The Left Ventricular dP/dt_max-End-Diastolic Volume Relation in Closed-Chest Dogs

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SUMMARY. I investigated the relation of the maximum rate of left ventricular pressure rise to the end-diastolic volume and the comparison of the maximum rate of left ventricular pressure rise-end-diastolic volume relation to the end-systolic pressure-volume relation, using the time-varying elastance model. These studies were performed in 11 dogs chronically instrumented to measure left ventricular pressure and determine left ventricular volume from three orthogonal dimensions. During vena caval occlusions, the relations between the maximum rate of left ventricular pressure rise and end-diastolic volume were described by straight lines ($r = 0.97 \pm 0.01$, mean $\pm$ SD). Dobutamine increased the slope of the maximum rate of left ventricular pressure rise-end-diastolic volume relation to $358 \pm 94\%$ of control. This increase was greater than the $244 \pm 61\%$ increase in the slope of the end-systolic pressure-volume relation ($P < 0.005$). The volume intercepts of the maximum rate of left ventricular pressure rise-end-diastolic volume relation and end-systolic pressure-volume relation were similar and were not significantly altered by dobutamine. The ratio of the slope of the maximum rate of left ventricular pressure rise-end-diastolic volume relation to the slope of the end-systolic pressure-volume relation divided by the time from end-diastole to end-systole was similar before ($2.2 \pm 0.7$) and after dobutamine ($2.3 \pm 0.7$, $P = \text{NS}$). Angiotensin II did not significantly alter the maximum rate of left ventricular pressure rise-end-diastolic volume relation generated by caval occlusion. Thus, consistent with the predictions of the time-varying elastance model, the maximum rate of left ventricular pressure rise-end-diastolic volume relation generated by caval occlusions is linear, and its slope may be a sensitive load-independent measure of left ventricular contractile performance. (Circ Res 56: 808-815, 1985)

IT has been proposed that left ventricular (LV) systolic pump function can be modeled as a time-varying elastance (Suga and Sagawa, 1974; Sunagawa and Sagawa, 1982). In this model, the left ventricle is considered to behave as an elastic structure that stiffens in a predictable manner during systole. The LV pressure, $P(t)$, at any time after the onset of contraction, $t$, is described by:

$$P(t) = E(t)(V(t) - V_o),$$

where $E(t)$ is the LV elastance at $t$, $V(t)$ the LV volume at $t$, and $V_o$ the minimal volume required for the LV to generate supra-atmospheric pressure. The LV elastance, $E(t)$, reaches a maximum value, $E_{max}$ at time $t_{max}$, which has been termed end systole. This end-systolic pressure-volume relation,

$$P_{ES} = E_{max}(V_{ES} - V_o),$$

has been the subject of much investigation. $E_{max}$, the slope of the $P_{ES}-V_{ES}$ relation, is a measure of the global inotropic state, and is relatively insensitive to changes in loading conditions in isolated canine hearts (Suga et al., 1973; Suga and Sagawa, 1974; Suga and Yamakoshi, 1977; Suga et al., 1979; Sagawa, 1978, 1981), conscious dogs (Sodums et al., 1984), and man (Grossman et al., 1977; Mehmel et al., 1981).

In isolated canine hearts, Suga and Sagawa (1974) demonstrated that $E(t)$ can be normalized by considering $E_{max}$ and $t_{max}$, so that:

$$E_N(t_N) = E(t)/E_{max},$$

where $t_N = t/t_{max}$ and $E_N(t_N)$ is a normalized elastance function that is similar for all ventricles. Thus, the LV elastance can be expressed as:

$$E(t) = E_{max}E_N(t_N).$$

Although the $P_{ES}-V_{ES}$ relation has been the subject of intense investigation, the more general time-varying elastance model has not been as widely studied in preparations other than the isolated heart. In addition to the $P_{ES}-V_{ES}$ relation, the time-varying elastance model also has implications concerning the relation between the maximum rate of rise of LV pressure ($dP/dt_{max}$) and the end-diastolic volume ($V_{ED}$).

