Intramural Myocardial Shortening in Hypertensive Left Ventricular Hypertrophy With Normal Pump Function

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**Background** In hypertensive left ventricular hypertrophy (LVH), intrinsic myocardial systolic function may be normal or depressed. Magnetic resonance tagging can depict intramural myocardial shortening in vivo.

**Methods and Results** Tagged left ventricular magnetic resonance images were obtained in 30 hypertensive subjects with LVH (mean LV mass index, 142±41 g/m²) and normal ejection fraction (mean, 64±9%) using spatial modulation of magnetization. In 26 subjects, circumferential myocardial shortening (%S) was compared with results obtained in 10 normal subjects at endocardium, midwall, and epicardium on up to 4 short-axis slices each. Similarly, in 10 subjects, midwall long-axis shortening at basal, midventricular, and apical sites was compared with results obtained in 12 normal volunteers. Circumferential %S was reduced in hypertensive subjects. Mean shortening was 29±6% at the endocardium in hypertensive subjects versus 44±6% in normal subjects (P=.0001); 20±6% at the midwall versus 30±6% (P=.0001); and 13±5% at the epicardium versus 21±5% (P=.0002). However, the transmural gradient in percent shortening from endocardium to epicardium in hypertensive subjects paralleled that in normal subjects. The normal base-to-apex gradient in circumferential %S was absent in LVH. In contrast to normal subjects, circumferential %S showed regional heterogeneity in hypertensive subjects, being maximal in the lateral wall and least in the inferior wall. Longitudinal shortening was also uniformly depressed in hypertensive subjects: 10±9% at the base versus 21±6% in normal subjects (P=.0001); 14±8% at the midventricle versus 18±3% (P=.03); and 14±8% at the apex versus 18±4% (P=.04).

**Conclusions** In hypertensive LVH with normal pump function, intramural circumferential and longitudinal myocardial shortening are depressed. (Circulation. 1994;89:122-131.)

**Key Words** • hypertension • hypertrophy • ventricles

In patients with hypertension, the increased risk of cardiac mortality, heart failure, and coronary artery disease associated with left ventricular hypertrophy (LVH) is well known.1,2 In such patients with uncomplicated hypertension and moderate LVH, conventional analyses of left ventricular pump function generally show normal to supernormal systolic function.3-5 However, numerous studies of myocardial contractile function in hypertrophied left ventricle in experimental models6-10 and a few in humans11-13 suggest that intrinsic myocardial performance may in fact be depressed in LVH with normal ejection fraction. Evaluation of segmental myocardial function in situ in humans has been limited to date by dependence on highly invasive methods such as surgical implantation of sonomicrometry crystals or metallic markers in the myocardium.14 Spatial modulation of magnetization (SPAMM), a new magnetic resonance tagging technique, permits noninvasive evaluation of myocardial deformation in humans, including circumferential and longitudinal segment shortening as well as transmural and regional differences in shortening.15,16 Therefore, we used SPAMM imaging to compare circumferential and longitudinal myocardial shortening in subjects with hypertensive LVH and normal left ventricular ejection fraction with that found in normal subjects.

**Methods**

**Subjects**

We studied 30 subjects with sustained hypertension defined as diastolic blood pressure >90 mm Hg and/or systolic blood pressure >150 mm Hg, with echocardiographic evidence of LVH (see Table 1). All subjects gave informed consent, and the study protocol was approved by the University of Pennsylvania’s Committee on Research Involving Human Subjects. Subjects were recruited from both inpatient medicine services and outpatient medical clinics at the Hospital of the University of Pennsylvania; they ranged in age from 30 to 78 years (mean, 49 years) and included 24 women and 6 men. None had clinical evidence of ischemic heart disease, echocardiographic segmental wall motion abnormalities, left ventricular dysfunction, significant valvular disease, or dynamic left ventricular outflow obstruction. Using newer Framingham criteria correcting for lean body mass, echocardiographic criteria for LVH included a mass/height index >130 g/m² in men and >96.8 g/m² in women.17 Left ventricular mass was determined in 26 subjects using an anatomically validated M-mode echocardiographic method, as modified for use of American Society of Echocardiography measurements.18,19 In 4 patients with M-mode recordings suggestive but not diagnostic for LVH, left ventricular mass estimates were made from two-dimensional echo images.
TABLE 1. Characteristics of Left Ventricular Hypertrophy Population

