Focalized Contractile Impairment at Hypertrophied Myocardium Proven in Consideration of Wall Stress in Patients With Hypertrophic Cardiomyopathy

Tadashi YAMAZAKI,1 MD, Jun-ichi SUZUKI,1 MD, Ryoichi SHIMAMOTO,1 MD, Taeko TSUJI,1 MD, Yuki OHMOTO,1 MD, Teruhiko TOYO-OKA,1 MD, Masao OMATA,1 MD, Kuni OHTOMO,2 MD, and Ryozo NAGAI,1 MD

SUMMARY

In hypertrophic cardiomyopathy (HCM) a hyperkinetic state is sometimes observed in spite of impaired systolic function in the hypertrophied myocardium. The aim of the present study was to determine the mechanism of this paradox.

Seventeen patients with HCM and 10 normal subjects underwent cine magnetic resonance (MR) imaging to measure percent systolic wall thickening and percent fractional shortening. The ratio of systolic radial wall stress of the LV at the hypertrophied myocardium over that at the nonhypertrophied myocardium was evaluated to describe the focal advantageous condition for wall thickening.

The ratio was 0.66 ± 0.36 at the start of contraction and 0.78 ± 0.31 at early-systole, indicating consistently smaller radial wall stress at the hypertrophied myocardium. Although the condition for contraction was favorable (a ratio less than 1.00), percent systolic wall thickening at the hypertrophied myocardium (23.0 ± 11.8%) was smaller than that at the nonhypertrophied myocardium (70.5 ± 32.3%). Smaller end-diastolic dimension (HCM group; 45.2 ± 4.2 mm, reference group; 48.9 ± 4.1 mm, P = 0.04) with a statistically identical value of systolic decrease in intraventricular dimension (HCM group; 19.7 ± 3.9 mm, reference group; 18.9 ± 3.2 mm, P = 0.60) yielded high percent fractional shortening in patients with HCM (43.5 ± 7.6%).

Although contractile impairment was proven at the hypertrophied region with low radial wall stress in the HCM group, the smaller end-diastolic dimension in this group resulted in high percent fractional shortening. (Int Heart J 2006; 47: 247-258)

Key words: Hypertrophic cardiomyopathy, Magnetic resonance imaging, Wall stress

DISARRAY of cardiac myocytes and proliferation of interstitial fibrosis1,2) due to the pathogenic gene specific to hypertrophic cardiomyopathy (HCM)3-10) must impair systolic capability as well as diastolic performance.11) Its global systolic...
function, however, has been shown to be preserved, and often reveals a hyperdynamic state.\textsuperscript{12,13} Possible explanations for this paradox include real observation of true hypercontractility in this disease entity, pseudo-normal contractility under the decreased left ventricular (LV) radial wall stress as a result of compensatory remodeling,\textsuperscript{14,15} pseudo-vigorousness by favorable afterload reduction with complication of mitral regurgitation due to outflow obstruction,\textsuperscript{16-19} or other unknown mechanisms.

Systolic wall thickening, ie, an increase in the wall thickness from end-diastole through end-systole, can be used as a parameter for regional contractile capability under the condition of normalized preload and afterload.\textsuperscript{20-22} Accordingly, analysis of regional systolic wall thickening in consideration of the regional radial wall stress holds a key to determining the mechanism of the abovementioned paradox.\textsuperscript{23-25} Cine magnetic resonance (MR) imaging can provide high temporal and spatial resolution sufficient to analyze systolic wall thickening and sequential radial wall stress during systole at the common regions on LV short-axis images.\textsuperscript{26} Therefore, the objectives of the present study were to elucidate regional contractile capability in consideration of radial wall stress and solve the paradox of a hyperdynamic state with contractile impairment by using MR imaging in patients with HCM without complication by mitral regurgitation.

