Load Independence of the Instantaneous Pressure-Volume Ratio of the Canine Left Ventricle and Effects of Epinephrine and Heart Rate on the Ratio

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ABSTRACT

As a means of assessing ventricular performance, we analyzed the time-varying ratio of instantaneous pressure, \( P(t) \), to instantaneous volume, \( V(t) \), in the canine left ventricle. Intraventricular volume was measured by plethysmography, while the right heart was totally bypassed. The cardiac nerves were sectioned, and an epinephrine infusion was used to alter the contractile state. The instantaneous pressure-volume ratio was defined as \( E(t) = P(t)/[V(t) - V_d] \), where \( V_d \) is an experimentally determined correction factor. We found that (1) all the \( E(t) \) curves thus defined were similar in their basic shape and attained their peak near the end of the ejection phase regardless of the mechanical load, the contractile state, or the heart rate, (2) under a constant heart rate and contractile state extensive changes in preload, afterload, or both did not alter the peak value of \( E(t) \), \( E_{\text{max}} \), or the time to \( E_{\text{max}} \) from the onset of systole, \( T_{\text{max}} \), and (3) these parameters of \( E(t) \) markedly changed with epinephrine infusion or increases in heart rate. At an epinephrine infusion rate of \( 2 \mu g/kg \text{ min}^{-1} \), \( E_{\text{max}} \) increased to \( 12.2 \pm 4.5 \) (SD) mm Hg/ml (\( n = 9 \)) from its control value of \( 6.6 \pm 1.2 \) mm Hg/ml before the infusion. Simultaneously, \( T_{\text{max}} \) shortened from \( 191 \pm 29 \) msec to \( 157 \pm 26 \) msec. Increases in the paced heart rate proportionally shortened \( T_{\text{max}} \) (45% per 100-beats/min change in heart rate) without any effect on \( E_{\text{max}} \). We concluded that \( E(t) \), represented by \( E_{\text{max}} \) and \( T_{\text{max}} \), explicitly reflects the ventricular contractility.

KEY WORDS

Frank-Starling mechanism ventricular compliance
pressure-volume diagram ventricular elastance
cardiometer contractility

don't change

It is well known that both the instantaneous pressure and the instantaneous volume in a beating ventricle are complex functions of end-diastolic volume, arterial blood pressure, heart rate, and inotropic background (1-5). Because of this complexity, many investigators have attempted to characterize the basic mechanical properties of ventricular contraction at the myocardial level (6, 7). Using a geometric model, the ventricular pressure and volume data have been reduced to myocardial fiber force, length, and shortening velocity variables and interpreted in the light of myocardial mechanics (6, 8). However, some researchers have recently questioned the validity of this method (9-13). Under these circumstances, studies of the ventricular contraction at the chamber level are important for a better understanding of cardiac performance.

Suga (14, 15) observed in the intact canine left ventricle during a given contractile state that the instantaneous ratio of ventricular pressure to absolute volume, \( P(t)/V(t) \), was almost independent of end-diastolic volume and arterial blood pressure. He also found that this ratio varied markedly with inotropic interventions (16). He temporarily concluded that the pressure-volume ratio could be used to characterize the ventricular contractility. However, an indicator-dilution technique and electromagnetic measurement of aortic blood flow were used for ventricular volume measurement in these studies, and the accuracy of the volume data was limited. For this reason, we reinvestigated the instantaneous pressure-volume ratio more accurately with an improved measurement of ventricular volume. The present study indicates that the original definition of the instantaneous pressure-volume ratio should be slightly modified and that the modified ratio explicitly reflects the contractile state of the ventricle.
VENTRICULAR PRESSURE-VOLUME RATIO

Methods

SURGICAL PREPARATION

Nine mongrel dogs (19–21 kg) were anesthetized with α-chloralose (60 mg/kg, iv) and urethane (600 mg/kg, iv). A midternal thoracotomy was performed under positive-pressure ventilation. After bilateral vagotomy, the stellate ganglia were removed. To collapse the right ventricle, venous return via the caval veins was drained into a reservoir 50 cm below heart level. A pump (Sarns model 3500) perfused the blood from the reservoir into the pulmonary artery as shown in Figure 1. The flow through this pump was fixed at about 80 ml/kg min⁻¹. Coronary venous return to the right heart was drained into the same reservoir through a catheter with multiple side holes by the negative hydrostatic pressure gradient. Body temperature was maintained at 37°C by warming the blood within the reservoir.

