A Force-Length-Time Relationship Describes the Mechanics of Canine Left Ventricular Wall Segments during Auxotonic Contractions

Hroar Piene and James W. Covell

SUMMARY We examined regional mechanics of the left ventricular free wall in naturally pumping dog hearts during β-blockade. Local systolic wall force (F) and segment length (L) were obtained with an auxotonic force gauge and an ultrasonic dimension gauge, both inserted at the equatorial level of the wall to measure F and L in the circumferential direction. Shortening velocity (−dL/dt) was obtained by differentiation of L. Preload and afterload were changed by acute caval and/or aortic occlusion so that a wide variation in F, L, −dL/dt, and dF/dt during shortening was obtained. In all experiments, F vs. L at identical time (t) after end-diastole (ED) fell on well-defined lines, irrespective of the −dL/dt values. Control F (at t = 200 ms) over the 0.5-cm wide gauge was 85.5 ± 11.5 g, and slope of the F vs. L line (τ = 200 ms) was equivalent to a drop of approximately 50% in F at 10% reduction in L. No defined relationship was observed between F, L, −dL/dt, and dF/dt values. However, by superimposing F, L, and −dL/dt curves from contractions of high EDL and high −dL/dt on those from contractions of low EDL and low −dL/dt, and comparing F and −dL/dt at identical L and t, a slightly lower F (difference 2.23 ± 1.09 g, P < 0.05) could be associated with the higher −dL/dt (difference 0.6 ± 0.1 muscle length/sec, P < 0.001). These data suggest that the F-L-t relationship is a valid descriptor of auxotonic contractions in the ventricular wall, and that the direct effect of shortening velocity on the wall force is modest.

The main body of knowledge about myocardial muscle mechanics stems from experiments with well-defined loading conditions, i.e., isotonic afterloads, produced in isolated preparations or even in the ventricular wall (Burns et al., 1973). In general, such studies convey the impression that there exists a well-defined relationship between instantaneous force, velocity, and length (Sonnenblick, 1965; Brutsaert et al., 1971; Burns et al., 1973). In the ventricular wall, however, contractions are normally not isotonic but auxotonic; i.e., the force changes continuously during the period of shortening as a reflection of the ongoing alterations in ventricular pressure and ventricular shape. The possibility exists that the simple picture of a unique force-velocity-length relationship is not valid under these more realistic circumstances, a notion which is supported by recent experiments on papillary muscle subject to physiological loading (Paulus et al., 1976). It is also likely that direct observations on instantaneous force, length, and shortening velocity in the ventricular wall may display a picture different from that obtained by the isolated fiber studies in view of the complicated structure of interweaving fibers encountered in the wall.

For these reasons, the present examination of the relationship between directly obtained regional wall force, dimension, and shortening velocity was undertaken. Dogs were anesthetized, artificially ventilated, and their chests opened. The left ventricular wall force and segment length were obtained over a broad range, and variations in these variables were accomplished by acute occlusions of the inferior vena cava or the aorta. For the wall segment length measurement, we employed an ultrasonic dimension gauge and for wall force determination an auxotonic force gauge (Feigl et al., 1967). The latter gauge underwent a series of tests in order to establish its applicability for the present purpose. Both gauges were inserted in the same wall region to obtain measurements valid for the same segment and direction, i.e., in the circumferential fiber direction at the equatorial level of the free left ventricular wall.

Methods

Animal Preparation

Eight male mongrel dogs (18–28 kg) were anesthetized (pentobarbital, 30 mg/kg, iv), and their hearts were exposed by combined mid-sternal and...
left 4th interthoracic space incisions during ventilation maintained with O2-enriched air at positive pressure. The pericardium was split and the heart suspended in a pericardial cradle. The preparation is shown schematically in Figure 1. Foley catheters (size 12 or 14) were advanced into the inferior vena cava (IVC) and into the aorta through the left brachiocephalic artery. By inflating the rubber balloons of the catheters, the IVC or aorta was occluded. Aortic pressure was obtained with a catheter inserted through the left carotid artery, and left ventricular pressure with a wide-bore steel cannula inserted into the ventricle through an incision at the apex. The fluid-filled catheter and steel cannula were connected to Statham P23Db pressure transducers. An auxotonic force gauge (Feigl et al., 1967) was positioned in the left ventricular wall at the equatorial level for measurement of total wall force in the direction of the circumferential fibers. Force was measured between two sets of three parallel pins which penetrated the wall completely. The pin array width was 0.5 cm and the interpin distance 2-3 mm in the operating gauge. The gauge compliance was 7-10^-4 mm/g. The procedure followed when inserting the gauge and approximating the two sets of pins to relax the muscle segment between them was according to the method of Burns et al. (1971).

