Left ventricular diastolic function assessed using Doppler tissue imaging in patients with hypertrophic cardiomyopathy: relation to symptoms and exercise capacity

Y Matsumura, P M Elliott, M S Virdee, P Sorajja, Y Doi, W J McKenna

Background: Conventional Doppler indices of left ventricular diastolic function do not correlate with symptoms or exercise capacity in patients with hypertrophic cardiomyopathy, because of their dependence on loading conditions. Diastolic mitral annular velocity measured using Doppler tissue imaging has been reported to be a preload independent index of left ventricular diastolic function.

Objective: To determine the relation between diastolic annular velocities combined with conventional Doppler indices and symptoms or exercise capacity in hypertrophic cardiomyopathy.

Methods: 85 patients with hypertrophic cardiomyopathy and 60 normal controls were studied. Diastolic mitral annular velocities, transmitral left ventricular filling, and pulmonary venous velocities were measured.

Results: Early diastolic velocities at lateral and septal annulus were lower in patients with hypertrophic cardiomyopathy than in controls (lateral Ea: 10 (3) v 18 (4) cm/s, p < 0.0001; septal Ea: 7 (2) v 12 (3) cm/s, p < 0.0001). Unlike conventional Doppler indices alone, transmitral early left ventricular filling velocity (E) to lateral Ea ratio correlated inversely with peak oxygen consumption (r = −0.42, p < 0.0001). Patients in New York Heart Association (NYHA) class III had a higher transmitral E to lateral Ea ratio (12.0 (4.6)) than those in NYHA class II (7.6 (3.1), p < 0.005) or class I (6.6 (2.6), p < 0.001).

Conclusions: Early diastolic mitral annular velocities are reduced in patients with hypertrophic cardiomyopathy. Unlike conventional Doppler indices alone, the transmitral E to lateral Ea ratio correlates with NYHA functional class and exercise capacity.

Methods

Patients

Eighty five consecutive patients (age 10–72 years; mean (SD) age, 38 (14) years; 56 male, 29 female) with hypertrophic cardiomyopathy were studied prospectively. The diagnosis of hypertrophic cardiomyopathy was based on the echocardiographic demonstration of unexplained left ventricular hypertrophy. Patients were selected by the following criteria: normal sinus rhythm; heart rate < 90 beats/min at the time of Doppler tissue imaging study; absence of moderate to severe mitral regurgitation; left ventricular ejection fraction > 50%; and normal left ventricular cavity dimensions. Cardioactive drug treatment was discontinued for at least five half lives before Doppler tissue imaging studies, except in 22 patients who continued to take amiodarone. The study cohort was compared with 60 age matched controls (age 9–69 years; mean (SD) age 37 (16) years; 30 male, 30 female) without signs or symptoms of heart disease.

Echocardiography

Imaging was done in the left lateral decubitus position using an Acuson 128 XP/10 (Mountain View, California, USA) with a multifrequency transducer equipped with Doppler tissue imaging software. Standard views for M mode and cross sectional studies were obtained. Standard techniques were employed for sizing the left ventricle and left atrium. The magnitude and distribution of left ventricular hypertrophy were assessed in the parasternal short axis plane by dividing the ventricle into four regions: anterior septum, posterior septum, lateral wall, and posteri wall. Wall thickness was measured at the levels of the...
mitral valve and the papillary muscles in each of the four segments. Maximum left ventricular wall thickness was defined as the greatest thickness in any single segment. A semi-quantitative point score of left ventricular hypertrophy (Wigle score) was calculated using a previously described method. Peak left ventricular outflow tract flow velocity was determined using continuous wave Doppler, and pressure gradients were calculated using the simplified Bernoulli equation. Transmitral left ventricular filling velocities at the tips of the mitral valve leaflets were obtained from the apical four chamber view using pulsed wave Doppler echocardiography. The transmitial left ventricular filling signal was traced manually and the following variables derived: peak velocity of early (E) and late (A) filling, E wave deceleration time, and E/A ratio. Isovolumic relaxation time was determined using continuous wave Doppler echocardiography in accordance with standard methodology. Pulmonary venous flow signals were recorded from the right upper pulmonary vein using pulsed Doppler with colour Doppler guidance. Peak velocity of systolic, diastolic, and atrial reversal signals were recorded.

