Serial M-mode Echocardiography in Severe Chronic Aortic Regurgitation

IAN G. MCDONALD, M.D., AND V. MICHAEL JELINEK, M.D.

SUMMARY Thirteen patients with severe chronic aortic regurgitation (mean age 52.5 years) were studied by serial M-mode echocardiography. When first studied, none had breathlessness caused by left ventricular failure (LVF). Nine of these patients remained asymptomatic over a mean period of 4 years, 3 months (no LVF group); the other four patients developed left ventricular failure with dyspnea after a mean interval of 3 years, 11 months (LVF group). For both of these groups, we compared the echocardiographic measurements from the first and last of the serial studies. For the LVF group, end-diastolic left ventricular internal dimension increased 14%, end-systolic dimension increased 35%, fractional shortening decreased 45% and left atrial dimension increased 62%. All of these changes were significant. For the No LVF group, the change in end-diastolic left ventricular internal dimension was not significant, but the 6% increase in end-systolic dimension, 10% reduction in fractional shortening and 25% increase in left atrial size were all statistically significant.

Although echocardiography could detect declining left ventricular function in a group of symptomatic patients with severe chronic aortic regurgitation, the reproducibility of the technique was limited in individual patients. Therefore, serial echocardiographic studies should be interpreted in conjunction with clinical assessment and other investigations.

PHYSICIANS often have difficulty deciding when to recommend aortic valve replacement in patients with severe chronic aortic regurgitation. Depressed myocardial function may persist after aortic valve replacement, and it has been suggested that the operation might be recommended in some patients who have a progressive increase in heart size even in the absence of symptoms. However, the asymptomatic patient often cannot be convinced of the necessity for the operation, and our enthusiasm for aortic valve replacement in such patients is still tempered by the small operative mortality and by the incidence of complications related to the prosthetic valve. Should surgery be deferred, myocardial function may progressively deteriorate so that the mortality of aortic valve replacement may be increased and postoperative improvement may be less certain. Indeed, many reports suggest that delaying aortic valve replacement might increase operative mortality, especially the late mortality, resulting in less recovery of left ventricular contraction and less symptomatic improvement. No generally accepted criteria for aortic valve replacement in asymptomatic patients have emerged; nor is it clear whether it is safe to continue medical treatment in the face of early symptoms until there is evidence of progressive deterioration. Echocardiography is an objective method that can be used to detect impaired left ventricular function. However, it is not clear whether serial M-mode echocardiography is sufficiently sensitive to detect declining left ventricular function and hence be of value in the clinical management of severe chronic aortic regurgitation. We analyzed our own experience over an 8-year period in an attempt to answer this question.

Patients

Fifteen patients with severe chronic aortic regurgitation were followed medically either because aortic valve replacement was not indicated on clinical grounds or because the patient refused surgery. Two patients were subsequently excluded because the echocardiograms were considered unsatisfactory. The 13 patients who remained in the study included 11 males and two females, with an average age of 52.5 years (table 1).

Severe aortic regurgitation was defined as an echocardiographic left ventricular stroke volume of 100 ml or more. This criterion was chosen, taking into account the relationship between left ventricular stroke volume and the severity of aortic regurgitation and the results of earlier study of patients with aortic regurgitation. Thus, Dodge et al. established that the left ventricular stroke volume in aortic regurgitation increased in direct proportion to the magnitude of regurgitation in an earlier cross-sectional study of patients with aortic regurgitation, the average value of the echocardiographic left ventricular stroke volume was 128.5 ml in severe chronic aortic regurgitation in the absence of left ventricular failure and 103.1 ml in the presence of failure.

Cardiac catheterization was performed in six of the 13 patients (patients 1, 4, 6, 10, 11 and 12) and was repeated in four to assess progress (patients 1, 10, 11 and 12). Coronary angiography and left ventricular angiography were performed in all of these patients and supine bicycle ergometer exercise was performed in all but patient 4. Left ventricular volumes and regurgitant fractions had been measured only in patient 12. In the remaining patients, the severity of regurgitation was estimated according to the following criteria: the size and amplitude of contraction of the left ventricular cavity, the appearance of the regurgi-
### Table 1. Clinical and Echocardiographic Data