A pair of ultrasonic dimension gauge crystals was inserted immediately adjacent to the force gauge to measure segment length changes in the same area and direction as the force measurement. The sound transit time between the two crystals was converted to segment length by assuming a sound velocity of 1.55 mm/μsec. The segment length signal was electronically differentiated with respect to time (RC filter) to obtain segment shortening velocity. Some degree of damping (3 dB down at 80 Hz) was necessary to avoid excessive noise in the signal. However, it introduced a time lag of 10-15 μsec in the differentiated signal compared to the original.

In two experiments, an additional pair of ultrasonic crystals was positioned on the inner ventricular wall at diametrically opposite points at the equatorial level for determination of the ventricular inner minor axis. These registrations were taken for comparison between in situ force measured with the gauge and force calculated from pressure and diameter according to an ellipsoid ventricular model.

Prior to experiments, the dogs were given propranolol (1 mg/kg) to prevent changes in contractility due to sympathetic reflexes evoked by the acute caval or aortic occlusions. In four experiments the hearts were electrically paced after the SA node had been crushed. A standard ECG was recorded in all experiments.

**Experimental Protocol and Data Analysis**

The experimental procedure is illustrated by the typical tracings of aortic and ventricular pressures, force (F), segment length (L) and shortening velocity (−dL/dt) shown in Figure 2, A and B. After a control period (left part of Fig. 2A and left panel of Fig. 2B), the IVC balloon was inflated (IVC occl. in Fig. 2A), and this resulted in lower end-diastolic (ED) L, lower peak F, and lower −dL/dt in the ejection period (second panel of Fig. 2B). The aortic balloon was then inflated (Ao. occl. in Fig. 2A) and the IVC occlusion released; this caused increased EDL and increased systolic F at continued low −dL/dt (panel 3 of Fig. 2B). When the aortic occlusion was released at a high EDL, high −dL/dt was produced at high levels of systolic F (panel 4 of Fig. 2B). Typical time courses of IVC and aortic occlusions and a total experimental run are shown in Figure 2A.

Great care was taken to exclude the possibility that cardiac contractility changed during the experimental runs. Contractility could in theory have been altered by two main factors: (1) sympathetic reflexes evoked by pressure alterations in the aorta arch and the carotids and (2) homeometric autoregulation ("Anrep" effect) due to alterations in ventricular pressure and wall stress development. To the first point, we systematically varied the position of the aortic balloon between the aortic root and the descending aorta. Sympathetic reflexes would then have been influenced in opposite directions, and, if they were pronounced, would have influenced the obtained relationships between F, L, and −dL/dt in different ways. However, the relationships between these variables were independent of the position of the aortic balloon, and we take this as (indirect) evidence for the non-importance of
sympathetic reflexes in these experiments. To the second point, the time periods of high or low ventricular pressure were made as short as the presently employed technique permitted, in order to limit development of homeometric autoregulation or its negative equivalent. After an experimental run, the recorded variables returned to the control levels within a short period of time (Fig. 2A), indicating that the load variations had no long-term effects on the basal circulatory state of the experimental animal.

The relationship between $F$, $L$, time after end-diastole ($t$), and $-dL/dt$ was examined by manually picking values from high-speed (100 mm/sec) paper chart pen recordings (Brush Clevite Instruments, model 2000). The load changes were repeated a number of times in each experiment in order to obtain a series of differently loaded beats without distributing influence from arrhythmias, which were easily evoked by the occlusions. For direct comparison of $F$ and $-dL/dt$ values at identical $L$ and $t$, curves of these variables were drawn on transparent paper with a sharp pencil and superimposed.

