The effects of pressure-induced right ventricular hypertrophy on left ventricular diastolic properties and dynamic geometry in the conscious dog


ABSTRACT  To determine whether chronic pressure overload and hypertrophy of the right ventricle alter the diastolic properties of the left ventricle, six adult dogs underwent banding of the pulmonary artery and were instrumented for studies 8 months later. Fourteen control dogs were also studied. Pressure and dimension data were collected from the dogs while they were awake and unsedated. The anterior-posterior, septal-free wall, and base-apex axis diameters of the left ventricle were measured with ultrasonic dimension transducers. Right and left ventricular pressures were measured with micro-manometers. Pulmonary arterial banding resulted in increased right ventricular/body mass ratios (2.70 ± 0.36 g/kg vs 1.52 ± 0.15 g/kg control; p ≤ .05) and increased left ventricular/body mass ratios (4.84 ± 0.64 g/kg vs 4.21 ± 0.49 g/kg control; p ≤ .05). Right ventricular peak systolic and end-diastolic pressures were higher among the banded dogs (50 ± 20/7 ± 5 mm Hg vs 31 ± 6/3 ± 2 mm Hg control; p ≤ .05). A rearrangement in the three-dimensional geometry of diastolic filling occurred in the banded dogs. Extension from unstressed diastolic dimension (strain) in the base-apex axis was significantly larger in the banded dogs at left ventricular transmural pressures of 12, 8, and 4 mm Hg; strains in the septal–free wall axis were significantly smaller at transmural pressures of 12 and 8 mm Hg. Normalized diastolic left ventricular pressure-volume data and midwall circumferential stress-strain data were fit to the Kelvin viscoelastic equation. The normalized pressure-volume relationships of the banded dogs lay significantly to the left of those of the controls, indicating a loss of left ventricular chamber compliance. The midwall circumferential stress-strain relationships of the banded dogs were also shifted to the left, indicating a loss of intrinsic myocardial compliance. Thus, during the course of right ventricular hypertrophy caused by right ventricular pressure overload, alterations in the mass, geometry, and material properties of the left ventricle occur. At 8 months the chamber compliance of the left ventricle is compromised by these changes. 


RECENT CLINICAL DATA suggest that in some forms of cyanotic congenital heart disease with pressure or volume overload of the pulmonary ventricle, the systemic ventricle may function abnormally and continue to function abnormally after operative correction.1–3 When dysfunction of the systemic ventricle is noted during the course of these diseases, it would be useful to identify a component of this dysfunction that is strictly attributable to elevated pressures in the pul-

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during early systole, and only during late ejection is there effective left ventricular contraction in the septal-free wall axis. After closure of the atrial septal defect and normalization of right ventricular pressures, septal geometry and left ventricular systolic function usually become normal. Similar changes in septal position and motion have been demonstrated during acute right ventricular hypertension induced by pulmonary arterial constriction in conscious dogs. The reversibility of these abnormalities in the setting of chronic right ventricular hypertension and their presence during acute right ventricular hypertension suggest that they are the direct result of elevated right-sided pressures rather than the byproduct of some change in the intrinsic properties of the left ventricular myocardium. The present study was undertaken to document whether the same or similar rearrangements in left ventricular geometry occur in a preparation of chronic right ventricular pressure overload, and to determine to what extent in the intact circulation left ventricular chamber compliance is altered by these rearrangements or by other concomitants of pressure-induced right ventricular hypertrophy.

Materials and methods

Experimental preparation. Six healthy adult dogs (20 to 30 kg) underwent banding of the pulmonary artery through a right thoracotomy. Right ventricular pressures were monitored during the procedure. The band was slowly tightened until peak systolic right ventricular pressure exceeded 80 mm Hg or until frequent ventricular extrasystoles developed. The ayzygos vein was ligated during this initial procedure to ensure inflow stasis during vena caval occlusions performed during subsequent studies.

Eight months later, these six animals and 14 controls of comparable size were subjected to a left thoracotomy under general anesthesia (pentobarbital 30 mg/kg) for the implantation of instrumentation to collect pressure and dimension data. The experimental preparation has been described previously. Briefly, three pairs of ultrasonic dimension transducers were implanted to measure the anterior-posterior minor axis, septal-free wall minor axis, and base-apex major axis of the left ventricle. The anterior-posterior minor axis and base-apex major axis transducers were sewn to the epicardium to measure external diameters. The septal-free wall diameter was measured from the septal midwall to the epicardium of the lateral free wall. Silicone rubber catheters were inserted into the right ventricle and left atrium so that during subsequent studies micromanometers could be introduced to measure right and left ventricular pressures. A third silicone rubber catheter closed at its distal end by a compliant silicone rubber balloon (1/4-inch thickness) was positioned in the left pleural cavity at the level of the aortic arch to measure intrapleural pressure. A fluid-filled polyvinyl chloride catheter was inserted through the left internal mammary artery into the aortic arch to measure aortic pressure. Inflatable silicone rubber occluders were placed around the two venae cavae. The electrical leads, catheters, and occluders were all exteriorized dorsal to the thoracotomy incision. The pericardium was left open and the chest closed. Postoperatively the dogs received intramuscular injections of dihydrostreptomycin (0.75 g) and penicillin (6 × 10^8 U) for 3 days.