**Derivation of the $dP/dt_{max}-V_{ED}$ Relation from the Time-Varying Elastance Model**

The time derivative of LV pressure ($dP/dt$) can be expressed in terms of LV elastance, as suggested by Sunagawa and Sagawa (1982), by differentiating Equation 1:

$$dP/dt = d(E(t)(V(t)-V_o))/dt.$$

Under normal conditions, $dP/dt$ reaches its maxi-
**Intraventricular Pressure Gradient**

The intraventricular pressure gradient is given by the product of the ventricular end-diastolic pressure (VED) and the dP/dtmax, which is assumed to be constant across the cardiac cycle. Thus,

\[ \frac{dP}{dt_{\text{max}}} = \frac{dE(t)}{dt_{\text{max}}} \]  

Since \( E_N(t) \) appears to be relatively constant in all ventricles (Suga and Sagawa, 1974; Sunagawa and Sagawa, 1982), the maximum value of its derivative should also be a constant, \( k \). Thus,

\[ \frac{dE}{dt_{\text{max}}} = k \frac{E_{\text{max}}}{t_{\text{max}}} \]  

Therefore, the time-varying elastance model of the LV predicts that the \( \frac{dP}{dt_{\text{max}}} - \text{VED} \) relation should be linear (Eq. 3). Furthermore, the slope of this relation, or \( \frac{dE}{dt_{\text{max}}} \), should be proportional to \( E_{\text{max}}/t_{\text{max}} \) (Eq. 4). Since \( E_{\text{max}} \) and \( t_{\text{max}} \) are both assumed to be independent of loading conditions, this relation should also be load independent. Since \( E_{\text{max}} \) increases in response to positive inotropic stimuli, while \( t_{\text{max}} \) decreases (Suga et al., 1973), the slope of the \( \frac{dP}{dt_{\text{max}}} - \text{VED} \) relation, which is proportional to their ratio, should be highly sensitive to changes in contractile function. The model also predicts that the volume intercept of the \( \frac{dP}{dt_{\text{max}}} - \text{VED} \) relation should be the same as the volume intercept \( (V_o) \) of the \( P_{ES} - V_{ES} \) relation. This study was thus undertaken to evaluate the above predictions of the time-varying elastance model in intact, chronically instrumented dogs.

**Methods**

**Instrumentation**

Eleven healthy, adult mongrel dogs were instrumented by a slight modification of a previously described technique (Little et al., 1984; Sodums et al., 1984). A sterile left lateral thoracotomy was performed under anesthesia with halothane (1–2%) following induction with xylene (1 mg/kg) and sodium thiopental (6 mg/kg). The pericardium was opened wide. A micromanometer pressure transducer (Konigsberg Instruments) and a polyvinyl catheter for transducer calibration (i.d. 1.1 mm) were inserted. Three pairs of ultrasonic crystals (5 MHz) were implanted in the endocardium of the LV to measure the anterior-posterior, septal-lateral, and base-apex (long axis) dimensions. Hydraulic occluder cuffs were placed around the inferior and superior venae cavae.

**Data Collection**

All studies were performed after full recovery from the thoracotomy (10 days to 2 weeks), with the dogs lying on their right sides in a sling. The LV catheter was connected to a pressure transducer (Statham P23DB) calibrated with a mercury manometer. The signal from the micromanometer was adjusted to match that of the catheter. The transit time of 5 MHz sound between the crystal pairs was determined and converted to distance assuming a constant velocity of sound in blood of 1.55 m/msec. The first derivative of LV pressure (dP/dt) was obtained by electronically differentiating the micromanometer signal using an RC circuit with a linear frequency response to above 70 Hz. The analog signals were recorded on an eight-channel oscillograph (Beckman Instruments) and digitized with an on-line analog-to-digital converter (Dual Control Systems) at 100 Hz and stored on a floppy disk memory utilizing a computer system (Zobex).

**Experimental Protocol**

The dogs were sedated with fentanyl (0.03–0.06 mg/kg) in combination with droperidol (1.5–3.0 mg/kg) and intubated. To prevent reflex changes in heart rate, the dogs were treated with atropine sulfate (0.2 mg/kg, iv), and were ventilated with room air. To minimize the effect of fluctuations in intrathoracic pressure, all data were recorded during 12-second periods while the dogs were apneic, with the glottis held open by the endotracheal tube (Little et al., 1984). The effect of dobutamine (10 µg/kg per min, iv) was assessed in six dogs. Data were recorded during a steady state, non-intervention period to obtain baseline values. The \( P_{ES} - V_{ES} \) and \( \frac{dP}{dt_{\text{max}}} - \text{VED} \) relations were then generated by sudden occlusion of the cavae. This caused a progressive fall in LV end-systolic pressure, volume, and \( \frac{dP}{dt_{\text{max}}} \) over a 12-second recording period (Fig. 1). Immediately after the recording period, the caval occlusion was released. After all parameters had returned to their baseline level, the caval occlusion was repeated. Then dobutamine was infused until a steady state had been achieved, and the caval occlusions were repeated.