Evaluation and Calibration of the Force Gauge

Direct calibration of the force gauge sensitivity in terms of mV per gram applied force was obtained by hanging calibrated weights from the gauge pins. The frequency response of the gauge was tested by a sudden release of the weight, thus obtaining its step response. The gauge sensitivity was found to be linear over 0-500 g, and the rise time for a step response was less than 1/200 sec at 90% of peak deflection. The in situ sensitivity of the force gauge was tested regularly in a strip of dead muscle cut from the heart at the end of experiments, and in two hearts by comparing the force directly obtained by the gauge with the calculated wall force according to pressure and diameter. By the first method (Burns et al., 1971), the relationship between applied weight and measured force was linear and "coupling factors" (i.e., measured force divided by calculated applied force according to the width of the gauge and the width of the muscle strip) ranged from 0.5 to 3 with median at 1.3. Following the analysis of Huisman (1977), this way of calibrating...
the gauge, in a piece of stretched, dead muscle, poorly reflect the situation in actively contracting muscle, and this method therefore was abandoned as a way of obtaining "true force." By the other method, recorded force was compared to calculated active force according to an often-used formula derived on basis of a thick-walled ellipsoid (Burns et al., 1971):

$$\text{force} = \text{gauge width} \cdot P \cdot B \cdot (1 - B^2/2A^2)$$

where \(P\) = ventricular pressure, \(B\) = minor hemi-axis obtained by ultrasonic crystals on the inner wall, and \(A\) = major hemi-axis measured as the distance from the gauge to apex in the excised heart. By taking values of \(P\) and \(B\) at peak \(P\) over a wide range of loading conditions, a linear relationship between measured force (in mV) and calculated force was obtained. Moreover, the slope of this line was close to the ideal 1:1 relationship between calculated force and observed force when the mV signal from the gauge was converted to force according to the directly observed gauge mV/g sensitivity, as demonstrated in Figure 3A. As a further test of the linearity of the relationship between true force and measured force, plots of pressure vs. force for isovolumic contractions were obtained, and these were linear for pressures above 25 mm Hg but slightly curved below this level. (This observation does not necessarily indicate a nonlinear relationship between actual and measured force; it may equally well be explained by change in ventricular wall configuration in early systole.)

Shortening of the tissue surrounding the gauge tends to narrow the gap between the gauge pins and thus to reduce the measured force even without any reduction in the true force. This effect may introduce a major systematic error in the force-length relationship obtained. The occurrence of such error is difficult to assess in the heart wall, but it may be tested in an isotonically loaded skeletal muscle preparation. In three dogs, the gracilis muscle was dissected free and loaded by a constant weight suspended from the muscle which was cut distally. The muscle was electrically stimulated via the nerve and the load chosen so as to achieve a total shortening of about 50% at tetanic contraction. These precautions were taken: (1) the gauge was inserted during tetanus and the pins approximated as much as possible (from 6 to 2 mm) to obtain efficient relaxation of the muscle between the pins; (2) part of the muscle lateral to the gauge was trimmed away to obtain uniform load in the region of force measurement (the final muscle strip was 3-5 cm wide). We then could observe no difference between measured force in unstimulated and stimulated (and shortened) isotonically loaded muscle. This is demonstrated in Figure 3B, which shows measured force (in mV) for the conditions of no load, loaded and unstimulated, stimulated at 1 Hz, vs. stimulated at 20 Hz (tetanic). This study indicated that the effect of shortening on measured force is minimal, which is the opposite finding of Huisman et al. (1977, 1980) in similar experiments. They found that measured force could drop substantially and even reverse sign during isotonically contractions. In a preliminary experiment when the gauge was inserted in stretched and unstimulated muscle, we obtained the same result as Huisman. We hypothesized that this could be due to the skeletal muscle being stretched far beyond \(L_{\text{max}}\) (length at maximum active tension) by the manipulation necessary when inserting the gauge. If this were so, subsequent approximation of the gauge pins most likely would tend to increase rather than decrease the force developed by the muscle segment between the pins, which must be functionally inactive in order to measure true muscle force with the gauge. By inserting the gauge in tetanized unloaded muscle this artifact apparently was avoided. The same precaution should not be necessary in cardiac muscle because the diastolic compliance in the my-
occardium is small in the region of $L_{\max}$. In this muscle, the segment between the pins is probably efficiently inactivated by reducing the pin distance from normally 6 mm during insertion to 2-2.5 mm under operation. When the pins were screwed together by the adjustment screw (shown as the horizontal screw in Fig. 1), a small, sometimes inverted or zero, signal was obtained at a long pin distance and the signal changed to a maximum positive deflection at a small pin distance. As described in Burns et al. (1971), recorded force vs. pin distance displays a plateau at which effective relaxation of the segment between the pins is assumed to have occurred.