To primarily vary the preload on the left ventricle, a miniature pressure transducer (Konigsberg P-21) was placed inside the ventricle through a small incision in the apex. The zero shift of this transducer due to temperature change was less than 0.1 mm Hg/°C, and the overall drift was less than 0.2%/°C of the output. The sensitivity was calibrated while the transducer was in a pressurizing air chamber, and then zero was established by immersing the transducer just below the surface of water at 37°C.

To measure instantaneous absolute volume of the left ventricular lumen, a modified cardiometer was used. The principle of this method involved assessing the volume changes from the air pressure changes in an airtight chamber in which the ventricle was enclosed (2–4). Since we wanted to measure instantaneous absolute intraventricular volume over 2 hours, we modified the classic cardiometer system to eliminate any air leak and temperature drift. The main modifications are as follows (Fig. 1). (1) A ventricular assist cup (SMEC) was lined with a very thin (0.05 mm) hemiellipsoidal polyurethane envelope. This envelope covered the ventricular surface and completely separated the air in the cardiometer interspace from the atmosphere, and it adhered to the ventricular surface by continuous negative-pressure suction. The unstressed volume of the envelope was much greater than that of the ventricular portion of the heart. (2) The cardiometer air space was connected to a 3-liter glass bottle to obtain a reasonably linear relation between the volume and the pressure changes inside the cardiometer system and at the same time to reduce back-pressure load on the ventricle. This bottle and the connecting tubing to the cardiometer cup were kept at 37 ± 0.1°C. (3) To further compensate for the air pressure changes associated with temperature changes in the surroundings, we placed an identical bottle in the bath, and connected a high-sensitivity differential pressure transducer (Beckman model 807-215-071) between the two bottles. Using these modifications, the observed pressure drift was equivalent to less than ±0.5 ml over 3 hours. The dynamic response of this cardiometer system to a step change in the air volume had a cutoff frequency of 15 Hz (see Appendix). Sensitivity of the cardiometer system was calibrated by injecting or withdrawing a known amount of air into or out of the cardiometer air system. Zero intraventricular volume was calibrated at the end of each experiment by withdrawing all the blood in the left ventricular lumen after stopping the right heart bypass pump.

Figure 2 shows the instantaneous left intraventricular volume and its time derivative as well as the left ventricular pressure and the ascending aortic blood flow recorded in a preliminary experiment. The time derivative of volume in the ejection phase appeared to be a mirror image of the aortic flow curve. This modified cardiometer could measure the instantaneous intraventricular volume with a reasonable accuracy for our purpose.

EXPERIMENTAL PROTOCOL

In this study we arbitrarily defined the control contractile state as the contractile state of a denervated ventricle before epinephrine infusion. To study the effect of changes in the contractile state on the instantaneous pressure-volume relation, the contractile
Effects of Changes in Loading Conditions on Emax and Tmax under the Control Contractile State

