Dynamic Geometry of the Left Ventricle in Mitral Regurgitation

By Pantel S. Vokonas, M.D., Richard Gorlin, M.D., Peter F. Cohn, M.D., Michael V. Herman, M.D., and Edmund H. Sonnenblick, M.D.

SUMMARY
High-speed biplane left ventricular (LV) cineangiograms were analyzed for changes in volume, shape, and dimensions in 35 patients. Ventriloculographic studies in ten normal subjects characterized by an ejection fraction (E.F.) of 67±2% and an end-diastolic volume (EDV) of 90±8 ml/m² were compared with results from 25 patients with isolated mitral regurgitation of varying severity. Patients with mitral regurgitation (MR) were subdivided according to whether or not the ejection fraction was normal. Those with normal E.F. (70±2%) were termed compensated MR (CMR) and had EDV 192±7 ml/m². Those with decreased E.F. 34±3% were termed decompensated MR (DMR) and had EDV 277±17 ml/m². In normal subjects no significant changes in LV dimensions were noted during the isovolumic phase of contraction while in patients with compensated MR the transverse axis shortened an average of 5.2% with no change in the longitudinal axis (L). Changes in geometry prior to ejection were less evident in the group with decompensated MR. In normal subjects during ejection the extent of circumferential fiber shortening was 38±1%, and longitudinal shortening was 18±1%. In CMR slightly greater changes were observed in LV dimensions. In DMR both circumferential and longitudinal shortening was significantly reduced (17±2% and 8±1%, respectively). Assuming an ellipsoidal model of the LV chamber, eccentricity (e) was calculated to assess the degree of roundness. In normal subjects, e increased from 0.85 at end-diastole to 0.92 at end-systole. In compensated MR, end-diastolic shape was more rounded with e increasing from 0.75 to 0.88 during systole. In decompensated MR there was only a small change in e from 0.70 to 0.73 during systole, indicating that a globular configuration persisted in systole as well as diastole.

These differences could not be satisfactorily explained in terms of etiology, age, regurgitant volume load or its duration. The differences between the two groups of patients were best expressed by the difference in ejection fraction and globularity of the LV. A relationship to absolute EDV between the two groups was less evident. These differences may be due to development of organic changes in the architecture of heart wall in those patients with decompensated MR.

Additional Indexing Words:
Cineventriculography Left ventricular volume Ejection fraction
Left ventricular pump performance Left ventricular dimensional changes
Left ventricular shape changes Isovolumic contraction Pre-ejection period

CARDIAC FAILURE can be brought about by primary disease of the myocardium, by insufficient myocardial blood flow in relation to need, and by the imposition of an externally applied load. The load can be either augmented pressure or volume. When greater load is caused by increased volume, alterations take place in the myocardium which are secondary to the applied load. These changes become a function of the intensity and duration of load and quite possibly other, as yet undefined factors.

This report will consider the effects of mitral regurgitation on the size, shape, and ejection volume, alterations take place in the myocardium which are secondary to the applied load. These changes become a function of the intensity and duration of load and quite possibly other, as yet undefined factors.

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pattern of the left ventricle. Primary changes which occur solely as a compensatory response to an excessive ejection volume will be differentiated from those which are possibly due to secondary architectural alterations in the wall of the heart. The findings in man will be related to those studies in animals which show a structural alteration in the myocardium as a consequence of chronic ventricular dilatation. Analysis of the data in the above-mentioned terms may make it possible to determine from the dynamic geometry of cardiac contraction when the ventricle has reached the stage of secondary myocardial structural change.

Methods

Data were derived from a detailed study of high-speed biplane ventriculograms obtained at the time of diagnostic cardiac catheterization in 35 patients. Ten patients with chest pain and normal coronary arteriograms were considered to have normal left ventricular function on the basis of normal resting hemodynamic findings, normal end-diastolic volumes (90 ± 10 ml/m²), and an ejection fraction greater than 55%. Twenty-five patients had isolated mitral regurgitation of varying severity. They were categorized according to whether ejection pattern was normal or abnormal. Fifteen with a normal ejection fraction (≥55%) were classified as compensated mitral regurgitation. This group included ten men (ages 17–66 years) and five women (ages 23–61 years). Mitral regurgitation was related to ruptured chordae tendineae in three of the men and to rheumatic valvular involvement in the remainder. The remaining group of ten patients had ejection fractions of less than 50% and were classified as uncompensated mitral regurgitation. This group consisted of six men (ages 51–70 years) and four women (ages 55–66 years). Mitral regurgitation was due to rheumatic valvar disease in six including one patient with a severe peribasilar leak following mitral valve replacement, possible ruptured chordae tendineae in three, and primary myocardial disease in one. All ten had massive cardiomegaly and clinically manifest congestive failure (Classes III–IV).

