Assessment of left ventricular mechanics in patients with asymptomatic aortic regurgitation: a two-dimensional echocardiographic study

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ABSTRACT We describe a noninvasive method for determining end-systolic meridional and circumferential wall stress and left ventricular architecture as the ratio of muscle to cavity area. With this technique, which uses two-dimensional echocardiography and cuff-determined values for systolic blood pressure, we assessed wall stress and left ventricular architecture in 15 normal subjects and 15 asymptomatic patients with severe chronic aortic regurgitation at rest and after load manipulations with sublingual nitroglycerin. Resting end-systolic meridional and circumferential stress were increased in patients with aortic regurgitation (113.9 ± 29 and 260 ± 50.7 × 10³ dynes/cm²) compared with those in normal subjects (85.6 ± 15.4 and 214.1 ± 28.4 × 10³ dynes/cm²) (both p < .01) and remained significantly greater after nitroglycerin. Meridional stress values obtained from two-dimensional echocardiographic studies correlated closely (r = .89) with values calculated from simultaneously recorded M mode echocardiograms. Ejection fraction in patients with aortic regurgitation and normal subjects were similar at rest (55 ± 10% vs 59 ± 6%) and were unchanged by nitroglycerin. In spite of the increased left ventricular mass in patients with aortic regurgitation (227 ± 60 g vs 130 ± 22 g in normal subjects), the mass-to-volume ratio and the ratio of muscle to cavity area in diastole in patients with aortic regurgitation were significantly lower than normal (0.90 ± 0.23 vs 1.30 ± 0.21 and 0.91 ± 0.23 vs 1.11 ± 0.18 [p < .005 and p < .02]). These differences were exaggerated after nitroglycerin, while concomitant changes in relative wall thickness were virtually undetected by M mode echocardiography. Thus this technique can be used for early recognition of afterload excess and changes in left ventricular architecture in patients with aortic regurgitation. Furthermore, the mean slopes of the circumferential stress-diameter and meridional stress-length lines, which represent load-independent indexes of myocardial contractile state, could be assessed and were similar in the group of patients with asymptomatic aortic regurgitation and normal subjects, indicating that overall myocardial contractility was still normal. We conclude that circumferential and meridional wall stress, myocardial contractility, and left ventricular architecture can be determined noninvasively. These measurements may prove to be useful in assessing patients with primary myocardial or valvular heart disease and determining their long-term management.


END-SYSTOLIC meridional stress, which can be evaluated by M mode echocardiography, is a readily determined quantitative index of left ventricular afterload and may have clinical and therapeutic implications. The relationship between meridional stress and left ventricular diameter may be an important load-independent index of myocardial contractile state. Relative wall thickness measured by M mode echocardiography has also been a useful descriptor of left ventricular short-axis architecture. However, there are potential limitations to the use of M mode echocardiography to measure left ventricular diameter and wall thickness. Among these are included the following: (1) there is a possibility of variability in repetitive measurements of left ventricular diameter and wall thickness, which is of special concern in patients with enlarged hearts; small changes in measurements of diameter and particularly of wall thickness could result in large discrepancies in left ventricular end-systolic wall stress. (2) The cross section of the left ventricle imaged by M mode echocardiography, the so-called ice pick view, is assumed to be representative of the left ventricle as a whole, and the presence of segmental
wall motion abnormalities, which would invalidate wall stress calculations, cannot be reliably excluded. 
(3) Because M mode echocardiography cannot measure the left ventricular long axis, no attempt can be made to assess circumferential stress, which is of much greater magnitude than meridional stress and may have a closer relationship to left ventricular emptying and ejection fraction. Strictly speaking, plots of end-systolic stress diameters should relate circumferential stress to left ventricular diameter, and meridional stress to ventricular length. We therefore devised a new noninvasive method of determining relative wall thickness, end-systolic meridional stress, and end-systolic circumferential stress by means of two-dimensional echocardiography, which may circumvent the important shortcomings of M mode echocardiographic techniques.

