Left Ventricular Filling in Dilated Cardiomyopathy: Relation to Functional Class and Hemodynamics

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Left ventricular systolic function does not correlate well with functional class in patients with dilated cardiomyopathy. To determine whether the correlation is better with Doppler indexes of left ventricular diastolic function, 34 patients with dilated cardiomyopathy (M-mode echocardiographic end-diastolic dimension >60 mm, fractional shortening <25%, increased E point-septal separation) were studied. Patients were classified into two groups according to functional class. Group 1 consisted of 16 patients in New York Heart Association functional class I or II; group 2 included 18 patients in functional class III or IV. Left ventricular dimensions, fractional shortening, left ventricular mass, meridional end-systolic wall stress, peak early and late transmitral filling velocities and their ratio, isovolumetric relaxation period and time to peak filling rate were computed from pulsed wave Doppler and M-mode echocardiograms and calibrated carotid pulse tracings. Right heart catheterization was performed in 20 of 34 patients.

No differences were observed between groups with regard to age, gender distribution, heart rate, blood pressure and M-mode echocardiographic-derived indexes of systolic function. Peak early filling velocity (72 ± 13 versus 40 ± 10 cm/s, p < 0.001) was higher and atrial filling fraction (27 ± 4% versus 46 ± 8%, p < 0.001) was lower in group 2 than in group 1. The ratio of early to late transmitral filling velocities was higher in group 2 patients (2.3 ± 0.5 versus 0.7 ± 0.2, p < 0.001). The duration of the isovolumetric relaxation period (53 ± 16 versus 85 ± 14 ms, p < 0.001) and the time to peak filling rate (121 ± 24 versus 154 ± 17 ms, p < 0.01) were significantly shorter in group 2.

All these differences occurred at a time when mean pulmonary capillary wedge pressure (31 ± 10 versus 11 ± 5 mm Hg, p < 0.01) was higher, stroke index was lower (23 ± 10 versus 12 ± 4 ml/beat per m², p < 0.001) and the grade of mitral regurgitation (2.4 ± 0.4 versus 1.1 ± 0.2, p < 0.001) was larger in group 2 patients.

Peak early transmitral filling velocities correlated significantly with mean pulmonary capillary wedge pressure (r = 0.86, n = 20) and the magnitude of mitral regurgitation (r = 0.74, n = 34) and inversely with stroke index (r = -0.61, n = 20). A strong correlation (r = 0.81) was also observed between mean pulmonary capillary wedge pressure and magnitude of mitral regurgitation.

Thus, in patients with dilated cardiomyopathy, diastolic transmitral filling of the left ventricle is determined by left atrial pressure and the severity of mitral regurgitation. Moreover, it correlates better with functional class than do indexes of left ventricular systolic function.

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Reduced functional capacity is a cardinal symptom of chronic congestive heart failure. The severity of functional impairment, however, correlates poorly with the degree of left ventricular systolic dysfunction (1). In addition, an increasing number of patients with signs and symptoms of congestive heart failure but without evidence of left ventricular systolic dysfunction are being recognized (2). These discrepancies have emphasized the importance of diastolic events in this setting and shifted the interest from systolic to diastolic left ventricular dysfunction.

Diastolic abnormalities are common in patients with dilated cardiomyopathy. Impaired left ventricular relaxation and abnormal diastolic left ventricular distensibility are well documented in the course of congestive heart failure (3). Yet, the correlation between diastolic dysfunction and the symptoms in patients with dilated cardiomyopathy remains to be defined. Recent studies (4) have shown the utility of

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Doppler echocardiography in assessing left ventricular diastolic filling. Indexes of diastolic function obtained with this technique correlate well and are probably superior to those obtained by contrast (5) or radionuclide (6,7) angiography.

The purpose of this study was to determine whether the diastolic left ventricular filling pattern assessed by pulsed wave Doppler echocardiography differs between symptomatic and asymptomatic patients with dilated cardiomyopathy despite a similar degree of left ventricular systolic dysfunction.

