Contractile State of the Left Ventricle in Man as Evaluated from End-systolic Pressure-Volume Relations

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SUMMARY  End-systolic pressure (PES), volume (VES), wall tension (TWS) and circumference (CW) of the human left ventricle were studied at cardiac catheterization in 24 subjects with varying degrees of left ventricular dysfunction. Acute alterations in systolic load consistently resulted in changes in VES and CW, with a smaller volume and circumference characterizing the lower systolic load in each subject. End systolic pressure-volume lines were constructed by plotting PES against VES at the higher and lower systolic load in each subject. The slope of the resultant lines was considerably steeper for normal than for poorly contractile left ventricles. VES, the volume axis intercept of the line (i.e., the theoretical VES at PES = 0) was significantly smaller for normal than for poorly contractile ventricles. Similar findings were noted for CW, the theoretic end-systolic circumference at zero end-systolic ventricular wall tension. Postextrasyolic potentiation resulted in decreased VES and CW with no change in PES and only a slight fall in TWS. In conclusion, end-systolic pressure-volume and tension-circumference relations reflect the contractile state of left ventricular myocardium. Quantitation of these relationships may provide a useful new approach to the assessment of myocardial function in man.

THE EXTENT OF MYOCARDIAL FIBER SHORTENING reflects the interaction of initial fiber stretch (preload), the load resisting systolic shortening (afterload), and intrinsic contractile state. As afterload increases, the extent of systolic fiber shortening falls, resulting in progressively greater end-systolic fiber lengths.1-3 Thus, end-systolic fiber length is apparently a direct function of afterload, and in experimental animals at any level of contractile state end-systolic pressure-volume, length-tension, and stress-strain relations have all been found to be essentially linear over the physiologic range.4-11 Furthermore, evidence suggests that the constants describing these linear relationships are independent of initial volume or preload, and are sensitive to changes in contractile state of the ventricular myocardium.9-11

This experimental approach to the assessment of myocardial contractility has not previously been applied to man. In the present study, left ventricular end-systolic pressure-volume and tension-circumference relations are described in a series of patients in whom alterations in left ventricular afterload were pharmacologically induced during cardiac catheterization. The effects of varying degrees of left ventricular dysfunction and of post-extrasyolic potentiation on the end-systolic pressure-volume and tension-circumference relationships are examined and compared to findings in a control group with normal ventricular function. The results indicate that end-systolic pressure-volume and tension-circumference relations of the human left ventricle are sensitive to alterations in contractile state and that quantitation of these relations may provide a new approach to the assessment of myocardial function in man.

Methods and Materials

Twenty-four patients who had undergone complete right and left heart catheterization with quantitative left ventricular cineangiography and simultaneous left ventricular or aortic pressure recording formed the study population. In sixteen subjects afterload was reduced with an organic nitrate. Hemodynamic and angiographic measurements were made before (control), and 15 minutes after the start of an intravenous infusion of sodium nitroprusside given at a rate sufficient to lower mean aortic pressure 15-20 mm Hg (nine subjects). Similar measurements were made before and after administration of 10 mg chewable (buccal absorption) erethrityl tetranitrate (three subjects) or 20 mg isosorbide dinitrate, p.o. (four subjects). In these subjects, heart rate was comparable in both states without atrial pacing. In three subjects, measurements were made before and 15 minutes after the start of an intravenous infusion of methoxamine given at a rate sufficient to raise aortic mean pressure by greater than 20 mm Hg; in these subjects, atrial pacing was utilized to assure comparable heart rates in the two states. In each study, quantitative left ventriculography together with simultaneous left ventricular or aortic pressure measurement was carried out in two states: before and during afterload manipulation.

Data were included in the analysis only when (a) ventriculograms and pressure tracings from both states were technically of high quality for quantitation of left ventricular volume and pressure, and (b) changes in mean aortic pressure for the isosorbide dinitrate and erethrityl tetranitrate studies were at least 10 mm Hg. In 19 subjects left ventricular volumes and pressures were determined at two states of systolic loading.

