Evaluation of Left Ventricular Contractile Performance Utilizing End-Systolic Pressure-Volume Relationships in Conscious Dogs

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SUMMARY. The relationship between left ventricular end-systolic pressure and volume has been proposed as a model of left ventricular contraction which may be useful for quantifying inotropic state independent of preload and afterload. Although the model has been well-validated in isolated hearts, systematic evaluation in conscious animals with an intact peripheral circulation has been limited. Accordingly, we derived end-systolic pressure-volume relationships in twelve conscious dogs, chronically instrumented to measure left ventricular pressure and dimensions from endocardial ultrasonic crystals in three orthogonal axes. We examined the linearity of the end-systolic pressure-volume relationship, its response to alterations of inotropic state and the peripheral circulation, and the influence of \( \beta \)-adrenergic reflexes. End-systolic pressure-volume relationships were constructed by linear regression of end-systolic pressure-volume coordinates produced by transient inferior vena caval occlusions during atrial pacing. The relations were highly linear; of 127 inferior vena caval occlusions, the correlation coefficient was 0.96 ± 0.05 (mean ± SD). The slope of the end-systolic pressure-volume relationship was not significantly altered either by a moderate resistive afterload induced by angiotensin II infusion, or by a moderate increase in preload produced by dextran, but was increased from 4.7 ± 2.3 to 6.5 ± 2.2 mm Hg/ml (\( P < 0.05 \)) in response to the positive inotropic stimulus of dobutamine. The volume intercept at zero end-systolic pressure was unaffected by dextran or dobutamine, but was decreased from 12 ± 8 to 5 ± 11 ml (\( P < 0.01 \)) by angiotensin II infusion, indicating a leftward shift of the end-systolic pressure-volume relationship. Pretreatment with propranolol to block \( \beta \)-mediated adrenergic reflexes did not affect the response to angiotensin or dextran. We conclude that linear end-systolic pressure-volume relationships can be derived in conscious dogs with intact sympathetic reflexes. The slope appears to reflect left ventricular contractile function and is independent of the level of afterload and preload. However, the relation is shifted leftward by high levels of arterial resistance, indicating that end-systolic pressure is a function, not only of end-systolic volume and inotropic state, but also of the peripheral circulation, in this intact animal model. (Circ Res 54: 731-739, 1984)
This study was undertaken to evaluate systematically the behavior of the end-systolic P-V relationship in conscious dogs, chronically instrumented to measure simultaneous left ventricular (LV) pressure and volume. Our goals were to examine in this model: (1) the linearity of the relationship over a range of cardiac pressures and volumes; (2) the response of the parameters m and Vp to alterations of inotropic state and the peripheral circulation; and (3) the influence of the β-adrenergic nervous system on the definition and characteristics of the end-systolic P-V relation in the intact animals.

**Methods**

**Instrumentation**

Twelve healthy, adult mongrel dogs (20-35 kg) were instrumented under halothane anesthesia, through a left lateral thoracotomy, using sterile technique (Robotham et al., 1983). The instrumentation (Fig. 1) included left atrial pacing wires, a high fidelity pressure transducer (P-18, Konigsberg Instruments) in the LV apex, a polyvinyl small-bore catheter adjacent to the micromanometer for calibration, three pairs of endocardial (5 MHz) ultrasonic crystals in the anterior-posterior (AP), septal-lateral (SL), and apex-base (LA) dimensions, and a hydraulic occluder around the inferior vena cava (IVC). A small-bore polyvinyl catheter (not illustrated) was inserted into the left atrial appendage for drug administration. The wires and tubing were tunneled subcutaneously to the neck where they could be easily exposed for subsequent studies. Animals were allowed to recover from surgery for 1-2 weeks.

**Data Collection**

All studies were performed with the dogs lying quietly on their right side in a sling. The LV catheter was connected to a Statham P231D pressure transducer calibrated from a mercury manometer; the zero reference point was the vertebral column. The LV pressure signal from the micromanometer was adjusted to match that obtained from the fluid-filled catheter. The first derivation of LV pressure (dP/dt), and the dimensions of the three crystal pairs were recorded on an eight-channel, forced ink-pen oscillograph (Beckman Instruments), at a paper speed of 100 mm/sec. The six data channels were also A-to-D converted at 10-msec intervals and stored on floppy disk memory utilizing a minicomputer system (Zobex).