Diagnostic right and left heart catheterizations were performed. Pressures were measured with P23Db strain gauges and recorded with a photographic recorder. Cardiac outputs were determined by the indocyanine green dye dilution method. Since stroke volume in normal patients determined by this method consistently underestimates angiographic or total stroke volume (TSV) in our laboratory, values for forward or “effective” stroke volume (FSV) were corrected by an appropriate regression equation relating indicator-dilution to angiographic stroke volumes in the normal group. (FSV = 0.78 (SV indocyanine green) + 31). The difference between TSV and FSV is regurgitant volume (RV) and the ratio of RV to TSV is regurgitant fraction (R.F.).

Left ventricular pressure and simultaneous electrocardiogram were recorded immediately prior to ventriculography to permit accurate timing of the mechanical events of the cardiac cycle.

Biplane cine-ventriculography was performed using a (No. 8 French) ventriculographic catheter passed via a retrograde femoral approach. Contrast medium (Renografin - 76) was injected into the left ventricle over a 2 to 3 second period from a power syringe (Viamonte-Hobbs) at a dose of 1 ml/kg. Each cine-ventriculogram was exposed in biplane at 100 frames per second and recorded on 16 mm Kodak XX film in the right and left anterior oblique projections. Simultaneous recordings of the electrocardiogram, brachial artery pressure and the cine-frame signal (indicating the exact instant of each cine-frame exposure) were made during the ventriculographic study to permit cross correlation of these parameters.

Selective cine coronary arteriography was performed following the ventriculographic procedure. Patients with significant obstructive coronary artery disease and a localized abnormality of LV contraction (asynnergy) were excluded from this study.

End-diastole was taken as the time 40 to 60 msec following the onset of the QRS complex of a simultaneously recorded cine-trace electrocardiogram and confirmed by direct measurement of this interval from left ventricular pressure tracings recorded immediately prior to ventriculography. Aortic valve opening was identified by observation of valve leaflet motion in the analysis of frame-by-frame film sequences during the pre-ejection period. Similarly, the duration of the pre-ejection period was confirmed by direct measurement of the interval from end-diastole to the instant that left ventricular pressure equaled the level of diastolic brachial artery pressure. End-systole was defined as the frame with the smallest planimetered area (or the maximum inward movement of the ventricular wall along both axes). Cardiac cycles which immediately followed ventricular premature beats were excluded.

Left ventricular volumes and ejection fraction were calculated by the area-length method of Dodge et al.1, 2

Left ventricular dimensions in each patient were corrected for image magnification and spherical distortion by means of a one-centimeter square grid (wire embedded in Lucite at 1 cm intervals) which was positioned and filmed in the midplane of the left ventricle in each projection following completion of the catheterization procedure.

Left ventricular length (L) was directly measured as the longitudinal axis of the LV chamber from the apex to the midpoint of the plane of the aortic valve (Fig. 1). Directly measured LV chamber diameter (D) was taken as a measured chord perpendicular to and bisecting the longitudinal axis (L). In addition, assuming the LV chamber to closely approximate a prolate ellipsoid, calculated LV diameter (D calc) was derived using the formula:

\[ D \text{ Calc} = \frac{4A}{\pi L} \]  

where A is the planimetered area of the LV chamber silhouette in each plane. These changes in longitudinal
### Table 1

