In Vivo Assessment of Left Atrial Contractile Performance in Normal and Pathological Conditions Using a Time-Varying Elastance Model

Brian D. Hoit, MD; Yanfu Shao, MD; Marjorie Gabel; Richard A. Walsh, MD

**Background** Contractile function of the ex vivo, isolated left atrium (LA) has been described by a time-varying elastance, but this atrial chamber property has not been shown in vivo.

**Methods and Results** Instantaneous LA pressure-volume (P-V) relations were studied in 12 anesthetized, autonomically blocked, atrially paced dogs. LA volume was calculated from orthogonal sonomicrometer pairs using a cast-validated formula. Data were collected during increases in LA pressure produced by a phenylephrine bolus (200 to 400 µg IV). Isochronal P-V points from 5 beats, representing a wide range of atrial pressures, were fitted by linear regression analysis (range of $R^2$, 0.92 to 0.99). There were significant time-dependent increases in increments of $E_{00}$ and small but statistically insignificant decreases in the volume axis intercepts $[V_{00}]$ of the instantaneous LA P-V relations during atrial contraction; maximal elastance ($E_{max}$) occurred 29±16 milliseconds before atrial end systole (minimal LA volume). $E_{max}$ was not significantly different than the slopes of either the nonisochronal end-systolic P-V relation ($E_{n0}$) or the nonisochronal maximal P-V relation ($E_{max}$): $5.5±2.8$, $4.3±1.5$, and $5.4±4.2$ mm Hg/mL, respectively. In 7 dogs, data were collected both before and after a rapid infusion of calcium gluconate (1 to 2 g IV). $E_{max}$ increased significantly with a calcium-induced increase in inotropic state ($4.5±1.6$ to $5.7±1.8$ mm Hg/mL, $P<.01$), but the volume axis intercept was unchanged ($3.6±0.7$ versus $3.4±1.9$, $P=NS$). In 4 additional dogs with heart failure (mean LA pressure, $26±6$ mm Hg) produced by 3 weeks of rapid right ventricular pacing, LA stroke volume was significantly greater than elastance determinations were similar to those of normal dogs. However, the effects of calcium infusion on LA function were attenuated in these animals.

**Conclusions** We conclude that (1) in the intact heart, LA contraction may be approximated by time-varying elastance with time-dependent changes in $E_{00}$ and that (2) LA systolic P-V relations using either the nonisochronal maximum P-to-V ratio or end systole may be useful as an estimate of $E_{max}$, are highly linear and sensitive to calcium-induced changes in inotropic state, and may be useful in identifying LA chamber adaptation to chronic hemodynamic loads. (*Circulation*. 1994; 89:1829-1838.)

**Key Words** • elastance • atrium • cardiac mechanics • heart failure

Although instantaneous left atrial pressure-volume relations have been described by a time-varying elastance in the isolated left atrium, this atrial chamber property has not been demonstrated in vivo. Assessment of atrial systolic elastance has been hampered by the lack of an accurate measurement of left atrial volume with adequate sampling frequency. Recently, we showed that left atrial volume can be estimated accurately with high temporal resolution sonomicrometry using two nearly orthogonal atrial dimensions. In the present study, we characterize left atrial contractile function in the pressure-volume domain using open chest, anesthetized dogs. We tested the hypotheses that left atrial function can be fitted to a time-varying elastance model in vivo and that maximal atrial systolic elastance is sensitive to changes in left atrial contractility. We also determined whether maximal elastance can be approximated with nonisochronal end-systolic pressure-volume relations. Finally, using these approaches, we examined the effects of congestive heart failure on left atrial systolic function.

**Methods**

Studies were performed in 12 heartworm-free mongrel dogs of either sex (22 to 27 kg) that were anesthetized with pentobarbital (30 mg/kg) and morphine sulfate (3 mg/kg SC), intubated, and ventilated with a positive-pressure respirator
(Harvard Apparatus). Adequate doses of anesthesia were administered as necessary, but no measurements were made until the animals had returned to a stable hemodynamic state. Arterial blood gases were monitored throughout the experiment, and supplemental oxygen and bicarbonate were administered as necessary to maintain a normal arterial blood Po2 and acid-base balance. A table warmer was used to ensure normothermia. The heart was exposed with a left lateral thoracotomy at the fourth intercostal space and was suspended in a pericardial cradle. A 7F micromanometer with lumen (Millar Instruments) was advanced into the left atrium via a pulmonary vein. Another 7F micromanometer with lumen (Millar Instruments) was advanced into the left ventricle through an apical stab wound. A femoral vein was cannulated to administer intravenous fluids. Pacing wires were sewn to the right atrial appendage.

