The Influence of Left Ventricular Late Diastolic Filling on the A Wave of the Left Ventricular Pressure Trace

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SUMMARY To study the influence of left ventricular (LV) late diastolic filling on the A wave of the LV pressure, simultaneously recorded echocardiographic LV dimensions and high-fidelity LV pressure measurements were taken in 24 patients. Group 1 comprised eight patients without LV hypertrophy (LVH) and LV end-diastolic pressure (LVEDP) < 13 mm Hg. Group 2 comprised 16 patients with LVH secondary to aortic stenosis, idiopathic hypertrophic subaortic stenosis, or hypertension and increased LVEDP. Patients in group 2 had significantly thinner left ventricles, decreased mitral E-to-F slopes, and larger A waves in the LV pressure curve. On the basis of end-diastolic chamber stiffness, we divided group 2 into two populations: 12 patients (group 2A) with end-diastolic chamber stiffness similar to that in group 1, and four patients (group 2B) with markedly elevated end-diastolic chamber stiffness. Patients in group 2A had a larger atrial contribution to LV filling than those with markedly abnormal stiffness (group 2B). Therefore, in LVH an increased A wave in the LV pressure may be related to either elevated end-diastolic chamber stiffness or augmented left atrial volume transport.

IN LEFT ventricular hypertrophy (LVH), the left ventricular end-diastolic pressure (LVEDP) is often increased, usually in association with a prominent A wave in the left ventricular pressure curve. The A wave reflects the rise in left ventricular pressure as a result of left atrial contraction; its increased magnitude in LVH has been attributed to increased left ventricular chamber stiffness; that is, a large change in pressure relative to the change in volume. However, recent angiographic and echocardiographic analyses have shown increased late diastolic filling in some patients with coronary artery disease, aortic stenosis, and idiopathic hypertrophic subaortic stenosis, reflecting augmented left ventricular filling secondary to a forceful atrial contraction. Although Grossman et al. studied the relationship of left atrial contraction and the left ventricular pressure A wave in a few patients with LVH secondary to aortic stenosis, none of their patients had unusually increased late diastolic filling. In this study, we have reexamined the relationship between the height of the A wave in the left ventricular pressure curve and the magnitude of the left atrial volume contribution to ventricular filling in patients with LVH.

Methods

Twenty-four patients undergoing diagnostic cardiac catheterization at the Mount Sinai Medical Center were studied. Simultaneous echocardiographic dimensions and high-fidelity pressure measurements of the left ventricle were recorded during catheterization either before injection of any contrast material or at least 20 minutes after contrast injection when heart rate, aortic pressure, and LVEDP had returned to baseline. All catheterizations were performed through the right brachial artery.

Eight patients (group 1) had no LVH on the ECG, and normal or borderline elevated LVEDP (≤ 13 mm Hg). Four of these patients had atypical chest pain without evidence of cardiovascular disease; one patient had one-vessel coronary artery disease with normal left ventricular function, and three had mild or
moderate aortic stenosis (aortic valve area > 1.0 cm²). Sixteen patients (group 2) had LVH by the ECG, as well as increased LVEDP (> 13 mm Hg). Six of these patients had severe aortic stenosis (aortic valve area < 1.0 cm²), five idiopathic hypertrophic subaortic stenosis, and five hypertensive heart disease. All patients were in normal sinus rhythm.

No patient had regional asynergy by right anterior oblique ventriculogram, and only three patients had significant coronary artery disease (> 70% decrease in luminal diameter) — one patient in group 1 and two patients in group 2. No patient had a history of myocardial infarction. Patients with aortic stenosis and more-than-mild aortic regurgitation demonstrated by angiography were excluded, as were patients with idiopathic hypertrophic subaortic stenosis and more-than-mild mitral regurgitation. No patient had associated mitral stenosis.

A #8F Millar catheter was used in all studies. The catheter was calibrated externally against a mercury reference, and drift was minimized by comparing the pressure before and after each measurement with a simultaneous lumen pressure from the side holes of the same catheter using a Statham P23Db transducer with a reference to a 0 level 5 cm below the angle of Louis. However, in two patients with severe aortic stenosis in whom retrograde catheterization of the aortic valve could not be accomplished with a high-fidelity catheter, fluid-filled catheters (#8F) were used for pressure measurement. We have obtained similar pressure contours in mid and late diastole between high-fidelity and fluid-filled catheters, so in these two patients the Millar catheter was placed in the ascending aorta and the delay in transmission between the Millar and a simultaneous Statham pressure was recorded (25–30 msec in each patient).

