Effect of Right Ventricular Pressure on the End-Diastolic Left Ventricular Pressure-Volume Relationship before and after Chronic Right Ventricular Pressure Overload in Dogs without Pericardia

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SUMMARY. We studied the effect of chronic right ventricular pressure overload on diastolic ventricular interdependence in dogs without pericardia, instrumented to measure left ventricular pressure, right ventricular pressure, and 3 left ventricular dimensions. We studied 12 dogs before (control) and nine dogs after 6 weeks of pulmonary artery constriction producing systolic right ventricular pressure ≥70 mm Hg. Compared to control, following pulmonary artery band there was greater (P < 0.01) interventricular septal mass (53 ± 15 vs. 35 ± 7 mg, mean ± sd), thickness (15 ± 2 vs. 10 ± 1 mm), and ratio of the surface area of the interventricular septal to total left ventricular surface area (0.38 ± 0.03 vs. 0.33 ± 0.02), but unchanged left ventricular free wall mass (81 ± 12 vs. 84 ± 14 mg) and thickness (11 ± 2 vs. 11 ± 2 mm). End-diastolic right and left ventricular pressures and left ventricular volume were varied by vena cava and pulmonary artery occlusions and releases. Volume was calculated as an ellipsoid and the data in each dog fit to: left ventricular pressure = a0 + a1V + a2V2 + a3V3 + a4V4 + bPRV, r > 0.91 in each dog. During control, b was similar, whether calculated from both pulmonary artery and vena cava occlusions (0.47 ± 0.09) or from vena cava occlusions alone (0.43 ± 0.11), and was greater than the ratio of the interventricular septal surface area to left ventricular surface area (0.33 ± 0.02, P < 0.05).

Following the pulmonary artery band, b decreased to 0.21 ± 0.10 (P < 0.05) and was less than the ratio of interventricular septal surface area to the left ventricular surface area which increased to 0.38 ± 0.03 (P < 0.05). We conclude that the effect of alterations in right ventricular pressure on the end-diastolic left ventricular pressure-volume relationship, independent of the pericardium, is reduced following the pulmonary artery band that produces interventricular septal hypertrophy. These results are consistent with the hypothesis that the effect of alterations of right ventricular pressure on the diastolic left ventricular pressure-volume relationship depends on the relative elastance of the interventricular septum and left ventricular free wall, and not simply on the ratio of the interventricular septal surface area to the left ventricular surface area. (Circ Res 54: 719-730, 1984)
diastole, then the transmural left ventricular pressure ($P_{LV}-P_{ex}$) should be a function ($F$) of the end-diastolic volume ($V_{LV}$) or:

$$P_{LV}-P_{ex} = F(V_{LV})$$

then combining with Equation 1 and rearranging:

$$P_{LV} = F(V_{LV}) + (S_{IVS}/S_{LV})P_{RV} + (1-S_{IVS}/S_{LV})P_{ren}.$$  

This implies that:

$$\frac{\partial P_{LV}}{\partial P_{RV}} = \frac{S_{IVS}/S_{LV}}{} (2)$$

Thus, if the effective left ventricular external pressure is given by Equation 1, then the effect of a change in right ventricular pressure on the left ventricular pressure when pericardial pressure and left ventricular pressure are held constant, will depend on the ratio of surface area of the septum to the total external surface area of the left ventricle.

This study was undertaken to test this prediction (Eq. 2) in intact, chronically instrumented dogs. The $\frac{\partial P_{LV}}{\partial P_{RV}}$ and $S_{IVS}/S_{LV}$ determined in the control situation and after 6 weeks of right ventricular pressure overload that increased $S_{IVS}/S_{LV}$ and produced right ventricular and septal hypertrophy without producing significant hypertrophy of the left ventricular free wall. When these observations were not consistent with Equation 2, we developed an alternative model (Appendix) that suggests that the effect of the right ventricular pressure on the left ventricular end-diastolic pressure-volume relationship depends on the relative elastance of the components of the left ventricle composed of the interventricular septum and the left ventricular free wall. Our observations are consistent with this model.

**Methods**

**Instrumentation**

Fourteen healthy, adult mongrel dogs (20–35 kg) were instrumented under halothane anesthesia through a left lateral thoracotomy using sterile techniques. The pericardium was widely resected between the phrenic nerves. Solid state micromanometer pressure transducers (P18, Konigsberg Instruments) and polyvinyl catheters for transducer calibration (ID 1.1 mm) were inserted through apical stab wounds into the left and right ventricular cavities (Fig. 1). A similar catheter was inserted into the left atrial appendage for blood sampling and the administration of drugs. Three pairs of ultrasonic crystals were implanted in the endocardium of the left ventricle to measure the anterior-posterior, septal-to-lateral, and base-to-apex dimensions (Badke, 1982; Robotham et al., 1983). Hydraulic occluders were placed around the inferior vena cava and the pulmonary artery. The wires and tubing were tunneled subcutaneously and brought out through the skin of the neck. The animals were allowed to fully recover from the surgery for 10 days to 2 weeks.