The remaining five subjects were selected on the basis of having single ventricular extra-systolic beats during quantitative biplane left ventriculography with simultaneous recording of left ventricular or aortic pressure. In these subjects the left ventricular end-systolic pressure-volume relations of control and post-extra-systolic potentiated beats could be compared.

For the total group of 24 subjects, left ventriculography was carried out using biplane 35 mm cineangiography (PA and lateral projection) in 16 subjects, and single plane 35 mm cineangiography (right anterior oblique projection) in eight subjects. Left ventricular volumes were determined by planimetry using the area-length method of Dodge and coworkers12 and Kasser and Kennedy,13 and a small computer

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interfaced with a sonic digitizer. Micromanometer-tipped angiographic catheters (Millar Mikrotip) were used in 16 subjects, permitting recording of high fidelity left ventricular pressure simultaneous with quantitative left ventriculography. In addition, systemic arterial pressure was recorded during ventriculography in all subjects using a fluid-filled catheter system attached to a P23Db Statham pressure transducer. The fluid-filled system has been tested in our laboratory and found to have a natural frequency of 25 Hz and a damping coefficient of .603.

Theoretical Considerations and Calculations

In the present study, we have made the following assumptions:

1) The left ventricular end-systolic pressure-volume relation is linear in man, as it has been shown to be in animal studies,6–11 such that:

\[ P_{ES} = mV_{ES} + b \]  

(1)

where \( P_{ES} \) and \( V_{ES} \) are left ventricular end-systolic pressure and volume respectively, \( m \) is the slope of the line describing their relations, and \( b \) is the pressure at \( V_{ES} = 0 \). The equation may also be expressed as:

\[ P_{ES} = m(V_{ES} - V_o) \]

where \( V_o = -b/m \), the volume at \( P_{ES} = 0 \).

2) End-systolic volume can be accurately determined from left ventricular cineangiograms as the smallest calculated volume from serial frames.

3) Left ventricular end-systolic pressure can be approximated by aortic dicrotic pressure. We have chosen aortic dicrotic pressure as “end-systolic” pressure since dicrotic pressure coincides with aortic valve closure (at which time left ventricular ejection is complete) and since it can be precisely identified in almost all subjects. The precise identification of end-systolic pressure using left ventricular pressure tracings alone is more difficult. Studies of left ventricular pressure-volume relations by Dodge and coworkers14 (their fig. 4), Mahler et al.9 (their figs. 2-5), Greene et al.16 (their figs. 3 and 7-9), and Suga and Sagawa\(^a\) (their figs. 3 and 4), indicate that peak left ventricular pressure is usually achieved close to the point of minimal left ventricular volume; that is, after most of the left ventricular stroke volume is ejected. In this regard, Wiggers points out that frequently “while aortic pressure is declining, the intraventricular pressure is rising” during late ejection\(^b\) (his fig. 2). Other investigators, studying left ventricular pressure-volume relations,17, 18 have found a left ventricular pressure plateau during ejection, such that peak and end-systolic pressure are nearly equal in magnitude although they occur at different points in time. For these reasons, we have also calculated end-systolic pressure-volume relations using peak left ventricular systolic pressure (tables 1 and 2, fig. 2).

4) It is assumed that left ventricular contractile state is not altered by the interventions utilized to vary systolic loading. In support of this last assumption are studies indicating that sodium nitroprusside, oral nitrates, and methoxamine have essentially no direct effect on myocardial contractility.19–25

The possibility of reflex changes in contractile state cannot be ruled out, but numerous studies indicate that such changes are negligible with the agents and afterload range used in this study, particularly if a steady state has been achieved.16–22, 26–28 In further support of this assumption is the fact that ventricular maximum dp/dt as determined from micromanometer tracings of left ventricular pressure in eight patients of the present study (patients 1, 2, 7, 8, 10, 14, 17 and 18 from table 1) showed no significant change with altered systolic loading (1778 ± 337 mm Hg/sec to 1595 ± 258 mm Hg/sec at the lower aortic pressure). The potential influence of ventriculography itself on left ventricular pressure and volume was previously examined by us. In subjects with either normal ventricular function or cardiomyopathy, a second ventriculogram, done at least 15 minutes after the first with no intervening drug administration, gave essentially identical left ventricular volumes and pressures.29