This study describes the two-dimensional echocardiographic assessment of end-systolic meridional stress and its relationship to left ventricular cavity length, end-systolic circumferential stress and its relationship with left ventricular internal diameter, and the ratio of circumferential to meridional stress. Normal subjects and patients with aortic regurgitation were studied at rest and after left ventricular load reduction with sublingual nitroglycerin. We also compared the values of end-systolic meridional stress and the ratio of muscle to cavity area calculated from two-dimensional echocardiographic data with those of meridional stress and relative wall thickness calculated from simultaneously recorded two-dimensionally directed M mode echocardiograms.

**Methods**

**Normal subjects.** This group was composed of 15 normal volunteers, three women and 12 men ranging in age from 24 to 35 years (mean 28). None had any history, symptoms, or signs of cardiac disease or hypertension. All had normal 12-lead electrocardiograms and were taking no medications.

**Aortic regurgitation.** This group comprised 15 asymptomatic patients with chronic severe aortic regurgitation. There were two women and 13 men ranging in age from 18 to 50 years (mean 31). Ten patients had undergone cardiac catheterization and had aortic regurgitation of angiographic grade III or IV out of IV, with no left ventricular aortic gradient of more than 10 mm Hg, no mitral regurgitation, and no other valvular lesions. Only one of the 15 patients underwent coronary arteriography, which revealed normal coronary arteries. Twelve of the remaining 14 patients were under 35 years of age. None had angina or segmental wall motion abnormalities on two-dimensional echocardiography, but all had dilated left ventricular cavities with marked volume overload and echocardiographically normal aortic valves. None of the patients had congestive heart failure and all were in sinus rhythm.

**Data acquisition.** The following data were recorded in each subject in the resting state after 5 min of recumbency and were repeated after administration of 0.4 mg of sublingual nitroglycerin:

1. Heart rate was monitored continuously on standard electrocardiographic lead II.
2. Cuff-determined systolic arterial blood pressure was measured in the left arm at 1 min intervals for at least 3 min at rest and for a minimum of 10 min after nitroglycerin. These values were used to represent end-systolic left ventricular pressure. We initially demonstrated that cuff-determined systolic blood pressure correlated with Millar micromanometer–determined left ventricular pressure in a mixed group of patients; in this study we demonstrated that this was also true in patients with aortic regurgitation (figure 1). Each systolic blood pressure recording was matched with the M mode strip chart recorder by an event marker and with the two-dimensional echocardiographic recordings by the frame counter.
3. M mode left ventricular echocardiograms at the tips of the papillary muscle were recorded at paper speeds of 50 mm/sec from Varian 3000R or 3400R two-dimensional phased-array ultrasonographs; we used the electronic M mode echocardiographic cursor to ensure that a true diameter of the left ventricle was sampled. M mode echocardiograms were recorded to correspond in time with the systolic blood pressure recordings.
4. Two-dimensional echocardiograms were obtained of the left ventricular short axis at the level of the tips of the papillary muscles from the parasternal position (figure 2) and of the apical four-chamber view so that the left ventricular long axis could be accurately measured (figure 3). Before and 3 min after nitroglycerin, approximately 10 to 20 cardiac cycles of left ventricular short axis were recorded, and the transducer was quickly moved to the left ventricular apex to obtain 10 to 20 cardiac cycles of the four-chamber view in order to minimize the interval between long- and short-axis left ventricular images.

**Data processing and analysis**

**M mode left ventricular echocardiograms.** M mode left ventricular echocardiograms containing a minimum of three cardiac cycles of similar cycle length at rest and 3 min after nitroglycerin were calibrated and digitized on a Hewlett-Packard 9821A desktop computer. End-diastolic left cavity diameter (LVD) and wall thickness (WT) were measured at the peak of the R wave on the electrocardiogram. End-systolic cavity diameter and wall thickness were identified at the time of appearance of the smallest left ventricular diameter. Left ventricular diameter determined by M mode echocardiography was measured from septal trailing edge to posterior wall leading edge, while posterior wall

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**FIGURE 1.** Correlation between cuff-determined systolic arterial pressure and Millar micromanometer–determined left ventricular pressure in 14 patients with chronic aortic regurgitation, five of whom had pressure perturbations with nitroglycerin or phenylephrine.
thickness was measured from leading edge to leading edge as described previously. From these data we assessed the end-diastolic and end-systolic relative wall thickness \( [h/R = (WT/LVD)/2] \) and used it as an index of left ventricular short-axis architecture.

