Contractile State of the Left Ventricle in Man

INSTANTANEOUS TENSION-VELOCITY-LENGTH RELATIONS IN PATIENTS WITH AND WITHOUT DISEASE OF THE LEFT VENTRICULAR MYOCARDIUM

By James H. Gault, M.D., John Ross, Jr., M.D., and Eugene Braunwald, M.D.

ABSTRACT

The contractile state of the left ventricle in man was analyzed by correlating left ventricular (LV) dimensional changes during contraction determined from cineangiograms, with simultaneous measurements of LV pressure. The mechanical characteristics of ventricular contraction were expressed quantitatively by deriving the extent and velocity of circumferential fiber shortening at the midwall and the time course of LV wall tension (stress); the instantaneous relations between tension, velocity, and length were then examined. In 6 patients without LV disease, wall tension became maximal soon after the onset of ejection, then declined rapidly; in 9 patients with LV disease, tension fell only slightly with continued ejection. The extent of shortening of the minor LV circumference was consistently less in patients with LV disease than in those without such disease. Velocity of circumferential fiber shortening throughout contraction ranged from 0.22 to 1.11 circumferences/sec in patients without LV disease and from 1.66 to 2.71 circumferences/sec in patients without LV disease, at comparable levels of wall tension (137 to 467 g/cm², and 175 to 409 g/cm², respectively). The initial rate of change of velocity of the circumferential fibers at the onset of ejection also was less than in the group without LV disease. The velocity of shortening of the contractile elements at maximum wall tension was 0.11 to 0.87 circumferences/sec in patients with LV disease and 1.46 to 2.04 circumferences/sec in patients without LV disease.

ADDITIONAL KEY WORDS left ventricular function tension stress fiber shortening cardiac muscle mechanics force-velocity relations

It has now been demonstrated in isolated cardiac muscle (1, 2) and in the intact canine left ventricle (3, 4) that the contractile state of myocardium can be described effectively in terms of the instantaneous relations between force, velocity, and fiber length. Standard hemodynamic measures such as the stroke volume, mean ejection rate, and intraventricular pressure provide only indirect information concerning the extent and velocity of fiber shortening and wall tension, and therefore efforts in several laboratories recently...
Left Ventricular Dimensions, Fiber Shortening, and Wall Tension in Man

