Simultaneous determination of left ventricular end-systolic pressure-volume and pressure-dimension relationships in closed-chest dogs

William C. Little, M.D., Gregory L. Freeman, M.D., and Robert A. O'Rourke, M.D.

ABSTRACT The left ventricular end-systolic pressure-volume relationship is a load-insensitive measure of left ventricular performance. The relationship at end-systole between left ventricular pressure and dimension is more easily obtained, but the conflicting results of previous studies make it unclear if it has the same properties as the left ventricular end-systolic pressure-volume relationship. To address this issue, 11 dogs were instrumented to measure left ventricular pressure and three orthogonal left ventricular dimensions. Left ventricular pressure and dimensions were varied by use of caval occlusion. Left ventricular volume was calculated as an ellipsoid. The left ventricular end-systolic pressure-volume relationship and each of the three end-systolic pressure-dimension relationships were described by straight lines ($r = .97 \pm .02$, mean ± SD). In six animals, dobutamine produced similar significant increases ($p < .01$) in the slope of the end-systolic pressure-volume relationship (244 ± 61% of control), the end-systolic pressure–anterior-posterior dimension relationship (248 ± 89%), the end-systolic pressure–septal-lateral dimension relationship (211 ± 95%), and the end-systolic pressure–basal-apical dimension relationship (210 ± 85%). The intercepts at zero pressure were relatively unchanged by dobutamine. In contrast, occlusion of the distal left anterior descending coronary artery in five animals produced a rightward shift of the left ventricular end-systolic pressure-volume relationship and the pressure–basal-apical dimension relationship, while the pressure–anterior-posterior dimension and pressure–septal-lateral dimension relationships were relatively unaffected. We conclude that the relationships between left ventricular end-systolic pressure and volume and left ventricular end-systolic pressure and each of three orthogonal left ventricular dimensions respond in a similar manner to global changes in contractility, but display different responses to regional ischemia. Thus, left ventricular end-systolic pressure-dimension relationships may be used to assess global but not segmental changes in left ventricular performance.


THE LEFT VENTRICULAR end-systolic pressure-volume relationship has been a subject of intensive study in the past several years.1,2 Studies in isolated, isovolumetric, and ejecting canine hearts,1,2 preinstrumented dogs,3 and in man4–5 have shown that the left ventricular end-systolic pressure-volume relationship is closely approximated by a straight line, and thus can be described by its slope and extrapolated intercept on the volume axis. This relationship is relatively independent of change in preload and incorporates a measure of afterload, the end-systolic pressure. Global changes in contractility influence the slope of the relationship, but have little influence on its volume intercept.1,3 The fact that the left ventricular end-systolic pressure-volume relationship is relatively insensitive to changes in loading conditions makes it attractive as a measure of cardiac performance since loading conditions are often difficult to control. This benefit is offset by the need for multiple determinations of left ventricular volume.

Because of the difficulty in measuring left ventricular volume, some investigators have replaced the end-systolic volume with a left ventricular dimension and the resulting end-systolic pressure-dimension relationship has been used to assess left ventricular performance.6–11 In clinical studies, the left ventricular end-systolic septal-lateral dimension has been measured by M mode echocardiography6–11 and in experimental studies the anterior-posterior left ventricular dimen-
sion has been determined with use of implanted ultrasonic crystals.\(^6,7\) Geometric considerations suggest that the linear left ventricular end-systolic pressure-volume relationship does not necessarily indicate that left ventricular end-systolic pressure-diameter relationships will be adequately described by a straight line. Some previous studies of the latter have only used a small number of points,\(^6,7,9\) so that the linearity of these relationships are difficult to assess.

Very little data is available on simultaneously generated pressure-volume and pressure-dimension relationships. Sagawa et al.\(^11\) have reported data from one isolated, perfused dog heart that suggest the relations respond in a similar fashion to inotropic stimulation. Data from other studies,\(^6,7\) however, indicate that the end-systolic pressure-dimension relationship may behave differently than the end-systolic pressure-volume relation. In a study on conscious dogs, Mahler et al.\(^6\) found that dobutamine shifted the left ventricular pressure-diameter relationship to the left, decreasing the volume intercept without changing the slope. Using a similar preparation, Sagawa et al.\(^11\) have shown preliminary data from four conscious dogs that demonstrate an inconsistent response of the end-systolic pressure-diameter relationship to inotropic stimulation. In two of these animals the relationship was shifted to the left, with little alteration of slope, and in two there was a change in slope with little change in volume intercept. In neither of these studies were the pressure-dimension relations compared with simultaneously acquired pressure-volume relationships. These conflicting data suggest that further comparison of pressure-volume and pressure-dimension relationships is required before they can be used interchangeably in the assessment of left ventricular performance.

