Right ventricular diastolic pressure-volume relations and regional dimensions during acute alterations in loading conditions

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ABSTRACT  Acute pharmacologically mediated parallel shifts in the left ventricular diastolic pressure-volume relation may be due to the restraining effect of the pericardium and/or leftward displacement of the interventricular septum. The existence and cause of this phenomenon in the right ventricle has not been studied in animals or in man. Accordingly, we altered right ventricular pressure with intravenous phenylephrine (0.2 to 0.3 mg) and nitroprusside (0.5 to 1.5 μg/kg/min) to achieve three disparate peak right ventricular pressures in nine normal subjects after partial autonomic blockade with atropine (1 mg) and propranolol (0.15 mg/kg). Simultaneous high-fidelity right ventricular pressures and biplane cineventriculographic volumes were acquired during the three resultant loading conditions. Right atrial pacing maintained heart rate constant at each pressure level. Peak right ventricular systolic pressure (23 ± 3 vs 31 ± 9 vs 45 ± 6 mm Hg, all p < .01) and right ventricular end-diastolic pressure (4 ± 2 vs 8 ± 4 vs 11 ± 3 mm Hg, all p < .01) were significantly different at low, medium, and high loading conditions, respectively. Right ventricular diastolic pressure-volume relations were, in parallel, shifted upward with altered loading in each patient. This was manifest by an unchanged dynamic chamber stiffness constant and a significant increase in the diastolic pressure volume y intercept at each load (1.98 ± 2.21 vs 5.33 ± 5.39 vs 8.51 ± 3.99 mm Hg, p < .05). Regional dimensional analysis of the orthogonal right ventricular contrast ventriculograms demonstrated that the observed increase in end-diastolic volume between low and high pressure (+26%, p < .01) was largely mediated by lengthening of the right ventricular septal-free wall segment (+10%, p < .05). We conclude that the right ventricular diastolic pressure-volume relation demonstrates parallel shifts in response to acute pharmacologically mediated alterations in load similar to those observed in the left ventricle. Although we cannot absolutely exclude shifting of the interventricular septum, pericardial restraint appears to be the major mechanism for this phenomenon in the right ventricle. 


THE LEFT VENTRICULAR diastolic pressure-volume relation may be altered by intrinsic factors such as chronic changes in chamber volume, chamber composition, muscle mass, or muscle properties or by ischaemia.1-3 However, studies in the isolated heart, intact animal, and man have also demonstrated that acute alterations in loading conditions may produce parallel shifts of the left ventricular diastolic pressure-volume relation. The mechanism(s) thought responsible for this phenomenon include pericardial restraint and ventricular interdependence mediated by transseptal pressure gradients and resultant leftward shifting of the interventricular septum. The relative contribution of these two extrinsic factors to passive ventricular diastolic chamber properties in man is uncertain. In particular, Ludbrook4 and Alderman5 and their colleagues have demonstrated parallel shifts in the left ventricular diastolic pressure-volume relation in response to pharmacologic alteration of load without a change in the chamber stiffness constant or elastic modulus; they used cineventriculography to measure left ventricular volumes in patients during cardiac catheterization. The existence and magnitude of this phenomenon have not been studied in the right ventricle because of its complex geometry and resultant difficulty in obtaining accurate volume determinations in animal preparations or in man. Accordingly, in the present investigation we used simultaneous high-fidelity right ventricular pres-
sures and our biplane cineangiographic approach to right ventricular volume measurement to assess whether a similar parallel shift occurs in the right ventricular diastolic pressure-volume relation when phenylephrine and nitroprusside are used to abruptly alter ventricular loading conditions. Regional dimensional analysis of the orthogonal end-diastolic cineventriculograms was used during the resultant volume changes to estimate changes in right ventricular geometry under these conditions.

Methods

Patients. The study population included nine subjects who were referred for cardiac catheterization to evaluate atypical chest pain. Each patient gave written informed consent on a form approved by our Institutional Review Board. There were six women and three men with a mean age of 49 ± 14 years (range 27 to 62 years). All patients had normal coronary anatomy documented by coronary cinearteriography, a normal electrocardiogram, and normal left and right ventricular function and wall thickness documented by M mode echocardiography. All nitrates, diuretics, and calcium entry-blocking drugs were discontinued at least 24 hr before cardiac catheterization and β-blocking drugs were discontinued at least 72 hr before cardiac catheterization.