In seven dogs, the effect of arterial vasoconstriction produced by the infusion of angiotensin II (0.5–2.5 µg/min) was assessed. In addition to atropine, these animals were also pretreated with propranolol (2 mg/kg, iv) to block \( \beta \)-adrenergically mediated changes in contractility. Two caval occlusions were performed before, and again after, the infusion of angiotensin II sufficient to raise the systolic arterial pressure by at least 40 mm Hg (Sodums et al., 1984).

**Data Analysis**

The stored digitized data were analyzed by computer algorithm (Sodums et al., 1984; Little et al., 1984). Baseline

**Figure 1.** Analog recording following caval occlusion. \( P_{LV} = \) LV pressure in mm Hg, \( D_{PA} = \) anterior-posterior LV dimension in mm, \( D_{SL} = \) septal-lateral LV dimension in mm, \( D_{LA} = \) long axis dimension in mm.
TABLE 1

<table>
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<th>Dobutamine</th>
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<tr>
<td>HR</td>
<td>168 ± 31</td>
<td>185 ± 28</td>
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<tr>
<td>PES</td>
<td>150 ± 32</td>
<td>160 ± 15</td>
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<tr>
<td>PED</td>
<td>8.1 ± 3.2</td>
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<tr>
<td>VES</td>
<td>36 ± 8.7</td>
<td>28 ± 8.8*</td>
</tr>
<tr>
<td>VED (ml)</td>
<td>35 ± 9.5</td>
<td>27 ± 8.6*</td>
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<tr>
<td>dP/dt max (mm Hg/sec)</td>
<td>48 ± 12</td>
<td>40 ± 12*</td>
</tr>
<tr>
<td>dP/dt min (mm Hg/sec)</td>
<td>2232 ± 740</td>
<td>3581 ± 915*</td>
</tr>
<tr>
<td>VED (ml)</td>
<td>-2470 ± 766</td>
<td>-3048 ± 431*</td>
</tr>
</tbody>
</table>

Results are expressed as mean ± SD; n = 6.

* P < 0.05, PES = LV end-systolic pressures (mm Hg); HR = heart rate; PED = LV end-diastolic pressure (mm Hg); VES = LV end-systolic volume (ml); VED = LV end-diastolic volume (ml); VED = LV end-ejection volume (ml); dP/dt max = peak value of time derivative LV pressure (mm Hg/sec); dP/dt min = peak negative value of dP/dt (mm Hg/sec).

pressure of at least 40 mm Hg, and that produced no extra systoles, were analyzed. The LV end-systolic pressure-volume data during the fall of LV pressure produced by the caval occlusions were fit to

\[ P_{ES} = E_{max}(V_{ED} - V_o), \]

using the linear least square technique. The LV VED and dP/dt max were fit to

\[ dP/dt_{max} = \frac{(dE/dt_{max})}{(V_{ED} - V_o)}, \]

where \( dE/dt_{max} \) is the slope of the relation and \( V_o \) is the volume intercept.

All results are summarized as the mean ± 1 SD, and the level of significance was \( P < 0.05 \). Multiple comparisons were performed by analysis of variance. Intergroup comparisons were performed by paired t-tests with an appropriate correction for the performance of multiple comparisons using the Bonferroni inequality (Glantz, 1981).

Postmortem Studies

At the conclusion of the experiments, the animals were killed and the hearts were examined to confirm the proper positioning of the instrumentation.

Results

A typical analog recording during a caval occlusion is shown in Figure 1. The LV pressure, dP/dt max, and the three LV dimensions decline to-
The infusion of dobutamine increased LV dP/dt max and decreased V ED and V ES (Table 1). The response of typical LV P ES-V ES and dP/dt max-V ED relations to the infusion of dopamine are shown in Figure 3. The individual regression information is shown in Tables 2 and 3. Both the P ES-V ES and dP/dt max-V ED relations were described by straight lines during control and after administration of dobutamine (r = 0.97 ± 0.01). Dobutamine markedly increased the slopes of both the LV P ES-V ES and dP/dt max-V ED relations. The increase in the slope of the dP/dt max-V ED relation (dE/dt max) (358 ± 94% of control) was greater than the increase in the slope of the P ES-V ES relation (244 ± 61% of control, P < 0.005) (Fig. 4). The ratios of dE/dt max to E max/t max were similar, 2.2 ± 0.7 during control and 2.3 ± 0.7 after dobutamine (P = NS). The volume intercepts of the control P ES-V ES and dP/dt max-V ED relations were similar (12.9 ± 6.3 and 9.4 ± 5.1 ml, P = NS) and were not altered significantly by dobutamine (14.5 ± 7.9 and 14.5 ± 8.9 ml, respectively, P = NS); although V o increased in five of six animals.