In the context of these assumptions, left ventricular end-systolic pressure-volume relations were characterized and the slope (\( m \)) and intercept (\( V_o \)) evaluated as indices of contractile state. In addition, left ventricular myocardial tensile force (\( F \)), wall tension (\( T \)) and circumference (\( C \)) were calculated from end-systolic pressure volume data utilizing formulae previously reported by others.26–28 Total tensile force was calculated as \( F = 1332P\pi R^2 \) where \( P \) is left ventricular pressure in mm Hg, \( R \) is the internal radius in centimeters calculated from the angiographic chamber volume and 1332 is the factor for converting mm Hg to dynes. Wall tension, or force per unit length of circumference (\( C = 2\pi R \)), was calculated at \( T, \) dynes/cm = \( F/C \). End systolic force-circumference and tension-circumference relations were characterized, and the slopes and intercepts evaluated in the same fashion as for the pressure-volume data.

Subjects in whom altered systolic loading was performed were divided into three groups based upon their resting left ventricular ejection fraction, and defined as having clearly normal left ventricular contractile function (group A, ejection fraction ≥ 0.60), intermediate left ventricular contractile function (group B, ejection fraction = 0.41–0.59), and poor left ventricular contractile function (group C, ejection fraction ≤ 0.40). In a fourth group of subjects (group D), the effect on left ventricular end-systolic pressure-volume relations of an inotropic stimulus produced by post-extrasystolic potentiation was examined. For these subjects \( m \) and \( V_o \) could not be determined since only one value of end-systolic pressure and volume is available at each contractile state. Accordingly, the effect of this intervention was evaluated in terms of direction and displacement of the end-systolic pressure-volume points.

Results

The diagnoses, heart rates, left ventricular volumes, pressures and ejection fractions, and aortic pressures are listed for each subject in table 1. It is evident that in each subject left ventricular end-systolic volume, end-diastolic volume and end-diastolic pressure were significantly lower at lower levels of systolic load. Average values for end-systolic volume and pressure (using dicrotic pressure) at both levels of systolic load are plotted for groups A, B and C in figure 1.
TABLE 1. Effects of Altered Systolic Loading and Inotropic Stimulation on Left Ventricular End-Systolic Pressure-Volume Relations

<table>
<thead>
<tr>
<th>Patient</th>
<th>Dx</th>
<th>Intervention</th>
<th>Heart rate (beats/min)</th>
<th>Left ventricular volume (cc/m²)</th>
<th>Ejection fraction</th>
<th>Left ventricular pressure (mm Hg)</th>
<th>Aortic pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>a/b</td>
<td>End-systolic b/a</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>MR</td>
<td>NTP</td>
<td>80/81</td>
<td>73/68</td>
<td>220/207</td>
<td>0.67/0.67</td>
<td>140/124</td>
</tr>
<tr>
<td>2</td>
<td>MR</td>
<td>NTP</td>
<td>84/84</td>
<td>61/57</td>
<td>166/172</td>
<td>0.70/0.70</td>
<td>125/102</td>
</tr>
<tr>
<td>3</td>
<td>MR</td>
<td>NTP</td>
<td>74/67</td>
<td>47/43</td>
<td>157/160</td>
<td>0.70/0.70</td>
<td>125/102</td>
</tr>
<tr>
<td>4</td>
<td>MR</td>
<td>NTP</td>
<td>60/60</td>
<td>51/46</td>
<td>166/172</td>
<td>0.70/0.70</td>
<td>125/102</td>
</tr>
<tr>
<td>5</td>
<td>MR</td>
<td>ETN</td>
<td>83/103</td>
<td>33/23</td>
<td>140/98</td>
<td>0.75/0.77</td>
<td>155/120</td>
</tr>
<tr>
<td>6</td>
<td>MR</td>
<td>ETN</td>
<td>96/90</td>
<td>71/63</td>
<td>201/161</td>
<td>0.65/0.61</td>
<td>130/135</td>
</tr>
<tr>
<td>7</td>
<td>CPNC</td>
<td>HBP</td>
<td>81/85</td>
<td>29/27</td>
<td>78/73</td>
<td>0.63/0.63</td>
<td>26/11</td>
</tr>
<tr>
<td>8</td>
<td>CPNC</td>
<td>Mx</td>
<td>78/78</td>
<td>42/36</td>
<td>117/99</td>
<td>0.64/0.63</td>
<td>180/146</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>80/81</td>
<td>51/46</td>
<td>156/136</td>
<td>0.69/0.69</td>
<td>143/116</td>
</tr>
</tbody>
</table>

