Altered Left Atrial Compliance After Atrial Appendectomy
Influence on Left Atrial and Ventricular Filling

Brian D. Hoit, Yanfu Shao, Liang-Miin Tsai, Rashmi Patel, Marjorie Gabel, and Richard A. Walsh

Previous studies have shown regional differences in atrial distensibility. We studied 12 open-chest dogs to test the hypothesis that left atrial compliance is decreased after removal of the left atrial appendage and to determine the effect of altered atrial compliance on atrial reservoir and conduit function. Sonomicrometer crystal pairs were used to measure the long- and short-axis diameters of the left atrium over a wide range of intracardiac pressures and volumes obtained by intravenous hetastarch infusion both before and after suture ligation of the left atrial appendage (appendectomy). Pulmonary venous flow was measured with an ultrasonic flowmeter, and transmitral flow velocities were measured with transthoracic Doppler echocardiography. After appendectomy, the diastolic pressure-volume relation was shifted upward and to the left in six of seven dogs. The mean dynamic stiffness constant of the left atrial diastolic pressure-volume relation was significantly greater after appendectomy than before (0.20±0.11 [mean±SD] versus 0.14±0.08 m·L⁻¹·mmHg⁻¹, p<0.01); the mean y intercept was slightly, but significantly, less after appendectomy (0.6±0.3 versus 1.3±0.6 mmHg, p<0.05). The left atrial reservoir volume (maximum minus minimum left atrial volume) was significantly less after appendectomy at matched left atrial pressures. The systolic to diastolic flow integral ratio of pulmonary venous flow (JPTI/KPTI), an index of the relative reservoir to conduit functions of the left atrium, increased significantly with volume infusion only before appendectomy; at matched left atrial pressure, JPTI/KPTI was significantly less afterwards. Similarly, the early diastolic transmitral velocity increased with volume infusion but was less at each level of left atrial pressure after appendectomy. We conclude that left atrial compliance decreases after appendectomy and is characterized by decreased relative reservoir to conduit function of the left atrium and decreased early left ventricular filling rate. (Circulation Research 1993;72:167–175)

KEY WORDS • left atrium • atrial compliance • atrial function • pulmonary venous flow

Atrial compliance is an important determinant of both cardiovascular performance and physiological physiology. In isolated canine atria, the slope of the left atrial pressure-volume relation was significantly greater without the appendage than with the appendage intact. We have recently shown that the left atrial appendage is more distensible than the body of the left atrium in vivo. Greater compliance of the appendage than body of the left atrium may be beneficial when left ventricular filling pressure is increased and atrial distensibility is decreased. However, both the relative contribution of appendage distensibility to the passive elastic chamber properties of the left atrium and its physiological importance are unknown. Accordingly, we tested the hypothesis that left atrial diastolic chamber compliance in vivo is greater with the appendage intact than after its removal. In addition, although recent studies have suggested that atrial compliance is an important determinant of diastolic left ventricular filling and atrial function, it has not previously been possible to alter atrial compliance without producing concomitant changes in other determinants of left atrial and ventricular filling in the intact heart. Therefore, an important goal of our study was to identify any changes in left atrial and ventricular filling owing to an isolated change in left atrial compliance.

Materials and Methods

Studies were performed in 16 heart worm–free mongrel dogs of either sex (20–32 kg) that were anesthetized with morphine sulfate (3 mg/kg s.c.) and á-chloralose (85 mg/kg i.v.), intubated, and ventilated with a positive-pressure respirator (Harvard Apparatus, South Natick, Mass.). Additional 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

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in a pericardial cradle. A 7F Goodale-Lubin catheter was advanced into the ascending aorta to record central aortic pressure. A femoral vein was cannulated to administer intravenous fluids, and an 8F catheter with a balloon of 10-ml capacity was advanced from the femoral vein into the inferior vena cava, just below the right atrium to vary systemic venous return. A 7F micromanometer with lumen (Millar Instruments, Houston, Tex.) was advanced into the left atrium via a pulmonary vein.

Pairs of 3-MHz sonomicrometers (6-mm diameter, Triton Technology Inc., San Diego, Calif.) were sewn to the anterior and posterior walls (long axis) and medial and lateral walls (short axis) of the left atrium. 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).

A 2-mm ultrasonic flow probe (Transonics Inc., Ithaca, N.Y.) was fitted loosely around the left upper pulmonary vein. These transit time ultrasonic flow probes measure volume flow rate and have been validated in vivo.11 Unlike electromagnetic flowmeters, they are not subject to artifacts when probe motion disrupts uniform electrical contact and do not require vessel occlusion to obtain a zero-flow recording. Ultrasonic contact was ensured by filling potential spaces between the vein and flow probe with coupling gel (Aquasonic 100, Parker Laboratories, Inc., Orange, N.J.). A limb-lead electrocardiogram was recorded throughout.