Pairs of 3-MHz sonomicrometers (6-mm diameter, Triton Technology Inc) were sewn to the anterior and posterior walls (long axis) and medial and lateral walls (short axis) of the left atrium as previously described.7 The posterior crystal was placed between the insertion of the right and left lower pulmonary veins, and the anterior crystal was oriented on the anterior surface of the left atrium to optimize the sonomicrometer signal. The lateral crystal was placed on the lateral surface of the left atrium, immediately caudal to the origin of the left atrial appendage, and the medial crystal was placed in the groove between the pulmonary artery and left atrium. The transit time of ultrasound between the two crystal pairs was measured with a multichannel sonomicrometer (Triton Technology, Inc).

The pressure signals from the micromanometers were matched to those of the fluid-filled catheters. Analog signals for left ventricular and left atrial pressures and atrial dimensions were digitized through an A-D board (Data Translation) interfaced to an IBM AT computer with a 2-millisecond sampling frequency and were stored on floppy disk.

Fluid-filled catheters were connected to Statham 23 dB pressure transducers with zero pressure set at the level of the mid right atrium. The ECG and analog signals for pressures and dimensions were recorded on-line at slow and rapid paper speeds (5, 25, and 100 mm/s) with a multichannel physiological recorder (Gould Inc).

**Experimental Protocol**

Autonomic blockade was accomplished using propranolol (1 mg/kg IV) and atropine (0.02 to 0.04 mg/kg IV).19 Constant heart rate was achieved by atrial pacing; the pacing rate was selected to eliminate competing rhythms and to permit separation of active (booster pump) from passive atrial emptying. Hemodynamic and dimensional data were recorded under steady-state baseline conditions and during abrupt increases in left atrial pressure and volume generated by bolus infusion of phenylephrine (200 to 400 μg IV) (see Fig 1). In 7 dogs, data were acquired both before and after a rapid intravenous infusion of calcium gluconate (1 to 2 g in 50 mL of 5% dextrose in water). Adequate time was allowed between interventions for hemodynamic and dimensional variables to return to baseline. All data were acquired with the respirator turned off at end expiration.

To determine the reproducibility of elastance determinations, multiple (three) left atrial pressure-volume loops were generated in 5 additional animals. Instrumentation was identical to that described in the larger study.

In 4 additional dogs, protocols were performed after myocardial dysfunction was produced by rapid right ventricular pacing.20 A unipolar pacemaker (SpectraX 5985, Medtronic)
Lead was placed in the right ventricular apex via the right external jugular vein under fluoroscopic visualization. A pulse generator programmed at 250 beats per minute was implanted in the subcutaneous tissue over the back of the neck. Three weeks after institution of rapid right ventricular pacing, the animals were anesthetized and instrumented as described above. After the initial left atrial pressure was recorded, intravenous furosemide (40 to 60 mg) was administered to lower the mean left atrial pressure. When necessary, phlebotomy was used to obtain a mean left atrial pressure of approximately 10 mm Hg.

Data Analysis

The left atrial dimension signals were analyzed as follows (Fig 2a). Left atrial end-diastolic dimension (LA_{ed}) was taken as the diameter immediately preceding the peak of the A wave of the left atrial pressure tracing. Left atrial end systole (LA_{es}) was taken as the minimal dimension at the end of left atrial contraction. Left atrial volume was modeled empirically as a general ellipsoid of revolution:

Left atrial volume = \pi/6(SAX)^2(LAX)

where SAX is the short or mediolateral axis, and LAX is the long or anteroposterior axis of the left atrium. Left atrial volume measured in this manner is highly correlated with true volume as determined by water displacement of atrial casts.\(^\text{17}\) True, or absolute, left atrial volume differs from the calculated, relative volume in proportion to the constants of the linear regression between calculated and true volumes. Left atrial stroke volume was calculated from individual pressure-volume loops (vide infra) as left atrial end-diastolic volume minus end-systolic volume. Left atrial ejection fraction was calculated as 100 \cdot (left atrial stroke volume/ left atrial end-diastolic volume).

