Pericardial Influences on Ventricular Filling in the Conscious Dog
An Analysis Based on Pericardial Pressure

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SUMMARY. Twenty-five dogs were chronically instrumented to investigate the effects of the normal pericardium on cardiac function. Pulse-transit ultrasonic transducers were implanted to measure multiple ventricular dimensions. The pericardium was incised transversely at the base of the heart and precisely reapproximated, so as to disturb its characteristics minimally. One week later, the dogs were studied in the conscious state, and left ventricular, right ventricular, pericardial, and pleural pressures were measured with matched micromanometers. Data were recorded before and after blood volume expansion. Absolute end-diastolic pericardial pressure varied directly with pleural pressure during the respiratory cycle. Transpericardial pressure (pericardial-pleural pressure) varied little with respiration and was related directly to ventricular diameter during the cardiac cycle with peak transpericardial pressure uniformly occurring at end-diastole. With volume infusion, normalized end-diastolic minor axis diameter and left ventricular transmural pressure (left ventricular-pleural pressure) increased significantly from 0.14 ± 0.01 and 9.5 mm Hg ± 1.0 mm Hg, respectively, in the control state to 0.20 ± 0.01 and 19.3 mm Hg ± 1.2 mm Hg after volume loading. End-diastolic transpericardial pressure also increased significantly from 2.3 ± 0.5 mm Hg to 4.1 ± 0.3 mm Hg, and represented approximately 21% of transmural left ventricular pressure. When measurements were obtained sequentially after implantation, transpericardial pressure was initially high but decreased with time, presumably due to pericardial creep. After volume loading, right ventricular end-diastolic transmural pressure averaged 9.6 mm Hg, and pericardial pressure constituted 42% of right ventricular pressure. Thus, pericardial restraining effects may predominantly influence right ventricular filling and affect the left ventricle through series interaction. In the normal conscious dog, transpericardial pressure remains low over the entire physiological range, and the direct influence of the normal pericardium on diastolic filling of the left ventricle appears to be minimal. (Circ Res 54: 173-184, 1984)

THE role of the pericardium in regulating cardiac function has generated considerable interest in recent years. Pericardial restriction of ventricular filling has been demonstrated using a variety of models, and several studies have suggested the pericardium to be a major determinant to left ventricular end-diastolic pressure (Hefner et al., 1961; Spotnitz and Kaiser, 1971; Glantz et al., 1978). However, pericardial restraining effects have not been quantified completely, and many previous studies utilized a resutured pericardium which may exaggerate restriction. In a classic study, Kenner and Wood (1966) showed that pericardial pressure remained low in dogs instrumented without thoracotomy or pericardiectomy, despite significant increases in ventricular filling pressures. Stokland et al. (1980) reported minimal restraint of the unviolated pericardium in open-chest dogs over the normal range of ventricular pressures. Finally, pericardial restriction of filling has been investigated in most studies by comparing ventricular diastolic pressure-volume characteristics, before and after pericardiectomy. Pericardial pressure rarely has been measured, and, in the absence of an effusion, the relationship between pericardial pressure and ventricular filling is unknown. Therefore, the present study was undertaken to develop a model allowing complete instrumentation of the heart while minimally disturbing pericardial properties. The constraining effect of the normal pericardium was quantified in terms of accurately measured pericardial pressure in the conscious chronically instrumented dog.

Methods

Experimental Preparations

Healthy adult dogs (22–34 kg) were instrumented for chronic studies. The dogs were anesthetized with sodium thiopental and ventilated with a volume respirator (Bennett MA-1) at 5 cm H₂O positive end-expiratory pressure. A left thoracotomy was performed under sterile conditions through the 5th intercostal space. Pneumatic occluders were positioned around both venae cavae. In eight dogs (group 1), a transverse pericardiectomy, 5 to 6 centimeters in length, was performed high over the base of the heart (Fig. 1A). Stay sutures were placed at the apices of the pericardiectomy, and the heart was delivered out of the pericardium (Fig. 1B). Pulse transit ultrasonic dimension transducers (Olsen et al., 1983) were placed across the
implanted to measure left ventricular minor axis diameter, major axis diameter, and transverse cardiac diameter (right ventricular freewall to left ventricular freewall diameter). Left atrial, pericardial, and pleural introducers were placed as described above, and the pericardiotomy was closed precisely.

Postoperatively, each dog was given a single dose of intramuscular ferric hydroxide (100 mg) and daily intramuscular injections of procaine penicillin G (200,000 U) and dihydrostreptomycin (250 mg). To prevent cardiac tamponade, the pericardial catheter was connected to a sterile closed drainage system for 24 hours after surgery. Thereafter, the catheter was aspirated daily and irrigated with 30 ml of saline under strict aseptic conditions. The pleural catheter also was aspirated daily, and the left atrial introducer was cleared every 3rd day and refilled with heparinized saline.