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>30-78 y (mean, 49±14)</td>
</tr>
<tr>
<td>LV mass index</td>
<td>99-272 g/m (mean, 142±41)</td>
</tr>
<tr>
<td>Body mass index</td>
<td>28±4</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>52%-88% (mean, 64±9)</td>
</tr>
<tr>
<td>Duration of hypertension</td>
<td>0.08-28 y (mean, 12±8)</td>
</tr>
<tr>
<td>h/r ratio</td>
<td>0.49±0.15</td>
</tr>
<tr>
<td>Heart rate</td>
<td>71±11 bpm</td>
</tr>
<tr>
<td>Systolic BP</td>
<td>158±31 mm Hg</td>
</tr>
<tr>
<td>Diastolic BP</td>
<td>100±19 mm Hg</td>
</tr>
</tbody>
</table>

LV indicates left ventricular; h/r ratio, ratio of wall thickness to chamber radius; bpm, beats per minute; and BP, blood pressure.

are actually orthogonal sets of parallel planes of reduced signal in three-dimensional space perpendicular to the imaging plane. Since the image plane is perpendicular to the planes of reduced signal, initial stripe spacing is the same throughout the cardiac volume. To time end systole, defined as the time of minimal LV cavity size through one slice, a single-slice, axial cine-MRI acquisition was performed at the level of the mitral valve with a 25-millisecond frame duration (TE of 13 milliseconds, TR equal to 25 milliseconds, 20° flip angle, flow compensation). To obtain data for circumferential shortening measurements, multiphase, multislice, short-axis SPAMM images of the left ventricle were then obtained from 13 milliseconds after the R-wave peak, defined as end diastole to end systole, in LVH subjects. For multiphase series, 4 to 5 midventricular slices were acquired at 4 to 5 time instances, and interslice delay was adjusted to ensure that the last multiphase image at each slice location was the end-systolic frame. In addition, the initial center-to-center stripe separation was chosen to optimize image quality, ranging from 7 to 10 mm among subjects. In 10 LVH subjects, long-axis multiphase series were acquired in a similar fashion (Fig 2). Heart rate, which affects imaging time, and time constraints limited the number of subjects for which both short- and long-axis series could be obtained. Long-axis planes were prescribed perpendicular to the short-axis planes imaged and perpendicular to the midseptum and lateral left ventricular wall, analogous to the echocardiographic four-chamber view. Four to five slices were imaged at 4 to 5 time instances, again from beginning to end systole. Total imaging time was approximately 1 hour, but this varied with heart rate. Because of the long duration of the SPAMM studies, it was not possible to perform additional untagged MRI imaging series to permit evaluation of LV mass, volume, and ejection fraction.

Since normal subjects were imaged for evaluation of circumferential shortening data early in our experience with the SPAMM technique, the imaging protocol for short-axis acquisitions differed slightly. Two temporally overlapped multiphase SPAMM acquisitions, extending from end diastole through systole and into early diastole were obtained with a fixed 60-millisecond interslice delay. In this case, end systole was defined as the time of maximal shortening as derived from the SPAMM images for each subject. Comparisons in LVH studies that included cine-SPAMM acquisitions indicated that end systole was timed to the same frame by maximal SPAMM shortening and smallest cavity area. Thus, the main difference between normal and LVH studies for circumferential shortening was that the maximal potential error in timing end systole was 40 milliseconds in normal subjects and 12.5 milliseconds in LVH patients. The 12 normal subjects in whom long-axis images were acquired were imaged with the same methods used in the hypertensive subjects, using cine MRI imaging to identify end systole and a variable interslice delay.
dial sites on anterior, lateral, septal, and inferoposterior walls. Only midventricular slices, falling within the mid 50% of the left ventricular long axis, were compared to ensure comparability of slice location. Segment locations were denoted relative to the left ventricular short-axis plane using anatomic markers (the septal insertions of the right ventricle).