* and b represent data in two states. For Groups A, B, and C, the data represent higher and lower systolic pressure states, respectively. For Group D, "a" represents control and "b" postextrasystolic beats. Statistics represent paired t-testing of b values against a values for each column. NS = not statistically significant.

Abbreviations: MR = mitral regurgitation; CPNC = chest pain, normal coronaries; AR = aortic regurgitation; HBP = high blood pressure; PVC = premature ventricular contraction; NTP = nitroprusside; ETN = etrithyl tetranitrate; Mx = methoxamine; Isor = isoradil; PVC = premature ventricular contraction; errors = standard error of the mean.

As can be seen, the slope of the left ventricular end-systolic pressure-volume relation was relatively steep in subjects with normal contractile function (group A) but became progressively less steep with greater degrees of impairment in contractile function. The extrapolated V₀ is small (32 cc/m²) for the group with normal contractile function, and larger (46 cc/m² and 100 cc/m²) for the groups with intermediate and poor contractile function, respectively. Similar results are obtained if peak systolic left ventricular pressure is used as the ordinate, as seen in figure 2.

For each individual patient, the two values for end-systolic pressure and volume listed in table 1 were used to determine that patient's end-systolic pressure-volume line. The slope (m) and intercept (V₀) of each line is given in table

![Figure 1](image1.png)  
**Figure 1.** Average values for left ventricular end-systolic volume and pressure at two levels of systolic load are plotted for subjects with normal contractile function (group A, ejection fraction ≥ 0.60), intermediate function (group B, ejection fraction = 0.41-0.59), and poor contractile function (group C, ejection fraction ≤ 0.40). Points represent average values for pressure and volume from table 1, and brackets indicate standard errors of the means. Volumes are indexed by body surface area in square meters (m²).

![Figure 2](image2.png)  
**Figure 2.** Average values for left ventricular end-systolic volumes and peak systolic pressure at two levels of systolic loading for groups A, B, and C.
2, and mean values (± standard errors) of m and V₀ for each group are shown in figure 3. Statistical analysis of the difference between these group means (unpaired t-test) showed that although there are statistically significant differences for both m and V₀ between subjects with normal (group A) and depressed (group C) ejection fractions, considerable overlap of individual values exists. Control values (i.e., values prior to afterload manipulation) for end-systolic volume and pressure in groups A, B, and C are plotted in figure 4. Although in individual subjects end-systolic volume was a variable, dependent on the level of systolic loading at the instant of measurement, nevertheless it is clear from figure 4 that resting end-systolic volume alone closely reflected overall left ventricular contractile performance, as measured by the ejection fraction, in the subjects studied. This may in part be a reflection of the narrow range of end-systolic pressures which characterized the resting state in our subjects as is also seen in figure 4.