Instrumentation and data acquisition. Each dog was allowed to recover from surgery for a week before being studied. Data were collected while the dogs were awake and unsedated. Left and right ventricular pressures were measured with catheter-tipped micromanometers (Millar PC-350). They were driven with Hewlett-Packard 8805C carrier preamplifiers and were zeroed and balanced to atmospheric pressure at 38°C. Zero drift of each transducer did not exceed 0.5 mm Hg during any study. The sonomicrometer used in these experiments was constructed in this laboratory. It converts the transit time of a pulse of ultrasound between two piezoelectric crystals into an analog signal. Since the velocity of sound is constant in tissues and blood, the measured transit time is directly proportional to the distance between the transducers. The sampling rate of the device is 1 kHz, and its resolution is 0.05 mm.

Pleural and aortic pressures were measured with external transducers (Statham P23Db) connected to fluid-filled catheters. A No. 6F catheter (U.S.C.I.) was inserted through the previously implanted pleural catheter to measure pleural pressure. The catheter-balloon system was filled with between 1.0 and 2.0 ml of saline before insertion of the No. 6F catheter. This volume was enough to fill the system with the No. 6F catheter in place and to measure 0.0 mm Hg pressure during testing before implantation. Aortic pressure was monitored with the polyvinyl chloride catheter previously implanted in the aortic arch. The external transducers were zeroed and balanced to atmospheric pressure at the mid chest level. The zero drift of the transducer measuring pleural pressure did not exceed 0.5 mm Hg during the course of any study.

Analog data representing pressures and dimensions were recorded onto magnetic tape with a Hewlett-Packard 3968A tape recorder. Data were collected from each dog during a baseline period and during a vena caval occlusion. To perform the vena caval occlusion, the vena caval occluders were inflated so that peak systolic left ventricular pressure was gradually reduced to 25 mm Hg over a 30 sec period.

Each dog was killed and autopsies were performed at the conclusion of the experiment. The position of the septal transducer was ascertained to be within 2 mm of the midwall position in each dog. The mass of the right ventricular free wall and the mass of the left ventricle including the interventricular septum were measured. The left ventricular papillary muscles were then removed and left ventricular mass again determined.

Data analysis. The analog signals representing pressures and dimensions were digitized at 5 msec intervals on a PDP 11/34 computer (Digital Equipment Corp.). The left ventricle was modeled as a generalized ellipsoidal shell with three orthogonal axes. The measured base-apex axis was considered the external major axis diameter of the shell. The measured anterior-posterior dimension was considered one of the two external equatorial minor axis diameters. The measured septal–free wall dimension was set equal to the external equatorial septal–free wall diameter minus one-half of a calculated equatorial wall thickness.

The dimension of left ventricular equatorial wall thickness was calculated from the three measured left ventricular axis dimensions and the postmortem mass of the left ventricle without its papillary muscles. The external volume (Ve) of the shell is equal to:

\[ Ve = \frac{\pi}{6}(a)(b)(c + 0.5h) \]  

(1)

where a, b, and c are the measured major axis, anterior-posterior or minor axis, and septal–free wall minor axis, respectively, and h is equatorial wall thickness. The inner volume (Vi) of the shell is equal to:

\[ Vi = \frac{\pi}{6}(a - 1.1h)(b - 2h)(c - 1.5h) \]  

(2)
Equation 2 assumes that the thickness of the shell at the base and apex (beneath the major axis transducers) is 55% of the equatorial wall thickness, a relationship previously validated by postmortem studies. 12 The mass (M) of the shell is equal to its volume multiplied by its specific gravity (1.07 g/cm³):

\[ M = 1.07(\text{Ve} - \text{Vi}) \]  

(3)

By substituting the postmortem mass of the left ventricle for M, h can be calculated from equations 1, 2, and 3. This single estimate does not account for the variability of wall thickness along the left ventricular equatorial circumference.

To quantify the chamber size of the left ventricle, intracavitary volume (Vi) was calculated from equation 2, and midwall equatorial circumference (L) was calculated as:

\[ L = 2(b - h) \int_0^{\pi/2} \sqrt{1 - k^2 \sin^2 \theta} \, d\theta \]  

(4)

where

\[ k^2 = \frac{(b - h)^2 - (c - 0.5h)^2}{(b - h)^2} \]  

(5)

For the purpose of analyzing diastolic force–dimension relationships, each of the measured and calculated left ventricular dimensions was normalized to a Lagrangian strain (fractional extension from unstressed dimension):

\[ D = (D - \text{Do})/\text{Do} \]  

(6)

where D is the Lagrangian strain of dimension D, and Do is the unstressed dimension of D. The unstressed dimensions of the three left ventricular axes, left ventricular volume, and midwall circumference were determined at maximal veno caval occlusion, when left ventricular transmural pressure was at a minimum, usually close to 0 mm Hg.