**Data Collection**

All studies were performed with the dogs lying on their right side in a sling. The right and left ventricular catheters were connected to Statham P23DB pressure transducers calibrated with a mercury manometer. The zero reference point was the vertebral column. The right and left ventricular pressure signals from the micromanometers were adjusted so that the end-diastolic and systolic pressures matched those obtained from the fluid-filled catheters. The transit time of the 5 MHz sound between the crystal pairs was determined and converted to distance, assuming a constant speed of sound in blood of 1.55 mm/sec (Franklin et al., 1973). High fidelity left and right ventricular pressure signals and the dimension signals from three crystal pairs were recorded on an 8-channel oscillograph (Beckman Instruments) at a paper speed of 25 mm/second. The analog signals were digitized with an on-line analog-to-digital converter (Dual Control Systems) at 10-msec intervals and stored on a floppy disk utilizing a minicomputer memory system (Zobex).

**Experimental Protocol**

The instrumented dogs were anesthetized with sodium thiopental, using the minimum dose (2–4 mg/kg) that permitted intubation. To minimize fluctuations in intrathoracic pressure, data were recorded during 12-second periods while the dogs were apneic following 15 seconds of hyperventilation. During the recording of data, the endotracheal tube was open to the atmosphere and the dogs were observed to be certain that they made no respiratory efforts.

**Control Studies**

Twelve dogs were studied in the control state. Data were recorded during a steady state period (Fig. 2) to document the stability of the signals and obtain baseline values. Then data were recorded during four transient inferior vena cava (Fig. 3) and pulmonary artery (Fig. 4) occlusions and releases. These vena cava and pulmonary artery occlusion and releases were used to generate a range of right and left ventricular pressures and left ventricular volumes.

**Chronic Right Ventricular Pressure Overload Studies**

Nine dogs were studied following 6 weeks of chronic right ventricular pressure overload produced by permanent inflation of the pulmonary artery occluder. The occluder was adjusted to maintain a right ventricular systolic pressure of greater than 70 mm Hg. Seven dogs had both control and chronic studies, while two dogs were studied only following chronic right ventricular pressure overload. One animal did not undergo chronic pulmonary artery banding and was studied again 6 weeks after the control measurements. In the chronic right ventricular pressure-overload animals, measurements were obtained during two steady state control periods and during four transient vena cava occlusions and releases. Fibrosis in the area of the pulmonary artery prevented the use of further pulmonary artery obstruction or release in these animals.

**Postmortem Studies**

At the conclusion of the experiment, the hearts were examined and the proper position of the instrumentation confirmed. In the pulmonary artery-banded dogs, the mass and the thickness of the right ventricular free wall, the interventricular septum, and the left ventricular free wall were determined. The surface area of the right ventricular side of the interventricular septum and the epican-
dial surface area of the remainder of the left ventricle was determined by planimetry. The total surface area of the left ventricle was the sum of these two areas. Determinations of surface areas were also made in 13 dogs which had undergone similar instrumentation but had not been subjected to chronic right ventricular pressure overload, and in 20 normal, uninstrumented dogs.

Data Analysis
The stored, digitized data were analyzed using a computer algorithm. Hemodynamic values in each dog were obtained by averaging the data obtained during the two nonintervention equilibrium periods. The data obtained during the pulmonary artery and vena cava occlusions and releases were analyzed at end-diastole. End-diastole was defined as the time at which the relative minimum of the left ventricular pressure occurred after the "a" wave. Only sinus beats with a recognizable "a" wave, and a cycle length greater than 400 msec, were analyzed. Left ventricular volume was calculated assuming a modified ellipsoidal geometry for the left ventricle, utilizing the equation:

\[ V_{LV} = \left( \frac{\pi}{6} \right) D_{AP} \cdot D_{SL} \cdot D_{LA} \]

where \( D_{AP} \) is the anterior-posterior dimension, \( D_{SL} \) is the septal-lateral dimension, and \( D_{LA} \) is the long axis or base-to-apex dimension.

We evaluated the effect of the changes in right ventricular pressure on the left ventricular end-diastolic pressure-volume relationship by approximating the pressure-volume relationship as a fourth order polynomial (Glantz, 1980) plus additional linear terms for right ventricular and pleural (\( P_{pnu} \)) pressures:

\[ P_{LV} = a_0 + a_1 V_{LV} + a_2 V_{LV}^2 + a_3 V_{LV}^3 + a_4 V_{LV}^4 + b P_{RV} + c P_{pnu} \]

where \( a_0, a_1, a_2, a_3, a_4, b, c \) are data constants. In the

FIGURE 1. Diagrammatic representation of the instrumentation.