Left atrial pressure-volume loops were generated off-line by plotting instantaneous left atrial pressure and volume data from phenylephrine runs every 2 milliseconds. Isochronal pressure-volume points from 5 beats, representing a wide range of left atrial pressures, were fitted by linear regression analysis according to a time-varying elastance model:

\[ E_{0}(t) = P_{0}(t)/[V_{0}(t) - V_{00}] \]

where \( E_{0}(t) \) is time-varying elastance, \( V_{00} \) is the volume axis intercept, and \( P_{0}(t) \) and \( V_{0}(t) \) are instantaneous isochronal pressure and volume, respectively. Data points were taken from the Y pressure trough to atrial end systole every 10 milliseconds. The maximal slope of the isochronal pressure-volume points was defined as \( E_{\text{max}} \). Linear regression analysis was also

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**Fig 2.** a, Analog recording of left atrial pressure and dimensions in time domain. Vertical lines indicate time of mitral valve opening (A), end of passive atrial emptying and onset of atrial diastasis (B), atrial end diastole (C), and atrial end systole (D). a and v represent respective venous pressure waves. Note that during "atrial diastasis" (between lines B and C), the two atrial dimensions move in opposite directions, indicating little net volume change and suggesting geometric rearrangements of the left atrium during this period. b, Left atrial pressure-volume loop from a single beat illustrating characteristic figure-of-eight configuration. Arrows indicate direction of loop as a function of time. A loop represents active atrial contraction. V loop represents passive filling and emptying of the left atrium. MVO indicates time of mitral valve opening; MVC, approximate time of mitral valve closure; LA_{es}, left atrial end systole; and LA_{ed}, left atrial end diastole.
TABLE 1. Hemodynamic Changes Produced by Phenylephrine Boluses

<table>
<thead>
<tr>
<th></th>
<th>LVSP, mm Hg</th>
<th>LVDP, mm Hg</th>
<th>LAPSP, mm Hg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Before bolus</td>
<td>111±16</td>
<td>7.6±2.6</td>
<td>10.0±2.7</td>
</tr>
<tr>
<td>After bolus</td>
<td>207±22</td>
<td>21.3±3.5</td>
<td>22.9±3.8</td>
</tr>
</tbody>
</table>

LVSP indicates left ventricular systolic pressure; LVDP, left ventricular end-diastolic pressure; and LAPSP, left atrial peak systolic pressure.

n=12.

applied to nonisochronal pressure-volume points at the time of left atrial end systole (minimal left atrial volume) and at the time of the maximal ratio of pressure to volume; the slopes of these linear fits were defined as \( E_a \) and \( E_{\text{pred}} \), respectively.

In each animal, \( E_0 \) and \( V_0 \) were calculated from simultaneous left atrial pressure-volume points (from 5 variably loaded beats) every 20 milliseconds for an entire cardiac cycle. Predicted \( P_c \) (from 1 of the 5 variably loaded beats selected at random) was calculated from \( E_0 \) and \( V_0 \) and the instantaneous volume \( V_c \) from that beat. The goodness-of-fit of atrial pressure and volume data to the linear time-varying elastance model was determined by comparing the predicted and measured left atrial pressures during one entire cardiac cycle.

Statistical Analysis

Hemodynamic, dimensional, and elastance data were compared before and after calcium infusion with Student's paired \( t \) tests. Values for \( E_{\text{max}} \), \( E_a \), and \( E_{\text{pred}} \) and their respective \( V_0 \) values were compared using one-way repeated-measures ANOVA (STATVIEW II, Abacus Concepts, Inc). Repeated-measures ANOVA was also used to compare the slopes and intercepts of the isochronal pressure-volume relation at various times during atrial systole. Linearity of the relations was evaluated by the coefficient of determination (\( R^2 \)) of the linear curve fit and by fitting the data to quadratic equations.\(^{21,22}\)

To compare the effects of increased inotropic state at varying left atrial end-diastolic volumes, beats at three matched levels of left atrial end-diastolic volume were selected from five of the studies, both before and after calcium infusion. The effects of left atrial end-diastolic volume and inotropic state on left atrial stroke volume were compared by two-way repeated-measures ANOVA (SUPER ANOVA, Abacus Concepts). The coefficient of variation (SD/mean) was used to describe the reproducibility of slope and intercept determinations. Unpaired \( t \) tests were used for comparisons between normal dogs and dogs with pacing heart failure. Unless otherwise specified, data are presented as mean±SD. A value of \( P<.05 \) was taken to indicate a significant difference.