Left ventricular transmural pressure (TMP) was calculated as the difference between left ventricular intracavity pressure (LVP) and pleural pressure (PP):

\[ \text{TMP} = \text{LVP} - \text{PP} \]  

(7)

The purpose of determining this transmural left ventricular pressure was simply to account for respiratory variation in left ventricular diastolic pressure. It does not represent an attempt to account for all of the external constraints to left ventricular filling. Thus the diastolic relationships between left ventricular transmural pressure and normalized axis or volume measurements do not account for these external constraints. Changes or abnormalities in these relationships may therefore reflect changes in the external constraints to left ventricular filling, e.g., increases in right ventricular diastolic pressure, that result in changes in left ventricular diastolic geometry. Changes in these relationships do not necessarily reflect any changes in the intrinsic stiffness of the left ventricular myocardium.

To examine the intrinsic stiffness of the left ventricular myocardium, not only must all external constraints be accounted for, but also must any alterations in left ventricular geometry. The relationship between average midwall circumferential wall stress and midwall circumferential strain was therefore used to describe the intrinsic compliance of a circumferential myocardial hoop at the equator of the left ventricle. To estimate midwall circumferential stress at the equator of the left ventricle, an effective external left ventricular pressure (ELVP) was calculated by assuming that two-thirds of the surface area of the left ventricle is surrounded by the pleural cavity and one-third is surrounded by the right ventricle:13

\[ \text{ELVP} = (2\text{PP} + \text{RVP})/3 \]  

(8)

The average midwall circumferential stress (σ) at the equator of the left ventricle was then calculated for a thin-walled ellipsoidal shell14:

\[ \sigma = \frac{\text{LVP} - 2h}{4h} \left\{ \frac{(c - 1.5h)(b - 2h) + (b - 2h)(c - 1.5h) + (b - 2h)(c - 1.5h)}{b - 2h + (c - 1.5h) + (a - 1.5h)^2} \right\} \]  

(9)

A computerized algorithm was used to identify the diastolic and ejection phases of the cardiac cycle. The beginning of diastole was marked at the minimum left ventricular pressure after ventricular systole. The end of diastole was marked at the minimum left ventricular pressure after atrial systole. The beginning of ejection was marked at the first time during systole that left ventricular pressure was equal to aortic pressure. End-ejection was marked during the rapid descent of left ventricular pressure (dP/dt ≥ 200 mm Hg/sec) at the first time aortic pressure exceeded left ventricular pressure by more than 5 mm Hg.

To characterize the static elastic diastolic properties of the left ventricle, pressure-strain and stress-strain data were selected from multiple (20 to 30) cardiac cycles during veno caval occlusions. Only data of low strain velocity (ds/dt ≤ 0.01 sec⁻¹ for each left ventricular axis, ds/dt ≤ 0.03 sec⁻¹ for midwall circumference, and ds/dt ≤ 0.1 sec⁻¹ for left ventricular volume) were analyzed, thereby minimizing the effects of the viscous filling properties of the left ventricle. Data were selected from the midexpiratory phase of the respiratory cycle to minimize respiratory variation in pressure and dimension. Where possible the data were fit by nonlinear least-squares regression to the Kelvin viscoelastic equation:

\[ \text{TMP} = \alpha(\text{e}^{\beta x} - 1) + \eta dP/dt + \gamma \]  

(10)

where α, β, η, and γ are parameters determined from the curve-fit, and dP/dt is strain velocity. The elastic parameters of the Kelvin equation are α and β; η is the viscous parameter. The parameter γ allows the derived curves to pass above or below the origin in those cases in which minimum left ventricular transmural pressure is not exactly zero (presumably when the micromanometers measuring left ventricular and pleural pressure were not precisely at the same level). Because only data of very low strain velocity were analyzed, the viscous term of equation 10, η dP/dt, was set equal to zero:

\[ \text{TMP} = \alpha(\text{e}^{\beta x} - 1) + \gamma \]  

(11)

Thus only the elastic component of the Kelvin model was used to account for the forces generated in filling the left ventricle. The suitability of equation 11 as a descriptor of the static elastic relationship between midwall circumferential stress and strain has previously been established.15 This modification of the Kelvin model has also been used empirically to characterize the diastolic relationships between each left ventricular axis length strain and transmural pressure as well as the left ventricular transmural pressure-volume strain relationship.16 Curve fits of data to equation 11 were considered satisfactory only if the estimated variance of γ on x was less than 1 mm Hg.
to compute circumferential strains at circumferential stresses of 40, 25, and 10 dyne $\times 10^3$/cm$^2$. Mean values of strain at each stress were computed for the two groups of dogs.

