the left ventricle. The t-area\textsubscript{min} value was also expressed as a percentage of the systolic interval (time interval from end diastole to end systole). Regional mean wall thickness was derived as the mean distance between epicardial and endocardial contours of each region. Ventriculographic measurements of wall thickness showed a good consistency with echocardiographic measurements in the present study (mean error, 5±4%).

The time constant Tst of regional wall stress decrease during isovolumic relaxation was calculated by the same method as Tp for regions 2–7. Although left ventricular wall stress may deviate from a monoexponential course with impairment of left ventricular relaxation, the mean correlation coefficient for this relation was 0.99 (range, 0.95−0.99) in the control group and 0.98 (range, 0.93−0.99) in the HCM group, which are close to the values reported by Pouleur et al5 and considered to be within acceptable limits for the use of the monoexponential fit. To assess regional differences in Tst, the coefficient of variation (%) for the Tst values of six regions of the left ventricle was calculated in each subject.

Statistical Analysis

Values are expressed as mean±SD. Analysis of variance with multiple comparison and linear regression analysis were used for statistical compari-

son. A probability value of less than 0.05 was considered significant.

Results

Hemodynamic and Volumetric Parameters

Hemodynamic and volumetric parameters are listed in Table 1. Compared with control subjects, left ventricular end-diastolic pressure was elevated in HCM patients. However, there was no significant difference in cardiac index. Left ventricular ejection fraction tended to be greater in the HCM group (range, 60–81%) than in the control group (range, 56–69%), but the difference was not statistically significant. Left ventricular IRT and Tp were prolonged (IRT, 84±13 versus 66±6 msec; Tp, 51±8 versus 36±5 msec; p<0.01), and peak (−)dP/dt and dP/dt(20/60) were reduced (peak (−)dP/dt, 1,114±165 versus 1,755±202 mm Hg/sec; dP/dt(20/60), 1.46±0.16 versus 2.15±0.14, respectively; p<0.01) in HCM patients.

Representative cases of left ventricular isovolumic pressure changes are shown in the left panels of Figure 1 together with insets of the (−)dP/dt upstroke patterns. In the control subject, the indexes of left ventricular relaxation are normal and the (−)dP/dt upstroke pattern is convex-upward (Figure 1, top panels). However, the patient with HCM showed prolonged Tp and IRT accompanied by the convex-downward (−)dP/dt upstroke pattern, which is quantified by the decreased dP/dt(20/60) value (Figure 1, bottom panels).

Of the 11 patients with HCM, five patients were found to have asymmetric septal hypertrophy (ASH) by biventriculography (mean wall thickness: septum, 19±2 mm; posterior wall, 12±2 mm), but the remaining six patients did not have ASH (four patients had increased wall thickness of both septum and posterior wall, and the other two patients had thickened posterior wall but normal septal wall thickness). These findings were consistent with those of echocardiography performed within 1 week of catheterization. No significant differences were observed between the patients with and without ASH with regard to the parameters for global left ventricular relaxation in the present study.

Regional Left Ventricular Relaxation

Regional left ventricular relaxation assessed by the isovolumic wall stress changes in a control subject
FIGURE 1. Plots of decrease of left ventricular (LV) pressure and regional wall stress during isovolumic relaxation period in a control subject (top panels) and a patient with hypertrophic cardiomyopathy (HCM; bottom panels). LV pressure and regional wall stress are plotted in logarithmic scale against elapsed time after end systole, and timing of mitral valve opening (MVO) is indicated by an arrowhead. (-)dP/dt is also depicted in insets. Left panels: In patient with HCM, time constants for LV pressure decrease (Tp) and isovolumic relaxation time (IRT) were prolonged compared with those of control subject. (-)dP/dt upstroke pattern is convex-upward in control subject and convex-downward with decreased ratio of dP/dt values 20 and 60 msec after peak (-)dP/dt [dP/dt(20/60)] in HCM patient. Right panels: Regional wall stress during isovolumic relaxation is shown for region 3 (anterior wall) and region 7 (inferior wall). In HCM patient, time constants for wall stress (Tst) in each region are greater than those of control subject. Note difference in Tst values between regions 3 and 7 in HCM patient (56 vs. 74 msec).

and a patient with HCM are shown in the right panels of Figure 1. The time constant for isovolumic regional wall stress decrease (Tst) was greater in the HCM patient than in the control subject for the corresponding regions, indicating impairment of regional relaxation in the HCM patient. It is interesting to note that in Figure 1, bottom panels, a considerable difference was observed in Tst values between
region 3 (56 msec) and region 7 (74 msec) in the HCM patient.