Values for left ventricular circumference, wall tension, and myocardial tensile force for each subject are given in table 3. As can be seen circumference was smaller at lower levels of tension and force for each subject in groups A, B, and C. Plots of the mean values for tension and force against circumference are shown in figures 5 and 6, respectively. In contrast to the findings with end-systolic pressure-volume relations (figs. 1 and 2), there was no progressive decrease in slope as ejection fraction declined. Substantial differences in C₀, the zero force or tension intercept, were observed among the groups. Of interest is the fact that C₀ calculated from force-circumference relations was nearly identical to C₀ calculated from tension-circumference relations.

The effect of post-extrasystolic potentiation was examined in the five subjects of group D, and results are presented in table 1 and figure 7. A substantial increase in left ventricular ejection fraction occurred (.38 ± .05 to .53 ± .08, P < 0.01) indicating an increase in inotropic state. As can be seen, the average end-systolic volume decreased without an associated change in end-systolic pressure. In the context of the end-systolic pressure-volume relationship found to apply to subjects in groups A, B, and C, this observation indicates movement to a higher contractile state and, presumably, a steeper end-systolic pressure-volume relationship (fig. 7).

**Discussion**

On the basis of animal studies, Mitchell and Wildenthal have stated that "observation of alterations in the end-
TABLE 3. Effects of Altered Systolic Loading and Inotropic Stimulation on Left Ventricular End-Systolic Circumference, Tension and Wall Force

<table>
<thead>
<tr>
<th>Patients</th>
<th>Normalized circumference (cm/m²)</th>
<th>Total tensile force (10⁶ dynes)</th>
<th>Wall tension (10⁹ dynes/cm)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>a/b</td>
<td>a/b</td>
<td>a/b</td>
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</tbody>
</table>

Group A

<table>
<thead>
<tr>
<th></th>
<th>16.3 / 15.9</th>
<th>26.9 / 17.7</th>
<th>16.6 / 11.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>2</td>
<td>13.4 / 12.9</td>
<td>17.2 / 11.8</td>
<td>12.8 / 9.1</td>
</tr>
<tr>
<td>3</td>
<td>14.0 / 13.6</td>
<td>18.5 / 12.4</td>
<td>13.1 / 9.1</td>
</tr>
<tr>
<td>4</td>
<td>14.4 / 14.0</td>
<td>24.4 / 17.2</td>
<td>16.9 / 12.2</td>
</tr>
<tr>
<td>5</td>
<td>12.5 / 11.1</td>
<td>18.9 / 11.7</td>
<td>15.1 / 10.6</td>
</tr>
<tr>
<td>6</td>
<td>16.1 / 15.5</td>
<td>31.7 / 25.5</td>
<td>19.7 / 16.4</td>
</tr>
<tr>
<td>7</td>
<td>12.0 / 11.7</td>
<td>22.8 / 15.2</td>
<td>19.0 / 13.0</td>
</tr>
<tr>
<td>8</td>
<td>13.5 / 12.9</td>
<td>25.3 / 17.9</td>
<td>18.7 / 13.9</td>
</tr>
</tbody>
</table>

Mean 14.0 / 13.5 23.2 / 16.2 16.5 / 11.9

P <0.005 <0.001 <0.001

Group B

<table>
<thead>
<tr>
<th></th>
<th>19.1 / 12.5</th>
<th>25.2 / 13.0</th>
<th>13.2 / 7.4</th>
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<tbody>
<tr>
<td>9</td>
<td>19.4 / 18.4</td>
<td>43.0 / 17.9</td>
<td>22.2 / 9.7</td>
</tr>
<tr>
<td>10</td>
<td>17.9 / 16.6</td>
<td>33.6 / 15.4</td>
<td>14.8 / 9.3</td>
</tr>
<tr>
<td>11</td>
<td>17.7 / 16.9</td>
<td>36.5 / 24.0</td>
<td>20.7 / 14.2</td>
</tr>
<tr>
<td>12</td>
<td>15.4 / 14.8</td>
<td>23.9 / 19.8</td>
<td>15.5 / 13.4</td>
</tr>
<tr>
<td>13</td>
<td>14.4 / 13.1</td>
<td>23.0 / 14.6</td>
<td>15.9 / 11.1</td>
</tr>
</tbody>
</table>