Protocol. Patients were premedicated with oral benadryl (50 mg) and diazepam (10 mg). After coronary cinearteriography had been completed No. 8F high-fidelity catheter was inserted into the right ventricle via the right antecubital vein (Millar Instruments, TC500 series, Houston). A No. 6F bipolar pacing catheter was positioned in the right atrial appendage and a No. 8F Berman angio graphic catheter was positioned in the right ventricular cavity near the apex through the right femoral vein. Each patient was then medicated with 1 mg of atropine and 0.15 mg/kg of propranolol before the research study in order to attenuate reflex autonomic effects on myocardial contractility consequent to altered load. All patients received an intravenous bolus of phenylephrine (0.2 to 0.3 mg) after control and six of the nine patients received nitroprusside (dose range 0.3 to 1.5 μg/kg/min) after phenylephrine in order to achieve three different loading conditions with widely disparate peak right ventricular pressures. During nitroprusside and phenylephrine infusion systemic peak systolic arterial pressure ranged between 100 and 250 mm Hg (mean arterial pressure 80 to 150 mm Hg) and peak right ventricular systolic pressures ranged between 17 and 50 mm Hg (table 1).

Hemodynamics. During each loading condition analog signals and cineframe markers were recorded at the same paced heart rate with an Electronics for Medicine VR-16 physiologic recorder at 100 mm/sec paper speed with 10 msec time lines. The surface electrocardiogram, the first derivative of right ventricular pressure development (dP/dt), and right ventricular pressures were recorded under each loading condition. To correct for hydrostatic pressure effects on the pressure sensor, the right ventricular high-fidelity pressure waveforms were matched to a fluid pressure that was balanced and calibrated with the external pressure transducer positioned at the midaxillary level. At the end of each study neither pressure sensor demonstrated thermal drift during the procedure; zero reference measurements before and after each dynamic recording were unchanged. Right ventricular pressure signals were recorded simultaneously with biplane cineventriculograms under the three loading conditions and cinepulse synchronization provided simultaneous pressure and volume every 16.6 msec. Analog-to-digital pressure conversion was accomplished in our laboratory as previously described.

Cineventriculography. Biplane right ventricular cineventriculography was performed at 60 frames/sec in the 30 degree right anterior oblique and 60 degree left anterior oblique/20 degree cranial angulations (CGR Angiopax) with a No. 8F Berman angio graphic catheter positioned in the right ventricular apex. Forty to fifty milliliters of meglumine diatrizoate (Renografin-76) was injected over a 3 to 4 sec at 450 pounds per square inch. Each cineventriculogram was performed during the end-expiratory phase of the respiratory cycle when simultaneous high-fidelity pressures were stable. Patients were carefully instructed during catheterization with regard to proper breathing technique in order to avoid the performance of a Valsalva maneuver. This approach was used to obviate any effect of intrapleural pressure on right ventricular intracavitary pressure during each hemodynamic state in every patient. Analysis was conducted on one of the first 3 sinus beats when the effect of iodinated contrast material on ventricular function is minimal. Ventricular ectopic and postventricular ectopic beats were rejected from analysis. Biplane right ventricular volumes were obtained by a method that has been previously validated in our laboratory with use of a modified Simpson’s rule algorithm. This approach, which divides the digitized biplane images into 100 parallel segments, correlates closely with normal adult right ventricular cast volumes determined by water displacement (n = 14, r = .97, SEE = 6 ml). Regional dimensional analysis was performed by computer algorithm, which provides a major and minor chord of the right ventricle in each orthogonal plane from the digitized raw data. The major right anterior oblique chord was defined as the ventricular dimension from the midpoint of the pulmonary valve to the right ventricular base, the minor right anterior oblique chord as the perpendicular dimension at the midpoint of the major right anterior oblique chord, the major left anterior oblique chord as the vertical dimension from the midpoint of the pulmonary valve to the right ventricular apex, and the septal-free wall chord as the perpendicular dimension between the midpoint of the major left anterior oblique chord and the right ventricular free wall.