From these tests we concluded that the gauge signal reliably reflects the force development in the ventricular wall, and we chose to calibrate the signal in terms of $g/mV$ according to the calibration line obtained by hanging weights from the gauge pins. The above considerations and conclusions are harmony with those of McHale and Greenfield (1973).

Results

Force-Length-Time Relationship

Force (F) and length (L) values were sampled at fixed points of time (t) over beats representing the control situation (no occlusions), reduced filling (caval occlusion), reduced filling and low stroke volume (aortic occlusion after caval occlusion), and increased filling with high stroke volume (release of caval and aortic occlusions). In all experiments the R-wave of the lead II ECG signal served as the time reference point.

Typical results from one experiment are shown on Figure 4, in which case the experiment was stored on magnetic tape, and force-length data were sampled during playback at 5-msec intervals by means of a computer system. Isochronic F-L relationships are shown at $t = 75, 125, 175$ msec. Apparently, all F-L datapoints fall closely on single lines. Analysis of line slopes revealed that lines of 20-msec time difference were statistically different at the 5% level ($t$-test) in the early part of systole ($t = 50-100$ msec). For the experiment of Figure 4 the slopes of isochrons are collected in Table 1 along with the correlation factors for the simple linear regression of F on L. These data demonstrate, in analogy with pressure-volume-time data for the whole ventricle (Suga and Sagawa, 1974; Suga et al., 1973), rapid increase of the slope of the F-L isochrons with time in the early part of the systole and thereafter a gradually diminishing rate of change in slope until a maximum is reached.

In other experiments, F and L data were sampled manually at $t = 100, 200, and, occasionally, at 300 msec if this point of time fell within systole. These data are collected in Figure 5, which shows one panel from each dog. In all dogs we obtained the picture of a well-defined F-L-t relationship describing the wall segment mechanics. Peak F for control beats (no occlusions) and F-L isochronic slopes at 200 msec from all dogs are collected in Table 2. These data showed substantial variation between the dogs, most probably reflecting different heart shapes. The position of the aortic balloon, which was in either the ascending or the descending aorta, was not found to have any influence on the obtained data. It is thus unlikely that sympathetic reflexes, which would have been evoked differently, played any part in these experiments.

Table 1

<table>
<thead>
<tr>
<th>Isochronic (msec)</th>
<th>A (g)</th>
<th>B (g/mm)</th>
<th>$R^2$</th>
<th>P</th>
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<tr>
<td>25</td>
<td>-262.91</td>
<td>45.84</td>
<td>0.956</td>
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<td>0.993</td>
<td>&lt;0.01</td>
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<tr>
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<td>65.77</td>
<td>0.998</td>
<td>&lt;0.01</td>
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<tr>
<td>225</td>
<td>-341.28</td>
<td>63.33</td>
<td>0.890</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Equation: $F = A + B \times L$
FORCE-LENGTH-TIME RELATIONSHIP IN VENTRICULAR WALL/Piene & Covell

![Graphs showing force-length-time relationship in ventricular wall](image)

**Table 2** Wall Force ($F^*$) at Midsystole ($t = 175$ msec) for Control Contractions; Slope of $F$ vs. $L$ Relationship at $t = 200$ msec; Heart Rate (HR) and End-Diastolic Pressure (EDP) at the Above Measurements