<table>
<thead>
<tr>
<th>Patient</th>
<th>Diagnosis</th>
<th>HR</th>
<th>Arterial P (mm Hg)</th>
<th>LVED P (mm Hg)</th>
<th>C.I.</th>
<th>Max. dp/dt</th>
<th>LV wall thickness (cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M.M.</td>
<td>ASD</td>
<td>88</td>
<td>115</td>
<td>9</td>
<td>2.60</td>
<td>2039</td>
<td>.69</td>
</tr>
<tr>
<td>W.C.</td>
<td>MS</td>
<td>57</td>
<td>110</td>
<td>9</td>
<td>3.23</td>
<td>1854</td>
<td>.75</td>
</tr>
<tr>
<td>R.B.</td>
<td>ASD</td>
<td>88</td>
<td>137</td>
<td>8</td>
<td>3.88</td>
<td>2279</td>
<td>.83</td>
</tr>
<tr>
<td>W.M.</td>
<td></td>
<td>94</td>
<td>116</td>
<td>8</td>
<td>2.33</td>
<td>2237</td>
<td>.91</td>
</tr>
<tr>
<td>J.S.</td>
<td>Functional murmur</td>
<td>105</td>
<td>140</td>
<td>7</td>
<td>5.37</td>
<td>1639</td>
<td>.90</td>
</tr>
<tr>
<td>E.D.</td>
<td>ASD</td>
<td>80</td>
<td>116</td>
<td>9</td>
<td>3.09</td>
<td>1845</td>
<td>.74</td>
</tr>
<tr>
<td><strong>AVERAGE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>E.T.</td>
<td>Myocard. dis.</td>
<td>65</td>
<td>102</td>
<td>11</td>
<td>2.50</td>
<td>1515</td>
<td>.74</td>
</tr>
<tr>
<td>A.S.</td>
<td>ASHD + mild MS</td>
<td>87</td>
<td>110</td>
<td>8</td>
<td>2.93</td>
<td>1020</td>
<td>.94</td>
</tr>
<tr>
<td>C.A.*</td>
<td>Myocard. dis.</td>
<td>80</td>
<td>140</td>
<td>17</td>
<td>2.36</td>
<td>1236</td>
<td>1.19</td>
</tr>
<tr>
<td>W.L.*</td>
<td>Myocard. dis.</td>
<td>90</td>
<td>90</td>
<td>25</td>
<td>1.49</td>
<td>475</td>
<td>.82</td>
</tr>
<tr>
<td>H.C.</td>
<td>ASHD/CHB</td>
<td>40</td>
<td>128</td>
<td>22</td>
<td>1.43</td>
<td>1054</td>
<td>.70</td>
</tr>
<tr>
<td>W.W.*</td>
<td>ASHD/MI</td>
<td>90</td>
<td>151</td>
<td>21</td>
<td>3.03</td>
<td>1452</td>
<td>.88</td>
</tr>
<tr>
<td>J.B.*</td>
<td>ASHD/MI</td>
<td>100</td>
<td>100</td>
<td>13</td>
<td>2.87</td>
<td>908</td>
<td>.88</td>
</tr>
<tr>
<td>J.M.</td>
<td>Myocard. dis.</td>
<td>69</td>
<td>115</td>
<td>16</td>
<td>2.44</td>
<td>1435</td>
<td>2.20</td>
</tr>
<tr>
<td>I.M.</td>
<td>Myocard. dis.</td>
<td>93</td>
<td>131</td>
<td>23</td>
<td>2.13</td>
<td>734</td>
<td>1.15</td>
</tr>
<tr>
<td><strong>AVERAGE</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*Patient receiving digitalis.

HR = heart rate; LV = left ventricle; ED = end-diastolic; ES = end-systolic; P = pressure; C.I. = cardiac index; BA = brachial artery; circ = circumference; VCF = velocity of circumferential fiber shortening; VCE = velocity of contractile state.

have been directed toward extending the principles of muscle mechanics to the assessment of ventricular function in man. In these studies, instantaneous tension in the wall of the human left ventricle was calculated from angiographic measurements of ventricular volume (5) or from estimations of the end-diastolic volume using the indicator-dilution method (6, 7) and assuming a constant rate of fiber shortening (7). However, calculation of the relations between mean tension and mean velocity during ejection using the latter techniques has not permitted clear separation of normal from abnormal ventricular function in man, and since the rate of fiber shortening is not constant during ejection (3, 4), it might be anticipated that an examination of instantaneous rather than mean relations between shortening velocity and wall tension, using a more direct approach, might provide a sensitive measure of contractile or inotropic state. Recently, this problem was approached in cardiac patients postoperatively by measuring the velocity of radiopaque markers that had been sutured to the ventricular epicardium during the operation (8). Although the force-velocity relations derived by this method were useful in analyzing directional changes in contractility, comparisons between patients were not possible.

This report presents methods for correlating the rate of instantaneous fiber shortening with left ventricular pressure and wall stress and describes its application to an analysis.
of left ventricular myocardial function in man. This approach has permitted a quantitative comparison of the contractile properties of the left ventricles of patients with and without myocardial dysfunction.

**Methods**

Fifteen patients aged 14 to 55 years were studied during diagnostic left heart catheterization. Their diagnoses are listed in Table 1. On the basis of clinical findings and standard hemodynamic measurements, six patients had normal left ventricular (LV) dynamics. This group included four patients with atrial septal defect, one with mitral stenosis and mild aortic stenosis (LV-aortic peak systolic pressure difference, 10 mm Hg), and one with a functional heart murmur. These six patients had sinus rhythm; their heart rates at the time the measurements were made ranged from 50 to 105/min, their brachial arterial pressures were normal, and their LV end-diastolic pressures were <12 mm Hg (9). The cardiac indices, determined by the indicator dilution technique, were normal in five patients and slightly reduced in one, ranging from 2.33 to 5.37 liters/min per M² (average 3.41).

