Left Ventricular Filling in Hypertrophic Cardiomyopathy: A Pulsed Doppler Echocardiographic Study

KATSU TAKENAKA, MD, ALI DABESTANI, MD, JULIUS M. GARDIN, MD, FACC, DANIEL RUSSELL, BS, SANDRA CLARK, AS, CCPT, ALICE ALLFIE, WALTER L. HENRY, MD, FACC

Orange, California

Abnormal left ventricular diastolic properties have been described in patients with hypertrophic cardiomyopathy. To evaluate the diastolic filling characteristics of the left ventricle in patients with this disease, pulsed Doppler echocardiography was used to study mitral flow velocity in 17 patients with hypertrophic cardiomyopathy (11 with and 6 without systolic anterior motion of the mitral valve) and 16 age-matched normal subjects. There were no statistically significant differences between patients with hypertrophic cardiomyopathy with and without systolic anterior motion with regard to ventricular septal thickness, left ventricular posterior wall thickness, left ventricular internal dimensions or the extent of hypertrophy evaluated by two-dimensional echocardiography.

Mitral regurgitation was detected by Doppler echocardiography in all 11 patients with and in 2 (33%) of the 6 patients without systolic anterior motion of the mitral valve. Early and late diastolic peak flow velocity, the ratio of late to early diastolic peak flow velocity and deceleration of early diastolic flow were measured from Doppler mitral flow velocity recordings. There were no statistically significant differences in these four indexes between the patients with systolic anterior motion and normal subjects. In contrast, the patients with hypertrophic cardiomyopathy without systolic anterior motion showed lower early diastolic peak flow velocity, higher ratio of late to early diastolic peak flow velocity and lower deceleration of early diastolic flow compared with the patients with systolic anterior motion and normal subjects, suggesting impaired left ventricular diastolic filling. These observed differences in mitral flow velocity between patients with hypertrophic cardiomyopathy with and without systolic anterior motion of the mitral valve may be explained by the more frequent occurrence of mitral regurgitation, which augments early diastolic left ventricular filling, or the less extensive myopathic process reported previously in patients with systolic anterior motion, rather than by differences in the extent of hypertrophy.

Methods

Study patients. Seventeen patients, 10 male and 7 female (age range 12 to 73 years, mean 34), were studied. The diagnosis of hypertrophic cardiomyopathy was based on echocardiographic demonstration of a septal to left ventricular posterior wall thickness ratio of greater than 1.3, a

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ventricular septal thickness of 20 mm or greater and a non-
dilated left ventricle in the absence of other acquired or congeneric heart disease.

The 17 patients with hypertrophic cardiomyopathy were
classified into two groups on the basis of M-mode echocardiographic findings of mitral valve motion. Eleven pa-
tients had an anterior leaflet of the mitral valve that made
contact with the interventricular septum in systole and were
grouped as having hypertrophic cardiomyopathy with sys-
tolic anterior motion of the mitral valve. In this group, there
were six male and five female patients (age range 16 to 54
years, mean 33). The remaining six patients had either no
or only minimal systolic anterior motion and were grouped
as having hypertrophic cardiomyopathy without systolic an-
terior motion of the mitral valve. There were four men or
boys and two women (age range 12 to 73 years, mean 37)
in this group. Nine patients (82%) in the group with and
four (67%) in the group without systolic anterior motion
were symptomatic (shortness of breath or chest pain, or
both). Five patients (45%) in the group with and two (33%)
in the group without systolic anterior motion were taking a
beta-adrenergic blocking drug (propranolol in six patients
and metoprolol in one patient) at the time of Doppler ex-
amination. No patient was taking a calcium channel blocker.

Sixteen normal subjects, 6 male and 10 female (age range
19 to 60 years, mean 38) served as the control group. They
had no clinical or echocardiographic evidence of cardiac
abnormality.