**Analysis of Hemodynamic and Ventriculographic Data**

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age</th>
<th>Sex</th>
<th>BAP</th>
<th>LVEDP</th>
<th>CI</th>
<th>PSSV</th>
<th>RV</th>
<th>EF</th>
<th>% ΔD</th>
<th>% ΔDv</th>
<th>% ΔL</th>
<th>cED</th>
<th>cES</th>
<th>Δe</th>
<th>RVm</th>
<th>RVm</th>
<th>% ΔDm</th>
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<tr>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>J.D.</td>
<td>35</td>
<td>M</td>
<td>121/66</td>
<td>3.3</td>
<td>60</td>
<td>—</td>
<td>—</td>
<td>96</td>
<td>60</td>
<td>39</td>
<td>38</td>
<td>21</td>
<td>0.87</td>
<td>0.94</td>
<td>0.07</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>W.B.</td>
<td>22</td>
<td>M</td>
<td>128/78</td>
<td>3.2</td>
<td>63</td>
<td>—</td>
<td>—</td>
<td>85</td>
<td>59</td>
<td>39</td>
<td>38</td>
<td>19</td>
<td>0.86</td>
<td>0.91</td>
<td>0.05</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>R.H.</td>
<td>47</td>
<td>F</td>
<td>122/75</td>
<td>3.3</td>
<td>52</td>
<td>—</td>
<td>—</td>
<td>81</td>
<td>52</td>
<td>40</td>
<td>38</td>
<td>20</td>
<td>0.86</td>
<td>0.92</td>
<td>0.06</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>L.T.</td>
<td>28</td>
<td>M</td>
<td>116/75</td>
<td>3.4</td>
<td>63</td>
<td>—</td>
<td>—</td>
<td>67</td>
<td>38</td>
<td>38</td>
<td>37</td>
<td>18</td>
<td>0.90</td>
<td>0.96</td>
<td>0.06</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>M.W.</td>
<td>43</td>
<td>F</td>
<td>140/80</td>
<td>3.1</td>
<td>58</td>
<td>—</td>
<td>—</td>
<td>121</td>
<td>34</td>
<td>41</td>
<td>42</td>
<td>19</td>
<td>0.83</td>
<td>0.91</td>
<td>0.08</td>
<td>—</td>
<td>—</td>
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<tr>
<td>H.P.</td>
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<td>F</td>
<td>142/80</td>
<td>3.3</td>
<td>58</td>
<td>—</td>
<td>—</td>
<td>63</td>
<td>15</td>
<td>45</td>
<td>43</td>
<td>25</td>
<td>0.81</td>
<td>0.92</td>
<td>0.09</td>
<td>—</td>
<td>—</td>
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<tr>
<td>M.N.</td>
<td>45</td>
<td>F</td>
<td>140/73</td>
<td>3.2</td>
<td>66</td>
<td>—</td>
<td>—</td>
<td>123</td>
<td>36</td>
<td>42</td>
<td>40</td>
<td>22</td>
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<td>0.89</td>
<td>0.07</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>M.B.</td>
<td>45</td>
<td>F</td>
<td>124/65</td>
<td>3.6</td>
<td>67</td>
<td>—</td>
<td>—</td>
<td>100</td>
<td>36</td>
<td>36</td>
<td>35</td>
<td>24</td>
<td>0.83</td>
<td>0.87</td>
<td>0.04</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>R.B.</td>
<td>43</td>
<td>F</td>
<td>115/65</td>
<td>3.5</td>
<td>69</td>
<td>—</td>
<td>—</td>
<td>112</td>
<td>45</td>
<td>33</td>
<td>33</td>
<td>14</td>
<td>0.85</td>
<td>0.94</td>
<td>0.09</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>R.C.</td>
<td>43</td>
<td>M</td>
<td>120/70</td>
<td>4.4</td>
<td>68</td>
<td>—</td>
<td>—</td>
<td>64</td>
<td>24</td>
<td>34</td>
<td>33</td>
<td>16</td>
<td>0.87</td>
<td>0.93</td>
<td>0.06</td>
<td>—</td>
<td>—</td>
</tr>
</tbody>
</table>

Mean ±SEM 7 ±1 3.4 ±0.1 63 ±2 — 90 ±8 30 ±3 61 ±5 67 ±2 38 ±1 37 ±1 18 ±1 0.85 0.92 0.07 — — —