\section*{METHODS}

\textbf{Diagnosis of HCM and population for analysis:} Patients who had negative T waves with negativity greater than 0.2 mV\textsuperscript{26,27} and/or deep Q waves greater than 0.4 mV\textsuperscript{28,29} on an electrocardiogram (ECG) underwent MR imaging (Figure 1). None of these patients had a long-term history of hypertension. A diagnosis of HCM was made when MR imaging demonstrated wall thickness equal to or greater than 15 mm on LV short-axis images in those patients with the abovementioned ECG abnormalities.\textsuperscript{26} Ten asymptomatic subjects who had neither ECG abnormalities nor histories of cardiac disease also underwent MR imaging. Complete MR analysis, as described below, was conducted in 17 randomly selected patients (maximum wall thickness: 20.6 ± 3.5 mm) with the diagnostic criterion for HCM (HCM group) and in the 10 reference subjects (reference group). All study subjects provided written informed consent and the MR procedure was approved by the institutional review board of the University of Tokyo Hospital. No subject had either mitral regurgitation or aortic stenosis.

\textbf{MR imaging:} MR\textsuperscript{30-33} examination was performed using a Magnetom Vision (Siemens, Erlangen, Germany) instrument with a 1.5 Tesla superconducting magnet. A cine loop of LV short-axis images was obtained using an ECG trigger gradient refocused sequence (turbo-fast low angle shots). Imaging parameters were
an echo time of 6.2 ms, flip angle of 30 degrees, data acquisition matrix of 140 × 256, and field of view of 350 × 350 mm. The time delay for the first data acquisition window as end-diastole was 0 ms after triggering the R wave and the window was moved toward the end of the cardiac cycle in increments of 80 ms. The entire LV was encompassed by acquisition of contiguous short-axis cine loops with a slice thickness of 10 mm without an interslice gap.

**Regional systolic increase in wall thickness and percent wall thickening:** End-systole was determined as the cardiac phase when the area of the blood pool of the LV was the smallest during the cardiac cycle. The systolic increase in wall thickness and percent systolic wall thickening were calculated using the following formulas:

\[
\text{(Systolic increase in wall thickness)} = (\text{end-systolic wall thickness}) - (\text{end-diastolic wall thickness})
\]

\[
\text{(Percent systolic wall thickening)} = \frac{(\text{systolic increase in wall thickness}) \times 100}{(\text{end} - \text{diastolic wall thickness})}
\]
In the HCM group the parameters were evaluated both at the hypertrophied myocardial wall and at the nonhypertrophied myocardial wall on LV short-axis images at the chordal level. In almost all patients, although the maximum amplitude of hypertrophied myocardium was located at the anterior portion of the interventricular septum at the basal level, this specific anatomical location was apt to be influenced by the partial volume effect of the LV outflow tract during end-systole and therefore instead of this location, the hypertrophied anterior wall was selected for evaluation as the site of hypertrophied myocardium.

In the reference group, the regional systolic increase in wall thickness and percent systolic wall thickening were evaluated at the anterior wall and the posterior wall at the chordal level on LV short-axis images (Figure 2).

**Ratio of radial wall stress at hypertrophy over that at nonhypertrophy:** In the HCM group, to compare regional wall stress at the hypertrophied myocardial wall with that at the nonhypertrophied myocardial wall in a single common patient, the ratio of regional radial wall stress measured at the hypertrophied myocardium over that obtained at the nonhypertrophied myocardium was obtained. The ratio was evaluated at the anatomical sites where the systolic increase in wall thickness and percent systolic wall thickening were measured. The ratio was obtained sequentially from end-diastole through late-systole in increments of 80 ms, ie, at the 3 cardiac phases of 0 ms, 80 ms, and 160 ms after the R wave was triggered on the ECG (Figure 1B-D). Radial wall stress was determined with the following formula at each cardiac phase:

\[ \text{Radial Wall Stress} = \frac{\text{Wall Thickness}}{\text{Eccentricity}} \]