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>AP (mm Hg)</th>
<th>CO (ml/kg min⁻¹)</th>
<th>Emax ± SD (mm Hg/ml)</th>
<th>Tmax ± SD (msec)</th>
<th>AP (mm Hg)</th>
<th>CO (ml/kg min⁻¹)</th>
<th>Emax ± SD (mm Hg/ml)</th>
<th>Tmax ± SD (msec)</th>
<th>AP (mm Hg)</th>
<th>CO (ml/kg min⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>90</td>
<td>100</td>
<td>6.9 ± 0.14</td>
<td>173 ± 2</td>
<td>115</td>
<td>150</td>
<td>6.9 ± 0.20</td>
<td>176 ± 5</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>2</td>
<td>80</td>
<td>70</td>
<td>8.4 ± 0.40</td>
<td>192 ± 2</td>
<td>115</td>
<td>100</td>
<td>8.3 ± 0.51</td>
<td>184 ± 3</td>
<td>55</td>
<td>55</td>
</tr>
<tr>
<td>3</td>
<td>95</td>
<td>70</td>
<td>7.1 ± 0.32</td>
<td>220 ± 3</td>
<td>120</td>
<td>95</td>
<td>6.0 ± 0.41</td>
<td>220 ± 3</td>
<td>65</td>
<td>65</td>
</tr>
<tr>
<td>4</td>
<td>125</td>
<td>85</td>
<td>7.3 ± 0.32</td>
<td>171 ± 2</td>
<td>130</td>
<td>145</td>
<td>6.4 ± 0.33</td>
<td>182 ± 5</td>
<td>85</td>
<td>55</td>
</tr>
<tr>
<td>5</td>
<td>90</td>
<td>80</td>
<td>5.6 ± 0.21</td>
<td>210 ± 3</td>
<td>100</td>
<td>150</td>
<td>5.2 ± 0.31</td>
<td>208 ± 2</td>
<td>70</td>
<td>45</td>
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<tr>
<td>6</td>
<td>100</td>
<td>80</td>
<td>8.2 ± 0.22</td>
<td>176 ± 3</td>
<td>120</td>
<td>135</td>
<td>7.8 ± 0.25</td>
<td>175 ± 2</td>
<td>65</td>
<td>45</td>
</tr>
<tr>
<td>7</td>
<td>85</td>
<td>60</td>
<td>5.4 ± 0.30</td>
<td>255 ± 3</td>
<td>100</td>
<td>100</td>
<td>5.7 ± 0.25</td>
<td>265 ± 3</td>
<td>55</td>
<td>35</td>
</tr>
<tr>
<td>8</td>
<td>105</td>
<td>85</td>
<td>7.6 ± 0.18</td>
<td>144 ± 1</td>
<td>150</td>
<td>120</td>
<td>7.2 ± 0.21</td>
<td>140 ± 2</td>
<td>70</td>
<td>45</td>
</tr>
<tr>
<td>9</td>
<td>90</td>
<td>75</td>
<td>5.5 ± 0.25</td>
<td>175 ± 2</td>
<td>125</td>
<td>125</td>
<td>5.5 ± 0.22</td>
<td>177 ± 2</td>
<td>75</td>
<td>40</td>
</tr>
</tbody>
</table>

P = mean aortic blood pressure and CO = cardiac output. P values were obtained using a paired t-test. There was no statistically significant difference of Emax and Tmax between load 1 and loads 2, 3, 4, or 5.

An example of fast (left) and slow (right) recordings of simultaneous tracings of intraventricular pressure, intraventricular volume (by plethysmography), the time derivative of intraventricular volume, and aortic blood flow (by an electromagnetic flowmeter).

![FIGURE 2](http://circres.ahajournals.org/)

An example of fast (left) and slow (right) recordings of simultaneous tracings of intraventricular pressure, intraventricular volume (by plethysmography), the time derivative of intraventricular volume, and aortic blood flow (by an electromagnetic flowmeter).
The text describes experiments on the left ventricular pressure-volume loops of a denervated heart. The loops were measured under control conditions and under enhanced contractile states with and without epinephrine infusion. The loops were used to calculate the ventricular pressure-volume ratio at different time points during the cardiac cycle:

1. **(ejection phase)**: The loop shows a decrease in volume with an increase in pressure, indicating ejection of blood from the ventricle.
2. **(isovolumic contraction phase)**: The volume remains constant while pressure increases rapidly.
3. **(isovolumic relaxation phase)**: Pressure decreases while volume remains constant, indicating relaxation of the ventricle.
4. **(diastolic filling phase)**: Volume increases with a decrease in pressure as the ventricle fills with blood.

The loops were calculated using the following equation:

\[
\frac{P_c}{(V_c - V_d)} = \text{Constant}
\]

where:
- \(P_c\) is the ventricular pressure at a particular time point.
- \(V_c\) is the absolute ventricular volume at the left uppermost corner.
- \(V_d\) is the correction volume.

The loops were used to determine the correction volume, which was found to be practically independent of the contractile state. This allowed for the calculation of the pressure-volume ratio at various time points under different loading conditions.