**Statistical methods.** To compare data from the two groups of dogs, group means were compared by unpaired t tests based on pooled variance. For descriptive purposes, the means and standard deviations of these data are presented in tables 1 through 3. Pooled variance was also used to establish 95% confidence limits about the mean values of strain for each group of dogs. These confidence limits are depicted graphically in figures 1 through 6.

**Results**

**Ventricular mass and geometry.** The means and standard deviations of left and right ventricular mass for the control and banded dogs are presented in table 1. The interventricular septum was included with the left ventricle for the purpose of these measurements. The masses of both the right and left ventricles were significantly greater among the banded dogs. Left ventricular mass was greater by 15%, and right ventricular mass was greater by 78%. The ratio of right to left ventricular mass was also significantly higher among the banded dogs.

In the banded dogs, changes in the geometric relationships between the unstressed dimensions of the three left ventricular axes were observed (table 1). There was a statistically significant increase in the ratio of unstressed anterior-posterior minor axis dimension to unstressed major axis dimension. The ratio of unstressed septal–free wall minor axis dimension to unstressed anterior-posterior minor axis dimension was smaller among the banded dogs, but this difference did not reach statistical significance. Similar differences existed between the end-diastolic relationships of these dimensions. The end-diastolic hemodynamic variables that correspond to these data are presented in table 2. The end-diastolic ratio of anterior-posterior minor axis dimension to base-apex major axis dimension was significantly larger among the banded dogs. The end-diastolic ratio of septal–free wall minor axis dimension to anterior-posterior minor axis dimension was significantly smaller among the banded dogs.

**Hemodynamics.** Hemodynamic variables obtained with the dogs at rest are shown in table 2. Mean values from 10 consecutive cardiac cycles were used to represent each dog. The banded dogs had significantly higher right ventricular pressures than the controls. The heart rates of the banded dogs were faster, but this difference between the two groups was not statistically significant. Although end-diastolic left ventricular volume was smaller and end-diastolic left ventricular pressure was lower in the banded dogs, these differences did not reach statistical significance. Left ventricular stroke volume was smaller in the banded dogs, but again this difference was not statistically significant. However, the banded dogs did have significantly smaller systolic ejection fractions than the controls.

**Left ventricular diastolic properties.** Figure 1 shows the left ventricular transmural pressure-volume strain relationships from the two groups of dogs. Mean values of strain for each group of dogs were computed at left ventricular transmural pressures between 0 and 20 mm Hg at 0.8 mm Hg increments. Curves have been fitted to these mean values of strain (equation 11). The 95% confidence limits about each mean were calculated and are also shown. The mean values of strain from the banded groups of dogs were significantly smaller.

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**TABLE 1**

Ventricular masses and left ventricular geometry

<table>
<thead>
<tr>
<th></th>
<th>Control (n = 14)</th>
<th>Pulmonary artery band (n = 6)</th>
</tr>
</thead>
<tbody>
<tr>
<td>LV mass (g/kg body mass)</td>
<td>4.21 ± 0.49</td>
<td>4.84 ± 0.64^</td>
</tr>
<tr>
<td>RV mass (g/kg body mass)</td>
<td>1.52 ± 0.15</td>
<td>2.70 ± 0.36^</td>
</tr>
<tr>
<td>RV mass/LV mass</td>
<td>0.36 ± 0.04</td>
<td>0.56 ± 0.10^</td>
</tr>
<tr>
<td>B/A</td>
<td>0.740 ± 0.039</td>
<td>0.858 ± 0.118^</td>
</tr>
<tr>
<td>C/B</td>
<td>0.881 ± 0.093</td>
<td>0.815 ± 0.093</td>
</tr>
<tr>
<td>EDB/EDA</td>
<td>0.818 ± 0.033</td>
<td>0.882 ± 0.071^</td>
</tr>
<tr>
<td>EDC/EDB</td>
<td>0.897 ± 0.096</td>
<td>0.803 ± 0.055^</td>
</tr>
</tbody>
</table>

Data are mean ± SD.

A$_i$ = unstressed base-apex major axis dimension; B$_i$ = unstressed anterior-posterior minor axis dimension; C$_i$ = unstressed septal–free wall minor axis dimension; EDA = end-diastolic base-apex major axis dimension; EDB = end-diastolic anterior-posterior minor axis dimension; EDC = end-diastolic septal–free wall minor axis dimension; LV = left ventricular; RV = right ventricular.

^p ≤ .05 by unpaired t test.