This study was undertaken to simultaneously determine the left ventricular end-systolic pressure-volume and three orthogonal left ventricular end-systolic pressure-dimension relationships. We compared their characteristics under control conditions as well as their responses to dobutamine and regional left ventricular dysfunction produced by coronary artery occlusion.

**Methods**

**Instrumentation.** Eleven healthy, adult, mongrel dogs were instrumented as we have previously described.\(^3,12,13\) In brief, a left lateral thoracotomy was performed in each dog by sterile techniques and the pericardium was opened widely. A micromanometer pressure transducer (Kongisberg, Pasadena, CA) and a catheter for transducer calibration were inserted through a left ventricular apical stab wound (figure 1). Three pairs of ultrasonic crystals were implanted in the endocardium of the left ventricle to measure the anterior-posterior (D\(_{AP}\)), septal-lateral (D\(_{SL}\)), and long axis or basal-to-apical (D\(_{LA}\)) dimensions. Inflatable hydraulic occluder cuffs were placed around the inferior and superior vena cava.

**Data collection.** After full recovery from the thoracotomy (10 days to 2 weeks) each dog was studied while lying on its side in a sling after sedation (with intravenous fentanyl [0.03 to 0.06 mg/kg] in combination with droperidol [1.5 to 3.0 mg/kg]) and intubation. Marked changes in heart rate were prevented by the intravenous administration of atropine sulphate (0.2 mg/kg).

The left ventricular catheter was connected to a Statham P23Db pressure transducer and calibrated with a mercury manometer. The zero reference point was the vertebral column. The left ventricular pressure signal from the micromanometer was adjusted to match the fluid-filled 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 signals were recorded on an eight-channel oscillograph (Beckman Instruments, Shiller Park, IL). Analog signals were digitized with an on-line analog-digital convertor at 10 msec intervals (100 Hz) and stored on a floppy disk memory system.

**Experimental protocol.** To minimize the influence of fluctuations in intrathoracic pressure, data were recorded over 12 sec periods while the dogs were apneic after a brief period of hyperventilation. During the recording period, the endotrachial tube was held open to the atmosphere and the dogs were observed to make certain they made no respiratory efforts.

Data were initially recorded during a steady-state control period to obtain baseline values. The control left ventricular end-systolic pressure-volume and pressure-diameter relationships were then generated by two transient vena caval occlusions (figure 2). The occlusion resulted in a 40 to 80 mm Hg drop in left ventricular systolic pressure. Dobutamine (10 \(\mu g/kg/min\)) was then infused in six animals. Signals were recorded during a steady-state period, and then the end-systolic pressure-volume and pressure-dimension relationships were again generated by two transient vena caval occlusions.

In five animals occluder cuffs were also placed around the left anterior descending coronary artery distal to the origin of a large diagonal branch. Transient inflation of this occluder during instrumentation produced apical cyanosis and dyskinesia without appreciable effect on the anterior or lateral left ventricular walls. These animals were studied after treatment with atropine and propranolol (2 mg/kg iv). Two caval occlusions were performed and then repeated 1 min after inflation of the coronary artery occluder.\(^13\)

**Postmortem study.** At the conclusion of the experiments, the animals were killed and their hearts were examined to confirm the proper positioning of the instrumentation.
Data analysis. The stored digitized data were analyzed with use of computer algorithms.\textsuperscript{3, 12, 13} Hemodynamic values in each dog were obtained by averaging the data obtained during the 12 sec steady-state recording periods. The data obtained during the vena caval occlusions were analyzed at end-systole. Only caval occlusions that produced at least a 40 mm Hg drop in left ventricular end-systolic pressure and contained no premature ventricular beats were analyzed. End-systole was defined at the time in which the ratio of the left ventricular pressure to volume became maximal.\textsuperscript{1, 2} End-diastole was defined as the Z point in the high-fidelity left ventricular pressure tracing. Left ventricular volume (V) was calculated from the three endocardial left ventricular dimensions\textsuperscript{3, 12, 13} with the equation
\[ V = \frac{\pi}{6} D_{ap} D_{sl} D_{la} \]

The end-systolic pressure and volume were fit by linear least squares to the following equation:
\[ P = E (V - V_o) \]

where \( P \) = left ventricular pressure; \( V \) = left ventricular end-systolic volume; \( E \) = slope of the left ventricular end-systolic pressure-volume relationship; \( V_o \) = the volume intercept of the end-systolic pressure-volume relationship. The left ventricular end-systolic pressure-volume relationship was evaluated by fitting the pressure-diameter data to the following equation:
\[ P = M (D - D_o) \]

where \( M \) = the slope of the left ventricular end-systolic pressure-volume relationship; \( D \) = the left ventricular dimension; \( D_o \) = the dimension intercept of the left ventricular end-systolic pressure-volume relationship.

