Quantitative Assessment of Left Ventricular Diastolic Stiffness in Man

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SUMMARY
An approach to the quantitative assessment of left ventricular (LV) diastolic stiffness in man has been developed utilizing strip-chart recordings of simultaneous ultrasonic LV dimensions, LV pressure, and electrocardiogram (ECG). In 23 patients without regional abnormalities of contraction, LV pressure, and LV internal diameter (D = distance between endocardial surfaces of LV posterior wall and septum at the plane of the mitral valve) were determined at the onset (P1, D1) and peak (P2, D2) of left atrial mechanical systole. In addition, left ventricular volumes, V1 and V2, were calculated from D1 and D2 using a regression formula for end-diastolic volume previously determined from biplane angiographic studies. This allowed calculation of ΔP/ΔD and ΔP/ΔV associated with the "a" wave of the LV pressure trace, and these ratios were utilized as measures of LV stiffness late in diastole.

Patients with LV hypertrophy by standard ECG criteria had much greater late diastolic stiffness (11 patients, ΔP/ΔD = 6.1 ± 1.1 mm Hg/mm, ΔP/ΔV = 1.0 ± 0.2 mm Hg/cc) than those without LV hypertrophy (12 patients, ΔP/ΔD = 1.8 ± 0.2 mm Hg/mm, ΔP/ΔV = 0.29 ± 0.04 mm Hg/cc, P < 0.001 for each ratio).

Comparison of the stiffness ratios showed significant variation among patients with different disease states. Thus, late diastolic stiffness was highest in patients with aortic stenosis (three patients, ΔP/ΔD = 8.9 ± 2.9 mm Hg/mm, ΔP/ΔV = 1.5 ± 0.5 mm Hg/cc), lowest in mitral stenosis (four patients, ΔP/ΔD = 1.5 ± 0.5 mm Hg/mm, ΔP/ΔV = 0.23 ± 0.06 mm Hg/cc), and intermediate in patients with aortic regurgitation (three patients, ΔP/ΔD = 4.8 ± 0.7 mm Hg/mm, ΔP/ΔV = 0.83 ± 0.12 mm Hg/cc) and mitral regurgitation (three patients, ΔP/ΔD = 3.2 ± 0.7 mm Hg/mm, ΔP/ΔV = 0.5 ± 0.1 mm Hg/cc).

It is concluded that the quantitative evaluation of LV diastolic stiffness obtained by this approach correlates well with the presence or absence of LV hypertrophy and with the underlying pathophysiology.

Additional Indexing Words:
LV pressure-volume relations LV compliance LV hypotrophy Elasticity LV stiffness LV distensibility

DIASTOLIC stiffness of the left ventricle (LV) is recognized to be a major determinant, along with myocardial contractile state, of left ventricular filling pressure and chamber size. Although studies have delineated the influence of a number of variables on left ventricular diastolic stiffness in experimental animals,1-5 little is known about this important property of the left ventricle in either normal man or patients with heart disease.6-9

Perhaps the major impediment to the study of LV diastolic stiffness in man has been the technical difficulty associated with simultaneous measurement of LV pressure and volume throughout diastole. The recent demonstration that pulsed ultrahigh-frequency sound waves can be successfully employed to monitor LV internal dimensions,10 and that those dimensions can be utilized in the accurate calculation of LV chamber volume11-13 has opened the possibility of a fresh approach to the study of diastolic pressure-volume relations in the human heart.
This report describes an approach to the assessment of LV diastolic stiffness in man, utilizing high-speed strip-chart recordings of simultaneous LV pressure and ultrasonically determined LV internal diameter.

**Methods and Materials**

Twenty-three patients undergoing complete right and left heart catheterization for diagnostic purposes formed the study population. All patients were in sinus rhythm, and diagnostic and hemodynamic data for each patient are detailed in Table 1. Patients were classified as to the presence (group A) or absence (group B) of electrocardiographic criteria for LV hypertrophy, based on examination of a 12-lead electrocardiogram for each patient and application of standard criteria for LV hypertrophy.