**Data Analysis**

The digitized, stored data were analyzed by means of a computer algorithm. End-diastole was defined as the Z-point of the high fidelity LV pressure tracing. Onset of ejection was taken at the time of maximum dP/dt. End-systole was defined as the maximum of the ratio of high fidelity LV pressure to volume (Sagawa, 1981), and end-ejection was defined at dP/dtmax (Abel, 1981). Beats with similar heart rates from 10-second recordings of data during steady state conditions were averaged from measurement of peak LV pressure, end-diastolic pressure, end-diastolic volume, heart rate, and dP/dtmax. Percent change of the anteroposterior diameter was calculated as the end-diastolic diameter minus the end-ejection diameter, divided by the end-diastolic dimension, times 100; mean Vcf, as the percent change in AP diameter divided by the ejection time; and ejection fraction, as the end-diastolic volume minus the end-ejection volume, divided by the end-diastolic volume, times 100 (Mahler et al., 1975a). Volume was calculated by assuming that the left ventricle was a general ellipsoid and that the three dimensions formed the principal axes of this structure, using the equation:

\[
\text{Volume} = \frac{\pi}{6} \times \text{AP} \times \text{SL} \times \text{LA}.
\]

Orientation of the crystal pairs in the three axes was confirmed by postmortem dissection of the left ventricle.

End-systolic P-V relations were constructed from end-systolic pressure-volume points obtained over a range of pressures and volumes produced by inflation of the IVC cuff occluder. During IVC occlusion, heart rate was kept constant by atrial pacing, utilizing small doses (0.1-0.5 mg) of atropine, as necessary, to prevent AV block. Individual beats with a heart rate 15% greater or less than the paced heart rate were excluded from the analysis. No effort was made to control for respiratory variation in pressure or volume. The end-systolic pressure-volume points from each IVC occlusion were subjected to least squared linear regression, starting with the highest end-
systolic volume. The slope, m, volume intercept, \( V_o \), and correlation coefficient, \( r \), of the end-systolic P-V relationship were then derived from each IVC cuff inflation. The mean values of m and \( V_o \) for each study condition in each dog were then obtained by averaging the slopes and volume intercepts of at least two separate IVC occlusions (average 2.7 occlusions for each study condition).

One hundred and twenty-seven IVC cuff inflations were utilized to generate 127 end-systolic P-V relationships for this study. Of these 127 relationships, 115 (91%) had an \( r \) value greater than or equal to 0.90; eleven had an \( r \) value greater than or equal to 0.82 but less than 0.90; and one had an \( r \) value of 0.77. The mean \( r \) value of the 127 relationships was 0.96 ± 0.05 (mean ± sd). The mean number of end-systolic pressure and volume coordinates for each of the 127 relationships was 12 ± 3.

Protocol

This study was performed in two portions. In the first, we obtained end-systolic P-V relationships during inotropic stimulation and during manipulation of preload and afterload in the presence of intact sympathetic reflexes in six dogs. In the second portion, the loading protocol was repeated in six additional dogs after pretreatment with 2 mg/kg propranolol (Ayerst Labs Inc.) to block beta-mediated sympathetic effects (Vatner et al., 1972).

During the first part, inotropic state was enhanced with a dobutamine (Eli Lilly) infusion of 10 \( \mu \)g/kg per min, and arterial pressure loading was performed over 10-15 minutes with an infusion of angiotensin II (Ciba Geigy Corp.) (0.5-2.5 \( \mu \)g/min), and volume loading was accomplished with an infusion of dextran (Pharmacia Labs) (500 ml over 5 minutes). After each infusion, all parameters were allowed to return to control values before proceeding with the next intervention. IVC occlusions were performed during control and during enhanced inotropic state, volume loading, and arterial pressure loading. During the second portion, IVC cuff inflations were performed during control, after propranolol, and during pressure and volume loading following propranolol.

In three dogs, at low cardiac volumes during IVC occlusion, an entrapment artifact near end-systole developed on the LV pressure tracing from the micromanometer. In these dogs, LV pressure from the fluid system was used to obtain end-systolic pressure after suitable correction for transmission delay. In order to assess the reliability of pressure derived from the fluid system for the construction of the end-systolic P-V relationship, we compared the slopes and volume intercepts of the end-systolic P-V relations obtained from the two methods of pressure recording in four dogs with both suitable micromanometer and fluid pressure signals. Neither the slopes (mean difference, 0.3 ± 0.8 mg Hg/ml [mean ± sd]) nor volume intercepts (mean difference, 1 ± 3 ml) were significantly different. Accordingly, we included data in the \( \beta \)-blocked portion of this study from the three animals in which only pressure from the fluid system was usable.