Simultaneous pressure-dimension measurements were recorded at the beginning of the electrocardiographic P wave, before the A wave of the left ventricular pressure trace (P1D1), at the peak of the A wave of the left ventricular pressure trace if present (P2D2), and at end-diastole (P3D3). End-diastole was defined as the point 0.04–0.06 second after the beginning of the QRS complex at the onset of the upward deflection in the left ventricular pressure trace. End-diastolic chamber stiffness was defined as P3-P1/D3-D1 or P2-P1/D2-D1 and divided by the average pressure \( \frac{P_1 + P_2}{2} \) (fig. 1).

Pressure was recorded at a gain scale of 0–40 mm Hg to determine chamber stiffness. For patients with a discrete peak of the A wave (P2D2) in the left ventricular pressure curve (nine patients), the value for stiffness was calculated using the peak of the A wave.

Since the use of the formula for end-diastolic chamber stiffness assumes an exponential diastolic pressure-volume relationship, pressure-dimension loops were also constructed in nine patients using pressures obtained from high-fidelity catheters. The relationship of \( \Delta P/\Delta D \) vs P was determined, and an average of six late diastolic points were plotted in each patient. These points were chosen beginning just before the A wave of the left ventricular pressure trace and ending at the A-wave peak, or at end-diastole. The \( \Delta P/\Delta D \) vs P plots could be fit by a linear equation in eight of nine patients with correlation coefficients of 0.79 to 0.99. The slope (Kp) of these lines was also determined.

The change in left ventricular diastolic dimensions between points D2 or D3 and D1 was defined as the atrial contribution to left ventricular filling, and was expressed either as an absolute value (in millimeters) or as a percent when normalized for diastolic dimension (D3 or D2-D1/D1). In addition, these dimensions were converted to volumes using the formula of Teichholz et al. and expressed as a percent when normalized for end-diastolic volume.

All echocardiographic-hemodynamic measurements were made at a paper speed of 100 mm/sec. Echocardiograms were recorded in standard fashion using Irex machines and 10 mm diameter, 2.25-MHz transducers. Additional echocardiographic data were obtained during each study in standard fashion. This included left atrial size, E-to-F slope of the anterior mitral valve leaflet, PR-minus-AC interval, and A-to-C slope of the mitral valve. Echocardiographic end-systolic and end-diastolic volumes and ejection fractions were also calculated. Posterior wall and interventricular septal measurements were made in diastole before the inscription of the left ventricular pressure A wave. Validation for using left ventricular echocardiographic dimensions in measuring left ventricular volumes throughout diastole has been previously reported.

All echocardiographic and hemodynamic data were digitized from the ultrasound and pressure data recordings using a SAC graph pen sonic digitizer. The data were processed and analyzed using a PDP-11/70 computer. Left ventricular pressure and echocardiographic dimensions at various portions of the cardiac cycle were analyzed and averaged individually over three consecutive beats, with less than a 10% variation between individual beats. Differences of 1 mm or less were consistently obtained on repeated evaluation for any single echocardiographic measurement. In addition, borders of the left ventricular posterior wall endocardium and left side of the interventricular septum were traced; simultaneous high-fidelity pressure measurements were also taken. Pressure-dimension and pressure-volume loops were determined. The basic system has been previously described.

Statistical analyses was performed using the t test for difference in means.

**Results**

Hemodynamic and echocardiographic data for all patients are shown in table 1. Patients in group 1 were significantly younger than patients in group 2. Patients in group 2 had significantly thicker interventricular septums and left ventricular posterior walls, larger left atrial sizes, and decreased E-to-F slopes compared with group 1 (table 2). Not only was LVEDP higher by definition in group 2, but the pa-
patients in this group also had significantly higher left ventricular pressure before the A wave as well as larger A waves in the left ventricular pressure trace. The atrial contribution to left ventricular filling, heart rate, PR interval, end-diastolic volume and ejection fraction were not significantly different between the two groups. Only one patient had an increased end-diastolic volume (>90 ml/m²). A representative echocardiogram of a patient of group 1 is shown in figure 2.