1. Patients with Normal Ventriculographic Studies

2. Patients with Compensated Mitral Regurgitation

| G.W. | 45  | F   | 134/76 | 21  | 2.0 | 50 | 90 | 69 | 211 | 71 | 140 | 67 | 38 | 36 | 14.7 | 0.76 | 0.87 | 0.09 | 19 | 0.21 | 4.5 |
| M.F. | 59  | F   | 105/62 | 20  | 4.0 | 62 | 60 | 49 | 182 | 60 | 122 | 67 | 40.7 | 36 | 14.7 | 0.74 | 0.90 | 0.16 | 19 | 0.32 | 5.3 |
| S.B. | 47  | M   | 125/85 | 10  | 2.0 | 47 | 56 | 54 | 149 | 45 | 103 | 70 | 40 | 41 | 23 | 0.78 | 0.89 | 0.11 | 15 | 0.27 | 5.0 |
| J.S. | 39  | M   | 120/64 | 10  | 2.7 | 61 | 73 | 55 | 191 | 57 | 134 | 70 | 41 | 40 | 22.3 | 0.65 | 0.79 | 0.14 | 20 | 0.27 | 5.2 |
| J.M. | 53  | M   | 139/64 | 11  | 2.0 | 51 | 79 | 61 | 209 | 79 | 130 | 62 | 35 | 33 | 22 | 0.69 | 0.78 | 0.09 | 18 | 0.23 | 4.3 |
| P.N. | 23  | F   | 95/43  | 7   | 4.2 | 70 | 21 | 23 | 152 | 61 | 138 | 60 | 34 | 31 | 14 | 0.79 | 0.91 | 0.12 | 6  | 0.29 | 2.1 |
| S.R. | 43  | M   | 80/52  | 22  | 2.4 | 53 | 114 | 68 | 232 | 65 | 167 | 72 | 41 | 42 | 22 | 0.78 | 0.92 | 0.14 | 27 | 0.24 | 5.9 |
| J.M. | 66  | M   | 180/86 | 25  | 2.7 | 53 | 113 | 68 | 202 | 36 | 166 | 82 | 30 | 47 | 24 | 0.77 | 0.90 | 0.13 | 36 | 0.32 | 9.0 |
| D.C. | 62  | M   | 132/99 | 9   | 2.1 | 49 | 89 | 65 | 181 | 51 | 135 | 78 | 43 | 44 | 25 | 0.78 | 0.89 | 0.11 | 23 | 0.26 | 6.5 |
| J.M. | 17  | M   | 149/78 | 3   | 3.2 | 54 | 92 | 63 | 176 | 30 | 146 | 83 | 37 | 45 | 25 | 0.81 | 0.93 | 0.12 | 29 | 0.32 | 8.4 |
| A.D. | 61  | M   | 152/75 | 10  | 1.8 | 45 | 104 | 70 | 216 | 67 | 149 | 69 | 37 | 37 | 23 | 0.74 | 0.87 | 0.13 | 21 | 0.20 | 4.9 |
| C.A. | 28  | F   | 106/60 | 11  | 2.8 | 54 | 96 | 64 | 214 | 64 | 150 | 70 | 40 | 38.5 | 16.7 | 0.73 | 0.88 | 0.15 | 20 | 0.21 | 4.8 |
| P.R. | 61  | F   | 96/61  | 11  | 1.3 | 43 | 50 | 54 | 143 | 65 | 50 | 35 | 36 | 19 | 0.78 | 0.91 | 0.13 | 9  | 0.18 | 3.2 |
| H.H. | 44  | M   | 96/62  | 11  | 1.5 | 45 | 86 | 66 | 199 | 68 | 131 | 66 | 37.5 | 35 | 20 | 0.75 | 0.85 | 0.10 | 16 | 0.19 | 4.0 |
| F.S. | 66  | M   | 115/63 | 14  | 3.3 | 63 | 90 | 63 | 219 | 60 | 156 | 71 | 41 | 39 | 26 | 0.70 | 0.84 | 0.14 | 24 | 0.26 | 5.5 |

Mean ±SEM 13 ±2 2.5 ±0.2 53 ±2 81 ±7 59 ±3 192 ±7 57 ±4 134 ±6 70 ±2 40 ±1 39 ±1 21 ±1 0.75 0.88 0.12 20.1 ±2 0.25 ±0.01 5.24 ±0.5
The hemodynamic and ventriculographic data for the three groups of patients presented in Table 1.

**Table 1.** Results

<table>
<thead>
<tr>
<th>Group</th>
<th>BAP (mm Hg)</th>
<th>LVEDP (mm Hg)</th>
<th>LVEF (%)</th>
<th>ESV (ml)</th>
<th>EDV (ml)</th>
<th>Stroke Volume (ml)</th>
<th>Mean Stroke Volume (ml)</th>
<th>Mean Stroke Volume (ml/m²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>120±10</td>
<td>90±10</td>
<td>60±5</td>
<td>60±5</td>
<td>100±10</td>
<td>80±10</td>
<td>50±10</td>
<td>2.5±0.5</td>
</tr>
<tr>
<td>Decompensated</td>
<td>120±10</td>
<td>90±10</td>
<td>60±5</td>
<td>60±5</td>
<td>100±10</td>
<td>80±10</td>
<td>50±10</td>
<td>2.5±0.5</td>
</tr>
</tbody>
</table>

The results were analyzed using a Student's t-test. The data were found to be normally distributed.

**Figure 1.** Dynamic geometry of mitral regurgitation. RAO: Right anterior oblique; LAO: Left anterior oblique.

**References:**


**Legend:**

- BAP: Brachial arterial pressure
- LVEDP: Left ventricular end-diastolic pressure
- LVEF: Left ventricular ejection fraction
- ESV: End-systolic volume
- EDV: End-diastolic volume
- CMR: Cardiac magnetic resonance
- TTE: Trans-thoracic echocardiography
- TEE: Trans-oesophageal echocardiography
- MR: Mitral regurgitation
mitral valvular lesion bore no consistent relation to the presence of a normal or low ejection fraction.

**Relations Between Left Ventricular End-Diastolic Pressure and Volume**

The relation of LVEDP to EDV is plotted in figure 2. Although a significant correlation for these data could not be demonstrated, the distribution suggests an apparent grouping for each patient category. The values for the majority of the patients with compensated MR are grouped to the right of the normal subjects while values for patients with decompensated MR are plotted even further rightward. While average LVEDP in compensated MR was moderately higher than in the normal group and even slightly higher in decompensated MR, considerable overlap of values for LVEDP was evident.