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**TABLE 2**

Hemodynamics

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Pulmonary artery band</th>
</tr>
</thead>
<tbody>
<tr>
<td>Heart rate (cycles/min)</td>
<td>115 ± 15</td>
<td>133 ± 32</td>
</tr>
<tr>
<td>Peak systolic RVP (mm Hg)</td>
<td>31 ± 6</td>
<td>50 ± 20^</td>
</tr>
<tr>
<td>End-diastolic RVP (mm Hg)</td>
<td>3 ± 3</td>
<td>7 ± 5^</td>
</tr>
<tr>
<td>Peak systolic TMP (mm Hg)</td>
<td>123 ± 10</td>
<td>121 ± 9</td>
</tr>
<tr>
<td>End-diastolic TMP (mm Hg)</td>
<td>13 ± 3</td>
<td>10 ± 3</td>
</tr>
<tr>
<td>End-diastolic LV volume (cm$^3$)</td>
<td>77.4 ± 26.0</td>
<td>66.6 ± 18.6</td>
</tr>
<tr>
<td>LV stroke volume (cm$^3$)</td>
<td>27.0 ± 12.9</td>
<td>17.3 ± 9.8</td>
</tr>
<tr>
<td>LV ejection fraction</td>
<td>0.345 ± 0.075</td>
<td>0.250 ± 0.097^</td>
</tr>
</tbody>
</table>

Data are mean ± SD.

LV = left ventricular; RVP = right ventricular pressure; TMP = left ventricular transmural pressure.

^p ≤ .05 by unpaired t test.
than those from the controls at 12, 8, and 4 mm Hg (table 3).

To determine to what extent in the banded dogs the smaller normalized volumes at any given left ventricular transmural pressure were the result of alterations in three-dimensional left ventricular geometry, the diastolic relationships between the individual normalized linear diameters and left ventricular transmural pressure were generated. The relationships between left ventricular transmural pressure and strain in the anterior-posterior axis are illustrated in figure 2. There were no significant differences in strain between the two groups of dogs at transmural pressures of 12, 8, and 4 mm Hg (table 3). Transmural pressure vs strain in the base-apex major axis has been plotted for the two groups of dogs in figure 3. At 12, 8, and 4 mm Hg, the strains in the banded dogs were larger than those in the controls. The relationship between left ventricular transmural pressure and strain in the septal–free wall axis could not be fit to equation 11 in three of the six banded dogs. The lack of adherence to an exponential form was the result of small strains at transmural pressures greater than 8 mm Hg (figure 4). Equation 11 could be fit to the data from the remaining three banded dogs and to the data collected from all of the controls. The individual diastolic relationships from the six banded dogs are shown in figure 4. The means and 95% confidence region of the strain data from the control group have also been illustrated. For the three dogs in which equation 11 could not be fit to the data, the curves were constructed by hand. Although statistical testing was not done, the pressure-strain relationships of four of the six banded dogs lay to the left of the control region at left ventricular transmural pressures greater than 8 mm Hg. At left ventricular transmural pressures of 12 mm Hg, the data from five of the six banded dogs lay to the left of the controls. The midwall circumferential stress-strain relationships are illustrated in figure 5. At 40, 25, and 10 dyne x 10^3/cm^2, the circumferential strains of the banded dogs were significantly smaller than those of the controls (table 3).

**Left ventricular dynamic geometry.** In all of the control dogs, shortening of the septal–free wall minor axis occurred throughout the ejection phase of the cardiac cycle. This was also true in four of the six banded dogs. In the remaining two banded dogs, however, there was dysynchronous shortening of the septal–free wall axis (figure 6). In these two dogs, septal–free wall shortening did not begin until after the beginning of ejection, and the majority of shortening occurred during relaxation and diastole of the subsequent cardiac cycle. Shortening in the anterior-posterior

![Graph](https://example.com/graph.png)

**TABLE 3**

<table>
<thead>
<tr>
<th>Diastolic data</th>
<th>TMP = 12 mm Hg</th>
<th></th>
<th>TMP = 8 mm Hg</th>
<th></th>
<th>TMP = 4 mm Hg</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Control</td>
<td>Banded</td>
<td>Control</td>
<td>Banded</td>
<td>Control</td>
<td>Banded</td>
</tr>
<tr>
<td>LV volume strain</td>
<td>2.89±0.86</td>
<td>1.93±0.77</td>
<td>2.40±0.73</td>
<td>1.54±0.57</td>
<td>1.66±0.56</td>
<td>1.03±0.40</td>
</tr>
<tr>
<td>Anterior-posterior minor axis strain</td>
<td>0.199±0.034</td>
<td>0.178±0.056</td>
<td>0.166±0.030</td>
<td>0.146±0.046</td>
<td>0.119±0.026</td>
<td>0.098±0.037</td>
</tr>
<tr>
<td>Base-apex major axis strain</td>
<td>0.080±0.023</td>
<td>0.147±0.054</td>
<td>0.066±0.020</td>
<td>0.115±0.039</td>
<td>0.046±0.016</td>
<td>0.074±0.026</td>
</tr>
<tr>
<td>σ = 40 dyne × 10^3/cm^2</td>
<td></td>
<td></td>
<td>σ = 25 dyne × 10^3/cm^2</td>
<td></td>
<td></td>
<td>σ = 10 dyne × 10^3/cm^2</td>
</tr>
<tr>
<td></td>
<td>Control</td>
<td>Banded</td>
<td>Control</td>
<td>Banded</td>
<td>Control</td>
<td>Banded</td>
</tr>
<tr>
<td>Midwall circumferential strain</td>
<td>0.404±0.078</td>
<td>0.305±0.074</td>
<td>0.353±0.062</td>
<td>0.262±0.059</td>
<td>0.244±0.058</td>
<td>0.182±0.039</td>
</tr>
</tbody>
</table>

Data are mean ± SD.