Echocardiographic studies. In the patients with hy-
pertrophic cardiomyopathy, five indexes were measured from

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Figure 1. Diastolic stop frame apical four chamber
view (upper panel) and apical long-axis view (lower
panel) from a normal subject. Sample volumes are
in the mitral orifice during diastole in both views.
Ao = aorta; LA = left atrium; LV = left ventricle;
RA = right atrium; RV = right ventricle.
Figure 2. Pulsed Doppler transmitral flow velocity tracing obtained from the apical position in a normal subject (37 year old woman) (left panel) and a patient with hypertrophic cardiomyopathy (HCM) with systolic anterior motion of the mitral valve (40 year old man) (right panel). DEF = deceleration of early diastolic flow in cm/s; PFVA = peak flow velocity during atrial systole in cm/s; PFVA/PFVE = ratio of peak flow velocity during atrial systole to peak flow velocity in early diastole; PFVE = peak flow velocity in early diastole in cm/s.

M-mode echocardiograms according to the methods described by Henry et al. (14): interventricular septal thickness (IVSth), left ventricular posterior wall thickness (LVPWth), left ventricular end-diastolic (LVDd) and end-systolic (LVDs) dimensions and left atrial dimension (all measured in millimeters). In addition, the ratio of ventricular septal thickness to left ventricular posterior wall thickness (IVSth/LVPWth), left ventricular percent fractional shortening (%FS) and the ratio of left ventricular wall thickness to end-diastolic dimension (Th/LVDd) were calculated as follows:

\[
%FS = \frac{[LVDd - LVDs] \times 100}{LVDd},
\]

\[
Th/LVDd = \frac{IVSth + LVPWth}{2 \times LVDd}.
\]

Two-dimensional echocardiographic hypertrophy point scores were determined using the point score system developed by Wigle et al. (15) to quantitate the extent of hypertrophy in patients with hypertrophic cardiomyopathy. In this system, the thickness of the basal ventricular septum (15 to 19, 20 to 24, 25 to 29 or > 30 mm) and the presence or absence of anterolateral wall extension are determined from the parasternal short-axis view at the level of the tips of the mitral leaflets. The length of septal involvement (basal one-third of septum, basal two-thirds of septum or whole septum) is evaluated from the apical four chamber view. The scores range from 1 to 10 points, 10 corresponding to the most extensive hypertrophy.

Doppler instrumentation and recording techniques. The ultrasound system used in this study combines a two-dimensional mechanical sector scanner with a range-gated Doppler flow velocity meter (Ultra Imager, Biosound Corp.) (16). The ultrasound frequencies of the transducers used were 3.5 and 2.25 MHz. Flow velocity signals and an electrocardiogram were recorded on a strip chart at an equivalent paper speed of 100 mm/s.

Subjects were examined in the left lateral position. A heat-sensitive respirometer was used to record the phase of respiration on the strip chart. The ultrasound transducer was placed on the cardiac apex to visualize the apical four chamber or apical long-axis view (Fig. 1). The sample volume was positioned in the left atrium to permit careful search for the systolic turbulent flow of mitral regurgitation. The diagnosis of mitral turbulent flow was made when early to mid-systolic or holosystolic turbulent flow was detected in the left atrium (17). The sample volume was then set in the mitral orifice on the atrial side at a level close to the tips of the mitral leaflets in diastole (Fig. 1). Because the angle between Doppler sampling direction and assumed direction of mitral blood flow was always less than 20° in this study, the error of blood flow velocity measurements caused by
Figure 4. Ratios of late diastolic to early diastolic peak mitral flow velocity (PFVA/PFVE) (left panel) and deceleration of early diastolic flow (DEF) measurements (right panel) for normal subjects (left columns) and patients with hypertrophic cardiomyopathy (HCM) (right columns). Symbols as in Figure 3.

this angle was less than 6%. Therefore, correction for the Doppler angle was not performed.