**Relations Between Total Stroke Volume and End-Diastolic Volume**

The relation of angiographic or total stroke volume to end-diastolic volume is plotted in figure 3. Patients with compensated MR by definition exhibit ejection fractions similar to the normal group but at larger end-diastolic volumes. Therefore, the total stroke volume is correspondingly increased.

Seven of ten patients with decompensated MR had larger end-diastolic volumes than the CMR group but their total stroke volumes were disproportionately lower. There was overlap between groups for both EDV and TSV indicating pump function could vary at any level of EDV.

**Figure 2**

*Relationship between left ventricular end-diastolic pressure (EDP) and end-diastolic volume (EDV). CMR = compensated mitral regurgitation; DMR = decompensated mitral regurgitation.*

**Figure 3**

*Relationship between total or angiographic stroke volume (TSV) and end-diastolic volume (EDV). Note the apparent separation of normal subjects and patients with compensated MR from those with decompensated MR as indicated by the corresponding lines of identity for ejection fraction. CMR = compensated mitral regurgitation; DMR = decompensated mitral regurgitation.*

**Relationship of Regurgitant Volume to Effective Stroke Volume**

Regurgitant volume and forward stroke volume are plotted in figure 4 to show the wide variation in regurgitant volume in the two groups. Patients with DMR had a reduced regurgitant volume in comparison with those who were compensated (DMR = 46 ± 6 ml/m², CMR = 81 ± 7 ml/m²).

**Figure 4**

*Relationship of regurgitant volume (RV) to forward stroke volume (FSV). Because regurgitant volume is derived from total stroke volume minus green dye stroke volume, no correlations are reported. The wide range of values is evident.*
Dynamic Changes During the Pre-Ejection Period

The time course of circumferential shortening for each of the patient groups is graphically summarized in figure 5. No significant changes in left ventricular dimensions were noted in normal patients during the pre-ejection period. In the groups with compensated MR, however, the minor axis (D) shortened an average of 5.2% with no change observed in the longitudinal axis (L). In decompensated MR, only insignificant detectable changes in geometry occurred prior to aortic valve opening despite some prolongation of the “pre-ejection” period. The dimensional changes observed in compensated MR represent an average volume change of 10.3% of end-diastolic volume and indicate that about one-fourth of the total regurgitant volume may be ejected before the aortic valve opens.

Although the slope of shortening in the minor axis (D) begins earlier in compensated MR than in normal subjects, these slopes are essentially identical during the ejection phase (\( \lambda = 0.2 \)). The decompensated patients, however, exhibit a significantly slower slope (\( \lambda = 0.1 \)) throughout systole.

**Correlation of the Extent of Dimensional Changes During Systole to the Ejection Fraction**

Because they are interrelated, correlations can be shown between shortening of either minor or the major axes and the ejection fraction (\( r = 0.99 \) and 0.88, respectively). Thus, ejection fraction can be derived from minor axis shortening (\( EF = 1.5 (\%\Delta D \text{ calc}) + 12.1 \pm 2.6 \)).

Dynamic Alterations of Left Ventricular Shape During Systole

In figure 6 the relationship between left ventricular volume and mean chamber eccentricity (e) is shown at end-diastole and end-systole. Patients with compensated MR had more rounded LV chamber configurations at end-diastole (0.75 ± 0.01) than in normal subjects (0.85 ± 0.01) while the degree of chamber roundness at end-diastole was greatest in patients with decompensated MR (0.70 ± 0.01). During systole, in both normal patients and those with compensated MR, the left ventricle changed from a globular shape at end-diastole to a more elongated configuration at end-systole as reflected by a significant increase in values for e in both groups (0.85 to 0.92 and 0.75 to 0.88, respectively). The slope of change in chamber eccentricity with

\[ * \text{Standard error of the estimate.} \]

![Figure 5](image)

**Figure 5**

Time-course of shortening of the midtransverse or minor axis (D) during the cardiac cycle. Note an average of 5.2\% shortening of D in the CMR group during the pre-ejection period compared to insignificant changes in decompensated MR. The slopes (\( \lambda \)) of the rate of shortening during mid-systole (brackets) are indicated.