End-diastolic meridional wall stress was computed in both groups at rest and after nitroglycerin with the formula developed by Grossman et al., \( \text{stress} = P \times R / 2h(1 + h/2R) \), as previously applied in our laboratory:

\[
\text{stress} = (1.33 \times 0.25 \times P [LVD]) / WT [1 + WT/LVD]
\]

where \( P \) = cuff-determined systolic pressure and the constant 1.33 converts mm Hg to dynes/cm².

**Two-dimensional left ventricular echocardiograms**

**SHORT AXIS.** For each subject before and after nitroglycerin, endocardial and epicardial images of the left ventricular short axis from at least five high-quality stop-action end-diastolic and end-systolic frames were traced on clear plastic overlays from a high-contrast television scan converter with X and Y axis calibration factors. To identify the exact end-systolic frame, we arbitrarily selected one occurring at the midpoint of the T wave on the electrocardiogram. To investigate whether selection of this particular frame was critical, we traced two frames before and two frames after it.

Tracings of left ventricular short-axis endocardium and epicardium were digitized with the orthogonal calibration factors on a Hewlett-Packard microcomputer to obtain the following:

1. total area \( (A_t) \) enclosed by the left ventricular epicardium and right side of the septum;
2. cavity area \( (A_c) \) by two methods — the papillary muscles were included as cavity for cavity volume and stress determinations, and \( A_c \) was digitized with the papillary muscles included as left ventricular wall for left ventricular mass determinations by our previously validated method;
3. muscle area \( (A_m) \) for stress determinations, obtained by subtracting \( A_c \) (including papillary muscles) from \( A_t \).

**APICAL FOUR-CHAMBER VIEW.** Endocardial and epicardial echocardiograms in the apical four-chamber view of the left ventricle in a minimum of five end-diastolic and five end-diastolic stop-action frames were traced and digitized to obtain left ventricular length \( (L) \), defined as the distance from the midpoint of the apical endocardium to the midpoint of the plane of the mitral valve anulus (figure 3).

The raw values for \( A_t, A_m, \) and \( L \) were corrected with regression equations developed for these echocardiographic instruments in our laboratory.9, 10 These corrected values were utilized to calculate:

1. End-diastolic and end-systolic volumes by the short-axis area-length method \( V = \frac{5}{6} A_t L \)
2. Fractional shortening expressed as percent change in left ventricular short-axis area
3. Ejection fraction
4. The ratio of short-to-long left ventricular axes:

\[
\frac{\sqrt{A_t/\pi}}{L}
\]

5. Left ventricular muscle mass \( (LVM) \) calculated as \( 1.055 \times 5/6(A_{Lm} - A_c) \). The reproducibility and interobserver variability of left ventricular volume and mass determination by two dimensional echocardiography has been previously reported from our laboratories.9, 10

6. Left ventricular end-systolic meridional wall stress \( (S_m) \):

\[
1.33 \times P \times A_c / A_t - A_c
\]

7. Left ventricular end-systolic circumferential wall stress \( (S_c) \):

\[
1.33 \times P \times \sqrt{A_c} \left( 1 - \sqrt[\sqrt{A_t} - \sqrt{A_c}] \right)
\]

\( *1.055 \) is the specific gravity of cardiac muscle.
The formulas for meridional and circumferential stress are modified from those of Mirsky, and the constant 1.33 represents the conversion factor from mm Hg to dynes/cm².

(8) Ratio of myocardial area $A_m$ to cavity area $A_L$ ($A_m/A_L$).

In addition, we assessed the relationship between (1) end-systolic meridional wall stress and left ventricular cavity length and (2) end-systolic circumferential stress and left ventricular internal diameter, assuming a linear model. We also determined the ratio of end-systolic circumferential wall stress to end-systolic meridional wall stress. A comparison was made between noninvasive end-systolic meridional stress calculated from two-dimensional echocardiographic images and those from simultaneous M mode echocardiographic recordings, and between relative wall thickness determined by M mode echocardiography and the ratio of muscle to cavity area calculated from two-dimensional images.

