Mechanism of Decreased Right and Left Ventricular End-Diastolic Volumes during Continuous Positive-Pressure Ventilation in Dogs

JAMES E. FEWELL, DANA R. ABENDSCHEIN, C. JEFFREY CARLSON, ELLIOT RAPAPORT, AND JOHN F. MURRAY

SUMMARY Continuous positive-pressure ventilation (CPPV) decreases cardiac output by decreasing right and left ventricular end-diastolic volumes. To investigate the mechanism(s), we measured cardiovascular responses to CPPV before and after opening the chest and holding the lungs away from the heart. Expiratory pressure was adjusted to achieve similar lung volumes when the chest was open and closed (12 cm H₂O). Increasing expiratory pressure, when the chest was closed and evacuated, decreased cardiac output, ventricular end-diastolic volumes, and transmural ventricular end-diastolic pressures measured relative to lateral and posterior epicardial surface pressure (P < 0.05). Transmural ventricular end-diastolic pressures measured relative to lateral pleural surface pressure did not change significantly, indicating that the increase in thoracic pressure was greater at the lateral and posterior epicardial surfaces than at the lateral pleural surface. Opening the chest and holding the lungs away from the heart eliminated the decrease in cardiac output and ventricular end-diastolic volumes during increased expiratory pressure. Pericardectomy did not affect the cardiovascular responses to increased expiratory pressure. We, therefore, conclude that decreased cardiac output and ventricular end-diastolic volumes during CPPV result from the effects of increased thoracic pressure on cardiac filling.


CONTINUOUS positive-pressure ventilation (CPPV, mechanical ventilation with positive end-expiratory pressure) decreases cardiac output (Cournand et al., 1948). Several investigators have suggested that this may result from a decrease in myocardial contractility (Lozeman et al., 1974; Manny et al., 1978a; Cassidy et al., 1978). However, we showed recently that neither isovolumic nor ejection phase indices of myocardial contractility changed during CPPV, but right and left ventricular end-diastolic volumes decreased significantly (Fewell et al., 1980). This indicated that CPPV decreased cardiac output in accordance with Starling’s law by decreasing end-diastolic volume of the ventricles. However, transmural right and left ventricular end-diastolic pressures, measured relative to lateral pleural surface pressure, did not change significantly.

If lateral pleural surface pressure is an accurate measure of pressure surrounding the heart during CPPV, then a decrease in ventricular end-diastolic volume without a change in transmural ventricular end-diastolic pressure must result from a decrease in ventricular end-diastolic compliance. However, if lateral pleural surface pressure underestimated the pressure surrounding the heart during CPPV, then a decrease in ventricular end-diastolic volume could result from a decrease in transmural ventricular end-diastolic pressure. In support of this latter explanation, Brookhart and Boyd (1947) found that lateral pleural surface pressure underestimated the pressure between the pericardium and lungs during continuous positive-pressure breathing (spontaneous breathing with positive end-expiratory pressure). These local variations in thoracic pressure could result from compression of the heart by the expanded lungs and/or pericardial traction caused by the depressed diaphragm. The purpose of this study was to investigate these mechanisms of decreased ventricular end-diastolic volumes during CPPV.

Methods

Experimental Groups

The dogs were grouped as shown in Table 1. Experiments in group 1 compared lateral pleural surface pressure and lateral and posterior epicardial surface pressures; transmural ventricular end-diastolic pressures were calculated relative to these.
pressures. Pressures were measured before and during CPPV when the chest was closed and evacuated after pericardectomy.

Experiments in group 2 were designed to determine whether decreased ventricular end-diastolic volumes during CPPV are caused by an increase in thoracic pressure. Cardiovascular responses to CPPV were measured before and after the chest was opened widely and the lungs held away from the heart.