**End-diastolic Chamber Stiffness**

Left ventricular end-diastolic chamber stiffness (table 3), in group 2 was 0.17 ± 0.03 (mm⁻¹) (mean ± SEM), compared with 0.15 ± 0.02 (mm⁻¹) in group 1 (p = NS). There was no difference in end-diastolic chamber stiffness among patients in group 1, whether or not they had cardiovascular disease. Furthermore, the value for end-diastolic chamber stiffness did not differ significantly in any patient with a discrete peak of the A wave in the left ventricular pressure trace, whether the A-wave peak (P₃D₃) or end-diastolic peak (P₂D₂) was used to calculate stiffness.

The chamber stiffness data in group 2 revealed two populations: 12 patients (group 2A) whose end-diastolic chamber stiffness was similar to that of group 1 (falling within 2 standard deviations of group 1) and four patients (group 2B) whose end-diastolic chamber stiffness was elevated greater than 2 standard deviations of that of group 1 (fig. 3). In the eight patients in whom the slope of the equation ΔP/ΔD vs P were determined, patients in group 1 and 2A were similar, with means of 3.4 and 5.5, respectively, while the two patients studied in group 2B had values >20.

Patients in group 2A had significantly larger atrial contributions to left ventricular filling, while the pre-A wave pressure and LVEDP were significantly greater in group 2B (table 3). The height of the A wave in group 2B was larger than in group 2A (15.4 ± 2.7 mm Hg vs 12.5 ± 1.8 mm Hg), but the difference was not significant. Although end-diastolic volume was significantly greater in group 2B, there was overlap with group 2A, and three out of four patients in group

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**Figure 1.** Representative echocardiographic-pressure recording. (left) Schematic representation of methods of measurement to calculate end-diastolic chamber stiffness. IVS = interventricular septum; L = left side of IVS; R = right side of IVS; PW = posterior wall of left ventricle; Endo = endocardium of PW; Epi = epicardium of PW; P₃,D₃ = left ventricular (LV) pressure and LV internal diastolic dimension, respectively, before A wave of LV pressure trace; P₂,D₂ = LV pressure and internal diastolic dimension at A-wave peak and P₃; D₃ = LV pressure and internal diastolic dimension at end-diastole. EDCS = end-diastolic chamber stiffness.

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EDCS = \frac{P₂-P₁}{D₂-D₁} / \frac{P₁+P₂}{2} \quad \text{or} \quad \frac{P₃-P₁}{D₃-D₁} / \frac{P₁+P₃}{2}
\]
2B had end-diastolic volumes in the normal range. Ejection fractions in group 2B were significantly lower than in group 2A and less than 50% in three patients. The mitral valve E-to-F slope was significantly greater in group 2B. All other hemodynamic and echocardiographic measurements were not significantly different between the two subgroups. Representative echocardiograms from patients of groups 2A and 2B are shown in figures 4 and 5. The atrial contribution to left ventricular filling in group 2A (5.1 ± 0.44 mm) was significantly greater (p < 0.05) than in group 1 (3.6 ± 0.71 mm). When normalized for diastolic dimension, the atrial contribution to left ventricular filling in group 2A (12.9%) was not significantly different from that in group 1 (8.9%) (0.075 < p < 0.10).

There was no significant correlation between end-diastolic stiffness and age, mitral E-to-F slope, posterior wall thickness, or interventricular septal thickness. Two patients in group 2B had a history of pulmonary edema, but no one in group 2A had such episodes. Otherwise, the duration and severity of symptoms between groups 2A and 2B were not different.

Patients with the highest values for end-diastolic chamber stiffness (group 2B) tended to have both the highest late diastolic pressure change and the smallest atrial contribution to left ventricular filling (table 3). Even when the atrial contribution to left ventricular filling was normalized for diastolic dimension or converted to volume, the values in group 2B were significantly smaller than in group 2A.

Three patients in group 2B had a shortened or borderline shortened PR-minus-AC interval (≤ 0.06 second), with a large notch on the A-to-C slope. The velocity of closure of the mitral valve (A-to-C slope) was also decreased or low-normal in these patients. Although the fourth patient had a normal PR-minus-AC interval (0.13 second) with a rapid A-to-C slope (330 mm/sec), he also had premature closure of the mitral valve in the absence of significant aortic regurgitation (fig. 6). Only two patients in group 1 and three in group 2A had shortened PR-minus-AC intervals; however, none of these patients had a large notch on the A-to-C slope. There was no correlation between either the PR-minus-AC interval or the A-to-C slope and end-diastolic chamber stiffness in patients in group 2.