LV = left ventricular; TMP = left ventricular transmural pressure; σ = left ventricular equatorial midwall circumferential stress.

*P ≤ .05 by unpaired t test.
LABORATORY INVESTIGATION—LEFT VENTRICULAR PERFORMANCE

FIGURE 2. Collective diastolic pressure-volume strain relationships in the anterior-posterior axis of the left ventricle. The 95% confidence intervals for strain are also indicated.

or axis and in the base-apex axis occurred throughout ejection in all of the control and banded dogs.

Discussion

The present set of experiments demonstrates that in the presence of right ventricular pressure overload of 8 months duration, the left ventricle (including the interventricular septum) undergoes a small degree of hypertrophy, a change in its three-dimensional diastolic geometry, and a decrease in its compliance as a chamber. The data also suggest that the perturbations in three-dimensional left ventricular geometry induced by chronic right ventricular hypertension can be reversed acutely by unloading the right ventricle. Our results are consistent with those of previous experimental studies that have demonstrated that left ventricular geometry and function are altered by short- and long-term changes in right ventricular loading. However, most of this earlier work was conducted in preparations in which the anatomic relationship between the two ventricles had been preserved but their physiologic arrangement as two pumps in series had been abolished. The results of these studies have suggested that left ventricular diastolic compliance is decreased in the presence of either acute or chronic pressure overload of the right ventricle. Most of the data suggest that this loss of compliance is the result of alterations in the three-dimensional geometry of the left

FIGURE 3. Collective diastolic pressure-strain relationships in the base-apex axis of the left ventricle. The 95% confidence intervals for strain are also indicated.

FIGURE 4. Collective diastolic pressure-strain relationship in the septal-free wall of the left ventricle for the control group of dogs. The individual pressure-strain relationships for the six banded dogs are also illustrated. The 95% confidence intervals for the strains of control dogs are indicated.

FIGURE 5. Collective diastolic relationships between circumferential stress and strain. The 95% confidence intervals for strain are also indicated.
ventricle. Leftward displacement and flattening of the interventricular septum have been observed in echocardiographic studies, and disproportionate decreases in diastolic septal-free wall dimension have been demonstrated when several left ventricular axis dimensions have been measured. Data collected from conscious dogs during a previous study in our laboratory suggested that during acute right ventricular hypertension, decreases in the compliance of the left ventricular chamber are purely the result of changes in three-dimensional left ventricular geometry and that the intrinsic compliance of the left ventricular myocardium is unaltered.

Several changes in the three-dimensional diastolic geometry of the left ventricle occurred in the present study. First, in the banded dogs, the external configuration of the left ventricle became more spherical in the sense that the ratio of the measured anterior-posterior short axis dimension to the measured base-apex long axis dimension was larger than that in the controls. This was true both for the end-diastolic and the unstressed dimensions of the left ventricle. This relative increase in anterior-posterior equatorial dimension compared with base-apex dimension may have been the result of a greater increase in equatorial wall thickness than basal or apical wall thickness and hence an increase in the ratio of external short- to long-axis dimensions. There was also a change in the end-diastolic equatorial geometry of the left ventricle. At end-diastole the ratio of septal-free wall dimension to anterior-posterior dimension in the banded dogs was significantly smaller than it was in the controls. This change in equatorial geometry, although still present when the left ventricle was emptied, was not statistically significant at zero transmural pressure. Since the right ventricular hypertension present in the banded dogs relented as the ventricles emptied during caval occlusions, it could be argued that this alteration in left ventricular equatorial geometry depended on the presence of elevated right ventricular pressures and diminished or vanished with acute unloading of the right ventricle. A similar alteration in end-diastolic left ventricular equatorial geometry has been demonstrated during acute pressure loading of the right ventricle. The most likely explanation for this phenomenon in both models is leftward displacement of the relatively compliant interventricular septum in response to a diminished interventricular pressure gradient.