Experiments in group 3 were designed to determine whether decreased ventricular end-diastolic volumes during CPPV are caused by pericardial traction due to the depressed diaphragm. After pericardectomy, cardiovascular responses to CPPV were measured before and after the chest had been opened widely and the lungs held away from the heart.

Animal Preparation

Sixteen mongrel dogs weighing between 20 and 25 kg were anesthetized by intravenous injection of a mixture of chloralose (50 mg/kg) and urethane (500 mg/kg); additional anesthetic was administered every 15 minutes to maintain a constant level of anesthesia. Each dog was placed supine, and the trachea was intubated with a cuffed endotracheal tube. The cuff was inflated to a gas-tight fit, and the lungs were ventilated by a volume ventilator (Harvard Apparatus respiration pump, model 607) set to deliver a tidal volume of 15 ml/kg at a frequency of 12 breaths/min. A catheter was inserted into a femoral artery and advanced to the ascending aorta for continuous monitoring of systemic arterial pressure and heart rate during the surgical procedure.

A midsternal thoracotomy and pericardiotomy were performed. The heart and great vessels were instrumented as described previously (Fewell et al., 1980). Briefly, micromanometers were placed in the apex of the left ventricle and the lateral wall of the right ventricle. Electromagnetic flow probes were placed around the ascending aorta and the main pulmonary artery. Thermocouples in 20-gauge needles were inserted into the ascending aorta and main pulmonary artery. Catheters were inserted into the right and left ventricles and the left atrium. A mushroom catheter was inserted into the pleural space at mid-right atrial level for measurement of lateral pleural surface pressure. In six dogs (group 1), a thin (2-mm) silicone rubber sheet (6-x 12-cm) containing two flat balloons (diameter, 2.5 cm) was sutured to the heart: one balloon was lateral to the right ventricle; the other was posterior to the left ventricle (Fig. 1). This device was used to measure lateral and posterior epicardial surface pressure.

Arterial blood gases and pH were measured intermittently to ensure adequate alveolar ventilation (Feigl and D'Alecy, 1972). Aortic blood temperature was maintained near 37°C by an external thermal blanket. The gains of the micromanometer amplifiers were adjusted so that systolic and diastolic pressures matched the reference ventricular pressures measured with fluid-filled catheters connected to Statham P23Db pressure transducers. Flow probes were calibrated in vivo by means of the dye dilution technique to simultaneously measure car-

- **Fig. 1** Schematic diagram of flat silicone sheet containing two pressure-sensitive balloons (A). The silicone sheet was sutured to the heart so that one balloon was lateral to the right ventricle and the other was on the posterior wall of the left ventricle (B, anterior view; C, posterior view).
Experimental Protocol

After completing the surgical procedure, we waited 60 minutes for the dog's hemodynamics to stabilize. Variables were then measured during a control period (end-expiratory pressure, 0 cm H₂O when the chest was closed and 3 cm H₂O when it was open) and during a period of 5-20 minutes after the expiratory pressure had been increased (end-expiratory pressure, 12 cm H₂O when the chest was closed and 10 cm H₂O when it was open). When the chest was open and pleural pressure was equal to atmospheric pressure, the expiratory pressure was adjusted to achieve a transpulmonary pressure similar to that present when the chest was closed and evacuated. Functional residual capacity was measured to verify that lung volumes were similar between the open- and closed-chest conditions. After 20 minutes, the expiratory pressure was returned to the control level, and dogs in groups 2 and 3 were prepared for the second experimental condition (Table 1). We allowed 30 minutes for the dog's hemodynamics to stabilize before the experimental protocol was repeated.

Variables were measured in the following sequence: arterial blood gases and pH, cardiovascular and respiratory pressures and cardiac output, functional residual capacity, ventricular volumes, and repeat functional residual capacity.

Experimental Measurements

Arterial Blood Gases and pH

Arterial blood samples were withdrawn from a femoral artery into heparinized syringes and were analyzed by a Corning 175 blood gas analyzer. Blood gas values were corrected to body temperature.

