Regional Left Ventricular Myocardial Contraction Abnormalities and Asynchrony in Patients With Hypertrophic Cardiomyopathy Evaluated by Magnetic Resonance Spatial Modulation of Magnetization Myocardial Tagging

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Global left ventricular (LV) pump function is generally preserved in patients with hypertrophic cardiomyopathy (HCM). However, it is unknown whether regional myocardial contractility is impaired, especially in nonhypertrophied regions. The purpose of this study was to evaluate regional LV myocardial contraction in patients with HCM using magnetic resonance (MR) spatial modulation of magnetization (SPAMM) myocardial tagging. The study group comprised 20 patients with asymmetric septal hypertrophy (HCM group) and 16 age-matched normal patients (control group), and data were collected using transthoracic M-mode and 2-dimensional echocardiography, and MR SPAMM myocardial tagging. The systolic strain ratio, maximum systolic strain velocity, and time from end-diastole to maximum systolic strain ($\Delta T$) in the anterior, ventricular septal, inferior and lateral regions for 2 LV short-axis sections at the levels of the chordae tendineae and papillary muscles were measured at 50-ms intervals by MR myocardial tagging. The end-diastolic anterior and ventricular septal wall thicknesses and LV mass index were significantly different between the HCM and control groups. The systolic strain ratio for all 4 walls, particularly the anterior and ventricular septal regions, was significantly lower in the HCM group. In the HCM group, the maximum systolic strain velocity was significantly lower and $\Delta T$ was significantly shorter for all 4 walls, particularly the anterior and ventricular septal regions. The standard deviation for the $\Delta T$, calculated from the $\Delta T$ for the 8 regions of the 2 LV short-axis sections, was significantly greater in the HCM group. In conclusion, regional LV myocardial contraction is impaired in both hypertrophied and nonhypertrophied regions, and systolic LV wall asynchrony occurs in patients with HCM. (Jpn Circ J 1999; 63: 442–446)

Key Words: Hypertrophic cardiomyopathy; Regional left ventricular systolic function; Spatial modulation of magnetization myocardial tagging

Magnetic resonance (MR) myocardial tagging has permitted the analysis of intramyocardial segmental function in normal volunteers and patients with myocardial disease. In particular, the spatial modulation of magnetization (SPAMM) method uses noninvasive recognition of markers for specific myocardial regions for analyzing the myocardial thickening or thinning during the cardiac cycle. Previous studies have reported that left ventricular (LV) contractility is impaired in the hypertrophied regions in patients with hypertrophic cardiomyopathy (HCM). However, there is controversy concerning whether contractility in the nonhypertrophied regions is impaired because some studies have reported that contractility is normal and other studies have reported decreased contractility. The present study therefore used MR SPAMM myocardial tagging to analyze regional myocardial contraction in the hypertrophied and nonhypertrophied regions of the LV wall in patients with HCM. In addition, we characterized the systolic LV wall asynchrony that occurs in this disease.

Methods

Patient Population
The study population consisted of 20 patients with asymmetric septal hypertrophy (HCM group; 12 men, 8 women; age range: 42±14 years) and 16 age-matched normal patients (control group; 10 men, 6 women; age range: 38±12 years). We enrolled the patients in sinus rhythm who met the following inclusion criteria: (1) normal coronary anatomy determined by coronary angiography, (2) no evidence of hypertension or moderate to severe valvular heart disease, (3) heart rate between 60 and 100 beats/min, (4) QT interval ≤420 ms, and (5) LV outflow obstruction <20 mmHg determined by continuous-wave Doppler echocardiography. The 16 normal patients visited hospital with the chief complaints of chest pain, palpitations, dyspnea or heart murmurs. Phonocardiography, routine echocardiography and cardiac catheterization...
LV Contraction in HCM Assessed by MR SPAMM

revealed no organic cardiac disease in the control group. The purpose of this study was fully explained to all patients, and informed consent was obtained.