Mean 17.3 / 16.2 29.7 / 17.5 18.3 / 11.5

P <0.001 <0.001 <0.001

Group C

<table>
<thead>
<tr>
<th></th>
<th>21.6 / 20.8</th>
<th>44.9 / 28.6</th>
<th>20.8 / 13.7</th>
</tr>
</thead>
<tbody>
<tr>
<td>15</td>
<td>21.3 / 20.5</td>
<td>40.9 / 30.5</td>
<td>19.2 / 14.8</td>
</tr>
<tr>
<td>16</td>
<td>21.9 / 21.4</td>
<td>47.9 / 41.8</td>
<td>21.8 / 15.5</td>
</tr>
<tr>
<td>17</td>
<td>21.7 / 21.3</td>
<td>44.2 / 37.7</td>
<td>20.3 / 17.7</td>
</tr>
<tr>
<td>18</td>
<td>20.4 / 20.2</td>
<td>46.7 / 36.9</td>
<td>22.8 / 18.2</td>
</tr>
</tbody>
</table>

Mean 21.4 / 20.8 44.9 / 35.4 20.9 / 16.8

P <0.01 <0.005 <0.005

Group D

<table>
<thead>
<tr>
<th></th>
<th>12.9 / 11.8</th>
<th>19.7 / 16.3</th>
<th>15.3 / 13.8</th>
</tr>
</thead>
<tbody>
<tr>
<td>20</td>
<td>18.4 / 16.8</td>
<td>32.5 / 27.1</td>
<td>17.6 / 16.1</td>
</tr>
<tr>
<td>21</td>
<td>13.1 / 10.0</td>
<td>14.6 / 9.6</td>
<td>11.1 / 9.0</td>
</tr>
<tr>
<td>22</td>
<td>14.3 / 13.9</td>
<td>22.5 / 21.9</td>
<td>15.7 / 15.7</td>
</tr>
<tr>
<td>23</td>
<td>18.8 / 16.4</td>
<td>41.9 / 31.5</td>
<td>22.3 / 19.2</td>
</tr>
</tbody>
</table>

Mean 15.5 / 13.8 25.6 / 21.4 16.4 / 14.9

P <0.01 <0.025 <0.025

*p* Aortic mean pressure used in place of dicrotic pressure in calculation of end-systolic force and tension.

Systolic volume may provide a useful key for differentiating changes in the contractile state of the left ventricle from changes induced by the Frank-Starling mechanism. [1] The present study supports the validity of that statement, and demonstrates the use of this concept in man. Twenty years ago, Holt examined factors influencing the degree of left ventricular emptying in dogs and found that despite an experimental design that resulted in a wide range of preloads, there was a linear relation between the length of ventricular muscle at the end of systole and the force exerted by that muscle at end systole. [4] Monroe and French [5] studied left ventricular pressure-volume relationships in the isolated dog heart using an experimental design in which the systolic load was varied from the extreme of zero pressure change to zero volume change during systole. Maximum left ventricular

![Figure 5](image_url)

**FIGURE 5.** Average values for left ventricular end-systolic wall tension ($T_{es}$) and circumference ($C_{es}$) at two levels of systolic loading for groups A, B, and C. Circumference is normalized for body surface area in square meters (m²).

Stroke volumes were developed by isobaric contractions, and maximum peak systolic pressures occurred with isovolumic contractions. When the load was varied to allow both pressure and volume to change in systole, the end-systolic pressure-volume points that resulted fell on a straight line. Epinephrine and digitalis glycosides increased the slope of

![Figure 6](image_url)

**FIGURE 6.** Average values for left ventricular total tensile force ($F_{es}$) and circumference ($C_{es}$) at two levels of systolic loading for groups A, B, and C.
The effect of post-extrasystolic potentiation on left ventricular end-systolic pressure-volume relations in the five subjects of group D. Data from figure 1 for groups A and B are included for reference. For group D, the solid dot represents average end-systolic pressure and volume for the control beat while the arrowhead represents average values for the post-extrasystolic potentiated beat. End-systolic volume decreased substantially without an associated change in end-systolic pressure.