<table>
<thead>
<tr>
<th>Experiment</th>
<th>$F$ (g/cm)</th>
<th>Slope of $F$ vs. $L$ (g/cm per mm)</th>
<th>Heart rate (beats/min)</th>
<th>EDP (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/9/79</td>
<td>60.6</td>
<td>73.5</td>
<td>107</td>
<td>3</td>
</tr>
<tr>
<td>10/19/79</td>
<td>96</td>
<td>14.5</td>
<td>108</td>
<td>5</td>
</tr>
<tr>
<td>10/26/79</td>
<td>153</td>
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<td>125</td>
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<td>11/2/79</td>
<td>96</td>
<td>80.5</td>
<td>117</td>
<td>2.5</td>
</tr>
<tr>
<td>11/9/79</td>
<td>33.5</td>
<td>29.8</td>
<td>115</td>
<td>5.5</td>
</tr>
<tr>
<td>11/26/79</td>
<td>84</td>
<td>48.6</td>
<td>107</td>
<td>9</td>
</tr>
<tr>
<td>1/10/80</td>
<td>94.5</td>
<td>66.8</td>
<td>133</td>
<td>4</td>
</tr>
<tr>
<td>1/17/80</td>
<td>86.5</td>
<td>46.4</td>
<td>112</td>
<td>5</td>
</tr>
</tbody>
</table>

Mean $85.9 \pm 6.5^\pm$ $8^E$ $11.7 \pm 8.3$

* $F$ is the value directly converted from mV to g according to the in vitro gauge calibration (see Methods). The gauge width was 0.5 cm in all experiments.

On the average, control $F$ at 200 msec was $85.5 \pm 11.5$ g (mean $\pm SE$). Assuming wall thickness to be 1.2 cm and using the value 0.5 cm for the gauge width, the estimated area of $F$ measurement was 0.6 cm². Hence, the above value of $F$ is equivalent with an average wall stress value of $142.5$ g/cm², which is in good agreement with the expected value calculated from ventricular pressure and heart shape (Burns et al., 1971). The slope of the F-L line at $t = 200$ msec was $54.5 \pm 8$ g per mm segment length change. As the average distance between the ultrasonic crystals was 8 mm, this value indicated an approximately 50% force drop at 10% shortening of the muscle. This accords well with the end-systolic force-length relationship for non-excised papillary muscle (Suga et al., 1977; according to their Figure 3A, a change in length from 13 to 12 mm would cause end-systolic force to drop from 50 to 25 g in their preparation).

When delineating the F-L relationship above, $-\frac{dL}{dt}$ was not taken into consideration. In Figure 6, upper panel, the F-L relationship at 175 msec is shown as filled circles and $-\frac{dL}{dt}$ is plotted as the height of the vertical bar connected with each F-L datapoint. Each point represents one beat of the series of differently loaded beats in one experimental run. It appears from this graph that the F-L relationship is well defined despite considerable variation of $-\frac{dL}{dt}$ between the points on the graph. Note in particular the points marked by arrows in the figure; the F and L values are almost identical despite considerable difference in $-\frac{dL}{dt}$. To show that this was a consistent finding irrespective of t, the lower panel of Figure 6 shows F vs. $t$ values at identical L over the series of differently loaded beats in the same experiment as shown in the upper panel. It appears that F was almost uninfluenced by the $-\frac{dL}{dt}$ value over the period of shortening.

![Graphs showing force-length vs. time](image)
**Figure 6** Force (F) vs. segment length (L) at constant t (175 msec) with actual shortening velocity (−dL/dt) shown as the height of a vertical bar connected with each datapoint, top panel. The arrows mark two contractions of almost identical L and F but with markedly different levels of −dL/dt. The lower panel shows values of F vs. t at identical L = 8.7 mm. −dL/dt values are again displayed as the height of the vertical bars. Note the well-defined positions of the datapoints in spite of the differences in −dL/dt.