Statistical methods. The significance of differences in measured and derived parameters of left ventricular function before and after nitroglycerin within the normal subjects and within the group of patients with aortic regurgitation was assessed with the paired t test. Unpaired t tests were used to test the significance of differences in parameters between the two populations.

Results

The range of resting heart rates and the mean increase after nitroglycerin were similar in the normal subjects and in patients with aortic regurgitation (table 1). There were also no differences between normal subjects and patients with aortic regurgitation in systolic blood pressure at rest or after nitroglycerin (table 1).

Left ventricular long-axis lengths were greater in patients with aortic regurgitation than in normal subjects at end-systole and end-diastole ($p < .005$) before and after nitroglycerin, but the percentage changes from systole to diastole in the two groups were similar at rest and were unchanged by nitroglycerin (table 1). Left ventricular diameter at end-systole and end-diastole was significantly greater in patients with aortic regurgitation than in normal subjects and changed little after nitroglycerin (table 1).

End-systolic and end-diastolic left ventricular volumes were both markedly increased in patients with aortic regurgitation at rest and approached three times the values for normal subjects (table 1). We calculated the left ventricular cavity short-axis area of the end-systolic frame arbitrarily selected for calculating volume in 10 patients (five normal and five with aortic regurgitation), and the mean interpatient volume of 10.16 cm² did not differ significantly from the two preceding frames (9.96 and 9.92 cm²) or the two following frames (10.20 and 10.13 cm²). This demonstrated that selection of a single frame to represent end-systole was not critical. Moreover, the mean values for intrapatient variability of the first and second preceding and succeeding frames from the frame selected was 1.2% and 2.9%, respectively. Fractional cavity shortening assessed as percent change in cavity area of left ventricular short axis was similar in patients with aortic regurgitation and normal subjects and did not change significantly after nitroglycerin (table 1, figure 4).

After nitroglycerin there was a marked reduction in left ventricular diastolic volume in both groups ($p < .01$), and although the absolute change in volume was significantly greater in patients with aortic regurgita-
TABLE 1
Heart rate, systolic blood pressure, left ventricular mass, and global left ventricular function in normal subjects and in patients with aortic regurgitation at rest and after nitroglycerin

<table>
<thead>
<tr>
<th>Patient group</th>
<th>Heart rate (bpm)</th>
<th>Systolic blood pressure (mm Hg)</th>
<th>LV cavity length (cm)</th>
<th>LV cavity diameter (cm)</th>
<th>LV volume (ml)</th>
<th>Ejection fraction in cavity area (%)</th>
<th>LV mass-volume ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Pre</td>
<td>69</td>
<td>126</td>
<td>8.6</td>
<td>7.5</td>
<td>13</td>
<td>4.7 ± 0.4</td>
<td>104</td>
</tr>
<tr>
<td></td>
<td>± 14</td>
<td>± 13</td>
<td>± 1.3 ± 0.7 ± 4</td>
<td>± 4</td>
<td>± 0.4 ± 0.4</td>
<td>± 16 ± 4</td>
<td>± 15 ± 4</td>
</tr>
<tr>
<td>Normal Post</td>
<td>75</td>
<td>117</td>
<td>8.3 ± 0.6 ± 4</td>
<td>7.3 ± 4</td>
<td>13</td>
<td>4.5 ± 0.3</td>
<td>92 ± 4</td>
</tr>
<tr>
<td></td>
<td>± 16</td>
<td>± 13</td>
<td>± 1.3 ± 0.5 ± 4</td>
<td>± 13 ± 4</td>
<td>± 0.6 ± 0.6</td>
<td>± 3 ± 4</td>
<td>± 34 ± 4</td>
</tr>
<tr>
<td>AR Pre</td>
<td>69</td>
<td>134</td>
<td>10.0 ± 0.3 ± 5</td>
<td>9.0 ± 6 ± 4</td>
<td>10</td>
<td>6.8 ± 0.9</td>
<td>274 ± 128</td>
</tr>
<tr>
<td></td>
<td>± 10</td>
<td>± 16</td>
<td>± 1.2 ± 1.3 ± 5</td>
<td>± 1.3 ± 4</td>
<td>± 1.1 ± 0.9</td>
<td>± 121 ± 89</td>
<td>± 18 ± 4</td>
</tr>
<tr>
<td>AR Post</td>
<td>74</td>
<td>123</td>
<td>9.8 ± 0.3 ± 5</td>
<td>8.9 ± 6 ± 4</td>
<td>10</td>
<td>6.6 ± 0.9</td>
<td>244 ± 114</td>
</tr>
<tr>
<td></td>
<td>± 11</td>
<td>± 20</td>
<td>± 1.2 ± 1.3 ± 5</td>
<td>± 1.2 ± 4</td>
<td>± 1.1 ± 1.1</td>
<td>± 115 ± 75</td>
<td>± 6 ± 11</td>
</tr>
</tbody>
</table>