Catheterization was carried out in the fasting state, following diazepam premedication (5-10 mg im). Brachial arteriotomy and retrograde left heart catheterization were performed with standard no. 8 French catheters in 14 patients, and with high-fidelity micro-manometer-tipped catheters (Statham SF-1 or Miller Mikro-Tip) in nine patients. All pressures were recorded on an Electronics for Medicine DR-12 recorder. Cardiac output was determined by both Fick and indicator dilution techniques in all patients. LV cineangiography was performed in each study (single-plane RAO in all patients, and additional LAO projection in three patients), and patients with regional abnormalities of LV contraction were excluded. Selective coronary cineangiography (Sones' technic) was performed in seven patients.

Immediately following cardiac output determination, but prior to angiography, a simultaneous photographic strip-chart recording of ECG, LV pressure, and ultrasonically determined LV septal and posterior wall motion (recorded with Smith-Kline Instruments Co. Eksoline-20 ultrasonoscope interfaced with the Electronics for Medicine recorder via an Electronics for Medicine UDA interface channel) was obtained at 100 mm/sec paper speed with 0.02-sec time lines. LV septal and posterior wall motion in a plane immediately below the mitral valve was obtained as previously described. High-quality recordings with clear delineation of posterior wall and septal endocardial surfaces could be obtained in approximately 70% of all studies, and only patients in whom high-quality recordings were obtained are included in this report. Thus, the 23 patients described represent a selected study population, derived from a total of 32 patients in whom this study was attempted.

**Theoretic Considerations and Calculations**

Pressure-geometry relations in early diastole may well represent a summation of physiologic properties, including incomplete ventricular relaxation, viscous and inertial properties of the ventricular myocardium, and true ventricular elastic properties. Because of the complexity which would necessarily be involved in analysis of such early diastolic pressure-geometry relations, it was decided to examine only late diastolic pressure-volume relations, which could more reasonably be interpreted as primarily reflecting true ventricular elastic properties. In this regard it was decided to examine the ventricular pressure and diameter increments associated with left atrial systole, and to compare

![Figure 1](http://circ.ahajournals.org/)

**Figure 1**

Photographic strip-chart recording of simultaneous echocardiogram, left ventricular pressure (LVP) and its first derivative, and ECG for a representative patient (R.C.). Actual record (left) is shown in traced form (right) where the technic of experimental measurement is illustrated. Distances between the endocardial surfaces of LV posterior wall and septum are shown as lines AB and CD at the onset and peak of left atrial systole, respectively. Corresponding LV pressures at the onset and peak of left atrial systole are shown as P1 and P2. These points and lines are defined in relation to the P wave of the electrocardiogram, as discussed in the text.

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## Summary of All Patient Data