Doppler tissue imaging
From the apical four chamber view, a 10 mm Doppler sample volume was placed at the lateral and septal margins of the mitral annulus. Care was taken to align the echo image so that the annular motion was parallel to the Doppler tissue imaging cursor. A Doppler velocity range of 30 to 30 cm/s was selected using the lowest wall filter settings and the minimum optimal gain. Doppler tissue imaging velocities were recorded at a sweep speed of 100 mm/s and stored on S-VHS videotape for later playback and analysis. All measurements were made in three cardiac cycles and averaged by one investigator. The following measurements were made from the Doppler tissue imaging recordings: early (Ea) and late (Aa) diastolic velocities, and deceleration time derived by linear extrapolation of Ea to baseline. The ratio of transmitial early left ventricular filling velocity (E) to early diastolic Doppler tissue imaging velocity of the mitral annulus (transmitial E/Ea) was calculated. This ratio has been reported to correlate with left ventricular filling pressure. Metabolic exercise testing
Eighty three patients underwent symptom limited exercise tests on an upright bicycle ergometer using a ramp protocol with simultaneous respiratory gas analysis and blood pressure recording. All exercise tests were performed within three to five days of the echocardiographic examination. Peak oxygen consumption (PVO2) was defined as the mean of the highest values obtained over the last 10 seconds of exercise.

Statistical analysis
Data are expressed as mean (SD). Group data were compared using the unpaired Student’s t test or analysis of variance (ANOVA) with Fisher’s PLSD test where appropriate. Linear regression analysis was used to compare continuous variables. A probability value of p < 0.05 was considered significant.

RESULTS
Patient characteristics
Forty three patients (51%) had dyspnoea (New York Heart Association (NYHA) functional class II (n = 37) and III (n = 6)), 24 (28%) had exertional chest pain, 32 (38%) had a history of unexplained syncope, and 19 (22%) had a history of palpitations. Nineteen patients (22%) had a family history of hypertrophic cardiomyopathy, and 23 (27%) had a family history of hypertrophic cardiomyopathy and premature (< 40 years old) sudden cardiac death. Maximum left ventricular wall thickness was 21 (4) mm (range 15–36 mm). The pattern of left ventricular hypertrophy was asymmetrical in 69 patients (81%), concentric in 12 (14%), and distal in three (4%). Left ventricular hypertrophy was confined to the posterior ventricular septum in one patient (1%). Twenty three patients (27%) had a resting left ventricular outflow tract gradient of more than 30 mm Hg.

Conventional echocardiographic findings in hypertrophic cardiomyopathy and controls
Conventional echocardiographic variables in patients with hypertrophic cardiomyopathy and controls are shown in Table 1. There were no significant differences in mean transmitial E and A wave velocities between patients and controls. Technically adequate pulmonary venous flow signals were detected in 56 patients with hypertrophic cardiomyopathy and in 48 controls. Peak systolic and atrial reversal velocities of pulmonary venous flow were higher in patients with hypertrophic cardiomyopathy than in controls. Peak diastolic velocity of pulmonary venous flow was lower in patients with hypertrophic cardiomyopathy than in controls.

