Mechanics of Left Ventricular Contraction in Chronic Severe Mitral Regurgitation

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SUMMARY

The mechanics of left ventricular contraction were studied during diagnostic cardiac catheterization using high-speed cineangiography in 11 patients with severe chronic mitral regurgitation. Compared with a group of previously studied normal subjects, most of the patients with mitral regurgitation demonstrated a reduced velocity of shortening \( V_{cf} \) during ejection at maximum wall stress, average = 1.01 circumferences/sec (circ/sec) (range 0.64–1.47 circ/sec). Maximum and mean \( V_{cf} \) values also were reduced in these patients, averaging 1.40 and 0.94 circ/sec, respectively. These findings are in contrast to those in acute experimental mitral regurgitation, and to observations of normal shortening velocities in chronic experimental volume overloading, in which left ventricular contraction velocity is augmented. Compared with normal subjects, patients with mitral regurgitation had significantly larger left ventricular end-diastolic circumferences and volumes, and higher total left ventricular stroke volumes. The mean regurgitant volume was 41% of the total stroke volume, of which an average of 46% was ejected into the left atrium prior to aortic valve opening. The ejection fraction and extent of fiber shortening were normal in all but two patients despite depressed shortening velocities in most. It is concluded that analysis of velocity in the ejection phase of left ventricular contraction is useful in detecting apparent alterations in inotropic state in the face of the altered loading conditions accompanying chronic mitral regurgitation. Further, favorable unloading conditions early during systole in patients with mitral regurgitation appear to mask the effects of a depressed inotropic state on the pumping function of the heart.

Additional Indexing Words:

Cineangiography Wall stress Shortening velocity Inotropic state Mitral insufficiency Force-velocity Mean velocity of fiber shortening

A CUTE EXPERIMENTAL mitral regurgitation causes reduced impedance to left ventricular ejection, accompanied by a rapid reduction in intramyocardial wall tension, more complete ventricular emptying, and an increased velocity of myocardial fiber shortening. However, it is not known if these acute alterations in left ventricular function also occur in the presence of chronic left ventricular dilatation and hypertrophy which accompany chronic mitral regurgitation. Accordingly, in patients with severe chronic mitral regurgitation, we utilized quantitative cineangiographic and hemodynamic technics to define left ventricular performance and to estimate myocardial contractility.

Methods

Eleven patients with clinical and hemodynamic evidence of severe mitral regurgitation comprised the study group. Their ages ranged from 7 to 62 years (mean 38 years). None of the patients had diastolic arterial hypertension ( > 90 mm Hg); four had systolic arterial pressures greater than 140 mm Hg at rest. Two of these (D.M. and F.W.) also had trivial aortic regurgitation. Nine were in New York Heart Association functional class III, and two were in class II. One patient (T.S.) was believed to have sustained rupture of mitral valve chordae tendineae 6 years prior to study. Two patients (M.R. and M.M.) had congenital mitral regurgitation, and the remaining eight patients had rheumatic heart disease. Two patients had a history suggestive of ischemic chest pain; in one patient (J.M.) coronary arteriograms were within normal limits. In the other patient (F.W.) coronary arteriograms were not performed. However, localized abnormalities of left ventricular wall motion were not observed in any of the left ventriculograms.
The patients were studied during diagnostic cardiac catheterization. Hemodynamic studies in adults were performed in the postabsorptive state following intramuscular injection of 100 mg of sodium pentobarbital. In all previous studies reported from this laboratory similar premedication was utilized. In patients, M.R. and M.M. premedication consisted of meperidine, 2 mg/kg and promethazine, 1 mg/kg.

Left heart catheterization was performed by transseptal and retrograde arterial technics in all patients. Left ventricular pressure was recorded during the cineangiogram in five patients using a Statham catheter-tip micromanometer, while in the remaining six patients left ventricular pressure was recorded by means of a conventional catheter-manometer system immediately prior to injection of contrast material. Although the use of a fluid-filled catheter may provide less accurate information than a catheter-tip micromanometer, derivative measurements were not made, and the results relative to contractility assessment were confirmed in each instance by calculation of the mean velocity of circumferential fiber shortening, a determination which does not require measurement of left ventricular pressure. During the cineangiogram, arterial pressure and the electrocardiogram were recorded at a paper speed of 200 mm/sec together with frame markers to indicate the precise moment of each radiographic exposure, as previously described. Biplane posteroanterior and lateral cineangiograms were obtained in six patients at 80 frames/sec while in the remaining five patients, the cineangiograms were exposed in the right anterior oblique projection at 60 or 75 frames/sec. These small differences in framing rate (maximum difference 12.5 vs 16.6 msec/frame) would not be expected to alter the results obtained. Indeed, in normal subjects previously reported from our laboratory, ejection fraction averaged 0.67 ± 0.09, results which are virtually identical to those obtained by Kennedy and his co-workers at much slower frame rates.