Methods

Study group. Thirty-four patients (30 men, 4 women, mean age 53 ± 14 years, range 32 to 75) with dilated cardiomyopathy were studied. Dilated cardiomyopathy was diagnosed by M-mode echocardiographic demonstration of a left ventricular end-diastolic dimension >60 mm, a left ventricular fractional shortening <25% and an increased E point–septal separation in the absence of primary valvular disease. Two-dimensional echocardiography revealed a dilated nonhypertrophic left ventricle with diffuse hypokinesia or akinesia in all patients; none had dyskinetic left ventricular wall motion or a parietal aneurysm. The presumptive causes of dilated cardiomyopathy are listed in Table 1.

Patients were further classified with respect to their functional status (according to the classification of the New York Heart Association). Sixteen patients (group 1: 14 men, 2 women, mean age 50 ± 7 years, range 36 to 64) were asymptomatic or only mildly symptomatic and were, therefore, considered to be in functional class I or II. The remaining 18 (group 2: 16 men, 2 women, mean age 57 ± 15 years, range 32 to 75) were symptomatic at rest or with mild exertion and were considered to be in functional class III or IV. Informed consent was given by all patients.

Instrumentation. M-mode, two-dimensional and pulsed wave Doppler echocardiographic examinations were performed with a Toshiba SSH 65A ultrasound imager, using a 3.5 or a 2.5 MHz wide-angle phased-array transducer with 48 channels. All examinations were recorded on videotape (Panasonic NV 8500), and calculations were made directly on the video screen by computerized planimetry utilizing a trackball. Carotid pulse tracings were obtained and recorded simultaneously on an Elema Schoenander polygraph at a paper speed of 50 mm/s. Patients were examined in the left lateral position, and all were in sinus rhythm at the time of examination.

M-mode echocardiographic measurements. Recordings were obtained from the left parasternal view, and measurements were made according to the recommendations of the American Society of Echocardiography (8). In addition to the usual variables and indexes of systolic function, left ventricular (LV) mass (9) and meridional end-systolic wall stress (ESSm [g/cm²]) (10) were calculated, using the following equations:

\[
LV\ mass = \left[ \left( \frac{[LVEDD + IVSth + PWth]^3}{4 \times PWth} \right) - LVEDD^3 \right] \times 1,055 - 14
\]

\[
ESSm = \left( 1.33 \times P_{ES} \times LVEDS \right) / \left( 4 \times PWth \left[ 1 + PWth/LVEDS \right] \right)
\]

where IVSth (cm) = interventricular septal thickness, LVEDD (cm) = left ventricular end-diastolic diameter, LVEDS (cm) = left ventricular end-systolic diameter, P_{ES} (mm Hg) = aortic pressure at end-systole and PWth (cm) = posterior wall thickness.

Carotid pulse tracings were used to obtain end-systolic pressure (11). Calibration was performed with assignment of systolic cuff pressure to the peak and diastolic cuff pressure to the nadir of the tracings. Linear interpolation to the level of the incisura was then performed to estimate end-systolic pressure.

Analysis of transmitral flow velocity profile. Pulsed wave Doppler recordings at the level of the mitral anulus were obtained from the apical four chamber view to study left ventricular filling. For each Doppler profile analyzed, the following variables were obtained: peak early (E) and late (A) transmitral filling velocities (cm/s) and their ratio, the time-velocity integral of the E and A waves (cm) and their ratio, the atrial filling fraction (calculated by dividing the component time-velocity integral by the total time-velocity integral), the acceleration and deceleration of the E and A waves (defined as the slope of the ascending and descending limb of these waves) and deceleration half-time (from peak velocity E to 71% of its initial value). The isovolumetric relaxation period (from aortic valve closure to beginning of transmitral flow) and the time to peak filling rate (from aortic valve closure to peak early transmitral filling velocity) were also computed.

Mitr al regurgitation. This was diagnosed and graded semiquantitatively (from 1 to 4) by Doppler color flow mapping as previously described (12).

Right heart catheterization. Ten patients from each group underwent right heart catheterization with fluid-filled catheters (7F thermodilution Swan-Ganz catheter, Edwards Lab-
oratories) connected to a Statham P23 ID strain gauge. Cardiac output was determined by either the Fick method or thermodilution. All hemodynamic data were obtained within 12 h of the Doppler echocardiographic study.