Results

Time-Varying Elastance

Phenylephrine boluses produced a wide range of left atrial peak systolic and left ventricular systolic and diastolic pressures (Table 1). An analog recording during a phenylephrine bolus is shown in Fig 1, and an example of a left atrial pressure-volume loop is shown in Fig 2b. The left atrial pressure-volume loop consists of a V loop, during ventricular systole, at which time the mitral valve is closed and the left atrium fills, and of an A loop, during atrial systole. The A loop begins at the trough of the left atrial pressure V wave (following passive atrial emptying) and represents active atrial contraction and relaxation. Fig 3a illustrates an ensemble of isochronal pressure-volume lines derived from the linear fits of pressure-volume data every 20 milliseconds during atrial systole from a single animal, and Fig 3b graphically depicts the mean isochronal pressure-volume relations from all 12 animals at selected times during atrial systole. The slope of the regression line at each time (\( t \)) is \( E_0 \), and the x-axis intercept is \( V_0 \). There was a significant increase in \( E_0 \) from atrial diastasis (3.7±1.6 mm Hg/mL) to the time of peak systolic pressure (4.6±2.3 mm Hg/mL) and to \( E_{\text{max}} \) (5.5±2.3 mm Hg/mL). Although time-dependent changes in \( V_0 \) were observed in each animal, changes were small, inconsistent, and statistically insignificant.

The linear fits of isochronal pressure-volume data were excellent (range of \( R^2 \), .92 to .99). As can be seen from the composite data illustrated in Fig 3b, neither maximal elastance nor minimal atrial volume (end systole) was coincident temporally with peak atrial systolic pressure; in the 12 dogs, \( E_{\text{max}} \) occurred 29.1±16.2 milliseconds before end ejection.

Left atrial pressure predicted from the time-varying elastance model is compared with measured left atrial
The left atrial end-systolic pressure-volume relation was also examined by fitting end-systolic pressure and volume data to a quadratic equation. The coefficient of the squared term was $-0.5\pm 4.8$ ($P=\text{NS}$ from 0), indicating that over the range of measured left atrial pressures and volumes, there were no significant deviations from linearity.\textsuperscript{21,22}

**Comparison of $E_{\text{max}}$ With Nonisochronal End-Systolic Relations**

For all 12 dogs, there were no significant differences between $E_{\text{max}}$ (5.5±2.8 mm Hg/mL) and the slopes of the nonisochronal pressure-volume relations either at atrial end systole (4.3±1.5 mm Hg/mL) or at the time of maximal pressure-to-volume ratio (5.4±2.2 mm Hg/mL). Similarly, there were no significant differences between the volume axis intercept of the isochronal maximal systolic pressure-volume relation (3.8±1.3 mL) and the intercepts of the nonisochronal pressure-volume relations either at atrial end systole (3.3±1.1 mL) or at the time of maximal pressure-to-volume ratio (3.3±1.4 mL). As seen in Fig 5, the correlations between $E_{\text{max}}$ and both $E_{\text{es}}$ and $E_{\text{maxP/V}}$ were excellent ($r=0.98$ and 0.95, respectively).

**Effects of Altered Inotropic State**

Representative left atrial pressure-volume loops at baseline and after calcium infusion are shown in Fig 6. Hemodynamic and elastance data before and after a calcium-induced increase in inotropic state are shown in Tables 3 and 4. Calcium infusion caused a significant increase in left ventricular systolic pressure, left ventricular peak +dP/dt, left atrial stroke volume, and ejection fraction; the atrially paced heart rate and mean left atrial pressure were unchanged. Stroke volume increased slightly but significantly with increased end-diastolic volume and was significantly greater after calcium infusion than before (1.2 versus 2.0 mL, 1.3 versus 2.4 mL, and 1.3 versus 2.3 mL at each matched level of end-diastolic volume, respectively). These data indicate that calcium infusion produced a positive inotropic response in atrial and ventricular myocardia. Increased atrial stroke volume was the result of significant percentage increases in fractional shortening of both the long and short axis (83.5±44.2% and 95.7±85.5%, respectively; $P=\text{NS}$, long versus short axis).