**Data Acquisition**

Each dog was trained to lie quietly on its right side, and groups I, II, and III were allowed to recover from implantation for 7 days before studies. Cardiac dimensions were measured by coupling the dimension transducers directly to a sonomicrometer designed and constructed in our laboratory. As the principle of Rushmer et al. (1956). A single pole filter produced a 6 db per octave attenuation above 100 Hz; therefore, the practical frequency response was 0 to 50 Hz. The minimum resolution of the dimension system was approximately 0.08 mm. Pressure measurements were obtained with high fidelity micromanometers (Millar PC-350) coupled to pressure amplifiers (Hewlett-Packard 8805-C). While the micromanometers had a frequency response in excess of 10 kHz, the pressure waveforms were filtered with an upper cut-off of 50 Hz by two-pole Butterworth filters. The manometers were pre-warmed in a water bath at 38°C and were calibrated simultaneously prior to each experiment. Used in this manner, the transducers had negligible temperature sensitivity and drift (less than 0.5 mm Hg/hour). At the time of study, the manometers were passed through the implanted silicone rubber catheters to obtain left ventricular, right ventricular, pleural, and pericardial pressures. The first side holes of the pleural and pericardial introducers were a standard distance from the external end of each catheter, and placement of the matched micromanometers at that point could be achieved reproducibly, with only the pericardium intervening. Analog data were recorded with an eight-channel FM tape recorder (Vetter, model A).

One hour prior to study, morphine sulfate (5–7 mg) was administered intramuscularly. The study protocol was identical for groups I, II, and III. Data were recorded in the conscious state prior to any intervention and then during three transient vena caval occlusions. As described previously (Rankin et al., 1976; Olsen et al., 1981), the cavae were occluded until the minor axis diameter reached a stable diastolic minimum where diastolic left ventricular transmural pressure was approximately 0 mm Hg. Each caval occlusion required about 20 seconds, and none exceeded 30 seconds. Adequate time was allowed between occlusions for physiological variables to return to control. The animals then were volume loaded by rapid intravenous infusion of 800–1200 ml of Normosol-R to achieve a left ventricular end-diastolic pressure of approximately 20 mm Hg. After volume loading, data were recorded during steady state conditions and again during vena caval occlusions over a wide range of filling pressures. Initial studies
of cardiac tamponade were undertaken in five of the group I dogs. An adaptor with a side port was connected to the pericardial introducer to allow infusion of 38°C sterile saline. Steady state and caval occlusion data were obtained in the conscious state as progressive levels of cardiac tamponade were produced by infusing 10-ml increments of saline into the pericardium. After completion of routine studies, one dog each from groups I and II was anesthetized, intubated, and ventilated. A thoracotomy was performed, and data were recorded before and after pericardectomy.

The multiple dimension preparations (group IV) were studied sequentially for 5 days after implantation. Steady state and vena caval occlusion data were obtained daily to examine temporal changes in transpericardial pressure. The relationship between minor axis diameter and other ventricular dimensions also was determined. On the 5th day of study, the dogs were volume loaded, and data were recorded at increasing levels of cardiac tamponade.

After completion of experiments, the dogs were killed and autopsied. Saline was infused to determine the integrity of the pericardiotomy, and representative pericardial biopsies were taken for histological examination. In two group I dogs, pericardial pressure-volume data were obtained immediately postmortem. The great vessels, cavae, and pulmonary veins were clamped, maintaining intracardiac volume constant. A micromanometer was passed into the pericardial introducer, and saline was infused into the pericardium. After each 5-ml increment of saline, steady state pericardial pressure was recorded for subsequent analysis.

**Data Analysis**

Analog data were digitized from FM tape by an A/D converter (ADAC, model 1012) at a sampling rate of 200 Hz. Total conversion time per channel (hardware and software) was approximately 30 μsec. Thus, the delay from the first to the eighth channel was 240 μsec; approximately 5% of the sampling interval. For 50 Hz signals on channels 1 and 8 (worst case), the phase delay was 4.5 degrees. Digital computer analysis was accomplished with a microprocessor (DEC, model PDP 11/23) and interactive programs developed in the authors' laboratory.