Discussion

Early diastolic left ventricular filling may be decreased in LVH. This has been suggested by a decrease in the "y descent" of the left atrial pressure curve in some patients with idiopathic hypertrophic subaortic stenosis and by a decreased E-to-F slope of the anterior mitral valve leaflet shown by echocardiography in some patients with LVH. Frame-by-frame angiographic analysis in some patients with coronary artery disease, aortic stenosis, or idiopathic hypertrophic subaortic stenosis has confirmed that the percentage of filling in early diastole is decreased compared with normals. As a result of or concomitant with decreased early diastolic filling, atrial contraction becomes forceful and prolonged, and may significantly augment left ventricular late diastolic filling above that in the normal ventricle. Angiography and recently echocardiography have confirmed increased late diastolic filling in some patients with aortic stenosis or idiopathic hypertrophic subaortic stenosis. Most of our patients with LVH previously studied by echocardiography had a large atrial contribution to left ventricular filling except when abnormal mitral valve closure was seen, i.e., a short PR-minus-AC interval with a large notch on the A-to-C slope. In the latter circumstances, the atrial contribution was small, and we postulated that these ventricles were stiffer in end-diastole. The hemodynamic data in the present study allow a better understanding of the relationship between the amount of filling and chamber stiffness in LVH.

In our patients with LVH and end-diastolic chamber stiffness similar to that in group 1 (group 2A), the presence of increased late diastolic filling suggests that in these patients, it is the volume of the atrial contribution rather than increased end-diastolic chamber stiffness that causes the increased A wave in the left ventricular pressure trace. Furthermore, the data indicate a spectrum of end-diastolic chamber stiffness in LVH, ranging from normal to markedly increased, in which patients with the largest A waves in the left ventricular pressure trace tended to have the highest values for end-diastolic chamber stiffness, and at the same time the smallest atrial contribution to left ventricular filling. The presence of normal end-diastolic chamber stiffness with a normal modulus of chamber stiffness (Kp) has also been reported by Peterson et al. in some patients with aortic stenosis and elevated end-diastolic pressure.

A short PR-minus-AC interval with a large A-to-C notch in the anterior mitral valve leaflet has been associated with increased LVEDP and abnormal dp/dt. Both findings would have been expected with more advanced left ventricular dysfunction and were present in three of the four patients of group 2B, but in none of the patients of the other groups. However, the PR-minus-AC interval alone could not discriminate between patients with normal or increased end-diastolic chamber stiffness, as it was also found in groups 1 and 2A. One of the patients of group 2B had premature closure of the mitral valve without a prolonged PR interval or significant aortic regurgitation. We cannot explain this finding.

The mechanism of the slightly more rapid E-to-F slope of the anterior mitral valve leaflet in group 2B patients compared with group 2A patients is unclear. This may be caused by changes in early diastolic filling related to left ventricular dilatation in patients with increased late diastolic stiffness.

The large ΔD in group 2A indicates the importance of the atrial contribution in determining the height of the A wave of the left ventricular pressure trace. Although group 2A ventricles had higher end-diastolic pressures compared with group 1 at comparable end-
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*Group 1—patients 1-8; group 2A—patients 9-20; group 2B—patients 21-24.
†Difference in pressure between points P₂ or P₃ and P₁.
‡Difference in LV interval diastolic dimensions between D₂ or D₃ and D₁.
§Atrial contribution to LV filling divided by D₁.
¶Pressure measured at beginning of P wave of ECG.
Abbreviations: LV = left ventricular; LVH = left ventricular hypertrophy; HR = heart rate; LVEDP = left ventricular end-diastolic pressure; LV-Ao grad = gradient between aorta and left ventricle; CI = cardiac index; LA = left atrial; EDV = end-diastolic volume; PW = posterior wall; IVS = interventricular septum; AC = atrial contribution; EDCS = end-diastolic chamber stiffness; CE = cannot evaluate; CAD = coronary artery disease; V = vessel; AS = aortic stenosis.