In patients in whom simultaneous left ventricular pressure recordings were not obtained, cardiac cycles with R-R intervals comparable to those obtained during control pressure recordings were chosen for analysis. In addition, the earliest well-opacified cardiac cycle following the injection was chosen for analysis. It has recently been demonstrated in our laboratory that little change in left ventricular contractility occurs during the first few beats after the injection of contrast material. Carleton did not observe an increase in left ventricular volume until the third beat following opacification of the left ventricle. Thus, the choice of early beats after opacification should tend to minimize effects of the contrast medium itself. Premature ventricular contractions and postextrasystolic beats were not analyzed. During atrial fibrillation both ejection fraction and fiber-shortening velocity may be affected by the end-diastolic volume of the beats chosen for analysis. Therefore, contractions were chosen with R-R intervals of sufficient length so as not to yield falsely low values for these measures. In the five patients with atrial fibrillation the R-R interval preceding each analyzed beat averaged 821 msec (range 640–964 msec), corresponding to an effective ventricular rate of 73 beats/min (range 62–94 beats/min). In patients in whom biplane cineangiograms were obtained left ventricular volumes were determined by the area-length method at end-diastole, at the time of opening of the aortic valve, and at end-systole.

Forward stroke volume was calculated by dividing the cardiac output (determined by the indicator-dilution method immediately prior to the cineangiogram) by the simultaneously occurring heart rate. Total left ventricular volume was calculated from the angiogram, and the regurgitant volume was taken as the difference between total stroke volume and forward stroke volume. In patients without mitral regurgitation good agreement has been found between angiographic stroke volume and stroke volume measured by dye dilution and Fick technic, and in 16 patients without valvular regurgitation we have found the average difference between the two determinations to be 11 ml (range 0–34 ml). In our own and in other studies the angiographic value has tended to be somewhat greater than the stroke volume calculated from the dye-dilution technic. The ejection fraction was derived by dividing the total stroke volume by end-diastolic volume, and the regurgitant fraction was calculated by dividing regurgitant volume by total stroke volume.

The velocity of circumferential fiber shortening (Vr) and the instantaneous left ventricular hoop stress (or wall tension) in the plane of the minor left ventricular circumference were determined from the correlated pressure and angiographic data in a manner reported previously. The left ventricular cavity silhouette was drawn frame-by-frame throughout systole. The long axis (L) of the left ventricle was drawn from the midpoint of the mitral valve plane to the ventricular apex, and the minor axis was constructed as a perpendicular to the long axis at its midpoint. An internal radius (ri) shortening curve (Fig. 1) was then constructed from frame-by-frame measurements during two successive cardiac cycles. The wall thickness (h) at the minor left ventricular circumference and the long axis were measured at end-diastole and at end-ejection, and the intervening points during contraction were calculated assuming a linear change throughout systole. Although we recognize that thickening of the left ventricular wall during systole may not always be linear, small errors in the estimation of wall thickness would tend to alter only slightly the absolute value of mean wall stress and would do little to alter the time at which peak stress occurs.

Mean left ventricular wall tension (stress) in g/cm² was calculated throughout contraction as:

\[
\text{wall stress} = P \frac{r_i \times \frac{2}{1 - \text{liters}^2 / h}}{\text{liters}^2 / h}
\]

where \(P\) = intracavitary pressure in g/cm². The instantaneous circumferential fiber shortening rate was computed at the midwall as 2 dr/dt, where \(r = r_i + h / 2\). The instantaneous velocity (Vr) at maximum tension was normalized by dividing by the instantaneous circumference, and the result was expressed in circ/sec. Similarly, mean Vr was normalized by...
The question of whether or not age affects calculations of normalized velocity has recently been studied in our laboratory. In 15 patients with normal left ventricular function (mean age 47 years, range 32–60), cineangiographic ejection fraction averaged 0.67 and mean Vₜₚ by cine averaged 1.66 circ/sec; no patient had either a reduced ejection fraction (<0.52) or depressed mean Vₜₚ (<1.2 circ/sec), and no differences between older and younger patients were observed.