![Figure 6](image)

**Figure 6**

Relationship between mean chamber eccentricity (e) and LV volume. Average values for chamber eccentricity (e) at end-diastole and for each of the patient groups are plotted with their respective end-diastolic and end-systolic volumes (mean ± SEM). Smaller values for e indicate a more rounded LV chamber configuration. CMR = compensated mitral regurgitation; DMR = decompensated mitral regurgitation; EF = ejection fraction.

\[ P < 0.05 \). Mean regurgitant fraction did not differ significantly (50 ± 5\% and 59 ± 3\%, respectively).
respect to LV volume for both groups was similar despite a more marked increase in $e$ ($\Delta e = 0.12 \pm 0.01$) in patients with compensated MR. Thus, the degree of eccentricity was dependent only on the volume per se, independent of diastole or systole. In contrast, in patients with decompensated MR not only was the shape of the end-diastolic chamber more spheroidal than in compensated MR, but only a small change in $e$ occurred, with persistence of a globular shape throughout systole. Thus the eccentricity per unit volume increased only minimally during systole. This minor change in $e$ ($\Delta e = 0.03 \pm 0.01$) accounts in part for the apparent digression from a hypothetical line relating chamber eccentricity to LV volume observed for these patients. There was a correlation between ejection fraction and the magnitude of change in chamber eccentricity between end-diastole and end-systole ($\Delta e$) in the entire population: E.F. = $282.4 (\Delta e) + 36.3 \pm 11.8$, $r = 0.75$.

Results of Treatment

In eight of the 15 patients with compensated MR, clinical symptoms of congestive heart failure led to surgical intervention (table 2). Corrective surgery was uncomplicated in all; seven underwent mitral valve replacement and a primary repair of ruptured chordae tendineae was performed in one patient. Clinical improvement was observed uniformly in these patients following operation. There was a change from AHA Class III to Class II in four patients and from Class III to Class I in four patients. The other seven patients with less severe symptoms received either no treatment or medical therapy alone and remained symptomatically unchanged during a follow-up period of approximately two years. Cardiac size decreased in two of seven following surgery although not to normal values and increased in one of six patients on medical therapy alone.

Six of ten patients with decompensated MR underwent mitral valve replacement. Clinical improvement was noted in three with change in American Heart Association Classification III to Classes II in two and to I in one patient. Two patients exhibited progressive deterioration following surgery culminating in death, eight months later (P.Z.) and 3.5 years later (F.O.). Of the four patients receiving medical treatment alone, one improved (N.W.) with decreased dyspnea and edema formation (change from Class IV to Class III); one was clinically unchanged; and two became progressively worse and died, one month and two years after catheterization. Cardiac size increased in three patients and decreased in two patients, one each in the medically and surgically treated groups. Four exhibited no change in heart size. The post therapy heart size remained grossly enlarged in all, however; reductions in diameter in the two cases were only of the order of 10%. The results of treatment on the hemodynamic status of three of these patients are summarized in table 3. In patient N.W., moderate clinical improvement resulted pari passu with bed rest and intensive digitalis and diuretic therapy. There was a rise in

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* Standard error of the estimate

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### Table 2

<table>
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<tr>
<th>Clinical Status*</th>
<th>Radiographic Heart Size</th>
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<tr>
<td></td>
<td>Improved</td>
</tr>
<tr>
<td>Compensated MR</td>
<td></td>
</tr>
<tr>
<td>Medically treated</td>
<td>7</td>
</tr>
<tr>
<td>Surgically treated</td>
<td>8</td>
</tr>
<tr>
<td>Decompensated MR</td>
<td></td>
</tr>
<tr>
<td>Medically treated</td>
<td>4</td>
</tr>
<tr>
<td>Surgically treated</td>
<td>6</td>
</tr>
</tbody>
</table>

* ± Change in AHA disability class.
† Cardiothoracic ratio > 50%.
‡ ± 10% of preoperative transverse cardiac diameter.
§ One patient had a normal heart size at initial study.
cardiac output and fall in LVEDP. The ejection fraction increased slightly but from an unchanged EDV. Patient P.Z. also had an unchanged EDV, but exhibited worsening of cardiac pump performance in the study done eight months after surgery even though mitral incompetence was corrected. Patient F.O. showed increasing EDV with an unchanged ejection fraction.

**Discussion**

**Characteristics of Patient Subgroups**

In this study, patients with MR were arbitrarily classified into two groups depending on whether the ejection fraction was normal or subnormal. This separation has permitted the further characterization of two subgroups with distinct hemodynamic and ventriculographic features. This classification of patients is not meant to preclude the possibility that early in the life history of MR there may be a stage when end-diastolic volume is normal and ejection fraction augmented. Because such patients are usually asymptomatic, they are rarely submitted to cardiac catheterization. In compensated MR, the ejection fraction was normal and an augmented total stroke volume was delivered from a significantly larger end-diastolic volume. Furthermore, during systole, the more rounded chamber configuration observed at end-diastole was progressively transformed to a more elongated shape in a manner qualitatively similar to the normal pattern of contraction. By comparison, patients with decompen-sated MR exhibited a reduced ejection fraction and an even larger end-diastolic volume than patients in the compensated group. In addition, the LV end-diastolic shape of patients with decompensated MR was the most globular of the three groups studied.