End-systolic regional wall stress was significantly lower and Tst was more prolonged for each region in the HCM group than in the control group (Table 2). Regional mean wall thickness was also increased in HCM patients compared with the control subjects. However, there were no significant differences in percent area changes during systole in any region between the control subjects and HCM patients.

Of the 66 regions examined in the 11 patients with HCM, regional mean wall thickness was within the normal range (less than or equal to mean±2 SD of the corresponding region of the control subjects) in 21 regions and increased in the remaining 45 regions. Tst was significantly increased in the regions with increased wall thickness (hypertrophied regions, 60±15 msec) compared with the regions with normal wall thickness (nonhypertrophied regions, 50±11 msec; p<0.01), although there were considerable variations in Tst in each group. The time to minimum regional area (t-area amax) was 0.32±0.04 seconds (94±11% of the systolic interval) in the nonhypertrophied regions, whereas it was 0.27±0.03 seconds (76±9% of the systolic interval) in the hypertrophied regions, which was significantly shorter (p<0.01) than that in the nonhypertrophied regions. During the isovolumic relaxation period, the regional area, which was normalized by end-diastolic area (EDA), tended to increase in the hypertrophied regions (6±5% of EDA) compared with that in the nonhypertrophied regions (2±4% of EDA, p<0.05). These findings indicate that regional contraction finished earlier and that the outward movement occurring during isovolumic relaxation was more pronounced in the hypertrophied regions than in the nonhypertrophied regions. During the subsequent rapid filling phase, however, the increase in regional area was significantly smaller in the hypertrophied regions (26±15% of EDA) than in the nonhypertrophied regions (37±14% of EDA, p<0.01). The mean rate of change in regional area during the rapid filling phase was also smaller in the hypertrophied regions (1.0±0.5 EDA/sec) than in the nonhypertrophied regions (1.5±0.5 EDA/sec, p<0.05).

The coefficient of variation for Tst values in six regions of the left ventricle was greater in HCM patients than in the control subjects (13±7% versus 7±3%, p<0.05). There were significant correlations between this coefficient of variation and Tp (r=0.80, p<0.01), IRT (r=0.79, p<0.01), and dP/dt(20/60) (r=−0.67, p<0.05) in the HCM group (Figure 2).

Discussion

Impaired left ventricular relaxation despite normal systolic function is a characteristic feature of HCM.7-15 This relaxation abnormality of the left ventricle was also demonstrated in HCM patients of the present study, in whom IRT and Tp were prolonged and peak (−)dP/dt was significantly lower (Table 1 and Figure 1). The IRT values in our results were shorter than those reported in the previous Doppler study.25 This discrepancy may be derived from our definition of end systole and mitral valve opening. We defined the end systole as 20 msec before peak (−)dP/dt because this point is close to the end shortening of the myocardium.3 However, the time difference between peak (−)dP/dt and aortic valve closure varies from 8 to 34 msec.24 In addition, angiographic determination of mitral valve opening has a maximum error of ±16.7 msec. These factors will induce the discrepancy of IRT values between previous studies and ours.

dP/dt(20/60) is a simplified index for the convexity of the (−)dP/dt upstroke pattern.22,26 When the (−)dP/dt upstroke pattern becomes convex downward, dP/dt(20/60) decreases, and this decrease reflects abnormality of the early-to-mid phase of left ventricular relaxation.22 Our result showed a significant decrease of dP/dt(20/60) in HCM patients compared with the control subjects (Table 1 and Figure 1). Theoretically, the convex-downward (−)dP/dt

Table 2. Parameters for Regional Ventricular Function

<table>
<thead>
<tr>
<th>Region</th>
<th>Control (n=10)</th>
<th>HCM (n=11)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>ES stress (kdyne/cm²)</td>
<td>Tst (msec)</td>
</tr>
<tr>
<td>2</td>
<td>147±49</td>
<td>38±5</td>
</tr>
<tr>
<td>3</td>
<td>172±50</td>
<td>36±10</td>
</tr>
<tr>
<td>4</td>
<td>116±50</td>
<td>40±10</td>
</tr>
<tr>
<td>5</td>
<td>90±48</td>
<td>40±10</td>
</tr>
<tr>
<td>6</td>
<td>188±64</td>
<td>37±5</td>
</tr>
<tr>
<td>7</td>
<td>194±45</td>
<td>35±5</td>
</tr>
</tbody>
</table>

