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 (t = 200 msec) was equivalent to a drop of approximately 50% in F at 10% reduction in L. No defined
relationship was observed between F, L, and −dL/dt. 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 after-
loads, 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; Brut-
saert et al., 1971; Burns et al., 1973). In the ventric-
ular wall, however, contractions are normally not
isotonic but auxotonic; i.e., the force changes con-
tinuously during the period of shortening as a re-
flection of the ongoing alterations in ventricular
pressure and ventricular shape. The possibility ex-
ists that the simple picture of a unique force-veloc-
ity-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 ventric-
ular wall may display a picture different from that
obtained by the isolated fiber studies in view of the
complicated structure of interweaving fibers en-
countered in the wall.

For these reasons, the present examination of the
relationship between directly obtained regional wall
force, dimension, and shortening velocity was un-
dertaken. Dogs were anesthetized, artificially ven-
tilated, 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 infe-
rior 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 direc-
tion at the equatorial level of the free left ventric-
ular wall.

Methods

Animal Preparation

Eight male mongrel dogs (18-28 kg) were anes-
ethetized (pentobarbital, 30 mg/kg, iv), and their
hearts were exposed by combined mid-sternal and
left 4th interthoracic space incisions during ventila-
tion 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 bal-
loons of the catheters, the IVC or aorta was oc-
cloded. 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 trans-
ducers. 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 =
1.55 mm/µsec. The segment length signal was elec-
dtronically 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 mi-
nor axis. These registrations were taken for com-
parison between in situ force measured with the
gauge and force calculated from pressure and di-
ameter according to an ellipsoid ventricular model.

Prior to experiments, the dogs were given pro-
pranolol (1 mg/kg) to prevent changes in contrac-
tility 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 veloc-
ity (−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 occlu-
sion 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 occlu-
sions and a total experimental run are shown in
Figure 2A.

Great care was taken to exclude the possibility
that cardiac contractility changed during the exper-
imental 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 autoreg-
ulation ("Anrep" effect) due to alterations in ven-
tricular 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 influ-
enced the obtained relationships between F, L, and
−dL/dt in different ways. However, the relation-
ships between these variables were independent of
the position of the aortic balloon, and we take this
as (indirect) evidence for the non-importance of

![Figure 1](https://example.com/figure1.png)

**Figure 1** Experimental preparation for the simulta-
aneous recording of ventricular wall force and segment
length. An auxotonic force gauge and an ultrasonic
dimension gauge were both inserted at the equatorial
level into the left ventricular free wall with the principal
axes of measurement in the hoop fiber direction. Occlud-
ing balloons were positioned in the inferior vena cava
and the aortic arch for acute variations of preload and
afterload.
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

![Figure 2 A: Time course of events during a typical experimental run (experiment 11/2/79). Variations in aortic pressure (AoP), left ventricular pressure (LVP), and segment length (L) are shown at low speed of the recording paper (50 mm/min). The periods of inferior vena cava occlusion (IVC occl.) and aortic occlusion (Ao. occl.) stand out clearly in the recorded pressures. In this experiment, the aortic balloon was in the ascending aorta, resulting in low pressure in the aortic arch and carotids (AoP tracing). In spite of this, no change in heart rate or LVP after the experimental run could be discerned, thus indicating effective β-blockade in the heart and no lasting effect on ventricular contractility evoked by the load variations. B: Obtained tracings of ECG (top), aortic pressure (AoP), left ventricular pressure (LVP), segment length (L), shortening velocity (dL/dt) and force (F, bottom), at high paper speed (experiment 1/10/80). The panels from left to right demonstrate the variations induced by the changes in preload and/or afterload. Left: control period; second panel: inferior vena cava occlusion; third panel: aortic occlusion; and right panel: final release of aortic occlusion. The L, dL/dt, and F data used for analysis are shown by the heavy lines in the L section.](http://circres.ahajournals.org/content/49/1/72.full.html)
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 hemiaxis 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 in 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 Husiman et al. (1977, 1980) in similar experiments. They found that measured force could drop substantially and even reverse sign during isometric contractions. In a preliminary experiment when the gauge was inserted in stretched and unstimulated muscle, we obtained the same result as Husiman. 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 Lmax. 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, and 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 isochronics 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 isochronics 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>
<thead>
<tr>
<th>Isochronic (msec)</th>
<th>A (g)</th>
<th>B (g/mm)</th>
<th>R²</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>25</td>
<td>-262.91</td>
<td>45.84</td>
<td>0.958</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>75</td>
<td>-320.32</td>
<td>57.89</td>
<td>0.987</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>125</td>
<td>-311.98</td>
<td>60.75</td>
<td>0.993</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>175</td>
<td>-324.42</td>
<td>65.77</td>
<td>0.998</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>225</td>
<td>-341.28</td>
<td>63.33</td>
<td>0.890</td>
<td>&lt;0.01</td>
</tr>
</tbody>
</table>