To determine any potential confounding influences of heart rate, left ventricular relaxation, diastolic compliance, and systolic function on appendectomy-induced alterations in left atrial and ventricular filling, four dogs were instrumented with a 7F micromanometer with lumen (Millar Instruments) in the left atrium and a pair of 3-MHz sonomicrometers (7-mm diameter, Triton Technology) on the anterior and posterior left ventricular epicardium. Pacing wires were sewn to the right atrial appendage. In these animals, left atrial micromanometers were not used.

The pressure waveforms from the micromanometer were matched to those of the fluid-filled catheter. Analog signals for aortic and left atrial pressures and atrial dimensions were digitized through an analog to digital board (Data Translation, Marlboro, Mass.) interfaced to an IBM AT computer with a 5-msec sampling frequency and stored on floppy disc.

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

A transesophageal imaging transducer (model 21362A, Hewlett-Packard Co., Palo Alto, Calif.) was covered with a disposable sheath, lubricated, and advanced into the esophagus behind the left atrium (approximately 45 cm from the incisors). This instrument consists of a 5-MHz imaging and 2-MHz Doppler phased-array transducer mounted on the distal tip of a 100-cm endoscope and has color flow-imaging capabilities. The analog signal from the pulmonary vein flow probe was patched into the auxiliary channel of the ultrasound system. Doppler echocardiographic transmural flow was sampled from the four-chamber equivalent long-axis view using color flow guidance. The sample volume was placed in the left ventricle at the tips of the mitral leaflets.

**Experimental Protocol**

Hemodynamic, dimensional, and flow data were recorded over a wide range of intracardiac volumes obtained by intravenous infusion of hetastarch (100 ml/min) prewarmed to 37°C. Inferior vena caval balloon occlusion was used to decrease atrial filling and pressure. Data were acquired during several stable hemodynamic states at each of 3–5–mm Hg increments of mean left atrial pressure with the respirator turned off at end expiration. To assess the presence or absence of hysteresis for the atrial diastolic pressure-volume relation, animals were given intravenous furosemide (60–80 mg) at the end of the volume infusion and were allowed to recover for approximately 60 minutes. Data were acquired at 3–5-mm Hg intervals as left atrial pressure and volume returned to baseline.

In seven dogs (group A), left atrial appendectomy was performed by placing a nontraumatic clamp around the base of the left atrial appendage, oversweeping the adjacent tissue with mattress sutures, and removing the clamp. Great care was taken to exclude as much of the appendage as possible without distorting the junction of the pulmonary veins and the atrial body or interfering with the atrial sonomicrometers. The integrity of the suture ligation was ensured by the inability to withdraw blood from the appendage with a needle and syringe. After an additional 30 minutes, the volume-infusion protocol was repeated.

In the four dogs instrumented with left ventricular sonomicrometers and micromanometers (group B), an identical protocol was performed with constant (atrially paced) heart rates.

Five dogs (group C) underwent two volume-infusion protocols (separated by 90 minutes) without an intervening appendectomy to serve as controls.

The experimental protocol was approved by the Institutional Animal Care and Use Committee at the University of Cincinnati.

**Data Analysis**

In addition to its function as a booster pump augmenting left ventricular filling during late diastole, the left atrium serves as a distensible reservoir for pulmonary venous blood flow stored during ventricular systole and as a conduit for pulmonary venous flow during early ventricular diastole.10 Therefore, we regarded pulmonary venous flow during ventricular systole and diastole as estimates of the relative atrial reservoir and conduit functions, respectively.

Pulmonary venous flow waveforms were analyzed for the peak systolic and the diastolic flows and the area under each component of the flow curve (flow velocity
integrals) (Figure 1). The derived values for each flow waveform included the ratio of peak systolic and diastolic velocities and their respective flow integrals. The analog signal of pulmonary venous flow was digitized from videotape using a Summagraphics Plus digitizer (Summagraphics Corp., Fairfield, Conn.) interfaced to a dedicated image analysis system (Freeland Medical, Indianapolis, Ind.) with customized software. Timing of the diastolic waveform was identified by the simultaneous Doppler velocity tracing of diastolic transmitral flow. When the systolic and diastolic waveforms overlapped, the systolic and diastolic flow velocity integrals were calculated by dropping a vertical line to the baseline from the intersection of the peak systolic and diastolic waves.