**Doppler estimation of cardiac output and stroke volume.** Continuous wave Doppler recordings at the level of the aortic valve were obtained from the apical five-chamber view to calculate stroke volume (13). Cross-sectional area of the aortic orifice was calculated from the maximal separation of the aortic cusps on the M-mode echocardiogram, assuming a circular orifice. Stroke volume was calculated by multiplying the total velocity-time integral by the aortic valve area. Patients with an abnormal aortic valve or mild aortic regurgitation, or both (n = 3), were excluded from this determination.

**Systolic pulmonary artery pressure.** This was estimated by application of the modified Bernoulli equation on the maximal tricuspid regurgitant flow velocity, whenever possible (14).

**Inter- and intraobserver variability.** Mean interobserver variability (and mean percent difference) was assessed for the determination of selected Doppler echocardiographic measurements: peak early transmitial filling velocity 3.4 cm/s (4.5%), range 1 to 10 cm/s; peak late (atrial) transmitial filling velocity 1.6 cm/s (3.6%), range 0 to 3 cm/s; E/A ratio 0.05 (2.1%), ratio 0.01 to 0.07; atrial filling fraction 2% (6.8%), range 1% to 3%; isovolumetric relaxation period 4.6 ms (6.4%), range 2 to 7 ms; and time to peak filling rate 3.6 ms (2.8%), range 1 to 6 ms. Mean intraobserver variability (and mean percent difference) were assessed for the determination of the same variables; peak early transmitial filling velocity 1.2 cm/s (1.9%), range 0 to 2 cm/s; peak late (atrial) transmitial filling velocity 1.6 cm/s (3.9%), range 0 to 4 cm/s; E/A ratio 0.03 (1.5%), range 0.02 to 0.05; atrial filling fraction 1% (3.8%), range 0% to 5%, isovolumetric relaxation period 1.8 ms (2.7%), range 0 to 5 ms; and time to peak filling rate 3.6 ms (2.7%), range 0 to 6 ms.

**Statistical analysis.** Values are expressed as mean values ± SD. Three to five consecutive beats were analyzed and averaged for each M-mode and Doppler measurement. Comparisons between the two groups were made with the unpaired Student’s t test, the Mann-Whitney test or the chi-square test for unpaired data, where appropriate. Relations between the different Doppler and hemodynamic variables were assessed by linear regression analysis. Statistically significant differences were defined as p < 0.05.

**Results**

Results are summarized in Tables 2 and 3. There were no differences in age, gender distribution, heart rate and arterial blood pressure between the two groups.

**M-mode echocardiographic data.** There were no differences between the two groups in most M-mode echocardiographic variables. However, left atrial dimension was significantly higher (53 ± 6 versus 41 ± 7 mm, p < 0.005) and left ventricular ejection time was significantly shorter (220 ± 60 versus 280 ± 30 ms, p < 0.05) in group 2. A prominent B notch on the M-mode echocardiogram of the mitral valve was also observed more frequently in group 2 patients (17 of 18 versus 3 of 16, p < 0.01).

**Transmitial filling dynamics.** Figure 1 illustrates representative transmitial Doppler velocity recordings obtained from a typical patient from each group. The mean values for the measured Doppler variables are listed in Table 2. Peak E velocities and the corresponding time-velocity integrals were significantly higher (72 ± 13 versus 40 ± 10 cm/s, p < 0.001) (Fig. 2) and peak A velocities (and the corresponding time-velocity integrals) were lower (31 ± 9 versus 57 ± 13 cm/s, p < 0.001) in group 2 patients compared with group 1. These differences in the time distribution of transmitial diastolic inflow resulted in a higher ratio of the peak velocities (and time-velocity integrals) in group 2 (2.3 ± 0.5 versus 0.7 ± 0.2, p < 0.001) (Fig. 3).