Figure 2. LV short-axis MR images at chordal level from subject in reference group. **Left panel:** end-diastolic image. **Right panel:** end-systolic image. Wall thickness at anterior and posterior walls and intraventricular dimension at both cardiac phases were measured on these images.
The radius of the curvature and wall thickness were measured at each cardiac cycle, ie, the start of contraction, early-systole, and late-systole. Accordingly, the ratio at each cardiac phase was calculated as follows:

\[
\text{(Ratio)} = \frac{(\text{radial wall stress at hypertrophy})}{(\text{radial wall stress at nonhypertrophy})}
\]

\[
= \frac{2 \times (\text{wall thickness at hypertrophy}) \times \left[ 1 + \frac{(\text{wall thickness at hypertrophy})}{2 \times (\text{radius at hypertrophy})} \right]}{2 \times (\text{wall thickness at nonhypertrophy}) \times \left[ 1 + \frac{(\text{wall thickness at nonhypertrophy})}{2 \times (\text{radius at nonhypertrophy})} \right]}
\]

where (radius at hypertrophy) and (thickness at hypertrophy) represent the radius of curvature and wall thickness measured at the hypertrophied myocardial wall, and (radius at nonhypertrophy) and (thickness at nonhypertrophy) indicate the radius of curvature and thickness evaluated at the nonhypertrophied myocardial wall.

The introduction of this ratio resulted in intraventricular pressure being cancelled out and thus it disappeared from the formula. Therefore, the ratio could be determined noninvasively by measuring LV wall thickness and the LV radius of curvature on MR short-axis images at each cardiac cycle.

**Intraventricular dimension and percent fractional shortening:** Anterior-posterior intravascular dimension was measured at end-diastole and at end-systole on short-axis MR images at the common chordal level where wall thickness and radius were evaluated. Percent fractional shortening was determined using the following formula:

\[
(\text{Percent fractional shortening}) = \frac{(\text{end-diastolic dimension}) - (\text{end-systolic dimension})}{(\text{end-diastolic dimension})} \times 100
\]

\[
= \frac{(\text{end-diastolic dimension}) - (\text{end-systolic dimension})}{(\text{end-diastolic dimension})} \times 100
\]
where (end-diastolic dimension) represents LV end-diastolic dimension and (end-systolic dimension) indicates LV end-systolic dimension in the anterior-posterior direction.

**Statistical analysis:** All values are expressed as the mean value with the standard deviation. Differences between 2 groups were tested by the paired t test or the unpaired t test and those among more than 2 groups were estimated with ANOVA. A P value less than 0.05 indicated a significant difference.

**RESULTS**

**LV wall thickness and percent systolic wall thickening:** Table I shows LV wall thickness and percent systolic wall thickening measured at the hypertrophied myocardial wall and at the nonhypertrophied myocardial wall in the HCM group and those evaluated at the anterior wall and at the posterior wall in the reference group. Percent systolic wall thickening obtained at the hypertrophied myocardium was smaller than that measured at the nonhypertrophied myocardium (\(P < 0.01\)) in the HCM group.

**Ratio of regional radial wall stress at the hypertrophied myocardial wall divided by that at the nonhypertrophied myocardial wall:** Figure 3 shows the time course of the ratio of regional radial wall stress at the hypertrophied myocardium divided by that at the nonhypertrophied myocardium at the common sites where the systolic increase in wall thickness and percent wall thickening were evaluated in the HCM group. Although the ratio was almost equal to 1.0 (0.98 ± 0.36) at late systole, it was less than 1.0 at the start of contraction (0.62 ± 0.36) and at early-systole (0.77 ± 0.33) (\(P < 0.01\)).