Volume Validation

LV volume was computed utilizing the crystal-determined dimensions, assuming a general ellipsoidal model for LV shape. Because the geometrical assumptions of this method may be altered by the changes of inotropic state or loading conditions employed in this study, we compared LV volumes calculated by this method to volumes obtained from geometrically independent techniques.

First, four dogs were additionally instrumented with an electromagnetic flow probe on the ascending aorta. In these animals, a range of steady state LV end-systolic volumes produced by incremental infusion of dobutamine and angiotensin II were calculated independent of geometry, using flow probe-derived measurements of stroke volume (SV) and radionuclide-derived measurements of ejection fraction (EF), by the formula:

\[
ESV = SV/EF - SV.
\]

Gated equilibrium radionuclide angiograms were obtained following in vivo red blood cell labeling with 20-30 mCi technetium-99m after the intravenous administration of stannous pyrophosphate. The dogs were positioned supine in a 30° right lateral position, and the \( \gamma \) camera was positioned in the 10° LAO/50° caudal tilt position which separated optimally the right and left ventricles in the plane of the interventricular septum. A 37 photomultiplier tube \( \gamma \) scintillation camera equipped with a low energy, all-purpose, parallel-hole collimator was used for image acquisition using a hardware zoom (2.0X). Image acquisition was such that count information in consecutive corresponding 30-msec frames of each cardiac cycle was summed and stored as images in the computer remote memory until each frame contained at least 2,000,000 counts. Using a semi-automated computer program (MDS MUDG), an LV region-of-interest for each image was defined, the activity in each LV region-of-interest during the cardiac cycle was determined, and an LV time-activity curve from these regions-of-interest was generated after background subtraction and temporal and spatial smoothing was completed. Background was obtained from an LV end-systolic paraventricular region. LV ejection fraction was calculated by subtracting end-systolic from end-diastolic counts and dividing by end-diastolic counts. This method of obtaining LV ejection fraction has been validated by comparison to the corresponding values obtained from simultaneous biplane contrast cineangiography (\( r = 0.93 \) (Starling et al., 1981)). End-systolic volumes measured by the crystal technique immediately after the radionuclide angiogram were compared to the radionuclide/flow probe-derived end-systolic volumes using least squares correlation. The results for the crystal-derived compared to the radionuclide-derived end-systolic volumes are contained in Table 1. For each dog there was a highly linear correlation between the values obtained by the two techniques (mean \( r \) value, 0.95 ± 0.02), although the relation was not that of the line-of-identity.

Next, four additional dogs were instrumented to allow

<table>
<thead>
<tr>
<th>Dog</th>
<th>Regression equation</th>
<th>( n )</th>
<th>( r )</th>
<th>SEE (ml)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>( V_c = 0.75 ) V_A + 24</td>
<td>9</td>
<td>0.94</td>
<td>3</td>
</tr>
<tr>
<td>2</td>
<td>( V_c = 0.52 ) V_A + 11</td>
<td>8</td>
<td>0.91</td>
<td>3</td>
</tr>
<tr>
<td>3 (#1*)</td>
<td>( V_c = 0.41 ) V_A + 14</td>
<td>6</td>
<td>0.95</td>
<td>2</td>
</tr>
<tr>
<td>3 (#2)</td>
<td>( V_c = 0.32 ) V_A + 1</td>
<td>8</td>
<td>0.96</td>
<td>2</td>
</tr>
<tr>
<td>4</td>
<td>( V_c = 0.54 ) V_A + 14</td>
<td>7</td>
<td>0.97</td>
<td>1</td>
</tr>
</tbody>
</table>

Table 1

Relation between Crystal-Derived and Radionuclide/Flow Probe-Derived End-Systolic Volumes in Four Dogs

Abbreviations: \( V_c \) = volume from ultrasonic crystals; \( V_A \) = volume from flow probe determined stroke volume and radionuclide determined ejection fraction; \( n \) = number of points; \( r \) = Pearson correlation coefficient; SEE = standard error of the estimate