Transmitral Doppler waveforms were analyzed for the peak early diastolic velocity, the deceleration time of the mitral flow velocity waveform in early diastole, and the peak late diastolic velocity. Deceleration time was measured as the time between the peak early velocity and the point where the linearly extrapolated deceleration slope crossed the baseline.

The left atrial dimension signals were analyzed as follows (Figure 2). Maximum left atrial dimension was taken as the largest atrial dimension occurring at the time of mitral valve opening (which corresponded to the y wave of the left atrial pressure tracing in Figure 2). Minimum left atrial dimension was taken as the smallest dimension after left atrial contraction. The long-axis/short-axis ratio of maximum left atrial dimension was used to identify any shape changes in the left atrial body after appendectomy.

Maximum and minimum left atrial volumes were estimated from a general ellipsoid of resolution without regression constants: left atrial volume=\( (SA)^2 \cdot (LA) \), where \( SA \) is the short (or mediolateral) axis and \( LA \) is the long (or anteroposterior) axis of the left atrium.

The atrial diastolic dynamic chamber stiffness constant (the reciprocal of compliance) was determined by fitting left atrial pressure–volume data derived from steady-state volume infusions to the exponential curve equation \( P=Ae^{Be} \) (Delta Graph, Deltapoint Inc., Monterey, Calif.), where \( P \) is left atrial pressure, the constant \( A \) is the y intercept, \( e \) is the base of the natural logarithm, \( k \) is the dynamic stiffness constant, and \( V \) is left atrial volume. Preappendectomy and postappendectomy atrial diastolic pressure–volume data were compared over a common range of mean left atrial pressure (5–20 mm Hg). The left atrial reservoir volume was

**FIGURE 1.** Simultaneous pulmonary venous (PV) flowmeter and Doppler transmitral waveforms. ECG, electrocardiogram; MV, mitral valve. Note the temporal relation between the peak systolic (J) and diastolic (K) PV flows and the early (E) and late (A) transmitral velocities.

**FIGURE 2.** Recordings illustrating the relation between left atrial (LA) pressure, LA long- and short-axis dimensions, pulmonary venous (PV) flow, and electrocardiogram (ECG). LA dimensions were measured at points indicated by the vertical lines: A, maximal LA dimension; B, minimum LA dimension. On the LA pressure tracing, a and v waves are labeled.
computed as maximum minus minimum left atrial volume.

For group B dogs, left ventricular end-diastolic dimension (LVEDD) was taken as the maximum left ventricular diameter, and left ventricular end-systolic dimension (LVESD) was taken as the minimum left ventricular diameter. Left ventricular shortening fraction was calculated as 100×(LVEDD−LVESD)/LVEDD. An index of left ventricular end-diastolic volume was calculated as % of LVEDD. The time constant of left ventricular relaxation was derived from the high-fidelity left ventricular pressure tracing using the method of Weiss et al. Data from 10–20 beats were averaged with the respirator turned off at end expiration.

**Statistical Analysis**

The coefficients and intercepts of the left atrial pressure-volume relation were compared before and after appendectomy with Student’s paired t tests (StatView II, Abacus Concepts, Inc., Berkeley, Calif.). For purposes of comparing the effect of appendectomy at varying atrial volumes, beats as close as possible to a mean left atrial pressure of 7, 13, and 20 mm Hg were selected from each study. Left atrial dimensions were analyzed from the original tracings with data averaged from three to five consecutive steady-state beats at each level of left atrial pressure, both before and after left atrial appendectomy. The effects of volume infusion and left atrial appendectomy on hemodynamic, dimension, and flow variables were compared by means of two-way repeated-measures analysis of variance (SUPERANOVA, Abacus Concepts). When a significant interaction was present (p<0.10), contrasts were used to identify where those differences were. Unless otherwise specified, data are presented as mean±SD. A value of p<0.05 was taken to indicate a significant difference.

**Results**

**Hemodynamic Measurements**

Hemodynamic measurements for group A dogs are given in Table 1. Volume infusion caused significant increases in mean left atrial and aortic pressures and small nonsignificant differences in heart rate. Mean aortic pressures were similar at each level of left atrial pressure before and after appendectomy. Heart rates were significantly lower after appendectomy than before.