Angiotensin II increased P ES from 105 ± 23 to 191 ± 19 mm Hg (P < 0.05) and also increased V ED, V ES, dP/dt max, and dP/dt min (Table 4). Because of the autonomic blockade, the heart rate was not altered, and t max remained nearly constant. Consistent with our previous observations (Sodums et al., 1984), the infusion of angiotensin II shifted the P ES-V ES relation to the left, as manifest by a decrease of the volume intercept from 18.0 ± 7.9 to 11.7 ± 7.6 ml (Fig. 5; Table 5). The slope of the P ES-V ES relation also decreased somewhat in response to angiotensin II (9.5 ± 4.1 to 6.3 ± 2.2 mm Hg/ml, P < 0.05). In contrast, the dP/dt max-V ED relation was not altered as much by angiotensin II (Fig. 5; Table 6). Although the slope and volume intercept of the dP/dt max-V ED relation were slightly, but not significantly, decreased in response to angiotensin II, a single line described the dP/dt max-V ED relation before and after angiotensin II (r = 0.982 ± 0.010) more adequately.

### Table 2

<table>
<thead>
<tr>
<th>Dog</th>
<th>n</th>
<th>r</th>
<th>E max</th>
<th>V o</th>
<th>n</th>
<th>r</th>
<th>E max</th>
<th>V o</th>
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<td>41</td>
<td>0.981</td>
<td>11.55</td>
<td>8.7</td>
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</tbody>
</table>

Mean ±SD: 7.7 ± 12.9

P vs. control: P < 0.005 NS

E max = slope of P ES-V ES relation in mm Hg/ml, V o = volume intercept of P ES-V ES relation in ml.

### Table 3

<table>
<thead>
<tr>
<th>Dog</th>
<th>r</th>
<th>dE/dt max</th>
<th>V o</th>
<th>t max</th>
<th>dE/dt max</th>
<th>E max/t max</th>
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<th>V o</th>
<th>t max</th>
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<td>978</td>
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Mean ±SD: 77.8 ± 9.4

P vs. control: P < 0.001 NS

dE/dt max = slope of dp/dt max-V ED relation in mm Hg/ml·sec, V o = volume intercept in ml, t max = time from end diastole to end systole in msec.
FIGURE 4. Comparison of the effect of dobutamine on the slope of the $P_{ES}-V_{ES}$ and $dP/dt_{max}-V_{ED}$ relations.

than a single regression line described the simultaneously determined $P_{ES}-V_{ES}$ relation ($r = 0.956 \pm 0.019, P < 0.05$). In one animal, the $dP/dt_{max}-V_{ED}$ relation (Fig. 6) did not remain linear at the higher $V_{ED}$ levels produced by angiotensin II infusion. At these higher $V_{ED}$ levels, the relationship flattened out. Only the linear portion of this curve ($V_{ED} < 33$ ml) was subjected to linear regression analysis.

Discussion

This study investigated several predictions suggested by the time-varying elastance model of the LV concerning the $dP/dt_{max}-V_{ED}$ relation and its link to the $P_{ES}-V_{ES}$ relation. Most of the results are consistent with these predictions. First, the relation between LV $dP/dt_{max}$ and the $V_{ED}$ is described by a straight line during acute preload reductions produced by caval occlusion. The $dP/dt_{max}-V_{ED}$ relation is relatively unchanged by increases in aortic pressure produced by dobutamine, the slope of the $dP/dt_{max}-V_{ED}$ relation is markedly increased (more so than the increase in $E_{max}$, the slope of the $P_{ES}-V_{ES}$ relation), while the volume intercept of the relation is relatively unchanged. Also, consistent with the time-varying elastance model, the volume intercept of the $dP/dt_{max}-V_{ED}$ relation is similar to the volume intercept of the $P_{ES}-V_{ES}$ relation.