Increases in inotropic state caused significant increases in $E_{\text{max}}$, $E_{\text{es}}$, and $E_{\text{maxP/V}}$, without significant changes in the respective volume intercepts. In addition, the contour of the atrial systolic pressure-volume trajec-

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**Table 2. Linear Regression Analysis Comparing Left Atrial Pressure Predicted from a Time-Varying Elastance Model and Measured Left Atrial Pressure**

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Slope, mm Hg/mL</th>
<th>Intercept, mL</th>
<th>$R$</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>0.97</td>
<td>0.6</td>
<td>.99</td>
</tr>
<tr>
<td>2</td>
<td>0.95</td>
<td>0.4</td>
<td>.94</td>
</tr>
<tr>
<td>3</td>
<td>1.00</td>
<td>-0.2</td>
<td>.98</td>
</tr>
<tr>
<td>4</td>
<td>0.98</td>
<td>0.4</td>
<td>.94</td>
</tr>
<tr>
<td>5</td>
<td>0.96</td>
<td>0.8</td>
<td>.99</td>
</tr>
<tr>
<td>6</td>
<td>1.10</td>
<td>-1.6</td>
<td>.99</td>
</tr>
<tr>
<td>7</td>
<td>0.97</td>
<td>0.6</td>
<td>.98</td>
</tr>
<tr>
<td>8</td>
<td>1.00</td>
<td>-2.6</td>
<td>.99</td>
</tr>
<tr>
<td>9</td>
<td>0.94</td>
<td>0.8</td>
<td>.98</td>
</tr>
<tr>
<td>10</td>
<td>1.01</td>
<td>-0.2</td>
<td>.99</td>
</tr>
<tr>
<td>11</td>
<td>1.00</td>
<td>0.2</td>
<td>.99</td>
</tr>
<tr>
<td>12</td>
<td>0.95</td>
<td>0.6</td>
<td>.98</td>
</tr>
<tr>
<td>Mean</td>
<td>0.99</td>
<td>0</td>
<td></td>
</tr>
<tr>
<td>SD</td>
<td>0.04</td>
<td>1.0</td>
<td></td>
</tr>
</tbody>
</table>

$n=12$. 

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**Fig 4.** a, Graph comparing measured pressure (○) with pressure predicted from elastance model (△). Pressure is predicted from $E_0$ and the $V_0$ derived from 5 variably loaded beats. The virtual superimposition of points indicates excellent linear fits of pressure and volume and confirms the accuracy of volume determinations. Data are plotted every 20 milliseconds throughout the cardiac cycle. See text for details. b, The slope (△) and volume axis intercept (○) of the isochronal pressure-volume relation are plotted every 20 milliseconds throughout the cardiac cycle. Note the time-varying behavior of elastance and the volume axis intercept.
Reproducibility of End-Systolic Left Atrial Pressure-Volume Relations

Elastance determinations were highly reproducible as indicated by the low coefficients of variation for the slopes (8.4±5.9%, 3.9±3.7%, and 12.1±12.4%) and intercepts (10.5±9.0%, 11.1±9.7%, and 30.3±33.1%) of the E\text{max}, E\text{cs}, and E\text{maxP/V} relations, respectively.

Discussion

There are two principal findings of this study. First, the instantaneous pressure-volume relation of the intact left atrium may be approximated as a time-varying elastance with time-dependent changes in E\text{0}, and second, maximal atrial systolic elastance (E\text{max}) is highly linear and sensitive to changes in inotropic state. These findings confirm and extend observations in the isolated, supported left atrium. In that study, linearity and time-dependence of E\text{0} and V\text{0} during atrial systole were demonstrated using computer-simulated left atrial loading conditions. Time dependence of E\text{0} and V\text{0} has also been reported in the isovolumically contracting isolated right atrium. However, our study is the first to demonstrate time-varying elastance behavior of the left atrium in the intact circulation. Moreover, we showed that left atrial systolic pressure-volume relations are highly linear in atra subjected to chronic hemodynamic overload (despite increased atrial end-systolic volumes). Although we did not specifically test for the load sensitivity of atrial systolic elastance, relative load independence of chamber elastance has been shown in the physiologically loaded, isolated left atrium.