For longitudinal shortening analysis, long-axis images were used in which all four cardiac chambers and the left ventricular insertion of the aorta were visualized. Selected stripe pairs were oriented perpendicular to the left ventricular long axis and to the endocardium. In the mid third of the left ventricle, longitudinal %S was determined at endocardial, midwall, and epicardial sites on the free wall and left ventricular endocardial, midwall, and right ventricular endocardial sites on the septum. For the base-to-apex analysis, longitudinal %S at all midwall sites from base to apex was determined and divided into basal, mid, and apical thirds. When stripe alignment was not suitable for interstripe distance measurements, segment lengths defined by stripe intersections were measured.

**Statistical Analysis**

Comparisons of mean circumferential %S at endocardial, midwall, and epicardial sites and among anterior, lateral, septal, and inferoposterior sites within each group of subjects were made using repeated-measures ANOVA with Scheffé subtesting. Similarly, comparisons of mean circumferential %S among more basal, midventricular, and more apical slices within each group were compared using repeated-measures ANOVA. Complete circumferential %S data sets from base to apex were available from 10 normal subjects and 18 LVH subjects. Likewise, for longitudinal %S, comparisons of mean midwall %S at three levels from base to apex and comparisons of longitudinal %S at midventricular transmural sites for septal and lateral walls within each group were made using repeated-measures ANOVA. Comparisons of septal and free wall long-axis shortening were made using paired t tests between mean values in the basal, mid, and apical thirds. Comparisons between normal and LVH subjects were made using unpaired t tests. Linear regression analysis was used to
evaluate the effects of LV mass index, relative wall thickness or h/r ratio, age, and reported duration of hypertension on mean %S in LVH subjects. To examine the effects of drug treatment, mean %S was compared between treated and untreated hypertensive subjects using unpaired t tests. Interobserver variability of %S was determined in a subset of 44 segments and evaluated using linear regression analysis.

Results

As depicted in Figs 1A and 1B, in normal human left ventricle in the short-axis plane, SPAMM interstripe distances decrease from end diastole to end systole because of circumferential myocardial shortening. There is a transmural gradient in circumferential shortening in normal subjects, with endocardial greater than epicardial shortening, resulting in convergence of stripes at the endocardium at end systole. Figs 1C and 1D show end-diastolic and end-systolic frames taken from a subject with hypertensive LVH and normal pump function. Myocardial cross-sectional area is increased, whereas end-systolic segment shortening appears reduced compared with the normal subject shown in top panel. However, end-systolic endocardial convergence of stripes is present. Figs 2A and 2B depict longitudinal shortening in a normal subject. At end systole (Fig 2B), interstripe distance decreases because of longitudinal shortening. Septal stripes stay relatively parallel because of the absence of a transmural gradient in shortening. The atrioventricular valve planes are translated toward the apex, which is fixed in position. End-diastolic (C) and end-systolic (D) longitudinal shortening in a left ventricular hypertrophy subject are shown. In contrast to normal, myocardial area is increased, and shortening is less in magnitude. LV indicates left ventricle.

Fig 2. End-diastolic (A) and end-systolic (B) long-axis images from a normal subject. At end systole, interstripe distance decreases because of longitudinal shortening. Septal stripes stay relatively parallel because of the absence of a transmural gradient in shortening. The atrioventricular valve planes are translated toward the apex, which is fixed in position. End-diastolic (C) and end-systolic (D) longitudinal shortening in a left ventricular hypertrophy subject are shown. In contrast to normal, myocardial area is increased, and shortening is less in magnitude.
measurements by our methods is good, with a correlation coefficient of 0.92 and a slope near unity. For the present study, we also determined interobserver variability of circumferential %S. Over a range of values from 1% to 43%, the correlation coefficient was 0.92, and the relation between results obtained by observers x and y was y=4.1+0.81x. All analyses were performed using results obtained by a single observer.