FIGURE 2. Control recording during the equilibrium period. \( P_{LV} \) = left ventricular pressure (mm Hg), \( P_{RV} \) = right ventricular pressure (mm Hg), \( D_{AP} \) = anterior-posterior left ventricular dimension (mm), \( D_{SL} \) = septal-lateral left ventricular dimension (mm), \( D_{LA} \) = base-apex left ventricular dimension (mm Hg).
In Equation 3, \( b \) is equal to \( \partial P_{LV}/\partial P_{RV} \). The data in each dog generated by both vena cava and pulmonary artery occlusions and releases during the control period, and during vena cava occlusions and releases following 6 weeks of chronic right ventricular pressure overload, were fit to Equation 3 using multiple least square regressions utilizing BMDP program 1R (Dixon et al., 1979). To allow
comparison with the pulmonary artery-banded dogs, the control measurements generated by only caval occlusions and releases were also fit in a similar manner to Equation 3.

Validation of Left Ventricular Volume Calculation

Left ventricular volume was calculated from the three ultrasonically determined left ventricular dimensions. This method is similar to that used and validated by others (Olsen et al., 1983; Visner et al., 1983), except that we determined endocardial dimensions directly, and thus subtraction of left ventricular wall thickness or wall volume was not necessary. This method of determining left ventricular volume takes into account changes in septal configuration that may occur during acute changes in right ventricular pressure and following chronic right ventricular pressure overload (Olsen et al., 1983). We have previously observed in four dogs that, during vena caval occlusions, the stroke volume calculated as the difference between the ultrasonically determined end-diastolic and end-systolic volumes was linearly related to the stroke volume simultaneously measured by an ascending aortic electromagnetic flow probe \( r > 0.97, \text{SEE} < 0.65 \text{ml} \). In one animal, (no. 10), these measurements were repeated following 6 weeks of pulmonary artery bandoing. Again, the calculated (CSV) and measured stroke volume (MSV) were linearly related \( r = 0.94, \text{SEE} = 0.77 \). The regression equations were similar (control: CSV = 1.1 MSV – 12.0; PA band: CSV = 1.0 MSV – 9.4).

Statistical Methods

The significance of the right ventricular pressure term in Equation 3 was tested using a two-tailed t-test (Dixon et al., 1979). Paired comparisons were by paired t-test. Comparison of groups was by unpaired t-tests (Glantz, 1981). Multiple comparisons were performed using analysis of variance. If an overall difference was present, the intergroup comparisons were performed using unpaired, two-tailed t-tests with an appropriate adjustment for multiple comparison using the Bonferroni inequality (Glantz, 1981). All results were summarized as the group mean ± 1 sd, and the level of significance was \( P < 0.05 \).

results

The baseline values obtained during the control period and after 6 weeks of pulmonary artery banding are found in Table 1. Representative analog recordings in a control dog during the equilibrium control period, and during inferior vena cava and pulmonary artery occlusions and releases, are shown in Figures 2, 3, and 4. The sudden occlusion of the inferior vena cava (Fig. 3) resulted in a prompt decrease in right ventricular diastolic pressure. Left ventricular end-diastolic pressure, and left ventricular anterior-posterior and long-axis end-diastolic dimension showed relatively little change during the first few beats after the sudden vena cava occlusion. However, coincident with the initial fall in right ventricular pressure, the end-diastolic septal-lateral dimension increased, resulting in an initial increase in left ventricular end-diastolic volume. Over the next several beats, presumably as the decreased right ventricular stroke volume was transmitted through the pulmonary circulation, left ventricular pressure and volume declined. Sudden release of the vena cava occlusion (Fig. 3) resulted in a prompt increase in right ventricular end-diastolic pressure. The left ventricular end-diastolic pressure and anterior-posterior and long axis dimensions were relatively unchanged initially; however, the end-diastolic septal-lateral dimension fell abruptly. Thus, the left ventricular end-diastolic volume initially declined after release of the vena cava occlusion. Over the next several beats, left ventricular pressure and dimensions steadily increased.

Following the sudden partial occlusion of the pulmonary artery (Fig. 4), right ventricular systolic and then diastolic pressures increased. Coincident with the initial increase in right ventricular end-diastolic pressure, the end-diastolic left ventricular septal-lateral dimension decreased. There was a less marked initial fall in the left ventricular end-diastolic anterior-posterior and long axis dimensions and pressure. Over the next several beats, the left ventricular dimensions and pressure declined. The sudden release of the pulmonary artery occlusion de-

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**Figure 5.** The left ventricular stroke volume calculated as the difference between the ultrasonically determined end-diastolic and end-systolic volumes is related by single linear regression to the stroke volume measured by an aortic flow probe both during inferior vena cava (IVC) and pulmonary artery (PA) occlusions.
increased right ventricular end-diastolic pressure. This was accompanied by a marked increase in the left ventricular end-diastolic septal-lateral dimension. Over the next several beats, the other left ventricular dimensions and end-diastolic pressure increased.

The vena cava and pulmonary artery occlusions and releases produced a variety of end-diastolic left ventricular pressures, volumes, and right ventricular pressures. These points are shown graphically in a dog before and after 6 weeks of pulmonary artery banding in Figure 6. Similar results were seen in animals in which there was an overlap of end-diastolic volume before and after banding.