**Force vs. Velocity of Shortening**

By superimposing curves of L, −dL/dt, and F obtained during two different loading conditions, we could obtain an estimate of the influence of −dL/dt on F. This is illustrated in Figure 7. For one of the beats shown, EDL was high and the aorta was not occluded, thus permitting high −dL/dt. For the other beat, the IVC and aorta both were occluded, resulting in low EDL and low −dL/dt. The objective of imposing these differences in the load was to obtain beats with identical L at some t in the interval of shortening (t = 100–200 msec), but with widely different values of −dL/dt. In Figure 7, t at identical L (crossing L curves) is denoted tL. In all cases in which the L tracings showed such a cross-over point, the F tracings also showed a similar cross-over, as shown in the same figure. The t at identical (crossing) F is denoted tF in Figure 7. The influence of −dL/dt on F then could be evaluated in two ways: (1) by examining tL and tF (if these were equal, this would mean that −dL/dt had no detectable influence on F); (2) when tL and tF were unequal, the difference in F at tL could be related to the simultaneous difference in −dL/dt. These data are collected in Table 3. There was no significant difference in tL and tF when all data (n = 15) were taken together (F = 0.21, Student’s t-test for paired comparison). At tL, the difference in F was hardly significant (2.23 g, P = 0.061). The direction of F difference was such that the higher −dL/dt was associated with lower F in most—but not in all—cases. The average difference in −dL/dt at tL was 4.68 mm/sec (P < 0.001), which was approximately 0.6 muscle length/sec. As the F level at tL was 75 g on the average, this difference in velocity was thus associated with a drop of approximately 3% in F. Included in Table 3 are data on dF/dt at tL. In all cases, the higher velocity was associated with a more negative dF/dt. For beats with low values of peak −dL/dt, dF/dt during shortening generally was found to take on a positive value (Fig. 7 and Fig. 2, panel 2). The difference in dF/dt at tL between the compared pairs of beats was highly significant (P < 0.001).

The above data indicate that velocity of shortening was not defined by force and length alone. To substantiate this further, plots of −dL/dt vs. L ("phase-plane" plots) for pairs of contractions that had identical time positions for L and F cross-over points (tL = tF) were produced. An example is shown in Figure 8. The left panel demonstrates the obtained F, L, and −dL/dt tracings; the F and L values were pairwise identical at t = 150 msec in this case. The right panel shows the two plots of −dL/dt vs. L for the period of muscle shortening. The plots are widely separated, in spite of having identical L and F at t = 150 msec (marked by arrows).
**Discussion**

The results of the present study demonstrate that the force development within a left ventricular wall segment can be described by a force-length-time relationship in analogy with the findings that the mechanics of the whole ventricle can be described by a pressure-volume-time relationship (Sa-gawa, review, 1978). It is intuitively reasonable that such analogy exists because ventricular pressure can be considered as being the overall result of wall tension in the various wall segments and the ventricular volume as being defined by wall geometry. Brady (1974) has suggested a tension-length-time relationship for the analytical description of an idealized myocardial fiber, and he has shown that the more conventional force-velocity relationship at isotonic afterloads will follow from this concept. According to his analysis, the force-length-time relationship can be transformed to a force-velocity-length relationship provided \( \frac{dF}{dt} = 0 \). The now almost classic experiments of Sonnenblick (1965) may convey the impression that, given a contractile state, a unique force-velocity-length relationship is valid under all loading conditions, a notion which seems strongly supported by others (Brutsaert et al., 1971). The present study indicates that that analysis no longer holds when one considers auxotonic contractions or, more specifically, contractions with neither constant nor zero \( \frac{dF}{dt} \). If one extends the analysis of the force-length-time relationship of Brady (1974) to include a varying \( \frac{dF}{dt} \), the same conclusion would be reached.

Still, a study of Weber and Janicki (1977) on isolated volume controlled dog hearts indicates that the ventricular contraction and its contractile state may be characterized uniquely by the relationship between calculated values of instantaneous force, velocity, and length, which is not the conclusion of the present study. The load variations imposed on the ventricle in that study were probably different from ours, however, since ours produced differences in both \( F \) and \( \frac{dF}{dt} \) between differently loaded ventricular contractions. Such variations are necessary in order to demonstrate clearly that the force-velocity-length relationship is not unique. Also in their data there is some evidence for this notion, as their Figure 4 (Weber and Janicki, 1977) shows pairs of contractions displaying at some instant identical force and length but different velocities. Two studies from Brutsaert's group demonstrate, as well, deviations from the claimed unique force-velocity-length relationship: a study of force and length relations at constant velocity (Brutsaert et al., 1972) demonstrates clearly that contractions under these conditions and contractions at isotonic afterload cannot be described by the same force-velocity-length relationship. More recent experiments, in which papillary muscle was subjected to physiological (auxotonic) loads (Paulus et al., 1976), showed that the relationship between instantaneous velocity, force, and length at increasing force deviated from that obtained at isotonic afterloads. It seems reasonable to conclude, therefore, from the evidence of the present study and the above citations, that the force-velocity-length relationship is dependent on the character of the load and thus cannot be used as a descriptor for either the wall mechanics or the contractility. On the other hand, the force-length-time framework, as presented in this study, seems to offer a comprehensive description of the mechanics of the wall segment, and the data indicate that its sensitivity to other variables, specifically the shortening velocity, is slight.

