Opening the pericardium during pulmonary artery constriction improves cardiac function

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Belenkie, Israel, Rozsa Sas, Jamie Mitchell, Eldon R. Smith, and John V. Tyberg. Opening the pericardium during pulmonary artery constriction improves cardiac function. J Appl Physiol 96: 917–922, 2004. First published October 24, 2003; 10.1152/japplphysiol.00722.2003.—During acute pulmonary hypertension, both the pericardium and the right ventricle (RV) constrain left ventricular (LV) filling; therefore, pericardiotomy should improve LV function. LV, RV, and pericardial pressures and RV and LV dimensions and LV stroke volume (SV) were measured in six anesthetized dogs. The pericardium was closed, the chest was left open, and the lungs were held away from the heart. Data were collected at baseline, during pulmonary artery constriction (PAC), and after pericardiotomy with PAC maintained. PAC decreased SV by one-half. RV diameter increased, and septum-to-LV free wall diameter and LV area (our index of LV end-diastolic volume) decreased. Compared with during PAC, pericardiotomy increased LV area and SV increased 35%. LV and RV compliance (pressure-dimension relations) and LV contractility (stroke work-LV area relations) were unchanged. Although series interaction accounts for much of the decreased cardiac output during acute pulmonary hypertension, pericardial constraint and leftward septal shift are also important. Pericardiotomy can improve LV function in the absence of other sources of external constraint to LV filling.

PULMONARY HYPERTENSION MAY CAUSE A Substantial decrease in left ventricular (LV) filling, thus reducing LV output by the Frank-Starling mechanism (4, 7–9, 13, 15, 16, 22, 24, 28–30, 34). Decreased right ventricular (RV) output due to increased RV afterload results in decreased LV filling (series interaction) and is clearly a major cause of the decreased cardiac output in acute pulmonary hypertension. However, the increased RV and decreased LV end-diastolic pressures decrease the transseptal pressure gradient; the decreased transseptal gradient causes a leftward septal shift and, together with pericardial constraint (direct ventricular interaction), also contributes to the decreased LV preload and output (7–9). It follows that reduction or removal of external constraint should reduce the negative impact of increased RV afterload. However, the degree to which pericardial constraint and its removal may alter the hemodynamic response to acute pulmonary hypertension remains uncertain (6, 8, 18). Our group (8) previously reported that opening the pericardium with the chest closed in severe experimental acute pulmonary embolism did not result in hemodynamic improvement. Because the chest remained closed in that study, the lack of improvement after the pericardium was opened may have been due to persistent constraint by other mediastinal structures, as suggested by our recent clinical study (10); this suggestion is supported by the fact that the pressure measured by the pericardial balloon transducer in the animal study did not return to zero after the pericardium was opened.

We therefore performed a study of acute pulmonary hypertension in an open-chest, closed-pericardium animal model to assess the effects of opening the pericardium in the absence of other mediastinal sources of constraint to LV filling. Our results are consistent with the concept that decreased RV output is the most important determinant of the hemodynamic response to acute pulmonary hypertension (9). However, we also show that removal of pericardial constraint can improve cardiac function substantially (despite persistent constraint to LV filling by increased RV pressure), therefore highlighting both the importance of pericardial constraint and the potential benefit of removing that constraint in acute pulmonary hypertension.