Left ventricular minor axis diameter was normalized using a Lagrangian strain definition:

$$\epsilon = (D - D_0)/D_0$$ (1)

where $\epsilon$ is the strain, $D$ is the instantaneous diameter, and $D_0$ is the minimum diastolic diameter obtained during a transient venous caval occlusion. Transmural pressures of the left and right ventricles were calculated as the difference between intracavitary and pleural pressures. Transpericardial pressure was obtained as pericardial pressure minus pleural pressure. First-time derivatives of both the pressure and dimension waveforms were computed with a running five-point polyorthogonal transformation. For assessment of steady state or venous caval occlusion data, only end-expiratory periods were analyzed. Diastatic data were selected automatically by the computer program with diastasis defined according to:

$$|d\epsilon/dt| \leq 0.05 \text{ sec}^{-1}.$$ (2)

As described previously (Rankin et al., 1977, 1980), diastatic pressure-strain data from each caval occlusion were computer fitted to an exponential function:

$$P = \alpha(e^\gamma - 1) + \gamma,$$ (3)

where $P$ is left ventricular transmural or transpericardial pressure, $\epsilon$ is diameter strain, $\alpha$ and $\beta$ are elastic coefficients describing the exponential curve, and $\gamma$ is an empirically derived constant* which allowed the pressure-strain curve to pass through the origin, accounting for any difference in hydrostatic levels of the transducers. Similar equations have been validated for both pericardium (Rabkin and Hsu, 1975) and myocardium (Glantz and Kernoff, 1975).

Data from the multidimensional preparations were used to calculate an index of biventricular volume using the formula for a general ellipsoid:

$$V = (\pi / 6) abc,$$ (4)

where $V$ is external biventricular volume, $a$ is left ventricular major axis diameter, $b$ is left ventricular minor axis diameter, and $c$ is transverse cardiac diameter. Volume data also were normalized with the Lagrangian strain equation (Eq. 1).

Statistical analysis within each group was performed using Student's $t$-test. Average end-diastolic values for left ventricular transmural pressure, transpericardial pressure, minor axis diameter, and strain at control conditions were compared statistically to values obtained after volume loading. Hotelling's $T^2$ test, a multivariate analog of Student's $t$-test (Hotelling, 1931), was used to compare $\alpha$ and $\beta$ values of left ventricular and pericardial pressure-strain relationships within each group and also between groups I and II.

**Results**

**Characteristics of Pericardial Pressure**

During the developmental phase of this study, fluid-filled catheters and balloons were used to measure pericardial pressure. Compared with the micromanometer method, both techniques yielded more motion artifacts, and the balloon consistently overestimated pericardial pressure. Placement of the micromanometer within the silicone rubber tube protected the manometer surface from impact artifacts, while the multiple side holes allowed free communication with the potential space of the pericardium. When the transducer was placed at different positions within the pericardium, dynamic pericardial pressure varied somewhat, depending on which cardiac chamber the manometer approximated. However, analyzing pericardial pressure only during the diastatic phases of the cardiac cycle minimized dynamic regional pressure differences, and the absolute diastatic pressure in various areas of the pericardium differed only by constant hydrostatic gradients.

Typical analog data from a conscious animal are shown in Figure 2 before and during a transient venous caval occlusion after volume loading. The absolute pericardial pressure varied both with respi-

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* First suggested to us in a personal communication by Carl E. Arentzen, M.D., University of Minnesota, Minneapolis, Minn.
ratory fluctuations in pleural pressure and with changes in ventricular diameter throughout the cardiac cycle. The relationship between pericardial pressure and cardiac volume was emphasized by the decline in pericardial pressure as minor axis diameter progressively decreased during the caval occlusion. Of interest was the finding that phasic respiratory variation in pericardial pressure persisted at a lower steady state level during maximal caval occlusion.

The close relationship between pleural pressure and pericardial pressure also can be seen in digital data from the same animal (Fig. 3). During inspiration, the pericardial pressure waveform appeared to be offset linearly by changes in pleural pressure. To delete the influence of pleural pressure, transpericardial pressure was used for data analysis. Transpericardial pressure varied directly with diameter during the cardiac cycle and was not significantly altered by respiration. Maximal transpericardial pressure consistently occurred at end diastole.

Despite eliminating respiratory variation, irregularities in the transpericardial pressure waveform remained (Fig. 3). These minor fluctuations appeared to be related to the first derivative of ventricular diameter and probably represented motion artifacts due to ventricular wall velocity (McDonald, 1974). The transpericardial pressure perturbations were greatest during rapid ventricular filling and ejection (when peak positive or negative diameter derivatives occurred) and were minimal during the diastatic periods selected for analysis.