In order to overcome the theoretic objection that calculation of velocity at a given tension and point in time may have limitations relative to active state duration, the mean rate of circumferential fiber shortening (mean Vₜₚ) also was calculated as previously described. With this approach, calculations of wall stress have proved unnecessary, and it has been demonstrated that mean Vₜₚ correlates well with estimates of Vₜₚ at maximum tension and is superior to indices derived from isovolumic force-velocity relations in differentiating patients with normal from those with abnormal left ventricular function. The term “circumferential fiber shortening” is used to describe dimensional changes in the minor left ventricular circumference, although it is recognized that these changes reflect the interaction of myocardial fiber bundles with different orientations to this circumference.

Results

Hemodynamic Values, Left Ventricular Volumes, and Dimensions

These data are summarized in table 1. Heart rate at the time of study averaged 76 beats/min ± 5 (SEM) (range 58–110 beats/min). Four patients (D.M., C.P., J.L, and H.G.) were in atrial fibrillation, and the remaining eight patients were in sinus rhythm. Cardiac indices averaged

Table 1

Hemodynamic Values, Left Ventricular Volumes

<table>
<thead>
<tr>
<th>Pt</th>
<th>Cardiac index (liters/min/m²)</th>
<th>Mean LAP (mm Hg)</th>
<th>LVEDP ml</th>
<th>LVEDP ml/m²</th>
<th>Total LV stroke volume (ml)</th>
<th>Ejection fraction</th>
<th>Regurgitant AVO</th>
<th>Total vol/ml</th>
<th>Regurgitant fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.M.</td>
<td>2.4</td>
<td>25</td>
<td>238</td>
<td>138</td>
<td>155</td>
<td>0.65</td>
<td>19</td>
<td>56</td>
<td>0.36</td>
</tr>
<tr>
<td>C.P.</td>
<td>2.5</td>
<td>24</td>
<td>175</td>
<td>108</td>
<td>98</td>
<td>0.56</td>
<td>26</td>
<td>46</td>
<td>0.47</td>
</tr>
<tr>
<td>J.L.</td>
<td>2.3</td>
<td>26</td>
<td>256</td>
<td>167</td>
<td>109</td>
<td>0.43</td>
<td>20</td>
<td>50</td>
<td>0.50</td>
</tr>
<tr>
<td>J.M.</td>
<td>2.8</td>
<td>32</td>
<td>200</td>
<td>121</td>
<td>91</td>
<td>0.46</td>
<td>18</td>
<td>31</td>
<td>0.34</td>
</tr>
<tr>
<td>F.W.</td>
<td>2.0</td>
<td>25</td>
<td>187</td>
<td>167</td>
<td>103</td>
<td>0.55</td>
<td>22</td>
<td>46</td>
<td>0.44</td>
</tr>
<tr>
<td>E.J.</td>
<td>2.3</td>
<td>27</td>
<td>424</td>
<td>230</td>
<td>185</td>
<td>0.56</td>
<td>37</td>
<td>80</td>
<td>0.37</td>
</tr>
<tr>
<td>M.R.</td>
<td>4.7</td>
<td>9</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>M.M.</td>
<td>8.0</td>
<td>10</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>J.S.</td>
<td>1.9</td>
<td>15</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>H.K.</td>
<td>1.9</td>
<td>11</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>T.W.</td>
<td>2.5</td>
<td>6</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
<td>—</td>
</tr>
<tr>
<td>Mean</td>
<td>3.0±</td>
<td>19.1±</td>
<td>247±</td>
<td>142±</td>
<td>124±</td>
<td>0.54±</td>
<td>23.7±</td>
<td>51.5±</td>
<td>0.41±</td>
</tr>
<tr>
<td>SEM</td>
<td>0.55</td>
<td>2.7</td>
<td>38±</td>
<td>21±</td>
<td>15±</td>
<td>0.03±</td>
<td>2.9±</td>
<td>6.6±</td>
<td>0.03±</td>
</tr>
</tbody>
</table>

Abbreviations: LA = left atrium; P = pressure; LVEDP = left ventricular end-diastolic pressure; AVO = aortic valve opening; SEM = standard error of the mean.
### Table 2