The diagrams illustrate the loops under control and enhanced contractile states with and without epinephrine infusion. The slope of the line drawn for the enhanced contractile state was significantly different from the control state, indicating a change in ventricular function.

For a detailed analysis of the loops and the calculation of the pressure-volume ratio, refer to the text for further discussion.
Effects of Epinephrine on Emax, Tmax, and [(dP/dt)/P]max

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Body weight (kg)</th>
<th>LV weight (g)</th>
<th>Vd (ml)</th>
<th>Range of preload (ml)</th>
<th>Range of afterload (mm Hg)</th>
<th>Heart rate (beats/min)</th>
<th>Emax ± sd (mm Hg/ml)</th>
<th>Tmax ± sd (msec)</th>
<th>(dP/dt)/Pmax (1/sec)</th>
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<tr>
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<td>19</td>
<td>75</td>
<td>4</td>
<td>21-40</td>
<td>75-155</td>
<td>145</td>
<td>7.0 ± 0.23</td>
<td>173 ± 7</td>
<td>27 ± 1.0</td>
</tr>
<tr>
<td>2</td>
<td>21</td>
<td>94</td>
<td>4</td>
<td>15-35</td>
<td>65-130</td>
<td>143</td>
<td>8.3 ± 0.68</td>
<td>189 ± 4</td>
<td>32 ± 2.7</td>
</tr>
<tr>
<td>3*</td>
<td>20</td>
<td>95</td>
<td>4</td>
<td>18-35</td>
<td>75-150</td>
<td>153</td>
<td>6.5 ± 0.68</td>
<td>222 ± 10</td>
<td>20 ± 2.5</td>
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<td>6</td>
<td>20-45</td>
<td>90-190</td>
<td>165</td>
<td>6.9 ± 0.51</td>
<td>184 ± 4</td>
<td>45 ± 2.2</td>
</tr>
<tr>
<td>5</td>
<td>20</td>
<td>93</td>
<td>6</td>
<td>16-36</td>
<td>55-165</td>
<td>125</td>
<td>5.5 ± 0.33</td>
<td>205 ± 13</td>
<td>33 ± 1.6</td>
</tr>
<tr>
<td>6</td>
<td>20</td>
<td>87</td>
<td>6</td>
<td>14-30</td>
<td>65-170</td>
<td>160</td>
<td>7.8 ± 1.20</td>
<td>175 ± 10</td>
<td>35 ± 1.3</td>
</tr>
<tr>
<td>7*</td>
<td>21</td>
<td>90</td>
<td>6</td>
<td>18-35</td>
<td>55-165</td>
<td>100</td>
<td>4.9 ± 0.32</td>
<td>250 ± 5</td>
<td>26 ± 1.1</td>
</tr>
<tr>
<td>8</td>
<td>20</td>
<td>90</td>
<td>4</td>
<td>16-35</td>
<td>80-185</td>
<td>150</td>
<td>7.4 ± 0.55</td>
<td>141 ± 3</td>
<td>45 ± 3.6</td>
</tr>
<tr>
<td>9*</td>
<td>20</td>
<td>90</td>
<td>5</td>
<td>27-42</td>
<td>75-165</td>
<td>117</td>
<td>5.5 ± 0.23</td>
<td>177 ± 3</td>
<td>29 ± 2.6</td>
</tr>
<tr>
<td>Mean</td>
<td></td>
<td></td>
<td>5 ± 1</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>46 ± 1.8</td>
</tr>
</tbody>
</table>

LV = left ventricle and Vd = correction volume (see text). Preload and afterload values represent left ventricular end-diastolic volume and peak developed pressure, respectively. P values indicate statistically significant differences between the control and the enhanced contractile states. a = ratio of Emax under the enhanced contractile state to that under control. s = ratio of Tmax under the control contractile state to that under the enhanced state. t = ratio of [(dP/dt)/P]max under the enhanced contractile state to that under the control state.

*Left ventricular pacing.

...This finding indicates that the pressure-volume ratio, Pc/(Vc-Vd), is markedly increased when the contractile state is enhanced.