Instantaneous pressure-volume relations are used extensively in physiological studies and to a lesser extent in clinical investigations to characterize ventricular contractility. Because of the relative simplicity in its derivation, end-systolic elastance (E\text{sn}), a modification of maximal elastance, is most often used. However, there is considerable debate regarding the linearity and reproducibility of E\text{sn}. The linearity of the atrial systolic pressure-volume relation in our study was evident from the high correlation coefficients of the linear curve fits. We also tested for curvilinearity by fitting end-systolic pressure-volume data to a second-order polynomial; the zero coefficient of the squared term of quadratic curve fits indicated that there were no significant deviations from linearity. It is likely, however, that curvilinearity exists at extremes of left atrial pressure and inotropic states that were not included in our analyses. Elastance determinations were highly repeatable, consistent with reproducibility of the E\text{sn} relation for both the left and the right ventricle. To minimize errors due to potential nonlinearity and the sensitivity of regression parameters to small changes in pressure-volume data, it is important to compare slopes and intercepts within an individual over a common, wide loading range.

An important finding of our study is that left atrial systolic pressure-volume relations using either the nonisochronal maximal pressure-to-volume ratio or end systole may be useful estimates of E\text{max}. Increased inotropic state was associated with increased E\text{max}, E\text{cs}, and E\text{maxP/V} without a change in the respective volume axis intercepts. Although E\text{maxP/V} most closely resembled E\text{max}, E\text{cs} was most sensitive to calcium-induced increases in atrial contractility, was most reproducible,
and was the simplest to derive. In dogs with heart failure, there was a nonsignificant trend toward increasing $E_{\text{max}}$ with calcium infusion, despite significant calcium-induced increases in $E_0$ and $E_{\text{maxP/V}}$. This apparent lack of concordance between isochronal and nonisochronal parameters probably reflects the small number of animals studied that had pacing-induced heart failure. Further studies are needed to determine whether these nonisochronal modifications of the time-varying elastance model describe accurately atrial contractility over a wider range of loading conditions and inotropic states.

An interesting finding of our study is that calcium infusion was associated with a change in the shape of the atrial pressure-volume loop (Fig 6). At baseline, atrial ejection continued beyond peak atrial systolic

![Table 3](image)

Table 3. Paired Hemodynamic Data at Baseline and After Calcium Gluconate Infusion

<table>
<thead>
<tr>
<th></th>
<th>Normal Dogs (n=7)</th>
<th>Pacing Failure Dogs (n=4)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>After Calcium</td>
</tr>
<tr>
<td>LVS, mm Hg</td>
<td>115±14*</td>
<td>134±21</td>
</tr>
<tr>
<td>LV dP/dt, mm Hg/s</td>
<td>1214±122*</td>
<td>1800±363</td>
</tr>
<tr>
<td>LAP, mm Hg</td>
<td>8.4±1.3</td>
<td>8.1±1.4</td>
</tr>
<tr>
<td>HR, bpm</td>
<td>106±9</td>
<td>103±5</td>
</tr>
<tr>
<td>LA SV, mL</td>
<td>0.8±0.2*</td>
<td>1.3±0.3</td>
</tr>
<tr>
<td>LA EF, %</td>
<td>11.3±2.7*</td>
<td>19±4.1</td>
</tr>
</tbody>
</table>

LVS indicates left ventricular systolic pressure; LV dP/dt, peak rate of rise of isovolumic left ventricular pressure; LAP, mean left atrial pressure; HR, heart rate; bpm, beats per minute; LA SV, left atrial stroke volume; and LA EF, left atrial ejection fraction. Data are mean±SD.

*P<.05 vs baseline.

†P<.05 vs corresponding column from normal dogs.
pressure; in contrast, after calcium infusion, atrial end systole occurred at about the same time as peak atrial systolic pressure. This change in the contour of the atrial systolic pressure-volume trajectory was associated with a decrease in the time from $E_{\text{max}}$ to end systole. As a result, the atrial $A$ loop resembled the shoulder of the right ventricular pressure-volume loop before and the left ventricular pressure-volume loop after calcium infusion. It has been postulated that the temporal delay between peak ejection pressure and end ejection in the right ventricle is a consequence of ventricular-vascular coupling.15 Thus, our data suggest that calcium infusion may have either direct or indirect effects on ventricular input impedance.