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**Table 3** Superposition of Contractions of Either High EDL and High \(-\frac{dL}{dt}\) or Low EDL and Low \(-\frac{dL}{dt}\) gave Identical \(L\) at \(t_f\), and Identical \(F\) at \(t_f\) (see Fig. 7)

<table>
<thead>
<tr>
<th>Experiment</th>
<th>(t_c) (sec)</th>
<th>(t_f) (sec)</th>
<th>(\Delta(-\frac{dL}{dt})) (m/m/sec)</th>
<th>(\Delta F) (g)</th>
<th>(\Delta(\frac{dF}{dt})) (g/sec)</th>
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<tr>
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<td>9.0</td>
<td>0</td>
<td>-1</td>
<td>-130</td>
</tr>
<tr>
<td>Mean</td>
<td>0.173</td>
<td>0.165</td>
<td>4.58</td>
<td>-2.23</td>
<td>-177</td>
</tr>
<tr>
<td>± SE</td>
<td>0.0094</td>
<td>0.0094</td>
<td>0.93</td>
<td>1.09</td>
<td>22</td>
</tr>
</tbody>
</table>

At \(t_c\), \(-\frac{dL}{dt}\) differed by \(\Delta(-\frac{dL}{dt})\), \(F\) differed by \(\Delta F\) and \(\frac{dF}{dt}\) differed by \(\Delta(\frac{dF}{dt})\).

**Figure 8** A pair of differently loaded contractions with identical \(F\) at identical \(L\) and \(t\) were compared in the \(-\frac{dL}{dt}\) vs. \(L\) projection ("phase-plane" plot), right panel. Note that the \(-\frac{dL}{dt}\) vs. \(L\) curves do not cross or coincide in spite of identical \(F\) and \(L\) at one instant (marked by the arrows).
The question still remains as to whether there exists a weak $-\Delta L/\Delta t$ dependence on $F$, in the sense that $-\Delta L/\Delta t$ influences developed $F$ at any given $L$ and $t$. In our experiments, this was analyzed in part by examining the velocity-related scatter of data around the observed $F$-$L$ line at a specific $t$ or the $F$-$t$ curve at specific $L$ (Fig. 6). As is evident from this figure, the influence was very modest and its presence could not be verified statistically by such graphs in any heart studied in the present series of experiments.

Data concerning isolated papillary muscle analyzed in a similar fashion were recently published and showed a significant reduction in developed tension with increasing shortening velocity (Leach et al., 1980). According to those data, fiber tension would drop below 50% of the value predicted by the force-length-time relationship established from isometric contractions when shortening velocity was 1 muscle length/sec or above. If those results are confirmed in experiments where the dead ends of the isolated papillary muscle cannot influence the results, they may point to a functional difference between papillary and ventricular wall muscle, as a velocity dependency of that magnitude should have been clearly evident in our experiments. By comparing more directly pairs of contractions of different preloads and afterloads yielding identical $L$ at certain $t$, we were able to assess a weak dependency between $P$-reduction and $-\Delta L/\Delta t$. The value obtained, 3% reduction in $P$ at $t$ around midsystole for 0.6 muscle length/sec of shortening velocity, is far smaller than the force-velocity dependency cited above. Also, recent experiments on isolated papillary muscles contracting as if they were part of the ventricular wall indicate that the end-systolic pressure-volume relation estimated from muscle $P$-$L$ data is dependent on the character of the afterload system, i.e., whether the load was changed by simulated variations in aortic compliance or peripheral resistance (Paulus et al., 1980). This may indicate that the isolated papillary muscle is not a good model with which to study the mechanics of the ventricular wall, as parallel observations are not seen in the intact heart, at least not in the right ventricle (Piene and Sund, 1980).

