The Significance of the Intact Pericardium for Cardiac Performance in the Dog

OLAV STOKLAND, MÅLFRID MOLAUG MILLER, JON LÆKVEN, AND ARNFINN ILEBEEK

SUMMARY The significance of the intact pericardium for cardiac performance was examined in 18 open-chest dogs. Myocardial chord lengths (MCL) in the right and left ventricle were measured simultaneously by ultrasonic crystals implanted in the myocardium of the anterior walls. In 14 dogs, the ultrasonic elements were inserted into the myocardium through needle openings in the pericardium (intact pericardium). In four other dogs, the elements were inserted through 6- to 7-cm-long incisions in the pericardium which were sutured afterward (sutured pericardium). Stroke volume was calculated in each of seven dogs with an intact pericardium from electromagnetic measurement of flow in the superior and inferior venae cavae. After blood volume expansion to about 13 mm Hg, the pericardium was opened and the end-diastolic pressure-MCL relationships and stroke volumes before and after pericardiectomy were compared. By opening the intact pericardium, the right and left ventricular end-diastolic MCL rose by 2.7 ± 0.7% and by 3.7 ± 1.1%, respectively, and stroke volume increased by 13 ± 4%. However, by reopening the sutured pericardium, the increases in both right and left ventricular end-diastolic MCL were clearly greater (12.2 ± 5.6% and 9.9 ± 2.9%, respectively), and the restrictive effect of the pericardium was therefore overestimated when the pericardium was not left intact. Thus, after a moderate blood volume expansion, the intact pericardium exerts a certain, although moderate restrictive effect on cardiac performance. Circ Res 47: 27-32, 1980

THE ROLE of the pericardium in cardiac function has interested cardiologists and physiologists for a long time and particularly the possibility that the pericardium might limit dilation of the various heart chambers. Whereas pressures in the heart chambers can be measured with great accuracy, considerable difficulties are associated with estimating their respective volumes. To estimate volume changes, however, miniature dimension gauges have been introduced into the myocardium or ventricular cavities in experimental animals by opening the pericardium widely. Thereafter, the pericardium has been closed by suture of the pericardial incisions (Glantz et al., 1978; Hefner et al., 1961; Prindle et al., 1973; Spotnitz and Kaiser, 1971). The elastic properties of the pericardium may, however, be changed by this handling, leading to misinterpretation of the obtained measurements of ventricular pressures and dimensions. Therefore, we implanted ultrasonic crystals into the left and right ventricular walls without opening the pericardium. The connecting leads of the ultrasonic crystals were used as threads mounted on curved needles (Fig. 1) and the crystals were sewn into the myocardium through the pericardium. Thus, we could regard the pericardium as intact in this study and myocardial chord lengths (MCL) between the crystals could be monitored continuously from both the right and left ventricles.

After cardiac dilation by blood volume expansion, a significant restraint by both the sutured pericardium (Glantz et al., 1978; Spotnitz and Kaiser, 1971; Hefner et al., 1961), and the intact pericardium (Shirato et al., 1978) has been demonstrated. However, none of these studies determined the effect of pericardiectomy on cardiac output. Therefore, to test the effect of the intact pericardium on cardiac performance, we abruptly opened the intact pericardium after elevation of the end-diastolic left ventricular pressure (LVP) to about 13 mm Hg by saline-dextran infusion during continuous measurement of cardiac output as well as right and left ventricular MCL. If the intact pericardium played no role in cardiac performance, no change should be expected to occur after pericardiectomy. If, on the other hand, the pericardium modifies cardiac performance, its effects could be quantified by these experiments. The effects of opening the intact pericardium also were compared with the effects of reopening a sutured pericardium.

Methods

Eighteen mongrel dogs of either sex and weighing 12–33 kg (mean 19.7 ± 1.8 kg) were anesthetized with intravenous sodium pentobarbital (25 mg/kg). At intervals, supplementary doses of 50 mg of sodium pentobarbital were given to maintain the anesthesia. The dogs were ventilated by a positive-pressure respirator (Cyclator Mark II, British Oxygen Co.). A transverse thoracotomy was performed...
in the 5th intercostal spaces with transection of the sternum. Arterial blood was repeatedly examined for pH, PCO₂ and PO₂ in an automatic pH blood gas analyzer (model 313, Instrumentation Laboratory Inc.). Appropriate measures were taken to keep the blood gases at normal levels.