Diastolic volumes, the calculated end-diastolic stiffness with the method used was not different between these two groups. However, as the use of echocardiography in deriving chamber stiffness precludes measuring minute dimensional changes (< 1 mm), we have sampled only a small segment of the pressure-dimension curve. In this segment, group 2A patients operate on a higher, although approximately parallel, pressure-dimension curve. The higher early diastolic pressures in group 2A suggest increased early diastolic chamber stiffness, which may be related to abnormal relaxation of the left ventricle in early diastole and to the degree of hypertrophy. It is likely that at higher left ventricular pressures, or if pressure-volume data were measured throughout diastole using angiographically determined ventricular volumes, groups 2A and 1 might have been more divergent. Group 2A patients could clearly be differentiated from group 2B patients by end-diastolic chamber stiffness, with a smaller ΔD and a larger ΔP in the latter. However, since end-diastolic volume and end-diastolic pressure were significantly greater in group
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TABLE 2. Echocardiographic-Hemodynamic Data in Groups 1 and 2  

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<tr>
<th>Age (years)</th>
<th>LA dimension (cm/m²)</th>
<th>Mitral E-to-F slope (mm/sec)</th>
<th>PW (mm)</th>
<th>IVS (mm)</th>
<th>ΔP (mm Hg)</th>
<th>Pre-A wave (mm Hg)</th>
<th>EDP (mm Hg)</th>
<th>EDCS (mm²)</th>
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<tr>
<td>37 ± 4.5</td>
<td>1.6 ± 0.2</td>
<td>92.2 ± 9.0</td>
<td>11 ± 0.4</td>
<td>11 ± 0.5</td>
<td>4.6 ± 0.7</td>
<td>6.4 ± 0.9</td>
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<td>0.15 ± 0.02</td>
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<td>54 ± 3.0</td>
<td>2.0 ± 0.1</td>
<td>58 ± 5.0</td>
<td>14.6 ± 0.4</td>
<td>17.6 ± 1.0</td>
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<td>16.2 ± 1.5</td>
<td>27.2 ± 2.1</td>
<td>0.17 ± 0.03</td>
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</table>

Values are mean ± SEM.  
Abbreviations: LA = left atrial; PW = posterior wall; IVS = interventricular septum; ΔP = difference in pressure between points P₁ or P₂ and P₃; Pre-A wave = pressure measured at beginning of P wave of ECG; EDP = end-diastolic pressure; EDCS = end-diastolic chamber stiffness.
2B, we cannot exclude preload-dependent changes in group 2A as the cause of some of these differences, even though group 2A patients had no evidence of volume depletion and 2B patients no evidence of volume overload. We feel that the greater end-diastolic stiffness in group 2B is more likely related to the greater left ventricular diastolic and systolic dysfunction in group 2B, which probably represents a later stage in the natural history of left ventricular hypertrophy. Because of this dysfunction, group 2B patients operate on a steeper segment of their pressure-volume curve than patients in group 2A. It would be interesting, however, to decrease diastolic pressure in group 2B patients either by altering preload or afterload and measure any change in end-diastolic stiffness.

The method for using echocardiography to measure chamber stiffness was first developed by McLaurin et al. Although their data showed increased end-diastolic chamber stiffness in all patients with aortic stenosis, we found markedly different values for end-diastolic chamber stiffness among our patients. We believe that these differences might partially be explained by the selection of patients. We studied a heterogeneous group of patients, presumably in different stages of disease. They represented only 60% of all patients with LVH who met our criteria for inclusion in this study, because high-quality echoes could not be obtained in the rest. Patients in group 2B with increased end-diastolic chamber stiffness were similar to the patients studied by Grossman, as the atrial contribution to left ventricular filling was similar to that in the respective control populations in both series.