The simple time-varying elastance model of LV function does not account for any effect of the characteristics of ejection on the LV systolic pressure generated at any LV volume (Suga and Sagawa 1974; Sunagawa and Sagawa, 1982). However, the LV pressure generated at any volume may be reduced somewhat when the stroke volume, ejection fraction, maximal velocity of ejection, or flow at end-systole are markedly altered (Suga and Yamakoshi, 1977; Suga et al., 1977; Hunter et al., 1983; Weber et al., 1982; Shroff et al., 1983; Maughan et al., 1984). These factors may account for the shift of the LV $P_{ES}-V_{ES}$ relation observed in this study and seen previously (Sodums et al., 1984) after the infusion of a vasoconstrictor. Interestingly, the LV $dP/dt_{max}-V_{ED}$ relation was not shifted as much by...
vanoconstriction. This may indicate that the simple
time-varying elastance model is a better descriptor
of the isovolumic phase of LV contraction than
during ejection, and that the $\frac{dP}{dt_{max}}$-$V_{ED}$ relation
may be affected less by alterations of the arterial
input characteristics than the $P_{ES}$-$V_{ES}$ relation. Under
conditions different than those employed in this
study, the predictions of the time-varying elastance
model may not be as accurate. For example, if the
stroke volume and rate of LV ejection were increased
due to a slow heart rate or vasodilation, the simple
time-varying elastance model may not be adequate
because of a much greater deactivating effect of
vasoconstriction. This may indicate that the simple
time-varying elastance model provides a conceptual link between the events
occurring during isovolumic contraction and at end
systole.

In this study, the slope of the $\frac{dP}{dt_{max}}$-$V_{ED}$ relation,
$\frac{dE}{dt_{max}}$, was roughly proportional to
$E_{max}/t_{max}$. The time-varying elastance model of the
LV predicts that this proportionality constant should be
equal to the maximum value of $\frac{dE_{n}}{dt_{n}}$ which is
similar in all ventricles. Suga and Sagawa (1974)
evaluated $E_{n}(t_{n})$ in a series of isolated hearts. Figure
9 of their paper indicates that the maximum value of
$\frac{dE_{n}}{dt_{n}}$ is approximately 1.4. This is somewhat
lower than the ratio of $\frac{dE}{dt_{max}}$ to $E_{max}/t_{max}$ found
in this study ($2.2 \pm 0.7$ control and $2.3 \pm 0.7$ with
dobutamine). However, the values obtained for
$\frac{dE}{dt_{max}}$ and $E_{max}/t_{max}$ from Figure 3 of Suga and
Sagawa's earlier study (1972) indicate that this ratio
is approximately 2, in closer agreement with the
observations of this study. The relationship between
$\frac{dE}{dt_{max}}$ and $E_{max}/t_{max}$ and the similarity of the
volume intercepts of the $\frac{dP}{dt_{max}}$-$V_{ED}$ and $P_{ES}$-$V_{ES}$
relations indicate that the time-varying elastance
model provides a conceptual link between the events
occurring during isovolumic contraction and at end
systole.

The observation that the slope of the $\frac{dP}{dt_{max}}$-$V_{ED}$ relation ($\frac{dE}{dt_{max}}$) showed a greater increase in
response to a positive inotropic stimulation than $E_{max}$

### Table 5

**Effect of Angiotensin II on the LV $P_{ES}$-$V_{ES}$ Relation**

<table>
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<tr>
<th>Dog</th>
<th>$n$</th>
<th>$r$</th>
<th>$E_{max}$</th>
<th>$V_o$</th>
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<th>6.3</th>
<th>11.7</th>
<th>9.1</th>
<th>17.5</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\pm$SEM</td>
<td>4.1</td>
<td>7.9</td>
<td>2.2</td>
<td>7.6</td>
<td>3.2</td>
<td>6.8</td>
</tr>
</tbody>
</table>

$P$ vs. control $< 0.05$ $P < 0.005$ NS NS

Abbreviations as in Table 1.