<table>
<thead>
<tr>
<th>Variable</th>
<th>HCM</th>
<th>Control</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cross sectional echocardiography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV dimensions</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End diastole (mm)</td>
<td>42 [5]</td>
<td>45 [4]</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>End systole (mm)</td>
<td>23 [5]</td>
<td>27 [4]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Fractional shortening (%)</td>
<td>46 [8]</td>
<td>41 [5]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Thickness</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>IVS (mm)</td>
<td>18 [5]</td>
<td>9 [1]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Posterior wall (mm)</td>
<td>11 [3]</td>
<td>9 [1]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>LA dimension (mm)</td>
<td>42 [6]</td>
<td>33 [5]</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Doppler echocardiography</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LV filling flow</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transmitral E (cm/s)</td>
<td>71 (21)</td>
<td>75 (15)</td>
<td>NS</td>
</tr>
<tr>
<td>Transmitral A (cm/s)</td>
<td>55 (23)</td>
<td>49 (13)</td>
<td>NS</td>
</tr>
<tr>
<td>E/A ratio</td>
<td>1.5 (0.7)</td>
<td>1.6 (0.6)</td>
<td>NS</td>
</tr>
<tr>
<td>E deceleration time (ms)</td>
<td>215 (69)</td>
<td>145 (30)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Isovolumic relaxation time (ms)</td>
<td>90 (19)</td>
<td>72 (12)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Pulmonary venous flow</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Peak systolic velocity (cm/s)</td>
<td>56 (14)</td>
<td>50 (11)</td>
<td>&lt;0.05</td>
</tr>
<tr>
<td>Peak diastolic velocity (cm/s)</td>
<td>43 (10)</td>
<td>51 (14)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Peak atrial systolic velocity (cm/s)</td>
<td>30 (16)</td>
<td>21 (6)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are mean (SD). A, late left ventricular filling velocity; E, early left ventricular filling velocity; HCM, hypertrophic cardiomyopathy; IVS, interventricular septum; LA, left atrial; LV, left ventricular.
Representative examples of lateral and septal mitral annular velocities measured using Doppler tissue imaging and transmitral left ventricular filling velocities in patients with hypertrophic cardiomyopathy (HCM) and controls are shown in fig 1. Mitral annular velocities in patients with hypertrophic cardiomyopathy and controls are shown in table 2. Early diastolic annular velocities were lower in patients with hypertrophic cardiomyopathy than in controls.

Doppler tissue imaging findings versus left ventricular hypertrophy, symptoms, and exercise capacity in hypertrophic cardiomyopathy

Although conventional Doppler indices did not correlate with the Wigle score, lateral Ea and septal Ea correlated with the Wigle score (lateral Ea: \( r = -0.35, p < 0.005 \); septal Ea: \( r = -0.31, p < 0.005 \)).

None of the conventional Doppler indices correlated with \( \text{PVO}_2 \). Lateral Ea was weakly correlated with \( \text{PVO}_2 \) (lateral Ea: \( r = 0.28, p < 0.05 \)). There was no correlation between septal Ea and \( \text{PVO}_2 \). The transmitral E to lateral Ea ratio was inversely correlated with \( \text{PVO}_2 \).

<table>
<thead>
<tr>
<th>Variable</th>
<th>HCM</th>
<th>Control</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lateral mitral annulus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lateral Ea (cm/s)</td>
<td>10 (3)</td>
<td>18 (4)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Lateral Aa (cm/s)</td>
<td>11 (4)</td>
<td>12 (3)</td>
<td>NS</td>
</tr>
<tr>
<td>Lateral Ea deceleration time (ms)</td>
<td>117 (38)</td>
<td>84 (19)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Transmitral E/lateral Ea</td>
<td>7.4 (3.2)</td>
<td>4.3 (1.0)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Septal mitral annulus</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Septal Ea (cm/s)</td>
<td>7 (2)</td>
<td>12 (3)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Septal Aa (cm/s)</td>
<td>8 (3)</td>
<td>10 (2)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Septal Ea deceleration time (ms)</td>
<td>123 (30)</td>
<td>101 (18)</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>Transmitral E/septal Ea</td>
<td>12.2 (9.6)</td>
<td>6.3 (1.4)</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Values are mean (SD).