<table>
<thead>
<tr>
<th>Pt</th>
<th>Age (yr)/Sex</th>
<th>Diagnosis</th>
<th>CO (liters/min)</th>
<th>HR (beats/min)</th>
<th>LVEDP (mm Hg)</th>
<th>LVEDV (cc)</th>
<th>ΔD (mm)</th>
<th>ΔV (cc)</th>
<th>ΔP (mm Hg)</th>
<th>ΔP/ΔD (mm Hg/mm)</th>
<th>ΔP/ΔV (mm Hg/cc)</th>
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<tbody>
<tr>
<td>1.</td>
<td>JM 50/M</td>
<td>AS</td>
<td>6.6</td>
<td>82</td>
<td>16</td>
<td>251</td>
<td>1.9 ± 0.2</td>
<td>11.2 ± 0.3</td>
<td>10.7 ± 0.3</td>
<td>5.7 ± 0.3</td>
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<td>AT 46/F</td>
<td>AS</td>
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<td>72</td>
<td>20</td>
<td>176</td>
<td>2.1 ± 0.3</td>
<td>12.7 ± 1.9</td>
<td>15.8 ± 0.7</td>
<td>6.5 ± 0.4</td>
<td>1.06 ± 0.07</td>
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<td>RB 53/M</td>
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<td>67</td>
<td>28</td>
<td>219</td>
<td>1.1 ± 0.1</td>
<td>6.4 ± 0.4</td>
<td>14.6 ± 0.7</td>
<td>2.5 ± 0.1</td>
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<td>4.</td>
<td>WH 62/M</td>
<td>AR</td>
<td>5.5</td>
<td>71</td>
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<td>305</td>
<td>1.5 ± 0.2</td>
<td>9.1 ± 1.3</td>
<td>9.0 ± 1.4</td>
<td>5.9 ± 0.2</td>
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<td>199</td>
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<td>9.0 ± 0.5</td>
<td>5.2 ± 0.2</td>
<td>3.4 ± 0.2</td>
<td>0.60 ± 0.02</td>
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<td>6.</td>
<td>OW 18/F</td>
<td>AR</td>
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<td>111</td>
<td>52</td>
<td>348</td>
<td>7.0 ± 0.6</td>
<td>39.2 ± 2.3</td>
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<td>0.90 ± 0.02</td>
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<td>MR, MS</td>
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<td>92</td>
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<td>246</td>
<td>1.9 ± 0.2</td>
<td>11.2 ± 0.9</td>
<td>7.5 ± 0.4</td>
<td>4.0 ± 0.2</td>
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<td>209</td>
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<td>1.9 ± 0.1</td>
<td>0.33 ± 0.01</td>
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<td>1.3 ± 0.1</td>
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<td>CAD</td>
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<td>92</td>
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<td>14.1 ± 1.6</td>
<td>14.3 ± 0.8</td>
<td>6.1 ± 0.4</td>
<td>1.0 ± 0.1</td>
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<td>PH 26/M</td>
<td>VSD</td>
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<td>91</td>
<td>21</td>
<td>343</td>
<td>1.4 ± 0.02</td>
<td>8.5 ± 1.1</td>
<td>11.5 ± 2.6</td>
<td>10.5 ± 1.0</td>
<td>1.8 ± 0.2</td>
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<td>20</td>
<td>268</td>
<td>2.3</td>
<td>13.5</td>
<td>12.1</td>
<td>6.1</td>
<td>1.0</td>
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<tr>
<td>SEM</td>
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<td></td>
<td>±0.4</td>
<td>±0.4</td>
<td>±19</td>
<td>±0.5</td>
<td>±2.8</td>
<td>±2.6</td>
<td>±1.1</td>
<td>±0.2</td>
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</table>

### Group A: LVH

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<tr>
<th>Pt</th>
<th>Age (yr)/Sex</th>
<th>Diagnosis</th>
<th>CO (liters/min)</th>
<th>HR (beats/min)</th>
<th>LVEDP (mm Hg)</th>
<th>LVEDV (cc)</th>
<th>ΔD (mm)</th>
<th>ΔV (cc)</th>
<th>ΔP (mm Hg)</th>
<th>ΔP/ΔD (mm Hg/mm)</th>
<th>ΔP/ΔV (mm Hg/cc)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>MM 36/F</td>
<td>MS</td>
<td>3.8</td>
<td>64</td>
<td>6</td>
<td>196</td>
<td>1.9 ± 0.2</td>
<td>11.4 ± 1.0</td>
<td>2.7 ± 0.2</td>
<td>1.4 ± 0.2</td>
<td>0.25 ± 0.04</td>
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<td>2.</td>
<td>RT 58/F</td>
<td>MS</td>
<td>4.7</td>
<td>76</td>
<td>5</td>
<td>190</td>
<td>4.8 ± 0.2</td>
<td>27.8 ± 1.2</td>
<td>2.2 ± 0.1</td>
<td>0.5 ± 0.0</td>
<td>0.08 ± 0.00</td>
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<td>3.</td>
<td>BF 40/F</td>
<td>MS</td>
<td>4.2</td>
<td>88</td>
<td>9</td>
<td>92</td>
<td>1.1 ± 0.1</td>
<td>7.6 ± 0.8</td>
<td>2.9 ± 0.2</td>
<td>2.7 ± 0.2</td>
<td>0.38 ± 0.02</td>
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<td>4.</td>
<td>JH 44/F</td>
<td>MS, mild</td>
<td>4.6</td>
<td>60</td>
<td>16</td>
<td>194</td>
<td>1.9 ± 0.2</td>
<td>11.7 ± 1.2</td>
<td>2.5 ± 0.1</td>
<td>1.3 ± 0.1</td>
<td>0.22 ± 0.01</td>
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<tr>
<td>5.</td>
<td>GP 50/F</td>
<td>Chest pain, normal coronaries</td>
<td>5.2</td>
<td>66</td>
<td>10</td>
<td>181</td>
<td>1.5 ± 0.1</td>
<td>8.8 ± 0.7</td>
<td>2.5 ± 0.2</td>
<td>1.7 ± 0.1</td>
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### Group B: No LVH