Coefficient of variation for Tst (%)
- HCM, hypertrophic cardiomyopathy; ES stress, end-systolic regional wall stress; Tst, time constant for isovolumic regional wall stress decrease; Area change, percent change in regional area from end diastole to end systole; WTh, regional mean wall thickness at end diastole.
- p<0.05 vs. control subject.
- tp<0.01 vs. control subject.
pattern indicates that left ventricular pressure is deviated from a monoexponential curve. Under such conditions, monoexponential fitting and the calculation of Tp would be a less precise assessment of left ventricular relaxation, and some investigators have tried to apply biexponential fittings to the left ventricular pressure decrease. However, for our results, the correlation coefficient for monoexponential fitting was reasonably high, so the calculated time constant is still considered to be useful for evaluation of left ventricular relaxation.

Assessment of Regional Relaxation and Its Nonuniformity

Pouleur et al reported that in patients with coronary artery disease, Tst was more prolonged in the
ischemic but still-contracting regions than in the normally perfused regions of the left ventricle. This suggests that regional variations of Tst become greater when the myocardium is regionally involved. The wide regional variation of Tst may lead to impairment of global left ventricular relaxation. To test this hypothesis, we measured Tst by calculating regional wall stress using the modified Janz method.5,19,20 The validity and limitation of this method were discussed in detail in previous studies.19,20 Like with Tp, mean Tst value was more prolonged in the corresponding regions of the left ventricle in HCM patients than in the control subjects (Table 2 and Figure 1). It is thus apparent that regional as well as global relaxation is impaired in HCM patients. In some regions, Tst was greater than Tp. An example is demonstrated by region 7 of the HCM patient in Figure 1, bottom panels, which indicates that regional relaxation abnormality may not be represented by measuring only the time course of global left ventricular pressure decrease.

The coefficient of variation for Tst was significantly greater in HCM patients than in the control subjects (Table 2), indicating a wide variation of Tst among the six regions of the left ventricle. Because the variation of Tst values indicates the variation of regional relaxation or the deviation from the uniformity of regional relaxation, the higher value for the coefficient of variation observed in HCM patients suggests the presence of nonuniform regional relaxation.

The mechanisms for the variation in regional relaxation are unclear at present, but there are some possible explanations. First, hypertrophy of regional myocardium may cause relaxation abnormality. In the present study, Tst values were greater in the regions with increased wall thickness (hypertrophied regions) than in those with normal wall thickness (nonhypertrophied regions). In the hypertrophied, nondilated left ventricle with normal systolic pressure, systolic wall stress is significantly reduced compared with the normal left ventricle.26,25 It is therefore thought that contraction load for the myocardial relaxation is lower in the hypertrophied ventricle than in the ventricle without hypertrophy and that muscle relaxation may be further impaired when contraction load is excessively reduced.26 This mechanism may operate in the hypertrophied regions in HCM patients. In addition, myoplasmic calcium removal is known to be slower in hypertrophied myocardium,30,31 which can cause deterioration of the relaxation process and result in prolongation of myocardial relaxation.1,11,12 Thus, in the hypertrophied regions in HCM, not only impaired myoplasmic calcium removal but also excessively reduced contraction load may contribute to the slower relaxation. Histological changes in the myocardium in the hypertrophied regions32 may also affect relaxation.

Tst was prolonged in the nonhypertrophied regions in HCM compared with control subjects, which is consistent with the findings of previous studies that demonstrated early diastolic abnormalities even in the regions without substantial hypertrophy in HCM.14,18 Cardiomyopathic tissue changes may exist in the regions without substantial hypertrophy and may cause this relaxation abnormality. However, it is also possible that the prolongation of Tst values in the nonhypertrophied regions may reflect the effects of the hypertrophied regions on the rate of decrease in global left ventricular pressure, which was used to estimate regional wall stress. In addition, there may be regional differences in diastolic pressure within the left ventricle.33,34 Such heterogeneity of pressure and the interaction of different regions would be expected to influence the regional relaxation rate, and further investigations are needed to elucidate their effects on Tst.