### Table 6

**Effect of Angiotensin II on the LV $\frac{dP}{dt_{max}}$-$V_{ED}$ Relation**

<table>
<thead>
<tr>
<th>Dog</th>
<th>$r$</th>
<th>$\frac{dE}{dt_{max}}$</th>
<th>$V_o$</th>
<th>$r$</th>
<th>$\frac{dE}{dt_{max}}$</th>
<th>$V_o$</th>
<th>$r$</th>
<th>$\frac{dE}{dt_{max}}$</th>
<th>$V_o$</th>
</tr>
</thead>
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<tr>
<td>2</td>
<td>0.996</td>
<td>66.1</td>
<td>14.2</td>
<td>0.987</td>
<td>62.1</td>
<td>2.7</td>
<td>0.990</td>
<td>65.4</td>
<td>4.4</td>
</tr>
<tr>
<td>5</td>
<td>0.996</td>
<td>77.0</td>
<td>23.4</td>
<td>0.900</td>
<td>81.7</td>
<td>22.4</td>
<td>0.986</td>
<td>87.2</td>
<td>24.8</td>
</tr>
<tr>
<td>7†</td>
<td>0.985</td>
<td>64.8</td>
<td>7.2</td>
<td>0.970</td>
<td>52.1</td>
<td>1.4</td>
<td>0.989</td>
<td>66.3</td>
<td>7.5</td>
</tr>
<tr>
<td>8†</td>
<td>0.987</td>
<td>105.0</td>
<td>19.7</td>
<td>0.982</td>
<td>96.1</td>
<td>17.7</td>
<td>0.986</td>
<td>103.3</td>
<td>19.2</td>
</tr>
<tr>
<td>9†</td>
<td>0.980</td>
<td>53.0</td>
<td>44.8</td>
<td>0.955</td>
<td>33.6</td>
<td>28.8</td>
<td>0.970</td>
<td>36.6</td>
<td>33.1</td>
</tr>
<tr>
<td>10</td>
<td>0.964</td>
<td>62.0</td>
<td>6.6</td>
<td>0.959</td>
<td>52.4</td>
<td>1.2</td>
<td>0.965</td>
<td>55.9</td>
<td>3.5</td>
</tr>
<tr>
<td>11</td>
<td>0.995</td>
<td>106.9</td>
<td>2.6</td>
<td>0.977</td>
<td>80.4</td>
<td>6.4</td>
<td>0.990</td>
<td>97.1</td>
<td>1.5</td>
</tr>
</tbody>
</table>

| Mean | 76.4 | 16.9 | 65.5 | 11.5 | 73.1 | 13.4 |
| $\pm$SEM | 21.6 | 14.4 | 21.6 | 11.3 | 23.9 | 12.3 |

$P$ vs. control NS NS NS NS

* Determined simultaneously with Table 5. Abbreviations as in Table 2.
† In animal 7, the LV $\frac{dP}{dt_{max}}$-$V_{ED}$ relation became nonlinear at high $V_{ED}$ (see Fig. 5). Only data
from the linear portion ($V_{ED} < 33$ ml) were analyzed.
is consistent with a previous observation of Suga et al. (1976). They compared the effects of baroreflex inotropic interventions on E_max and dP/dt_max in open-chest canine LV preparations contracting isovolumically at a constant volume. In their study, dP/dt_max showed greater changes than E_max in response to changes in contractility.

The results of this study are consistent with previous observations that dP/dt_max is preload dependent (Mason, 1969; Mahler et al., 1975; Wallace et al., 1963; Schmidt and Hoppe, 1978). These earlier studies assessed LV preload, using the LV end-diastolic pressure and not V_{ED}. Due to the nonlinear relation of LV end-diastolic pressure and V_{ED}, the dP/dt_max-V_{ED} relation cannot be directly deduced from these studies. Also, consistent with the observations of this study, Reeves et al. (1960) found in open-chest dogs that the relation between dP/dt_max and a measure of LV end-diastolic stretch was approximated by a straight line, whose slope was increased by epinephrine. Similarly, Quinones et al., (1976) reported that the ratio of dP/dt_max to the LV end-diastolic circumference increased in response to isoproterenol.

Most previous studies have found that dP/dt_max increases somewhat in response to elevations of arterial pressure. This increase in dP/dt_max can usually be attributed to an increase in the LV end-diastolic pressure and, thus, presumably, V_{ED} (Mason, 1969). However, Wallace et al., (1963) found, in a canine right-heart bypass preparation, that a sudden increase in aortic pressure increased dP/dt_max before the end-diastolic pressure increased. Others (Wildenthal et al., 1969; Furnival et al., 1970) have found that such sudden increases in aortic diastolic pressure do not alter dP/dt_max when it occurs prior to aortic valve opening.

