Wall Thickness and Diastolic Properties of the Left Ventricle

By William Grossman, M.D., Lambert P. McLaurin, M.D., Sally P. Moos, Miltiadis Stefadouros, M.D., Daniel T. Young, M.D.

SUMMARY

Diastolic properties of the left ventricle (LV) are probably influenced by several factors, including completeness of ventricular relaxation, composition of the ventricular wall, and wall thickness. This study has utilized a combined ultrasonic and hemodynamic technique to examine the influence of LV posterior wall thickness at end diastole (hₚ) on LV diastolic characteristics in 24 patients with various forms of heart disease. The slope of late diastolic LV pressure-diameter relations (∆P/ΔD) was calculated and used as a measure of effective diastolic stiffness (S) late in diastole. S was normalized for average LV pressure during the interval of measurement (P) as S/P, called Sₓ, LV end diastolic pressure (LVEDP), volume index (LVEDVI), and mass index (LVMI) were measured in each patient during the same study at which hₚ, S, and Sₓ were determined.

The range of hₚ was 5.6 to 18.6 mm; it was highest in a patient with aortic stenosis, and lowest in those with mitral stenosis. Linear regression of hₚ against S, Sₓ and LVEDP showed significant correlation, with r = 0.85, 0.75, and 0.74 respectively (P < 0.001 for each regression analysis). Poor correlation was noted with LVEDVI, ∆P, and ∆D. Of 12 patients with LV hypertrophy (LVH) by ECG, four had normal hₚ (7.9 ± 1.0 mm) and eight had abnormal hₚ (13 ± 6.6 mm). Those with normal hₚ had nearly normal values for S (3.5 ± 0.5 mm Hg/mm) while those with abnormal hₚ showed significant increases in S (7.7 ± 1.5 mm Hg/mm), indicating that LVH may alter S only insofar as there is an associated increase in hₚ. Consistent with this was the observation that within the group of patients having increased LVMI, LVMI itself was a poor predictor of S (r = 0.50, NS) while hₚ remained an excellent predictor of S (r = 0.86, P < 0.001). In summary, this study suggests that wall thickness is an important determinant of left ventricular diastolic stiffness and pressure, and that wall thickness appears to predict diastolic stiffness independent of the presence or absence of LVH or increased LV mass.

Additional Indexing Words:
Left ventricular end diastolic pressure   Echocardiography   Left ventricular hypertrophy
Left ventricular diastolic stiffness   Left ventricular mass index   Ventricular compliance

DIASTOLIC PROPERTIES of the left ventricle are probably influenced by multiple factors, including completeness of ventricular relaxation, composition of the ventricular wall, and ventricular wall thickness. The completeness of left ventricular relaxation in man has recently been examined and found to be an important determinant of diastolic pressure and compliance, particularly in patients with ischemic heart disease.1-3 Changes in the composition of the ventricular wall, as with hypertrophy4 or the fibrosis of diffuse coronary artery disease,5-7 have been reported to result in increased diastolic stiffness of the left ventricle, but the role of these changes has not been clearly separated from the possible influence of concomitant alterations in wall thickness.

Recently, the study of diastolic left ventricular characteristics in man has been approached by use of a combined hemodynamic and ultrasonic technique to quantify the left ventricular pressure-diameter relation in late diastole.4, 8-9 In the present study, we have utilized this approach to examine...
the role of left ventricular wall thickness as a determinant of diastolic properties of the left ventricle in 24 patients with various forms of heart disease.

Methods

Twenty-four patients undergoing complete left and right heart catheterization for diagnostic purposes formed the study population. Included were 14 patients with severe chronic left ventricular volume overload, three with mitral stenosis, three with chest pain and normal coronary arteries, and one each with severe aortic stenosis, idiopathic cardiomyopathy, amyloidosis, and minimal aortic stenosis and insufficiency. All patients were in sinus rhythm, and diagnostic and hemodynamic data for each patient are detailed in table 1.

Catheterization was carried out in the fasting state, following diazepam (5–10 mg i.m.) premedication. Brachial arteriotomy and retrograde left heart catheterization were performed with standard #8 French catheters in 16 patients, and with high fidelity micromanometer tipped catheters* in eight patients. All pressures were recorded on an Electronics for Medicine DR-12 recorder. Zero reference point for pressure measurement was taken as the midchest with the patient supine. Left ventricular cineangiography was performed in each study, and patients with regional abnormalities of contraction were excluded.

Immediately prior to angiography a simultaneous strip chart recording of ECG, left ventricular pressure, and ultrasonically determined septal and posterior wall motion in the plane of the mitral valve (recorded with a Smith-Kline Ecoline 20A ultrasonoscope interfaced with the Electronics for Medicine recorder) was obtained as previously described. Differentiation of posterior wall endocardium from epicardium was aided by sudden damping of the intensity of the ultrasonic beam in all cases, and by injection of indocyanine green dye into the left ventricular chamber whenever possible (fig. 1).