**Mitral flow measurements (Fig. 2).** Three mitral flow velocity indexes were measured: peak flow velocity in early diastole in centimeters per second, peak flow velocity during atrial systole in centimeters per second and deceleration of early diastolic flow in centimeters per square second (9). In addition, the ratio of peak flow velocity during atrial systole to peak flow velocity in early diastole was calculated. Measurements were made from the beat with the highest early diastolic peak flow velocity, in the expiratory phase of respiration when a respiration curve was available. Because we found no differences in mitral flow velocity measurements between the apical four chamber and apical long-axis views (18), the view that showed the best signal to noise ratio and least spectral dispersion was used for measurements. Peak flow velocities in early diastole and during atrial systole were measured at the midpoint of the Doppler flow velocity spectrum at the point of maximal blood flow velocity. Deceleration of early diastolic flow was measured as the slope of a straight line drawn through the peak of early filling flow velocity and a point at 50% of early diastolic peak flow velocity on the descending portion of the early filling flow velocity curve.

**Data analysis.** All results of this study were expressed as the mean ± 1 SD. Differences between two groups were tested by Student’s unpaired t test. Differences among three groups were tested by one-way analysis of variance, and significant differences between the groups were determined by the Scheffé test.

**Results**

All patients had normal sinus rhythm at the time of study. There were no statistically significant differences in the mean heart rate at the time of examination among normal subjects (66 ± 9 beats/min), patients with hypertrophic cardiomyopathy with systolic anterior motion of the mitral valve (64 ± 6 beats/min) and those without systolic anterior motion (69 ± 11 beats/min).

**Hypertrophic cardiomyopathy (Fig. 3 and 4).** When all 17 patients with hypertrophic cardiomyopathy (Fig. 2)
were considered together and their data compared with those from the 16 normal subjects, peak flow velocity in early diastole (45 ± 17 cm/s) was lower (p < 0.01) than the normal value (60 ± 9 cm/s) (Fig. 3). In contrast, peak flow velocity during atrial systole (40 ± 17 cm/s) in patients with hypertrophic cardiomyopathy was not significantly different from the normal value (38 ± 8 cm/s) (p > 0.05). The ratio of late to early diastolic peak flow velocity in patients with hypertrophic cardiomyopathy (0.99 ± 0.58) was higher than normal (0.66 ± 0.19) (p < 0.05) (Fig. 4). Deceleration of early diastolic flow (246 ± 137 cm/s²) was reduced (p < 0.01) in patients with hypertrophic cardiomyopathy compared with that in normal subjects (399 ± 110 cm/s²).

Comparison of hypertrophic cardiomyopathy with and without systolic anterior motion (Fig. 5 to 9). To gain further insight into the results, the 17 patients with hypertrophic cardiomyopathy were classified into those with and without systolic anterior motion (Fig. 5). In the 11 patients with systolic anterior motion, peak flow velocity in early diastole (53 ± 17 cm/s) (Fig. 6), peak flow velocity during atrial systole (34 ± 11 cm/s) (Fig. 7), the ratio of late to early diastolic peak flow velocity (0.69 ± 0.25) (Fig. 8) and deceleration of early diastolic flow (302 ± 133 cm/s²) (Fig. 9) were not significantly different from normal mean values (p > 0.05).

In the six patients without systolic anterior motion, peak flow velocity in early diastole (33 ± 10 cm/s) was lower (p < 0.01) (Fig. 6), but peak flow velocity during atrial systole (50 ± 22 cm/s) (Fig. 7) was not significantly different (p > 0.05) compared with mean values in normal subjects (Fig. 6 and 7). The ratio of late to early diastolic peak flow velocity (1.55 ± 0.63) was higher than normal (p < 0.01) (Fig. 8). Deceleration of early diastolic flow (144 ± 72 cm/s²) was lower in the patients without systolic anterior motion compared with data from the normal subjects (p < 0.01) (Fig. 9).

Mitr val regurgitation was detected by pulsed Doppler echocardiography in all 11 patients with systolic anterior motion (early to mid-systolic turbulence in 4 patients and holosystolic turbulence in 7). It was seen in 2 (33%) of the 6 patients without systolic anterior motion (early to mid-systolic turbulence in both patients).