The left ventricular end-diastolic pressure-volume relationship was well approximated by the fourth order polynomial plus the linear term of right ventricular pressure (Eq. 3), both in the control situation (Table 2) and following chronic right ventricular pressure overload (Table 3). The right ventricular pressure term had a significant effect on the left ventricular pressure-volume relationship in all animals, except one dog after chronic right ventricular pressure overload. In the control animals, \( \frac{dP_{LV}}{dP_{RV}} \) was similar, whether determined from the points generated by both vena cava and pulmonary artery occlusions and releases (0.47 ± 0.09) or from points generated by vena cava occlusions and releases alone (0.43 ± 0.11) (Table 2). \( \frac{dP_{LV}}{dP_{RV}} \) calculated by either method was greater than the ratio of the septal surface area to the total left ventricular surface area determined in similarly instrumented animals (0.33 ± 0.02, \( P < 0.01 \)) (Table 4). The ratio of the septal surface area to the total surface area of the left ventricle was similar in the instrumented control dogs and in 20 uninstrumented animals (0.33 ± 0.02 vs. 0.33 ± 0.03). Following chronic right ventricular pressure overload, the right ventricular and interventricular septal mass and thickness were increased, but the left ventricular free wall mass and thickness were not significantly changed (Table 4). The ratio of the surface area of the septum to the surface area of the left ventricle increased from 0.33 ± 0.02 in the control animals to 0.38 ± 0.03 in the animals following 6 weeks of pulmonary artery banding (\( P < 0.05 \)) (Fig. 7).

Following 6 weeks of right ventricular pressure overload, the \( \frac{dP_{LV}}{dP_{RV}} \) was decreased to 0.21 ± 0.10, from the similarly determined control value of 0.43 ± 0.11 (\( P < 0.05 \)). Following right ventricular pressure overload, \( \frac{dP_{LV}}{dP_{RV}} \) was less than the ratio of the surface area of the septum to the surface area of the left ventricle (0.21 ± 0.10 vs. 0.38 ± 0.03, \( P < 0.05 \)).

The fall in \( \frac{dP_{LV}}{dP_{RV}} \) that occurred following chronic right ventricular pressure overload did not occur in the one animal (dog 11) who was observed over a similar period without pulmonary artery banding. Initially, \( \frac{dP_{LV}}{dP_{RV}} \) was 0.367 ± 0.028, after 6 weeks of sham pulmonary artery banding \( \frac{dP_{LV}}{dP_{RV}} \) was 0.468 ± 0.035.

To help determine whether the decrease in \( \frac{dP_{LV}}{dP_{RV}} \) that occurred after chronic right ventricular pressure overload was due to a decrease in left ventricular volume, \( \frac{dP_{LV}}{dP_{RV}} \) was determined in one animal (dog 10) following 6 weeks of pulmonary artery banding both before and after the infusion of 500 ml of dextran over 5 minutes. Left ventricular end-diastolic volume increased from 38.4 to 42.7 ml, but \( \frac{dP_{LV}}{dP_{RV}} \) was relatively unchanged (0.229 ± 0.064 before dextran, 0.144 ± 0.11 after dextran).

**Discussion**

We determined the effect of alterations of right ventricular pressure on the end-diastolic left ventricular pressure-volume relationship in chronically instrumented, closed chest dogs. The pericardium was removed from these animals and thus the external pressure for the left ventricular free wall was determined by the pleural pressure. We held this pressure constant by performing the measurements during post-hyperventilation apnea with the glottis held open by an endotrachial tube. Measurements were made at end-diastole in beats with cycle lengths greater than 400 msec so that the effects of ventricular relaxation and viscoelastic effects of filling should be minimized (Janicki and Weber, 1980b). Under these conditions, the pressure-volume relationship should be primarily determined by the passive characteristics of the left ventricle. Right ventricular pressure was altered by sudden occlusion and release of the inferior vena cava and the pulmonary artery. Because of the pulmonary transit time, rapid changes were produced in right ventricular pressure while left ventricular pressure initially remained relatively constant and then slowly declined with occlusions or increased with releases (Figs. 3 and 4).

The left ventricular volume was calculated from...
three orthogonal endocardial dimensions assuming modified ellipsoidal geometry for the left ventricle in which the volume is proportion to the product of the three dimensions (Olsen et al., 1983; Walley et al., 1982; Grover and Glantz, 1983). Despite the changes of left ventricular geometry that occur with acute vena caval and pulmonary artery constriction and chronic right ventricular pressure overload, we observed that the stroke volume determined from the calculated ventricular volumes was linearly related to the flow probe-measured stroke volume. Although the relation was not the line of identity, these results indicate that this method provides a consistent index of left ventricular volume despite the changes of left ventricular geometry. These findings are in agreement with those of Olsen et al. (1983.)