**Myocardial Mechanics and Dimensions**

<table>
<thead>
<tr>
<th>Pt</th>
<th>ED internal cm</th>
<th>Shortening of internal cm</th>
<th>Maximum ( V_{slt} ) (midwall)</th>
<th>( V_{slt} ) (midwall) at max T</th>
<th>Mean ( V_{slt} ) endocardial surface (circ/sec)</th>
<th>ED tension (mm Hg)</th>
<th>Ejection duration (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td>D.M.</td>
<td>20.5</td>
<td>11.9</td>
<td>6.6</td>
<td>31</td>
<td>36.4</td>
<td>1.61</td>
<td>275</td>
</tr>
<tr>
<td>C.F.</td>
<td>18.4</td>
<td>11.4</td>
<td>4.6</td>
<td>26</td>
<td>32.5</td>
<td>1.53</td>
<td>194</td>
</tr>
<tr>
<td>J.L.</td>
<td>22.3</td>
<td>14.6</td>
<td>3.5</td>
<td>16</td>
<td>15.7</td>
<td>0.64</td>
<td>232</td>
</tr>
<tr>
<td>J.M.</td>
<td>19.0</td>
<td>11.5</td>
<td>4.3</td>
<td>23</td>
<td>26.1</td>
<td>1.29</td>
<td>290</td>
</tr>
<tr>
<td>F.W.</td>
<td>20.3</td>
<td>9.7</td>
<td>4.0</td>
<td>20</td>
<td>20.3</td>
<td>0.93</td>
<td>501</td>
</tr>
<tr>
<td>E.J.</td>
<td>26.8</td>
<td>14.6</td>
<td>8.2</td>
<td>31</td>
<td>33.6</td>
<td>1.16</td>
<td>224</td>
</tr>
<tr>
<td>M.R.</td>
<td>22.9</td>
<td>21.2</td>
<td>9.1</td>
<td>40</td>
<td>40.9</td>
<td>1.98</td>
<td>215</td>
</tr>
<tr>
<td>M.M.</td>
<td>17.9</td>
<td>14.4</td>
<td>6.3</td>
<td>35</td>
<td>23.4</td>
<td>1.28</td>
<td>144</td>
</tr>
<tr>
<td>J.S.</td>
<td>21.9</td>
<td>15.6</td>
<td>6.2</td>
<td>28</td>
<td>31.0</td>
<td>1.49</td>
<td>358</td>
</tr>
<tr>
<td>H.K.</td>
<td>19.7</td>
<td>12.2</td>
<td>7.1</td>
<td>36</td>
<td>37.5</td>
<td>1.89</td>
<td>208</td>
</tr>
<tr>
<td>T.W.</td>
<td>18.8</td>
<td>12.3</td>
<td>6.7</td>
<td>36</td>
<td>28.7</td>
<td>1.61</td>
<td>295</td>
</tr>
<tr>
<td>Mean</td>
<td>20.8±</td>
<td>13.6±</td>
<td>6.1±</td>
<td>29.3±</td>
<td>29.5±</td>
<td>1.40±</td>
<td>267±</td>
</tr>
<tr>
<td>SEM</td>
<td>0.78</td>
<td>0.93</td>
<td>0.54</td>
<td>2.3</td>
<td>2.3±</td>
<td>0.12</td>
<td>29.3±</td>
</tr>
</tbody>
</table>

Abbreviations: ED = end-diastolic; circ = circumference; \( V_{slt} \) = velocity of circumferential fiber shortening; max T = maximum tension.

### LV Stroke Volume Index, ml/M²

**Figure 2**

- **Retrograde**
  - Volume index 40
  - Volume index 20
  - Volume index 0

- **Antegrade**
  - Volume index 40
  - Volume index 20
  - Volume index 0

**Normal**

- Volume index 40
- Volume index 20
- Volume index 0

**Mitral Valve Regurgitation (MR)**

- Volume index 40
- Volume index 20
- Volume index 0

The internal major axis circumference of the left ventricle at the mid-diastolic phase averaged 20.8±0.7 cm in our laboratory (35 ml/m², range 20-47 ml/m²). The increased in circumference corresponding to the dilated left ventricle at mid-diastolic phase, 20.8±0.7 cm (normal = 19.8±0.6 cm, P<0.05) (fig. 2), was significantly larger than the average value of 17.5 cm found in normal subjects (range 17-23 cm, normal = 19.8±0.6 cm, P<0.05). The left ventricular end-diastolic volume (Vd) was 250 ml/m². Moderate-to-severe pulmonary arterial hypertension was found in eight patients and in normal subjects.