**The duration of the isovolumetric relaxation period (53 ± 16 versus 85 ± 14 ms, p < 0.001) and the time to peak filling rate (121 ± 24 versus 154 ± 17 ms, p < 0.01) were also significantly shorter in group 2. Marked differences in the slope of the descending limb of the E wave were observed**

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**Table 2. Clinical and Echocardiographic Data in 34 Patients**

<table>
<thead>
<tr>
<th></th>
<th>Group 1 (n = 16)</th>
<th>Group 2 (n = 18)</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical data</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Age (yr)</td>
<td>50 ± 7</td>
<td>57 ± 15</td>
<td>NS</td>
</tr>
<tr>
<td>HR (beats/min)</td>
<td>73 ± 22</td>
<td>87 ± 20</td>
<td>NS</td>
</tr>
<tr>
<td>BP (mm Hg)</td>
<td>97 ± 11</td>
<td>98 ± 15</td>
<td>NS</td>
</tr>
<tr>
<td><strong>M-mode echocardiography</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>LVEDD (mm)</td>
<td>68 ± 9</td>
<td>74 ± 9</td>
<td>NS</td>
</tr>
<tr>
<td>FS (%)</td>
<td>19 ± 4</td>
<td>17 ± 5</td>
<td>NS</td>
</tr>
<tr>
<td>Mass (g)</td>
<td>327 ± 76</td>
<td>374 ± 90</td>
<td>NS</td>
</tr>
<tr>
<td>E (cm/s)</td>
<td>40 ± 10</td>
<td>72 ± 13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AFF (%)</td>
<td>46 ± 8</td>
<td>27 ± 4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/A</td>
<td>0.73 ± 0.2</td>
<td>2.3 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td><strong>Doppler echocardiography</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>SI (ml/m²)</td>
<td>38 ± 6</td>
<td>23 ± 5</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>RV/RA (mm Hg)</td>
<td>11.1 ± 0.2</td>
<td>2.4 ± 0.4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>IVRP (ms)</td>
<td>85 ± 14</td>
<td>53 ± 16</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>tPFR (ms)</td>
<td>154 ± 17</td>
<td>121 ± 24</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>E (cm/s)</td>
<td>40 ± 10</td>
<td>72 ± 13</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>AFF (%)</td>
<td>46 ± 8</td>
<td>27 ± 4</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>E/A</td>
<td>0.73 ± 0.2</td>
<td>2.3 ± 0.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>

**AFF = atrial filling fraction; BP = mean blood pressure; E = peak early transmitial filling velocity; E/A = ratio of early to late transmitial peak velocities; ESS = meridional end-systolic wall stress; FS = fractional shortening; HR = heart rate; h/R = thickness/radius ratio; IVRP = isovolumetric relaxation period; LVEDD = left ventricular end-diastolic dimension; MR = mitral regurgitation; SI = stroke index; tPFR = time to peak filling rate; RV/RA = systolic tricuspid pressure gradient.**
Mitral regurgitation. Mitral regurgitation was detected in all 34 patients by Doppler color flow mapping. However, it was mild in each group 1 patient (mean grade 1.1 ± 0.2) and moderate to important in most group 2 patients (mean grade 2.4 ± 0.4). This difference was statistically significant (p < 0.001).

Hemodynamic findings (Table 3). Right heart catheterization was carried out in 20 patients (10 from each group) at a time close to the echographic study. Mean capillary wedge pressure (31 ± 10 versus 11 ± 5 mm Hg, p < 0.001) and mean pulmonary artery pressure (42 ± 7 versus 19 ± 6 mm Hg, p < 0.001) were significantly higher in group 2 patients compared with group 1. Cardiac index and stroke index were lower in group 2 patients (respectively, 2.042 ± 727 versus 3.021 ± 582 ml/min per m², p < 0.001 and 23 ± 10 versus 38 ± 5 m/min per m², p < 0.001). In addition to these invasive hemodynamic data, cardiac output and estimates of systolic pulmonary pressure were obtained by Doppler recording in all patients. A close correlation between Doppler and invasive determinations was found in the subgroup of patients who underwent both investigations (r = 0.87, standard error of the estimate (SEE) = 300 ml, p < 0.001 for cardiac output; r = 0.91, SEE = 6 mm Hg, p < 0.001 for systolic pulmonary pressure).

Figure 1. A, Representative pulsed wave Doppler tracings from a typical patient from each group. B, A schematic representation of the transmitral velocity profile of each patient. Note the shorter isovolumetric relaxation period, the higher early filling velocity and the smaller atrial contribution to left ventricular filling in the patient from group 2 (right). IVRP = isovolumetric relaxation period; MVO = mitral valve opening; NYHA = New York Heart Association functional class.
Discussion

The results of our study indicate that highly symptomatic patients with dilated cardiomyopathy (functional class III or IV) show marked differences in left ventricular filling dynamics compared with asymptomatic or mildly symptomatic (functional class I or II) patients despite a similar degree of left ventricular systolic dysfunction. These differences (higher early diastolic filling velocity, reduced atrial filling fraction and shorter isovolumetric relaxation period and time to peak filling rate in group 2) were related to the magnitude of mitral regurgitation, left atrial pressure and stroke volume, suggesting that left ventricular filling pressures and volumes play a major role in early diastolic left ventricular filling.