**Group I**

End-diastolic data from dogs with a precisely closed transverse pericardiotomy are presented in Table 1. End-diastolic strain (mean ± sem) averaged 0.14 ± 0.01 in the control state and increased significantly to 0.20 ± 0.01 with volume loading. This increase in ventricular diameter was associated with a significant increase in left ventricular transmural end-diastolic pressure from 9.5 ± 1.0 mm Hg at control to 19.3 ± 1.2 mm Hg after volume loading. End-diastolic transpericardial pressure increased significantly from 2.3 ± 0.5 mm Hg in the control state to 4.1 ± 0.3 mm Hg with volume loading. The restraining effect of the pericardium could be inferred by comparing these pressures. Even after volume loading, transpericardial pressure constituted only 21% of the difference between left ventricular end-diastolic pressure and pleural pressure.

Data from one of the group I studies are shown in Figure 4A with transmural left ventricular pressure and transpericardial pressure plotted vs. minor axis strain. These diastatic measurements were obtained from multiple cardiac cycles over the range of ventricular volumes produced by a vena caval occlusion. The divergence of the curves was similar in every experiment, and transpericardial pressure remained low over the entire physiological range.
These findings may be contrasted with pressure-strain data obtained from one of the group II dogs (Fig. 4B), where closure of the vertical pericardiotomy with the edges overlapping resulted in significant restraining effects.

The mathematical descriptors $\alpha$, $\beta$, and $\gamma$ from all

![Figure 4. Diastatic left ventricular (LV) transmural and transpericardial pressure-strain relationships in typical dogs from group I (panel A) and group II (panel B).](http://circres.ahajournals.org/)

group I dogs are listed in Table 2. The low values of $\gamma$ confirm the accurate placement of the pressure transducers with only small differences in hydrostatic levels. Using Hotelling's $T^2$ test of the $\alpha$ and $\beta$ coefficients, the ventricular and pericardial curves were significantly different ($P < 0.001$). Average pressure-strain curves from all studies (Fig. 5) demonstrated a minimal contribution of the pericardium to left ventricular pressure over the physiological range.

Representative effects of various interventions, including anesthesia, thoracotomy, and pericardiotomy, on left ventricular transmural pressure-strain relationships are shown in Figure 6. When the pericardiotomy was opened in a group I dog at 1 week after instrumentation, the end-diastolic minor axis diameter increased from 58.3 to 59.1 mm (1.4%). During studies of cardiac tamponade, a minimum of 50 ml of pericardial fluid was necessary to produce hemodynamically significant changes in ventricular filling (Fig. 7A). In each panel, the solid line represents the curve fit from the control caval occlusion using true transmural pressure (left ventricular—pericardial pressure) for the regression. With infusion of additional volumes of saline, pericardial pressure increased markedly and left ventricular dimensions decreased. Severe tamponade resulted in near equalization of left ventricular and pericardial pressures and progressive leftward shifting of the transmural pressure-strain curve. End-diastolic minor axis diameter approached the minimum obtained during the control caval occlusion ($D_0$). Subtracting pericardial pressure (as the external pressure) from cavitary left ventricular pressure (Fig. 7B) eliminated the apparent leftward shifts in the curves.

### Group II

In dogs with overlapping pericardial closure, end-diastolic diameter in the control state was 59.1 ± 2.2 mm, and minor axis strain was 0.09 ± 0.01. Control

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**TABLE 1**

End-Diastolic Data from Group I Dogs before and after Volume Loading

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>Control</th>
<th>Volume loaded</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>$D$ (mm)</td>
<td>$\epsilon$</td>
</tr>
<tr>
<td>1</td>
<td>67.3</td>
<td>0.18</td>
</tr>
<tr>
<td>2</td>
<td>58.9</td>
<td>0.11</td>
</tr>
<tr>
<td>3</td>
<td>59.0</td>
<td>0.14</td>
</tr>
<tr>
<td>4</td>
<td>65.4</td>
<td>0.17</td>
</tr>
<tr>
<td>5</td>
<td>68.4</td>
<td>0.13</td>
</tr>
<tr>
<td>6</td>
<td>57.1</td>
<td>0.11</td>
</tr>
<tr>
<td>7</td>
<td>61.6</td>
<td>0.10</td>
</tr>
<tr>
<td>8</td>
<td>53.8</td>
<td>0.14</td>
</tr>
<tr>
<td>Mean</td>
<td>61.4</td>
<td>0.14</td>
</tr>
<tr>
<td>SEM</td>
<td>1.8</td>
<td>0.01</td>
</tr>
</tbody>
</table>

$D =$ anterior-posterior minor axis diameter of the left ventricle; $\epsilon =$ normalized minor axis diameter; LVTMP = transmural left ventricular pressure; PCP = absolute pericardial pressure; tPC = transpericardial pressure.