Figure 7. The effect of post-extrasystolic potentiation on left ventricular end-systolic pressure-volume relations in the five subjects of group D. Data from figure 1 for groups A and B are included for reference. For group D, the solid dot represents average end-systolic pressure and volume for the control beat while the arrowhead represents average values for the post-extrasystolic potentiated beat. End-systolic volume decreased substantially without an associated change in end-systolic pressure.

In the present study, steepness of the slope of the left ventricular end-systolic pressure-volume relation appeared to reflect left ventricular contractile state. Although the three lines of figure 1 tend to converge at lower end-systolic pressures, their intercepts at zero end-systolic pressure, $V_0$, are different. If $V_0$ may be thought of as the volume to which a given ventricle would contract if it were totally unloaded (i.e., zero pressure load resisting further ejection of blood at end systole), then it should reflect the theoretical maximum pumping capability of a given ventricle. Similarly, if $C_n$ may be thought of as the minimum length to which a circumferential myocardial fiber would contract if there were no force or tension resisting further shortening at end systole, then this theoretic quantity should reflect the max-

Figure 8. A schematic representation of the theoretical relationship of ventricular preload, afterload and contractility for isovolumic and ejecting beats. In the left panel, isovolumic ($A \rightarrow A'$, $B \rightarrow B'$) and ejecting ($B \rightarrow C \rightarrow A'$) pathways illustrate the identity of isovolumic and ejecting end-systolic pressure-volume relations. The effect of increased myocardial contractility (right panel) is to produce a higher pressure in isovolumic beats ($B \rightarrow B'$), and a smaller end-systolic volume in ejecting beats ($B \rightarrow C \rightarrow A'$). Note that the end-systolic volume $A''$ at the higher contractile state is independent of end-diastolic volume or preload, in that it is the final volume for ejecting beats originating from both the higher ($B \rightarrow C \rightarrow A' \rightarrow A''$) and lower ($A \rightarrow A' \rightarrow A''$) preloads.
imum shortening capability for the muscle composing the ventricular walls. \( V_0 \) and \( C_0 \) might then be considered the theoretic counterparts of \( P_0 \) and \( T_0 \), the maximum pressure and wall tension a ventricle can develop at zero shortening (isovolumic maximum, point \( B' \), fig. 8 left), with the exception that \( V_0 \) and \( C_0 \) should be independent of preload, while \( P_0 \) and \( T_0 \) are clearly influenced by preload.

From a practical viewpoint, it should be emphasized that there is considerable overlap of values for \( m \) and \( V_0 \) among the subjects in this study. It is of interest that end-systolic volume (or circumference) alone showed good discrimination of normal from poor contractile function as reflected in the ejection fraction (fig. 4). In this regard, it is worth noting that Mitchell and colleagues examined left ventricular volumes in the dog using biplane cinefluorography and found that at a constant inotropic state, the left ventricle appears always to return to the same end-systolic dimensions no matter what the end-diastolic dimensions.\(^{36}\) In Mitchell’s studies, end-systolic volume alone seemed to be independent of preload and sensitive to changes in inotropic states. In the present study, sensitivity of end-systolic volume to sudden changes in inotropic state was clearly demonstrated in response to post-extrasystolic potentiation (fig. 7). Recently Weisfeldt and co-workers\(^{38}\) have examined the relation between end-systolic pressure and volume in man, and have found it to be sensitive to the changes in inotropic state associated with post-extrasystolic potentiation. Their findings are similar to those observed in the present study for group D subjects.