<table>
<thead>
<tr>
<th>TABLE 1. Hemodynamic and Left Atrial Volume Data at Three Levels of Left Atrial Pressure in Group A Dogs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Low LA pressure</strong></td>
</tr>
<tr>
<td>Mean LA pressure (mm Hg)</td>
</tr>
<tr>
<td>Mean aortic pressure (mm Hg)</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
</tr>
<tr>
<td>Maximum LA volume (ml)</td>
</tr>
<tr>
<td>LA reservoir volume (ml)</td>
</tr>
</tbody>
</table>

LA, left atrial; APP, appendectomy; bpm, beats per minute. Values are mean±SD (n=7 dogs).

*p<0.05 for low vs. mid LA pressure; †p<0.05 for low vs. high LA pressure; ‡p<0.05 for mid vs. high LA pressure; §p<0.05 for before vs. after APP.

**Left Atrial Compliance**

A representative example of the pressure-volume relation of the left atrial body before and after appendectomy is shown in Figure 3. Pressure-volume curve fits in each dog both before and after appendectomy were excellent (range of r² values, 0.87–0.99 and 0.91–0.99, respectively). For all seven dogs, the dynamic stiffness constant of the left atrial diastolic pressure–volume relation was greater (0.20±0.11 versus 0.14±0.08 ml⁻¹, p<0.01), and the y axis intercept was slightly but significantly less after appendectomy (0.6±0.3 versus 1.3±0.6 mm Hg, p<0.05).

**Left Atrial Volumes**

Left atrial volumes for group A dogs are given in Table 1. Maximum left atrial body volume increased significantly during volume infusion, but the effect of appendectomy as determined from the analysis of variance was not significant. However, there was a significant statistical interaction between the effects of volume infusion and appendectomy; thus, for a similar increase in left atrial pressure, the change in left atrial volume was greater before appendectomy than afterwards. In all animals, the pressure-volume relation displayed hysteresis; i.e., at matched left atrial pressures, left atrial volume was greater when left atrial pressure and volume were falling during recovery than during volume...
venous flow (Figure 4). As a result, the mean left atrial volume at the low level of left atrial pressure was significantly greater after appendectomy than before appendectomy.

Left atrial reservoir volume increased significantly during volume infusion both before and after appendectomy. However, after appendectomy, left atrial reservoir volume was significantly less at each level of left atrial pressure.

The long-axis/short-axis ratios of maximal left atrial dimension were similar before and after appendectomy, indicating that the surgically induced changes in atrial distensibility did not differentially affect the long and short axes of the left atrial body.

**Pulmonary Venous Flow and Mitral Flow Doppler Velocimetry**

Peak systolic and diastolic flows (Table 2) increased significantly during volume infusion. Peak systolic flow decreased at matched left atrial pressures after appendectomy, although these changes did not achieve statistical significance; peak diastolic flow did not change after appendectomy. The peak systolic/diastolic ratio did not change significantly with volume infusion, but at each level of left atrial pressure, the ratio was significantly less after appendectomy.

With volume infusion, integrated pulmonary venous flow (Table 2) during systole increased significantly and was unchanged during diastole. As a result, volume infusion caused an increase in the systolic/diastolic integral flow ratio. In contrast, after appendectomy, the systolic/diastolic integral flow ratio failed to increase with volume infusion. Also, after appendectomy, integrated pulmonary venous flow decreased during systole and increased during diastole, but these changes were not statistically significant. However, the ratio of integrated systolic to diastolic flow decreased significantly after appendectomy.

The peak early mitral velocity (Table 2) increased significantly with volume infusion; after appendectomy, the peak early mitral velocities were significantly less at each level of left atrial pressure. The early transmitral deceleration time and late diastolic transmitral velocity could be measured in only five of the seven dogs. The late transmitral velocity did not change significantly with volume infusion but decreased after appendectomy; as a result, the early to late diastolic transmitral velocity ratio increased after appendectomy. The transmitral deceleration time decreased significantly with volume infusion and after appendectomy.

In the four group B dogs (Table 3), the heart rate, time constant of left ventricular relaxation, left ventricular end-diastolic volume estimates, and fractional shortening were unchanged by appendectomy. The coefficient of the monoexponential left atrial pressure–volume relation was greater after appendectomy than before (0.15±0.01 versus 13±0.01 ml⁻¹). Heart rates were similar before and after appendectomy. In addition, changes in pulmonary venous flow profiles and early transmitral Doppler velocities in response to volume infusion and appendectomy were similar to those in the larger study (data not shown).