*Statistically significant compared to control values ($P < 0.005$) by Student's $t$-test for paired data.
TABLE 2

Left Ventricular and Pericardial Static Pressure-Strain Relationships in Group I Dogs after Volume Loading

<table>
<thead>
<tr>
<th>Dog no.</th>
<th>( \alpha ) (mm Hg)</th>
<th>( \beta ) (mm Hg)</th>
<th>( \gamma )</th>
<th>( \Sigma Sq/Pt )</th>
<th>( \alpha ) (mm Hg)</th>
<th>( \beta ) (mm Hg)</th>
<th>( \gamma )</th>
<th>( \Sigma Sq/Pt )</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>4.75</td>
<td>9.24</td>
<td>1.7</td>
<td>2.07</td>
<td>1.23</td>
<td>13.16</td>
<td>-0.9</td>
<td>1.08</td>
</tr>
<tr>
<td>2</td>
<td>1.87</td>
<td>14.06</td>
<td>-0.8</td>
<td>0.07</td>
<td>0.03</td>
<td>21.42</td>
<td>0.2</td>
<td>0.00</td>
</tr>
<tr>
<td>3</td>
<td>1.52</td>
<td>21.77</td>
<td>-0.1</td>
<td>1.48</td>
<td>0.01</td>
<td>38.22</td>
<td>0.8</td>
<td>0.28</td>
</tr>
<tr>
<td>4</td>
<td>4.93</td>
<td>7.22</td>
<td>0.9</td>
<td>0.33</td>
<td>0.29</td>
<td>9.40</td>
<td>0.9</td>
<td>0.11</td>
</tr>
<tr>
<td>5</td>
<td>5.60</td>
<td>7.21</td>
<td>0.0</td>
<td>0.33</td>
<td>0.09</td>
<td>9.78</td>
<td>-0.2</td>
<td>0.39</td>
</tr>
<tr>
<td>6</td>
<td>4.49</td>
<td>6.87</td>
<td>0.3</td>
<td>0.33</td>
<td>0.01</td>
<td>39.60</td>
<td>-0.3</td>
<td>0.12</td>
</tr>
<tr>
<td>7</td>
<td>5.98</td>
<td>6.70</td>
<td>0.0</td>
<td>0.33</td>
<td>0.14</td>
<td>18.15</td>
<td>0.4</td>
<td>0.10</td>
</tr>
<tr>
<td>8</td>
<td>5.20</td>
<td>14.41</td>
<td>1.2</td>
<td>0.35</td>
<td>0.42</td>
<td>19.91</td>
<td>-0.2</td>
<td>0.10</td>
</tr>
<tr>
<td>Mean</td>
<td>4.29</td>
<td>11.00</td>
<td>0.4</td>
<td>0.28</td>
<td>21.20*</td>
<td>0.0 (NS)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SEM</td>
<td>0.64</td>
<td>2.06</td>
<td>0.3</td>
<td>0.16</td>
<td>4.54</td>
<td>0.2</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

LVTMP = left ventricular transmural pressure (left ventricular-pleural pressure); TPCP = transpericardial pressure; \( \epsilon \) = the normalized minor axis diameter; \( \alpha, \beta, \) and \( \gamma \) = the mathematical descriptors of the exponential pressure-strain relationship. \( \Sigma Sq/Pt \) is the sum of squares deviation of the predicted data points from the measured data points divided by the number of data points and indicates the goodness of fit about the regression line. A lower value indicates a better fit, and \( \Sigma Sq/Pt \) of less than 2.5 indicates a goodness of fit with a confidence level of greater than 95%.

* Statistically significant (\( P < 0.001 \)) by Hotelling’s \( T^2 \) test. NS = non-significant.

left ventricular end-diastolic pressure was 11.7 ± 2.1 mm Hg, and transpericardial pressure averaged 4.9 ± 0.5 mm Hg. With volume loading, end-diastolic diameter increased to 60.1 mm ± 2.3 mm and minor axis strain to 0.11 ± 0.01 (\( P < 0.01 \)). Associated with this small change in ventricular diameter were large increases in both ventricular and pericardial pressures. Transmural left ventricular pressure rose to 20.0 ± 1.0 mm Hg, and transpericardial pressure increased to 10.3 ± 0.6 mm Hg. (Fig. 4B). When pericardiectomy was performed in a group II dog, minor axis diameter increased from 60.4 to 64.3 mm (6.4%).