<table>
<thead>
<tr>
<th>Pt</th>
<th>Sex</th>
<th>Age (years)</th>
<th>Cause of AR</th>
<th>Dyspnea class</th>
<th>BP (mm Hg)</th>
<th>Chest radiograph</th>
<th>Interval (years, months)</th>
<th>LVIDd (cm)</th>
<th>LVIDs (cm)</th>
<th>FS (%)</th>
<th>LVSV (ml)</th>
<th>LA (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>M</td>
<td>16</td>
<td>Rheumatic</td>
<td>I</td>
<td>116/56C</td>
<td>0.59 + LVH</td>
<td>8.3</td>
<td>5.8</td>
<td>30</td>
<td>207</td>
<td>4.3</td>
<td></td>
</tr>
<tr>
<td>2</td>
<td>M</td>
<td>18</td>
<td>Rheumatic</td>
<td>I</td>
<td>165/40</td>
<td>0.57 0 LVH</td>
<td>7.6</td>
<td>5.3</td>
<td>30</td>
<td>172</td>
<td>3.5</td>
<td></td>
</tr>
<tr>
<td>3</td>
<td>M</td>
<td>18</td>
<td>Rheumatic</td>
<td>I</td>
<td>150/20</td>
<td>0.55 0 LVH</td>
<td>7.4</td>
<td>4.9</td>
<td>36</td>
<td>176</td>
<td>4.4</td>
<td></td>
</tr>
<tr>
<td>4</td>
<td>M</td>
<td>25</td>
<td>Rheumatic</td>
<td>I</td>
<td>170/58C</td>
<td>0.63 0 LVS</td>
<td>7.2</td>
<td>4.8</td>
<td>33</td>
<td>164</td>
<td>4.2</td>
<td></td>
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<tr>
<td>5</td>
<td>M</td>
<td>33</td>
<td>Rheumatic</td>
<td>I</td>
<td>135/50</td>
<td>0.49 0 LVH</td>
<td>6.0</td>
<td>3.7</td>
<td>38</td>
<td>122</td>
<td>2.1</td>
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<td>6</td>
<td>M</td>
<td>29</td>
<td>Rheumatic</td>
<td>I</td>
<td>108/35</td>
<td>0.49 0 LVH</td>
<td>6.0</td>
<td>4.2</td>
<td>30</td>
<td>101</td>
<td>2.8</td>
<td></td>
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<tr>
<td>7</td>
<td>M</td>
<td>37</td>
<td>Rheumatic</td>
<td>I</td>
<td>145/65</td>
<td>0.52 0 LVH</td>
<td>7.1</td>
<td>5.5</td>
<td>23</td>
<td>117</td>
<td>5.5</td>
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<td>8</td>
<td>M</td>
<td>48</td>
<td>Unknown</td>
<td>I</td>
<td>120/35</td>
<td>0.53 0 N</td>
<td>6.4</td>
<td>4.4</td>
<td>31</td>
<td>121</td>
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<td>9</td>
<td>M</td>
<td>21</td>
<td>Unknown</td>
<td>I</td>
<td>140/50</td>
<td>0.47 0 LVH</td>
<td>6.3</td>
<td>4.6</td>
<td>27</td>
<td>104</td>
<td>4.6</td>
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<tr>
<td>10</td>
<td>M</td>
<td>36</td>
<td>Rheumatic</td>
<td>I</td>
<td>130/42C</td>
<td>0.65 + LVS</td>
<td>8.5</td>
<td>6.6</td>
<td>22</td>
<td>170</td>
<td>2.2</td>
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<tr>
<td>11</td>
<td>M</td>
<td>50</td>
<td>Unknown</td>
<td>I</td>
<td>143/50C</td>
<td>0.61 + LVH</td>
<td>7.0</td>
<td>5.2</td>
<td>26</td>
<td>125</td>
<td>3.4</td>
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<tr>
<td>12</td>
<td>F</td>
<td>56</td>
<td>Rheumatic</td>
<td>I</td>
<td>147/48C</td>
<td>0.57 + LVH (D)</td>
<td>6.2</td>
<td>4.2</td>
<td>32</td>
<td>115</td>
<td>2.4</td>
<td></td>
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<tr>
<td>13</td>
<td>M</td>
<td>51</td>
<td>Unknown</td>
<td>I</td>
<td>135/40</td>
<td>0.55 + LVS</td>
<td>7.0</td>
<td>4.6</td>
<td>34</td>
<td>158</td>
<td>3.8</td>
<td></td>
</tr>
</tbody>
</table>