Aa, late diastolic velocity of mitral annulus; DTI, Doppler tissue imaging; Ea, early diastolic velocity of mitral annulus; HCM, hypertrophic cardiomyopathy; transmitral E/lateral Ea, ratio of transmitral early left ventricular filling velocity to early diastolic velocity of lateral mitral annulus; transmitral E/septal Ea, ratio of transmitral early left ventricular filling velocity to early diastolic velocity of septal mitral annulus.
correlated with $P_{VO2}$ ($r = -0.42, p < 0.0001$). This inverse correlation was seen in patients with and without left ventricular outflow tract obstruction ($r = -0.40, p < 0.05$; and $r = -0.40, p < 0.005$, respectively).

Three groups of the patients were distinguished: those with $P_{VO2}$ (ml/kg/min) $> 30$, those with $P_{VO2}$ between 20 and 30, and those with $P_{VO2} < 20$. The patients with $P_{VO2} < 20$ had a significantly higher transmitral $E$ to lateral $E_a$ ratio than those with $P_{VO2} > 30$ ($8.6 (3.7)$ $\pm$ $5.9 (2.2)$; $p < 0.005$) (fig 2). Patients in NYHA class III had a higher transmitral $E$ to lateral $E_a$ ratio ($12.0 (4.6)$) than those in NYHA class II ($7.6 (3.1)$; $p < 0.005$) or class I ($6.6 (2.6)$; $p < 0.0001$) (fig 3).

**DISCUSSION**

This study shows that early diastolic mitral annular velocities measured using Doppler tissue imaging are reduced in patients with hypertrophic cardiomyopathy. Unlike conventional Doppler indices alone, the transmitral $E$ to lateral $E_a$ ratio correlated with NYHA functional class and exercise capacity.

**Conventional echocardiographic assessment of diastolic function in hypertrophic cardiomyopathy**

Many invasive pressure studies have shown that patients with hypertrophic cardiomyopathy have a spectrum of diastolic abnormalities, including increased mean left atrial and left ventricular end diastolic pressures, prolonged time constant of relaxation, and increased effective chamber and myocardial stiffness. Most clinical studies have used non-invasive methods to assess diastolic function—in particular, pulsed wave Doppler interrogation of transmitral left ventricular filling velocities. Some previous studies showed that characteristic findings based on mitral inflow patterns are lower $E$ wave velocity, prolonged $E$ wave deceleration time, higher $A$ wave velocity, and an $E/A$ ratio $< 1.0$, which are clearly differentiated from normal inflow patterns in normal subjects. However, the overlap is considerable. Recent studies showed that most of the patients had a normal (or pseudonormalised) mitral inflow pattern.

An invasive study produced some important results: the mitral inflow velocity curve variables and the mean left atrial pressure were not related in patients with hypertrophic cardiomyopathy. Because of the complexity of the multiple and interrelated factors that determine left ventricular diastolic filling, the mitral inflow velocity curve is strongly influenced by factors independent of diastolic properties, such as loading conditions and age. The limitations of conventional Doppler indices in patients with hypertrophic cardiomyopathy are illustrated in this study by the fact that, with the exception of $E$ deceleration time and

**Diastolic mitral annular velocities and clinical features in hypertrophic cardiomyopathy**

Previous studies in hypertrophic cardiomyopathy have shown that the transmural diastolic velocity gradient in the left ventricular posterior wall is reduced. Our study confirms that early diastolic mitral annular velocities are reduced in patients with hypertrophic cardiomyopathy. Lateral $E_a$ and septal $E_a$ correlated with the WIGLE score. Nevertheless, the correlation coefficients were modest, suggesting that diastolic longitudinal dysfunction is also determined by factors independent of severe hypertrophy, such as myocardial fibrosis, myocyte disarray, and diastolic ventricular interaction.

Our study also shows that, unlike conventional Doppler indices alone, the transmitral $E$ to lateral $E_a$ ratio correlates with NYHA functional class. It also shows that this ratio correlates with $P_{VO2}$ in patients with hypertrophic cardiomyopathy with and without left ventricular outflow tract obstruction. As it has been shown recently that left ventricular filling pressures in patients with hypertrophic cardiomyopathy correlate with the transmitral $E$ to lateral $E_a$ ratio, these observations support the long-held belief that dyspnoea and exercise intolerance in patients with hypertrophic cardiomyopathy are related largely to raised left atrial pressures.