Nine patients had LV myocardial disease. Three had idiopathic cardiomyopathy, two had idiopathic left ventricular hypertrophy, and four had arteriosclerotic heart disease. In one of the last four patients, there was associated mitral stenosis of minimal degree (mean pressure difference across mitral valve, 2 mm Hg); in another (H.C.), complete heart block had recently developed with a ventricular rate of 40/min. The remaining eight patients had sinus rhythm, with heart rates ranging from 58 to 92/min. The

---

### Table 1: Contractile Properties of Left Ventricles

<table>
<thead>
<tr>
<th>ED internal circ (cm)</th>
<th>ED tension (g/cm²)</th>
<th>Shortening of internal circ (cm)</th>
<th>%ED</th>
<th>Maximum Von (midwall)</th>
<th>Corresponding tension (g/cm²)</th>
<th>Von (midwall)</th>
<th>Corresponding tension (g/cm²)</th>
</tr>
</thead>
<tbody>
<tr>
<td>13.9</td>
<td>41</td>
<td>5.7</td>
<td>41.2</td>
<td>31.3</td>
<td>2.33</td>
<td>271</td>
<td>23.2</td>
</tr>
<tr>
<td>14.6</td>
<td>35</td>
<td>4.5</td>
<td>30.5</td>
<td>24.7</td>
<td>1.66</td>
<td>270</td>
<td>23.3</td>
</tr>
<tr>
<td>16.2</td>
<td>47</td>
<td>4.8</td>
<td>29.5</td>
<td>30.4</td>
<td>1.72</td>
<td>409</td>
<td>26.6</td>
</tr>
<tr>
<td>14.5</td>
<td>39</td>
<td>5.1</td>
<td>35.2</td>
<td>37.7</td>
<td>2.42</td>
<td>255</td>
<td>30.4</td>
</tr>
<tr>
<td>12.9</td>
<td>36</td>
<td>5.5</td>
<td>42.2</td>
<td>36.0</td>
<td>2.71</td>
<td>175</td>
<td>30.6</td>
</tr>
<tr>
<td>14.7</td>
<td>42</td>
<td>6.9</td>
<td>46.9</td>
<td>36.7</td>
<td>2.63</td>
<td>298</td>
<td>28.9</td>
</tr>
<tr>
<td>14.5</td>
<td>40</td>
<td>5.4</td>
<td>37.6</td>
<td>32.8</td>
<td>2.25</td>
<td>280</td>
<td>27.2</td>
</tr>
<tr>
<td>19.7</td>
<td>47</td>
<td>3.7</td>
<td>18.8</td>
<td>19.3</td>
<td>0.93</td>
<td>316</td>
<td>12.6</td>
</tr>
<tr>
<td>17.1</td>
<td>45</td>
<td>3.3</td>
<td>19.1</td>
<td>20.5</td>
<td>1.11</td>
<td>234</td>
<td>16.7</td>
</tr>
<tr>
<td>26.4</td>
<td>86</td>
<td>1.0</td>
<td>3.8</td>
<td>7.8</td>
<td>0.26</td>
<td>330</td>
<td>7.8</td>
</tr>
<tr>
<td>26.6</td>
<td>167</td>
<td>1.0</td>
<td>3.8</td>
<td>6.8</td>
<td>0.23</td>
<td>351</td>
<td>4.1</td>
</tr>
<tr>
<td>21.8</td>
<td>123</td>
<td>5.4</td>
<td>24.6</td>
<td>20.3</td>
<td>0.94</td>
<td>467</td>
<td>17.9</td>
</tr>
<tr>
<td>22.4</td>
<td>121</td>
<td>1.6</td>
<td>7.0</td>
<td>12.0</td>
<td>0.48</td>
<td>377</td>
<td>12.9</td>
</tr>
<tr>
<td>23.1</td>
<td>81</td>
<td>2.8</td>
<td>12.3</td>
<td>19.6</td>
<td>0.81</td>
<td>305</td>
<td>18.9</td>
</tr>
<tr>
<td>17.8</td>
<td>42</td>
<td>2.6</td>
<td>14.8</td>
<td>21.5</td>
<td>0.93</td>
<td>137</td>
<td>18.1</td>
</tr>
<tr>
<td>26.8</td>
<td>85</td>
<td>1.1</td>
<td>4.1</td>
<td>6.6</td>
<td>0.22</td>
<td>386</td>
<td>3.5</td>
</tr>
<tr>
<td>22.4</td>
<td>89</td>
<td>2.5</td>
<td>12.0</td>
<td>15.0</td>
<td>0.66</td>
<td>322</td>
<td>12.5</td>
</tr>
</tbody>
</table>