The geometry of the elastic constraints to left ventricular diastolic filling was also altered in the banded dogs. It should be emphasized that the relationships between normalized axis dimension and left ventricular transmural pressure illustrated in figures 2 to 4 were constructed simply to document changes in the dynamic and static geometry of left ventricular filling. They cannot be used to examine changes in the intrinsic muscle properties of the left ventricular myocardium because they do not account for the effective external constraints to left ventricular filling or for changes in geometry of the left ventricular chamber. Because local wall thickness, local transmural pressure, and local curvature were not estimated, no definitive conclusions regarding local wall stresses and the separate compliances of the left ventricular free wall and interventricular septum can be drawn from these relationships. Compared with the controls, the left ventricles of the banded dogs were less compliant to extension from unstressed dimension in the septal-free wall axis (figure 4) and more compliant in the base-apex axis (figure 3). The decreased extension in the septal-free wall axis is again similar to that observed during acute right ventricular hypertension and is most likely the result of changes in the external constraints of the left ventricle (reduced transseptal pressures at any given diastolic left ventricular pressure with leftward displacement of the interventricular septum). The dependence of this phenomenon on the presence of elevated right ventricular pressures is supported by the fact that strains in the septal-free wall axis were not significantly smaller in the banded dogs when both ventricles were emptied sufficiently to reduce diastolic left ventricular transmural pressure to below 8 mm Hg (figure 4). The increase in extension in the base-apex axis at any given left ventricular transmural pressure
observed in the banded dogs (figure 3) has not been observed during acute right ventricular pressure overload. It must be assumed, therefore, that this change is the result of more gradual alterations in the geometry and material properties of the left ventricle that accompany chronic right ventricular hypertension.

To examine the intrinsic stiffness of the left ventricular myocardium in an equatorial hoop of the left ventricle, the relationship between midwall circumferential stress and strain was constructed. The calculation of stress in this relationship normalizes forces in the left ventricular wall both for external constraints and for left ventricular geometry. Both pleural and right ventricular pressure have been incorporated into the determination of effective external pressure for calculating this wall stress. The leftward shift of the stress-strain relationship in the banded dogs suggests that the intrinsic compliance of the left ventricular myocardium has been altered. It cannot be determined from these data where in the equatorial circumference of the left ventricle this change has occurred. Therefore, it is possible that only the septal myocardium was affected without any change in the properties of the left ventricular free wall. Conversely, the left ventricular free wall may have been the only portion of the myocardium affected. The leftward shift of the normalized diastolic pressure-volume relationship (figure 1) and the decreased chamber compliance of the left ventricle in the banded dogs were probably the result of the aforementioned geometric rearrangements as well as a change in the intrinsic material properties of the left ventricular myocardium. In the setting of acute right ventricular hypertension, the normalized left ventricular diastolic pressure-volume relationship is also shifted to the left by smaller extensions in the septal-free wall axis at any given left ventricular transmural pressure. However, no significant change in the circumferential stress-strain relationship was observed during acute right ventricular hypertension, suggesting that a change in the intrinsic compliance of the left ventricular myocardium did not contribute to the decrease in chamber compliance. In our banded dogs, the increase in left ventricular myocardial stiffness, suggested by the leftward displacement of the midwall circumferential stress-strain relationship, may have been the result of the small degree of left ventricular hypertrophy that occurred in these animals. There are data to suggest that loading-induced hypertrophy of the left ventricular myocardium can result in alterations in intrinsic myocardial compliance. Previous experimental studies from this laboratory and others have demonstrated an increase in myocardial stiffness during the development of left ventricular hypertrophy induced by chronic left ventricular pressure overload. Mirsky and Laks, working with excised hearts, also demonstrated a time-dependent increase in left ventricular muscle stiffness in the presence of left ventricular hypertrophy induced by pressure overload of the right ventricle.

It is also possible that a decrease in septal compliance without any change in the material properties of the left ventricular free wall accounted for this difference in intrinsic myocardial compliance between the two groups of animals. Data from previous studies have suggested that the material properties and compliance of the interventricular septum are altered by chronic right ventricular hypertension. Using statistical methods, previous investigators have demonstrated significant correlations between left and right ventricular diastolic pressures during interventions that acutely alter right ventricular loading. The data from a recent study by Little et al. demonstrated that this statistical coupling between the diastolic pressures in the two ventricles is also present after 6 weeks of sustained right ventricular hypertension. However, in their animals with chronic pulmonary arterial constriction, the statistically derived coupling factor between left and right ventricular diastolic pressures was smaller than that derived from the controls. In the authors' model, this suggested that during the course of chronic right ventricular hypertension, a decrease in septal compliance had occurred and that transient changes in right ventricular and transseptal pressures produced smaller displacements of the septum and changes in left ventricular geometry. Again, this finding of a change in the material properties of at least a portion of the left ventricular chamber after a period of sustained right ventricular hypertension is consistent with our present findings.

It might also be argued that since the interventricular septum was included in the mass of the left ventricle, septal hypertrophy alone accounted for the small increase in left ventricular mass observed in the present study. It was assumed that the septum comprises approximately one-third of the left ventricular wall, then a 45% increase in septal mass alone would account for the 15% increase overall in left ventricular mass. However, a previous study of dogs after pulmonary arterial banding demonstrated that after 7 weeks there are significant increases in both left ventricular free wall and septal mass. No mechanism for this biventricular response has ever been clearly documented, although it has been postulated that the left ventricular myocardium may respond to elevated levels of circulating humoral factors in response to pressure.
loading of the right ventricle. There is no evidence in the present study to suggest that the interventricular septum obstructed left ventricular outflow in the banded dogs, and there was no significant difference between maximum systolic left ventricular pressures in the two groups of dogs.