In normal subjects, no regional differences in %S were observed between anterior, lateral, septal, and inferoposterior sites (Table 2). In contrast, circumferential shortening in hypertensive subjects was not uniform (P=.0003). Shortening was greatest at lateral wall sites, and there were significant differences between lateral and both septal and inferior sites (P<.05).

In normal subjects, as previously reported, a base-to-apex gradient in circumferential shortening was observed with greater apical shortening (P=.0002). In contrast, no significant base-to-apex gradient was found in LVH (Table 2), although a tendency for greater apical shortening was observed.

Midwall longitudinal %S was also significantly depressed in LVH subjects (Table 3). At the base, mean %S was 10±6% in LVH versus 21±6% in normal subjects (P=.0001). At the midventricular level, mean %S was 14±8% in LVH subjects versus 18±3% in normal subjects (P=.03). Mean %S in apical slices was 14±8% in LVH subjects in contrast to 18±4% in normal subjects (P=.04). This reduction in shortening was also seen in comparisons of septal and free wall %S (Table 3). Free wall %S was 12±8 in LVH subjects versus 20±5 in normal subjects (P<.0001), and septal %S was 13±9 in LVH subjects versus 18±4 in normal subjects (P<.004).

Overall, septal and free wall longitudinal shortening did not differ significantly in either group. However, there was a base-to-apex gradient in free wall shortening in normal subjects, with higher %S at more basal sites (P=.0001) that was not present in LVH (Table 4). Conversely, there was a reverse gradient in septal base-to-apex shortening, with higher %S at midventricular and apical sites in LVH (P<.0001) that was not present in normal subjects.

Analysis of septal longitudinal %S across the wall showed no differences among LV endocardial, midwall, and right ventricular endocardial shortening in either group. However, in the free wall, shortening was higher at endocardial sites in both normal (P=.01) and LVH (P=.04) subjects (Table 5). As expected, this transmural gradient was less in magnitude than that seen with circumferential shortening.

Linear regression analysis in LVH subjects showed no significant relations between segment shortening and LV mass index, relative wall thickness, age, or reported duration of hypertension. Since there was a systematic age difference between LVH subjects and normal subjects (mean age, 49 years in LVH subjects versus 29 years in normal subjects), we also compared subgroups of subjects below 41 years (LVH subjects, n=7; mean age, 34 years; control subjects, n=10; mean age, 29 years), selecting this cutoff to include a sufficient number of LVH subjects for comparison. The difference in circumferential %S between LVH and normal subjects in this subgroup was similar to that in the entire population and remained highly significant (Table 6). Thus, age differences cannot explain our results. There was no significant difference between mean %S in treated and untreated hypertensive patients.

**Discussion**

Left ventricular hypertrophy is a major adaptive response to chronic pressure overload and an important risk factor in patients with hypertension. However, controversy exists with respect to myocardial function in moderate hypertensive LV. The purpose of this study was to compare circumferential and longitudinal myocardial shortening in subjects with uncomplicated hypertensive LV and normal subjects using a new magnetic resonance tagging technique. Our results indicate that myocardial segment shortening in human subjects

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**Table 2. Mean Circumferential Percent Shortening in Normal Subjects and in Left Ventricular Hypertrophy Subjects**

<table>
<thead>
<tr>
<th>Segment Shortening ±SD (%)</th>
<th>Normal</th>
<th>LVH</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Region</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Anterior</td>
<td>26±12</td>
<td>21±11</td>
</tr>
<tr>
<td>Lateral</td>
<td>30±10</td>
<td>24±9</td>
</tr>
<tr>
<td>Inferior</td>
<td>31±11</td>
<td>19±10*</td>
</tr>
<tr>
<td>Septal</td>
<td>34±15</td>
<td>21±10*</td>
</tr>
<tr>
<td>P (ANOVA)</td>
<td>NS</td>
<td>.0003</td>
</tr>
<tr>
<td><strong>Level</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Basal</td>
<td>25±7</td>
<td>20±8</td>
</tr>
<tr>
<td>Midventricular</td>
<td>30±7†</td>
<td>22±4</td>
</tr>
<tr>
<td>Apical</td>
<td>33±4†</td>
<td>23±4</td>
</tr>
<tr>
<td>P (ANOVA)</td>
<td>.0002</td>
<td>NS</td>
</tr>
</tbody>
</table>

LVH indicates left ventricular hypertrophy.