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<th>Pt</th>
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<th>Diagnosis</th>
<th>CO (liters/min)</th>
<th>HR (beats/min)</th>
<th>LVEDP (mm Hg)</th>
<th>LVEDV (cc)</th>
<th>ΔD (mm)</th>
<th>ΔV (cc)</th>
<th>ΔP (mm Hg)</th>
<th>ΔP/ΔD (mm Hg/mm)</th>
<th>ΔP/ΔV (mm Hg/cc)</th>
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</thead>
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<tr>
<td>7.</td>
<td>HJ 37/F</td>
<td>Chest pain, normal coronaries</td>
<td>5.6</td>
<td>70</td>
<td>14</td>
<td>237</td>
<td>1.1 ± 0.1</td>
<td>6.9 ± 0.6</td>
<td>2.1 ± 0.2</td>
<td>1.9 ± 0.1</td>
<td>0.30 ± 0.02</td>
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<tr>
<td>8.</td>
<td>JK 48/M</td>
<td>Minimal CAD</td>
<td>6.0</td>
<td>65</td>
<td>15</td>
<td>182</td>
<td>3.1 ± 0.4</td>
<td>18.2 ± 2.3</td>
<td>5.4 ± 0.5</td>
<td>1.8 ± 0.1</td>
<td>0.30 ± 0.03</td>
</tr>
<tr>
<td>9.</td>
<td>RC 53/F</td>
<td>MR, MS, AR</td>
<td>4.3</td>
<td>71</td>
<td>11</td>
<td>142</td>
<td>1.7 ± 0.2</td>
<td>10.3 ± 1.4</td>
<td>5.2 ± 0.2</td>
<td>3.2 ± 0.3</td>
<td>0.54 ± 0.05</td>
</tr>
<tr>
<td>10.</td>
<td>MH 25/F</td>
<td>Coarc, mild</td>
<td>5.3</td>
<td>90</td>
<td>10</td>
<td>142</td>
<td>3.9 ± 0.4</td>
<td>21.5 ± 1.4</td>
<td>4.1 ± 0.2</td>
<td>1.1 ± 0.1</td>
<td>0.19 ± 0.01</td>
</tr>
<tr>
<td>11.</td>
<td>SW 37/F</td>
<td>Coarc, moderate</td>
<td>8.0</td>
<td>80</td>
<td>9</td>
<td>245</td>
<td>1.9 ± 0.2</td>
<td>11.3 ± 1.3</td>
<td>4.3 ± 0.1</td>
<td>2.4 ± 0.3</td>
<td>0.40 ± 0.05</td>
</tr>
<tr>
<td>12.</td>
<td>DB 32/M</td>
<td>Mod pulm HT</td>
<td>6.1</td>
<td>83</td>
<td>12</td>
<td>258</td>
<td>4.2 ± 0.3</td>
<td>25.3 ± 2.0</td>
<td>4.5 ± 0.6</td>
<td>1.1 ± 0.1</td>
<td>0.17 ± 0.01</td>
</tr>
</tbody>
</table>

Mean | 42 | -- | ±0.3 | ±0.3 | ±13 | ±0.4 | ±2.1 | ±0.4 | ±2.2 | ±0.4 |

| P   | NS | NS | <0.05 | <0.01 | NS | NS | <0.001 | <0.001 | <0.001 |

**Abbreviations**: VSD = ventricular septal defect; CAD = coronary artery disease; AR = aortic regurgitation; AS = aortic stenosis; MR = mitral regurgitation; MS = mitral stenosis; LVH = left ventricular hypertrophy; Coarc = aortic coarctation; pulm HT = pulmonary hypertension; LVEDP and LVEDV = left ventricular end-diastolic pressure and volume; HR = heart rate; CO = cardiac output; ΔP, ΔV, ΔD = see text; SEM = standard error of the mean.
these increments and their ratio (ΔP/ΔD) among the various patients studied.