In recent experiments with an isolated dog heart preparation, Suga et al. (1980) have extended their pressure-volume-time data (for review see Sagawa, 1978) to include the influence of flow, and have reported the following relationship between ventricular pressure (normalized to 100) and flow: \[ \%P = 98 - 0.23 \times (-\Delta V/\Delta t) \] (Eq. 1 in their Table 2). Assuming cylindrical ventricular geometry and a ventricular volume at midsystole of 25 ml, a difference in velocity of shortening in the hoop fibers of 0.6 muscle length/sec between two contractions would be equivalent to a difference in flow of 30 ml/sec which, according to the above equation, would lead to a pressure drop of $0.23 \times 30 = 6.9\%$. This value is somewhat greater but of the same order of magnitude as the presently obtained wall force drop of 3% for the same shortening velocity.

The nature of the force drop associated with the rate of shortening as assessed in the present study is not clear. It may be a simple viscosity effect, meaning that part of the force developed within the contractile elements is consumed in overcoming internal friction and not available for external work, or it may be an inactivation of the contractile machinery such as that seen during rapid release of stretched muscle fibers (Brady, 1968). It is even possible that the observed $F$ vs. $-\Delta L/\Delta t$ dependency reflects a history dependency between contractility and loading and so there is no true causality in the observed drop in $F$ and $-\Delta L/\Delta t$.

It is highly unlikely that altered contractility due to sympathetic nervous reflexes can have influenced our results, as the dogs were heavily $\beta$-blocked and no other manifestations of a change in sympathetic tone (heart rate, blood pressure) could be observed. In our view, the level of myocardial inotropy is defined by the instantaneous $F$-$L$ relationship. Rapid alteration of the contractile state, e.g., as a result of homeometric autoiregulation, would manifest itself as spread of the $F$-$L$ datapoints, which would obscure the picture of well-defined $F$-$L$ isochronics. The scatter in our data is small, however, and we conclude therefrom that the hearts were at a constant, or almost constant, level of inotropy during the period of each experimental run.

Apart from being implicit in ventricular models used to study the dynamic behavior of the cardiovascular system (Beneken, 1964; Synder et al., 1968), the notion that the ventricular wall behaves like an elastic body of time-varying elasticity has received extensive experimental support, in particular by the studies carried out by Suga, Sagawa, and coworkers (Suga and Yamakoshi, 1976; Sagawa, review, 1978). This notion is in harmony with the presently obtained results: the elasticity of the wall in the direction of measurement is at each instant during the systole given by the $F$-$L$ line for that instant. This idea may possibly be extended to include anisotropy of the myocardial wall, which would mean that the elasticity and its time variation is different from segment to segment and in different directions within a segment. The anatomical substrate for this would be the change in myocardial fiber angle and distribution over the ventricular wall (Streeter and Hanna, 1973). To construct a mathematical ventricular model on this basis would be a problem of formidable complexity, but it is intuitively reasonable that the final result would be a well defined relationship between pressure, volume, and time, as the experiments on the whole ventricle indicate. In this study we have restricted ourselves to obtaining $F$-$L$ data at one site and in one direction in each heart, but some variation in site and direction must have occurred between the different hearts. Still, we obtained qualitatively the same results. This lack of variabil-
ility between the results in the various ventricular walls may give support to the above idea.

In conclusion, these experiments on naturally pumping hearts demonstrate that, over a broad range of preloads and afterloads, the mechanical performance of a myocardial wall segment during systole is well described by a relationship between force, length, and time after end-diastole. This was hardly unexpected in light of experimental evidence for a well-defined relationship between pressure, volume, and time observed for both the left and right ventricles (Sagawa, 1978; Maughan et al., 1978; Piene and Sund, 1980). However, the data question the validity of regarding the velocity trajectory in relation to the length and force variables as a unique descriptor of myocardial contraction in the ventricular wall.

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A force-length-time relationship describes the mechanics of canine left ventricular wall segments during auxotonic contractions.

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