METHODS

Instrumentation. The protocol was approved by the University of Calgary Animal Care Committee. After premedication with 0.75 mg/kg morphine sulfate intravenously, six mongrel dogs of either sex weighing 20–25 kg were anesthetized, initially with sodium thiopental (10–15 mg/kg intravenously) and then with intravenous fentanyl citrate (50 μg/kg followed by 20–50 μg·kg⁻¹·h⁻¹). The animals were then intubated and ventilated with a 70% nitrous oxide-30% O₂ mixture with a constant-volume respirator (model 607, Harvard Apparatus, Natick, MA). Through a midline sternotomy, the pericardium was opened ventrally with two perpendicular incisions, one along the base of the ventricles at the level of the atroventricular groove and the other along the base-to- apex axis. LV and RV pressures were measured with 8-Fr catheter-tipped transducers with reference lumens (model SPC-485A, Millar Instruments, Houston, TX) inserted through a carotid artery and femoral vein, respectively. Aortic and right atrial pressures were measured with fluid-filled catheters inserted through a femoral artery and jugular vein, respectively. Pericardial pressure was measured over the lateral surface of each ventricle with flat, fluid-filled balloon transducers (6, 7). A cuff constrictor was placed on the proximal pulmonary artery to increase RV afterload, and an ultrasonic flow probe (Transonic Systems, Ithaca, NY) was implanted on the aorta to measure LV stroke volume. Septum-to-LV free wall, LV anteroposterior, and septum-to-RV free wall diameters were measured by sonomicrometry (Sonometrics, London, ON, Canada). The pericardium was closed by reapproximating the edges of the incisions without causing the contents to be tight (27). The chest was maintained widely open with the lungs retracted. A signal from the respirator was used to identify end-expiratory cardiac cycles, and a single lead ECG was recorded.

Conditioned signals (model VR16, PPG Biomedical Systems, Lenexa, KS) were recorded on a personal computer. The analog signals

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Values are means ± SE. Alv, left ventricular (LV) area; LVAP, LV anteroposterior diameter; LVEDP, LV end-diastolic pressure; RVSP, peak right ventricular (RV) systolic pressure; LVSP, peak LV systolic pressure; PAC, pulmonary constriction; PAC + OP, open pericardium during PAC; Pplv and Pprv, pericardial pressure over the LV and RV, respectively; RVEDP, RV end-diastolic pressure; TLVEDP, transmural LVEDP; SLVFW and SRVFW, septum-to-LV and septum-to-RV free wall diameters, respectively; RV, stroke volume; SW, stroke work; TSG, transseptal pressure gradient. *P < 0.05, compared with previous value.

Table 1. Hemodynamic and dimensional changes during PAC and when the pericardium was opened

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>PAC</th>
<th>PAC + OP</th>
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</thead>
<tbody>
<tr>
<td>RVSP (mmHg)</td>
<td>29.4 ± 1.9</td>
<td>58.3 ± 7.6*</td>
<td>53.4 ± 5.3</td>
</tr>
<tr>
<td>LVEDP (mmHg)</td>
<td>8.2 ± 0.3</td>
<td>12.1 ± 1.1*</td>
<td>8.7 ± 0.8*</td>
</tr>
<tr>
<td>TSG (mmHg)</td>
<td>10.3 ± 0.6</td>
<td>7.6 ± 0.9*</td>
<td>4.9 ± 0.6*</td>
</tr>
<tr>
<td>Pplv (mmHg)</td>
<td>2.0 ± 0.4</td>
<td>−4.7 ± 1.1*</td>
<td>−3.7 ± 0.9</td>
</tr>
<tr>
<td>Pprv (mmHg)</td>
<td>8.0 ± 0.6</td>
<td>8.0 ± 0.7*</td>
<td>1.6 ± 0.4*</td>
</tr>
<tr>
<td>TLVEDP (mmHg)</td>
<td>7.0 ± 0.6</td>
<td>9.3 ± 1.0*</td>
<td>2.1 ± 0.7*</td>
</tr>
<tr>
<td>SLVFW (mm)</td>
<td>2.1 ± 0.3</td>
<td>−1.8 ± 0.7*</td>
<td>2.0 ± 0.6*</td>
</tr>
<tr>
<td>SRVFW (mm)</td>
<td>27.2 ± 3.1</td>
<td>32.1 ± 3.1*</td>
<td>33.8 ± 3.3</td>
</tr>
<tr>
<td>LVSP (mmHg)</td>
<td>918 ± 182</td>
<td>918 ± 182</td>
<td>918 ± 182</td>
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<tr>
<td>RVEDP (mmHg)</td>
<td>8.2 ± 0.3</td>
<td>12.1 ± 1.1*</td>
<td>8.7 ± 0.8*</td>
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<tr>
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<td>918 ± 182</td>
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<td>918 ± 182</td>
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Fig. 1. Plots illustrating the hemodynamic and dimensional changes at baseline, during pulmonary artery constriction, and after opening the pericardium while the constriction was maintained. LVAP, left ventricular (LV) anteroposterior diameter; LVEDP, LV end-diastolic pressure; RVSP, peak RV systolic pressure; LVSP, peak LV systolic pressure; PAC, pulmonary constriction; PAC + OP, open pericardium during PAC; Pplv and Pprv, pericardial pressure over the LV and RV, respectively; RVEDP, RV end-diastolic pressure; TLVEDP, transmural LVEDP; SLVFW and SRVFW, septum-to-LV and septum-to-RV free wall diameters, respectively; RV, stroke volume; SW, stroke work; TSG, transseptal pressure gradient. *P < 0.05 compared with previous value.