We found that alterations in right ventricular pressure, even in the absence of the pericardium, have a significant effect on the normal left ventricular diastolic pressure-volume relationship. A 1 mm Hg increase in right ventricular pressure produced, on the average, greater than 0.4 mm Hg upward shift of the left ventricular pressure volume relationship. Six weeks of right ventricular pressure overload produced right ventricular and interventricular septal hypertrophy, but not significant left ventricular free wall hypertrophy. This intervention decreased the effect of alterations in right ventricular pressure on the left ventricular pressure-volume relationship to less than one half the control level. This decreased effect of alterations of right ventricular pressure does not appear to be due to a decrease in left ventricular volume, or to occur after instrumentation, if the right ventricle is not exposed to chronic pressure overload. These findings indicate that the diastolic ventricular interdependence seen under normal circumstances may not be applicable to clinical situations in which the right ventricle is subjected to a chronic pressure overload.

The right ventricular and pericardial pressures make up the external pressures for the left ventricle. Thus, changes in the right ventricular and pericardial pressures would be expected to alter the left ventricular pressure-volume relationship. The usual manner to account for the effect of an external pressure on a structure is to subtract the external pressure from the intracavitary pressure to calculate the distending or transmural pressure. In the case of the left ventricle, this is difficult, since the left ventricular external pressure is not uniform: the right ventricular pressure acts on the interventricular septum, and the pericardial pressure acts on the left ventricular free wall. In the intact animal, the right ventricular and pericardial pressures are not independent, but are interrelated by the pressure-volume relationship of the pericardium and the cardiac chambers (Refsum et al., 1981; Tyberg et al., 1978). Mirsky and Rankin (1978) have suggested, as a simplifying assumption, that the external pressure for the left ventricle can be calculated as the weighted average of the right ventricular and left ventricular pressures. The weighting factor is the proportion of the surface area of the left ventricle on which each pressure acts. Our study allows us to examine this hypothesis by testing one of its implications, \( \frac{dP_{LV}}{dP_{RV}} = \frac{S_{LV}}{S_{RV}} \). Our results are not consistent with this prediction. In the control situation, \( \frac{dP_{LV}}{dP_{RV}} \) was greater than \( \frac{S_{LV}}{S_{RV}} \), which is about one third. Following chronic right ventricular...
Table 2

The Effect of Alterations in Right Ventricular Pressure on the Left Ventricular End-Diastolic Pressure-Volume Relationship during Control

<table>
<thead>
<tr>
<th>Dog</th>
<th>n</th>
<th>r</th>
<th>dP_\text{LV}/dP_\text{RV} ± SEE</th>
<th>P</th>
<th>n</th>
<th>r</th>
<th>dP_\text{LV}/dP_\text{RV} ± SEE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>91</td>
<td>0.946</td>
<td>0.621 ± 0.045</td>
<td>&lt;0.0001</td>
<td>43</td>
<td>0.958</td>
<td>0.372 ± 0.054</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>2</td>
<td>152</td>
<td>0.957</td>
<td>0.397 ± 0.028</td>
<td>&lt;0.0001</td>
<td>85</td>
<td>0.915</td>
<td>0.327 ± 0.085</td>
<td>&lt;0.0002</td>
</tr>
<tr>
<td>3</td>
<td>109</td>
<td>0.990</td>
<td>0.479 ± 0.015</td>
<td>&lt;0.0001</td>
<td>68</td>
<td>0.983</td>
<td>0.500 ± 0.037</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>4</td>
<td>116</td>
<td>0.918</td>
<td>0.294 ± 0.047</td>
<td>&lt;0.0001</td>
<td>71</td>
<td>0.946</td>
<td>0.246 ± 0.023</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>5</td>
<td>85</td>
<td>0.929</td>
<td>0.588 ± 0.034</td>
<td>&lt;0.0001</td>
<td>53</td>
<td>0.951</td>
<td>0.543 ± 0.037</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>6</td>
<td>134</td>
<td>0.982</td>
<td>0.500 ± 0.012</td>
<td>&lt;0.0001</td>
<td>107</td>
<td>0.983</td>
<td>0.505 ± 0.013</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>7</td>
<td>113</td>
<td>0.991</td>
<td>0.411 ± 0.016</td>
<td>&lt;0.0001</td>
<td>55</td>
<td>0.976</td>
<td>0.404 ± 0.018</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>8</td>
<td>115</td>
<td>0.983</td>
<td>0.550 ± 0.027</td>
<td>&lt;0.0001</td>
<td>50</td>
<td>0.981</td>
<td>0.595 ± 0.028</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>9</td>
<td>94</td>
<td>0.976</td>
<td>0.523 ± 0.032</td>
<td>&lt;0.0001</td>
<td>51</td>
<td>0.963</td>
<td>0.533 ± 0.095</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>10</td>
<td>85</td>
<td>0.956</td>
<td>0.426 ± 0.045</td>
<td>&lt;0.0001</td>
<td>42</td>
<td>0.949</td>
<td>0.298 ± 0.145</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>11</td>
<td>110</td>
<td>0.980</td>
<td>0.367 ± 0.028</td>
<td>&lt;0.0001</td>
<td>55</td>
<td>0.980</td>
<td>0.383 ± 0.042</td>
<td>&lt;0.0001</td>
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<tr>
<td>12</td>
<td>85</td>
<td>0.962</td>
<td>0.490 ± 0.022</td>
<td>&lt;0.0001</td>
<td>41</td>
<td>0.976</td>
<td>0.440 ± 0.041</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Mean ± SD 0.47 ± 0.09 0.43 ± 0.11 (P = NS)