The manner in which the left atrial chamber adapts to chronic pressure and volume overload is poorly understood. This is partly the result of limitations of previous experimental designs and the techniques used to analyze atrial function. With the exception of chronic mitral regurgitation, left atrial mechanics have not been studied carefully and longitudinally in animal models. The subset of animals modeled with rapid right ventricular pacing demonstrate for the first time that in response to left ventricular myocardial contractile dysfunction, there is increased left atrial diastolic distensibility (increased left atrial volume at matched left atrial pressure) and maintained atrial systolic function (increased left atrial stroke volume) and unchanged left atrial ejection fraction (at matched left atrial and ventricular pressures and heart rate) and atrial force generation (systolic elastance). Although elastance determinations were not normalized for atrial volume, increased atrial size should decrease elastance; in contrast, we observed a nonsignificant increase in all three elastance determinations. Further work is needed to characterize the morphological and biochemical correlates of this adaptive response, to determine the sensitivity of systolic pressure-volume relations to atrial myocardial contractile dysfunction, and to ascertain the most appropriate size or geometric normalization for $E_{\text{max}}$.

There is controversy over whether time-varying elastance is a property fundamental to cardiac muscle or to the complex organization of the cardiac chamber. In isolated cat trabecula, the shape of the isochronal “pressure-volume” relation was time dependent, and $E_{\text{max}}$ was dependent on the history of contraction (ie, load).28 Although it is likely that the pressure-volume relation is influenced by shortening deactivation and viscoelastic effects in the intact heart, the similarity in time-varying elastance between the right ventricle and left atrium, ie, chambers with vastly different chamber geometries, fiber orientations, and wall thicknesses, suggest that time-varying elastance is a property fundamental to cardiac muscle.

**Critique of the Methods**

The limitations of a time-varying elastance approach to characterize cardiac chamber contractility are well known.24–26 Despite its shortcomings, however, time-varying elastance may provide a useful theoretical framework for understanding left atrial contractile performance. The linearity, reproducibility, relative load independence, and sensitivity to altered inotropic state provide considerable advantages over currently used methods of assessing atrial function.

Phenylephrine boluses were used to define left atrial pressure-volume relations. We blocked the reflex adrenergic and muscarinic effects on heart rate and left atrial performance using pacing, propranolol, and atropine. In the isolated, perfused left ventricle, $E_{\text{max}}$ was insensitive to a wide range of computer-simulated arterial impedances.29 In another study, phenylephrine decreased the slope of the nonisochronal left ventricular end-systolic pressure-volume relation, but not isochronal $E_{\text{max}}$.30 However, in these studies, there was a small but significant leftward shift of $V_o$. In contrast, Freeman et al31 have shown in conscious dogs that the method (eg, inferior vena cava occlusion, angiotensin II, and methoxamine infusions) used to generate the obligatory range of data points influences both the slope and intercept of end-systolic pressure-volume relations. These variable results may be the result of the influence of altered arterial loading on the timing of end systole, which affects $E_{\text{max}}$ (and other nonisochronal slope determinations) to a greater extent than $E_{\text{max}}$.32 Alternatively, nonlinearity of the pressure-volume relation at the extremes of pressure and volume may produce an apparent shift of the pressure-volume relation. Regardless of the cause, it is important to interpret cautiously end-systolic pressure-volume relations that are derived using different methods of load alteration and that are

**Table 4. Paired Left Atrial Elastance Values at Baseline and After Calcium Gluconate Infusion**

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<td>4.5±1.6*</td>
<td>5.7±1.8</td>
</tr>
<tr>
<td>$E_{\text{s}}$, mm Hg/mL</td>
<td>3.9±0.9*</td>
<td>5.3±1.1</td>
</tr>
<tr>
<td>$E_{\text{maxPV}}$, mm Hg/mL</td>
<td>4.2±1.7*</td>
<td>5.5±1.4</td>
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<tr>
<td>$V_{\text{o max}}$, mL</td>
<td>3.6±0.7</td>
<td>3.4±1.0</td>
</tr>
<tr>
<td>$V_{\text{o s}}$, mL</td>
<td>3.3±0.7</td>
<td>3.3±1.0</td>
</tr>
<tr>
<td>$V_{\text{o maxPV}}$, mL</td>
<td>3.2±1.3</td>
<td>3.3±1.0</td>
</tr>
</tbody>
</table>