Changes in right and left ventricular MCL were measured by an ultrasonic technique as described by Bugge-Asperheim et al. (1969). The ultrasonic transmission time was recorded continuously between two piezo-electric crystals of lead zirconate-titanate (0.5 x 1 x 3 mm) sewn into the myocardium: one pair in the anterior wall of the right ventricle and one pair in the anterior wall of the left ventricle (Fig. 1). The crystals were molded in epoxy resin and connected with thin insulated copper wires which could be sewn into the myocardium with the crystals. In 14 dogs, the crystals were sewn through the intact pericardium. In four other dogs, a pericardiectomy, about 6-7 cm long, over the anterior wall of the right and left ventricle, was performed to give access to the myocardium. When the crystals had been sewn into the myocardium, the pericardial incisions were closed by 4-6 interrupted sutures. Care was taken not to diminish the original pericardial space and minimize overlap of the pericardial edges. In all dogs the crystals were sewn into the myocardium 8-15 mm apart and at a depth from the epicardial surface of 3-5 mm in the left ventricle and at a depth of 1-3 mm in the right ventricle. The positions of the crystals were adjusted until a correct ultrasonic signal was visualized on an oscilloscope. The distance between them is called the MCL and corresponded to the main direction of muscle shortening as verified by post-mortem examination.

In seven dogs with intact pericardium, total venous return, coronary blood flow excluded, was measured by a square wave electromagnetic flowmeter (Nycotron, Drammen) with flow probes on the superior and inferior venae cavae. The azygos vein was ligated. The diameter of the probes chosen was slightly less than the diameter of the veins in order to obtain a good fit, and probes used were those whose gap could be closed. Care was taken to prevent tilting of the probes by fixing the cables to the surrounding structures. True zero flow was obtained by occluding the vessels with a snare downstream to the probes. Stroke volume was calculated by dividing total flow in the veins cavae by heart rate.

Left and right ventricular pressures (LVP and RVP) were measured by Statham pressure transducers (P 23 Gb and P 23 Db) connected to polyethylene catheters introduced through the left carotid artery and through the azygos or jugular vein, respectively. The first derivative of LVP, dP/dt, was continuously recorded with an RC differentiating circuit connected to the output of the left ventricular pressure channel.

**Experimental Procedure**

The blood volume was expanded by infusion of dextran (Macrodex 6% "Pharmacia") and saline (NaCl 0.9%) through a femoral vein. All hemodynamic measurements were obtained at end-expiration. During steady state with an end-diastolic LVP of about 13 mm Hg, the pericardial sac in 13 dogs was opened widely. Care was taken not to change the heart's position in the thorax. Right and left ventricular MCL, pressures, and flow were compared immediately before and after pericardiectomy. Usually an interval of less than 4 minutes was required to open the pericardium completely. The saline-dextran infusion then was stopped and 20 mg of furosemide injected. Thus, hemodynamic data were recorded both during blood volume expansion with an intact pericardium and during return of the blood volume to control levels with the pericardium opened. In another dog, blood volume expansion with saline was induced three times consecutively with the pericardium intact and then once again after the pericardium had been widely opened.

**Statistics**

Each dog served as its own control, and the statistical probability of difference was calculated using Wilcoxon's test for paired or unpaired comparisons (Snedecor and Cochran, 1967). $P < 0.05$ was regarded as statistically significant.

**Results**

Figure 2 shows tracings from one experiment before and after removal of the intact pericardium. The end-diastolic MCL of both the right and the left ventricle increased when the pericardium was removed and mean flow in the venae cavae and the amplitude of pulsatile flow increased. The changes in end-diastolic MCL in the individual experiments, when the intact pericardium was opened, are presented in Figure 3 (upper part). Right ventricular end-diastolic MCL increased in 11 of 13 dogs and
**Figure 2** Tracings demonstrating hemodynamic effects of opening the intact pericardium after saline/dextran infusion in an open-chest dog weighing 16 kg. By pericardiotomy, stroke volume rose from 16.0 to 18.4 ml. LV dP/dt = first derivative of LVP; LVDP = diastolic LVP; SVC = superior vena cava; IVC = inferior vena cava; RV MCL = right ventricular MCL; LV MCL = left ventricular MCL.

remained unchanged in two. Left ventricular end-diastolic MCL also increased in 11 dogs, but remained unchanged in one and decreased in another.

**Figure 3** Effects on right and left ventricular end-diastolic MCL in each dog of opening the intact pericardium (upper panel) and of reopening the sutured pericardium (lower panel).