---

**Table I. Wall Thickness and Percent Systolic Wall Thickening**

<table>
<thead>
<tr>
<th></th>
<th>Diastolic wall thickness (mm)</th>
<th>Systolic wall thickness (mm)</th>
<th>Percent systolic wall thickening (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>HCM group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hypertrophied myocardial wall</td>
<td>Mean 17.9±*</td>
<td>21.9±*</td>
<td>23.0±*</td>
</tr>
<tr>
<td>Nonhypertrophied myocardial wall</td>
<td>Mean 10.8±*</td>
<td>18.1±*</td>
<td>70.5</td>
</tr>
<tr>
<td></td>
<td>SD 2.7</td>
<td>3.2</td>
<td>11.8</td>
</tr>
<tr>
<td></td>
<td>SD 1.3</td>
<td>1.9</td>
<td>32.3</td>
</tr>
<tr>
<td><strong>Reference group</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior wall</td>
<td>Mean 8.4</td>
<td>14.8</td>
<td>80.9</td>
</tr>
<tr>
<td></td>
<td>SD 1.9</td>
<td>2.7</td>
<td>36.1</td>
</tr>
<tr>
<td>Posterior wall</td>
<td>Mean 7.9</td>
<td>15.1</td>
<td>101.4</td>
</tr>
<tr>
<td></td>
<td>SD 1.8</td>
<td>2.5</td>
<td>61.7</td>
</tr>
</tbody>
</table>

* Significant difference versus nonhypertrophied myocardial wall (\(P < 0.01\))
* Significant difference versus anterior wall in reference group (\(P < 0.01\))
* Significant difference versus posterior wall in reference group (\(P < 0.01\))
Intraventricular dimensions and percent fractional shortening: Table II displays the intravascular dimensions and percent fractional shortening. LV end-diastolic and end-systolic dimensions in the HCM group were smaller than those in the reference group ($P < 0.05$). Although there was no statistical difference between the 2 groups, percent fractional shortening in the HCM group was slightly greater than that in the reference group ($P = 0.15$).
**DISCUSSION**

**Evidence of contractile impairment of the hypertrophied myocardium in HCM:** The results of analysis in the HCM group demonstrated that percent systolic wall thickening at the hypertrophied myocardial wall was smaller than that at the non-hypertrophied myocardial wall (Table I), and also revealed that regional radial wall stress at the hypertrophied wall was consistently smaller than that at the non-hypertrophied wall from the start of contraction through late-systole with favorable conditions for systolic contraction at the hypertrophied region (Figure 3). Moreover, percent systolic wall thickening at the nonhypertrophied myocardial wall was slightly smaller than that in the reference group. Although these results did not directly suggest impaired contractility in the HCM group due to a lack of information on radial wall stress for comparison between the HCM group and the reference group, these observations imply, in the very least, the existence of impaired contractile ability at the hypertrophied region when compared with that at the nonhypertrophied region in the HCM group.

**Demonstration of hyperkinetic observation in HCM:** In spite of strong indication of the existence of contractile dysfunction at the hypertrophied region in the HCM group, percent fractional shortening in this group was more than 40% in the current study. Although comparison of percent fractional shortening between the HCM group and the reference group did not directly imply comparison of contractile ability because of the lack of comparison of radial wall stress between the 2 groups, percent fractional shortening in the HCM group was slightly greater than that in the reference group ($P = 0.15$) (Table II).

**Solution of the paradox in HCM:** Possible explanations should be proposed for solving the paradoxical discrepancy between impairment of contractile capability and LV hyperdynamic observation described as high percent fractional shortening. Attention should perhaps be focused on the pitfall that exists when LV contractile capability is discussed using parameters that are dependent on intraventricular measurements such as percent fractional shortening and/or ejection fraction. Direct information on myocardial contraction including percent systolic wall thickening should be taken into account. Table III summarizes the increase in the sum of the anterior wall thickness and the posterior wall thickness during systole, decrease in dimension from the anterior epicardial edge to the posterior epicardial edge in systole, decrease in the intraventricular dimension in systole, and again LV end-diastolic dimension and percent fractional shortening in the HCM group and in the reference group (Figure 4). Although percent systolic wall thickening in the HCM group was much less than that in the reference group, the systolic increases in the sums of the anterior and posterior wall thicknesses were almost identical in the 2 groups. This can be explained by the fact that massive myocardium with smaller systolic wall thickening can attain a total
amplitude of increase in wall thickness that almost corresponds to the normal value. Moreover, the systolic decrease in the dimension between the 2 epicardial edges was slightly greater in the HCM group than in the reference group ($P = 0.07$). The small difference in the systolic increase in wall thicknesses between the 2 groups and the greater systolic decrease in epicardial-epicardial dimension in the HCM group contributed to the value associated with the systolic decrease in intraventricular dimension in the HCM group, which was comparable to that in the reference group, because the systolic decrease in intraventricular dimension was calculated using the following formula:

\[
(systolic \ decrease \ in \ intraventricular \ dimension) = (end-diastolic \ dimension) - (end-systolic \ dimension) + (systolic \ increase \ in \ sum \ of \ anterior \ and \ posterior \ wall \ thicknesses)
\]

\[
= (end-diastolic \ dimension) + (anterior \ wall \ thickness) + (posterior \ wall \ thickness)
\]

\[
= (end-systolic \ dimension) + (anterior \ wall \ thickness) + (posterior \ wall \ thickness)
\]

\[
+ (systolic \ increase \ in \ sum \ of \ anterior \ and \ posterior \ wall \ thicknesses)
\]

\[
+ (systolic \ decrease \ in \ epicardial-epicardial \ dimension)
\]

Table III. Summary of Intraventricular Dimension and Fractional Shortening in HCM and Reference Groups

<table>
<thead>
<tr>
<th></th>
<th>Systolic increase in sum of anterior and posterior wall thicknesses (mm)</th>
<th>Systolic decrease in epicardial-epicardial dimension (mm)</th>
<th>Systolic decrease in intraventricular dimension (mm)</th>
<th>End-diastolic dimension (mm)</th>
<th>Fractional shortening (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCM group</td>
<td>Mean 11.3</td>
<td>8.4</td>
<td>19.7</td>
<td>45.2</td>
<td>43.5</td>
</tr>
<tr>
<td></td>
<td>SD 3.8</td>
<td>3.4</td>
<td>3.9</td>
<td>4.2</td>
<td>7.6</td>
</tr>
<tr>
<td>Reference group</td>
<td>Mean 13.6</td>
<td>5.3</td>
<td>18.9</td>
<td>48.9</td>
<td>39.0</td>
</tr>
<tr>
<td></td>
<td>SD 4.7</td>
<td>4.7</td>
<td>3.2</td>
<td>4.1</td>
<td>7.5</td>
</tr>
</tbody>
</table>

$P$ value 0.19 0.07 0.60 0.04 0.15

Figure 4. Schematic representation of intraventricular dimension and wall thickness on LV short-axis plane. **Left panel:** scheme for end-diastole. **Right panel:** scheme for end-systole. Dimension between anterior epicardium and posterior epicardium decrease during contraction.

\[
(systolic \ decrease \ in \ intraventricular \ dimension) = (end-diastolic \ dimension) - (end-systolic \ dimension) + (systolic \ increase \ in \ sum \ of \ anterior \ and \ posterior \ wall \ thicknesses)
\]

\[
+ (systolic \ decrease \ in \ epicardial-epicardial \ dimension)
\]
(systolic decrease in intraventricular dimension) = (left ventricular end-diastolic dimension) – (left ventricular end-systolic dimension)
= (systolic decrease in epicardial-epicardial dimension) + (systolic increase in anterior wall thickness and posterior wall thickness)

Percent fractional shortening was calculated as follows:

\[
\text{Percent fractional shortening} = \frac{\text{systolic decrease in intraventricular dimension} \times 100}{\text{left ventricular end-diastolic dimension}}
\]

Thus, a similar numerator (systolic decrease in intraventricular dimension) over a smaller denominator (LV end-diastolic dimension) yielded high percent fractional shortening in the HCM group. It is clear that neither afterload reduction due to mitral regurgitation nor low radial wall stress at the nonhypertrophied region contributed favorably to the hyperdynamic observation, ie, high percent fractional shortening.

**Conclusion:** Even if a hyperkinetic state was observed, impaired contractility was strongly indicated in patients with HCM under the favorable condition of low radial wall stress at the hypertrophied myocardium. Smaller end-diastolic dimension contributed to high percent fractional shortening in HCM.

**REFERENCES**