Figure 3B shows P-V loops measured in the same dog and under the same control contractile state as in Figure 3A. During this run, arterial blood pressure was fixed while cardiac output was varied fourfold. In spite of this wide variation in cardiac output, the left uppermost corners of the P-V loops were on or very close to the same solid line that was drawn for the P-V loops in A, indicating that the pressure-volume ratio, Pc/(Vc-Vd), is insensitive to the imposed changes in preloaded end-diastolic volume.

**DEFINITION AND SIMILARITY ANALYSIS OF THE INSTANTANEOUS PRESSURE-VOLUME RATIO CURVE**

The discussion in the preceding section is concerned with the pressure-volume ratio at a particular time point near the end of the ejection phase. We examined the time course of the pressure-volume ratio curve over the entire cardiac cycle as well. To discuss the entire ratio curve, we defined the pressure-volume ratio at any time point in one cardiac cycle as E(t) = P(t)/[V(t) - Vd], where P(t) = instantaneous intraventricular pressure, V(t) = instantaneous intraventricular volume, and Vd = the fixed correction volume.

Figure 4 shows the instantaneous pressure-volume ratio curve, E(t), calculated from intraventricular pressure and volume under load-1 conditions. Comparison of the E(t) curves obtained in the control contractile state (left) with those obtained in the enhanced contractile state under a 2-μg/kg min⁻¹ epinephrine infusion (right) showed that the peak value of E(t), Emax, markedly increased and that the time to Emax from the onset of systole, Tmax, considerably shortened with enhancement of the contractile state. However, the two E(t) curves under the different contractile
states had similar shapes in spite of their marked differences in height and width. To rigorously compare the basic shape of \( E(t) \) curves recorded under different contractile states, the \( E(t) \) curves were normalized so that their \( E_{max} \) and \( T_{max} \) values were unity. Figure 5 shows the results of such a comparison. The solid circles and the open circles show mean values (±sd) of the normalized \( E(t) \) curves under the control contractile state and the enhanced contractile state (2-μg/kg min\(^{-1}\) epinephrine infusion), respectively, under load-1 conditions in all nine preparations. Evidently, all the normalized \( E(t) \) curves obtained under different contractile states have a common shape.

Similarly, we compared the shape of the \( E(t) \) curves obtained under various conditions of loading and heart rate. The crosses and the triangles in Figure 5 represent mean values (±sd) of the \( E(t) \) curves from one preparation when the heart was contracting under five different loading conditions and at three different heart rates, respectively, under the control contractile state. These mean values were statistically indistinguishable from those under different contractile states at any normalized time point.

From the similarity analysis we concluded that all the \( E(t) \) curves, if normalized with respect to \( E_{max} \) and \( T_{max} \), would reduce to a single curve, \( E_N(t_N) \), with a unique shape regardless of the dog, the loading conditions, the contractile state, or the heart rate. Therefore, \( E_{max} \) and \( T_{max} \) can be considered the characteristic parameters of the instantaneous pressure-volume ratio curve.

Note that \( E_{max} \) is nothing but the pressure-volume ratio at the left uppermost corner of a P-V loop and that \( T_{max} \) is the time required for a pressure-volume data point to move from the end-diastolic point to the left uppermost corner along the P-V loop.

**LOAD INDEPENDENCE OF \( E_{max} \) AND \( T_{max} \) AND THEIR SENSITIVITY TO EPINEPHRINE**

The two parameters \( E_{max} \) and \( T_{max} \) were not affected by wide variations in loading conditions under a given contractile state. Listed in Table 1 are the \( E_{max} \) and \( T_{max} \) data from all nine dogs under the control contractile state and the five different loading conditions previously defined. Using a paired \( t \)-test, we could not find any statistically significant difference of \( E_{max} \) and \( T_{max} \) between load 1 and loads 2, 3, 4, or 5, as the \( P \) values indicate.