There were no statistically significant differences (p > 0.05) between patients with hypertrophic cardiomyopathy with and without systolic anterior motion in the M-mode echocardiographic indexes or two-dimensional echocardiographic hypertrophy point scores except for left atrial dimension (Table 1).
Discussion

Left ventricular filling in hypertrophic cardiomyopathy. A number of indexes have been used to study the diastolic characteristics of the left ventricle in patients with hypertrophic cardiomyopathy. One of the most widely used has been the rate of early diastolic left ventricular filling, which has been obtained as the first derivative of the left ventricular volume curve (dV/dt). In previous studies of hypertrophic cardiomyopathy, contrast left ventriculography (2,19,20), radionuclide left ventriculography (8,11) or M-mode echocardiography (3-7,10) has been used to assess changes in left ventricular volume. However, the small size and irregular shape of the left ventricle in patients with hypertrophic cardiomyopathy create technical problems that may interfere with the accurate measurement of left ventricular size by either contrast ventriculography or M-mode echocardiography. In addition, the hypertrophied papillary muscles occupy a greater percentage of the small ventricular cavity of patients with hypertrophic cardiomyopathy (2,3).

Recently, measurement of mitral flow velocity by pulsed Doppler echocardiography has been reported (12,13) to be useful in assessing left ventricular diastolic filling characteristics. This measurement has been used because transmitral flow velocity obtained by pulsed Doppler echocardiography has been shown (9,12,13,20) to have a close relation with the rate of diastolic left ventricular filling (dV/dt) in the absence of aortic regurgitation or ventricular septal defect. Because Doppler measurements of mitral flow velocity are not likely to be affected by the irregular geometry of the left ventricle, they appear to be well suited for evaluating the left ventricular diastolic filling properties in patients with hypertrophic cardiomyopathy.

Several investigators (1,5,7,9,10) have reported a decrease in the rate of early diastolic filling in patients with hypertrophic cardiomyopathy. Kitabatake et al. (9) studied mitral flow in 13 patients with hypertrophic cardiomyopathy using pulsed Doppler echocardiography. They found a reduced peak flow velocity in early diastole, a slower deceleration of early diastolic flow and a normal peak flow velocity during atrial systole. These results are in accord with the mean values of the four mitral flow indexes in our total group of 17 patients with hypertrophic cardiomyopathy. Lorell et al. (10) also reported a reduction in the peak rate of early diastolic filling (dD/dt) using M-mode echocardiography. Although they did not classify their patients into those with and without a left ventricular outflow pressure gradient, their data showed that dD/dt was higher in patients with a gradient (95 ± 44 mm/s) than in patients without a gradient (55 ± 20 mm/s).

Other investigators (2-4,6,8,11,19,20) found no reduc-
The results of several previous echocardiographic studies of diastolic ventricular filling characteristics in patients with hypertrophic cardiomyopathy. These findings suggest that factors other than the extent of hypertrophy may be of importance in the differences in left ventricular wall thickness to end-diastolic dimension. Values are expressed as the mean ± 1 SD.

### Table 1. Indexes of Wall Thickness and Chamber Size in 17 Patients With Hypertrophic Cardiomyopathy

<table>
<thead>
<tr>
<th></th>
<th>IVS (mm)</th>
<th>LVPW (mm)</th>
<th>LVDd (mm)</th>
<th>LVDs (mm)</th>
<th>LAD (mm)</th>
<th>IVS/LVPW</th>
<th>%FS</th>
<th>Th/LVDd</th>
<th>Hypertrophy Point Scores</th>
</tr>
</thead>
<tbody>
<tr>
<td>HCM with SAM (n = 11)</td>
<td>28 ± 5</td>
<td>11 ± 3</td>
<td>43 ± 6</td>
<td>20 ± 4</td>
<td>49 ± 9*</td>
<td>2.6 ± 0.7</td>
<td>53 ± 8</td>
<td>0.46 ± 0.11</td>
<td>7.7 ± 1.1</td>
</tr>
<tr>
<td>HCM without SAM (n = 6)</td>
<td>23 ± 4</td>
<td>11 ± 3</td>
<td>38 ± 8</td>
<td>20 ± 7</td>
<td>40 ± 8</td>
<td>2.3 ± 0.9</td>
<td>50 ± 8</td>
<td>0.46 ± 0.13</td>
<td>7.2 ± 1.8</td>
</tr>
</tbody>
</table>

*p < 0.05 compared with the mean value in patients without systolic anterior motion of the mitral valve. %FS = percent fractional shortening of the left ventricle. HCM = hypertrophic cardiomyopathy; IVS = interventricular septal thickness; IVS/LVPW = ratio of ventricular septal thickness to left ventricular posterior wall thickness; LAD = left atrial dimension; LVDd = left ventricular end-diastolic dimension; LVDs = left ventricular end-systolic dimension; LVPW = left ventricular posterior wall thickness; SAM = systolic anterior motion of the mitral valve; Th/LVDd = ratio of left ventricular wall thickness to end-diastolic dimension.