Left ventricular pressure and ultrasonically measured internal diameter were determined at the onset (P₁, D₁) and peak (P₂, D₂) of left atrial mechanical systole, as defined below and as illustrated in figure 1. In the patients studied with standard catheters, no correction for catheter delay was made since this delay (10–14 msec in our laboratory) is small compared with the interval between P₁ and P₂, which averaged 120 msec in this study. Volumes V₁ and V₂ were calculated from the LV internal diameters D₁ and D₂, measured from the ultrasonic trace, according to the method of Fortuin et al., previously reported from this laboratory. The formula, used, V = 59D - 153, was developed by Fortuin as a regression equation for end-diastolic volume based on bplane LV angiographic measurements as a reference. The onset of left atrial mechanical systole was defined as occurring 80 msec after the onset of the P wave of the ECG, and P₁ and D₁ were determined at this point. The peak of left atrial systole was defined as the peak of the atrial (“a”) wave in the LV pressure trace (fig. 1). In some patients there was no clearly defined ventricular “a” wave, and in that circumstance P₂ and D₂ were obtained at the time of LV end-diastolic pressure, defined as 40 msec after the onset of the QRS in the ECG.

ΔP and ΔD (defined as P₂-P₁, D₂-D₁) thus represented end-diastolic pressure and diameter increments occurring in association with atrial mechanical systole. It should be emphasized that ΔP and ΔD are not necessarily produced by left atrial systole since in certain patients, those with severe aortic regurgitation for example, ΔP and ΔD may result at least in part from blood entering the LV from the aorta. This should not alter the significance of ΔP or ΔD as late diastolic changes in pressure and geometry which may be assumed to reflect primarily true ventricular elastic properties. ΔP/ΔV, where ΔV = V₂-V₁, was similarly calculated in each study.

All measurements were performed in five cycles for each patient, and the values reported represent averages over these five cycles, with their standard errors. As seen in table 1, standard errors were quite small compared with the magnitude of the measurement, supporting the reproducibility of the method.

Data were analyzed by standard statistical methods, using Student’s t test for unpaired data.

**Results**

Table 1 details pertinent clinical and hemodynamic data for all 23 patients. The patients were divided into two groups, based upon the presence (group A) or absence (group B) of electrocardiographic evidence of LV hypertrophy. As can be seen from the table, patients with LV hypertrophy had much greater late diastolic increments in pressure per unit change in diameter (ΔP/ΔD = 6.1 ± 1.1 mm Hg/mm) or calculated volume (ΔP/ΔV = 1.0 ± 0.2 mm Hg/cc) than patients without LV hypertrophy (ΔP/ΔD = 1.8 ± 0.2 mm Hg/mm, ΔP/ΔV = 0.29 ± 0.04 mm Hg/cc, P < 0.001 for each ratio). This is illustrated graphically in figure 2.

This increased diastolic stiffness was associated primarily with a greater late diastolic pressure increment for the group with LV hypertrophy: for group A, ΔP = 12.1 ± 2.6 mm Hg, while for group B, ΔP = 3.4 ± 0.4 mm Hg. The late diastolic internal diameter and volume increments were similar in both groups, implying that the atrial contribution to diastolic filling is preserved in patients with left ventricular hypertrophy despite the cost associated with an increased filling pressure.

Although late diastolic internal diameter and calculated volume increments were similar in both groups, there was wide individual patient variation within each group. Thus, ΔD varied from 1 to 7 mm, and calculated ΔV varied from 6 to 39 cc in patients with hypertrophy, and examination of table 1 shows that stiffness ratios for individual patients could not be predicted from knowledge of ΔP or ΔV alone.

This increased diastolic stiffness was associated with a larger end-diastolic volume (268 ± 19 cc) in those patients with LV hypertrophy as compared with those without LV hypertrophy (186 ± 13 cc, P < 0.01). Similarly, LV end-diastolic pressure
tended to be higher in those patients with LV hypertrophy (20 ± 3.6 mm Hg) than in those without LV hypertrophy (11 ± 1 mm Hg, P < 0.05). Cardiac output and index were essentially the same in those with hypertrophy (5.3 liters/min and 2.9 liters/min/m²) as in those without hypertrophy (5.2 liters/min and 2.9 liters/min/m²).