Cardiovascular and Respiratory Pressures and Cardiac Output

The following pressures were measured at end-expiration: right and left ventricular end-diastolic pressures, right and left ventricular peak-systolic pressures, lateral pleural surface pressure, lateral epicardial surface pressure, and posterior epicardial surface pressure. Before the pressures were measured at the epicardial surface of the heart, the balloons were adjusted to their predetermined optimum volume, i.e., balloon volume at which pressure was not generated by the elastic property of the balloon. The 10-90% response time to a square-wave pressure change of 30 mm Hg was 10 ± 0.82 (mean ± 1 SD) msec for the balloons used in this study. Cardiac output was determined from the flow tracing. The pressure and flow tracings were recorded on an Electronics for Medicine DR-8 recorder. An aneroid manometer was incorporated into the ventilator circuit opposite the endotracheal tube port for continuous monitoring of proximal airway pressure. Transmural ventricular end-diastolic pressures were calculated relative to lateral pleural surface pressure (end-diastolic pressure minus lateral pleural surface pressure), lateral epicardial surface pressure (end-diastolic pressure minus lateral epicardial surface pressure), and posterior epicardial surface pressure (end-diastolic pressure minus posterior epicardial surface pressure).

Functional Residual Capacity

Functional residual capacity was measured in duplicate by the closed-circuit method using helium as the tracer gas (Comroe et al., 1962). Functional residual capacity was calculated from the formula:

\[ \text{FRC} = \%\text{He initial} - \%\text{He final} / \%\text{He final} \times \text{initial volume} \]

and corrected to body temperature, pressure, and saturation.

Ventricular Volumes

Right and left ventricular volumes were measured by the thermodilution technique described in detail elsewhere (Fewell et al., 1980; Keroes and Rapaport, 1972).

Statistical Analysis

Statistical analysis was performed using Student's paired t-test. For each experimental condition, we tested the null hypothesis that the mean of each variable after elevation of the expiratory pressure was equal to the corresponding mean during the control period. Comparisons were selected "a priori."

Results

A typical pressure tracing showing the relation between lateral pleural surface pressure, lateral epicardial surface pressure, and posterior epicardial surface pressure during intermittent positive-pressure ventilation and CPPV is shown in Figure 2. Lateral and posterior epicardial surface pressures increased more than lateral pleural surface pressure when positive end-expiratory pressure was applied. Thus, changes in pressure on the lateral pleural surface underestimated changes in pressure on the lateral and posterior epicardial surfaces of the heart (Table 2). Transmural right and left ventricular end-diastolic pressures, measured relative to lateral
increased expiratory pressure. However, we think pressure (PESP), when the chest was closed and evacu-
ated, did not change significantly when expiratory pressure was increased. However, transmural right and left ventricular end-
diastolic pressures, measured relative to lateral and posterior epicardial surface pressure, decreased signifi-
cantly ($P < 0.05$).

Increasing the expiratory pressure decreased cardiac output by 40% when the pericardium was closed and the chest was closed and evacuated (Table 3). End-diastolic volumes decreased significantly. Increasing the expiratory pressure when the chest was closed and evacuated after pericardectomy produced cardiovascular changes similar to those observed when the pericardium was closed.

Increasing the expiratory pressure did not signifi-
cantly change cardiac output or ventricular end-
diastolic volumes when the chest was opened wide and the lungs held away from the heart (Table 4). A small but consistent decrease in left ventricular peak systolic pressure was measured.

Increasing expiratory pressure caused a small increase in $P_aCO_2$ and decrease in pH. No significant changes in $P_aO_2$ occurred.