**Extent of myopathic process.** A second factor is that there is a difference in the severity and extent of the microscopic myopathic process between patients with hypertrophic cardiomyopathy with and without left ventricular outflow obstruction (28,29). The microscopic abnormalities of myocardium were present in the ventricular septum but were either absent or rarely found in the left ventricular free wall of patients with obstructive hypertrophic cardiomyopathy. In contrast, microscopic myocardial abnormalities were extensively distributed throughout both the septum and free wall of patients with nonobstructive hypertrophic cardiomyopathy studied at necropsy even though, in these patients, the septum and free wall compared were thinner than in the group with obstruction. These observations are consistent with the concept that patients with nonobstructive hypertrophic cardiomyopathy whose left ventricular free wall is involved more extensively by the primary myopathic process have more abnormal diastolic filling characteristics compared with patients with obstructive hypertrophic cardiomyopathy whose free wall is less extensively involved by the myopathy.

**Mitral regurgitation.** A third factor that might have influenced our results is the effect of mitral regurgitation on diastolic left ventricular filling. Support for this possibility comes from the experience of Hatle and Angelsen (30), who found that a high left atrial-left ventricular pressure gradient in early diastole due to an increased V wave in the left atrium in patients with mitral regurgitation increases the velocity of forward mitral flow in early diastole. This increase in transmural flow velocity appears to be limited to early diastole as a result of rapid equalization of pressure. Animal experiments (31) also have shown that peak early diastolic filling rate is strongly influenced by the left atrial pressure at the onset of filling as well as by the left ventricular relaxation rate. In addition, early diastolic mitral flow or peak left ventricular filling rate has been shown (32,33) to be increased in animals and patients with pure mitral regurgitation. In patients with outflow obstruction, mitral regurgitation has been reported to be frequently present, whereas it is uncommon in patients without obstruction (17,34–42). Kinoshita et al. (17) recently reported, using...
Doppler echocardiography, that mitral regurgitation is usually present in patients with hypertrophic cardiomyopathy and systolic anterior motion, but is mild or absent in patients without systolic anterior motion. In addition, they found that the extent of the early to mid-systolic turbulence into the left atrium was less than that of the holosystolic turbulence, suggesting a milder degree of mitral regurgitation.

In the present study, holosystolic turbulence was found only in patients with systolic anterior motion. Thus, the difference in the frequency and severity of mitral regurgitation between patients with and without systolic anterior motion may be the cause of the differences in the early diastolic Doppler flow measurements between the two groups of patients with hypertrophic cardiomyopathy. In other words, the presence of mitral regurgitation may mask abnormal diastolic function in patients with hypertrophic cardiomyopathy and systolic anterior motion.

Age. Although age has been reported to affect mitral flow velocity (43,44), this factor is not likely to explain the difference in Doppler measurements because the two groups of patients were similar in age.

Conclusions. It appears that, among patients with hypertrophic cardiomyopathy, those without systolic anterior motion of the mitral valve have abnormal left ventricular filling in diastole whereas diastolic filling values are not significantly different from normal in those with systolic anterior motion. Although the cause of the differences in the early diastolic flow measurements between patients with and without systolic anterior motion is unclear, such differences exist and may prove to be of importance to the understanding of the pathophysiology of patients with hypertrophic cardiomyopathy.

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References


31. Ishida Y, Mesner JS, Tsujikoka K, et al. Peak rapid filling rate may not reflect left ventricular relaxation properties when left atrial pressure compensates for changes in loading conditions (abstr). Circulation 1984;70(suppl II):II-349.