NTG = nitroglycerin; LV = left ventricular; AR = aortic regurgitation.

\(^a\)p < .001 denotes significant difference in resting or postnitroglycerin values from normal.

\(^b\)p < .005 denotes significant difference in resting or postnitroglycerin values from normal.

In spite of marked left ventricular hypertrophy and almost a twofold increase in left ventricular mass, the mass-to-volume ratio was significantly lower than normal (0.90 ± 0.23; p < .001), indicating inadequate hypertrophy or mass/volume mismatch. It remained significantly less than normal after nitroglycerin, increasing to 1.02 ± 0.29 (table 1).

Relative wall thickness (h/R ratio) calculated from M mode echocardiograms was similar in the two groups at end-diastole and end-systole at rest (table 2). However, the ratios of left ventricular muscle area \(A_m\) to cavity area \(A_c\) determined from digitized, two-dimensional, short-axis end-diastolic and end-systolic frames were significantly greater in normal subjects than in patients with aortic regurgitation (p < .025 and p < .05, respectively) (table 2).

Diastolic relative wall thickness determined by M

![FIGURE 4. Left ventricular fractional shortening, expressed as percent change in two-dimensional echocardiographic left ventricular short-axis cavity area in patients with aortic regurgitation compared with normals. Mean values did not differ significantly either before or after nitroglycerin in the two groups.](http://circ.ahajournals.org/DownloadedFrom)
mode echocardiography changed little after nitroglycerin in the two groups, while systolic relative wall thickness in normal subjects increased and became significantly greater than that in patients with aortic regurgitation (p < .025) (table 2). The ratio of muscle area to cavity area at end-systole and end-diastole were significantly different in patients with aortic regurgitation than in normal subjects but increased by the same amount at end-diastole (7%) and end-systole (10%) after nitroglycerin (table 2).

The ratio of short to long left ventricular axes, a simple expression of cavity shape at end-systole and end-diastole, was significantly different in the two groups at rest (table 2), with the larger values in patients with aortic regurgitation indicating a more spherical shape. After nitroglycerin, the left ventricular axis ratio remained constant in both groups, demonstrating that load reduction did not result in any major change in left ventricular shape or configuration and that there was no tendency to selectively reduce short axis to achieve a more normal ellipsoid shape in patients with aortic regurgitation.

M mode and two-dimensional echocardiographic end-systolic meridional wall stress was significantly greater in patients with aortic regurgitation than in normal subjects at rest and remained so after nitroglycerin (table 2, figure 6). The decrease in end-systolic stress in patients with aortic regurgitation after nitroglycerin was comparatively greater than that occurring in normal subjects (figure 6). However, when normalized to resting values, the changes in end-systolic wall meridional stress in the two groups were no different. Two-dimensional echocardiographic estimations of end-systolic meridional stress in the two groups correlated closely with determinations from simultaneously recorded M mode echocardiograms (r = .89) (figure

### TABLE 2
Left ventricular architecture and end-systolic meridional and circumferential stress in normals and patients with aortic regurgitation at rest and after nitroglycerin