Comparison of ΔP/ΔD and ΔP/ΔV values showed the anticipated variation among patients with different disease states, and this is illustrated in figure 3. There it can be seen that these ratios were low in patients with predominant mitral stenosis, significantly increased in patients with major aortic regurgitation or mitral regurgitation, and high in patients with aortic stenosis.

Linear regression plots of LV end-diastolic pressure against ΔP/ΔD and ΔP/ΔV showed poor correlation, with r values of 0.53 and 0.54, respectively. Similarly, linear regression of LV end-diastolic volume against ΔP/ΔD and ΔP/ΔV showed failure of significant correlation with r values of 0.41 and 0.46, respectively. These last data indicate that neither LV end-diastolic pressure nor volume, taken individually, is predictive of the slope of LV pressure-volume relations in late diastole.

Discussion

The present investigation has explored a new approach to the quantitative assessment of LV diastolic stiffness in man. Studies of simultaneous pressure and geometry changes during late diastole in 23 patients suggest that the quantitative evaluation of diastolic stiffness obtained by this approach correlates well with the presence or absence of LV hypertrophy, and with the underlying pathophysiology. Those patients in whom heart disease imposed a primary burden on the left ventricle showed significant increases in left ventricular diastolic stiffness. This was true even when electrocardiographic criteria for LV hypertrophy were not present, as can be seen in patient R.C. (mixed mitral regurgitation and stenosis, ΔP/ΔD = 3.2 mm Hg/mm, ΔP/ΔV = 0.54 mm Hg/cc) from group B in table 1. In contrast, patients in whom heart disease did not primarily affect the left ventricle showed much lower values for diastolic stiffness. This is well illustrated by patients R.T. (pure mitral stenosis, ΔP/ΔD = 0.5 mm Hg/mm, ΔP/ΔV = 0.08 mm Hg/cc), D.B. (chronic obstructive lung disease with moderate pulmonary hypertension, ΔP/ΔD = 1.1 mm Hg/mm, ΔP/ΔV = 0.17 mm Hg/cc), and G.P. (chest pain with normal coronary arteries, ΔP/ΔD = 1.7 mm Hg/mm, ΔP/ΔV = 0.29 mm Hg/cc).

If late diastolic pressure-geometry relations are truly exponential, as has been suggested in animal experiments, then the ratios studied in this investigation represent “effective” diastolic stiffness at the particular volume at which each left ventricle was operating at the time of the study. Normalization of these ratios by relating them to the pressure or volume at which they were measured might then give a characterization of the entire pressure-volume plot, independent of the operating volume. If the stiffness ratios in our study are normalized for pressure (ΔP/ΔV/P₁), there is still clear separation between patients with LVH (ΔP/ΔV/P₁ = 125 ± 11 × 10⁻³cc⁻¹) and those without LVH (ΔP/ΔV/P₁ = 38 ± 6 × 10⁻³cc⁻¹, P < 0.01), as well as among the various subgroups listed in figure 3. However, it should be emphasized that the applicability of exponential analysis to LV diastolic compliance in man has not been established. Furthermore, it is of interest that in a recent study by McCullagh, Covell, and Ross data are presented which suggest that late diastolic pressure-diameter relations can be quite reasonably approximated by a linear regression over the range of physiologic pressures in the conscious dog. Mathematical analysis of multiple points from late diastole will clearly be needed to determine the applicability of either linear or exponential analysis to late diastolic pressure-geometry relations in man.

It seems reasonable to speculate that the increased diastolic stiffness present in many of the patients in this study may have both desirable and undesirable clinical consequences. One obvious disadvantage of the increased stiffness is that an increased pressure will be required for diastolic filling of the left ventricle, and this increased pressure, transmitted directly backward upon the pulmonary capillaries, may result in pulmonary congestion and edema.

The increased diastolic stiffness may, however, have desirable consequences in special situations. In aortic regurgitation (patient O.W. table 1) increased diastolic stiffness may tend to limit left ventricular dilatation, thereby tending to protect these patients against the phenominal increases in wall tension (and therefore myocardial oxygen requirements) associated with large increases in end-diastolic volume, as dictated by the Law of Laplace. In this setting, increased diastolic stiffness of the left ventricle may have the additional advantage of acting in concert with a lowered

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systemic vascular resistance to encourage the antegrade flow of blood in the aorta.