**Study Protocol**

**Transthoracic Echocardiography** Transthoracic M-mode and 2-dimensional short-axis echocardiograms were...
recorded with a commercially available ultrasound diagnostic system (Toshiba SSA-380A, Toshiba Corp, Tokyo, Japan) with a 2.5 MHz probe. The LV end-diastolic dimension (LVDd) and LV end-systolic dimension (LVDs) were determined by M-mode echocardiography. The end-diastolic ventricular septal thickness (VSth), end-diastolic LV lateral wall thickness (LWth), end-diastolic LV inferior wall thickness (IWth), and end-diastolic anterior wall thickness (AWth) were determined by 2-dimensional short axis echocardiography. The percent LV fractional shortening (%FS) and LV mass index (LVMI), corrected for body surface area (BSA), were calculated using the following equations:

\[%FS(\%) = \frac{\text{LVDd} - \text{LVDs}}{\text{LVDd}} \times 100\]

\[\text{LVMI} (\text{g/m}^2) = \frac{1.04 \times [(\text{LVDd} + \text{VSth} + \text{LWth})^3 - \text{LVDd}^3] - 13.6)}{\text{BSA}}\]

**MR Myocardial Tagging**  
The LV long-axis view was acquired in the supine position using an MR imaging apparatus (MAGNETOM 63 SP, Siemens Co, Ltd, Munich, Germany). Two short-axis sections were obtained at the levels of the chordae tendineae and papillary muscles based on the LV long-axis view (Fig 1). The tag was labeled synchronously at end-diastole as defined by the beginning of the R wave on ECG. Subsequently, MR myocardial taggings were performed between end-diastole and end-systole (0–400 ms) using the following parameters: repetition time, 50 ms; echo time, 9 ms; matrix size, 256 x 128 pixels; slice thickness, 7 mm; and tag size, 7 mm. Tags were determined between the mid-wall and subendocardium in the anterior, ventricular septal, inferior and lateral walls of the respective short-axis section. The lengths of the tags extending to the center of the LV cavity were measured at 50-ms intervals during systole for the 8 regional myocardial walls. The strain ratio for each region of the myocardial wall was calculated at 50-ms intervals during systole using the following equation:

\[\text{strain ratio (\%)} = \frac{(a - a')}{a} \times 100\]

where a is the tag distance forward the center of the LV cavity at end-diastole, and an is the distance of tag lengthening during each 50 ms (Fig 2). The systolic strain velocity (\(\Delta V\)) for each myocardial wall region also was calculated at 50-ms intervals during systole using the following equation:

\[\Delta V (\text{cm/s}) = \frac{(an - an')}{0.5}\]

where an – an’ is the difference in the distance of tag lengthening during each 50 ms; and the maximum systolic strain velocities (\(\Delta V\)) for the 8 respective regions (ie, maximum values for the mean strain velocities measured at 50-ms intervals during systole) were determined. The interval from end-diastole to the maximum systolic strain (\(\Delta T\)) also was determined for the 8 regions. The mean values for the strain ratios, \(\Delta V\) and \(\Delta T\) for the 2 short-axis sections were calculated for the anterior, ventricular septal, inferior and lateral walls. The time-strain ratio plots for each wall were constructed, and the standard deviation of the \(\Delta T\) (SD-\(\Delta T\)), which was calculated from the \(\Delta T\) for each of the 8 regions, was determined.

**Statistical Analysis**
Values are expressed as the mean±SD. Mean values obtained for the control and HCM groups were compared by unpaired Student’s t test. Mean values for the MR tagging variables for the 4 LV walls were compared by analysis of variance (ANOVA) and Scheffe’s F test. A p value <0.05 was considered statistically significant.

**Results**

**Clinical and M-Mode and 2-Dimensional Echocardiographic Variables**  
There were no significant differences in heart rate, LVDs, %FS, IWth and LWth between the control and HCM groups (Table 1). The LVDd was significantly lower in the HCM group than in the control group. In contrast, the AWth, VSth and LVMI were significantly greater in the HCM group than in the control group.