Circulation Research, Vol. XXII, April 1968
brachial arterial pressures were normal in all nine patients. Seven of the nine had abnormal LV dynamics at rest. The LV end-diastolic pressure at rest was elevated in seven patients (>12 mm Hg) and normal in two, and the cardiac index was below normal in five (<2.50 liters/min/"") in two patients (E.T., A.S.), both of whom reported symptoms of left heart failure, LV dynamics at rest were normal, but the hemodynamic responses to exercise were abnormal (10, 11). Conventional chest roentgenograms in these two patients revealed no evidence of LV enlargement. Five patients were receiving a digitalis preparation (Table 1).

The cineangiogram from which the measurements of LV dimensions were made was performed for diagnostic purposes in all but 2 patients, whose informed consent for this part of the procedure was obtained.

The hemodynamic study was performed in the postabsorptive state after giving sodium pentobarbital 100 mg, intramuscularly. A Corinod needle was placed in the left brachial or left radial artery. Left heart catheterization was performed by the retrograde arterial technique, by transseptal puncture (12), or by introducing a catheter into the left heart via an atrial septal defect. A catheter-tip micromanometer was introduced into the left ventricle to permit the recording of high-fidelity LV pressure pulses (13). To avoid ventricular premature beats, the left ventricle was visualized by injection of contrast material proximal to the left ventricle, either through a catheter introduced into the left atrium by transseptal puncture or via an atrial septal defect, or through a catheter in the pulmonary artery.

The patient was positioned in the right anterior oblique projection, and in midinspiration 45 to 75 ml of radiographic contrast material was injected over 2 to 3 seconds with a power syringe while cineangiograms were exposed at 60 frames/sec on 35-mm cineangiographic film (Fig. 1). During the cineangiogram, LV pressure and its first derivative from the micromanometer, LV pressure from the catheter lumen, and the brachial arterial pressure, were recorded simultaneously at 200 mm/sec on a photographic recorder and also directly on the cine film using the cinetrace system (14). To minimize the effects of contrast material on ven-

1Hypaque, 90% or Renovist, 69%.
2Electronics for Medicine, White Plains, New York.
CONTRACTILE STATE OF LEFT VENTRICLE IN MAN

Measurements of the radius of the minor LV circumference (upper tracing), determined at 16.7-msec intervals from successive cine frames during ejection, are correlated with simultaneous LV pressure (lower tracing) recorded by catheter-tip micromanometer. Circles and squares represent LV pressure and the averages of duplicate measurements of LV radius from each of two successive cycles in one patient originating from the same end-diastolic pressure and reaching the same peak systolic pressure. Dashed vertical lines indicate the onset and end of ejection. LVEDP = left ventricular end-diastolic pressure.

The LV cavity silhouette was drawn in outline, frame by frame, throughout systole. The long axis of the left ventricle was taken as the line from the midpoint of the mitral valve plane to the LV apex. The internal radius of the minor LV circumference was measured from each outline drawing, perpendicular to and at the midpoint of the long axis (Fig. 1), correction being made for x-ray magnification (15). Duplicate measurements of internal radius were made in each of two successive beats originating from the same LV end-diastolic pressure and reaching the same peak LV pressure. A curve representing internal radius throughout contraction was then drawn to fit these measurements (Fig. 2). In all studies, the maximum deviation of these measurements from the constructed curve ranged from 0.8 to 2.3% (average 1.8%).