Data analysis. Pressure-volume loops were derived from simultaneous right ventricular pressures and volumes at 16.6 msec throughout the cardiac cycle, as demonstrated in figure 1. The dynamic elastic chamber stiffness constant was derived from the simultaneous pressures and volumes starting from the lowest diastolic pressure to the right ventricular end-diastolic pressure identified at the peak of the R wave of a simultaneous electrocardiogram. For this analysis we used a monexponential function: P = be^(-Ct), where P = diastolic pressure;
V = right ventricular volume; \( K_C \) = dynamic elastic chamber stiffness constant; b = diastolic pressure volume y intercept.\(^{10}\) This monoeponential model may provide an imprecise fit of the left ventricular diastolic pressure-volume relation near end-diatole.\(^1 \)\(^5 \)\(^10\) However, it provided a significant fit of the pressure-volume data points during each intervention, with the exception of those from patient 2, in which case a flat curve yielded \( K_C \) values of zero during high loading conditions. Changes in the calculated \( K_C \) were used to quantitate whether the observed shifts in the diastolic pressure-volume relation were due to alterations in chamber dynamics or extrinsic factors. The extrapolated diastolic pressure y intercept at zero volume mathematically defined the relative position of the pressure-volume curve at low, medium, and high loading conditions.

**Statistical analysis.** All data are presented as the mean ± 1 SD. Multiple comparisons were analyzed by a repeated-measures analysis of variance with use of a standard statistical program (BMDP2V). When the analysis of variance revealed a significant F statistic the Neuman-Keuls multiple-range test was used to determine significant differences among group means. A p value of .05 or less was considered indicative of a significant difference.

**Results (tables 1 and 2)**

By study design, the heart rate did not differ under low, medium, and high loading conditions (94 ± 7 vs 93 ± 6 vs 93 ± 5 beats/min). Mean peak right ventricular systolic pressure differed significantly under each loading condition (23 ± 3 vs 31 ± 9 vs 45 ± 6 mm Hg, p<.01), as did the right ventricular end-diastolic

**TABLE 1**

Individual hemodynamic data and right ventricular chamber stiffness constants during pharmacologically altered loading