**Abbreviations:** LVP = left ventricular failure; AR = aortic regurgitation; BP = blood pressure; Class = New York Heart Association classification; C = intra-arterial blood pressure measured at cardiac catheterization; CTR = cardiothoracic ratio; PVC = pulmonary venous congestion; Interval = time between serial echocardiograms; LVID = left ventricular hypertrophy; LVS = left ventricular strain; (D) = taking digitalis; LVIDd = end-diastolic left ventricular internal dimension; LVIDs = end-systolic left ventricular internal dimension; FS = fractional shortening; LVSV = left ventricular stroke volume; LA = left atrial dimension; 0 = no pulmonary venous congestion; + = mild or moderate congestion; ++ = severe congestion.
tant jet, opacification of the left ventricle and the rate of clearing of contrast from this chamber.\textsuperscript{14} Cardiac catheterization was not clinically indicated in the remaining seven patients; in these patients, the severity of aortic regurgitation was confirmed by the clinical signs, in particular by the blood pressure (see table 1) and the severity of left ventricular dilatation and hypertrophy indicated by the chest radiograph and electrocardiograph. None of these patients had significant aortic stenosis, disease of another heart valve, ischemic heart disease, evidence of unrelated myocardial disease or hypertension. Significant aortic stenosis was defined as a peak systolic gradient across the aortic valve of 10 mm Hg or more and, for those patients not subjected to cardiac catheterization, slowing of the rate of upstroke of the indirect carotid pulse recording.\textsuperscript{18}

During the period of serial echocardiography, the usual indication for aortic valve replacement in our Cardiology Unit was clinical left ventricular failure. This was defined as breathlessness that could, clinically, be reasonably attributed to pulmonary venous congestion proved by chest radiography. Four patients developed clinical left ventricular failure during the period of serial study (LVF group) and nine did not (no LVF group).

Methods

Echocardiography

Our technique has been described previously.\textsuperscript{15} The description included the method of standardization, measurement of end-diastolic and end-systolic left ventricular internal dimensions (LVID\textsubscript{d}, LVID\textsubscript{s}), left atrial dimension, calculation of an index of myocardial contraction, fractional shortening (FS)

$$FS = \frac{LVID_d - LVID_s}{LVID_d} \times 100$$

and left ventricular stroke volume. Left ventricular volumes were calculated from the left ventricular internal dimension according to the method of Teichholz.\textsuperscript{18} Errors in the estimation of end-diastolic and end-systolic left ventricular internal dimensions are additive in the calculation of the index fractional shortening and cubed in the estimation of left ventricular stroke volume. Hence, we took particular care in reproducing the correctly standardized left ventricular echocardiogram\textsuperscript{19} in serial recordings and in measuring left ventricular dimensions.

Statistical Analysis

For comparison of data from the two groups we used the $t$ test to assess differences in mean values of each variable in the light of scatter of results. A second type of comparison was also necessary: assessment of the significance of differences in echocardiographic variables between serial studies in one individual patient. The reproducibility of serial left ventricular echocardiograms differs for each subject, depending mainly on the quality of the study and ease of standardization. Although the reproducibility for the patient can be considered informally when making clinical decisions, insufficient data prevent us from calculating statistical reproducibility of measurements for each individual. Therefore, we used average values for reproducibility. Reproducibility was established separately for a group of clinically stable patients with severe left ventricular volume overload due to either aortic or mitral regurgitation (table 2).

The study included 12 males and three females with an average age of 38 years. These patients were studied twice by the same technician, with a mean interval between studies of 27 days. The criteria for a technically acceptable echocardiogram and the methods of routine checking by the supervising physician were identical to our laboratory routine. Significant changes (measured by paired $t$ test) were considered to be more than 2 standard deviations from the mean variation between the paired studies. Thus, a significant change in end-diastolic left ventricular internal dimension was 4 mm, end-systolic dimension 6 mm, fractional shortening 9% and left atrial dimension 8 mm.

Results

Data from serial echocardiography and relevant clinical information are summarized in table 1. Changes in echocardiographic measurements between the first and last of the serial studies are summarized in table 3.