*P<.05 vs lateral; †P<.05 vs basal.
TABLE 3. Mean Midwall Longitudinal Shortening in Normal Subjects and in Left Ventricular Hypertrophy Subjects

<table>
<thead>
<tr>
<th>Level</th>
<th>Segment Shortening ±SD (%)</th>
<th>f Test (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
<td>LVH</td>
</tr>
<tr>
<td>Basal</td>
<td>21±6</td>
<td>10±9</td>
</tr>
<tr>
<td>Midventricular</td>
<td>18±3</td>
<td>14±8</td>
</tr>
<tr>
<td>Apical</td>
<td>18±4</td>
<td>14±8</td>
</tr>
<tr>
<td>Wall</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal</td>
<td>18±4</td>
<td>13±9</td>
</tr>
<tr>
<td>Free</td>
<td>20±5</td>
<td>12±8</td>
</tr>
</tbody>
</table>

LVH indicates left ventricular hypertrophy.

with uncomplicated hypertensive LVH and normal LV pump function is depressed when compared with that found in normal subjects. Furthermore, in LVH, regional heterogeneity of segment shortening was more marked than in the normal left ventricle. Finding a generalized reduction in intramural segment shortening combined with normal pump function may at first seem paradoxical. However, geometric considerations alone may account for the apparent paradox. When LV diastolic wall thickness is increased by hypertrophy, less intramural percent segment shortening is necessary for the same absolute systolic wall thickening and resultant displacement of the endocardium.25 Pump function indices, which reflect only LV cavity emptying, may thus be insensitive to impaired myocardial performance in this setting.

The increased regional heterogeneity of circumferential segment shortening observed in hypertrophied left ventricle may reflect differences in regional geometry within the left ventricle, operating through the LaPlace effect. Heng et al26 have hypothesized that increased LV pressure could have differential effects on regional wall stress in different regions of normal left ventricles because of differences in local radii of curvature. Such regional heterogeneity of geometric determinants of wall stress could be more marked in hypertrophied ventricles. Alternatively, if myocyte orientation within the ventricular wall in pressure-overload hypertrophy differed from normal, reduced circumferential shortening and larger longitudinal and radial components could result. Examining regional midwall segment shortening in normal canine left ventricle using ultrasonic segment length gauges, Lew and LeWinter27 found greater circumferential than longitudinal shortening in the anterior wall but similar shortening in the two directions in the posterior walls. Subsequently, assessing finite strains in anterior and posterior ventricular walls, Villarreal and Lew28 found a preferential increase in end-systolic circumferential strain in the anterior wall and preferential increase in longitudinal strain in the posterior wall. Thus, altered myocardial fiber orientation in LVH could explain reduced segment shortening found in a single plane, either in a region or throughout the left ventricle. However, our data indicate that shortening is reduced in two orthogonal planes, making it unlikely that altered fiber orientation plays an important role in our results with respect to either regional heterogeneity or overall reduction in shortening in LVH.

Pharmacological effects could contribute to our findings. Antihypertensive agents with negative inotropic effects could have reduced segment shortening in LVH. However, there was no significant difference between mean %S in pharmacologically treated and untreated hypertensive subjects.