<table>
<thead>
<tr>
<th>Patient No./sex</th>
<th>Body weight (kg)</th>
<th>RV systolic loading</th>
<th>HR (bpm)</th>
<th>RVP (mm Hg)</th>
<th>RVEDP (mm Hg)</th>
<th>RVEDV (ml)</th>
<th>RVESV (ml)</th>
<th>( K_C ) (mm Hg/ml)</th>
<th>b (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1/F 78</td>
<td>Low(^a)</td>
<td>109</td>
<td>20</td>
<td>90</td>
<td>21</td>
<td>0.005</td>
<td>0.25</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium</td>
<td>104</td>
<td>22</td>
<td>2</td>
<td>130</td>
<td>28</td>
<td>0.004</td>
<td>−0.27</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High(^b)</td>
<td>103</td>
<td>36</td>
<td>6</td>
<td>119</td>
<td>32</td>
<td>0.003</td>
<td>4.23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>2/F 50</td>
<td>Low</td>
<td>89</td>
<td>17</td>
<td>148</td>
<td>57</td>
<td>0.003</td>
<td>1.43</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medium(^b)</td>
<td>85</td>
<td>43</td>
<td>15</td>
<td>164</td>
<td>97</td>
<td>0</td>
<td>16.03</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High(^b)</td>
<td>92</td>
<td>50</td>
<td>15</td>
<td>170</td>
<td>94</td>
<td>0</td>
<td>15.83</td>
<td></td>
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</tr>
<tr>
<td>3/F 61</td>
<td>Low(^a)</td>
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<td>26</td>
<td>133</td>
<td>34</td>
<td>0.002</td>
<td>1.03</td>
<td></td>
<td></td>
</tr>
<tr>
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<td>34</td>
<td>5</td>
<td>156</td>
<td>38</td>
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<td>1.23</td>
<td></td>
<td></td>
</tr>
<tr>
<td>High(^b)</td>
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<td>51</td>
<td>11</td>
<td>144</td>
<td>41</td>
<td>0.003</td>
<td>7.23</td>
<td></td>
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<tr>
<td>4/M 88</td>
<td>Low(^a)</td>
<td>91</td>
<td>27</td>
<td>209</td>
<td>98</td>
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<td>2.93</td>
<td></td>
<td></td>
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<tr>
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<td>9</td>
<td>224</td>
<td>114</td>
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<td>4.23</td>
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<td></td>
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<tr>
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<td>238</td>
<td>130</td>
<td>0.003</td>
<td>9.13</td>
<td></td>
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</tr>
<tr>
<td>5/F 67</td>
<td>Low(^a)</td>
<td>95</td>
<td>24</td>
<td>169</td>
<td>67</td>
<td>0.003</td>
<td>−0.17</td>
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<tr>
<td>Medium</td>
<td>91</td>
<td>25</td>
<td>7</td>
<td>207</td>
<td>80</td>
<td>0.003</td>
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<tr>
<td>High(^b)</td>
<td>90</td>
<td>37</td>
<td>12</td>
<td>242</td>
<td>86</td>
<td>0.002</td>
<td>6.83</td>
<td></td>
<td></td>
</tr>
<tr>
<td>6/M 88</td>
<td>Low</td>
<td>100</td>
<td>26</td>
<td>162</td>
<td>73</td>
<td>—</td>
<td>—</td>
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</tr>
<tr>
<td>Medium(^b)</td>
<td>100</td>
<td>35</td>
<td>7</td>
<td>196</td>
<td>84</td>
<td>0.004</td>
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<tr>
<td>High(^b)</td>
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<td>9</td>
<td>193</td>
<td>99</td>
<td>0.004</td>
<td>4.73</td>
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</tr>
<tr>
<td>7/F 94</td>
<td>Low(^a)</td>
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<td>22</td>
<td>122</td>
<td>32</td>
<td>0.004</td>
<td>1.63</td>
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<tr>
<td>Medium</td>
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<td>23</td>
<td>5</td>
<td>139</td>
<td>45</td>
<td>0.003</td>
<td>1.33</td>
<td></td>
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</tr>
<tr>
<td>High(^b)</td>
<td>91</td>
<td>46</td>
<td>12</td>
<td>202</td>
<td>53</td>
<td>0.004</td>
<td>5.43</td>
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<td></td>
</tr>
<tr>
<td>8/M 89</td>
<td>Low(^a)</td>
<td>89</td>
<td>25</td>
<td>202</td>
<td>76</td>
<td>0.003</td>
<td>6.93</td>
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<tr>
<td>Medium</td>
<td>89</td>
<td>30</td>
<td>12</td>
<td>178</td>
<td>76</td>
<td>0.002</td>
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<tr>
<td>High(^b)</td>
<td>89</td>
<td>49</td>
<td>14</td>
<td>237</td>
<td>110</td>
<td>0.001</td>
<td>13.03</td>
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<tr>
<td>9/F 60</td>
<td>Low</td>
<td>95</td>
<td>21</td>
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<td>0.004</td>
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<td>Medium(^b)</td>
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<td>127</td>
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<td>63</td>
<td>0.004</td>
<td>6.33</td>
<td></td>
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</tr>
</tbody>
</table>

\(\text{RV} = \text{right ventricular}; \text{HR} = \text{heart rate}; \text{RVP} = \text{peak RV pressure}; \text{RVEDP} = \text{RV end-diastolic pressure}; \text{RVEDV} = \text{RV end-diastolic volume}; \text{RVESV} = \text{RV end-systolic volume}; \text{K}_C = \text{dynamic chamber stiffness constant}; \text{b} = \text{pressure intercept of the RV pressure-volume relation.}
\)

\(^{a}\)Nitroprusside.

\(^{b}\)Phenylephrine.

\(^{p} < .05: \text{low} < \text{medium}, \text{medium} < \text{high}; ^{2p} < .01: \text{low} < \text{medium}, \text{medium} < \text{high}; ^{3p} < .01: \text{low} < \text{medium and high.}
TABLE 2
Regional biplane cineangiographic right ventricular dimensions during pharmacologically altered loading (mean ± SD, n = 9)