Certain limitations of the present study must be emphasized. First, linearity of the end-systolic pressure-volume relation was assumed, since only two values of end-systolic pressure and volume were determined for each subject. To validate this assumption, at least three data points (and therefore at least three ventricular angiographic studies using the methodology described above) would be required for each subject. However, in support of the assumption of linearity are the careful studies of Monroe and French,\(^{38}\) Suga and Sagawa,\(^{38}\) and Weber et al.\(^{38, 41}\) in the isolated heart, and of Mahler and co-workers in the conscious animal.\(^{38}\) All of these investigators found precise linearity of end-systolic pressure-volume relations over the physiologic range.

A second limitation of this study is the assumption of constant inotropic state at the two levels of systolic loading for groups A, B and C. While there is no way to confirm or refute this assumption in the absence of a universally agreed upon index of myocardial contractility, the agents used to alter systolic load in this study have been previously shown to have minimal effects on various measures of myocardial contractility in isolated cardiac muscle,\(^{43}\) as well as intact animals and man.\(^{44-49}\) Clearly the possibility of centrally mediated reflex changes in contractility cannot be completely ruled out, but against any major reflex influences in our subjects are (a) the lack of significant changes in maximum \( dp/dt \) in the two states, and (b) the absence of any significant change in heart rate with the altered loading. Reflex adjustments, were they to occur, might be expected to increase inotropic state at the lower arterial pressure, due to baroreceptor mediated sympathetic activity. This would have the effect of shifting the lower point of each line in figures 1 and 2 to the left (smaller end-systolic volume at any given end-systolic pressure). This in turn would give lower values for \( m \) and \( V_0 \) than would be the case at constant inotropic state. Further studies utilizing adrenergic blockade will be needed to clarify this point.

Third, it must be acknowledged that end-systolic volume may be difficult to measure with accuracy because of infolding of the trabeculae carnae, and because of problems in tracing the blood-muscle border in ventricular hypertrophy secondary to a pressure overload. It is not possible to quantify the magnitude of the error here, but studies in our laboratory using left ventricular casts from postmortem specimens indicate that it may become appreciable when the chamber volume is less than 30 cc.

It might well be asked what advantage, if any, is offered by end-systolic pressure-volume analysis as an approach to the assessment of left ventricular inotropic state. Since this study did not attempt a comparison between end-systolic pressure-volume analysis and other more widely utilized approaches to the assessment of contractility, we cannot definitively answer this question. However, there are at least three theoretic advantages of end-systolic pressure-volume analysis as an approach to the assessment of myocardial contractility. First, the relation has been shown to be preload independent,\(^{38, 39}\) aiding differentiation from changes in ventricular performance mediated by the Frank-Starling mechanism. This gives the end-systolic pressure-volume relation approach a distinct advantage over ejection fraction, which Mitchell and co-workers have shown to be affected by end-diastolic volume.\(^{40}\) Second, the analysis is independent of any assumptions concerning muscle models and the arrangement of contractile, elastic, and viscous components. This, of course, has been a major problem with regard to the interpretation of the so-called “isovolumic indices.”\(^{50, 51}\) Third, afterload is incorporated into the analysis, so that changes observed assess contractility rather than the usual mixed changes of contractility and afterload. In contrast, so-called “ejection phase indices” of contractility (e.g., velocity of circumferential fiber shortening, ejection fraction, systolic ejection rate) may be substantially altered by varying afterload, without any change in contractile state.\(^{40}\) As pointed out earlier, end-systolic volume alone separated patients with differing degrees of left ventricular dysfunction in this study. This may, however, be more a fortuitous reflection of similar levels of systolic loading (fig. 4) in the various groups studied. Use of the end-systolic pressure-volume relationship should still give valid assessment of ventricular contractile state even if wide swings in aortic pressure occurred at the time of study.

In conclusion, this study has examined left ventricular end-systolic pressure-volume and tension-circumference relations in man, with particular attention to the effects of altered systolic loading and post-extrasystolic potentiation. The results are consistent with animal studies performed under a variety of experimental conditions,\(^{42-44}\) and support the potential usefulness of the end-systolic pressure-volume relationship as an index of myocardial contractile state in man.

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