**Discussion**

These experiments show that CPPV decreases transmural ventricular end-diastolic pressure measured relative to lateral and posterior epicardial surface pressures. This indicates that the decrease in ventricular end-diastolic volumes results at least in part from a decrease in transmural ventricular end-diastolic pressures. However, this does not ex-
clude the possibility that a decrease in ventricular end-diastolic compliance may participate in de-
creasing ventricular end-diastolic volumes. Opening the chest widely and holding the lungs from the heart eliminated the decrease in ventricular end-
diastolic volumes and cardiac output during increased expiratory pressure. Pericardectomy did not affect the cardiovascular responses to increased expiratory pressure. We conclude that decreased cardiac output and ventricular end-diastolic vol-
umes during CPPV result from the effects of in-
creased thoracic pressure on cardiac filling.

Others have reported that opening the chest does not eliminate the decrease in cardiac output during increased expiratory pressure. However, we think this apparent discrepancy can be explained by dif-
ferences in the experimental designs of these stud-
ies. Humphreys et al. (1937) measured cardiac out-
put in dogs during a control period of spontaneous breathing and during several brief periods of con-
tinuous lung inflation after the chest was opened widely. Continuous lung inflation decreased cardiac output in most cases when compared with sponta-
neous breathing. However, opening the chest alone has been shown to decrease cardiac output (Fer-
moso et al., 1964). Furthermore, Humphreys et al. (1937) acknowledged that opening the chest did not prevent the lungs from compressing the heart during lung inflation. Thus, the decrease in cardiac output probably resulted from the loss of normally negative pleural pressure when the chest was opened and compression of the heart by the ex-
panded lung. In the experiments reported here, control variables were measured after the chest had been opened and the transmural left atrial pressure adjusted (measured relative to lateral pleural sur-
face pressure) to the control level measured when the chest was closed and evacuated. Furthermore, the lungs were held away from the heart during increased expiratory pressure. Thus, we avoided a change in transmural ventricular end-diastolic pressure due to opening the chest and compression of the heart by the lungs.

Manny et al. (1978b) compared the cardiovascu-
lar responses to increased expiratory pressure in two groups of dogs. In one group, the chest was closed and evacuated; in the other group, the chest was opened and the ribs were resected. Increasing the expiratory pressure by 15 cm $H_2O$ decreased cardiac output in both groups. However, it is diffi-
cult to compare the responses between the two groups because the increase in lung volume was much greater in open-chested than in closed-
chested dogs. Extreme lung expansion can produce

<table>
<thead>
<tr>
<th>Expiratory pressure (cm $H_2O$)</th>
<th>0</th>
<th>12</th>
</tr>
</thead>
<tbody>
<tr>
<td>$L_PSP$</td>
<td>$-2.5 \pm 0.9$</td>
<td>$0.7 \pm 0.7^*$</td>
</tr>
<tr>
<td>$L_ESP$</td>
<td>$-1.3 \pm 1.3$</td>
<td>$3.6 \pm 1.2^*$</td>
</tr>
<tr>
<td>$P_ESP$</td>
<td>$0.0 \pm 1.4$</td>
<td>$5.2 \pm 1.1^*$</td>
</tr>
<tr>
<td>$RVEDP_{TM}$ ($L_PSP$)</td>
<td>$4.0 \pm 0.9$</td>
<td>$4.6 \pm 2.1$</td>
</tr>
<tr>
<td>$RVEDP_{TM}$ ($L_ESP$)</td>
<td>$3.4 \pm 1.7$</td>
<td>$1.7 \pm 2.4^*$</td>
</tr>
<tr>
<td>$RVEDP_{TM}$ ($P_ESP$)</td>
<td>$2.1 \pm 1.4$</td>
<td>$0.1 \pm 1.6^*$</td>
</tr>
<tr>
<td>$LVEDP_{TM}$ ($L_PSP$)</td>
<td>$6.4 \pm 1.9$</td>
<td>$6.1 \pm 2.2$</td>
</tr>
<tr>
<td>$LVEDP_{TM}$ ($L_ESP$)</td>
<td>$5.3 \pm 2.3$</td>
<td>$3.2 \pm 1.9^*$</td>
</tr>
<tr>
<td>$LVEDP_{TM}$ ($P_ESP$)</td>
<td>$4.0 \pm 2.5$</td>
<td>$1.6 \pm 1.4^*$</td>
</tr>
</tbody>
</table>

Values are means $\pm 1$ SD for six dogs.