<table>
<thead>
<tr>
<th></th>
<th>Major RAO (mm)</th>
<th>Minor RAO (mm)</th>
<th>Major LAO free wall (mm)</th>
<th>RV end-diastolic volume (ml)</th>
<th>RV end-diastolic pressure (mm Hg)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low pressure</td>
<td>102.5 ± 1.4</td>
<td>74.8 ± 0.8</td>
<td>94.3 ± 1.0</td>
<td>148 ± 2</td>
<td>4 ± 2</td>
</tr>
<tr>
<td>High pressure</td>
<td>106.7 ± 1.8</td>
<td>76.8 ± 0.6</td>
<td>95.9 ± 1.0</td>
<td>186 ± 48</td>
<td>11 ± 3*</td>
</tr>
<tr>
<td>% change low vs high</td>
<td>+4%</td>
<td>+2%</td>
<td>+3%</td>
<td>+10%</td>
<td>+26%</td>
</tr>
</tbody>
</table>

 Major RAO = dimension from pulmonary valve to RV base in the 30 degree right anterior oblique projection; Minor RAO = orthogonal dimension at the midportion of the major RAO chord; Major LAO = dimension from the pulmonary valve to the RV apex in the 60 degree left anterior oblique + 20 degree cranial angulation; RV septal-free wall = orthogonal dimension between the midportion of the major LAO chord and the RV free wall; other abbreviations are as in table 1.

*p ≤ .05 vs low.

pressure (4 ± 2 vs 8 ± 4 vs 11 ± 3 mm Hg, p<.01). Corresponding peak systolic femoral arterial pressures ranged between 100 and 250 mm Hg (mean arterial pressure 80 to 150 mm Hg). The mean right ventricular end-diastolic volume increased at each loading condition but differed significantly only at low and medium loads (148 ± 42 vs 169 ± 35 ml, p<.01) and at low and high loads (148 ± 42 vs 186 ± 48 ml, p<.01). Biplane right ventricular end-diastolic regional dimensional analysis revealed a concomitant significant increase only in the right ventricular septal to free wall chord (+10%, p<.05; table 2). The mean right ventricular end-systolic volumes were significantly different under each loading condition (54 ± 26 vs 68 ± 29 vs 79 ± 33 ml, p<.01).

The calculated chamber stiffness constant did not differ at low, medium, and high loading conditions (0.003 ± 0.001 vs 0.003 ± 0.002 vs 0.003 ± 0.001 mm Hg/ml); the pressure axis y intercept increased significantly (1.98 ± 2.21 vs 5.33 ± 5.39 vs 8.51 ± 3.99, all p<.05). The diastolic pressure-volume relationships were apparently shifted in parallel, with no obvious change in slope in each of the nine study patients during the phenylephrine infusion (figure 2).

FIGURE 2. Right ventricular pressure-volume loops for each of the nine study patients demonstrating a parallel upward shift in the diastolic pressure-volume relation with progressive increases in right ventricular loading. --- = low; --- = medium; —— = high.
However, because some patients presented with low baseline right ventricular filling pressures, there was no visible separation between the low and medium loading condition during infusion of nitroprusside in patients 1, 3, 4, and 7, while in patients 5 and 8 there was a clear separation of the diastolic pressure-volume relation under all three loading conditions when baseline filling pressures were more elevated before the nitroprusside infusion. This observation is also consistent with the findings of Alderman and Glantz in a study of the left ventricular diastolic pressure-volume relation in patients during cardiac catheterization in whom nitroprusside was used to alter load.

Discussion

A number of studies in both animals and man have evaluated the determinants of the left ventricular diastolic pressure-volume relation. By contrast, right ventricular diastolic pressure-volume relations have not been examined due to the difficulty in obtaining accurate estimates of volume in this complex geometric chamber. In the present investigation we determined alterations in the right ventricular diastolic pressure-volume relation and regional dimensions consequent to acute pharmacologically mediated changes in loading with a human cast-validated cineventriculographic method previously developed in our laboratory. Three widely separated levels of right ventricular pressure were achieved with phenylephrine and nitroprusside infusions in nine patients with normal coronary anatomy and ventricular function. Right ventricular regional dimensional analysis revealed that resultant increases in end-diastolic volumes between low and high pressures were largely mediated by an increase in the distance between the right ventricular septum and free wall. Our results demonstrate a parallel upward shift of the diastolic pressure-volume curves during progressive increases in right ventricular pressure without a change in the right ventricular chamber stiffness constant. This effect is apparent in figure 2 and is quantitated by the resultant changes in the extrapolated pressure axis y intercepts, which differed significantly at low, medium, and high pressures. Our data strongly suggest that increases in total pericardial volume rather than shifting of the interventricular septum is the mechanism for this phenomenon in the right ventricle.