<table>
<thead>
<tr>
<th>Patient group</th>
<th>NTG</th>
<th>No.</th>
<th>M mode h/R ratio (Diastolic, Systolic)</th>
<th>2D A_2/A_1</th>
<th>Ratio of short to long axis (Diastolic, Systolic, ESMS, ESCS, CS/MS)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal Pre</td>
<td>15</td>
<td>0.36, 0.87</td>
<td>1.11, 2.03</td>
<td>0.56, 0.46</td>
<td>85.6, 214.1, 2.59</td>
</tr>
<tr>
<td>Normal Post</td>
<td>15</td>
<td>0.37, 0.96</td>
<td>1.19, 2.26</td>
<td>0.55, 0.46</td>
<td>72.0, 184.0, 2.59</td>
</tr>
<tr>
<td>AR Pre</td>
<td>15</td>
<td>0.35, 0.75</td>
<td>0.91, 1.64</td>
<td>0.68, 0.55</td>
<td>113.9, 260.0, 2.31</td>
</tr>
<tr>
<td>AR Post</td>
<td>15</td>
<td>0.36, 0.80</td>
<td>0.97, 1.79</td>
<td>0.66, 0.55</td>
<td>99.4, 230.0, 2.38</td>
</tr>
</tbody>
</table>

NTG = nitroglycerin; 2D = two-dimensional echocardiographic; ESMS = end-systolic meridional stress; ESCS = end-systolic circumferential stress; AR = aortic regurgitation.

Statistical comparisons significant difference in resting or postnitroglycerin values from normal: 'p < .005; "p < .01; 'p < .025; "p < .05.
7). However, the two-dimensional echocardiographic values were systematically higher than those obtained from M mode echocardiographic data because conventional wall thickness measurements overestimate true mean left ventricular wall thickness and left ventricular mass as previously demonstrated in our laboratory.\(^7\)

This overestimation of wall thickness would result in a higher h/R ratio and thus a lower estimate of wall stress. The two-dimensional echocardiographic method used in this study incorporated a regression correction that compensated for a similar systematic overestimation of myocardial cross-sectional area by two-dimensional echocardiography. Thus the stress calculations have been corrected for image error by the two-dimensional method but not by the M mode method.

One objective of nitroglycerin administration was to enable us to examine the relationship of end-systolic meridional stress to the left ventricular long axis. We used the slope of these constructs as an index of myocardial contractility, the normal subjects being a comparator for the patients with aortic regurgitation. Although the stress length lines for patients with aortic regurgitation were displaced to the right (figure 8), the slopes in the normal subjects and patients with aortic regurgitation were similar, indicating that in spite of afterload excess, myocardial contractility was normal.

Mean end-systolic circumferential wall stress was greater in patients with aortic regurgitation than in normal subjects both at rest (p < .005) and after nitroglycerin (p < .01) (table 2, figure 9), but the reduction in mean circumferential stress in patients with aortic regurgitation after nitroglycerin was similar to that in normal subjects (table 2, figure 9). The relationship of end-systolic circumferential wall stress to the left ventricular internal diameter in patients with aortic regur-

**FIGURE 6.** End-systolic meridional stress determined by two-dimensional echocardiography was significantly different in normals and patients with aortic regurgitation both before and after nitroglycerin (NTG).

**FIGURE 7.** Correlation between two-dimensional and M mode echocardiographic assessments of end-systolic meridional wall stress (ESMS) (r = 0.89).

**FIGURE 8.** Slopes of the end-systolic meridional stress-length lines were similar in the 15 normals (y = -376.1818 + 71.8182x) and the 15 patients with aortic regurgitation (y = -576.7579 + 76.3158x). Filled symbols represent the mean resting values; open symbols represent postnitroglycerin values.
gitation as a group, similar to that relationship between meridional stress and cavity length, was displaced to the right of normal, but the slope, also an index of myocardial contractile function, was virtually identical to that in the normal subjects (figure 10). In the one patient with aortic regurgitation and decreased ejection fraction, not only was meridional and circumferential stress the highest but also the slopes of the stress-length and stress-diameter relationships varied most from normal, indicating impaired left ventricular contractility.