Statistical methods. Comparisons before and after the infusion of dobutamine were made by paired t test.\textsuperscript{14} The accuracy of the linear fits of the end-systolic pressure-volume and pressure-diameter relationships were assessed by the Pierson correlation coefficient. All results are summarized as the mean \pm SD, and the level of significance was taken as \( p < .05 \).

Results

Because of the pretreatment with atropine, heart rate increased only slightly during the infusion of dobutamine (185 \pm 28 vs 168 \pm 31 beats/min, \( p = NS \)). As expected, dobutamine produced an increase in peak left ventricular dp/dt (3581 \pm 915 vs 2232 \pm 740 mm Hg/sec, \( p < .05 \)) and reduced left ventricular end-diastolic pressure (2.0 \pm 2.1 vs 8.1 \pm 3.2 mm Hg, \( p < .05 \)) and end-systolic volume (28.3 \pm 8.8 vs 36 \pm 8.7 ml, \( p < .5 \)), while the end-systolic pressure was relatively unchanged (160 \pm 15 vs 150 \pm 32 mm Hg, \( p < .05 \)).

End-systolic pressure-volume and pressure-dimension data. The relationship between the left ventricular end-systolic pressure and volume and the left ventricular end-systolic pressure and each of the three orthogonal left ventricular dimensions in a typical animal are shown in figure 3. The regression information on data from each animal is contained in table 1. Both during control and after the infusion of dobutamine the left ventricular end-systolic pressure-volume relationships were described by straight lines (\( r \geq .95 \)). Similarly, the relationships between the left ventricular end-systolic pressure and each of the three left ventricular dimensions were also linear (\( r > .93 \) in all but two instances; tables 2 to 5). As expected, the infusion of dobutamine produced an increase in the slope of the left ventricular end-systolic pressure-volume relationship (from 7.7 \pm 2.9 to 18.6 \pm 7.7 mm Hg, \( p < .05 \)). This was associated with little change in the volume intercept (12.9 \pm 6.3 vs 14.5 \pm 7.9 ml, \( p = NS \)). Dobutamine produced a similar change in each of the three left ventricular end-systolic pressure-dimension relationships (tables 1 to 4, figure 4). In each instance, the slope of these relationships markedly increased in response to the infusion of dobutamine, while there was little change in the dimension intercepts. The magnitude of the slope change in response to dobutamine was similar for the end-systolic pressure-volume relationship and each of the three end-systolic pressure-dimension relationships (figure 4).

The effect of regional ischemia produced by distal left anterior descending coronary artery occlusion is

\[ \begin{array}{c|c|c|c|c|c}
\text{Dog No.} & n & r & V_o & \text{Control} & \text{Dobutamine} \\
\hline
1 & 36 & .995 & 7.19 & 9.9 & 40 & .981 & 11.55 & 8.7 \\
2 & 61 & .978 & 10.69 & 17.7 & 28 & .950 & 27.78 & 18.5 \\
3 & 60 & .985 & 11.75 & 8.2 & 63 & .964 & 25.13 & 9.24 \\
4 & 39 & .990 & 3.96 & 8.6 & 49 & .986 & 9.66 & 11.5 \\
5 & 71 & .983 & 6.74 & 9.4 & 71 & .964 & 23.35 & 10.2 \\
6 & 28 & .996 & 5.99 & 23.5 & 36 & .969 & 14.18 & 28.8 \\
\hline
\text{Mean} & & 7.7 & 12.9 & 18.6^a & 14.5 & 7.7 & 14.5 \\
\pm SD & & 2.9 & 6.3 & 7.9 & & & & \\
\hline
\end{array} 
\]

\( n = \) number of points.
\( ^a p < .05. \)
shown in figure 5 and tables 5 to 8. As expected from previous reports coronary artery occlusion produced a rightward shift in the left ventricular end-systolic pressure-volume relationship, increasing the volume intercept from 14.8 ± 8.3 to 16.6 ± 8.1 ml (p < .02). The end-systolic pressure-D$_{SA}$ relationship showed a similar shift, with an increase in the intercept (p < .01) and little change in the slope. The pressure-D$_{DA}$ and the pressure-D$_{SL}$ relationships were relatively unaffected by distal left anterior descending occlusion.

**Discussion**

This study demonstrates that in closed-chest dogs the left ventricular end-systolic pressure-volume relationship and each of three orthogonal left ventricular end-systolic pressure-dimension relations show a similar response to the infusion of dobutamine. Both the pressure-volume and pressure-dimension relationships showed a marked increase in slope with little change in volume intercept as a result of inotropic stimulation.
The similarity of these relations under control conditions and after dobutamine infusion indicates that the use of left ventricular end-systolic pressure-dimension relationships as indexes of changes in global cardiac performance is warranted.