Abbreviations: IVC + PA = data generated by inferior vena cava and pulmonary artery occlusions and releases. IVC = data generated by inferior vena cava occlusion and releases, r = multiple correlation coefficient of fit to Equation 3 (see text), P_LV/P_RV = coefficient of P_RV term in Equation 3, SEE = standard error of the estimate, P = significance of P_RV term in Equation 3.

Table 3

Effect of Alterations in Right Ventricular Pressure on the Left Ventricular End-Diastolic Pressure-Volume Relationship after 6 Weeks of Right Ventricular Pressure Overload Determined by FVC Occlusion

<table>
<thead>
<tr>
<th>Dog</th>
<th>n</th>
<th>r</th>
<th>dP_\text{LV}/dP_\text{RV} ± SEE</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>68</td>
<td>0.935</td>
<td>0.279 ± 0.081</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>4</td>
<td>91</td>
<td>0.906</td>
<td>0.173 ± 0.020</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>5</td>
<td>109</td>
<td>0.965</td>
<td>0.022 ± 0.026</td>
<td>NS</td>
</tr>
<tr>
<td>6</td>
<td>101</td>
<td>0.990</td>
<td>0.262 ± 0.007</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>7</td>
<td>67</td>
<td>0.975</td>
<td>0.210 ± 0.016</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>9</td>
<td>57</td>
<td>0.994</td>
<td>0.320 ± 0.006</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>10</td>
<td>61</td>
<td>0.930</td>
<td>0.229 ± 0.064</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>13</td>
<td>165</td>
<td>0.968</td>
<td>0.124 ± 0.011</td>
<td>&lt;0.0001</td>
</tr>
<tr>
<td>14</td>
<td>58</td>
<td>0.975</td>
<td>0.312 ± 0.035</td>
<td>&lt;0.0001</td>
</tr>
</tbody>
</table>

Mean ± SD 0.21 ± 0.10

Abbreviations are the same as in Table 2; dog numbers also correspond to those in Table 2. Similar numbers indicate observations in the same animal. Dogs 10 and 11 did not have control observations.

Table 4

Anatomic Data in Control Animals and after 6 Weeks of Right Ventricular Pressure Overload (PA Band)

<table>
<thead>
<tr>
<th>Group</th>
<th>Body wt (kg)</th>
<th>SIVS (mg)</th>
<th>RV wt (mg)</th>
<th>RV thickness (mm)</th>
<th>IVS wt (mg)</th>
<th>IVS thickness (mm)</th>
<th>LFW wt (mg)</th>
<th>LVFW thickness (mm)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control (n = 13)</td>
<td>25 ± 4</td>
<td>0.33 ± 0.02*</td>
<td>48 ± 8</td>
<td>5 ± 1</td>
<td>35 ± 7</td>
<td>10 ± 1</td>
<td>84 ± 14</td>
<td>11 ± 2</td>
</tr>
<tr>
<td>PA band (n = 9)</td>
<td>26 ± 4</td>
<td>0.38 ± 0.03*</td>
<td>71 ± 7*</td>
<td>10 ± 1*</td>
<td>53 ± 15*</td>
<td>15 ± 2*</td>
<td>81 ± 12 (NS)</td>
<td>11 ± 2 (NS)</td>
</tr>
</tbody>
</table>

All data mean ± sd. Abbreviations: WT = weight; SIVS/SIVL = ratio of surface area of the interventricular septum to total surface area of the left ventricle; RV = right ventricle; IVS = interventricular septum; LFW = left ventricular free wall; NS = no significant difference when compared to control

* P < 0.01 vs control

pressure overload, \( \frac{dP_{\text{LV}}}{dP_{\text{RV}}} \) and SIVS/SIVL changed in opposite directions. SIVS/SIVL increased but \( \frac{dP_{\text{LV}}}{dP_{\text{RV}}} \) decreased and was now significantly less than SIVS/SIVL.

The mathematical development of an alternative model is presented in the Appendix. This model, in agreement with the analysis proposed by Sunagawa et al. (1981) to quantify end-systolic ventricular interdependence, suggests that the effect of alterations in right ventricular pressure on the left ventricular diastolic pressure-volume relationship depends on the relative elastance (or slope of the pressure-vol-
our observations that this intervention decreases the effect of alterations in right ventricular pressure on the left ventricular pressure-volume relationship, and thus it may be a reasonable first approximation of the relative elastances of these structures. Our data suggest that this may not always be the case, especially when there is septal hypertrophy.