**Table 2. Pulmonary Venous Flow and Transmitral Doppler Velocimetry at Three Levels of Left Atrial Pressure in Group A Dogs**

<table>
<thead>
<tr>
<th></th>
<th>Low LA pressure</th>
<th></th>
<th>Mid LA pressure</th>
<th></th>
<th>High LA pressure</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Before APP</td>
<td>After APP</td>
<td>Before APP</td>
<td>After APP</td>
<td>Before APP</td>
</tr>
<tr>
<td>Peak J (ml/min)</td>
<td>147±49</td>
<td>129±53</td>
<td>195±71*</td>
<td>168±72*</td>
<td>255±83§§</td>
</tr>
<tr>
<td>Peak K (ml/min)</td>
<td>166±49</td>
<td>160±73</td>
<td>208±70*</td>
<td>213±94*</td>
<td>253±69§§</td>
</tr>
<tr>
<td>Peak J/K</td>
<td>0.88±0.10†</td>
<td>0.83±0.11</td>
<td>0.93±0.14†</td>
<td>0.81±0.12</td>
<td>1.02±0.21†</td>
</tr>
<tr>
<td>JFT1 (ml)</td>
<td>34.2±14.5</td>
<td>32.5±15.4</td>
<td>46.8±18.1*</td>
<td>42.0±21.5</td>
<td>59.4±16†§</td>
</tr>
<tr>
<td>KFT1 (ml)</td>
<td>28.9±7.8</td>
<td>33.8±17.2</td>
<td>32.2±10.1</td>
<td>42.0±18.7</td>
<td>30.0±9.7</td>
</tr>
<tr>
<td>JFT1/KFT1</td>
<td>1.18±0.34</td>
<td>1.04±0.44</td>
<td>1.48±0.42</td>
<td>1.0±0.24</td>
<td>2.12±0.84†§</td>
</tr>
<tr>
<td>Peak E (cm/sec)</td>
<td>67.5±10.2†</td>
<td>56.8±11.8</td>
<td>78.5±6.9††</td>
<td>67.1±7.3*</td>
<td>91.1±12.4†‡</td>
</tr>
<tr>
<td>Peak A (cm/sec)</td>
<td>45.6±11.9†</td>
<td>27.8±7.9</td>
<td>50.2±14.8†</td>
<td>35.4±9.7</td>
<td>47.8±8.6†</td>
</tr>
<tr>
<td>Peak E/A</td>
<td>1.6±0.3†</td>
<td>2.1±0.5</td>
<td>1.6±0.4†</td>
<td>1.9±0.6</td>
<td>1.6±0.3†</td>
</tr>
<tr>
<td>Decel (msec)</td>
<td>81±13†</td>
<td>72±8</td>
<td>67±3†</td>
<td>64±8*</td>
<td>62±6†§</td>
</tr>
<tr>
<td>L/S ratio</td>
<td>1.87±0.30</td>
<td>1.87±0.37</td>
<td>1.79±0.23</td>
<td>1.81±0.32</td>
<td>1.76±0.21†</td>
</tr>
</tbody>
</table>

LA, left atrial; APP, appendectomy; J, systolic pulmonary venous flow; K, diastolic pulmonary venous flow; FTI, flow time integral; E, early diastolic transmitral velocity; A, late diastolic transmitral velocity; Decel, early diastolic deceleration time; L/S, ratio of long to short axis. Values are mean±SD (n=7 dogs).

*p<0.05 for low vs. mid LA pressure; †p<0.05 for before vs. after APP; t*<0.05 for low vs. high LA pressure; §p<0.05 for mid vs. high LA pressure.
Control Dogs

In the five control dogs with a sham appendectomy (Table 4), the left atrial diastolic stiffness constant and y intercept of the pressure–volume relations were similar for each volume-loading protocol (0.14±0.05 versus 0.17±0.07 ml⁻¹ and 2.5±1.0 versus 2.6±1.1 mm Hg, respectively; both p=NS). Moreover, both the pattern of pulmonary venous flow and the early transmitral velocity were similar at each level of left atrial pressure before and after sham appendectomy; rapid heart rates precluded measurement of early diastolic deceleration time and late diastolic transmitral velocity. Thus, the changes in left atrial compliance, pulmonary vein flow, and peak early transmitral velocity could not be attributed to temporally related changes in the experimental preparation or to the effect of a rapid volume load and subsequent diuresis.

