Impact of pericardial restraint on right atrial mechanics during acute right ventricular pressure load

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Submitted 28 May 2002; accepted in final form 9 September 2002

Maniar, Hersh S., Sunil M. Prasad, Sydney L. Gaynor, Celeste M. Chu, Paul Steendijk, and Marc R. Moon. Impact of pericardial restraint on right atrial mechanics during acute right ventricular pressure load. Am J Physiol Heart Circ Physiol 284: H350–H357, 2003. First published September 12, 2002; 10.1152/ajpheart.00444.2002.—Optimization of right atrial (RA) mechanics is important for maintaining right ventricular (RV) filling and global cardiac output. However, the impact of pericardial restraint on RA function and the compensatory role of the right atrium to changes in RA function; conductance catheter; pulmonary artery occlusion. Data were collected before and after pericardiotomy. With the pericardium intact and partial PA occlusion, RA elastance increased by 28% (P < 0.04), whereas RA stiffness tended to rise (P = 0.08). However, after pericardiotomy, there was a significant fall in both RA elastance (54%, P < 0.04) and stiffness (39%, P < 0.04), and subsequent PA occlusion failed to induce a change in elastance (P > 0.19) or stiffness (P > 0.84). After pericardiotomy, RA elastance and stiffness fell dramatically, and the compensatory response of the right atrium to elevated RV afterload was lost. The ability of the right atrium to respond to changes in RV hemodynamics is highly dependent on pericardial integrity.

THE RIGHT ATRIUM is a dynamic structure whose role is to promote filling of the right ventricle while minimizing pressure in the venous circulation. Optimization of right atrial (RA) function is important for maintaining right ventricular (RV) filling and global cardiac output during periods of stress. However, the physiological changes that impact RA mechanics, the compensatory role of the right atrium during changes in RV afterload (pulmonary hypertension) (11, 27), and the influence of pericardial restraint on normal RA function remain poorly characterized.

The importance of pericardial restraint has previously been demonstrated for the right and left ventricles and the left atrium (2, 3, 7, 8, 10, 16, 21, 24, 30, 31, 34). The pericardium plays an important role in ventricular interdependence (2, 3, 7, 8, 10, 16, 24, 30, 31, 34), and, with respect to the left atrium, pericardiotomy induces changes in compliance that effect both passive and active ventricular filling (16, 21). Previous investigators have noted that atrial compliance can substantially influence cardiac performance (20, 21, 23, 37, 39), and, whereas these studies have focused on the left atrium, the concepts are of great interest and may be applicable to the anatomically distinct right heart. In a computer model, Suga (37) found that increased left atrial compliance markedly improved cardiac performance and concluded that a “flexible atrium” would substantially improve the output of the heart. Others have predicted that early ventricular filling increases directly with atrial compliance (39); however, data are insufficient from intact subjects to support these theories.

Historically, the right atrium has been difficult to study because of its amorphous architecture and the complex interplay that occurs among the atrium, ventricle, and systemic and coronary venous circulation. In the current study, using conductance technology to provide instantaneous assessment of RA volume (9, 12, 18, 29), the systolic and diastolic pressure-volume (P-V) relations of the right atrium were quantified at rest and during increased RV afterload with the pericardium closed and open. It was hypothesized that the pericardium plays a crucial role in modulating RA mechanics and that elimination of pericardial restraint would have a significant impact on the compensatory response of the right atrium to increased RV afterload.

MATERIALS AND METHODS

Surgical Preparations

Eight healthy sheep of either sex (25–30 kg body wt) were premedicated with ketamine hydrochloride (27 mg/kg im), anesthetized with pentothal sodium (6.8 mg/kg iv), intubated, and ventilated (Siemens; Munich, Germany) with supplemental inhalational isoflurane (1.5–3%). Pulse oximetry, continuous ECG, and arterial blood gases were monitored.