**Left Ventricular End-diastolic and End-systolic Volumes**

- Volume 30±0.55 liters/m²
- Volume 19-80 liters/m²

**Left Ventricular End-diastolic and End-systolic Pressures**

- Pressure 250 dynes/sec/cm²
- Pressure 20-47 dynes/sec/cm²

**Left Ventricular Stroke Volume Index**

- Index ml/m²
- Index ml/min/m²
ventricular stroke volume × heart rate/m²) averaged 5.0 ± 0.4 liters/min/m² (fig. 3). The regurgitant volume averaged 51.5 ± 6.6 ml (range, 31–80 ml), or 41 ± 3% of the total left ventricular stroke volume. A substantial portion of the left ventricular stroke volume, averaging 23.7 ± 2.9 ml, or 46% of the total regurgitant volume, was ejected into the left atrium prior to aortic valve opening (fig. 2).

Left ventricular ejection fraction was normal in four of the six patients so studied (table 1), and the average percent change of end-diastolic circumference was reduced in only three patients with mitral regurgitation (table 2).

**Tension-Velocity Relations**

Estimates of left ventricular inotropic state were derived from the velocities of circumferential fiber shortening (Vcf). The values for Vcf at maximum wall stress (max T) were normalized for instantaneous left ventricular circumference. Despite levels of maximum wall tension comparable to normal and increased resting fiber lengths, Vcf at max T was almost uniformly depressed (1.01 ± 0.08 circ/sec), compared with the mean value for the normal subjects in our laboratory (1.74 ± 0.10 circ/sec, P < 0.001). Only one patient with mitral regurgitation (C.P.) had a normal value (table 2). Mild-to-moderate depression of Vcf at max T occurred in patients with mitral regurgitation who had both normal and abnormal hemodynamic findings (tables 1 and 2; fig. 1).

The maximum velocity of circumferential fiber shortening (max Vcf), without normalization for circumference, averaged 29.5 ± 2.3 cm/sec (range 15.7–40.9), and only three patients fell below the normal range (23–46 cm/sec) at corresponding levels of wall stress that were not significantly different from normal (265 ± 9 g/cm², range 63–409). Despite increased resting fiber lengths and normal levels of wall stress, no patient with mitral regurgitation exhibited a supranormal max Vcf. In addition, when max Vcf (rather than Vcf at maximum wall stress) was expressed as a normalized value per unit of instantaneous circumference, the average value was 1.40 ± 0.12 circ/sec, which was significantly lower than the mean found in normal subjects (2.10 ± 0.10 circ/sec, P < 0.001).

End-diastolic wall stress averaged 52.4 g/cm² and was slightly but not significantly higher in patients with mitral regurgitation than in normal subjects (table 2). Maximum wall stress averaged 301 ± 27 g/cm² (range 208–505), exceeding the normal range in only one patient (F.W.) in whom systolic arterial hypertension also was present. The maximum rate of stress or tension development (dT/dt) in patients with mitral regurgitation was not significantly different from that observed in patients with normal left ventricular function without valvular regurgitation (5020 ± 750 vs 5144 ± 1270 g/cm²/sec).

Representative patterns of instantaneous Vcf during ejection and wall stress during a single contraction are shown in figure 4. In the normal

![Figure 3](image)

**Figure 3**

(Left) Left ventricular (LV) end-diastolic and end-systolic volumes for control subjects (circles) and patients with mitral regurgitation (triangles) are shown. (Right) Left ventricular index (forward plus regurgitant stroke volumes) for control subjects and patients with mitral regurgitation. Arrows indicate average values.

![Figure 4](image)

**Figure 4**

Representative plots of wall stress (TENSION) vs velocity (VCF) for a control subject, and two patients with mitral regurgitation. In the control subject, contraction begins at a low end-diastolic tension, and shortening does not begin until tension has increased significantly. In the patients with mitral regurgitation (the patient in the center panel has relatively normal myocardial function, and the patient on the right has depressed myocardial function) end-diastolic tension is higher, and shortening begins immediately with the onset of contraction. Arrows indicate the sequence of the plots during ventricular contraction. The control subject had an atrial septal defect (ASD).