Comparison of group II with group I revealed that left ventricular transmural end-diastolic pressure did not differ significantly in the control state or after volume loading. Minor axis diameter did not differ in the control state, but increased less in group II after volume loading to the same ventricular pressure (\( P < 0.01 \)), indicating constraint of ventricular filling due to overlapping pericardial closure. Transpericardial pressure was significantly higher at control and after volume loading. Pericardial contribution to left ventricular end-diastolic pressure, derived from the ratio of pericardial to ventricular pressure, was 42% in the control state and increased to 51% after volume infusion.

The mathematical descriptors of pressure-strain...
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GROUP III

In the group III dogs, average transpericardial pressure after volume loading was 4.0 mm Hg, and mean left ventricular transmural end-diastolic pressure was 18.2 mm Hg. These values were virtually identical to those in group I. Average right ventricular transmural end-diastolic pressure under the same conditions was 9.6 mm Hg. Thus, transpericardial pressure constituted 42% of right ventricular end-diastolic pressure, twice the effect observed for the left ventricle.

GROUP IV

In the multidimensional preparations, all ventricular diameters decreased similarly during occlusion of the venae cavae, and the onset of the decline was virtually simultaneous (Fig. 8). The relationship between minor axis diameter and calculated biventricular volume during a caval occlusion after volume loading is shown in Figure 9A and appeared to be highly linear in each dog studied. During cardiac tamponade (Fig. 9B), there seemed to be no significant deviation from the linear relationship obtained during vena caval occlusion (solid regression line). End-diastolic data from sequential studies in one of the multidimension preparations are shown in Figure 10. Both biventricular volume and minor axis diameter increased with time after implantation. Left ventricular transmural pressure remained relatively constant, while transpericardial pressure progressively decreased. Therefore, the pressure effectively distending the ventricle (left ventricular minus pericardial pressure) increased, consistent with the change in ventricular dimensions.

POSTMORTEM STUDIES

Pericardial pressure-volume data from one of the postmortem studies are shown in Figure 11. With relationships (α, β, γ) obtained for the group II animals after volume loading were 5.78 ± 0.81, 16.60 ± 1.54, and 0.4 ± 0.2 mm Hg for the ventricle, and 2.50 ± 0.43, 18.60 ± 2.50, and 0.2 ± 0.2 mm Hg for the pericardium. These relationships were significantly different from group I (Table 2), and produced curves that were shifted upward and to the left. The average relationships for each group were similar to the representative animals shown in Figure 4.

FIGURE 7. Diastatic pressure-strain data obtained during caval occlusions in the same dog as Figure 6. In each panel, the solid line represents the curve fit from the control caval occlusion using true transmural pressure (left ventricular-pericardial pressure). Panel A: with pleural pressure subtracted as the external pressure, a slight difference was observed from the true pressure-strain relationship even with the pericardium empty. With tamponade, there was a progressive leftward shift of the curve, producing an apparent change in ventricular compliance. Panel B: when true transmural pressure was calculated, all data fell along the control curve, demonstrating that ventricular compliance was unchanged at moderate levels of tamponade.

FIGURE 8. Analog data from a multidimension preparation after volume loading in the control state and during a vena caval occlusion.
intracardiac volume held constant, infusion of 100 ml of saline into the pericardium increased pericardial pressure more than during the pre-mortem experiments. In each case, the pericardial pressure-volume curve was relatively flat over the lower volume range and became steep only after infusion of 60–80 ml. At autopsy, only minimal fibrinous adhesions were found, generally located directly beneath the pericardial suture line or over the dimension transducers. Histological examination of pericardial specimens from all dogs revealed a mild acute and chronic inflammatory infiltrate. Only minimal thickening of the pericardium was observed, and in no case was pericardial fibrosis noted.

Discussion

Previous studies of intact animals have demonstrated low pericardial pressures under normal conditions. Adamkiewicz (1873) performed transthoracic cannulation of the pericardium and observed
negative pericardial pressure. Using similar techniques, Kenner and Wood (1966) increased the afterload of the left and right ventricles, and despite marked increases in cardiac filling pressure, pericardial pressure remained low. The relationship between pericardial pressure and pleural pressure was examined by Morgan and associates (1965), who uniformly observed low pericardial pressure in normal dogs. Shirato and coworkers (1978) reported a mean pericardial pressure in conscious dogs of 8.2 mm Hg after volume loading, but the corresponding left ventricular end-diastolic pressure was almost 30 mm Hg. During control conditions in Shirato’s study, pericardial pressure was only 1.5 mm Hg, and in the absence of pathological conditions, substantially higher pericardial pressures have been recorded only when balloons were used to measure pressure (Holt et al., 1960).