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Throughout the experiment. Supplemental oxygen and sodium bicarbonate were administered as necessary to maintain a normal acid-base balance and arterial blood oxygen tension between 100 and 200 mmHg, and a table warmer was used to ensure normothermia. Micromanometer-tipped pressure catheters (Millar Instruments; Houston, TX) were zeroed in a 37°C water bath for 30 min before insertion. A 7-Fr pressure catheter (Millar MPC-500) was advanced through the left carotid artery to the ascending aorta to record central aortic pressure. A median sternotomy was performed, leaving the pericardium intact. Ultrasonic flow probes (10- to 12-mm perivascular probes with a T206 flowmeter, Transonic Systems; Ithaca, NY) were placed around the superior (SVC) and inferior vena cava (IVC) −1 cm from the caval-atrial junction to measure RA inflow. A tourniquet was positioned around the distal main pulmonary artery (PA) to permit acute RV afterload manipulation via partial PA occlusion. Tourniquets were also positioned around the SVC and IVC to allow transient vena caval occlusion (preload alteration). A 1-cm incision was made in the pericardium over the anterior RV free wall, and a 7-Fr pressure catheter (Miller MPC-500) was positioned in the mid-RV cavity to record RV pressure (RVP). A second 1-cm incision was made over the atrioventricular groove to place a vascular loop around the coronary sinus so that it could be temporarily occluded during periods of data collection to prevent coronary venous return. A third 1-cm incision was made in the pericardium over the RA appendage, and a 6-Fr combined P-V conductance catheter (Millar SPR-766) was positioned along the long axis of the atrium so that its tip rested at the RA-IVC junction (Fig. 1). This catheter position has previously been shown to accurately reflect changes in RA volume; the catheter tip position was verified by manual palpation before data acquisition (29). A micromanometer −2 cm from the distal end of the catheter allowed simultaneous measurement of RA pressure (RAP).

The combined P-V conductance catheter was custom designed with 12 equally spaced (4 mm) electrodes and dual-field conductance technology. We found this spacing to be most appropriate for the right atrium, as opposed to conventional catheters designed for the ventricular chambers. The conductance-pressure catheter was connected to a signal processor and conditioner (Sigma 5DF, CD Leycom/Cardiodynamics; Zoetermeer, The Netherlands) to determine RA chamber conductance and, thereby, measure instantaneous relative RA volume. Total RA volume was divided into four to five segmental volumes as shown in Fig. 1; the most proximal segment was excluded if the electrodes did not all reside within the RA cavity. To further ensure volume sampling accurately reflected changes in atrial (versus caval) volume, each volume segment was individually assessed for its synchronization and phase relationship to the other atrial segments. Segmental conductance signals (G) were combined to yield the total volume (V) as follows

\[ V(t) = \frac{1}{\alpha} L^2 \cdot \rho \cdot \sum_{i=1}^{5} G(t) - G_i \]

where \( L \) is the interelectrode distance, \( t \) is time, \( \rho \) is blood resistivity, \( \alpha \) is the conductance gain factor, \( i \) is the segment number, and \( G_i \) is the parallel conductance constant (36). The boundaries of the atrium (extending from the IVC and SVC) were defined by the relative changes in conductance that occur at the atrial wall. This methodology is potentially better suited than alternative techniques for ensuring adequate sampling of the geometrically complex atrial chamber. As described by previous authors, relative RA volume was determined assuming that parallel conductance was zero (9). In five animals, changes in conductance-derived RA volume were correlated with changes in flow-derived RA volume. Conductance-derived changes in RA volume were determined during RA filling, from the time of minimum RA volume to the time of tricuspid valve opening (time of maximum RA volume). Simultaneously, RA inflow was also calculated during RA filling by integrating and adding SVC and IVC flow. During this time period, the tricuspid valve is closed, allowing direct comparison of RA inflow to the change in RA chamber volume. Note that during these measurements coronary venous inflow into the RA was suspended by temporary occlusion of the coronary sinus. In all five animals, conductance-derived changes in RA volume correlated in a highly linear fashion with flow-derived changes (\( r^2 = 0.94 \)).

**Experimental Protocol**

To evaluate the effects of the pericardium on RA function, baseline data were initially recorded with the pericardium...
intact. Partial PA occlusion was then performed to produce approximately a 50% rise in maximum RVP. Data were obtained during this period of increased RV afterload. The PA tourniquet was subsequently released, and the RVP was allowed to return to its baseline level. In seven of eight animals, a pericardiectomy was then performed, and baseline data were recorded with the pericardium open. Partial PA occlusion was again performed to produce a 50% rise in maximum RVP, and data were recorded during increased RV afterload in the open pericardium setting.