These results differ from those reported by Mahler et al., who found that inotropic stimulation produced a change in the dimension intercept, not the slope of the left ventricular end-systolic pressure-dimension relationship. The studies differ in that we evaluated the pressure-dimension relationships at peak elastance, as originally proposed by Suga and Sagawa, while Mahler et al. evaluated the relationship at end-ejection. When the arterial circulation is influenced by the infusion of a vasoconstrictor, such as used in their study, the end-ejection pressure-volume relationship may not accurately reflect that at end-systole. Marked alterations in the arterial circulation produced by vasoconstrictors may also influence the position of the left ventricular end-systolic pressure-volume relation.

Furthermore, in the study of Mahler et al., the relationships were determined from only two points, and the data from all the animals were grouped before analysis. As can be seen in table 3 of their article, there is substantial interanimal variability in the end-systolic pressures and dimensions. Our results show, however, that in each animal the infusion of dobutamine produced a change in the slope of the end-systolic pressure-dimension relationship.

### TABLE 2

<table>
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<tr>
<th>Dog No.</th>
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<tr>
<td>±SD</td>
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<td>8.3</td>
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</table>

<sup>a</sup>p < .05.

### TABLE 3

<table>
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</tr>
<tr>
<td>±SD</td>
<td>±3.4</td>
<td>±3.8</td>
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</table>

<sup>a</sup>p < .05.
systolic pressure-dimension relationship generated by caval occlusion, with little change in the volume intercept.

It is important to point out that the similarities in the pressure-volume and pressure-dimension relationships apply to all three orthogonal left ventricular dimensions. Clinical studies commonly use the $D_{al}$ obtained with M mode echocardiography, while animal studies use the $D_{ap}$ obtained with piezoelectric crystals. Our data indicate that either of these methods will produce pressure-dimension relationships that accurately reflect the pressure-volume relation during global changes in contractility.

We also assessed the response of the end-systolic pressure-dimension relationships to regional ischemia. Consistent with the observations of Sunagawa et al.\textsuperscript{15} in isolated, isovolumetric hearts and our observations in intact dogs,\textsuperscript{13} regional ischemia produced a parallel rightward shift of the left ventricular end-systolic pressure-volume relationship. This apical ischemia shifted...
the end-systolic pressure-D_{LA} relationship, but had little effect on the pressure-D_{AP} and pressure-D_{SL} relations. This result indicates that left ventricular end-systolic pressure-dimension relations are not adequate to assess the effects of regional abnormalities, such as those that may occur in patients with ischemic heart disease, on global left ventricular performance. Similarly, pressure-dimension relationships may not accurately reflect the left ventricular pressure-volume relation when the left ventricular configuration is markedly altered.

Since our method of volume calculation was based on the three left ventricular dimensions, it is important to demonstrate their accuracy. This method is similar to that used and validated by Olsen et al.,\textsuperscript{20} except that we determined the left ventricular endocardial dimensions directly and thus subtraction of left ventricular wall volume was not necessary. We have previously observed that this method of left ventricular volume calculation provides a consistent index of left ventricular volume ($r > .97$) despite marked changes in left ventricular configuration.\textsuperscript{3,12,13} Furthermore, our prior studies have shown that the end-systolic pressure-volume relationship generated by this method behaves like that generated in isolated dog hearts in which volume is measured directly.\textsuperscript{3,13} Thus, our results show a true similarity of the left ventricular end-systolic pressure-volume and the pressure-dimension relationships.

There are several factors that must be considered when applying our data to clinical situations. This study was performed after opening the pericardium, after the infusion of atropine to minimize changes in heart rate, and during apnea to minimize the effects of alterations of intrathoracic pressure. The animals were also sedated. These controlled conditions were used in our study to produce the most accurate assessment of the parameters of interest. In the clinical setting, where these variables are not subject to strict control, the pressure-volume or pressure-dimension relationships generated may be somewhat less accurate.

In conclusion, we have shown that the relationship between left ventricular end-systolic pressure and each of three orthogonal left ventricular dimensions are lin-

### Table 5

<table>
<thead>
<tr>
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<th>LAD occlusion</th>
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$\Delta p < .02$, compared with control.

### Table 6

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<td>Mean</td>
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### Table 7

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### Table 8

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<tbody>
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$\Delta p < .01$, compared with control.
ear and respond to dobutamine in the same manner as the left ventricular end-systolic pressure-volume relationship. In contrast, all of the left ventricular end-systolic pressure-dimension relationships did not accurately reflect the effect of regional ischemia on the global left ventricular end-systolic pressure-volume relationship. Thus, it appears that left ventricular end-systolic pressure-dimension relations may be useful in assessing global but not regional changes in left ventricular performance.

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