Ventricular interaction in animal preparations. Previous studies with a variety of preparations have defined the relative role of ventricular interaction and pericardial restraint in mediating parallel shifts in the left ventricular diastolic pressure-volume relation under altered loading conditions. In the postmortem isolated heart preparation Taylor and Laks and their colleagues demonstrated that increased right ventricular volume shifts the left ventricular diastolic pressure-volume relation upward in the absence of the pericardium, since under these conditions a positive diastolic pressure gradient between the right and left ventricles may shift the interventricular septum and compromise left ventricular volume. In the isolated beating heart Bemis and Santamore and their colleagues demonstrated that independent loading of one ventricle shifted the diastolic pressure-volume relation of the contralateral ventricle upward. They also determined that shifting of the interventricular septum decreased chamber dimensions of the left ventricle during right ventricular loading.

More recent studies in the isolated heart have elucidated the importance of pericardial restraint in mediating ventricular interdependence. Spadaro et al. used an intraventricular balloon to record left ventricular volume during progressive increases in right ventricular filling pressure with the pericardium widely unop- posed, partially closed, and completely closed. The left ventricular diastolic pressure-volume relation was, in a leftward and parallel manner, shifted upward under each condition, but the effect was greatly augmented with the pericardium closed. Janicki and Weber demonstrated a parallel upward shift of the right ventricular diastolic pressure-volume relation with the pericardium closed during progressive increases in left ventricular volume using a similar preparation. Furthermore, Maruyama et al. demonstrated that independent increases in the volume of each of the four cardiac chambers shifted the pressure-volume relation of the other three chambers upward and to the left in the postmortem isolated heart. This effect was observed with or without the pericardium but was greatly accentuated by the closed pericardium.

Although isolated heart studies demonstrate a tight coupling of the right and left ventricular diastolic pressures that is augmented by the pericardium, they are nonphysiologic since the volume of one ventricle is independently increased. However, in the canine right heart bypass preparation in situ, Glantz et al. demonstrated that the left ventricular diastolic pressure-volume relation was shifted upward and to the left by volume expansion. This effect was greatly attenuated by pericardiectomy. Tyberg and Shirato and their colleagues demonstrated similar findings during volume loading in the anesthetized and the awake prein- strumented dog, respectively. In both of these studies the parallel left ventricular diastolic pressure-volume
shifts were largely absent on removal of the pericardium.

Although these and other studies demonstrate the importance of the pericardium in mediating changes in the passive diastolic pressure-volume relation, Tyson et al.\textsuperscript{21} have cautioned that the experimental preparation may introduce a significant artifactual pericardial restriction. In their study of the preinstrumented dog, resuturing a small pericardial incision at the base of the heart produced significantly lower intrapericardial pressures when compared with a similar reapproximation of the more conventional longitudinal incision from base to apex.\textsuperscript{21} Consequently, they concluded that the effects of the normal undisturbed pericardium on diastolic filling may be less than that reported in the instrumented animal.

**Ventricular interaction in man.** In man large upward shifts in the left ventricular diastolic pressure-volume relation have been observed during infusion of angiotensin\textsuperscript{4} and during isometric handgrip exercise.\textsuperscript{22} Conversely, parallel downward shifts have been reported during nitroglycerin\textsuperscript{4, 23} and nitroprusside\textsuperscript{5, 24} infusions. These studies were performed during cardiac catheterization using high-fidelity fluid-filled catheters and left ventricular volumes to obtain pressure-volume data points. Previous investigations differed from the present study in that many patients had coronary artery disease or valvular heart disease and were taking cardioactive drugs at the time of cardiac catheterization. Therefore, acute ischemia or valvular regurgitation could not be excluded during alteration of load. Despite these potential limitations, these studies demonstrate parallel shifts in the left ventricular diastolic pressure-volume relation in response to pharmacologic alterations in load similar to those that we observed in the right ventricle in normal patients.