**Pathophysiologic Consequences of Mitral Regurgitation**

In the presence of mitral regurgitation the mitral orifice acts as a pressure-dependent outlet for the left ventricle in parallel with the aortic outlet. The major consequence of this situation is that when the shortening capacity of the left ventricle is normal, ventricular volume is rapidly reduced during the pre-ejection phase of systole, which in turn reduces the systolic tension required in the ventricular wall. This in turn further enhances contractile element shortening. Accordingly, the mechanical advantage of reduction in volume and tension during systole permits delivery of a large total left ventricular stroke volume. If deterioration of myocardial function develops, a further increase in end-diastolic volume (the Frank-Starling mechanism) becomes necessary to maintain total left ventricular stroke volume.

The consequences of an increase in end-diastolic volume are multiple. When volume is increased to a certain point, reduction in size during systole is minimized and wall tension will increase rather than decrease during systole, and the mechanical advantage of regurgitation of blood into the left atrium may be lost. This places an increasing afterload on the left ventricle. If diastolic volume remains chronically enlarged there are at least three demonstrable effects on the ventricle itself. First, the ventricle assumes a more globular shape. Theoretically, this may further augment regurgitant flow by changing the configuration of the mitral apparatus. Second, the sarcomeres, the individual contractile units of muscle, move up their intrinsic

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**Table 3**

<table>
<thead>
<tr>
<th>Patient</th>
<th>BAP mm Hg</th>
<th>LVEDP mm Hg</th>
<th>CI</th>
<th>EDV ml/m²</th>
<th>ESV ml/m²</th>
<th>TSV ml/m²</th>
<th>EF %</th>
<th>%ΔD</th>
<th>%ΔL</th>
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<tr>
<td>N.W.* A</td>
<td>145/110</td>
<td>28</td>
<td>1.0</td>
<td>220</td>
<td>148</td>
<td>72</td>
<td>33</td>
<td>11.5</td>
<td>9.0</td>
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<tr>
<td>B</td>
<td>115/70</td>
<td>10</td>
<td>1.9</td>
<td>216</td>
<td>134</td>
<td>82</td>
<td>38</td>
<td>17</td>
<td>11.0</td>
</tr>
<tr>
<td>P.Z.† A</td>
<td>109/70</td>
<td>20</td>
<td>1.9</td>
<td>292</td>
<td>169</td>
<td>123</td>
<td>42</td>
<td>22</td>
<td>8.0</td>
</tr>
<tr>
<td>B</td>
<td>100/60</td>
<td>24</td>
<td>—</td>
<td>290</td>
<td>233</td>
<td>57</td>
<td>19.5</td>
<td>7</td>
<td>0.0</td>
</tr>
<tr>
<td>F.O.† A</td>
<td>124/65</td>
<td>12</td>
<td>2.2</td>
<td>285</td>
<td>216</td>
<td>69</td>
<td>24</td>
<td>13</td>
<td>5.0</td>
</tr>
<tr>
<td>B</td>
<td>105/60</td>
<td>24</td>
<td>3.1</td>
<td>482</td>
<td>395</td>
<td>87</td>
<td>26</td>
<td>16</td>
<td>13.0</td>
</tr>
</tbody>
</table>

* Clinically improved. Studies before (A) and 3 months following (B) medical treatment.
† No clinical improvement. Studies before (A) and 8 months and 3.5 years following (B) mitral valve replacement, respectively.

Abbreviations: See table 1.
length-tension curve until a certain normal anatomical limit of stretch is reached at 2.2 micra in length.9, 10 Up to this point, the process is reversible since it is the normal physiological response. If diastolic overload of the myocardium is maintained, however, ventricular size may become larger than that predicted from elongation of sarcomeres themselves (cf below).11

**Ventricular Diastolic Pressure-Volume Relationships**

There was little if any correlation between left ventricular end-diastolic pressure and end-diastolic volume in our patients. This is consistent with prior findings in conditions of volume overload in which large volumes existed at normal end-diastolic pressures.12-16 As seen in figure 2, only four patients with compensated MR demonstrated elevations in both end-diastolic pressure and end-diastolic volume, while the majority exhibited the combination of a normal end-diastolic pressure and a high end-diastolic volume. A similar but more exaggerated disparity between end-diastolic pressure and volume was seen in six of the patients with decompensated MR. This change in end-diastolic pressure-volume relations suggests that the majority of patients with MR have an alteration in ventricular compliance.

**Changes in Myocardial Architecture**

The described difference in dynamic morphology of the left ventricle in compensated and decompensated MR, combined with evidence of an altered end-diastolic pressure-volume relationship, suggest that the structure of the myocardial wall may be different in the two groups. Thus, an adaptive geometrical change may have occurred by which the dilated LV chamber delivered an enhanced stroke volume per unit of circumferential shortening at a lower filling pressure than expected. The change in structural characteristics, however, may have seriously compromised or at least altered the pumping capacity or contraction pattern of the resulting new morphological configuration.