* Indicates a difference, at the 0.05 level of significance, from the mean of the control period.
Table 3  Effect of Increasing Expiratory Pressure on Cardiovascular and Respiratory Variables When the Chest Was Closed and Evacuated

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pericardium closed</th>
<th>Pericardium removed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0 cm H2O</td>
<td>12 cm H2O</td>
</tr>
<tr>
<td></td>
<td>0 cm H2O</td>
<td>12 cm H2O</td>
</tr>
<tr>
<td>Functional residual capacity (ml)</td>
<td>339 ± 67</td>
<td>312 ± 45</td>
</tr>
<tr>
<td>Lateral pleural surface pressure (mm Hg)</td>
<td>-1.6 ± 0.9</td>
<td>-1.8 ± 0.3</td>
</tr>
<tr>
<td>Cardiac output (ml/min)</td>
<td>2236 ± 498</td>
<td>2615 ± 730</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>160 ± 13</td>
<td>143 ± 11</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>13.9 ± 2.4</td>
<td>18.5 ± 5.7</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>End-diastolic pressure (mm Hg)</td>
<td>3.1 ± 1.0</td>
</tr>
<tr>
<td></td>
<td>34.8 ± 8.3</td>
<td>34 ± 9</td>
</tr>
<tr>
<td></td>
<td>20 ± 6</td>
<td>17 ± 4</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>End-diastolic pressure (mm Hg)</td>
<td>3.5 ± 1.4</td>
</tr>
<tr>
<td></td>
<td>113.5 ± 12.0</td>
<td>108.8 ± 7.1</td>
</tr>
<tr>
<td></td>
<td>33 ± 7</td>
<td>36 ± 10</td>
</tr>
<tr>
<td></td>
<td>19 ± 4</td>
<td>18 ± 5</td>
</tr>
</tbody>
</table>
| Values are means ± 1 SD for five experiments. | * Indicates a difference, at the 0.05 level of significance, from the mean of the control period.

Table 4  Effect of Increasing Expiratory Pressure on Cardiovascular and Respiratory Variables When the Chest Was Open and the Lungs Were Held Away from the Heart

<table>
<thead>
<tr>
<th>Variable</th>
<th>Pericardium closed</th>
<th>Pericardium removed</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>3 cm H2O</td>
<td>10 cm H2O</td>
</tr>
<tr>
<td></td>
<td>3 cm H2O</td>
<td>10 cm H2O</td>
</tr>
<tr>
<td>Functional residual capacity (ml)</td>
<td>436 ± 109</td>
<td>372 ± 75</td>
</tr>
<tr>
<td>Lateral pleural surface pressure (mm Hg)</td>
<td>2446 ± 815</td>
<td>2546 ± 742</td>
</tr>
<tr>
<td>Cardiac output (ml/min)</td>
<td>156 ± 20</td>
<td>141 ± 18</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>15.5 ± 3.9</td>
<td>18.3 ± 6.0</td>
</tr>
<tr>
<td>Stroke volume (ml)</td>
<td>5.2 ± 0.7</td>
<td>3.8 ± 1.6</td>
</tr>
<tr>
<td>Right ventricle</td>
<td>36.8 ± 14.0</td>
<td>42.9 ± 6.7</td>
</tr>
<tr>
<td></td>
<td>35 ± 10</td>
<td>33 ± 12</td>
</tr>
<tr>
<td>Left ventricle</td>
<td>5.6 ± 2.2</td>
<td>5.0 ± 1.5</td>
</tr>
<tr>
<td></td>
<td>117.8 ± 21.2</td>
<td>121.6 ± 16.9</td>
</tr>
</tbody>
</table>
| Values are means ± 1 SD for five experiments. | * Indicates a difference, at the 0.05 level of significance, from the mean of the control period.