RESULTS

Hemodynamic changes. Table 1 lists and Fig. 1 depicts the hemodynamic and dimensional changes during pulmonary constriction and when the pericardium was opened. Pulmonary artery constriction doubled peak RV systolic pressure to 58.3 ± 7.6 mmHg and decreased peak LV systolic pressure a mean of 18 mmHg, both significantly. The increase in RVSP (from 8.2 ± 0.3 to 12.1 ± 1.1 mmHg) and the decreases in LVEDP (from 10.3 ± 0.6 to 7.6 ± 0.9 mmHg) and in the transseptal pressure gradient (from 2.0 ± 0.4 to −4.7 ± 1.1 mmHg) were all significant. Pericardial pressure over the RV
increased significantly (from 7.0 ± 0.6 to 9.3 ± 1 mmHg) but was unchanged (8 mmHg) over the LV. Transmural LVEDP decreased significantly (from 2.1 ± 0.3 to −1.8 ± 0.7 mmHg). The septum-to-RV free wall diameter increased by 18%, and the septum-to-LV free wall diameter decreased by 16%, both significantly, whereas the LV anteroposterior diameter remained unchanged. As a result, LV area decreased significantly by 18%. LV stroke volume and stroke work decreased significantly (by 50 and 58%, respectively). When the pericardium was opened widely (without changing the degree of pulmonary artery constriction), the changes in peak RV and LV systolic pressures were not significant, the transseptal pressure gradient remained unchanged, and pericardial pressure over both ventricles decreased significantly to just above zero. However, RVEDP and LVEDP decreased to 8.7 ± 0.8 and 4.9 ± 0.6 mmHg, respectively, transmural LVEDP increased to 2.0 ± 0.6 mmHg, and LV area increased, all significantly. The increase in the septum-to-LV free wall diameter (6%) was significant, and the LV anteroposterior and RV diameters did not change significantly. LV stroke volume and stroke work increased significantly by 35 and 40%, respectively, compared with before pericardiomy.

Figure 2 depicts the pooled-data relations between normalized stroke work and normalized LV area (Fig. 2A, top), transmural LVEDP and normalized (%) LV area (middle), and normalized (%) stroke work and transmural LVEDP (bottom) in all the animals. As can be seen in Fig. 2A, pulmonary artery constriction caused a substantial decrease in LV stroke work and LV area. Pericardiomy improved LV function by improving LV filling (increased LV area), but stroke work remained significantly and substantially reduced compared with baseline because LV filling was still significantly decreased compared with before pulmonary artery constriction (series effect). In Fig. 2A, middle, the conventional calculation for transmural LVEDP was used; in Fig. 2B, middle, we used one-half instead of one-third for the contribution of RVEDP for the calculation of transmural LVEDP to illustrate how a small change in that calculation might alter the LVEDP-LV area relation. As can be seen in both Fig. 2A and Fig. 2B, the transmural LVEDP-LV area relations (using both calculations of transmural pressure) are in keeping with the fact that both are measures of LV preload. The stroke work-transmural LVEDP relation (bottom) was more linear in Fig. 2B than in Fig. 2A, indicating that, from assumptions of ventricular geometry, which may not be accurate in this model, a very small change in the calculation could account for the less precise relation in Fig. 2A. Similarly, the RV diameter-transmural RVEDP relation suggests that RV myocardial compliance did not change (Fig. 3, A); however, the RV stroke work-RV diameter relation (B) suggests that contractility decreased during pulmonary artery constriction and improved after the pericardium was opened.