The use of a combined ultrasonic and hemodynamic technique in the analysis of left ventricular diastolic stiffness has been previously reported from this laboratory and the theoretical considerations relevant to this analysis need not be repeated in detail here. Basically, the slope of the late diastolic pressure-diameter relation at the time of left atrial systole was measured in each patient, as illustrated in figure 2, and this slope, \( \Delta P/\Delta D \), was used as a measure of effective left ventricular stiffness (S) late in diastole. If \( S \) is related to the average pressure (\( \bar{P} \)) during the interval of measurement (\( \bar{P} = [P1 + P2]/2 \)), we may define the normalized stiffness as \( S/\bar{P} \), called \( S_\perp \).

Left ventricular posterior wall thickness (\( h_p \)) was measured echocardiographically in each patient as the distance between endocardial and epicardial surfaces at end diastole. This technique has been previously

* Mikrotip, Millar Instruments, Houston, Texas.

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**Figure 1**

Photographic strip chart recording of simultaneous echocardiograms, left ventricular pressure (LVP), and ECG. The left-hand panel is recorded at 100 mm/sec with 20 msec timelines, while the right hand panel is recorded at 50 mm/sec without timelines. Multiple echoes resulting from the injection (arrow) of 5 cc indocyanine green dye through the LV catheter fill the ventricular cavity and confirm the identity of LV septum and posterior wall (PW) endocardium. PW thickness at end diastole is designated as \( h_p \).
## Table 1

### Posterior Wall Thickness and Diastolic Characteristics

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age (yr)/sex</th>
<th>Diagnosis</th>
<th>$h_p$ mm</th>
<th>$S$ mm</th>
<th>$S_n$ $10^3$ mm$^{-1}$</th>
<th>LVEDP mm Hg</th>
<th>$\Delta P$ mm Hg</th>
<th>$\Delta D$ mm</th>
<th>LVEDVI cc/m$^2$</th>
<th>LVMI gm/m$^2$</th>
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<tbody>
<tr>
<td>1) JH</td>
<td>44/F</td>
<td>MS</td>
<td>5.6</td>
<td>1.3</td>
<td>1.72</td>
<td>8.8</td>
<td>2.5</td>
<td>1.9</td>
<td>116</td>
<td>71</td>
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<td>2) RT</td>
<td>58/F</td>
<td>MS</td>
<td>6.2</td>
<td>0.5</td>
<td>1.28</td>
<td>5</td>
<td>2.2</td>
<td>4.8</td>
<td>86</td>
<td>71</td>
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<td>3) CW</td>
<td>44/M</td>
<td>MS</td>
<td>6.1</td>
<td>2.3</td>
<td>3.40</td>
<td>8.7</td>
<td>4</td>
<td>1.8</td>
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<td>4) JM</td>
<td>52/M</td>
<td>CPNC</td>
<td>10.0</td>
<td>2.9</td>
<td>3.79</td>
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<td>72</td>
<td>101</td>
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<td>5) CL</td>
<td>56/F</td>
<td>CPNC</td>
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<td>2.9</td>
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<td>7) EMeQ</td>
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<td>8) VW</td>
<td>48/M</td>
<td>AR</td>
<td>8.8</td>
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<td>9) TS</td>
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<td>AR</td>
<td>15.0</td>
<td>13.6</td>
<td>3.93</td>
<td>40.4</td>
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<td>10) LS</td>
<td>52/F</td>
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<td>11.0</td>
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<td>11) OB</td>
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<td>7.6</td>
<td>3.53</td>
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<td>12) CS</td>
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<td>AR</td>
<td>13.5</td>
<td>11.9</td>
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<td>13) JL</td>
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<td>5.8</td>
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<td>21</td>
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<td>14) JD</td>
<td>33/F</td>
<td>AR, MR</td>
<td>10.2</td>
<td>5.0</td>
<td>2.82</td>
<td>25</td>
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<td>15) HH</td>
<td>17/M</td>
<td>AR, MR</td>
<td>7.9</td>
<td>2.0</td>
<td>1.53</td>
<td>18.6</td>
<td>11.1</td>
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<td>16) YO</td>
<td>17/F</td>
<td>MR</td>
<td>7.0</td>
<td>2.3</td>
<td>1.55</td>
<td>6</td>
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<td>17) PG</td>
<td>28/M</td>
<td>MR</td>
<td>6.7</td>
<td>4.0</td>
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<td>18) JC</td>
<td>22/F</td>
<td>MR</td>
<td>5.9</td>
<td>3.7</td>
<td>4.40</td>
<td>7</td>
<td>4.8</td>
<td>1.3</td>
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<td>19) SH</td>
<td>25/M</td>
<td>MR</td>
<td>10.0</td>
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<td>25.7</td>
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<td>53/M</td>
<td>Severe AS</td>
<td>18.6</td>
<td>14.6</td>
<td>7.49</td>
<td>28</td>
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<td>21) JK</td>
<td>21/M</td>
<td>Minimal AR, AS</td>
<td>8.3</td>
<td>3.5</td>
<td>2.01</td>
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<td>10.2</td>
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<td>22) PH</td>
<td>26/M</td>
<td>VSD</td>
<td>12.0</td>
<td>10.5</td>
<td>4.77</td>
<td>21</td>
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<td>23) LD</td>
<td>38/F</td>
<td>Amyloidosis</td>
<td>13.0</td>
<td>6.6</td>
<td>3.65</td>
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<td>24) PR</td>
<td>62/F</td>
<td>Cardiomyopathy</td>
<td>8.6</td>
<td>6.7</td>
<td>3.33</td>
<td>28.5</td>
<td>19.8</td>
<td>3.1</td>
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Linear regression against $h_p = r$  
$t = 0.85$  
$P < 0.001$  