cardiopulmonary changes which might not occur in the intact animal (Maulsby and Hoff, 1962). Furthermore, it is possible that marked expansion of the lungs could lead to greater vagal stimulation (Daly et al., 1967; Coleridge et al., 1965) and prostaglandin release (Said et al., 1972; Berry et al., 1977) than would occur in the intact animal. The fact that nervous and/or humoral factors affect peripheral vascular resistance during increased expiratory pressure was shown in our study by decreased left ventricular peak-systolic pressure when cardiac output was unchanged. To avoid the effects of extreme expansion of the lungs, we adjusted the expiratory pressure to produce similar changes in lung volumes at end-expiration when the chest was opened and closed.

Transmural ventricular end-diastolic pressures, measured relative to lateral pleural surface pressure, did not change significantly during increased expiratory pressure. However, when measured relative to lateral and posterior epicardial surface pressures, transmural ventricular end-diastolic pressures decreased significantly, indicating that the increase in thoracic pressure was greater at the lateral and posterior epicardial surfaces of the heart than at the lateral pleural surface. These results agree with the finding of others [Brookhart and Boyd, 1947; Prewitt and Wood, 1979 (Appendix);
Wise et al., 1979]. Our pressure measurements, as well as those of others, have not excluded the possibility that pericardial traction due to the depressed diaphragm could further increase epicardial surface pressure during CPPV (our epicardial surface pressure measurements were made after pericardectomy; Brookhart and Boyd (1947) and Prewitt and Wood (1979) measured pressure between pericardium and lung; Wise et al. (1979) measured epicardial surface pressure when the chest was open, which could significantly attenuate diaphragmatic depression during CPPV). However, it is unlikely that pericardial traction plays an important role because pericardectomy did not affect the cardiovascular responses to increased expiratory pressure.

Cassidy et al. (1978) and Scharf et al. (1979) measured epicardial surface pressure using cylindrical balloons attached to catheters and introduced into the pericardial sac. Transmural atrial pressures did not change during CPPV, and close correlation was observed between changes in both esophageal pressure and epicardial surface pressure (Cassidy et al., 1978) and lateral pleural surface pressure and epicardial surface pressure (Scharf et al. 1979). However, Agostoni (1972) has shown that if pressure outside a long balloon is not uniform, the gas within the balloon may be shifted to the point at which the surrounding pressure is lower. The pressure recorded by a relatively long balloon approximates the lowest pressure on its surface (Mead, 1961). It is possible that expansion of the lungs during CPPV could result in nonuniform pressure being exerted upon the balloons which could shift its internal volume. Furthermore, experimental manipulations changed the position of the balloons in the pericardial sac (Cassidy et al., 1978).

Although our study does not explain the apparent differences between lateral pleural surface pressure and lateral epicardial surface pressure-posterior epicardial surface pressure, we can speculate on some possible causes. Brookhart and Boyd (1947) have suggested that the local variations in thoracic pressure which occur during increased expiratory pressure are the result of local distortion of the elastic lung tissue surrounding the heart. If lung inflation results in uniform tension being exerted on the lateral chest wall and the heart, the resulting pressure around the heart would be higher because of the heart’s smaller radius of curvature. Thus, the greater increase in epicardial surface pressure may result from compression of the heart by the expanded lungs. Another possibility is that measuring pressure in a small pneumothorax may not be an accurate reflection of true lateral pleural surface pressure. If pressure is measured in a bubble with a small radius of curvature, the retractive forces of the lungs may be partially counterbalanced by the surface tension of the bubble (Agostoni, 1972). The size and shape of the small pneumothorax also may be altered when the lungs are inflated, using positive pressure.

Acknowledgments
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