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patient without mitral regurgitation, contraction began from a low end-diastolic stress, and shortening (ejection) did not begin until wall stress had increased significantly. Once ejection had begun, velocity and stress rose rapidly together, and velocity continued to rise during ejection, as stress declined. In the patient with mitral regurgitation and a moderately abnormal V_{et} at maximum stress (J.M.), end-diastolic wall stress was higher and shortening began immediately with the onset of ventricular contraction. The rate of velocity increase and max V_{et} level were lower than normal, and stress continued to rise after velocity began to decline. A similar pattern of ejection was seen in the patient with mitral regurgitation and a more depressed V_{et} (J.L.).

**Mean Velocity of Wall Shortening**

The mean rate of circumferential fiber shortening (mean V_{et}) at the left ventricular minor equator averaged 0.94 ± 0.08 circ/sec (range 0.50–1.386) and differed significantly from that of normal patients in our laboratory (1.50 ± 0.09 circ/sec, range 1.27–2.03, P < 0.001). Mean V_{et} was reduced in all patients with an abnormal V_{et} at maximum wall stress (table 2), being normal in only one patient (C.P.)

**Discussion**

It is well known that patients with chronic, severe mitral regurgitation can remain clinically asymptomatic for many years despite a considerable regurgitant volume. In contrast, patients with other forms of chronic left ventricular volume overload, such as aortic regurgitation, do not appear to fare as well. Experimentally, acute mitral regurgitation leads to a significant reduction in calculated myocardial wall tension, as well as an increased extent and rate of wall shortening, whereas aortic regurgitation produces a small increase in wall tension. Since wall stress is a major determinant of myocardial O_2 consumption, it has been suggested on the basis of such acute animal experiments that alterations in myocardial mechanics may favorably influence O_2 requirements in mitral regurgitation, and thereby play a role in the preservation of adequate ventricular performance over many years. Accordingly, it seemed desirable to analyze left ventricular performance and myocardial contractility in patients with chronic advanced mitral regurgitation in order to assess their relevance to the acute experimental animal model. All of the patients in this series had chronic, severe mitral regurgitation. However, five of the 11 had normal cardiac indices at rest, and the left ventricular index, which includes both antegrade and regurgitant flows, was normal or above normal in all six patients in whom it was measured. Therefore, as in acute experimental mitral regurgitation, hemodynamic performance in chronic mitral regurgitation tends to be preserved and frequently is greater than normal.

Two factors identified by this study which may account for the maintenance of left ventricular performance are increased diastolic volume and reduction of afterload. A primary compensatory response to acute volume overload is the Frank-Starling mechanism, augmented end-diastolic fiber-length-improving ventricular ejection by increasing both the rate and force of contraction. In the present study, the left ventricular end-diastolic volume index was above the upper limit of normal in all but one patient with mitral regurgitation, and the average left ventricular circumference index was 38% above that of control subjects. Thus, the normal forward cardiac index in many patients undoubtedly resulted in part from augmented left ventricular resting end-diastolic fiber length. Reduction in cardiac index in long-term follow-up studies of patients with mitral regurgitation may reflect either increased regurgitant volumes or more likely, the development of left ventricular myocardial disease as discussed below. A second potential compensatory mechanism is the reduced afterload afforded by the low-impedance pathway to ventricular ejection via the regurgitant leak. In our patients, although mean left atrial pressure was abnormally high (18 ± 3 mm Hg), it nevertheless was considerably lower than mean systolic pressure (91 mm Hg) at any moment during ventricular contraction; hence, impedance to ventricular emptying was always lower than normal, and calculated myocardial wall tension, expressed as average stress per unit of myocardial wall thickness, did not rise to abnormal levels. As in chronic experimental volume overloading, it would appear that normal wall stress values in the minor equator reflect an altered major-minor axis ratio, increased average wall thickness, and enhanced early emptying in patients with mitral regurgitation. Almost half of the total regurgitant volume, or 19% of the total left ventricular stroke volume, was ejected into the left atrium prior to the opening of the aortic valve, confirming our previous observation. During what is normally the “preejection” period, therefore, a portion of the left ventricular contractile activity was expressed in terms of fiber shortening rather

*Circulation, Volume XLVII, June 1973*
than exclusively in tension development. Since the work of myocardial fiber shortening is accomplished at a lower energy cost than the work of tension development, it is likely that O₂ demands are less in chronic mitral regurgitation than in chronic aortic insufficiency despite comparable levels of preload, observations which are consistent with those following experimental production of acute mitral and aortic regurgitation.