* Dog 3 was studied twice (on two separate days).
the simultaneous measurement of ascending aortic flow with an electromagnetic flow probe and LV volume from the three orthogonal ultrasonically determined left ventricular dimensions. Similar to the protocol to produce the end-systolic pressure-volume relations, a range of ventricular volumes were produced by IVC occlusion in the control situation, and after the infusion of angiotensin II or volume loading with dextran. The crystal-derived stroke volume, calculated as end-diastolic left ventricular volume—end-ejection left ventricular volume, was compared with the simultaneously measured stroke volume from the aortic flow probe (Fig. 2; Table 2). In each animal, the calculated and flow probe-measured stroke volumes during IVC occlusions during control, angiotensin II infusion, or after dextran loading were related by a single linear regression ($r > 0.97$, $SEE < 1.0$ ml).

**Statistical Analysis**

Statistical analysis was performed by analysis of variance for repeated measures and paired t-tests, as appropriate. Where analysis of variance revealed a significant F-statistic, the Newman-Keuls test was utilized to determine significant difference of individual means from control (Winer, 1971). A $P$ value of less than 0.05 was taken to signify statistical significance.

The study was approved by the Institutional Laboratory Animal Committee.

**Results**

Figure 3 is a sample analog recording of a single IVC occlusion. Depicted are LV $dP/dt$, high fidelity LV pressure, and the anteroposterior, septolateral, and the long axis dimensions. The arrow designates the time of cuff inflation, after which there was a progressive fall in $dP/dt$, LV pressure, and the three dimensions. The anteroposterior, septolateral, and long axis dimensions were utilized to calculate instantaneous LV volume assuming the formula for a general ellipsoid. During this cuff inflation, end-systolic pressure and volume coordinates from these beats with successively decreasing pressures and volumes were utilized to construct the end-systolic P-V relationship.

Figure 4 is an example of the end-systolic P-V relationships obtained during control and during the infusion of dextran, angiotensin II, and dobutamine.
demonstrated results similar to those in Figure 4. With angiotensin II, there was a significant increase in peak LV pressure from 113 ± 16 to 157 ± 18 mm Hg (P < 0.01). LV end-diastolic pressure also rose from 3 ± 5 to 9 ± 7 mm Hg (P < 0.01). The slope of the end-systolic P-V relationship did not change during the angiotensin II infusion; however, the volume at zero end-systolic pressure (V₀) was decreased 62% from 12 ± 8 ml at control to 5 ± 11 ml with angiotensin II (P < 0.01), indicating a leftward parallel shift of the end-systolic P-V relation during this intervention.

With dextran, LV end-diastolic pressure and volume rose significantly (from 3 ± 5 to 15 ± 6 mm Hg and 58 ± 20 to 68 ± 21 ml, respectively, P < 0.01). Heart rate also increased from 121 ± 15 to 151 ± 25 beats/min (P < 0.05) as the atrial pacemaker was overridden by the spontaneous sinus rate. However, with dextran, neither the slope nor the volume intercept of the end-systolic P-V relationship was changed from control values.

With dobutamine, there were significant increases in ejection fraction, %ΔD, mean Vcf, and dP/dtmax, (all P < 0.05), demonstrating a positive inotropic effect from the agent. The slope of the end-systolic P-V relationship increased significantly by 38% from 4.7 ± 2.3 to 6.5 ± 2.2 mm Hg/ml (P < 0.05). V₀, although somewhat larger, did not change significantly from control.