Dyskinetic systolic shortening in the septal–free wall axis was demonstrated in two of the six banded dogs in our study. Similar dyskinesia in the septal–free wall axis, severe enough to compromise systolic stroke volume and ejection fraction, was a constant finding during acute right ventricular hypertension induced by pulmonary arterial constriction. This similarity between the abnormality in dynamic left ventricular geometry observed in the two banded dogs and that observed during acute right ventricular hypertrophy again suggests that the rearrangements in left ventricular geometry induced by chronic right ventricular pressure overload are the result of elevated right ventricular pressures and should be reversible with the restoration of normal right ventricular hemodynamics. Hemodynamic variables (most importantly heart rate) were not controlled sufficiently to determine whether systolic function was significantly compromised in the two banded dogs with dyskiniesia in the septal–free wall axis.

The changes in left ventricular geometry we have documented in this study are similar to those that have been reported in patients with chronic pressure or volume overload of the right ventricle. Data from these clinical studies have suggested that in some cases the abnormalities in dynamic geometry are responsible for diminished left ventricular diastolic compliance and impaired systolic performance. There has been considerable speculation as to whether these abnormalities are the direct result of increased right ventricular pressures and flows or whether they are manifestations of alterations in the intrinsic material properties of the left ventricle. After the surgical closure of an atrial septal defect, the abnormalities in septal position and motion soon relent which suggests that these geometric rearrangements are the direct result of right ventricular hemodynamic abnormalities. The similarity between these geometric rearrangements and those observed during acute right ventricular hypertrophy also suggests that right ventricular hypertension in and of itself can cause these abnormalities and that they will relent when normal pressures are restored in the chronically hypertensive right ventricle. However, the increase in left ventricular myocardial stiffness demonstrated in this study suggests that the material properties of at least a portion of the left ventricle are altered by chronic right ventricular hypertension. If there is an anatomic substrate for this change in muscle stiffness, it would be unlikely to regress immediately after normalization of right ventricular pressures.

Changes in the material properties of the systemic ventricle may account at least in part for the impairment of systemic ventricular function in patients with cyanotic congenital heart disease. This dysfunction does not always completely relent with operative correction and restoration of normal hemodynamics. Chronic hypertension in the pulmonary ventricle is usually a component of these disease complexes. When changes in systemic ventricular geometry identical or similar to those observed in this study are observed in these patients, it might be anticipated that closer to normal compliance and systolic dynamic geometry will be present after pressures are reduced in the pulmonary ventricle. However, on the basis of chronic right ventricular hypertension alone, there may be more lasting changes in the material properties in at least some portion of the systemic ventricle that will contribute to postoperative systemic ventricular dysfunction.

The limitations of the methods used in this study have been discussed previously. In brief, most clinical and experimental data suggest that the shape of the left ventricle deviates from that of an ellipsoidal shell during chronic right ventricular pressure overload. This is the result of leftward septal displacement that is often accompanied by flattening of the septal surface or even bowing and convexity toward the left ventricle. Modeling of the left ventricle as an ellipsoidal shell permits computation of wall thickness, midwall circumference, and chamber volume from the three measured axis dimensions. If the left ventricle is deformed into a crescentic shape during the course of chronic right ventricular pressure overload, measurements of additional left ventricular chords and wall thickness would be necessary to describe its geometric configuration and provide more precise estimates of volume, circumference, and stress. In addition, the equatorial thickness of the left ventricle was assumed to be homogeneous for the purpose of determining its dimension from measurements of left ventricular mass and linear axis dimensions. This assumption may not be entirely valid in the banded dogs, in which the hypertrophy and hence thickness of the septum may have been greater than that of the left ventricular free wall. Thus left ventricular free wall thickness may have been somewhat overestimated in the banded dogs. Because left ventricular free wall thickness was subtracted from the measured dimensions of both the
septal-free wall and anterior-posterior diameters to obtain midwall and endocardial diameters, the midwall circumference and chamber volume of the left ventricle may have been slightly underestimated in the banded dogs (equations 2 and 4).

In summary, we have shown that during the process of pressure-induced right ventricular hypertrophy, the mass, geometry, and material properties of the left ventricle are altered. In the face of these abnormalities, left ventricular chamber compliance is decreased. Right ventricular hypertension seems to be a necessary substrate for some of the alterations in three-dimensional left ventricular geometry, since acute unloading of the two ventricles by vena caval occlusion tends to normalize the relationship between diastolic left ventricular transmural pressure and septal-free wall dimension. The similarity between the geometric abnormalities induced by acute and chronic pressure overload at the right ventricle also suggests that these abnormalities require the presence of some degree of right ventricular hypertension and are reversible with restoration of normal right ventricular pressures. However, the loss of intrinsic myocardial compliance that was observed may have an anatomic substrate that is related to the small amount of left ventricular hypertrophy that was also observed. If this is the case, it is unlikely that removal of the obstruction of right ventricular outflow would immediately correct this abnormality.

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