Other studies have inferred pericardial influences by measuring changes in ventricular diastolic pressure-volume relationships after pericardiectomy. In isolated hearts, Spotnitz and Kaiser (1971) demonstrated a 34% contribution by the pericardium to a left ventricular end-diastolic pressure of 20 cm H2O (14.7 mm Hg). Using a similar model, Janicki and Weber (1980) found that pericardiectomy resulted in a downward shift of the ventricular diastolic pressure-volume curve by 4.6 mm Hg at an average left ventricular diastolic pressure of 20 mm Hg. These data suggested a pericardial contribution of 23% to left ventricular end-diastolic pressure, results quantitatively similar to those of the present study.

Hefner et al. (1960) observed a marked constraining effect of the pericardium in open-chest dogs at left ventricular end-diastolic pressures above 10 mm Hg. Similar results were reported by Glantz and associates (1978), who suggested that the pericardium substantially influenced left ventricular filling. In Glantz’s study, pericardiectomy produced significant increases in left ventricular minor axis area and a shift to the right of the left ventricular diastolic compliance curve. However, data were obtained well beyond the physiological range of filling pressures, and the pericardium had been opened vertically from the aortic arch to beyond the cardiac apex. Despite careful closure, pericardial retraction may have occurred during the length of time necessary for instrumentation, which included right heart bypass.

More recently, Stokland et al. (1980) instrumented dogs both with and without major pericardiectomy. After volume infusion to a ventricular end-diastolic pressure of 13 mm Hg, the pericardium was opened. The maximal increase in left ventricular myocardial chord length was 9.9% in hearts with a resutured pericardium and only 3.7% when the intact pericardium was opened. In contrast to the results of Glantz and coworkers (1978), Stokland’s data suggested minimal restriction of ventricular filling by the intact pericardium. The difference in results may be attributable to the lower range of filling pressures examined in Stokland’s study, or to the limited pericardiectomy which resulted in physiology more closely resembling normal. Thus, extent of pericardiectomy may be one experimental variable explaining differences in previous studies.

Resuturing the pericardium may have affected previous experimental results by magnifying cardiac restraining effects in several ways. First, in closing the pericardiectomy, the edges may be overlapped to such an extent that pericardial capacity is reduced. Gibbon and Churchill (1931) noted that closure of the pericardium required careful technique. When experimental closure produced hemodynamic rearrangements, reopening the pericardiectomy resulted in marked improvement. With a precisely closed pericardium, subsequent pericardiectomy produced no change. Second, intraoperative shrinkage or retraction of the pericardium, as observed during clinical cardiac surgery (Cunningham et al., 1975), may occur during instrumentation of the heart, and the pericardium will enclose a smaller volume when resutured, even if closed exactly. This effect would be greatest in acute studies in which the resutured pericardium was used to represent normal physiology. Again, comparison to conditions after pericardiectomy would overestimate the effects of the normal pericardium.

In general, care must be taken in extrapolating principles of physiology from isolated hearts or open-chest preparations to the intact subject, and the combination of ventricular dimension data and simultaneously measured ventricular, pericardial, and pleural pressures has not been available in previous reports. Therefore, the chronically instrumented, awake dog was chosen for the present study, and the pericardiectomy was placed over the great vessels well away from the cardiac chambers, maintaining pericardial capacity by precise reapproximation of the pericardial edges. Since the heart was delivered out of the pericardial sac, minimal distortion of the pericardium occurred during instrumentation. To avoid a second thoracotomy and data acquisition at a different time, analysis was based on comparison of simultaneously measured pericardial and left ventricular pressures. Finally, the effect of the pericardium on ventricular filling was evaluated 1 week after instrumentation, allowing pericardial properties to return toward normal. Although pericardiectomy was necessary in this preparation, the physiology of the normal pericardium seemed to be relatively preserved.

Delaying experiments for a week after implantation appeared to be very important in reproducing normal pericardial physiology. Data from the dogs studied sequentially suggested that substantial limitation of ventricular filling was present immediately after instrumentation but reversed with time. This early restraining effect may have been related to pericardial retraction occurring during instrumentation, and reversal of this effect may be analogous to pericardial creep (Rabkin et al., 1974; LeWinter et
Thus, pericardial contributions to left ventricular pressure were greater in group II, indicating minimal pericardial reserve capacity and extension beyond pericardial elastic limits even over the physiological range of filling pressures.