Increased afterload could account for depressed circumferential shortening in LVH subjects. However, both noninvasive and invasive studies of the geometric determinants of LV wall stress in untreated and treated hypertensive subjects with compensated LVH and normal ejection fraction have shown that hypertrophy is

TABLE 4. Mean Midwall Longitudinal Shortening From Base to Apex in Normal Subjects and in Left Ventricular Hypertrophy Subjects

<table>
<thead>
<tr>
<th>Level</th>
<th>Segment Shortening ±SD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Normal</td>
</tr>
<tr>
<td></td>
<td>Free Wall</td>
</tr>
<tr>
<td>Basal</td>
<td>25±5</td>
</tr>
<tr>
<td>Midventricular</td>
<td>17±3*</td>
</tr>
<tr>
<td>Apical</td>
<td>17±2*</td>
</tr>
<tr>
<td>P (ANOVA)</td>
<td>.0001</td>
</tr>
</tbody>
</table>

LVH indicates left ventricular hypertrophy.

*P<.05 basal vs midventricular and apical at the free wall in normal subjects.

TABLE 5. Mean Longitudinal Shortening at Free Wall Transmural Sites in Normal Subjects and in Left Ventricular Hypertrophy Subjects

<table>
<thead>
<tr>
<th>Segment</th>
<th>Segment Shortening ±SD (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal (n=57)</td>
<td>LVH (n=57)</td>
</tr>
<tr>
<td>Endocardial</td>
<td>20±7</td>
</tr>
<tr>
<td>Midwall</td>
<td>18±5</td>
</tr>
<tr>
<td>Epicardial</td>
<td>15±7*</td>
</tr>
<tr>
<td>P (ANOVA)</td>
<td>.01</td>
</tr>
</tbody>
</table>

LVH indicates left ventricular hypertrophy.

*P<.05 endocardial vs epicardial.
TABLE 6. Mean Circumferential Percent Shortening at Transmural Sites in Normal Subjects and in Left Ventricular Hypertrophy Subjects Under 41 Years

<table>
<thead>
<tr>
<th>Segment</th>
<th>Normal (n=10)</th>
<th>LVH (n=7)</th>
<th>t Test (P)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Endocardial</td>
<td>44±6</td>
<td>30±7</td>
<td>.0006</td>
</tr>
<tr>
<td>Midwall</td>
<td>30±6</td>
<td>21±8</td>
<td>.02</td>
</tr>
<tr>
<td>Epicardial</td>
<td>22±5</td>
<td>11±6</td>
<td>.002</td>
</tr>
</tbody>
</table>

LVH indicates left ventricular hypertrophy.

fully compensatory, so that estimates of mean midwall stress, a good index of afterload seen by the myocardium, are normal.3,5,13,29

Reduced preload could also result in reduced circumferential shortening in LVH. We did not directly measure hemodynamic determinants of myocardial preload in this study. However, previous invasive hemodynamic studies of hypertensive heart disease by others have not shown sufficient preload reduction to account for reduced segment shortening in mild hypertrophy.3,13 Furthermore, the principal potential mediator of reduced end-diastolic wall stress in LVH is an increase in the ratio of wall thickness to chamber radius, or h/r ratio. In our hypertensive group, there was no relation between h/r ratio and segment shortening results. The fact that we obtained similar results in the presence and absence of diuretic administration also makes a preload effect less likely.

Changes in myocardial perfusion in cardiac hypertrophy have been studied extensively.3,20,32 It is generally established that pressure-overload hypertrophy with normal pump function in animals and in humans is associated with normal myocardial perfusion at rest and impairment in coronary vascular reserve.31 Impaired perfusion with exercise may occur in the subendocardium in the setting of marked hypertrophy with impaired pump function.32,33 Since our studies were performed in the resting state and our hypertensive subjects had normal pump function and moderate hypertrophy, diminished myocardial perfusion is an unlikely explanation for the observed findings.

Mechanical tethering of myocytes or myocyte bundles by collagen or adjacent fibers or fiber bundles may occur within the ventricular wall and could become more marked within a hypertrophied LV wall, caused either by altered collagen matrix, as suggested by Weber et al.,34 or the increase in wall thickness itself. Such tethering could in turn account for the observed decrease in segment shortening. At present, no experimental methods are available for assessment of possible mechanical tethering within intact ventricular wall. However, the repeated demonstration of abnormal mechanical function in papillary muscles, trabeculae, and isolated myocytes from animal models of pressure overload suggest that mechanical tethering is unlikely to be the sole explanation for our observations.6,8-10,35