In contrast, \( E_{max} \) markedly increased and \( T_{max} \) significantly decreased from their control values when the contractile state was enhanced by a 2-μg/kg min\(^{-1}\) epinephrine infusion. The \( P \) values in

![FIGURE 5](image)

*Comparison of mean values of the magnitude of many normalized pressure-volume ratio curves (ε\(_{en}\)) at each normalized time point (t\(_{en}\)). The vertical bars indicate ±sd. The two equations on the figure show the process of normalization. Symbols are explained in the text.*
Table 2 indicate this fact. Also given in Table 2 are the values of \( \frac{(dP/dt)}{P} \)max for the control and the enhanced contractile states. In parallel with those changes in Emax and Tmax, \( \frac{(dP/dt)}{P} \)max significantly increased from its control value with enhancement of the contractile state.

Under a 1-\( \mu \)g/kg min\(^{-1}\) epinephrine infusion, Emax increased \( 69 \pm 41\% \) (sp) and Tmax decreased \( 21 \pm 9\% \); under a 4-\( \mu \)g/kg min\(^{-1}\) epinephrine infusion, Emax increased \( 125 \pm 58\% \) and Tmax decreased \( 43 \pm 19\% \) from their control values.

From all of these results, we concluded that Emax and Tmax are independent of wide variations in preload and afterload conditions under a given contractile state but that both Emax and Tmax very sensitively change with changes in the contractile state of the ventricle.

**CONSTANCY OF Emax AND ALTERATION OF Tmax IN RESPONSE TO HEART RATE CHANGES**

Increases in heart rate, produced by pacing during a given contractile state, significantly shortened Tmax but had no effect on Emax. The mean value of the rate of shortening of Tmax per 100-beats/min increase in heart rate caused by pacing was \( 45 \pm 10\% \) (sp) under both the control and the enhanced contractile states. As shown in Table 2, however, the increases in heart rate were always associated with epinephrine infusion in nonpaced preparations. The mean value of the rate of shortening of Tmax per 100-beats/min increase in heart rate caused by epinephrine infusion was \( 129 \pm 56\% \) and was significantly greater than the mean value in the paced hearts \( (P < 0.05) \). The mean rate of increase in \( \frac{(dP/dt)}{P} \) max per 100-beats/min increase in heart rate caused by pacing was \( 49 \pm 25\% \) (sp). Statistical test showed that this value was equal to the rate of shortening of Tmax associated with changes in paced heart rate.

**Discussion**

Warner (19), DeFares et al. (20), Beneken (21), and Rideout (22) used “reciprocal capacitance or compliance” or “elastance” as a parameter relating instantaneous intraventricular pressure to volume in their models. We purposely avoided the use of these terms since elastance or reciprocal compliance more commonly means the ratio of incremental changes in pressure and volume. Recently, Templeton et al. (23) studied the volume stiffness defined as the incremental pressure-volume ratio \((\Delta P/AV)\) of the isovolumically contracting left ventricle during one cardiac cycle. They found that within one cardiac cycle the volume stiffness increased and then decreased with time in linear proportion to the concomitant ventricular pressure. The volume stiffness studied by Templeton et al. (23) is different in many respects from our instantaneous pressure-volume ratio, \( E(t) \), and a direct comparison between the two is not possible at the moment. Rather the physiological meaning of \( E(t) \) is more closely related to the concept of time-varying elastance or reciprocal compliance. Therefore, our present analysis gives a physiological basis to those cardiac models.

We found supportive evidence for the concept of \( E(t) \) in the work of other investigators. Downing and Sonnenblick (24) showed in cat papillary muscle that length-tension curves obtained from isotonic contractions were virtually identical to those obtained from isometric contractions. This finding is illustrated in Figure 6A, which is a reproduction of Figure 1B in their paper. The figure shows that, for any given force to be developed, the muscle shortens to the same final length regardless of the initial length and the mode of contraction. We think that this basic property of myocardial contraction manifested itself in our observation of the load independency of Emax. The force-length curve intercepted the fiber length axis at some positive length (10 mm in the example shown in

**FIGURE 6**

A: Length-tension curve obtained by isometric and isotonic contractions during a contractile state. B: Length-tension curves before and after the addition of norepinephrine. (Reproduced from Figs. 1B and 3 of Downing and Sonnenblick [26] with the permission of the authors and publisher.) In A the different symbols show the data points obtained from different initial fiber lengths. Three solid rectilinear lines indicate the pathway of fiber contraction. In B the solid and the broken curves show the length-tension curves during the control and the enhanced contractile states, respectively.
VENTRICULAR PRESSURE-VOLUME RATIO

Fig. 6A). In Figure 6B, we reproduced Figure 3 from the same paper. As shown, when the contractile state was enhanced by norepinephrine the slope of the force-length curve became steeper, but the intercept remained unchanged.