The hemodynamic effects of opening the intact pericardium are summarized in Table 1. The increments in end-diastolic MCL of the right and left ventricles were not significantly different and averaged 2.7 ± 0.7% and 3.7 ± 1.1%, respectively. In the left ventricle, myocardial shortening (the difference between end-diastolic and end-systolic MCL) increased by 27 ± 8% (P < 0.0002), whereas in the right ventricle, myocardial shortening did not increase significantly. Stroke volume rose by 13 ± 4% (P < 0.02) when the intact pericardium was re-

### Table 1  Effects of Opening the Intact Pericardium

<table>
<thead>
<tr>
<th></th>
<th>Control</th>
<th>Pericardiectomy</th>
<th>Difference</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Left ventricle</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>End-diastolic MCL (mm)</td>
<td>13.77 ± 0.89</td>
<td>14.24 ± 0.88</td>
<td>0.47 ± 0.12</td>
<td>&lt;0.005</td>
</tr>
<tr>
<td>Myocardial shortening (mm Hg)</td>
<td>1.43 ± 0.12</td>
<td>1.75 ± 0.12</td>
<td>0.32 ± 0.08</td>
<td>&lt;0.0002</td>
</tr>
<tr>
<td>End-diastolic pressure (mm Hg)</td>
<td>12.7 ± 1.6</td>
<td>12.6 ± 1.8</td>
<td>-0.1 ± 0.4</td>
<td>NS</td>
</tr>
<tr>
<td>Systolic pressure (mm Hg)</td>
<td>124 ± 7</td>
<td>127 ± 7</td>
<td>3 ± 2</td>
<td>NS</td>
</tr>
<tr>
<td>dP/dt (mm Hg/sec)</td>
<td>2370 ± 230</td>
<td>2380 ± 205</td>
<td>10 ± 110</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Right ventricle</strong></td>
<td></td>
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<tr>
<td>End-diastolic MCL (mm)</td>
<td>14.25 ± 0.80</td>
<td>14.60 ± 0.78</td>
<td>0.35 ± 0.08</td>
<td>&lt;0.0005</td>
</tr>
<tr>
<td>Myocardial shortening (mm Hg)</td>
<td>2.47 ± 0.25</td>
<td>2.53 ± 0.25</td>
<td>0.06 ± 0.12</td>
<td>NS</td>
</tr>
<tr>
<td>End-diastolic pressure (mm Hg)</td>
<td>9.7 ± 0.9</td>
<td>8.0 ± 1.0</td>
<td>-1.7 ± 0.5</td>
<td>&lt;0.005</td>
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<tr>
<td>Systolic pressure (mm Hg)</td>
<td>31 ± 2</td>
<td>31 ± 3</td>
<td>0 ± 1</td>
<td>NS</td>
</tr>
<tr>
<td><strong>Common parameters</strong></td>
<td></td>
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<tr>
<td>Stroke volume (ml)</td>
<td>20.9 ± 2.6</td>
<td>23.2 ± 2.6</td>
<td>2.3 ± 0.7</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>Heart rate (beats/min)</td>
<td>156 ± 12</td>
<td>157 ± 13</td>
<td>1 ± 2</td>
<td>NS</td>
</tr>
</tbody>
</table>

Values are mean ± SEM of experiments in 13 anesthetized, open-chest dogs. (Stroke volume was examined in seven dogs.) dP/dt = first derivative of left ventricular pressure; NS = not significant.
moved. Systolic pressure and heart rate were not affected by the pericardiectomy. Left ventricular dP/dt and end-diastolic pressure remained unchanged, whereas end-diastolic RVP decreased by 1.7 ± 0.5 mm Hg ($P < 0.005$). As shown in Figure 4, the increase in left ventricular end-diastolic MCL was associated with increased stroke volume both after saline-dextran infusion and after pericardiectomy.

The findings of an increased end-diastolic MCL in both ventricles, together with unchanged or even reduced end-diastolic pressures, strongly suggest that the end-diastolic pressure-volume relationship was altered in both ventricles following pericardiectomy. This is more closely examined in Figure 5, which shows the end-diastolic pressure-MCL relationships of the right and left ventricle in one experiment. With the pericardial sac open, the end-diastolic pressure-MCL curves were shifted to the right in both ventricles. End-diastolic RVP was reduced by pericardiectomy, whereas end-diastolic LVP remained unchanged. The end-diastolic pressure-MCL curves were clearly separated at high end-diastolic pressures.

To determine whether the observed changes in the end-diastolic pressure-MCL curves could be explained by a shift of curves (hysteresis) during loading and unloading, such curves were recorded during saline loading and unloading thrice before pericardiectomy in one dog (Fig. 6). No hysteresis was found, and at high end-diastolic pressures the curves almost completely overlapped. After pericardiectomy, however, a shift to greater volumes of both ventricles was obtained (Fig. 7).

**Figure 4** Effects of blood volume expansion (●) and of opening the pericardium (○) on left ventricular end-diastolic MCL and on stroke volume in seven atropinized open-chest dogs weighing 21.0 ± 2.3 kg. Control values for stroke volume and MCL are normalized to 10 ml and to 10 mm, respectively. Other values are means ± SEM.

**Discussion**

This study shows that the intact pericardium exerts a moderate but significant restraint on cardiac dilation at a moderate degree of blood volume
expansion. At an average end-diastolic LVP of 13 mm Hg, stroke volume rose by 13 ± 4% after pericardiotomy.