**MR Myocardial Tagging Variables**  
Time-strain ratio plots for the anterior, ventricular septal, inferior and lateral walls of the LV are depicted in Fig 3. In all 4 walls, particularly the ventricular septal and LV anterior walls, the systolic strain ratios were significantly lower (Fig 3), the \(\Delta V\) was significantly lower (Fig 4), and the \(\Delta T\) was significantly shorter (Fig 5, left) in the HCM group than in the control group. The SD-\(\Delta T\) was significantly greater in the HCM group than in the control group (Fig 5, right).

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Table 1  Clinical and M-Mode Echocardiographic Variables

<table>
<thead>
<tr>
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<th>Control (n=16)</th>
<th>HCM (n=20)</th>
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<tr>
<td>HR (beats/min)</td>
<td>74±14</td>
<td>70±11</td>
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<tr>
<td>LVDd (cm)</td>
<td>4.4±0.5</td>
<td>3.8±0.4**</td>
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<tr>
<td>LVDs (cm)</td>
<td>2.6±0.4</td>
<td>2.4±0.5</td>
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<tr>
<td>%FS (%)</td>
<td>41±10</td>
<td>38±89</td>
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<tr>
<td>AWth (cm)</td>
<td>0.9±0.2</td>
<td>1.8±0.5***</td>
</tr>
<tr>
<td>VSth (cm)</td>
<td>1.1±0.3</td>
<td>2.2±0.6***</td>
</tr>
<tr>
<td>IWth (cm)</td>
<td>1.0±0.2</td>
<td>1.1±0.3</td>
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<tr>
<td>LWth (cm)</td>
<td>1.1±0.3</td>
<td>1.3±0.4</td>
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<tr>
<td>LVMI (g/m²)</td>
<td>106±26</td>
<td>212±55**</td>
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*p<0.01, **p<0.0001 vs control group.

HCM, hypertrophic cardiomyopathy; HR, heart rate; LVDd, left ventricular end-diastolic dimension; LVDs, left ventricular end-systolic dimension; %FS, percent fractional shortening of the left ventricle; AWth, end-diastolic anterior wall thickness; VSth, end-diastolic ventricular septal thickness; IWth, end-diastolic inferior wall thickness; LWth, end-diastolic lateral wall thickness; LVMI, left ventricular mass index.

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Discussion

The location and magnitude of LV hypertrophy varies in patients with HCM. Previous studies\textsuperscript{10-14} have reported that regional myocardial contractility generally is impaired in the hypertrophied regions despite a normal LV ejection fraction in patients with HCM. In contrast, changes in myocardial contractility in the nonhypertrophied regions remain the subject of controversy. The LV lateral and inferior walls, which are nonhypertrophied in patients with HCM, exhibit normal or hyperkinetic motion to compensate for hypo- or dyskinetic motion in the hypertrophied LV anterior wall and ventricular septum in patients with asymmetric septal hypertrophy\textsuperscript{12,15} However, it has been reported that myocardial abnormalities exist not only in the LV anterior wall and ventricular septum, but also in the LV inferior and lateral walls and the right ventricular free wall of patients with HCM\textsuperscript{13,14}.

In the present study, the LV myocardial strain ratio determined by MR SPAMM myocardial tagging decreased markedly during systole in the hypertrophied LV anterior wall and ventricular septum, although the strain ratio also decreased in the nonhypertrophied LV inferior and lateral walls, in keeping with the results reported by Unverferth et al\textsuperscript{13} and Takagi et al.\textsuperscript{14} In patients with HCM, contractility per gram of myocardium decreases, although the LV ejection fraction is preserved by a decrease in afterload.\textsuperscript{17} Therefore, various indices reflecting myocardial contractility decrease easily when end-systolic LV wall stress increases.\textsuperscript{18} The results of the present study obtained by MR SPAMM myocardial tagging demonstrate a decrease in contractility per gram of myocardium in patients with HCM.