There is a large body of observations that right ventricular pressure affects the left ventricular pressure-volume relationship (Taylor et al., 1967; Kelly et al., 1971; Bemis et al., 1974; Elzinga et al., 1974; Santamore, 1976; Glantz et al., 1978; Janicki and Weber, 1980a; Bove and Santamore, 1981; Lorell et al., 1981; Maughan et al., 1981; Spadaro et al., 1981; Maruyama et al., 1982; Olsen et al., 1983). This effect is greater when the pericardium is intact, presumably since alterations in right ventricular pressure influence both the interventricular septum and the pericardial pressure, which affects the lateral wall of the left ventricle (Glantz et al., 1978; Tyberg et al., 1978; Refsum et al., 1981). The results of several of these studies can be compared, at least qualitatively, to our own control observations.

Bemis et al. (1974) found in isolated canine hearts without pericardia, in which left ventricular volume was determined by radiographic tracking of endocardial markers, that \( \Delta P_{LV} / \Delta P_{RV} \) was 0.45, in close agreement with our control observations. Glantz et al. (1978) found in open-chest dogs that the right ventricular pressure was the most important determinant of left ventricular pressure, more important than left ventricular dimensions when the pericardium was intact. After removing the pericardium, the effect of right ventricular pressure was decreased, but it still had a significant effect on the left ventricular diastolic pressure-volume relationship in four of the five dogs studied. After the pericardiotomy, the "coupling coefficient" or \( \Delta P_{LV} / \Delta P_{RV} \) was greater than 0.40 in these four animals. Lorell et al. (1981), in a study of the isovolumic bearing canine
left ventricle, found that—in the control situation—alterations in right ventricular pressure produced a non-parallel shift of the left ventricular diastolic pressure-volume relationship. At constant left ventricular volume, they observed \( \frac{dP_{LV}}{dP_{RV}} \) to be approximately 0.4, also in agreement with our control observations.

Other studies in isolated dog hearts without pericardia have shown less influence of the right ventricular pressure on the left ventricular diastolic pressure-volume relationship (Janicki et al., 1980a; Maughan et al., 1981; Sparado et al., 1981). In these studies, the mitral valve orifice was occluded with a rigid disc to prevent prolapse of the left ventricular balloon into the left atrium. In some studies, the tricuspid annulus was also occluded (Janicki, 1980; Maughan, 1981). It is possible that these occluder discs may have decreased the mobility and stiffened the interventricular septum, thus decreasing the effect of the right ventricular pressure on the left ventricular pressure-volume relationship. Maruyama et al. (1982) may have avoided this problem by occluding the mitral and tricuspid orifices with thin, rubber plugs. Without the pericardium, they observed \( \frac{dP_{LV}}{dP_{RV}} \) was 0.28, less than our control observations, but greater than the mean value observed following chronic right ventricular pressure overload.

The effect of alterations of right ventricular on the diastolic left ventricular pressure-volume relationship, seen in our study, may be magnified by postoperative fibrosis and adhesions on the left ventricular free wall. Such adhesions were seen to develop around the wires exiting from the lateral wall of the left ventricle, but in no case did we observe fibrosis overlying the epicardium. The postoperative changes might increase the left ventricular free wall stiffness. The model presented in the Appendix predicts that such a change would increase \( \frac{dP_{LV}}{dP_{RV}} \) by increasing \( E_r \).

Our method of analysis (Eq. 3) may also have influenced our observations. Any variable that was not entered into the fit that may influence the pressure-volume relationship (i.e., aortic pressure, coronary perfusion pressure, heart rate) might potentially increase the effect attributed to right ventricular pressure. Equation 3 accounts only for a parallel shift of the left ventricular pressure-volume relationship in response to alterations in right ventricular pressure. If there is a nonparallel shift, the value of \( \frac{dP_{LV}}{dP_{RV}} \) calculated from the fit of Equation 3 will be a weighted average of \( \frac{dP_{LV}}{dP_{RV}} \) over the range of pressures and volumes observed. The decrease in \( \frac{dP_{LV}}{dP_{RV}} \) seen after chronic right ventricular pressure overload might not be due to septal hypertrophy, but, instead, may result from some other consequence of the intervention (such as the increased right ventricular volume or changes in the configuration of the left ventricle).

Our results in the control group indicate that the \( \frac{dP_{LV}}{dP_{RV}} \) is equal to about one-half, and thus, if our model is correct, indicates that the free wall and septal elastances are approximately equal. Since the interventricular septum is smaller than the left ventricular free wall, one would expect that the elastance of the septal component would be less than the elastance of the free wall. Thus, our results, interpreted in terms of the analysis presented in the Appendix, indicate that the interventricular septum may be very compliant. Kent et al. (1978) evaluated the relative stiffness of the left ventricular free wall and septum by ultrasonically measuring septal and free wall segment lengths during volume loading in open-chest dogs. When expressed in terms of left ventricular pressure, the end-diastolic stiffness of the septum and free wall were similar. When calculated using the trans-septal pressure (left ventricular-right ventricular pressure) the septal stiffness was very low. Similarly, the marked shifts in interventricular septal position seen echocardiographically in response to relatively small changes in the transseptal pressure gradient produced by right ventricular pressure overload, pacing, volume loading, or the Mueller maneuver, also suggest that the septum behaves as a very compliant structure (Tanaka et al., 1980; Little et al., 1982; Kingma et al., 1982; Guzman et al., 1981).