The ratio of orthogonal wall stresses, i.e., circumferential to meridional stress, was significantly different in the two groups (p < .005) (table 2). In spite of the dramatic reduction in meridional and circumferential stress after nitroglycerin, this ratio remained constant in both normal subjects and patients with aortic regurgitation, as did the ratio of short to long axis, indicating that there were no major changes in the left ventricular configuration with perturbations in left ventricular loading.

Discussion

Using high-quality two-dimensional echocardiography and cuff-determined systolic blood pressure, we calculated relative wall thickness and end-systolic meridional and circumferential wall stress noninvasively. This technique allowed more extensive sampling of the left ventricle than possible with M mode echocardiography and with the knowledge that there were no segmental wall motion abnormalities, which have been reported in patients with aortic regurgitation.\textsuperscript{13} End-systolic meridional stress calculated from two-dimensional echocardiograms for normal subjects and for patients with aortic regurgitation corresponded closely with those calculated from simultaneously recorded M-mode echocardiograms. This was important because noninvasively determined end-systolic meridional stress calculated from M mode echocardiograms has correlated (r = .96) with values obtained at cardiac catheterization.\textsuperscript{1}

End-systolic stress is of interest for two reasons. First, it is the load that limits left ventricular ejection and thus provides a useful quantitative index of afterload at the myocardial level.\textsuperscript{14, 15} Second, by altering end-systolic stress, one can assess the myocardial force-length relationship at end-systole and use it as an

![FIGURE 9. End-systolic circumferential stress determined by two-dimensional echocardiography was significantly greater in patients with aortic regurgitation than in normals both before and after nitroglycerin (NTG).](image)

![FIGURE 10. The slopes of the end-systolic meridional stress-diameter lines (y = −218.1333 + 90.6667x in normals, and y = −370.4000 + 96.6667x in patients with aortic regurgitation), and end-systolic circumferential stress-diameter lines (y = −458.1334 + 200.6667x in normals, and y = −732.2800 + 198.0000x in patients with aortic regurgitation) were similar in the two groups. Filled symbols represent mean values for the two groups at rest; open symbols represent postnitroglycerin values.](image)
index of myocardial contractility that is independent of load. Two-dimensional echocardiography permitted calculation of left ventricular volume and end-systolic circumferential stress. It also allowed detection of changes in the ratio of short to long left ventricular axis, and the ratio of circumferential to meridional stress before and after load manipulation and nitroglycerin. Previous studies based on M mode echocardiography have used only meridional stress or calculated circumferential stress assuming a fixed left ventricular axis ratio. However, axis ratio can vary widely because of changes in cavity shape, and circumferential stress is the proper load to relate to short axis dimension changes, since it accounts for the bulk of left ventricular emptying.

Heart rate and cuff-determined systolic blood pressure were similar in normal subjects and in patients with aortic regurgitation at rest and after nitroglycerin and could not account for the difference in cavity volumes, ejection fraction, or wall stress between the two groups. Relative wall thickness (M mode) is virtually constant in the normal human and was normal in the patients with aortic regurgitation at rest. After nitroglycerin, diastolic relative wall thickness in patients with aortic regurgitation did not change, while systolic relative wall thickness was significantly less than that in the normal subjects in spite of the presence of left ventricular hypertrophy. The ratio of muscle to cavity area in patients with aortic regurgitation was also significantly less than normal at rest, and these differences were exaggerated after nitroglycerin, indicating that differences in short-axis architecture may be detected better by two-dimensional echocardiography than by M mode echocardiography.

The ability to measure both long and short left ventricular axes with two-dimensional echocardiography enabled a simple description of cavity shape. The ratio of short to long axes in patients with aortic regurgitation was significantly greater than that in normal subjects, indicating that the left ventricle was more spherical and therefore accommodated a greater volume of blood per unit perimeter. There was no change in axis ratio in either group after nitroglycerin, showing that left ventricular shape did not change during manipulation of left ventricular load.