Wall thickness of the left ventricle was measured from the cineangiogram in the plane of the minor LV circumference (Fig. 1) at end-diastole and at end-systole, correction being made for x-ray magnification. Measurement of LV wall thickness in the right anterior oblique projection is subject to potential error from superimposition of the right ventricular wall. However, contrast visualization of the right ventricle in 6 of the 15 patients, some of whom had right ventricular enlargement, demonstrated that the right ventricular wall did not interfere with measurement of wall thickness at the midportion of the left ventricle. In addition, it was possible in many patients to delineate further the outer margin of the LV wall by visualization of lateral branches of the left anterior descending coronary artery. Moreover, in the six subjects with normal LV function, the LV wall thicknesses at end-diastole averaged 0.8 cm, a value in close agreement with that determined from angiograms made in the frontal projection in normal subjects (5, 16).

The opening of the aortic valve was identified as the time when LV pressure equaled brachial arterial diastolic pressure, corrected for any difference between the latter and central aortic diastolic pressure. Left ventricular wall tension in grams per square centimeter (stress) was computed at 16.7 msec intervals throughout systole with the aid of a digital computer as

$$\text{wall tension} = \frac{P \cdot r}{L} \left(1 - \frac{2r^2}{L^2}\right) \frac{1}{h} \quad (17),$$

where $P = LV$ intracavitary pressure in grams per square centimeter, $r = \text{instantaneous internal radius in centimeters}$, $L = \text{long axis in centimeters}$ and $h = \text{wall thickness, also expressed in centimeters}$. In these computations $h$ and $L$ were measured at end-diastole and end-systole, intermediate points being calculated assuming a linear change in wall thickness and length. This equation was employed to account for the influence of changes in ventricular shape on circumferential hoop stress in the same ventricle during the course of contraction and in ventricles of differing shapes. This approach, therefore, should have obviated in large part the problems implicit in the assumption of a constant geometric form for the left ventricle. The force acting at the internal minor LV circumference was assumed to be

---

Circulation Research, Vol. XXII, April 1968

IBM 1620.
Some support for using internal radius has been provided by the studies of Hefner et al. (18), who demonstrated that total tension, computed as a function of internal radius, correlated rather closely with directly measured tension. Equations derived for thin-walled structures underestimate the peak stress computed from known stress distributions for passively distended thick-walled elastic cylinders (5, 19), especially as the magnitude of wall thickness increases relative to internal radius. However, these equations appear to provide a reasonably accurate estimate of average wall stress (19, 20).

The peak rate of tension development was determined from the slope of the tension-time relation. The total duration of systolic tension was measured from the onset of isometric contraction to the point during isometric relaxation at which tension equaled that at the onset of contraction.

The extent of unloading of the ventricle during contraction, termed the "fractional decrease in afterload," was calculated as the difference between the maximum systolic tension and that existing at end-ejection, expressed as a percentage of maximum systolic tension.

Velocity of circumferential fiber shortening was computed at the LV midwall as $2\pi \frac{dr}{dt}$ (where $r = r_0 + \frac{h}{2}$). Velocity of circumferential fiber shortening was corrected for the corresponding instantaneous midwall LV circumference ($circumference = 2\pi r$) and expressed as circumferences per second. In addition, a mean velocity of shortening of the internal circumference was computed in each patient by dividing the extent of shortening of this circumference by the ejection time. The initial rate of change of velocity of the circumferential fibers at the midwall was determined in each patient as the average.

**FIGURE 3**

LV cavity silhouettes drawn from cineangiographic frames exposed at end-diastole (outer silhouettes) and end-systole (inner silhouettes), are shown in two patients with normal LV function (A, B) and in two patients with LV disease (C, D).
slope of the fiber shortening curve during the 50 msec following the onset of ejection. The term "circumferential fiber shortening" is employed to describe the characteristics of dimensional changes in the minor LV circumference, recognizing that these changes reflect the net result of the interaction of fiber bundles with different orientations to this circumference.

**Figure 4**

A: Total systolic shortening of the minor internal LV circumference (vertical axis) in patients with normal LV function (circles) and in patients with LV myocardial disease (triangles). B: Extent of circumferential shortening expressed as percent of end-diastolic circumference. Horizontal bars in both panels indicate the average values for each group.