At the conclusion of the experiment, the animals were euthanized using pentothal sodium (1 g iv) followed (after 2 min) by potassium chloride (80 meq iv), and proper positioning of the catheters was confirmed. All animals received humane care in compliance with the “Principles of Laboratory Animal Care” formulated by the National Society for Medical Research and the National Institutes of Health Guide for the Care and Use of Laboratory Animals. The study was approved by the Washington University School of Medicine Animal Studies Committee and conducted according to Washington University policy.

Data Acquisition

During each data acquisition run, ECG, RAP, RVP, aortic pressure, SVC flow, IVC flow, and RA conductance signals were acquired and processed using a 16-channel analog-to-digital converter board and recorded using a dedicated Pentium III computer system with custom-designed software (Conduct-PC, CD Leycom/Cardiodynamics). Data were recorded at a sample frequency of 200 Hz. To minimize the effects of intrathoracic pressure variation, the respirator was temporarily interrupted at end-expiration during data collection for 10–15 s. After steady-state data were obtained (3–5 beats), slow, progressive bivacal occlusion was performed to generate RA P-V loops over a wide physiological range of filling pressures. Data acquisition runs were repeated in triplicate, and all runs containing premature ventricular contractions were excluded from subsequent off-line analysis. Sufficient time was allowed between runs for hemodynamic stabilization (3–5 min).

Data Analysis

RA stiffness. Static RA diastolic stiffness (i.e., 1/compliance) was defined as the slope of the “atrial end-diastolic” P-V relation (Fig. 2). Atrial end-diastolic pressure (RAPA,ED) and volume (RAV,ED) points were determined at the time of maximum RA volume (corresponding to tricuspid valve opening and the RAP V wave) for each cardiac cycle during preload reduction (slow vena caval clamping). By least-squares linear regression, a straight line was fitted to the following equation (32)

\[
\text{RAP}_{A,ED} = \text{RA stiffness} \cdot (\text{RAV}_{A,ED} - V_0)
\]

where RA stiffness (in mmHg/ml) and \(V_0\) (in ml) are the slope and volume-axis intercept, respectively.

RA elastance (contractility). RA contractile performance (Fig. 2) was assessed using the atrial end-systolic P-V relationship (chamber elastance) (1, 22). Atrial end-systolic pressure (RAPA,ES) and volume (RAV,ES) points were determined for each cardiac cycle during preload reduction, and, by least-squares linear regression, a straight line was fitted to the following equation

\[
\text{RAP}_{A,ES} = E_{A,ES} \cdot (\text{RAV}_{A,ES} - V_0)
\]

where \(E_{A,ES}\) (in mmHg/ml) and \(V_0\) (in ml) are the slope (RA chamber elastance) and volume-axis intercept, respectively.

RESULTS

Figure 3 illustrates typical RA P-V loops taken from one animal at baseline and during partial PA occlusion with the pericardium intact. For all eight animals, the RA P-V loop was a figure-eight. Atrial diastole (filling) occurred from point A to point B and was followed by passive RA emptying (point B to point C). Atrial contraction (point C) initiated RA systole and the “atrial kick,” closing the loop at point A. During partial PA occlusion and after pericardiectomy, the P-V loop remained a figure-eight.

Table 1 summarizes the hemodynamic data during all interventions. There was no significant change in heart rate \((P > 0.47)\) or mean aortic pressure \((P > 0.76)\) with partial PA occlusion or after pericardiectomy. RV end-diastolic pressure \((P > 0.15)\), mean RAP \((P > 0.10)\), and maximum \((P > 0.56)\) and minimum \((P > 0.36)\) RA volume similarly did not change with partial PA occlusion or after pericardiectomy.

Pericardium Intact

Figure 4 illustrates the hemodynamic response of one animal (same animal as depicted in Fig. 3) to acute...
Partial PA occlusion with the pericardium intact. For all animals, with partial PA occlusion, maximum RVP increased by 43% (P < 0.004; Table 1). In response to the acute rise in RV afterload, RA elastance and stiffness both increased (Table 2). The effects of partial PA occlusion on a typical sequence of P-V loops obtained during progressive inflow occlusion with the pericardium intact (same animal as in Fig. 2) are illustrated in Fig. 5A. For all animals, the 28% rise in RA elastance from 0.18 ± 0.10 to 0.24 ± 0.16 mmHg/ml was statistically significant (P < 0.04; Table 2). With partial PA occlusion, atrial end-systolic V₀ did not change (P > 0.48), but atrial end-diastolic V₀ increased (P < 0.04). The mean correlation coefficients for elastance and stiffness within the intact pericardium were 0.94 ± 0.04 and 0.95 ± 0.04, respectively.