On the other hand, previous studies have emphasised that raised left atrial pressure is not a major determinant of exercise capacity in hypertrophic cardiomyopathy. Lele and colleagues suggest that stroke volume augmentation—which is determined by exercise diastolic filling characteristics—is the major determinant of peak exercise capacity in affected individuals. However, there is a limitation in that the study patients were not classified according to the presence or absence of left ventricular outflow obstruction.

Chikamori and colleagues assessed the relation of exercise capacity to indices of resting systolic and diastolic function using a nuclear technique in patients with and without a left ventricular outflow gradient. Their study suggests that there are different mechanisms of exercise limitation in hypertrophic cardiomyopathy: in patients with a left ventricular outflow gradient at rest, the main determinants of exercise limitation were impaired left ventricular and left atrial systolic performance; in those without a gradient, however, diastolic function at rest was a more important factor in the limitation of exercise performance.

A recent study showed that maximum oxygen consumption correlated with the left atrial fractional shortening, which is closely related to left ventricular end diastolic pressure at rest. These results support the role of left ventricular diastolic dysfunction at rest in limiting the exercise capacity of patients with hypertrophic cardiomyopathy. It still seems to be controversial whether or not left ventricular diastolic pressure and function at rest are major determinants of exercise capacity in hypertrophic cardiomyopathy, and the true mechanism of exercise limitation remains unclear. In our present study, the correlation between the transmitral $E$ to lateral $E_a$ ratio and $P_{VO2}$ was relatively modest, suggesting that other factors such as a reduced stroke volume response, ventilation/perfusion mismatch, and abnormal peripheral oxygen utilisation also influence exercise.
Doppler tissue imaging in hypertrophic cardiomyopathy

251

limitation. Further studies are needed to determine the exact mechanisms of impaired exercise tolerance.

Conclusions

Early diastolic mitral annular velocities are reduced in patients with hypertrophic cardiomyopathy and are related to the magnitude of left ventricular hypertrophy. The transmitral E to lateral Ea ratio correlates with NYHA functional class and exercise capacity.

ACKNOWLEDGMENTS

MSV was supported by a grant from the British Heart Foundation. We thank Gillian C Smith, Brian Mist, Annie O'Donoghue, and Shaughan Dickie for their assistance with this report. This study was presented in part at the 16th Annual Congress of the American College of Cardiology, New Orleans, March 1999.

Authors’ affiliations

Y Matsumura, P M Elliott, M S Virdee, P Soroja, W J McKenna, Department of Cardiological Sciences, St George’s Hospital Medical School, London SW17, UK

Y Doi, Department of Medicine and Geriatrics, Kochi Medical School, Kochi, Japan

REFERENCES


Left ventricular diastolic function assessed using Doppler tissue imaging in patients with hypertrophic cardiomyopathy: relation to symptoms and exercise capacity

Y Matsumura, P M Elliott, M S Virdee, P Sorajja, Y Doi and W J McKenna

Heart 2002 87: 247-251
doi: 10.1136/heart.87.3.247

Updated information and services can be found at:
http://heart.bmj.com/content/87/3/247

These include:

References
This article cites 36 articles, 8 of which you can access for free at:
http://heart.bmj.com/content/87/3/247#BIBL

Email alerting service
Receive free email alerts when new articles cite this article. Sign up in the box at the top right corner of the online article.

Topic Collections
Articles on similar topics can be found in the following collections

- Hypertension (3006)
- Hypertrophic cardiomyopathy (314)
- Drugs: cardiovascular system (8842)
- Clinical diagnostic tests (4779)

Notes

To request permissions go to:
http://group.bmj.com/group/rights-licensing/permissions

To order reprints go to:
http://journals.bmj.com/cgi/reprintform

To subscribe to BMJ go to:
http://group.bmj.com/subscribe/