**Figure 5**

In the upper panels, LV wall tension is plotted against time in a patient with normal LV function (A) and in two patients with LV myocardial disease (B, C). The vertical dashed lines in each panel indicate the limits of the ejection period, and the arrows the maximum level of tension. In the lower panels, the instantaneous relation between velocity of circumferential fiber shortening (VCF) (vertical axis) and wall tension (horizontal axis) are shown throughout ejection in each patient. Circ = circumferences; arrows indicate direction of the tension-velocity loop in each lower panel.

*Circulation Research, Vol. XXII, April 1968*
Results

The findings in all 15 patients are summarized in Table I.

Left Ventricular Dimensions and the Extent of Fiber Shortening.—In the patients with left ventricular disease, the LV cavity silhouettes were larger and more spherical than normal (Fig. 3, C and D). The major-minor axis ratios averaged 1.4/1.0 at end-diastole and 1.5/1.0 at end-systole in the patients with LV disease, and were significantly smaller (P < .001) than in patients without LV disease, in whom they averaged 1.9/1.0 and 2.4/1.0 respectively. The internal circumference at end-diastole was significantly greater, and the extent of shortening of this circumference during systole was consistently less than in the patients without LV disease (Fig. 4). The extent of shortening at the midwall also was reduced, decreasing by an average of 8.2% and 27.6% in patients with and without LV disease, respectively. Shortening of the LV internal diameter in the major axis (L) was significantly reduced, averaging 7.4% in the patients with, and 18.6% in those without, LV disease (P < .001).

Left Ventricular Wall Tension.—Maximum total wall tension was generally comparable in the two groups of patients (Table I). In all six patients without left ventricular disease, LV myocardial wall tension during contraction reached a maximum level soon after the onset of ejection and then declined rapidly (Fig. 5, A), while in the patients with LV disease tension was sustained at a relatively high level throughout most of systole (B and C). The peak rate of tension development during isometric systole was generally greater in patients without LV disease, ranging from 3832 to 6737 (avg = 5168 g/cm² - sec) as compared to values of from 1826 to 4731 g/(cm² - sec) (avg 3107 g/cm² • sec) in the patients with LV disease (P < .01).

The fractional decrease in afterload, or the difference between maximum systolic tension
and that existing at end-ejection, expressed as a percentage of maximum systolic tension, was significantly less in patients with LV disease, averaging 25.5% and 50% in the patients with and without LV disease, respectively ($P < .001$). End-diastolic tension was significantly higher in patients with LV disease ($P < .001$) and constituted a significantly greater percentage of maximum tension ($P < .01$).

Left Ventricular Fiber Shortening Rate.—The initial upslope of the curve of circumferential fiber shortening was always reduced in patients with LV disease (Fig. 6). The initial rate of change of velocity of the circumferential fibers averaged 553 cm/sec² in patients without, and 194 cm/sec² in patients with, LV disease, respectively ($P < .001$). Maximum velocity of circumferential fiber shortening occurred an average of 159 msec after the onset of isometric contraction in patients without LV disease and 186 msec in patients with LV disease; maximum velocity occurred 95 msec and 123 msec after the onset of ejection, respectively, in the two groups. These times did not differ significantly between the two groups. The mean velocity of fiber shortening calculated at the internal circumference in patients without LV disease ranged from 18.0 to 27.5 cm/sec (avg 23.3 cm/sec), and from 5.1 to 15.2 cm/sec (avg 10.2 cm/sec) in patients with LV disease.

Left Ventricular Tension-Velocity Relations.—The pattern of instantaneous relations between tension and velocity during the course of ejection consistently differed in the two groups of patients (Fig. 5, lower panels). In the patients without LV disease (W.M.), the tension-velocity relation exhibited a broad counterclockwise loop, since tension increased and then began to decline while velocity continued to rise; velocity subsequently was sustained while tension fell, and tension at end-ejection was always lower than at the onset of ejection. In the patients with LV disease, tension increased proportionately more than velocity during the first half of the ejection period, and in contrast to patients without LV disease, velocity did not continue to rise after peak tension but fell progressively as tension diminished. Therefore, the instantaneous tension-velocity relation during ejection exhibited a narrow loop, and in addition, tension at end-ejection was greater than at the onset of ejection (A.S. and C.A.).