Pericardium Open
Standard hemodynamics did not change in the baseline state when the pericardium was open (P > 0.15 for all; Table 1); however, there was a significant fall in both RA elastance and RA chamber stiffness (Table 2).

Table 1. Hemodynamic effects of acute partial/PA occlusion before and after pericardectomy

<table>
<thead>
<tr>
<th></th>
<th>Pericardium Closed</th>
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<th>Pericardium Open</th>
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<tbody>
<tr>
<td></td>
<td>Baseline</td>
<td>PA occlusion</td>
<td>Baseline</td>
<td>PA occlusion</td>
</tr>
<tr>
<td>Heart rate, beats/min</td>
<td>109 ± 14</td>
<td>99 ± 16</td>
<td>115 ± 17</td>
<td>104 ± 13</td>
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<tr>
<td>Mean aortic pressure, mmHg</td>
<td>48 ± 10</td>
<td>45 ± 13</td>
<td>45 ± 16</td>
<td>44 ± 11</td>
</tr>
<tr>
<td>Maximum RVP, mmHg</td>
<td>26 ± 6</td>
<td>37 ± 11*</td>
<td>23 ± 3</td>
<td>33 ± 12*</td>
</tr>
<tr>
<td>End-diastolic RVP, mmHg</td>
<td>6 ± 3</td>
<td>6 ± 3</td>
<td>5 ± 2</td>
<td>5 ± 3</td>
</tr>
<tr>
<td>Mean RA pressure, mmHg</td>
<td>4 ± 2</td>
<td>5 ± 2</td>
<td>4 ± 2</td>
<td>4 ± 1</td>
</tr>
<tr>
<td>Maximum RA volume, ml</td>
<td>44 ± 10</td>
<td>49 ± 12</td>
<td>49 ± 9</td>
<td>54 ± 10</td>
</tr>
<tr>
<td>Minimum RA volume, ml</td>
<td>38 ± 9</td>
<td>40 ± 9</td>
<td>41 ± 6</td>
<td>46 ± 7</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 8 for pericardium closed and 7 for pericardium open. PA, pulmonary artery; RVP, right ventricular pressure; RA, right atrial. *P < 0.05 for PA occlusion vs. baseline; P > 0.15 for all pericardium open vs. closed. Repeated-measures ANOVA was used for all comparisons.
and Fig. 5B). In the baseline state, RA elastance fell by 54% from 0.18 ± 0.10 mmHg/ml with the pericardium intact to 0.09 ± 0.03 mmHg/ml with the pericardium open (P < 0.04). Similarly, RA stiffness fell by 39% from 0.11 ± 0.06 mmHg/ml with the pericardium intact to 0.07 ± 0.04 mmHg/ml with the pericardium open (P < 0.04). \( V_0 \) for both the atrial end-systolic and atrial end-diastolic relations also decreased significantly (P < 0.05 for both).

With the pericardium open, partial PA occlusion produced a 40% rise in maximum RVP (P < 0.03) compared with the baseline state (Table 1). However, in contrast to what occurred when the pericardium was intact, PA occlusion no longer induced any changes in RA elastance or RA chamber stiffness (Table 2 and Fig. 5C). Without pericardial restraint, RA elastance was 0.09 ± 0.03 mmHg/ml at baseline and 0.10 ± 0.01 mmHg/ml with PA occlusion (P > 0.19). Similarly, RA stiffness was 0.07 ± 0.04 mmHg/ml at baseline and 0.08 ± 0.02 mmHg/ml with PA occlusion (P > 0.84). In addition, with the pericardium open, partial PA occlusion had no effect on the atrial end-systolic \( V_0 \) (P > 0.56) or atrial end-diastolic \( V_0 \) (P > 0.11). The mean correlation coefficients for elastance and stiffness within the open pericardium were 0.97 ± 0.03 and 0.94 ± 0.07, respectively.