DISCUSSION

In the present study in which acute pulmonary artery constriction caused substantial hemodynamic deterioration, opening the pericardium in the absence of constraint to ventricular filling by other mediastinal structures quickly resulted in partial hemodynamic improvement (LV stroke volume and stroke work increased by more than one-third compared with before pericardiomy). However, stroke volume and stroke work...
OPENING THE PERICARDIUM

Fig. 3. Transmural RVEDP-RV diameter (A) and RV diameter stroke work-RV diameter (B) relations. SW_{svfw}, RV diameter stroke work; TRVEDP, transmural RVEDP. Values are means ± SE. See Fig. 1 for other abbreviations.

only improved to approximately two-thirds of baseline, which highlights the important contribution of decreased RV output (series interaction) to the response to pulmonary artery constriction. Despite the fact that the RV remained dilated after opening the pericardium, removal of pericardial constraint (but not the constraint due to increased RV diastolic pressure) increased transmural LV end-diastolic pressure (despite the decreased intracavitary pressure) and, consequently, LV end-diastolic volume and stroke volume, which underscores the important contribution of pericardial constraint to decreased LV filling and output. Thus, as shown previously in our laboratory (7–9), when the contribution of pericardial constraint to intracavitary pressure is decreased during acute pulmonary hypertension, transmural pressure may increase despite the decrease in intracavitary pressure. The data suggest that, although decreased RV systolic function accounts for much of the hemodynamic deterioration during acute pulmonary hypertension, constraint to LV filling also plays an important role. Taken together with the results from the acute pulmonary embolism model in which the pericardium was opened while the chest remained closed (8) and our laboratory’s recent study in patients during open-heart surgery (10), the data suggest that, in the absence of an intact pericardium, constraint by other mediastinal structures may limit LV filling substantially.

Ventricular interaction in pulmonary hypertension. As shown previously, acute pulmonary constriction increased RV and decreased LV end-diastolic pressures, which resulted in a decreased transseptal pressure gradient and a leftward septal shift (4, 13, 18, 22, 28, 30, 34). The increased pericardial pressure over the RV and absence of change in pericardial pressure over the LV is consistent with a nonuniform response to increased RV afterload, which our laboratory reported previously (29). As a result of the leftward septal shift and no change in the anteroposterior diameter, LV end-diastolic volume decreased (4, 7, 8, 11, 16, 18, 22, 30, 34), which is consistent with the decreased transmural LVEDP. Although we would anticipate similar responses to similar degrees of acute pulmonary hypertension due to other causes (for example, the pseudoallergic reaction to complement activation (31)), we do not have the data to verify that. The effects of chronic pulmonary hypertension associated with a variety of conditions on ventricular interaction have also been documented previously (1, 3, 14, 21, 26). Thus leftward septal shift may compromise LV filling, but the contribution of pericardial constraint to the decreased LV preload has not been defined. In the absence of heart failure, substantial pericardial constraint seems unlikely because pericardial and right atrial pressure are similar (33). However, if right-sided heart failure is present, this implies increased pericardial pressure because pericardial and RV end-diastolic pressure increase similarly (they may not increase similarly in the presence of RV hypertrophy, however).

The results from the present study support and extend our previous observations in an experimental pulmonary embolism model (7–9). In those experiments, the decreased LV stroke work could be fully explained by the decrease in LV end-diastolic volume (no change in LV contractility). The important new concept was that the decreased cardiac output is partly caused by underfilling of the LV due to increased external constraint (pericardial and septal) and not just due to the series mechanism (decreased RV output). To summarize, volume loading after embolism with the pericardium closed increased constraint to LV filling and decreased transmural LVEDP, LV end-diastolic volume, and stroke work, despite the increased intracavitary LVEDP. Subsequent volume removal caused hemodynamic improvement by increasing transmural LVEDP, LV end-diastolic volume, and stroke work, despite the decreased intracavitary LVEDP. However, with the pericardium open, embolism was better tolerated and subsequent volume loading increased LV filling and improved cardiac function; i.e., RV output could increase further if constraint to LV filling was reduced. Transmural LVEDP- and LV stroke work-end-diastolic volume relations indicated no change in LV myocardial compliance or contractility, indicating that changes in LV preload accounted for the changes in LV performance during embolism and subsequent volume manipulation.