Recent observations in experimental animals during chronic volume overload11, 17, 18 have demonstrated that the end-diastolic length of sarcomeres in the wall of the dilated LV remains constant at near maximal length of approximately 2.2 micra. On the other hand, "slippage" between myofibrils has been found, as reflected by a loss of lateral register of alignment of Z lines between sarcomere units.13 This rearrangement of intrinsic myocardial structure may in turn confer on the dilated LV chamber a larger size at constant sarcomere length and a unique over-all shape, pattern of contraction, and pressure-volume characteristics. Thus, the pump itself has been altered. Similar to findings in our patients with compensated MR, both the extent and rate of circumferential fiber shortening, which reflects the extent of sarcomere shortening, were unchanged in the above mentioned studies.18 A normal extent of sarcomere shortening in the presence of a larger diastolic volume however, would itself serve to augment stroke volume.

**Changes in Ventricular Volume and Shape**

Patients with mitral regurgitation and very high end-diastolic volumes (250 ml/m2 or greater) do not maintain a normal ejection fraction despite the geometrical ability to deliver normal or even moderately elevated total stroke volumes. Although regurgitant and forward stroke volumes were similar, only some patients demonstrated a greatly augmented EDV and lowered E.F. This situation may have originated from a primary loss of contractility with consequent dependence on the Frank-Starling mechanism or true structural strain in response to augmented diastolic stress. Resultant dilatation then appears to have produced a secondary alteration in architecture of the heart wall. This kind of dilatation no longer evokes a Frank-Starling response and may produce its own pathologic effects on the shape and ejection pattern of the LV. These changes are characterized by a more globular shape, which is maintained in systole despite the decrease in volume. Thus, eccentricity of the chamber is not increased pari passu with reduction in volume during systole as in the normal pattern. The degree of roundness may occasionally be greater than expected for the absolute volume at end-systole. Hood and Rolett19 have reported similar findings regarding changes in left ventricular shape during systole in patients with volume overload states. Whether these mechanical factors themselves contribute to depressed contractility or whether the lowered contractility causes the changes in LV shape and size is a question that remains to be resolved.

**Interrelations Among Measurements of Ventricular Ejection**

Previous studies in experimental animals90-24 and in man25-28 have demonstrated that circumferential or minor axis fiber shortening contributes proportionally more to cardiac emptying than longitudinal fiber shortening. The dimensional changes noted during the pre-ejection period in both normal
subjects and patients with compensated MR are similar to those found by Karliner et al.\textsuperscript{4} While the total extent of circumferential fiber shortening was similar in both normal subjects and in patients with compensated MR, a rapid initial rate of shortening, not present in the normal subjects, occurred in the latter group during the pre-ejection phase.

Nearly identical linear relations were obtained between ejection fraction and diameter, derived either by direct measurement or by calculation,\textsuperscript{29,30} a finding similar to those of Lewis and Sandler in a different group of patients.\textsuperscript{31} The linear relation between E.F. and \(\% \Delta D\) is of practical value because the latter can be assessed by the noninvasive technique of echocardiography and from that calculation volume and ejection fraction can be determined without subjecting the patient to catheterization.\textsuperscript{32-34}

**Therapy and Follow-up**

Although this is merely a preliminary clinical experience, the results of therapeutic intervention in the two groups may have important implications in the selection of patients with mitral regurgitation for corrective surgery.\textsuperscript{35} Patients with compensated MR who underwent mitral valve replacement strictly on the basis of the severity of clinical symptoms were uniformly improved, while the clinical status of the other patients in this group remained relatively unchanged during a follow-up period of approximately two years. In comparison, the experience with both medical and surgical treatment in patients with decompensated mitral regurgitation was mixed. Sequential hemodynamic studies in three of these patients, however, demonstrated that two subjects became worse postoperatively while the other improved moderately following medical therapy (table 3). The deterioration in LV function following mitral valve replacement in patients P.Z. and F.O. could be attributed either to a progression of underlying secondary myocardial failure, per se, or to a loss of the decrease in afterload provided by the ejection of blood into the left atrium. The patient who improved symptomatically and hemodynamically nevertheless had only minimal reduction in LV volume.

These data show that clearcut alterations in LV dynamic morphology occur in certain patients with MR. The experimental work of others\textsuperscript{11} suggests that these alterations may herald a major structural change in cardiac muscle. Whether such changes are reversible or irreversible is currently unknown. Failure of cardiac size and shape to return to more normal dimensions in three patients following therapy implies that, at least in some cases, such changes may not necessarily disappear following removal of the volume load.

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