Discussion

The major finding of this study is that compliance of the left atrium decreases (dynamic stiffness constant increases) after the atrial appendage is removed and that this isolated change in atrial compliance is associated with significant changes in left ventricular and left atrial filling and atrial function. The steeper slope of the left atrial pressure–volume relation after appendectomy in vivo confirms and extends findings from an in vitro study in isolated hearts that compared pressure–volume data of the left atrium with and without the appendage. These findings are also of interest in view of an in vivo study in dogs instrumented with sonomicrometers on the left atrial body and appendage; this study demonstrated that the left atrial appendage is more distensible than the left atrial body. Differential atrial distensibility may be due to regional differences in stress distribution or myofibrillar orientation or to inhomogeneous elastic properties of the atrial myocardium; a direct comparison of the material properties of the left atrial body and appendage will be necessary to make this distinction. Whether the effects of left atrial appendectomy on left atrial body compliance are due to changes in atrial geometry or to loss of a region with different

TABLE 3. Left Atrial Volumes, Left Ventricular Performance, Pulmonary Venous Flow, and Transミtal Doppler Velocimetry at Constant Heart Rate and Three Levels of Left Atrial Pressure in Group B Dogs

<table>
<thead>
<tr>
<th></th>
<th>Low LA pressure</th>
<th>Mid LA pressure</th>
<th>High LA pressure</th>
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<tbody>
<tr>
<td></td>
<td>Before APP</td>
<td>After APP</td>
<td>Before APP</td>
</tr>
<tr>
<td>LA pressure (mm Hg)</td>
<td>6.8±1.5</td>
<td>6.9±1.4</td>
<td>13.3±1.0</td>
</tr>
<tr>
<td>Heart rate* (bpm)</td>
<td>108±15</td>
<td>110±11</td>
<td>108±15</td>
</tr>
<tr>
<td>Maximum LA volume (ml)</td>
<td>14.3±6.8</td>
<td>14.0±6.2</td>
<td>19.6±9.2</td>
</tr>
<tr>
<td>LV end-diastolic volume (ml)</td>
<td>73±17</td>
<td>71±19</td>
<td>82±21</td>
</tr>
<tr>
<td>Time constant of LV relaxation (msec)</td>
<td>43.3±10.3</td>
<td>42.4±7.7</td>
<td>49.1±11.5</td>
</tr>
<tr>
<td>Fractional LV shortening (%)</td>
<td>7.4±1.9</td>
<td>7.2±2.4</td>
<td>7.8±1.6</td>
</tr>
<tr>
<td>JFTI (ml)</td>
<td>21.1±6.4</td>
<td>26.9±13.8</td>
<td>36.5±21.3</td>
</tr>
<tr>
<td>KFTI (ml)</td>
<td>21.2±6.7</td>
<td>23.2±9.4</td>
<td>27.2±14.0</td>
</tr>
<tr>
<td>JFTI/KFrI</td>
<td>1.03±0.28</td>
<td>1.16±0.35</td>
<td>1.47±0.89</td>
</tr>
<tr>
<td>Peak E (cm/sec)</td>
<td>55.5±11.4</td>
<td>51.5±10.0</td>
<td>60.5±10.7</td>
</tr>
<tr>
<td>Decel (msec)</td>
<td>87±20</td>
<td>80±11</td>
<td>70±23</td>
</tr>
</tbody>
</table>

LA, left atrial; APP, appendectomy; bpm, beats per minute; LV, left ventricular; JFTI, systolic flow velocity integral; KFTI, diastolic flow velocity integral; E, early diastolic transmitral velocity; Decel, early diastolic deceleration time. Values are mean±SD (n=4 dogs).

*p>Atrially paced.

TABLE 4. Hemodynamic Left Atrial Volume and Pulmonary Venous Flow Data at Three Levels of Left Atrial Pressure in Control (Group C) Dogs

<table>
<thead>
<tr>
<th></th>
<th>Low LA pressure</th>
<th>Mid LA pressure</th>
<th>High LA pressure</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>Sham APP</td>
<td>Baseline</td>
</tr>
<tr>
<td>Mean LA pressure (mm Hg)</td>
<td>7.6±0.8</td>
<td>7.1±0.6</td>
<td>14.0±1.9*</td>
</tr>
<tr>
<td>Mean aortic pressure (mm Hg)</td>
<td>81±23</td>
<td>91±11</td>
<td>83±14</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>143±37</td>
<td>151±22</td>
<td>146±42</td>
</tr>
<tr>
<td>Maximum LA volume (ml)</td>
<td>15.8±6.6</td>
<td>15.1±7.1</td>
<td>20.2±5.9*</td>
</tr>
<tr>
<td>LA reservoir volume (ml)</td>
<td>3.3±1.8</td>
<td>3.2±1.4</td>
<td>5.9±1.8*</td>
</tr>
<tr>
<td>Peak J (ml/min)</td>
<td>136±44t</td>
<td>261±94</td>
<td>143±43</td>
</tr>
<tr>
<td>Peak K (ml/min)</td>
<td>166±38</td>
<td>181±91</td>
<td>237±93</td>
</tr>
<tr>
<td>Peak J/K</td>
<td>0.86±0.14</td>
<td>0.91±0.19</td>
<td>0.87±0.11</td>
</tr>
<tr>
<td>JFTI (ml)</td>
<td>29.3±9.0</td>
<td>33.0±16.3</td>
<td>39.8±17.7</td>
</tr>
<tr>
<td>KFTI (ml)</td>
<td>22.5±7.9</td>
<td>20.9±12.1</td>
<td>27.6±9.3</td>
</tr>
<tr>
<td>JFTI/KFrI</td>
<td>1.33±0.22</td>
<td>1.68±0.29</td>
<td>1.40±0.25</td>
</tr>
</tbody>
</table>