### Abbreviations: $h_p$ = posterior wall thickness; LVEDP, LVEDVI, and LVMI = left ventricular end diastolic pressure, end diastolic volume diastolic volume index, and mass index; $S$ = effective diastolic stiffness late in diastole; $\Delta P$, $\Delta D$ = the LV pressure and diameter increments associated with left atrial systole; $S_n$ = normalized $S$ for average LV pressure. MS = mitral stenosis; CPNC = chest pain with normal coronaries; AR = aortic regurgitation; MR = mitral regurgitation; AS = aortic stenosis; VSD = ventricular septal defect; $r$ = coefficient of linear correlation; $t$ = test statistic for the linear regression; $P$ = probability.
described by others,\textsuperscript{11-13} and reported to show excellent correlation with angiographically and directly measured left ventricular wall thickness. Only patients in whom echocardiographic records were of sufficient quality to permit accurate identification of posterior wall epicardial and endocardial surfaces were included (figures 1 and 2), and this was possible in approximately 70% of studies performed in our laboratory. Patients were instructed to maintain normal quiet respiration during recording. Where significant respiratory variation in pressures was observed, measurements were made and averaged over an entire respiratory cycle; otherwise, measurements were averaged over five beats. Ventricular end diastolic volumes were calculated from end diastolic diameters in each patient, according to the method of Feigenbaum et al.,\textsuperscript{14} by simply cubing the end diastolic diameter. All volumes were indexed for body surface area. Left ventricular mass was calculated for each patient from echocardiographic wall thickness and end diastolic diameter, according to the method of Troy, Pombo, and Rackley.\textsuperscript{12} This method has been reported by them to show excellent correlation with left ventricular mass calculated from biplane left ventricular angiograms. Values obtained were indexed for body surface area in each patient. Statistical analysis was carried out using standard techniques for linear regression analysis, \( t \) statistics for testing linear regression, and the unpaired \( t \) test for analysis of variance.\textsuperscript{15}

**Results**

Left ventricular posterior wall thickness, \( h_p \), ranged from 5.6 to 18.6 mm. In this series of 24 patients the highest value was noted in patient RB with severe aortic stenosis, while the lowest value was recorded in patient JH with mitral stenosis.

Linear regression of \( h_p \) against effective left ventricular diastolic stiffness showed strong correlation \((S = h_p -4.87; r = 0.85, P < 0.001)\) as illustrated in figure 3. Significant correlation was also found between \( h_p \) and normalized diastolic stiffness \((S_n = 0.313 h_p -0.019; r = 0.75, P < 0.001)\), and left ventricular end diastolic pressure \((LVEDP = 23.4 h_p -3.15; r = 0.74, P < 0.001)\). Poor correlation was noted with \( \Delta P, \Delta D \), and left ventricular end diastolic volume index. All linear regression data are summarized in table 1.

Patients with left ventricular hypertrophy (LVH) by standard electrocardiographic criteria\textsuperscript{16} tended to have thicker posterior walls \((h_p = 11.6 \pm\)
LV DIASTOLIC WALL THICKNESS

This study has investigated the influence of wall thickness on diastolic properties of the left ventricle. The results suggest that wall thickness is a major determinant of left ventricular diastolic stiffness and pressure, but correlates poorly with diastolic chamber size. One might speculate that this scheme of things has the very important physiologic consequence of maintaining wall stress nearly constant. By itself, increased wall thickness tends to decrease wall stress by distributing diastolic forces over a greater area. A concomitant increase in those diastolic forces* would restore wall stress toward normal, but unless accompanied by an increase in ventricular diastolic stiffness, such an increase in diastolic force would lead to progressive dilatation. The increased stiffness thus preserves the normality of wall stress and minimizes dilatation, but at the cost of an elevated left ventricular filling pressure and its accompanying clinical manifestations of pulmonary congestion and edema. The importance of wall thickness as a determinant of left ventricular wall stress has been pointed out by Hood, Rackley, and Rolett, and the relationship between diastolic stiffness and sarcomere stretch has been thoroughly reviewed in a recent editorial by Levine.