No LVF Group

These nine patients were studied over a mean period of 4 years, 3 months. Comparison of the group mean values for echocardiographic measurements recorded at the first and last study disclosed no significant change in left ventricular end-diastolic internal dimension, but there were statistically significant changes for the end-systolic internal dimension, fractional shortening and left atrial dimension (table 3). Thus, end-systolic dimension increased 6% ($p < 0.05$), fractional shortening decreased 10% ($p < 0.05$) and left atrial dimension increased 25% ($p < 0.01$). The average rates of increase of left ventricular end-
TABLE 4. Comparison of First and Last Serial Study

<table>
<thead>
<tr>
<th></th>
<th>LVIDd</th>
<th>LVIDs</th>
<th>FS</th>
<th>LA</th>
</tr>
</thead>
<tbody>
<tr>
<td>n</td>
<td>(cm)</td>
<td>(cm)</td>
<td>(%)</td>
<td>(cm)</td>
</tr>
<tr>
<td>No LVF group</td>
<td>9</td>
<td>6.92</td>
<td>4.80</td>
<td>30.88</td>
</tr>
<tr>
<td></td>
<td></td>
<td>±0.75</td>
<td>±0.63</td>
<td>±4.23</td>
</tr>
<tr>
<td></td>
<td>7.11</td>
<td>5.12</td>
<td>27.90</td>
<td>4.17</td>
</tr>
<tr>
<td></td>
<td>±0.81</td>
<td>±0.65</td>
<td>±4.38</td>
<td>±1.48</td>
</tr>
<tr>
<td>LVF group</td>
<td>4</td>
<td>7.17</td>
<td>5.15</td>
<td>28.5</td>
</tr>
<tr>
<td></td>
<td></td>
<td>±0.83</td>
<td>±0.90</td>
<td>±4.77</td>
</tr>
<tr>
<td></td>
<td>8.23</td>
<td>6.92</td>
<td>16.0</td>
<td>4.68</td>
</tr>
<tr>
<td></td>
<td>±0.53</td>
<td>±0.78</td>
<td>±3.81</td>
<td>±0.46</td>
</tr>
</tbody>
</table>

Values are mean ± sd.

Abbreviations: LVIDd = end-diastolic left ventricular internal dimension; LVIDs = end-systolic left ventricular internal dimension; FS = fractional shortening; LA = left atrial dimension; LVF = left ventricular failure.

diastolic and end-systolic dimension were 0.45 and 0.75 mm per year, respectively, and the average rate of decline of fractional shortening was 0.7% per year (table 4).

Comparison of individual patients, using the reproducibility criteria of the control study, indicated that only patient 6 had a significant increase in both end-diastolic and end-systolic left ventricular internal dimensions, and patient 3 had a significant increase in end-diastolic dimension only. No patient had a change in fractional shortening that was statistically significant. In seven patients left atrial dimension increased significantly.

LVF Group

These patients were studied over a mean period of 5 years, 7 months. During this period, group mean end-diastolic left ventricular internal dimension increased 14% between first and last serial study (p < 0.02), end-systolic dimension increased 35% (p < 0.01), the mean value of fractional shortening decreased 45% (p < 0.05) and left atrial dimension increased 62% (p < 0.05). The average time from the first echocardiographic study to left ventricular failure was 3 years, 11 months. During this time, the mean rates of increase of end-diastolic and end-systolic left ventricular internal dimensions were 2.05 and 3.21 mm per year, respectively, and the rate of decline of fractional shortening was 2.3% per year (table 4).

Each patient had a significant increase in end-diastolic and end-systolic left ventricular internal dimensions and in the left atrial dimension; fractional shortening fell significantly in three of the four patients.

Patient 7 (fig. 1) was of particular interest because fractional shortening was subnormal (23%) at the initial study and did not change significantly over the next 5 years; during this time he remained asymptomatic, with no change in physical signs, ECG or chest radiograph.