In order to evaluate the effect of \( \beta \)-mediated sympathetic reflexes upon the end-systolic P-V relationship during the different states of the peripheral circulation, six additional animals were studied before and after propranolol and during the infusion of angiotensin II and dextran after \( \beta \)-blockade. The group results are listed in Table 4. The slope of the end-systolic P-V relationship was not significantly different from control after propranolol, during angiotensin II infusion, or dextran infusion, when compared by analysis of variance. Following propranolol, the infusion of angiotensin II or dextran did not significantly affect the slope of the end-systolic P-V relationship. The value of V₀ was significantly lower with angiotensin II, compared to control (—1 ± 4 vs. 6 ± 5 ml, P < 0.05). In order to verify that the decrement in V₀ during the angiotensin II infusion represented a leftward shift of the end-systolic P-V relation, and was not due solely to extrapolation to zero pressure, we selected beats with similar end-systolic volumes from \( \beta \)-blocked control and \( \beta \)-blocked angiotensin II cuff occlusions, and then compared corresponding end-systolic pressures. End-systolic volume was matched within 1 ml from six beats in six dogs (31 ± 5 ml with propranolol and 31 ± 5 ml with angiotensin II). At these matched end-systolic volumes, the end-systolic pressure during the angiotensin II, \( \beta \)-blocked cuff inflations was significantly greater (144 ± 9 mm Hg) than during the \( \beta \)-blocked cuff inflations prior to angiotensin II (117 ± 14 mm Hg; P < 0.01). Thus, the infusion of angiotensin II did indeed result in a leftward parallel shift of the end-systolic P-V relationship unrelated to an intact \( \beta \)-adrenergic nervous system.
To facilitate a qualitative comparison of the response of the slope of the end-systolic P-V relation (m), the ejection fraction, and dP/dt max during the various interventions to alter inotropic state and the peripheral circulation, the data from Tables 3 and 4 are plotted as average percent change from control in Figure 5. The slope, m, was slightly, but not significantly, decreased in response to preload augmentation with dextran while dP/dt max and EF were increased. Although the change in m due to the positive inotropic stimulus of dobutamine appears less than that of dP/dt max, it is greater than that of the ejection fraction. A similar order of sensitivity of the three indices to the negative inotropic effect of propranolol is also evident.

**Discussion**

This study demonstrates that highly linear end-systolic P-V relationships can be obtained, irrespective of the respiratory cycle, and in the presence of intact sympathetic reflexes. Positive inotropic stimulation increases the steepness of the end-systolic P-V relationship without a change in the volume intercept. Moreover, the slope of the relationship remains relatively unchanged by maneuvers which alter the major determinants of the peripheral circulation (i.e., blood volume and arterial resistance). However, elevation of peripheral resistance with angiotensin II appears to shift the end-systolic P-V relation leftward, resulting in a higher end-systolic pressure for any end-systolic volume. With the exception of this parallel leftward shift induced by higher resistive afterload, these findings in the conscious dog are similar to the concepts proposed by Suga and Sagawa (1974), based on experiments in isolated hearts.

Blockade of ß-mediated sympathetic reflexes by propranolol appears to have little influence upon the end-systolic P-V relationship or its response to alterations in the peripheral circulation. Although a
negative inotropic stimulus would have been expected to depress the value of m, the decrement in the slope after β-blockade was not significant. In part, this failure to demonstrate a significant change with application of analysis of variance for repeated measures may relate to the intrinsic variation among animals within each treatment group. Alternatively, the small decrement may also reflect the low level of sympathetic tone in the resting, conscious dog (Vatner et al., 1972). Importantly, an increase in preload produced by dextran or afterload by angiotensin II did not significantly alter the slope of the relationship compared to the β-blocked control state, indicating that the effects seen in dogs without propranolol are not mediated by alterations in sympathetic drive to the ventricle. In particular, the infusion of angiotensin II during β-blockade produced a significant reduction in $V_0$, just as in the non-β-blocked state. Accordingly, this leftward parallel shift associated with an increase in arterial resistance does not result from sympathetically mediated changes in ventricular contractile function.

Although the slope of the end-systolic P-V relation appears to reflect LV contractile function, it is not obviously superior to the more traditional indices. However, compared to ejection fraction, percent change in AP diameter, mean Vcf, and dP/dt_max, the slope, m, was the only parameter which revealed a qualitative decrease in response to both augmentation of left ventricular preload and resistive afterload (Fig. 5, Table 3). This property of m may be of some value where LV preload, but not contractility, are augmented, and isovolumic and ejection phase indices are "spuriously" elevated (Mahler et al., 1975a). The ejection fractions in our study are somewhat lower than the angiographic ejection fraction in normal humans, but are consistent with previous results in instrumented, conscious dogs (Olsen et al., 1983; Visner et al., 1983).