In this study, we could not document a direct correlation between the degree of LVH and end-diastolic

<table>
<thead>
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<th>Table 3. Echocardiographic-Hemodynamic Data in Groups 2A and 2B</th>
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<tr>
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<tr>
<td>EDCS (mm⁻¹)</td>
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<tr>
<td>E-to-F slope (mm/sec)</td>
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<tr>
<td>ΔD (mm)</td>
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<tr>
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</tr>
<tr>
<td>EDP (mm Hg)</td>
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<tr>
<td>EDV (ml/m²)</td>
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<tr>
<td>Ejection fraction</td>
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Abbreviations: EDCS = end-diastolic chamber stiffness; ΔD = atrial contribution to left ventricular filling; Pre-A Wave P = pressure measured at beginning of P wave of ECG; ΔP = difference in pressure between points P₁ or P₃ and P₁; EDP = end-diastolic pressure; EDV = end-diastolic volume.
FIGURE 4. Echocardiographic-pressure recordings of two patients in group 2A with large end-diastolic volume changes in addition to large A waves in the left ventricular pressure trace. A) A patient with asymmetrical septal hypertrophy secondary to idiopathic hypertrophic subaortic stenosis. B) A patient with symmetrical left ventricular hypertrophy secondary to aortic stenosis.

FIGURE 5. Echocardiographic-pressure recording of a patient from group 2B with symmetrical left ventricular hypertrophy secondary to aortic stenosis showing a small end-diastolic volume change with a large A wave in the left ventricular pressure trace. The pressure trace was obtained from a fluid-filled catheter.
chamber stiffness. Although some patients with the thickest left ventricles had the highest values for end-diastolic chamber stiffness, there was considerable overlap. As Grossman et al.22 have shown, a direct relationship between end-diastolic chamber stiffness and the degree of LVH, the differences between our data and their data might also be related to patient selection. In addition, it has recently been shown that the collagen content of the left ventricle may be increased in patients with aortic stenosis.23 Perhaps it is the amount of fibrosis, in addition to wall thickness, that influences end-diastolic chamber stiffness.

End-diastolic chamber stiffness was increased in patients in group 2B compared with that in group 1. However, group 1 does not contain normal persons, but rather patients with atypical chest pain, coronary artery disease, and even aortic stenosis. Nevertheless, we assume that the patients in group 1 probably have normal end-diastolic chamber stiffness. Not only was the calculated end-diastolic chamber stiffness similar in all patients in group 1 regardless of diagnosis, but the values were in the same range as a group of controls previously reported by Grossman et al.7

There are several problems inherent in the use of the echocardiogram in measuring left ventricular volume. Difficulties in identification of the endocardium from other structures, i.e., chordae, in addition to the fact that the resolution of the echocardiogram in the order of 1 mm, represent possible sources of error in measuring small volume changes. However, reproducibility in measuring these changes has been excellent and only the highest quality echocardiograms were chosen and precisely analyzed using a computerized, echocardiographic-hemodynamic program.

Another source of error is the calculation of chamber stiffness using the formula outlined in our methods, since it does not consider the influence of viscous or inertial properties of muscle on the diastolic pressure-volume relationship. Gaasch et al.,24 and recently Kennish et al.,25 have shown the importance of viscous properties in interpreting pressure-volume data especially during atrial systole. Although theoretically, viscous effects cannot be excluded in our patients with LVH and a large atrial contribution to left ventricular filling, they probably account for only a small increment in pressure, and therefore have questionable significance in interpretation of our data.

In conclusion, in patients with LVH secondary to aortic stenosis, idiopathic hypertrophic subaortic stenosis, or hypertension, an increased A wave in the left ventricular pressure curve with an increase in LVEDP may be related to augmented atrial volume transport rather than increased left ventricular end-diastolic chamber stiffness. In patients who have the largest A waves in the left ventricular pressure curve, and the smallest atrial contribution to left ventricular filling, end-diastolic chamber stiffness is considerably increased, and in these patients the high LVEDP is undoubtedly related to increased end-diastolic chamber stiffness. These patients may have a more advanced stage of LVH that occurs in some patients before significant dilatation of the left ventricle. A decreased ejection fraction in three of the four patients with significantly increased end-diastolic chamber stiffness is consistent with the advanced stage of their disease. As patients in group 2B tend to have a smaller atrial contribution to left ventricular filling than patients in group 2A, this finding might be an important noninvasive indicator of markedly increased left ven-

**Figure 6.** Representative mitral valve echocardiograms from two patients in group 2B. A) A large notch on A-to-C slope. B) Early mitral valve closure (arrow) with a rapid A-to-C slope of the mitral valve.
tricular end-diastolic chamber stiffness in patients with LVH, especially in the presence of abnormal mitral valve closure. Because the number of patients in this study is small, more patients should be evaluated to determine the clinical relevance of our findings.

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