Suga and Sagawa (1972) have derived the force-velocity relation from the time-varying elastance model. The force-velocity relation is related by appropriate scaling factors to the relation of E(t) to [dE(t)/dt]_E, and this equation relates to the time-varying elastance model. The peak value of dE(t)/dt or dE/dt_max in their figure is relatively constant during an increase in LV systolic pressure or an increase in V_{ED}, but increases in response to the infusion of positive inotropic agent, epinephrine. Since dE(t)/dt_max is the slope of the dP/dt_max-V_{ED} relationship, our results are consistent with these observations of Suga and Sagawa (1972).

In one animal in this study, the dP/dt_max-V_{ED} relation became nonlinear at high V_{ED}. This may be a manifestation of the flat portion of the Frank-Starling relationship. The time-varying elastance model treats the ventricle as a perfectly elastic structure in which pressure and volume are linearly related at all volumes. It is clear that the real LV must have a limit above which further increase in volume will not result in a continued linear increase in dP/dt_max or LV systolic pressure. This dP/dt_max-V_{ED} relation may reach this limit sooner than the P_{ES}-V_{ES} relationship, since V_{ED} is larger than V_{ES}. The observations of the linearity of the P_{ES}-V_{ES} relation and the data in the other animals in this study indicate that this limit is not usually reached in the physiological range of LV volumes.

The derivation of the dP/dt_max-V_{ED} relation described in the introduction depends on several assumptions that may not be completely accurate. First, LV volume may not be constant during isovolumic systole, as some volume is ejected into the aortic and mitral valves. Second, the volume correction factor (V_o) may not be constant early in systole (Suga and Sagawa, 1974). Finally, dP/dt_max may not always occur during isovolumic systole, but instead may in some circumstances be reached shortly after aortic valve opening. This is most likely to occur after vasodilation or when the LV systolic performance is depressed (Wildenthal et al., 1969; Quinones et al., 1976). However, the agreement of our results with the predictions of the time-varying elastance model (i.e., equations 3 and 4) suggests that these factors do not have a substantial effect under the conditions of this study.

The results of this study suggest that the LV dP/dt_max-V_{ED} relation is a sensitive, load-independent index of LV performance. However, before this can be applied, several limitations of this study must be considered. First, this study was performed after
opening of the pericardium. Second, although the study was performed in close-chest animals, the conditions were carefully controlled. Measurements were obtained during periods of apnea to avoid the confounding influences of changes in intrathoracic pressure. The animals were treated with atropine to avoid the influences of alterations in heart rate during caval occlusion, and with atropine and propranolol to prevent reflex changes in contractile state during angiotensin II administration. Finally, the dP/dt_{max}-V_{ED} relations were generated by acute preload reduction. The effect of changing loading conditions by other methods and the variability of the relation over time remain to be determined.

In conclusion, this study demonstrates that in chronically instrumented dogs LV dP/dt_{max} and the V_{ED} are linearly related during caval occlusions. The relation is not altered by arterial vasoconstriction, and the slope of the dP/dt_{max}-V_{ED} relation appears to be more sensitive to positive inotropic stimulation than E_{max}, the slope of the P_{ES}-V_{ES} relation. These results are consistent with predictions of the time-varying elastance model of the LV and support its use as a conceptual framework for the understanding of LV systolic performance.

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References


Little WC, O'Rourke RA (1985) Effect of regional ischemia on the left ventricular end-systolic pressure-volume relation in chronically instrumented dogs. J Am Coll Cardiol 5: 297-302


Mahler F, Ross J Jr, O'Rourke RA, Covell JW (1975) Effects of changes in preload, afterload and inotropic state on ejection and isovolumic phase measures of contractility in the conscious dog. Am J Cardiol 35: 626-634

Mason DT (1969) Usefulness and limitations of the rate of rise of intraventricular pressure (dP/dt) in the evaluation of myocardi al contractility in man. Am J Cardiol 23: 516-527


Schmidt HD, Hoppé H (1978) Preload dependence of dP/dt_{max}, V_{CS max} and calculated V_{max} compared to the inotropic sensitivity of these indices of cardiac contractility. Basic Res Cardiol 73: 380-393


Suga H, Kitabatake A, Sagawa K (1979) End-systolic pressure-volume relations determine stroke volume from fixed end-diastolic volume in the isolated canine left ventricle under a constant contractile state. Circ Res 44: 238-249


INDEX TERMS: Left ventricular dP/dt • Pressure-volume relations • Left ventricular performance
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W C Little

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