The increased stroke volume caused by pericardiotomy could be due to increased activation of the Frank-Starling mechanism, increased inotropic stimulation, or decreased afterload. However, there was no evidence of increased myocardial inotropy during pericardiotomy as judged from the LV dP/dt, and systolic LVP remained constant, indicating no decrease in afterload. Because the pericardium was opened during steady state conditions, the increase in MCL was not caused by the saline-dextran infusion. Changes in ventricular shape might, however, have influenced the evaluation of ventricular volume both in our and other studies during pericardiotomy (Bartle et al., 1968; Bartle and Hermann, 1967; Carleton, 1929; Glantz et al., 1978; Hefner et al., 1961), but cannot account for the increase in stroke volume observed in our study. Because of constant inotropy and afterload, the increase in stroke volume in the present study therefore can be explained only by increased activatedization of the Frank-Starling mechanism through increased end-diastolic ventricular volume.

On reopening a previously sutured pericardium, we found that cardiac dimensions increased significantly more than on opening an intact pericardium. These findings indicate that the restrictive function of the pericardium observed by others during reopening of a sutured pericardium (Glantz et al., 1978; Hefner et al., 1961; Spotnitz and Kaiser, 1971) might have been overestimated. Glantz and coworkers found the left ventricular square area to be about 20% greater with the pericardium reopened than with the pericardium closed at an end-diastolic LVP of 8 mm Hg; at a higher end-diastolic pressure, the effect of reopening the sutured pericardium was even greater. In the present study, an increase in left ventricular end-diastolic dimension of approximately 4% was found on opening the intact pericardium at an end-diastolic pressure of about 13 mm Hg. The quantitative disagreement between our data and those of Glantz et al. might also, to some extent, be due to the opening of the right ventricle in their study, whereas any artificial effects due to ventriculotomy were avoided in our study.

Shirato et al. (1978) studied the left ventricular pressure-length curve during volume loading before and after removal of the pericardium. They kept the pericardium intact and compared the pressure-length curves of capture beats during cardiac pacing with and without pericardium, in four conscious dogs, but did not correlate these findings to changes in cardiac pump function. At an end-diastolic LVP of about 8 mm Hg, they found an increase in myocardial segment length of the left ventricle of 2.2% which correlates well with the increases found in the present study.

The altered diastolic pressure-MCL relationships of both ventricles observed in our study when the pericardium was opened, have been interpreted as a restrictive effect of the pericardium on both ventricles during moderate volume loading. Another possibility is, however, as pointed out by Glantz et al. (1978), that only filling of the relatively thin-walled right ventricle is restricted by the pericardium. By pericardiotomy, improved filling of the right ventricle would increase right ventricular stroke volume and subsequently left ventricular preload. Simultaneously, the decrease in end-diastolic pressure initiated increased myocardial inotropy through Frank-Starling mechanism, increased inotropic stimulation, or decreased afterload.
stolic RVP observed in the present experiments would increase the septal transmural pressure gradient and allow a bulging of the septum toward the right ventricle. Relief of right ventricular restriction by pericardiotomy would thus tend to increase left ventricular volume by two mechanisms, i.e., by increasing its filling and by septal displacement. Such an interaction between the two ventricles through displacement or alterations in function of the interventricular septum has been discussed extensively (Bemis et al., 1974; Glantz et al., 1978; Laks et al., 1967; Ludbrook et al., 1979; Moulopoulos et al., 1965; Ross, 1979; Shabetai, 1978; Shirato et al., 1978; Stool et al., 1974, Taylor et al., 1967).

However, the results observed both in our study and in others, can in part be explained by the restrictive effect of the pericardium on the most thin-walled structure enclosed within the pericardium, namely the right atrium. When we opened the pericardium, we immediately observed a substantial increase in right atrial volume. With a total absence of atrial systole, cardiac output may decrease by up to 30% (Skinner et al., 1963). Thus, the increase in cardiac output of 13% in this study could be explained by relief of atrial restraint during pericardiotomy.

Although the pericardium restricts cardiac dilation in the acute phase of volume loading, it does not appear to restrict cardiac function in the chronic state (Bartle and Hermann, 1967; Prindle et al., 1973). The most likely explanation for this finding is that the pericardium undergoes morphological changes concurrent with the development of chronic heart dilatation.

The present study on open-chest dogs demonstrates that, by opening the intact pericardium after a moderate blood volume expansion, the end-diastolic pressure-MCL relationship is changed in both the right and the left ventricles. By opening of the intact pericardium, the pump function of the heart is improved. The intact pericardium accordingly exerts a certain but only a moderate effect on cardiac performance.

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