Numerous studies in small mammals provide evidence that pressure-overload hypertrophy leads to alterations in contractile function.6-10 Furthermore, decreases in coronary flow and myocardial oxygen consumption have been found.10 In larger mammals, depression of systolic function in pressure-overload hypertrophy has been less consistently demonstrated. Spann et al.36 demonstrated depressed myocardial function in pressure-overloaded cat right ventricles produced by pulmonary banding, but subsequent studies in similar models demonstrated gradual improvement over time.37,38 Recently, Dinda et al35 studied isolated myocytes from right ventricles of cats with pulmonary artery banding and found decreases in contractile function as well as in calcium transients. Sasayama et al36,40 demonstrated normal wall stress-diameter loops in dogs with LVH produced by sustained aortic constriction. However, using similar aortic banding techniques, Gaasch et al41 found statistically significant decreases in midwall shortening in “compensated” LVH dogs. Finally, Hittinger et al43 demonstrated significant differences in wall thickening in dogs with LVH from aortic banding compared with control dogs.

Prior studies in human subjects also have been inconsistent. Several have shown normal to supernormal indices of pump function in compensated hypertensive LVH.3,5,29 Our own echocardiographic studies have indicated that patients with LVH caused by hypertension and normal pump function have normal end-systolic stress and normal stress-shortening relations.42 However, Takahashi et al41 showed decreased contractile performance using the linear wall stress-diameter relation in hypertensive patients with marked LVH. Shimizu et al,43 using invasive hemodynamic and ventriculographic methods, reported depressed calculated midwall fractional shortening in hypertensive subjects with LVH and decreased calculated midwall circumferential stress using a modified ellipsoidal model with concentric two-shell geometry. It has been suggested that an explanation for the discrepancy between findings in large and small mammals may be the relative insensitivity of the prior methods used to evaluate systolic performance in larger animals.43 Until the advent of magnetic resonance tagging techniques, noninvasive methods were not available for determination of intramural segmental myocardial function in humans.

Alterations in contractile function often have a molecular basis in models of pressure-overload hypertrophy. In hearts of species that normally have significant amounts of V1 myosin isoenzymes, such as rabbit and rat, changes in myosin ATPase activity and isoenzyme pattern to V3 can be demonstrated early in response to pressure overload.44 In contrast, in V3-predominant species, such as human, pig, and dog, myosin isoenzyme alterations appear to be less important factors.45 Shifts in myosin light-chain isoforms and associated heavy-chain isoforms have been demonstrated in hypertensive, hypertrophied baboons.46,47 Altered creatinine kinase energetics have also been demonstrated in pressure-overload hypertrophy by Ingwall and others.56,48 Furthermore, Osbaken et al.,49 have recently demonstrated altered creatinine kinase kinetics in a canine model of chronic renovascular hypertension-induced hypertrophy. Abnormalities in calcium uptake, binding, transients, and calcium-ATPase of the sarcoplasmic reticulum have been demonstrated in hypertrophied animals and humans.35,51-54

The present study provides no data to support or refute the relevance of the potential mechanisms con-
considered above to our results. However, given the other studies cited, it does not appear likely that alterations in organ level physiology (loading and perfusion) or intramural tethering are the principal mechanisms at work. More fundamental changes in myocyte biology in hypertrophy may be more important, but few data are available in humans to support this view.

Our methods and results have important limitations. As with any new method, a need exists to consider the validity and the reliability of segmental shortening determinations derived from magnetic resonance tagging techniques. Conventional ECG-gated cardiac magnetic resonance images are constructed from data acquired over hundreds of cardiac cycles and many respiratory cycles. Such temporal averaging may be a source of error. Resolution is also a limiting factor for measurement of interstripe distances of 7 mm or less, with current pixel size of 1.88 mm (y-axis) by .94 mm (x-axis) interpolated to 0.88 mm². However, we have obtained data showing good correlations between circumferential segment shortening by magnetic resonance tagging and high-resolution implanted sonomicrometry crystals in canine acute myocardial infarction.55 Similar agreement with sonomicrometry for wall thickening has been reported using magnetic resonance tagging by Lima et al.56 Furthermore, intraobserver and interobserver reproducibility of our results are quite good.