Table 1 Simple Linear Regression of Isochronic Force (F) and Length (L) Data in a Typical Experiment (of Fig. 4)
FORCE-LENGTH-TIME RELATIONSHIP IN VENTRICULAR WALL/Piene & Covell

Figure 5  Force-length data at 100, 200, and occasionally 300 msec (if within systole) for all experiments. Direct calibration values are displayed on both axes. Encircled datapoints represent control contractions.

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>
<td>80.5</td>
<td>125</td>
<td>3</td>
</tr>
<tr>
<td>11/2/79</td>
<td>153</td>
<td>80.5</td>
<td>117</td>
<td>2.5</td>
</tr>
<tr>
<td>11/9/79</td>
<td>113</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>6</td>
</tr>
<tr>
<td>1/10/80</td>
<td>84.5</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 ± 11.5 g

* 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 ± 11.5 g (mean ± 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 ± 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, -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 -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 -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 -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 -dL/dt value over the period of shortening.
F was hardly significant (2.23 g, \( P = 0.061 \)). The direction of F difference was such that the higher \(-\frac{dL}{dt}\) was associated with lower F in most—but not in all—cases. The average difference in \(-\frac{dL}{dt}\) at \( t_L \) was 4.58 mm/sec \((P < 0.001)\), which was approximately 0.6 muscle length/sec. As the F level at \( t_L \) 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 \( \frac{dF}{dt} \) at \( t_L \). In all cases, the higher velocity was associated with a more negative \( \frac{dF}{dt} \). For beats with low values of peak \(-\frac{dL}{dt}\), \( \frac{dF}{dt} \) during shortening generally was found to take on a positive value (Fig. 7 and Fig. 2, panel 2). The difference in \( \frac{dF}{dt} \) at \( t_L \) 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 \(-\frac{dL}{dt}\) vs. L ("phase-plane" plots) for pairs of contractions that had identical time positions for L and F cross-over points \((t_L = t_F)\) were produced. An example is shown in Figure 8. The left panel demonstrates the obtained F, L, and \(-\frac{dL}{dt}\) tracings; the F and L values were pairwise identical at \( t = 150 \) msec in this case. The right panel shows the two plots of \(-\frac{dL}{dt}\) 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).

**Force vs. Velocity of Shortening**

By superimposing curves of L, \(-\frac{dL}{dt}\), and F obtained during two different loading conditions, we could obtain an estimate of the influence of \(-\frac{dL}{dt}\) 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 \(-\frac{dL}{dt}\). For the other beat, the IVC and aorta both were occluded, resulting in low EDL and low \(-\frac{dL}{dt}\). The objective of imposing these differences in the load was to obtain beats with identical L at some \( t \) in the interval of shortening \((t = 100–200 \text{ msec})\), but with widely different values of \(-\frac{dL}{dt}\). In Figure 7, \( t \) at identical L (crossing L curves) is denoted \( t_F \). 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 \( t_L \) in Figure 7. The influence of \(-\frac{dL}{dt}\) on F then could be evaluated in two ways: (1) by examining \( t_L \) and \( t_F \) (if these were equal, this would mean that \(-\frac{dL}{dt}\) had no detectable influence on F); (2) when \( t_L \) and \( t_F \) were unequal, the difference in F at \( t_L \) could be related to the simultaneous difference in \(-\frac{dL}{dt}\). These data are collected in Table 3. There was no significant difference in \( t_L \) and \( t_F \) when all data \((n = 15)\) were taken together \((P = 0.21, \text{ Student's } t\text{-test for paired comparison})\). At \( t_L \), the difference in
TABLE 3  Superposition of Contractions of Either High EDL and High -dL/dt or Low EDL and Low -dL/dt gave Identical L at tL and Identical F at tF (see Fig. 7)