The measures of left ventricular ejection velocity used to estimate left ventricular inotropic state were depressed in almost every patient. These reduced values were observed in patients having a wide range of clinical features and hemodynamic findings, including two children with mitral regurgitation in whom no rheumatic activity was present. This evidence for the presence of depressed left ventricular contractility assumes greater significance when it is recognized that in experimental acute mitral regurgitation the velocity of ventricular contraction is higher than normal. Moreover, in chronic experimental volume overloading produced by arteriovenous fistula, mean Vₚₚ normalized for circumference and percent shortening of the minor equator are unchanged and remain relatively normal during progressive chronic left ventricular dilatation, unless heart failure supervenes. Both of these measures were depressed, however, in the patients in the present study. Additional evidence for impaired myocardial function can be found in the pattern of ventricular ejection. The patients studied initiated left ventricular contraction from an augmented left ventricular end-diastolic volume, but at the conclusion of systole, ventricular volumes were still abnormally large. This finding is in contrast to that in animals with acute experimental mitral regurgitation in which the left ventricle, although dilated at end-diastole, contracted to a normal end-systolic volume leading to an increased ejection fraction. Of the six patients in whom ventricular volumes were measured, normal ejection fractions were found in four and mildly reduced values in two. Thus, a normal ejection fraction does not necessarily indicate the absence of depressed function, and indeed three of the four patients with a normal ejection fraction had low shortening velocities. A similar disparity between hemodynamic performance and myocardial mechanics was observed by Cohn and associates.

The mechanism for the apparent depression of inotropic state evidenced in these studies remains uncertain. Some experimental studies have indicated that hypertrophy per se causes depression of myocardial contractility induced by pressure overload, and in this group of patients left ventricular hypertrophy was clearly present. This question continues to remain in dispute, however. It is possible that reduced velocity of fiber shortening could be related to early rapid shortening of the muscle fibers due to the regurgitant leak, a mechanism which in isolated muscle can cause a decrease in shortening velocity. This mechanism appears unlikely to be the sole cause of reduced shortening velocities, since in acute experimental mitral regurgitation these velocities appear to be increased. Nevertheless, some caution must be expressed in attributing the reduced shortening velocities observed in this study solely to depressed inotropic state.

From previous experimental studies of force-velocity relations in isovolumic contractions and ejecting beats after chronic volume overloading, and of the prejection period in other studies on chronic experimental dilatation, it would be expected that chronic ventricular dilatation and hypertrophy per se do not necessarily impair myocardial performance per unit of circumference. Thus, it appears that a true reduction inotropic state has been demonstrated in many of these patients. On the other hand, one of the young patients (M.R.) had near-normal velocity values, and a second older patient (C.P.) had normal values, and it might be anticipated that in patients with milder or less prolonged forms of mitral regurgitation, myocardial contractility may be preserved. Whether or not analysis of isovolumic prejection phase pressure data in man, a procedure not attempted in the present analysis, which has recently been suggested to be independent of the presence of mitral regurgitation, will detect depression of myocardial function in patients with mitral regurgitation remains to be established. As indicated earlier, however, recent studies suggest that in the absence of mitral regurgitation, velocities during ejection are more reliable for separating normal from abnormal left ventricular contractility.

The finding that despite normal or above normal left ventricular hemodynamic performance, left ventricular myocardial contractility appeared to be depressed in most of these patients with chronic severe mitral regurgitation underscores the difficulties inherent in analyzing inotropic state by standard means under chronically altered mechanical loading conditions. Thus, the favorable unloading of the left ventricle provided by mitral
regurgitation masked the usual tendency of depressed inotropic state to reduce the ejection fraction and other hemodynamic measures of myocardial function.

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Mechanics of Left Ventricular Contraction in Chronic Severe Mitral Regurgitation

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Circulation. 1973;47:1252-1259
doi: 10.1161/01.CIR.47.6.1252

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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Correction

Eckberg DL et al.: Circulation 47: 1252, 1973. On page 1253, the formula should read

\[
\text{wall stress} = P \cdot r_1 \left(1 - \frac{2r_1^2}{L^2}\right) / h
\]

where \(P\) = intracavitary pressure in g/cm², \(r_1\) = internal left ventricular cavity radius, \(h\) = wall thickness at the minor left ventricular circumference, and \(L\) = long axis of the left ventricle.