Maximum velocity of circumferential fiber shortening at generally comparable levels of wall tension was always lower in the patients with LV disease (avg 15.0 cm/sec) than in those without LV disease (avg 32.8 cm/sec).
The relations between tension and maximum velocity of fiber shortening and contractile element velocity expressed as muscle lengths or circumferences per second also were consistently different in the two groups of patients, as shown in Figure 7. In the patients with LV disease, maximum tension (the point at which contractile element velocity was measured) occurred an average of 147 msec after the onset of isometric systole, a value not significantly different from that in patients without LV disease, in whom it averaged 109 msec.

Discussion

It has been demonstrated in the canine left ventricle that the preload, the afterload, and the level of contractility are the primary determinants of the manner in which the myocardial fibers shorten (3, 4). These considerations require that if analysis of the characteristics of fiber shortening is to provide a sensitive means of comparing the level of contractile state in the normal and abnormal ventricle, then both afterload and diastolic fiber length must be known.

In patients with abnormal LV function, velocity of circumferential fiber shortening was consistently reduced throughout ejection when compared with that in patients with normal LV function at comparable levels of wall tension. To compare velocity among different patients, it was corrected by dividing by the corresponding instantaneous circumference; thus, velocity was expressed per unit of circumferential length, a term analogous to muscle lengths per second in isolated muscle. Correction of shortening velocity in this manner, of course, does not take into consideration the influence of end-diastolic muscle length or instantaneous length during contraction, both of which have been shown to be important determinants of instantaneous velocity (4, 21). Although it was not possible to examine velocity of fiber shortening or of contractile elements in patients without LV disease at fiber lengths comparable to those in patients with LV disease, the greater initial fiber lengths in the latter group would not be expected to decrease velocity relative to that of the patients without LV disease at comparable levels of wall tension and contractility. Support for this contention is provided by studies in isolated muscle (21), and by recent observations in our laboratory that in the intact canine left ventricle velocity of fiber shortening and that of contractile elements generally are unchanged or increased when diastolic volume and stroke volume are increased by transfusion, despite augmentation of wall tension. No correlation was observed in the present study between heart rate and velocity of fiber shortening. Under experimental conditions, changes in heart rate substantially greater than the differences observed between our patients are required to produce a significant change in the force-velocity relation (22).

In addition to abnormalities in the time course of tension development, there were considerable reductions in the extent of fiber shortening in patients with LV disease (Fig. 4), a conclusion reached in studies employing indicator-dilution measurements of the ejected fraction (7, 8) and evident in studies in which ventricular volume and ejected fraction were calculated angiographically (23, 24). These findings also are consistent with recent observations in acute experimental heart failure indicating that the extent of LV fiber shortening is reduced, despite substantial elevation of the LV end-diastolic volume (25).

It would be desirable to measure, in addition to velocity of fiber shortening, the shortening velocity of the contractile elements throughout the cardiac cycle in the normal and failing heart. However, the coefficient of series elasticity (26) could differ substantially in the normal and abnormal left ventricle, and therefore calculation of contractile element velocity throughout contraction was not attempted. It was possible, nonetheless, to determine this velocity at maximum wall tension, when the rate of extension of the series elastic component is zero and velocity of the contractile elements equals that of circumferential fiber shortening (27); velocity of
contractile elements determined in this fashion was consistently reduced in patients with LV disease.

It is recognized that variations in the duration of active state could have influenced the measurements of peak velocity of fiber shortening and velocity of contractile elements at peak tension. However, these variables were lower throughout the cardiac cycle in patients with LV disease than in those with normal LV function. In addition, the differences in time to peak tension in the two groups were not significant, and there were only small differences in the time at which maximum velocity occurred. Also, in acute (25) and chronic (28) experimental ventricular failure the duration of active state does not appear to be abbreviated. Finally, it has been shown in isolated cardiac muscle that there is a considerable plateau of active state (29, 30). Therefore, it is considered unlikely that variations in the time course of active state between the two groups could explain the observed differences in velocity.