Several potential limitations of this study need to be considered. The first potential limitation is the technique utilized for LV volume measurement. Although ultrasonic crystals in three dimensions and a general ellipsoidal model have been utilized and validated for the calculation of LV volume (Rankin et al., 1976), these calculations are based on geometric assumptions about LV shape at end-diastole and end-systole. In particular, LV internal shape at end-systole is less likely to be ellipsoidal, due to a variable amount of volume displacement by the papillary muscles. In our study, we validated the crystal method for calculating end-systolic volume by comparing it to geometrically independent techniques. Although the relationship between the calculated volumes and the measured volumes, using other techniques, was not the line of identity, the crystal technique and the geometrically independent approaches were linearly related, despite potential changes in LV geometry that may occur during the interventions employed in this study. Therefore, the crystal measurement of LV volume yields an index of LV volume. Since end-systolic pressure is linearly related to this index in these conscious animals, it follows that end-systolic pressure is also linearly related to true end-systolic volume, and that the behavior of the relationship in response to interventions will be similar.

A second potential limitation of our methods is that changes in preload or afterload altered the inotropic state through activation of baroreceptor reflexes. Most of these changes would have occurred through the β-adrenergic limb of the sympathetic nervous system (Sarnoff et al., 1960). Importantly, if baroreflex-derived changes in sympathetic tone were a significant factor in the generation of the end-systolic P-V relation in the autonomically intact animal, then end-systolic pressure-volume points during the later portion of IVC occlusions would be displaced leftward compared to the "ideal" end-systolic P-V line. Accordingly, $V_0$ should have been smaller prior to propranolol, compared to the value obtained after sympathetic reflex attenuation. In general, this was not observed; in fact, $V_0$ was slightly smaller after propranolol, although this change was not significant. Since our results were similar before and after pretreatment with propranolol, we suspect that such baroreceptor reflexes have little effect on the generation of the end-systolic P-V relation by IVC occlusion, or on the response of the relationship to changes in the peripheral circulation. This finding is consistent with the study of Vatner et al., who found little influence of the carotid sinus reflex on myocardial contractility in the conscious dog (Vatner et al., 1972). This may relate to the low basal level of sympathetic stimu-
lation in the dog or to the exogenous control of the heart rate by atrial pacing in our study. Whether similar findings would be present in man, or when heart rate is allowed to vary spontaneously, is uncertain.

The explanation for the small leftward parallel shift of the end-systolic P-V relationship produced by an increase in arterial resistance is not entirely clear. There are several potential explanations for this phenomenon. Of greatest concern would be that the level of inotropic state was enhanced through the Anrep effect, or directly by the angiotensin II. This seems unlikely in that: (1) the Anrep effect is seen with abrupt, not gradual increases in aortic pressure and even in these circumstances is not marked in conscious dogs (Vatner et al., 1974); (2) positive contractile interventions increase the slope of the end-systolic P-V relation, and the slope during angiotensin II was similar to the control slope; (3) any positive inotropic effects of angiotensin II mediated through sympathetic stimulation (Farr and Grupp, 1967), should have been blocked by pretreatment with propranolol; and (4) Sunagawa et al. (1981) have recently reported a similar leftward shift produced by elevated arterial resistance in an isolated heart preparation ejecting into a model of the peripheral circulation. Thus, other non-inotropic factors would appear to be responsible for the leftward parallel shift of the end-systolic P-V relation seen during angiotensin II infusion.

The original formulation of the end-systolic pressure-volume model proposed that the time to \( E_{\text{max}} \) was independent of cardiac loading and only a function of inotropic state (Sagawa et al., 1977; Sagawa, 1978). Subsequently, Elzinga and Westerhof have suggested that the time to \( E_{\text{max}} \) is, in fact, load-dependent, and will increase in response to an elevation in afterload (Elzinga and Westerhof, 1981), perhaps shifting the end-systolic P-V relationship leftward. A second potential explanation relates to the difficulty in defining the time of end-systole in the intact preparation. Although we defined end-systole as the time in which the ratio of LV pressure to volume is maximal, as suggested by Sagawa (1981), the pressure-volume loop of individual beats often demonstrates a substantial "shoulder" near end-ejection which makes the precise timing of end-systole difficult. Last, the leftward parallel shift may be related to ventricular internal resistance during ejection (Hunter et al., 1983; Schropp et al., 1983). According to their model, end-systolic pressure is not only a function of end-systolic volume but also of end-systolic flow. At higher flows, end-systolic pressure is lower than that predicted by a pure elastance model. At higher peripheral resistance, due to angiotensin II infusion, end-systolic flow at any end-systolic volume might be lower than at control, resulting in a higher end-systolic pressure. Further studies will be required in order to differentiate between these potential mechanisms.

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Sodums et al./End-Systolic P-V Relations in Conscious Dogs

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