Determinants of left ventricular filling dynamics. The major determinant of left ventricular early diastolic filling is the instantaneous left atrial to left ventricular pressure difference during early diastole (15,16). Recent combined hemodynamic and Doppler flow studies (17) across the mitral valve, demonstrated a close correlation between peak atrioventricular pressure gradient and peak acceleration of transmitral early inflow and its corresponding peak velocity. In

Table 4. Correlation Coefficients Between Doppler and Hemodynamic Data

<table>
<thead>
<tr>
<th></th>
<th>PCWP* (mm Hg)</th>
<th>PAP* (mm Hg)</th>
<th>RV/RA* (mm Hg)</th>
<th>MR†</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVRT (ms)</td>
<td>-0.71</td>
<td>-0.72</td>
<td>-0.80</td>
<td>-0.72</td>
</tr>
<tr>
<td>E wave (cm/s)</td>
<td>0.86</td>
<td>0.84</td>
<td>0.89</td>
<td>0.74</td>
</tr>
<tr>
<td>E/A</td>
<td>0.94</td>
<td>0.94</td>
<td>0.89</td>
<td>0.81</td>
</tr>
<tr>
<td>AFF (%)</td>
<td>-0.82</td>
<td>-0.80</td>
<td>-0.89</td>
<td>-0.79</td>
</tr>
<tr>
<td>MR</td>
<td>0.81</td>
<td>0.83</td>
<td>0.82</td>
<td></td>
</tr>
</tbody>
</table>

*a = 20 studies; †n = 23 studies; ‡n = 34 studies. Abbreviations as in Tables 2 and 3.

a significant positive correlation between peak early mitral inflow velocity and mean pulmonary capillary wedge pressure (r = 0.86), mean pulmonary artery pressure (r = 0.84) and systolic tricuspid pressure gradient (r = 0.89). A significant inverse correlation was observed between peak early transmitral filling velocity and forward stroke volume (r = -0.61). Peak E wave also correlated significantly with the magnitude of mitral regurgitation (r = 0.74).

Atrial filling fraction. There was a significant inverse correlation between atrial filling fraction and mean pulmonary capillary wedge pressure (r = -0.82).

Mitral regurgitation. The severity of mitral regurgitation correlated strongly with mean pulmonary capillary wedge pressure (r = 0.82), mean pulmonary artery pressure (r = 0.83) and systolic tricuspid pressure gradient (r = 0.82).

Ischemic versus nonischemic cardiomyopathy. Six of the 16 group 1 patients and 6 of the 18 group 2 patients had nonischemic cardiomyopathy (Table 5). No difference between subgroups was observed, either for transmitral filling dynamics or hemodynamic findings.
Figure 4. Ratio of early to late transmitral filling velocities (E/A) (A), E wave amplitude (B) and atrial filling fraction (C) closely correlated with mean pulmonary capillary wedge pressure (PCWP) in 20 patients. The linear regression equations are given and illustrated along with standard error of the estimate (SEE) and correlation coefficient ($r$).

contrast, the deceleration rate was more related to the magnitude of the pressure reversal (17). Many factors, often acting in opposite ways, influence this instantaneous pressure gradient. These factors include the left ventricular relaxation rate (18), early diastolic left ventricular chamber distensibility (19), left atrial compliance (20) and left atrial pressure at the time of mitral valve opening (namely, the pressure crossover) (18,21). The net effect on early diastolic left ventricular filling will depend on the relative interplay and importance of each of these factors.