The potential mechanism(s) responsible for parallel shifts in the diastolic pressure-volume relation in response to acute alterations in loading include changes in intrinsic myocardial factors or external constraints on the ventricular chambers. Variations in intrinsic chamber properties are highly unlikely since multiple investigations have demonstrated this phenomenon with interventions and pharmacologic agents that are devoid of direct myocardial effects. Extrinsic factors including pleural pressure, pericardial restraint, and ventricular interaction mediated through shifting of the interventricular septum may produce acute parallel shifts in the ventricular diastolic pressure-volume relation. A deep inspiration or performance of a Valsalva maneuver during cineventriculography will shift the pressure-volume relation downward or upward by changing cardiac chamber pressure. In the present investigation all cineventriculograms were obtained during expiration in the absence of a Valsalva maneuver. Alderman and Glantz\textsuperscript{5} measured intraesophageal pressures during pharmacologic interventions and found that, although pressures vary widely among patients there is minimal variance in the same individual during sequential interventions. Therefore, the shifts of the pressure-volume curves result from the particular intervention rather than respiratory artifact.

Ventricular interaction is difficult to evaluate in the conscious human because of the inability to accurately measure simultaneous right and left ventricular volumes. However, Ludbrook et al.\textsuperscript{4} have demonstrated the importance of right ventricular filling pressure in determining the left ventricular diastolic pressure-volume relation.\textsuperscript{4} In their study amyl nitrite caused no downward displacement of the left ventricular diastolic pressure-volume relation when compared with nitroglycerin, which produced a similar reduction in mean arterial pressure but shifted the pressure-volume relation downward. This phenomenon was attributed to the failure of amyl nitrite to decrease right ventricular diastolic pressure in contrast to the significant decrease in right ventricular filling pressure resulting from nitroglycerin infusion. Whether this effect was mediated by shifting of the interventricular septum, pericardial restraint, or both is uncertain.

Animal studies have demonstrated that the interventricular septum shifts to the left and decreases the septal to free wall left ventricular dimension shortly after pulmonary artery banding.\textsuperscript{19, 25, 26} Tanaka et al.\textsuperscript{26} have also reported a flattening of the interventricular septum toward the left ventricle in the two-dimensional echocardiographic parasternal short-axis view in patients with chronic pressure overload of the right ventricle. However, during acute pharmacologic alterations in loading conditions in the intact circulation both ventricular chambers are more likely to be simultaneously subjected to the change in load to produce a balance in end-diastolic and end-systolic fiber stress across the ventricles. This situation differs from that in the isolated heart in which one ventricle is loaded independently of the other, the intact animal preparation in which the pulmonary artery is abruptly banded, and the patient in whom the right ventricle is subjected to a chronic pressure overload. The results of the present investigation and other studies of the left ventricle suggest that the stress across the interventricular septum may be uniformly distributed because the same relative increase or decrease in pressure and volume compared with baseline values is noted in both ventricles before acute
load manipulation.3, 5, 27 The proposed mechanism whereby the pericardium may produce shifts in both right and left diastolic pressure-volume relations is as follows27: when the pericardium is dilated beyond its unstressed volume any increase in pericardial volume will lead to an increase in pericardial pressure. Alterations in atrial and/or ventricular volume may lead to changes in pericardial pressure and hence to parallel shifts in the ventricular pressure-volume relation. This hypothesis has recently been confirmed and quantified for the left ventricle by Junemann et al.27 using computed tomography in anesthetized closed-chest dogs.

In conclusion, right ventricular diastolic pressure-volume relations demonstrated a parallel shift similar to that previously observed in the left ventricle during acute pharmacologic alterations of load. Analysis of biplane orthogonal regional end-diastolic dimensions revealed that resultant increased volumes were largely mediated by lengthening of the distance between the septum and the right ventricular wall. Thus, the restraining effect of the pericardium rather than shifting of the interventricular septum appears to be the mechanism for this phenomenon in the right ventricle. In the intact circulation when acute alterations in arterial and venous pressures affect all four heart chambers simultaneously and total cardiac volume is varied, pericardial restraint rather than shifting of the interventricular septum may be the predominant mechanism mediating these changes in passive diastolic properties of the ventricles. Simultaneous measurement of pressures and precise septal to free wall dimensions of both ventricles are required to definitively exclude shifting of the interventricular septum as a contributory factor under these conditions.

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