The consideration of the effect of right ventricular pressure as merely an external pressure of the interventricular septum does not take into account the possibility that deformations of the septum may influence the diastolic properties of the left ventricular free wall by altering the configuration of the left ventricle or influencing common fiber bundles. As well, the analysis contained in the Appendix ignores the role of the atria and the interatrial septum, which, during diastole, may also contribute to ventricular interdependence (Maughan et al., 1981; Maruyama et al., 1982).

In conclusion, we have demonstrated that, in preinstrumented animals without pericardia, alterations in right ventricular pressure can significantly shift the left ventricular diastolic pressure-volume relationship independent of changes in pericardial or pleural pressures. Following chronic right ventricular pressure overload, which produces right ventricular and interventricular septal hypertrophy, the effect of alterations of right ventricular pressure on the left ventricular pressure-volume relationship is reduced. These observations are consistent with the hypothesis that the effect of alterations of right ventricular pressure on the left ventricular diastolic pressure-volume relationship depends on the relative elastance of the portions of the left ventricle composed by the interventricular septum and the left ventricular free wall.

Appendix

The left ventricle is considered to be divided into two compartments (Fig. 8). Blood can distribute
freely between the two compartments, so the intracavitary pressures are the same ($P_{LV}$). The compartment composed by the intraventricular septum has, as its external pressure, the right ventricle pressure ($P_{RV}$). The other compartment composed of the free wall of the left ventricle has, as its external pressure, the pericardial pressure ($PP$). The pressure-volume relationships of the two components at a fixed $PP$ and $P_{RV}$ are given by:

$$P_{LV} = f_S(V_S); \quad P_{LV} = f_F(V_F);$$

where $P_{LV}$ = intraluminal left ventricular pressure, $V_S$ = volume of the septal compartment, and $V_F$ = volume of the free wall compartment (Fig. 6). The volume of the left ventricle ($V_T$) is the sum of the volumes of the two compartments:

$$V_T = V_S + V_F$$

This relationship and $f_S$ and $f_F$ determine the pressure-volume relationship, $P_{LV} = f(V_T)$, of the combined system. Increasing right ventricular pressure by an incremental amount, $\Delta P_{RV}$, will shift the pressure-volume relationship of the septal compartment ($f_S$) upward by this amount. This will shift volume into the free wall compartment of the left ventricle but will not alter the free wall pressure-volume relationship ($f_F$). The upward shift of $f_S$ by $\Delta P_{RV}$ will shift $f_S$ toward the left by $\Delta V_S$, where:

$$\Delta V_S = \Delta P_{RV}/E_S; \quad \Delta P_{RV} \text{ is very small} \quad (4)$$

where $E_S = \partial f_S/\partial V_S$. Since $V_T = V_S + V_F$, this will result in a leftward shift of the combined pressure-volume relationship, $f_T$, by the same amount, $\Delta V_S$. $f_T$ will be shifted to the left by $\Delta P_{LV}$ where:

$$\Delta P_{LV} = \Delta V_S \cdot \frac{\partial f_T}{\partial V_T} \quad (5)$$

$\partial f_T/\partial V_T$ can be evaluated as follows:

$$\frac{\partial f_T}{\partial V_T} = \lim \frac{\Delta P_{LV}}{\Delta V_T}$$

$$\Delta V_T = \Delta V_S + \Delta V_F$$

$$\Delta V_S = \Delta P_{LV}/E_S$$

$$\Delta V_F = \Delta P_{LV}/E_F$$

where

$$E_F = \partial f_F/\partial V_F.$$ 

Therefore,

$$\frac{\partial f_T}{\partial V_T} = \frac{E_F \cdot E_S}{E_F + E_S} \quad (6)$$

Substituting equations 6 and 4 into equation 5 gives:

$$\Delta P_{LV} = \Delta P_{RV} \cdot E_F/(E_S + E_F)$$

therefore,

$$\frac{\partial P_{LV}}{\partial P_{RV}} = E_F/(E_S + E_F)$$

Thus, at constant left ventricular volume and pericardial pressure, the change in LV pressure produced by an alteration in right ventricular pressure will depend on the relative elastance of the intraventricular septum and the left ventricular free wall. By similar reasoning it is seen that:

$$\frac{\partial P_{LV}}{\partial P_{RV}} = E_S/(E_S + E_F)$$

Therefore, an effective external pressure ($P_{ext}$) for the left ventricle can be calculated as:

$$P_{EXT} = \frac{(E_F/(E_S + E_F)) \cdot P_{RV} + (E_S/(E_S + E_F)) \cdot P_F}{E_F/(E_S + E_F) - P_{RV} + E_S/(E_S + E_F) \cdot P_F}$$

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References


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