$E_{\text{max}}$ indicates maximal atrial systolic elastance; $V_{\text{o max}}$, respective volume axis intercept; $E_{\text{s}}$, atrial end-systolic elastance; $V_{\text{o s}}$, respective volume axis intercept; $E_{\text{maxPV}}$, maximum pressure-to-volume ratio; and $V_{\text{o maxPV}}$, respective volume axis intercept.

*P<.05 vs baseline.
†P<.05 vs corresponding column from normal dogs.
constructed from points with different ranges of pressure and volume.

Instantaneous atrial pressure-volume analysis requires accurate estimates of dynamic left atrial volume with high temporal resolution. In the present study, we calculated left atrial volume using two nearly orthogonal sonomicrometer pairs on the body of the left atrium. We recently demonstrated the validity of this technique. Although this validation was based on geometric assumptions of left atrial volume at the time of mitral valve opening, changes in atrial circumference are generally symmetrical. Because absolute atrial volumes were not used in this study, our values for elastance cannot be compared with values reported for the left and right ventricles. However, elastance values computed using left atrial volume regression constants were similar to those reported in the isolated left atrium. A potential limitation is that studies were performed in anesthetized, open chest animals. Recent studies suggest that end-systolic pressure-volume relations of the left ventricle may be variable in conscious animals. Thus, our results should be extrapolated to the conscious animal with caution. Although studies were performed with an open pericardium, the left atrial end-diastolic dimension-shortening relation is unaffected by pericardiectomy.

Finally, sonomicrometers were necessary for determination of atrial elastance. Sonomicrometry is highly invasive and not suited for clinical use. Currently there are no clinically applicable methods for left atrial volume determination that have sufficient temporal resolution for pressure-volume analyses. Therefore, until a relatively noninvasive method of measuring continuous atrial volume with high sampling frequency is developed, the clinical usefulness of atrial elastance remains in question.

Clinical Implications

The importance of the atrial booster pump is dependent on the timing of atrial systole, venous return, vagal stimulation, left ventricular end diastolic pressures, and left ventricular functional reserve. Despite considerable study, the atrial contribution to left ventricular filling and cardiac output remains controversial, especially in patients with abnormal left ventricular performance. This is due, in part, to a lack of indices that characterize atrial performance independent of left atrial end-diastolic volume (an estimate of atrial preload) and left ventricular diastolic pressure (an estimate of atrial afterload). The clinical relevance of the atrial systolic contribution to left ventricular filling is underscored by the considerable interest in dual-chamber pacemakers that maintain atrioventricular synchrony and by the attempts to restore and maintain atrial systole in patients with atrial fibrillation. In addition, although studies have suggested an increase in atrial systolic function in patients with ischemic and hypertensive disease, few have accounted for variable degrees of atrial myocardial contractile dysfunction. Therefore, a reproducible and relatively load-independent measure that is sensitive to changes in atrial contractility should clarify the contribution of atrial booster pump function to cardiovascular performance. Our study suggests that despite its shortcomings, approaches based on time-varying elastance behavior of the left atrium may be useful to describe left atrial contractile behavior in situ. Finally, the analytical framework of the pressure-volume relation affords the opportunity for studying energetic aspects of atrial work in a manner analogous to the left ventricle.

Acknowledgments

This work was supported in part by National Institutes of Health grant HL-33579, American Heart Association, Ohio Affiliate, grant SW-91-09, and a Grant-in-Aid from the American Heart Association, with funds contributed in part by the American Heart Association, Ohio Affiliate (9300680). The authors would like to thank Norma Burns for her secretarial assistance and Gary Flesher and Tom Frede for their technical assistance.

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In vivo assessment of left atrial contractile performance in normal and pathological conditions using a time-varying elastance model.

B D Hoit, Y Shao, M Gabel and R A Walsh

Circulation. 1994;89:1829-1838
doi: 10.1161/01.CIR.89.4.1829

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