Left ventricular volumes were greatly increased in patients with aortic regurgitation. After nitroglycerin, left ventricular volume in both groups decreased significantly, and although the absolute changes in diastolic cavity volume were significantly greater in patients with aortic regurgitation, their percent changes were similar. The reduction in left ventricular volume in patients with aortic regurgitation after nitroglycerin was not achieved by change in left ventricular long axis but by reduction in left ventricular cavity cross section. This initially appeared inconsistent with the lack of change in diastolic radius measured by M mode echocardiography but was probably explained by the fact that the cross-sectional area is dependent on the second power of the radius and changes in area were more easily detected than those in radius alone. Thus there may be an advantage of two-dimensional over M mode echocardiography in detecting such subtle variations. Regardless of the greater left ventricular volume and different cavity configurations, mean fractional shortening and ejection fraction in patients with aortic regurgitation and normal subjects were similar and unaffected by nitroglycerin.

In spite of the left ventricular hypertrophy in patients with aortic regurgitation, the mass-to-volume ratio was significantly reduced and remained abnormal after nitroglycerin, indicating mass-to-volume mismatch or inadequate left ventricular hypertrophy. Inadequate left ventricular hypertrophy has been regarded as a major contributor to the pump dysfunction in patients with aortic regurgitation, but in our patients overall myocardial contractile function remained normal.

Assessment of end-systolic wall stress with two-dimensional echocardiography allowed more detailed examination of myocardial muscle function and permitted identification of afterload excess in the patients with aortic regurgitation. After nitroglycerin, wall stress decreased in the majority of patients with aortic regurgitation. These transient reductions in wall stress with nitroglycerin suggested to us that afterload reduction with vasodilators, which has been advocated in the treatment of asymptomatic aortic regurgitation, may prove efficacious in patients with asymptomatic aortic regurgitation.

When end-systolic meridional stress was plotted against left ventricular cavity length, the slopes of the stress length lines connecting the resting values to those obtained after nitroglycerin were similar in the two groups. This indicated that myocardial contractility in the patients with aortic regurgitation considered as a group was normal. This was also true when left ventricular long axis was substituted for left ventricular internal dimension measured from M mode or two-dimensional echocardiograms.

The end-systolic meridional stress-length and stress-diameter relationships were constructed from small changes in left ventricular size. The rationale for this was based first on the concern that larger changes in left ventricular size might be associated with barore-
ceptor reflex-mediated changes in contractile state; second, we sought a practical and safe method for clinical application in outpatients. Although these small changes may potentially increase the variability of the slopes of the stress-length and stress-diameter determinations, the meridional stress-diameter slopes assessed by M mode and two-dimensional echocardiography were similar in the normal subjects and in patients with aortic regurgitation. This concordance of results obtained by these two different techniques strongly suggested that the myocardial contractile state was normal in the two groups. Circumferential wall stress was markedly increased in patients with aortic regurgitation and remained significantly different from normal after nitroglycerin. When circumferential wall stress was plotted against left ventricular diameter, this relationship in patients with aortic regurgitation was shifted to the right of normal but the slopes were virtually identical, similar to the meridional stress-length relationships, indicating that myocardial contractility in the group of patients with aortic regurgitation was normal.

The ratios of circumferential to meridional end-systolic stress were different in the two groups, which probably reflected differences in cavity shapes. These differences were maintained after nitroglycerin, which is consistent with the absence of any change in left ventricular axis ratio when left ventricular loading was altered.

One limitation of this technique, however, is that it should not be applied to patients with segmental abnormalities due to coronary artery disease, since the stress calculations assume uniformity of myocardial contractility.

Noninvasive assessment of end-systolic meridional and circumferential stress may provide a more physiologic basis on which to study patients with aortic regurgitation. Measurement of left ventricular diameter, length, and wall stress before and after small perturbations in left ventricular loading with short-acting agents such as nitroglycerin allows longitudinal assessment of myocardial contractility and detection of afterload excess at serial follow-up visits. In addition, this technique may provide a means of recognizing the onset of decreased myocardial contractility early, manifested as departure from the normal slopes of the stress-length and stress-diameter relationships. This may also prove useful in characterizing the left ventricular architectural changes in the early postoperative period after aortic valve replacement, when left ventricular remodeling is occurring most rapidly, and in identifying persistence of afterload excess in patients with malfunction of a prosthetic aortic valve. However, long-term prospective studies are needed to determine whether clinical decisions and recommendations can be made from these data.

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