During isovolumic relaxation, the increase in regional area was greater in the hypertrophied regions than in the nonhypertrophied regions. That is, in the left ventricle with asymmetric hypertrophy in HCM, outward wall movement during isovolumic relaxation, which has also been observed by other investigators,7,10,35 is more pronounced in the hypertrophied regions. This event was associated with prolongation of Tst in the hypertrophied regions. In the present study, the time to minimum regional area (t-area\textsubscript{min}) was significantly shorter in the hypertrophied regions than in the nonhypertrophied regions, a finding that suggests that compared with the nonhypertrophied regions, myocardial contraction proceeds faster and terminates earlier in the hypertrophied regions, probably because of reduced afterload. This earlier completion of contraction may facilitate early onset of relaxation in the hypertrophied regions, leading to early onset of the myocardial fiber lengthening. Because outward wall motion increases the regional area and reduces the wall thickness, the rate of decrease in wall stress during isovolumic relaxation decreases, leading to impaired relaxation in the hypertrophied regions.

Another possible explanation for the variation of regional relaxation is regional myocardial ischemia. It is known that impaired left ventricular relaxation is closely related to asynchrony in ischemic and normal myocardium during coronary occlusion.3,6 On the one hand, decreased capillary density relative to myocardial mass and reduced coronary vasodilator reserve were observed in myocardium with hypertrophy by chronic pressure load.36 In the clinical setting, scintigraphic investigations revealed abnormal myocardial perfusion, which indicates regional ischemia in HCM patients.37,38 Therefore, myocardial ischemia—subendocardial ischemia, in particular—may be present in some regions of the left ventricle in HCM patients,37–40 and this can cause slow and asynchronous regional relaxation.

Limitations

The present study has some limitations with regard to the collection of hemodynamic and angiographic data. In HCM patients, severe obliteration of the left ventricular cavity can lead to at least two critical problems in interpretation of data: obliteration of the
apical region of the left ventricular cavity at end systole may lead to misinterpretation of wall dynamics in this region, and catheter entrapment by the obliterated cavity may cause an artifact on pressure tracings. We reviewed the left ventriculogram of each patient to determine the extent of these problems, and none of our patients showed cavity obliteration severe enough to significantly affect ventriculographic data or the morphology of left ventricular pressure and its \((-\frac{dP}{dt})\) upstroke pattern. The second limitation is that there was no significant difference in left ventricular ejection fraction between the control and HCM groups, although previous studies have reported increased ejection fraction in patients with HCM.\(^{29,41}\) This may be in part because none of our HCM patients had severe cavity obliteration or prominent papillary muscle shadow protrusion, both of which can lead to an increase in ejection fraction. In addition, it is possible that our HCM patients had early deterioration of systolic function. In a previous study,\(^{29}\) depressed myocardial contractility was also suggested in some patients with HCM. Third, ASH is thought to be one of the morphological characteristics of HCM, and it was observed in five of the 11 patients in the present study. Although no significant differences were found in the indexes for global left ventricular relaxation between patients with and those without ASH in our study group, it is possible that the disproportionately hypertrophied septal wall caused regional relaxation abnormality. However, this was not assessed in the present study because Janz’s formula could not be applied to the interventricular septum, which is part of both ventricles. Therefore, early diastolic septal wall dynamics in HCM remains to be elucidated.

In the present study, the nonuniformity of regional relaxation in HCM was closely related not only to IRT and Tp but also to the \((-\frac{dP}{dt})\) upstroke pattern assessed by \(dP/dt(20/60)\) (Figure 2). The convex-downward configuration of the \((-\frac{dP}{dt})\) upstroke pattern may reflect asynchronous onset of regional relaxation. Thus, our finding strongly suggests that regional nonuniformity is closely related to the impairment of left ventricular relaxation in nonobstructive HCM patients, although further investigations are necessary to clarify the cause-and-effect relation between regional nonuniformity and relaxation abnormality. In a previous study, Bonow et al\(^{18}\) suggested that an improvement of global left ventricular filling by administration of verapamil may be mediated by reduction in regional nonuniformity.

Left ventricular relaxation abnormality is known to affect ventricular filling dynamics and may exacerbate clinical symptoms in patients with HCM. Therefore, optimal modulation of the nonuniformity appears to be an important consideration in the management of HCM.

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References


KEY WORDS • hypertrophic cardiomyopathy • left ventricular relaxation • regional wall stress • nonuniformity
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