LA, left atrial; APP, appendectomy; bpm, beats per minute; J, systolic pulmonary venous flow; K, diastolic pulmonary venous flow; FTI, flow time integral. Values are mean±SD (n=5 dogs).

*p<0.05 vs. corresponding value for low LA pressure; †p<0.05 vs. corresponding value for mid LA pressure; ‡p<0.05 vs. corresponding value for sham APP.
distensibility cannot be answered by the present study. Regardless of the mechanism, we have shown that left atrial appendectomy makes the left atrial body stiffer without concomitant changes in left ventricular compliance or relaxation.

Although there were significant differences in the left atrial diastolic stiffness constant after appendectomy, left atrial volumes at matched left atrial pressures were not significantly different before and after appendectomy. This may have been due, in part, to a time-dependent increase in left atrial volume after the initial intravascular volume infusion (see below). Nevertheless, there was a significant statistical interaction between the effects of intravascular volume infusion and appendectomy, indicating that the change in left atrial pressure for a given change in volume was greater after appendectomy than before appendectomy.

Theoretical models of the circulation have suggested that atrial compliance has important effects on left ventricular filling. In an electrical analogue model, atrial compliance increased, cardiac performance improved by virtue of left atrial reservoir function. In that study, although mean left atrial pressure was lower (facilitating pulmonary venous return during ventricular systole), left atrial pressure during ventricular diastole was relatively high, resulting in a greater left atrial–ventricular diastolic gradient and increased ventricular filling. We have shown previously that, for similar abrupt increases in left atrial volume, reduced operative atrial compliance results in a larger increase in left atrial pressure at the time of mitral valve opening but a smaller change in the atroventricular pressure gradient and left ventricular peak lengthening rate. In a lumped parameter analogue model, for a given left atrial pressure and rate of left ventricular relaxation, early left ventricular filling increased directly with atrial compliance. However, the present study is the first to demonstrate the influence of altered atrial compliance on left ventricular filling in vivo.

Recently, it has been suggested that analysis of pulmonary venous flow (left atrial inflow) may be used to explain left ventricular filling dynamics and to estimate left atrial pressure. Although early investigations supported the view that the pattern of pulmonary venous flow is determined primarily by transmission of the right ventricular pressure pulse, recent data suggest that left atrial and left ventricular systolic function are the major determinants of phasic left atrial filling via the pulmonary veins. In the present study, we have shown that left atrial compliance is an important independent determinant of the pattern of pulmonary venous flow by using an experimental protocol that produced an isolated change in atrial compliance. Thus, alterations in atrial compliance in various disease states should be taken into consideration when the pattern of pulmonary venous flow is used to estimate left atrial pressure or to assess left ventricular diastolic function.

The ability of the left atrium to use the Frank-Starling mechanism suggests a physiologically important interaction between atrial compliance and booster pump function. In this regard, we recently showed that the left atrial appendage was more distensible and shortened to a greater extent than the body of the left atrium. Although relatively rapid heart rates precluded accurate measurement of atrial booster pump function from the left atrial sonomicrometer signals in the present study, analysis of the peak late diastolic transmural velocity suggested that, at matched levels of left atrial pressure, atrial systolic function decreased after appendectomy. The lack of a change in pulmonary venous flow ratios after sham appendectomy makes it unlikely that left atrial systolic function deteriorated during the protocol or was unfavorably affected by repeated volume infusions. Thus, our data support the hypothesis that atrial booster pump function varies directly with atrial compliance.