The poor correlation between wall thickness and diastolic chamber size suggests that left ventricular volume overload, which was responsible for the enlarged diastolic chamber size in 14 of the 24 patients in this study, is not a particularly potent stimulus to increased wall thickness. In contrast, pressure overload, which produced the greatest increase in wall thickness seen in this study (patient #20, RB), was associated with no increase in diastolic chamber size.

In this regard, it might be well to comment on the role of hypertrophy as a determinant of left ventricular diastolic stiffness. A diagnosis of left ventricular hypertrophy by standard ECG criteria correlates well with increased left ventricular mass. This increased mass may be so distributed as to minimize increases in wall thickness, as was observed in four of the 12 patients in this study with LVH by ECG criteria. As noted above, those with LVH and normal wall thickness had lower

$\Delta P/\Delta D$, a measure of left ventricular diastolic stiffness, against posterior wall thickness at end diastole, $h_p$. A strong correlation was observed, suggesting that wall thickness is a useful predictor of left ventricular diastolic stiffness.

A more precise measure of left ventricular hypertrophy, the left ventricular mass index, also tended to correlate with increased $h_p$ ($r = 0.64$, $P < 0.01$) and with $S$ ($r = 0.72$, $P < 0.01$). However, if only those with increased left ventricular mass* are examined, left ventricular mass index becomes a poor predictor of $S$ ($r = 0.50$, NS) or $h_p$ ($r = 0.23$, NS), but within this group $h_p$ remains an excellent predictor of $S$ ($r = 0.86$, $P < 0.001$). This suggests that wall thickness is a determinant of ventricular diastolic stiffness independent of the presence or absence of an increased left ventricular mass.

**Figure 3**

Diastolic forces here are a function of diastolic pressure and chamber size. For a spherical model, stress ($\sigma$) is related to pressure ($P$), radius ($R$) and wall thickness ($h$) as $\sigma = PR/2h$. Thus, increases in wall thickness must be accompanied by increased pressure or radius if wall stress is to remain constant.
values for effective stiffness (S) than those with LVH and abnormal wall thickness. Previously we had reported4 that LVH correlated quite well with left ventricular diastolic stiffness: it would appear from the present data that within the population of all patients exhibiting LVH by ECG criteria, wall thickness acts as a further and independent predictor of stiffness. This is supported by the observation that even in the absence of LVH, increased h, was associated with increased S, as noted in patient LD with amyloidosis.

In further support of this hypothesis is the data concerning left ventricular mass. Patients with increased total left ventricular mass may show wide variation in wall thickness, depending on whether concentric hypertrophy or series replication of sarcomeres has been the predominant pathway leading to the increased mass. In this study, within the subgroup of patients having increased left ventricular mass, the mass itself was a poor predictor (r = 0.50, P = 0.15) of diastolic stiffness, while wall thickness remained an excellent predictor (r = 0.86, P < 0.001) of stiffness. This supports the contention that wall thickness is a major determinant of diastolic left ventricular stiffness, independent of the presence or absence of increased left ventricular mass.

Certain limitations of this study must be emphasized. First, wall thickness was not determined directly (e.g., at surgery or autopsy) in our patients, but rather by an indirect ultrasonic technique. We have relied upon the work of others11-15 who have reported an excellent correlation between direct measurements and those made utilizing the ultrasonic method. Second, it is possible that ventricular filling may occur in a different fashion in thick-walled as opposed to thin-walled ventricles. Thus, if long axis lengthening plays a more significant role in either condition than does internal diameter (minor axis) lengthening, a consistent bias might be introduced by reliance on only internal diameter for characterizing changes in diastolic geometry. Third, posterior wall thickness may not be representative of wall thickness in the rest of the left ventricle. This might be especially true in conditions associated with asymmetric hypertrophy (such as hypertrophic subaortic stenosis) or fibrosis (coronary disease with regional disorders of contraction). Concern about this possibility has led us to exclude such patients from the present study, but the possibility of asymmetric changes cannot be ruled out.

In summary, we have examined the influence of wall thickness on diastolic properties of the left ventricle in 24 patients. The results suggest that wall thickness is an important determinant of left ventricular diastolic stiffness and pressure, and that wall thickness appears to predict diastolic stiffness independent of the presence or absence of LVH.

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