<table>
<thead>
<tr>
<th>Experiment</th>
<th>tL (sec)</th>
<th>tF (sec)</th>
<th>Δ(-dL/dt) (mm/sec)</th>
<th>ΔF (g)</th>
<th>Δ(dF/dt) (g/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>10/9/79</td>
<td>0.16</td>
<td>0.15</td>
<td>1.75</td>
<td>-5.5</td>
<td>-190</td>
</tr>
<tr>
<td>10/19/79</td>
<td>0.18</td>
<td>0.18</td>
<td>2.5</td>
<td>-7.5</td>
<td>-175</td>
</tr>
<tr>
<td>10/26/79</td>
<td>0.15</td>
<td>0.14</td>
<td>1.5</td>
<td>5</td>
<td>150</td>
</tr>
<tr>
<td>11/2/79</td>
<td>0.17</td>
<td>0.17</td>
<td>3.5</td>
<td>0</td>
<td>-430</td>
</tr>
<tr>
<td>11/9/79</td>
<td>0.18</td>
<td>0.19</td>
<td>6.5</td>
<td>3.5</td>
<td>-105</td>
</tr>
<tr>
<td>11/26/79</td>
<td>0.20</td>
<td>0.20</td>
<td>2.5</td>
<td>0</td>
<td>-120</td>
</tr>
<tr>
<td>1/10/80</td>
<td>0.10</td>
<td>0.10</td>
<td>9.7</td>
<td>-3</td>
<td>-125</td>
</tr>
<tr>
<td>0.17</td>
<td>0.16</td>
<td>1.7</td>
<td>9.0</td>
<td>0</td>
<td>325</td>
</tr>
<tr>
<td>0.10</td>
<td>0.09</td>
<td>9.0</td>
<td>-1</td>
<td>-130</td>
<td></td>
</tr>
<tr>
<td>Mean ± SE</td>
<td>0.173 ± 0.165</td>
<td>4.58</td>
<td>-2.23</td>
<td>-177</td>
<td></td>
</tr>
</tbody>
</table>

At tL, -dL/dt differed by Δ(-dL/dt), F differed by ΔF, and dF/dt differed by Δ(dF/dt).

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 (Sagawa, 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 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 dF/dt. If one extends the analysis of the force-length-time relationship of Brady (1974) to include a varying 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 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.

Figure 8: A pair of differently loaded contractions with identical F at identical L and t were compared in the -dL/dt vs. L projection ("phase-plane" plot), right panel. Note that the -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 $-dL/dt$ dependence on $F$, in the sense that $-dL/dt$ 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/second 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 a certain $t$, we were able to assess a weak dependency between $F$-reduction and $-dL/dt$. The value obtained, 3% reduction in $F$ at $t$ around midsystole for 0.6 muscle length/second 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 $F$-$L$ 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: $\%P = 98 - 0.23 \times (-dV/dt)$ (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/second 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. $-dL/dt$ dependency reflects a history dependency between contractility and loading and so there is no true causality in the observed drop in $F$ and $-dL/dt$.

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 autoadjustment, would manifest itself as spread of the $F$-$L$ datapoints, which would obscure the picture of well-defined $F$-$L$ isochonics. The scatter in our data is small, however, and we conclude therefore 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-
ity 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.

Acknowledgments

The technical skills of R. Pavelec and M. Hill and the secretarial skills of J. Johnson and G. Strom are gratefully acknowledged.

References


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

H Piene and J W Covell

doi: 10.1161/01.RES.49.1.70

_Circulation Research_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1981 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/49/1/70

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/