The following hypothesis can be proposed on the basis of present data. In asymptomatic or mildly symptomatic patients with dilated cardiomyopathy (our group I patients) and no significant mitral regurgitation, left atrial pressure is normal or low at rest (22). When left atrial pressure is normal (or low), the main determinant of early transmitral inflow appears to be the left ventricular relaxation rate (23). Initially, when relaxation is altered, as is often the case in cardiomyopathy (3), there is reduced early filling, a delay in mitral valve opening (prolonged isovolumetric relaxation period) and slower dissipation of the atrioventricular (AV) pressure gradient (18). Because early diastolic filling is reduced, the contribution of atrial systole to left ventricular filling increases, as a compensatory mechanism to maintain stroke volume.

Conversely, when left atrial pressure increases, the early diastolic AV pressure gradient and, consequently, the early filling velocity tend to increase and return toward a more “normal” or even “supernormal” pattern, despite the presence of altered relaxation. Furthermore, when atrial pressure is markedly elevated, as it was in the majority of our group 2 patients, left ventricular pressure rises rapidly to a plateau at the end of early diastolic filling (with reversal of the AV pressure gradient), resulting in an abrupt cessation of transmitral inflow, a rapid deceleration of transmitral flow velocity and, sometimes, diastolic mitral regurgitation. This abnormal filling pattern, resembling a restrictive pattern, is thought to be at the origin of the $S_3$ sound in patients with cardiomyopathy (24). It is also associated with a marked reduction in the duration of the isovolumetric relaxation period and with

Table 5. Doppler and Hemodynamic Findings in Ischemic and Nonischemic Subgroups

<table>
<thead>
<tr>
<th></th>
<th>Group 1</th>
<th></th>
<th>Group 2</th>
<th></th>
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</thead>
<tbody>
<tr>
<td></td>
<td>No.</td>
<td>IVRP (ms)</td>
<td>E Wave (cm/s)</td>
<td>E/A</td>
</tr>
<tr>
<td>Ischemic</td>
<td>10</td>
<td>84 ± 10</td>
<td>42 ± 10</td>
<td>0.7 ± 0.2</td>
</tr>
<tr>
<td>Nonischemic</td>
<td>6</td>
<td>88 ± 21</td>
<td>36 ± 8</td>
<td>0.6 ± 0.2</td>
</tr>
<tr>
<td>Ischemic</td>
<td>12</td>
<td>54 ± 16</td>
<td>75 ± 12</td>
<td>2.3 ± 0.6</td>
</tr>
<tr>
<td>Nonischemic</td>
<td>6</td>
<td>51 ± 16</td>
<td>65 ± 12</td>
<td>2.1 ± 0.3</td>
</tr>
</tbody>
</table>

There were no significant differences between patients with ischemic or nonischemic cardiomyopathy. Abbreviations as in Tables 2 and 3.
decreased atrial filling fraction, perhaps as a consequence of atrial systolic failure or elevated left atrial afterload.

Far from being static and permanent once installed, these different filling patterns should be regarded as a dynamic continuum that may change depending on loading conditions and progression of the underlying disease. Recent observations by Valantine et al. (25) support this hypothesis. They enrolled nine severely symptomatic patients (functional class III) with dilated cardiomyopathy and a left ventricular filling pattern resembling a restrictive pattern in a 6 month therapeutic trial with metoprolol. After completion of the trial, marked improvement in functional capacity, ejection fraction and pulmonary pressure was noted, together with significant modifications in the transmitral inflow pattern (that is, marked prolongation in the duration of the isovolumetric relaxation period and deceleration time and slight decrease in early filling velocity).

Influence of mitral regurgitation of transmitral filling dynamics. The contribution of mitral regurgitation to our findings deserves some comment. Previous studies have reported that mitral regurgitation can result in increased transmitral flow (16) and inflow velocities (5). In the present study, as in the report of Takenaka et al. (26), a strong correlation was observed between peak early diastolic transmitral inflow velocities and the magnitude of mitral regurgitation, detected by Doppler color flow mapping. Bhatia et al. (27), however, failed to demonstrate any significant relation between the transmitral inflow pattern and either the presence or magnitude of mitral regurgitation in 54 patients with dilated cardiomyopathy. One explanation for these discrepancies may be that the volumetric importance of mitral regurgitation is not an independent determinant of early diastolic filling.