In group III studies, transmural end-diastolic left and right ventricular pressures (ventricular-pleural pressure) were higher than those obtained in similarly instrumented animals with the pericardium left widely open after implantation (Olsen et al., 1983). However, if ventricular filling pressures had been calculated using pericardial pressure as the external pressure, the values would have been remarkably similar to those in Olsen’s study. Not surprisingly, the effect of the pericardium on the right ventricle in the present study appeared to be much greater than that exerted on the left ventricle. In fact, it is likely that, at any physiological state, the thin-walled right ventricle is affected disproportionately by pericardial constraining forces (Armstrong et al., 1982) or increased intrathoracic pressure (Rankin et al., 1982). Whereas the pericardium may modulate direct ventricular interaction (Janicki and Weber, 1980), series interaction due to right ventricular constraint may be a more important determinant of left ventricular function (Olsen et al., 1983).

While comparison of pericardial and ventricular pressures may quantify the effect of the pericardium, cavitary ventricular pressure alone is not adequate to assess ventricular diastolic pressure-volume relationships. Calculation of transmural pressure is required in closed-chest subjects, as demonstrated by the work of Fowler et al. (1959) and Shirato et al. (1978). When cavitary left ventricular pressure in Shirato’s study was plotted vs. dimension with the pericardium intact, different curves were obtained for various interventions; after pericardiectomy, the curves became superimposed. By calculating transmural pressure as left ventricular pressure minus pericardial pressure in a reanalysis of the original data (Shabetai et al., 1979), a single curve was obtained for all interventions before and after pericardiectomy. Similar results were noted in the present experiments (Fig. 7). Therefore, with physiological changes in ventricular volume or during cardiac tamponade, concomitant changes in pericardial pressure may occur which must be taken into consideration when assessing ventricular transmural pressure or compliance.

Transient vena caval occlusions provide hemodynamic measurements over a wide range of diastolic volumes and allow data acquisition to be virtually instantaneous for the given experimental conditions (Olsen et al., 1981). One problem with using vena caval occlusions to investigate pericardial physiology is that pericardial pressure might decrease earlier than left ventricular pressure during the initial phase of the occlusion when right ventricular volume falls. In actual fact, the initial decrement in pericardial and left ventricular pressures differed by only one or two cardiac cycles in every study, and a precipitous decline in transpericardial pressure
was never observed. It also appeared that minor axis diameter reflected dynamic changes in the volume of both ventricles, as demonstrated by the linear relationship between minor axis diameter and calculated biventricular volume. This finding is surprising, since right ventricular volume might be expected to decrease during a vena caval occlusion before left ventricular dimensions begin to fall. However, it is well documented that the ventricular septum shifts into the unloaded right ventricle during the initial phase of a caval occlusion (Olsen et al., 1981a, 1983). The resultant increase in left ventricular septal-freewall diameter is accompanied by a decrease in minor axis diameter, with minimal change in left ventricular volume. Thus, when right ventricular volume decreases during the early phase of a vena caval occlusion, ventricular interaction results in a decline in minor axis diameter which is proportional to the change in biventricular volume. Stated differently, minor axis diameter is not just a left ventricular measurement but is dependent on changes in the volumes of both ventricles via direct ventricular interaction. Therefore, minor axis diameter data in group I experiments should validly reflect pericardial restrictive properties over the entire range of ventricular volumes.

The pericardial pressure-volume relationship is the ultimate descriptor of pericardial properties. Static pericardial pressure-volume curves obtained immediately postmortem in this study (Fig. 11) were similar to those reported previously (Holt, 1960), and could be used to infer pericardial reserve capacity. The biexponential nature of the relationship is characteristic of a stiff membrane which exerts little restriction until its capacity is exceeded. As first described by Cohnheim (1889), pericardial pressure remained low over the physiological range of volumes, but increased precipitously with continued infusion of fluid, to the point that a small change in volume resulted in a large increment in pressure. In the present study, pericardial pressure data from group I indicated that pericardial restriction was not augmented during intravascular volume expansion. Thus, with physiological changes in cardiac size, pericardial volume was varied over the flat portion of the curve. Even after volume expansion (Fig. 7A), infusion of at least 50 ml of fluid into the pericardium was required in the conscious dog before ventricular function was affected. Therefore, normal intrapericardial volume was somewhat less than pericardial reserve capacity. In conclusion, the results of this study suggest that ventricular end-diastolic volume and myocardial compliance are the major determinants of left ventricular end-diastolic pressure, and that pericardial restraint is minimal under conditions of normal pericardial capacity.

References

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INDEX TERMS: Pericardial pressure • Ventricular filling • Diastolic properties • Pericardium
Pericardial influences on ventricular filling in the conscious dog. An analysis based on pericardial pressure.

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*Circ Res.* 1984;54:173-184
doi: 10.1161/01.RES.54.2.173

Circulation Research is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7330. Online ISSN: 1524-4571

The online version of this article, along with updated information and services, is located on the World Wide Web at:
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