In the present study, the direct measurement of LV dimensions allowed for the influence of instantaneous ventricular shape in the computations of tension, largely obviating the errors implicit in indirect methods which assume a constant geometric figure during contraction and in different patients. We assumed that the radius in the plane selected was representative of all radii of the minor LV circumference throughout the cardiac cycle. It has been shown in angiographic studies that the diameters of the minor LV circumferences measured in the frontal and lateral projections differ by less than 10% (31), and direct measurements of casts made from the chambers of normal canine left ventricle arrested in systole or diastole confirmed this view (32). Therefore we believe that the error is small in deriving circumferential shortening from the radius in one plane.

In previous studies, in which indicator-dilution techniques were employed, mean rate of fiber shortening was correlated with mean wall tension in patients with and without cardiac dysfunction, using a thin-walled spheroidal model (6, 7). The explanation for at least some of the overlap in the values for normal and diseased hearts obtained with that approach may be found in the lack of geometric uniformity between the normal and abnormal ventricle, a factor not assessed by indicator-dilution techniques. As shown in the present study, the relative shortening of the minor LV axis, particularly in patients with normal LV function, exceeds that of the major axis. Therefore, computations based on a spheroidal LV model may underestimate both the extent and velocity of shortening of most of the cardiac fibers in the normal ventricle. This contention is supported by the finding in the present study that the mean velocity of fiber shortening at the internal circumference of patients without LV disease was 23.3 cm/sec, while values of 13.4 (6) and 15.2 cm/sec (7) have been found in similar subjects by the indicator-dilution technique. Similar considerations apply to the use of a single geometric figure in the calculation of myocardial wall stress. The magnitude of the forces acting on the minor circumference are dependent on the shape of the ventricle, specifically on the relation between the major and minor axis lengths (17). For example, the mechanical advantage afforded by the more spheroidal configuration of the ventricles in patients with LV disease resulted in a relatively lower wall tension than would have been derived assuming an ellipsoidal model.

To permit a quantitative comparison of LV wall stress among individual patients, the tension was corrected for mean wall thickness. In the present study, LV wall thickness increased by an average of 32% in patients without, and 23% in patients with, LV disease from end-diastole to end-systole. These values are similar to the dynamic changes in wall thickness observed in contracting canine ventricles (33) and to the differences in wall thickness observed between canine ventricles fixed at end-diastole and at end-systole (32).

The present study has demonstrated that the function of the left ventricle in intact man can be analyzed quantitatively in terms...
of the mechanical characteristics of ventricular contraction. Most of the patients with LV disease studied were selected because they had obvious hemodynamic evidence of LV dysfunction in the resting state. In two patients, however, abnormal LV function defined by standard hemodynamic measurements was evident only during the stress of exercise; nevertheless, the tension-velocity-length relations in the resting state clearly distinguished these two patients from those with normal LV function. It has been shown in animals that the force-velocity relation provides a more sensitive description of changes in contractile state than the ventricular function curve, and it may be anticipated that the approach described in this report will permit the detection of abnormal myocardial function in patients without other hemodynamic evidence of cardiac dysfunction. By focusing on the mechanical function of the ventricular muscle per se, these techniques also offer the advantage of permitting assessment of cardiac function in the presence of abnormal function of the cardiac valves. While it is recognized that the techniques described are relatively complex, it may be anticipated that the quantitative information gathered by this approach will provide a foundation upon which simpler indices of myocardial function can be based.

References


Contractile State of the Left Ventricle in Man: Instantaneous Tension-Velocity-Length Relations in Patients With And Without Disease of the Left Ventricular Myocardium

JAMES H. GAULT, JOHN ROSS, Jr. and EUGENE BRAUNWALD

doi: 10.1161/01.RES.22.4.451

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1968 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circres.ahajournals.org/content/22/4/451

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in Circulation Research can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to Circulation Research is online at:
http://circres.ahajournals.org/subscriptions/