Therefore, although it is the RV that is “stressed” during acute pulmonary hypertension, constraint to LV filling (by the pericardium and increased RV diastolic pressure) plays an important role in the hemodynamic response. Considered together with the results of our laboratory’s recent study (6), which verified that the pericardium may provide substantial constraint to LV filling, removal of that constraint by opening the pericardium during acute pulmonary hypertension should improve LV filling and, therefore, cardiac function. This should be true, provided that the other mediastinal structures do not provide an alternative source of constraint. Therefore, the lack of hemodynamic improvement after the pericardium
was opened in our laboratory’s previous study in the closed-chest animal model of pulmonary embolism may have been due to persistent constraints by other mediastinal structures, as suggested by the observation that pressure in the pericardial balloon did not return to zero after the pericardium was opened (8). This is also in keeping with our laboratory’s demonstration of constraint in patients during open-heart surgery despite the pericardium being left open before sternal closure (10).

LV compliance and contractility. The transmural LVEDP-LV area and LV stroke work-LV area relations and the stroke work-transmural LVEDP relations support our conclusion that LV myocardial compliance and contractility were unchanged. However, the relations with transmural LVEDP were more monotonic when we applied a slightly different algorithm for the contribution by RVEDP to LV constraint; the improved relations with this correction suggest that the surface area of the septum compared with the LV free wall in this model in which the anatomy is grossly distorted by the pulmonary artery constriction and subsequent removal of the pericardium was different from the closed-pericardium models in which the algorithm was validated (6, 25). When the pericardium is closed, the free wall, approximately two-thirds of the LV, is covered by the pericardium and approximately one-third of the LV surface is constrained by RV pressure. Because we did not image the LV in the present study, it is not clear what the relative proportions were after pericardial opening during pulmonary constriction. Our data suggest that the septum may have comprised one-half of the surface under those conditions.

RV compliance and contractility. The transmural RV pressure-RV diameter relation suggests that RV compliance did not change during the interventions (19, 32). However, RV contractility appears to have decreased during pulmonary artery constriction and improved after pericardial opening. We do not have sufficient data to address this apparent change.

Clinical implications. In the present study, we demonstrate a significant contribution of external constraint by the pericardium to decreased LV function during acute pulmonary hypertension. The results explain the lack of benefit from opening the pericardium in our laboratory’s previous study of acute pulmonary embolism (8), and, together with our other work (10), highlight the potential importance of external constraint by the lungs and mediastinum as well as the pericardium. In view of renewed interest in pulmonary embolectomy for severe acute pulmonary embolism (2), it appears reasonable to consider the possibility that pericardiotomy alone might result in some hemodynamic improvement after acute pulmonary embolism. Certainly, the potential benefit of embolectomy and pericardiotomy might be limited by RV dysfunction (23) so that our experimental model might not accurately reflect the pathophysiology in the most severely affected patients. Nevertheless, we have anecdotal experience of dramatic hemodynamic improvement when the pericardium was opened in a patient with acute pulmonary embolism who underwent open-heart surgery to remove a right atrial thrombus. Without ignoring the salutary effects of embolectomy, our results suggest that the pericardiotomy, per se, may provide some benefit as well. In a broader sense, the results improve our understanding of how constraint to LV filling may be clinically important. For example, reduced constraint may contribute to improved hemodynamics when the chest is left open after open-heart surgery (5, 12, 17, 20) when it is difficult to maintain an adequate circulation after closure of the pericardium and chest, particularly in the presence of pulmonary hypertension.

In summary, in our model of acute pulmonary hypertension, in which external constraint to LV filling contributes substantially to the hemodynamic consequences of acute RV pressure loading, we demonstrated the potential benefit from removal of constraint caused by the pericardium. Taken together with previous work, the data suggest that constraint to LV filling by the other mediastinal structures can also reduce LV filling significantly and should be considered, particularly after open-heart surgery when constraint may also be increased by collections of blood or effusions.

GRANTS

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REFERENCES