Time-dependent alterations in the passive length–tension relation (hysteresis) are well characterized in isolated muscle and in the intact ventricle. Large increases in left ventricular pressure and volume cause rightward shifts of the left ventricular pressure–dimension and stress–strain relations, and both the rate and extent of pressure change influence the magnitude of the rightward pressure–dimension shift. In our study, volume was infused relatively quickly to high (supraphysiological) mean left atrial pressures. Thus, it is likely that our experimental protocol exaggerated time-dependent alterations in the left atrial pressure–volume relation. Left ventricular diastolic viscoelastic effects are also dependent on diastolic filling time. Although heart rates were not controlled in our larger study, left atrial filling time (during ventricular systole) is less influenced by changes in heart rate than is left ventricular filling time (during ventricular diastole). Moreover, in group B dogs with constant (atrially paced) heart rates, appendectomy caused similar changes in atrial compliance, pulmonary venous flow profiles, and Doppler transmural waveforms. Thus, it is unlikely that differences in left atrial filling time in this study significantly influenced the time-dependent changes in the left atrial pressure–volume relation. It is of interest that the time-dependent change in the passive chamber dimension was nearly twice as great in the left atrium as that observed previously in the left ventricle. Although these differences likely reflect differences in chamber distensibility, we cannot exclude the possibility that differences in shape changes, theoretical models, and experimental designs may be responsible.

Critique of the Methods
We calculated relative, not absolute, left atrial volumes, which we considered sufficient, since each animal served as its own control. A related criticism is that the geometric assumptions used for volume estimates differ before and after appendectomy. Although previous studies have shown that left atrial size calculated from a single echocardiographic dimension correlates highly with left atrial area and volume as measured from cineangiography, we calculated left atrial volumes from two orthogonal dimensions in an attempt to minimize the effects of changing atrial geometry with both volume infusion and appendectomy. It should be recognized that the simple monoeponential curve fit is an empiric approach that defines the direction and magnitude of pressure–volume shifts; physiological interpretation of coefficients should be made with great caution.

The use of the systolic/diastolic ratio as an index of the relative atrial reservoir to conduit function merits discussion. Reservoir function represents the net volume of left atrial flow during ventricular systole from
atrial end systole to mitral valve opening. Since blood does not leave the left atrium during this period, the reservoir volume is equivalent necessarily to the pulmonary venous flow during ventricular systole. Left atrial conduit flow represents the total atrial flow minus reservoir and atrial systolic blood flow and, except for an insignificant volume that crosses the atrioventricular valve during isovolumic contraction, occurs during early ventricular diastole. 10 Thus, pulmonary venous flow during early left ventricular diastole is a measure of conduit flow. Since blood flow was measured in only one pulmonary vein, the systolic and diastolic flow integrals represent only a fraction of the reservoir and conduit volumes; however, the ratio of integrated systolic to diastolic flow provides an index of their relative contribution to atrial function.

It is possible that suture ligation of the left atrial appendage influenced atrial distensibility by restricting motion of the adjacent atrial body. However, at each level of left atrial pressure, the ratio of the maximum left atrial dimension in the long and short axis was unchanged by appendectomy. Since the sonomicrometer on the lateral wall of the atrial body was adjacent to the suture line, it is unlikely that restricted motion along the appendectomy site can explain our findings.

Studies were performed without the pericardium. Because of its restraining properties, the pericardium is likely to influence both the magnitude of left atrial pressure-volume shifts and the time-dependent alterations in the pressure-volume relation. However, it is unlikely to alter qualitatively the effect of appendectomy.

Finally, there may be limitations due to the experimental design. It is possible that repeated volume infusions and the time required to complete the protocol changed left atrial and/or ventricular function. However, in sham-operated dogs there were no significant differences in the stiffness constant or intercept of the left atrial pressure-volume curve or the pattern of pulmonary venous flow. Thus, it is unlikely that our results were due to nonrandomized interventions, the effects of the hemodilution, or deterioration of the experimental preparation over time.

Summary and Clinical Implications

We have shown that left atrial compliance decreases after ligation of the atrial appendage in vivo. This change in compliance is associated with decreased atrial reservoir function manifested by a smaller reservoir volume and alterations in left atrial and left ventricular filling. The decreased systolic/diastolic ratios we observed after appendectomy are consistent with relative decreases in reservoir function and relative increases in conduit function of the left atrium. These findings have clinical implications insofar as the left atrial pressure–volume relation is a major determinant of left atrial hypertension and symptoms of heart failure. Furthermore, the reclamation of stored or potential energy (reservoir function) may contribute to left ventricular filling and is likely to become important in states in which augmented atrial filling is essential for maintaining left ventricular preload (e.g., hypertension and coronary artery disease). Thus, it is reasonable to postulate that the appendage modulates the relation between pressure and volume in the left atrium and becomes important in states of left atrial pressure and volume overload.

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