There is, indeed, increasing evidence that mitral regurgitation affects left ventricular filling, more through the increase in left atrial pressure that accompanies the regurgitation than through the volumetric importance of the regurgitation. Keren et al. (28-30) showed that in the absence of mitral regurgitation, left atrial pressure usually decreases during ventricular systole because of both left atrial relaxation (28,29) and systolic caudal displacement of the AV junction (30). This decrease generates a pressure gradient between the pulmonary veins and the left atrium and contributes to atrial refilling, despite only slight changes in left atrial pressure. In patients with dilated cardiomyopathy, Keren et al. (30) reported that left ventricular dysfunction was associated with disturbed left atrial filling from the pulmonary veins through both altered left atrial relaxation (long-standing left atrial enlargement and hypertrophy) and reduced systolic mitral anulus motion. Nevertheless, in the absence of significant mitral regurgitation, forward systolic pulmonary venous flow usually persisted, indicating normal left atrial depressurization during ventricular systole. In contrast, the development of significant mitral regurgitation impaired the systolic phase of pulmonary venous flow, so that all atrial filling occurred during ventricular diastole. These findings suggest that the development of mitral regurgitation in patients with dilated cardiomyopathy is associated with a substantial increase in left atrial pressure, so that the normal systolic forward pulmonary venous flow return is abolished. This may help to explain the deleterious effects of functional mitral regurgitation in patients with dilated cardiomyopathy.

In the present study, a significant correlation was observed between the severity of mitral regurgitation and estimates of left atrial pressure (pulmonary capillary wedge pressure), suggesting that mitral regurgitation could have triggered the increase in left atrial pressure in our patients. It is noteworthy that the majority of group 2 patients had significant mitral regurgitation (grade >2), whereas most group 1 patients had only minimal mitral regurgitation. It is tempting to attribute the higher left ventricular filling pressures and filling velocities as well as the severity of symptoms in group 2 patients to the presence of more significant mitral regurgitation.

Study limitations. The lack of invasive measurement of left atrial or pulmonary capillary wedge pressure in some patients could be seen as a significant limitation to the present study. However, we attempted to evaluate the pulmonary artery pressure noninvasively by using continuous wave Doppler echocardiography in those patients for whom invasive data were not available. By application of the modified Bernoulli equation on maximal tricuspid regurgitant flow velocities, this method was reported (14) to correlate closely with invasive determinations of right ventricular systolic pressure, which is also our experience. In the absence of primary pulmonary disease or long-standing postcapillary pulmonary hypertension, marked discrepancies between pulmonary artery pressure and left atrial pressure are uncommon. Thus, we consider the noninvasive assessment of pulmonary artery pressure to be reliable and, to some extent, indicative of the left ventricular filling pressures.

A second possible limitation is that mitral inflow velocities measured by pulsed wave Doppler ultrasound do not directly translate into transmitral volume flow rate. The instantaneous transmitral flow volume is the product of the instantaneous transmitral flow velocity and the instantaneous mitral anulus cross-sectional area, which is known to vary throughout diastole. Nevertheless, significant correlations between transmitral filling velocities (and derived flow volume using a constant value for mitral anulus area measured on two-dimensional echocardiograms) and angiographic measurements of instantaneous volume flow variations have been reported (5), indicating that the transmitral flow velocity profile accurately reflects the pattern of left ventricular filling.

Clinical implications. The assessment of the left ventricular filling pattern by pulsed wave Doppler echocardiography may play an important role in the evaluation and follow-up of patients with dilated cardiomyopathy. The
prevalence of altered relaxation and decreased left ventricular distensibility is quite high in this group of patients. Hence, the pattern of transmitral filling can be regarded as indicative of the left ventricular filling pressures. Patients with reduced early filling, a prolonged isovolumetric relaxation period and increased atrial filling fraction are likely to have normal or low filling pressures and to be asymptomatic or mildly symptomatic. Those patients with normal or increased early filling, a short isovolumetric relaxation period, a relatively small atrial contribution to left ventricular filling and significant mitral regurgitation are likely to have elevated left atrial pressures and more severe symptoms.

Conclusions. In patients with dilated cardiomyopathy, the diastolic transmitral filling pattern appears to correlate well with functional status. Moreover, it provides important information regarding the level of left ventricular filling pressures. Further prospective studies seem to be warranted to evaluate the role and efficacy of serial measurements in assessing the natural history of this disease and the effects of therapy.

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References