Previous investigators have explored both qualitative and quantitative approaches to the analysis of LV diastolic compliance and distensibility in man. Using an angiographic technic for LV volume determination, Dodge and co-workers have examined the slopes of diastolic pressure-volume curves and made comparative judgments about compliance by relating the values to volumes at which the slopes were determined. They have pointed out that simple ratios of volume increments to pressure increments vary throughout diastole, passing through infinity at the nadir of the pressure curve. In an excellent study Bristow and his colleagues have specifically analyzed the late diastolic pressure and volume increments associated with left atrial systole, using angiographic technics. Their data on five normal subjects, as calculated from their figure 4, give an approximate mean \( \Delta P/\Delta V \) of 0.31 mm Hg/cc/m² during the last 200 msec of diastole. If \( \Delta P/\Delta V \) in the nonhypertrophied group of the present study is similarly indexed for body surface area, the resultant value is 0.46 mm Hg/cc/m². Although this is somewhat higher than the value calculated from Bristow's data, it must be recalled that our nonhypertrophied patients were by no means normal subjects, and

Figure 3

Variation in diastolic stiffness of the left ventricle in patients with different disease states. Both \( \Delta P/\Delta D \) (solid circles) and \( \Delta P/\Delta V \) (open circles) tended to be low in patients with mitral stenosis, high in patients with aortic stenosis, and intermediate in patients with aortic or mitral regurgitation. Bars represent the mean value for each group, and open and closed circles show individual patient values.
that there was considerable difference in methodology between the two studies, particularly with regard to the time interval between points $P_1$, $V_1$, and $P_2$, $V_2$.

Several limitations of the method described in this report should be considered. First, the method can only be legitimately applied at present in patients without regional abnormalities of left ventricular contraction. In patients displaying such abnormalities, the assumptions underlying calculation of LV chamber volume from a single echocardiographic dimension are invalidated. While it might be argued that asynergy in contraction pattern is a systolic abnormality, not necessarily invalidating echocardiographic assumptions about diastolic geometry, further studies comparing echocardiographic with biplane angiographic diastolic volume determinations in patients with left ventricular asynergy would be required before the current technic could be reasonably applicable to such patients. Second, even in patients with uniform LV contractile patterns, one might question the comparative applicability of echocardiographic diameter and volume determinations in patients with diverse cardiovascular abnormalities, where the left ventricular chamber geometry might vary from ellipsoidal to spherical. Although several investigators have shown excellent correlations between echocardiographic and angiographic volumes for large groups of patients, consistent bias introduced for specific groups (e.g., mitral stenosis vs aortic regurgitation) might tend to introduce bias artifactually into the comparisons of derived values among such groups.

Third, it should be pointed out that the echocardiographically determined $\Delta D$ and $\Delta V$ utilized in this study were not verified by angiographic measurements in the same patients. This investigation has relied on previous reports which supports a close correlation between results obtained by the two technics. Since each patient is being compared with himself as a control (i.e., $D_2$ and $P_2$ are being compared with $D_1$ and $P_1$) and this study is thus examining a ratio of changes ($\Delta P/\Delta D$), the absolute accuracy of the pressures or diameters measured becomes less important.

In support of the method, it should be pointed out that it offers several advantages over the angiographic technics previously utilized for the study of diastolic pressure-volume relations in man. Prominent among these advantages is the possibility for repeated sampling over consecutive beats; the ability to sample at any desired interval (since the data are obtained and recorded in analog form); the ability to measure changing diastolic geometry without altering cardiac function by the act of measurement itself; and finally, the possibility for studying effects of various physiologic variables by repeated measurements throughout the course of an individual study.

In summary, high-speed strip-chart recordings of simultaneous LV pressure and ultrasonically determined LV internal diameters have been utilized in the development of a new approach to the quantitative assessment of LV diastolic stiffness in man. Studies in 23 patients suggest that the quantitative evaluation of diastolic stiffness obtained by this approach correlates well with the presence or absence of LV hypertrophy, and with the underlying pathophysiology.

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