The effect of through-plane cardiac motion on our results must also be considered. Because of through-plane motion, different myocardium is present in each image plane at end systole and end diastole. However, since the three-dimensional sets of stripe planes used are all orthogonal to the short-axis image plane, the initial stripe separations in the short-axis plane are uniform throughout the myocardium. Since the stripes reflect magnetic “labeling” of protons in the tissue, only myocardial shortening can change stripe separation at a later time in the cardiac cycle. Thus, the change from end-diastolic to end-systolic stripe separation is a valid measure of shortening in the myocardium found in the image plane at end systole, even though that myocardium may not have been imaged at all at end diastole.

The imaging protocols used for comparing circumferential segment shortening in normal subjects and LVH subjects also differed slightly. This resulted in a slightly larger potential error in timing end systole in normal subjects than in hypertensive subjects. However, such an error should bias results toward diminished shortening in normal subjects, whereas our results were opposite. Moreover, longitudinal shortening studies were performed with similar methods in both study groups, and results were comparable to those obtained for circumferential shortening. Thus, we believe the impact of this factor on our results is minimal. The cost and complexity of the MRI SPAMM imaging protocol and analysis precluded repeating studies of circumferential shortening in normal subjects with techniques identical to those used in LVH subjects.

This study is also limited by considerations relative to the study population. Echocardiograms were not available in normal control subjects, many of whom were imaged before this project was conceived. Furthermore, the length of the SPAMM MRI data acquisitions precluded additional MRI imaging for quantitation of LV mass, volume, and ejection fraction. Thus, the normality of our control subjects is substantiated mainly by historical information and the cine-MRI and SPAMM MRI images obtained. No quantitative statistical comparisons of ventricular anatomy, wall stress, and pump function between normal and LVH subjects were performed. However, echocardiographic normal values have been published extensively from many laboratories, including our own.18-20,42 Moreover, definitions of LVH were based on the extensive Framingham database.1,17 The normal and LVH groups studied also differed significantly in age (mean age of 29 years in normal subjects versus 50 years in LVH subjects). Several studies demonstrate a decline in LV pump function with age.57-59 We did not find a significant relation between age and %S in our patients, and subgroup analysis using data from the 7 LVH patients under age 41 years still showed a significant difference from normal subjects. Nonetheless, age effects require further evaluation.

We found no significant relations between circumferential shortening and LV mass index, relative wall thickness, age, or reported duration of hypertension. However, given sample size limitations and the limited range of variation of these variables in the hypertensive group, further evaluation of these issues is required. Treatment regimens were not evaluated because of sample size limitations and lack of randomization among treated groups. Finally, the definition of hypertrophy used in this study normalized LV mass for height, not weight or BSA. This approach, developed from the Framingham database,17 reflects the component of hypertrophy that is due to obesity per se as well as that attributable to hypertension. Since many hypertensive subjects are obese, omission of such individuals would have greatly limited the applicability of our findings. Fewer of our hypertensive subjects had hypertrophy when LV mass was normalized for BSA, probably because of the moderate hypertension and hypertrophy present in the group. These subjects did not differ in segmental function from other hypertensive subjects. However, given our limited sample size, potential differences between subgroups in the hypertensive population, including lean and obese subjects, require further assessment.

Conclusions

Circumferential and longitudinal myocardial shortening is depressed in patients with uncomplicated LVH caused by hypertension. The significance and etiologic mechanisms remain to be determined. However, it appears unlikely that pharmacological effects or alterations in myocardial loading or perfusion can account for these results. Thus, more fundamental alterations in cardiac myocyte function and composition may be present even in moderate human hypertensive hypertrophy. This study exemplifies the usefulness of magnetic resonance tagging in the investigation of hypertensive heart disease. This new noninvasive technique should be an important tool for evaluation of segmental myocardial function in other common cardiac diseases.

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