Monroe et al. (25, 26) studied the pressure-volume relation of isolated canine left ventricle as it contracted isovolumically, auxotonically, or isobarically. We found in their reports that the maximally contractile state was enhanced by norepinephrine but the intercept remained unchanged.

As shown, when the line irrespective of the mode of contraction and the end-diastolic volume. The volume axis intercept of this line drawn by us through their data points had a positive value. This undoubtedly corresponds to Vd that we observed. Again, the slope of the line increased with epinephrine infusion without any noticeable shift of the volume axis intercept. Similar findings to these were observed by Urschel et al. (27) and Taylor et al. (28) in the canine left ventricle. These findings by other investigators are quite consonant with the present results of the load independence of Emax of the left ventricle.

From the similarity analysis of the shape of the E(t) curve we concluded that all E(t) curves have a unique basic shape. The shape is invariant with dogs, loading conditions, heart rates, and contractile states as seen from Figure 5. The single curve, Eτ(tτ), in Figure 5 enables mathematical description of any E(t) curve once Emax and Tmax values are specified. The mathematical description is given by E(t) = Emax - E N (t/Tmax).

The necessity of both the Emax and Tmax parameters for characterizing the E(t) curve is obvious from the findings that the relative sensitivities of Emax and Tmax (represented by α and β in Table 2) to a given change in inotropic background were different in individual dogs. Also, we could not find any significant correlation of changes in Emax and Tmax among individual dogs. In other words, we could not estimate one parameter by knowing the other in a given dog. Therefore, to characterize the instantaneous pressure-volume ratio curve, we must know Emax and Tmax simultaneously. The lack of a close correlation between the two parameters seems consistent with the work of Reeves and Hefner (29), who measured isometric force generated by ventricular wall muscle. They observed that the relative sensitivities of the peak developed force and the duration of contraction to different inotropic agents were not equal. A similar discrepancy was also observed by Sonnenblick (30, 31) in isolated papillary muscle with respect to the relative sensitivities of myocardial force and shortening velocity to different inotropic agents such as norepinephrine, strophanthidin, and calcium.

Based on our findings and their consistency with those in the literature, we conclude that the instantaneous pressure-volume ratio curve, E(t), can be represented by Emax and Tmax and that changes in these parameters explicitly reflect the variations in the contractile state of the ventricle.

Appendix

The pressure, P, and the volume, V, of N moles of air are related to the absolute temperature, T, by PV = nRT, where R is the gas constant of air. To accurately know a small change in V from an observed change in P, T should be constant. In our cardiometer system, volume changes occurred much faster than the heat exchange through the air reservoir wall. Therefore, T changed transiently because of the change in internal energy caused by the adiabatic volume change. Owing to the transient temperature change in our system, a step change in volume did not produce a step change in pressure but some overshoot in pressure, as shown in the top of Figure 7. This transient pressure overshoot could be eliminated, as shown in the middle of this figure, by adding an electric filter to the output of the pressure signal conditioner. The filter is shown in the circuit diagram at the bottom of the figure. By adjusting the values of capacitance (C) and resistance (R) in the circuit, we could obtain compensated pressure tracings which were always proportional in amplitude to the input volume changes and had no delay within the frequency range of ventricular volume change.

![Figure 7](http://circres.ahajournals.org/)

**Simultaneous recordings of the uncompensated (top) and the compensated (middle) pressure signals when the air volume was changed in steps in the cardiometer system.**

The signal compensation was achieved by a filter circuit shown in the bottom of this figure. R1, R2, and C were appropriately determined so that a step signal without any over- or under-shoot could be obtained on the recorder as the air volume in the cardiometer was changed in steps.
References


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