Oki et al have reported that the peak systolic LV wall motion velocities evaluated by pulsed tissue Doppler imaging decreased not only in the hypertrophied ventricular septum, but also in the nonhypertrophied lateral wall in patients with asymmetric septal hypertrophy.\textsuperscript{19} Their result lends support to myocardial damage being present throughout the LV wall even in patients with asymmetric septal hypertrophy\textsuperscript{13}. The present study demonstrates that MR SPAMM myocardial tagging can detect decreases in $\Delta V$ (ie, velocity of LV myocardial contraction) in both the hypertrophied LV anterior wall and ventricular septum and the nonhypertrophied LV inferior and lateral walls in patients with asymmetric septal hypertrophy, although the time resolution of MR SPAMM myocardial tagging is inferior to that obtained by pulsed tissue Doppler imaging. However, MR SPAMM myocardial tagging allows analysis of myocardial thickening or thinning during any phase of the cardiac cycle.

Schwammenthal et al have demonstrated that myocardial contraction in the hypertrophied region ends in the early phase of systole, resulting in marked differences in LV myocardial contraction time between the hypertrophied and nonhypertrophied regions in patients with HCM and LV outflow obstruction.\textsuperscript{6} Moreover, Hayashida et al have reported premature completion of the myocardial contraction in the hypertrophied region in patients with HCM, but no LV outflow obstruction.\textsuperscript{20} Therefore, LV wall asynchrony occurs because of non-uniform myocardial wall thickening in patients with HCM. In the present study using MR SPAMM myocardial tagging, the max$\Delta V$ and the $\Delta T$ were significantly lower in all 4 walls, particularly the hypertrophied LV anterior wall and ventricular septum, in the HCM group than in the control group, and the standard deviation of the $\Delta T$ was significantly greater in the HCM group than in the control group. Therefore, it was clarified that LV wall asynchrony occurs in patients with HCM. These findings might reflect the pathologic characteristics of the myocardium in patients with HCM, such as myocardial disarray or fibrosis. Therefore, MR SPAMM myocardial tagging may be useful for long-term follow-up of patients with HCM, including during the transition to the dilated phase of HCM.\textsuperscript{21}

Regional myocardial function and rotation of the heart have been evaluated using surgically implanted markers in the myocardium.\textsuperscript{22} However, the development of MR myocardial tagging has facilitated the detailed evaluation of abnormalities in regional LV myocardial function not.
only in the setting of HCM, but also in hypertensive heart disease, ischemic heart disease and dilated cardiomyopathy. Three-dimensional MR imaging is a recent development. The refinement of MR SPAMM myocardial tagging is expected to facilitate the understanding of the pathophysiology in cardiovascular diseases. Current studies are aimed at improving the technical aspects of MR SPAMM, including the reduction of tag size, shortening of imaging intervals, improved image resolution, and shortening the examination time.

Study Limitations

In the present study imaging intervals were fixed at 50 ms. Therefore, it is conceivable that there was a lag in the imaging during systole, especially 350 ms after end-diastole. To minimize this lag, the study population was limited to patients in normal sinus rhythm and with a QT interval ≤420 ms. We were primarily interested in examining the period from end-diastole to maximum regional contraction. Therefore, a slight lag at end-systole most likely did not influence the results of the present study.

The tag size of 7 mm is also a limiting factor for precise measurements. Although we selected the tag between the mid-wall and subendocardium in all patients, it is possible to exhibit some dislocation of the tag in this setting, especially at the nonhypertrophied walls.

Another potential problem is the displacement of tagging in the short-axis view during MR imaging due to translation of the entire heart along the long axis during LV contraction. However, because myocardial tags were labeled at right angles to the short-axis view in the present study, an imaging stripe in the short axis view was preserved throughout the cardiac cycle. Moreover, Lima et al. have reported a significant correlation between wall thickening along the short axis measured by MR imaging and thickening determined by implanted sonomicrometry crystals. Therefore, the short-axis strain ratio used in the present study precisely reflects myocardial contraction.

In conclusion, regional LV myocardial contraction is impaired in both the hypertrophied and nonhypertrophied regions, and systolic LV wall asynchrony occurs in patients with HCM. MR SPAMM myocardial tagging is a noninvasive and useful method for evaluating regional LV myocardial contraction abnormalities and asynchrony in this disease.

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References