Discussion

Myocardial Impairment in Chronic Severe Aortic Regurgitation

Chronic severe left ventricular volume overload is known to cause myocardial damage. The extent of clinical disability has been related to the age of the patient and, by inference, to the duration of volume overload. Left ventricular damage has also been demonstrated by a variety of techniques in both animals and man when the chamber has been subjected to prolonged overload, but clinical detection of declining left ventricular myocardial function can be difficult even with the aid of the chest radiograph and ECG. Symptoms of left ventricular failure indicate a poor prognosis with continued medical treatment. Unfortunately, important symptoms such as breathlessness or chest pain are often hard to assess when they occur without any objective changes in investigations and may be attributable to anxiety, which tends to be reinforced by repeated clinical reassessments. Nor are radiographic or electrocardiographic changes always easy to interpret. Although radiographic evidence of pulmonary venous congestion is important, its interpretation is subjective and, in some of our patients, some redistribution of pulmonary blood flow could be discerned for many years before symptoms of left ventricular failure developed. Severe cardiac enlargement is an unfavorable sign, especially if it is progressive, but our studies have demonstrated that an increase in cardiothoracic ratio may be caused by progressive left atrial enlargement, with no change in left ventricular size or contraction, as in patients 3, 4, 5, 6 and 8. Furthermore, the prognostic significance of this finding is not yet known. Severe electrocardiographic left ventricular hypertrophy is also prognostically unfavorable but may appear only when left ventricular failure is obvious or may be obscured by the effects of digitalis.

Myocardial Impairment Detected by M-mode Echocardiography

The severity of left ventricular dilatation and of reduction of fractional shortening demonstrated by echocardiography have been related to the likelihood of early deterioration of left ventricular function with
progression to failure. Thus, early left ventricular failure was shown to be more likely when the end-systolic dimension was greater than 5.5 cm and a progressive fall in fractional shortening more likely when the left ventricular internal dimensions were more than 40% above the upper limits of normal (corresponding to LVIDd > 6.5 cm, LVIDs > 4.2 cm). We studied too few patients to allow us to test these conclusions. Thus, only two of our patients had an end-systolic dimension greater than 5 cm at the time of initial study, and one of them developed left ventricular failure during serial study. The end-diastolic dimension was greater than 6.5 cm and the end-systolic dimension greater than 4.2 cm at initial study in three of the four patients who developed left ventricular failure in our study but also in six of the nine patients who did not.

Our results suggest that the decline in left ventricular function in asymptomatic patients with severe chronic aortic regurgitation is slow but does accelerate in the few years before the onset of left ventricular failure (table 4). Thus, at the time of initial study of patients who developed left ventricular failure, the fractional shortening was 29% and the index was subnormal in only one of the four patients at that time; however, fractional shortening declined to an average value of 20% during the 4-year period between the initial study and the appearance of dyspnea due to left ventricular failure. Such a rapid decline might reflect acceleration of the degenerative changes in the overloaded myocardium. Alternatively, the onset of renal sodium retention might cause left ventricular dilatation, resulting in an increase in mural stress and hence left ventricular afterload. In this way, there might be a terminal vicious circle of progressively declining myocardial function with increasing left ventricular dilatation and progressively increasing afterload.

Limitations of M-mode Echocardiography

The interpretation of serial M-mode echocardiographic measurements in chronic severe aortic regurgitation is hampered by two major problems: limitations of the reproducibility of the technique and a reservation that changes in fractional shortening may not always accurately reflect declining myocardial function in aortic regurgitation with left ventricular failure. The left ventricular echocardiogram is usually easy to record in patients with left ventricular volume overload but our experience in this study and our routine practice has highlighted some specific problems limiting reproducibility. For example, echoes from adjacent portions of the interventricular septum are often recruited serially and superimposed during systolic contraction, a phenomenon that causes underestimation of the end-systolic left ventricular internal dimension and overestimation of fractional shortening and ejection fraction. In addition, our control study demonstrated that, despite careful technique, small variations in standardization of the measured tracing could result in relative large fluctuations in left ventricular dimensions between consecutive studies.

The second problem is that the use of fractional shortening as an index of myocardial contraction assumes that the cross section of the left ventricle contracts symmetrically, and this may not be strictly true in patients with aortic regurgitation and left ventricular failure. In fact, there is evidence that shortening of the echocardiographic left ventricular internal dimension, which is expressed as fractional shortening, may overestimate contraction of the left ventricle as a whole. The important implication is that impairment of left ventricular contraction may actually be more severe than the echocardiogram suggests and this would only become apparent if left ventricular angiography were performed.
The results of this study and our clinical experience have not encouraged us to rely on M-mode echocardiographic data alone when assessing individual asymptomatic patients with chronic severe aortic regurgitation. We believe that serial echocardiograms should be evaluated in conjunction with the clinical assessment and other investigations, particularly when deciding whether to recommend cardiac catheterization with a view to aortic valve replacement.

References
Serial M-mode echocardiography in severe chronic aortic regurgitation.
I G McDonald and V M Jelinek

Circulation. 1980;62:1291-1296
doi: 10.1161/01.CIR.62.6.1291

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