**DISCUSSION**

Previous studies have suggested that the pericardium tends to equalize pressure evenly among the four cardiac chambers (28, 38). The right atrium and ventricle, as thin-walled chambers, have relatively limited intrinsic stiffness and are, therefore, more likely to be dependent on pericardial influence than their counterparts on the left side of the heart. The current findings show that the impact of the pericardium on RA mechanics is substantial. With the pericardium intact, when RV afterload increased acutely consequent to partial PA occlusion, RA elastance increased by 28% (P < 0.04) and RA stiffness tended to rise (P = 0.08). The increase in chamber stiffness, typically considered a maladaptive response with respect to ventricular function, may be an adaptive response for the right atrium. The mechanisms responsible for increased RA elastance and stiffness with PA occlusion are unclear but may involve similar homeometric, neurohumoral responses as have been suggested for the right ventricle in response to similar changes in afterload (11).

Serving multiple functions during the cardiac cycle, the right atrium acts as a reservoir during atrial filling (storing blood when the tricuspid valve is closed) and then as both a conduit (passive blood transfer from the cava to the ventricle) and pump (atrial contraction) when the valve is open (14, 17, 33). The tendency for RA chamber stiffness to increase suggests that the right atrium acts more as a conduit than a reservoir during acute pulmonary hypertension to improve RV filling. These findings are consistent with those of Hoit and Gobel (18), who found that increased left atrial stiffness helped maintain left ventricular preload in a model of left atrial failure. We hypothesize that by optimizing the balance between reservoir and conduit function, the right atrium can maximize RV filling to maintain RV preload and pari passu right heart output in times of stress. The impact of changes in RA chamber stiffness and elastance on the composite functions of the right atrium (reservoir, conduit, and pump) remains unknown and will require further study.

With pericardiectomy, RA elastance fell by 54% and RA chamber stiffness fell by 39%, presumably due to the loss of direct restraint from the pericardium. For the left atrium, Hoit and colleagues (21) similarly demonstrated a fall in left atrial stiffness with loss of pericardial restraint, even at physiological pressures. The significance of pericardial restraint demonstrated in this study is particularly noteworthy as it occurred even in the setting of low overall atrial pressures. The impact of pericardial restraint would have likely been greater at higher RA pressures. This inability to account for pericardial restraint is perhaps a potential confounder of previous studies of atrial mechanics that were performed in open pericardial settings, with higher atrial pressures, and presumably larger, abnormally distended atria (20, 29).

A significant finding of this current study was the loss of the compensatory atrial response to acute elevation in RV afterload after the pericardium was opened. Chamber stiffness and elastance of the right atrium no longer increased with partial PA occlusion, as they had when the pericardium was intact, possibly as the result of the loss of coupling with the surrounding cardiac chambers. Mechanical interactions between the left and right ventricles and between the left and right atria are significantly enhanced with an intact pericardium (7, 21, 24, 28, 30, 34). In addition, the vertical, in-series interaction between the cham-
bers on each side of the heart (atrioventricular coupling) has an impact on atrial filling and emptying properties (4, 28). While there are some data to suggest that an intact pericardium is beneficial during acute RV failure, the importance of pericardial restraint on preserving RA function has not previously been well characterized (6, 8). These current data suggest that the pericardium modulates the compensatory response of the right atrium to changes in RV afterload.

Potential Limitations

Although RA conductance volume was not corrected for parallel conductance (resistance to current due to surrounding tissues) (36), the analytic methods employed in this study were not dependent on absolute volume measurements and were consistent with previous studies involving the right atrium (9, 12, 29). Relative conductance-derived volume changes correlated highly to relative volume changes calculated with caval flow analysis. Second, the slope of the end-systolic and end-diastolic P-V relations were fitted to a straight line, and, whereas linear fitting of the behavior of the P-V loop may not be accurate over a large range of volumes and pressures, the goal of this study was to address changes within a physiological range, where differences between linear and exponential fitting are negligible (25, 32, 35). Furthermore, for the left atrium, these indexes have shown sensitivity and accuracy in assessing atrial function during load manipulation and inotropic stimulation in a relatively load-independent manner (1, 22). Similarly, although pericardial pressures were not measured in this study, we suspect that the use of transmural pressures (subtracting pericardial pressure from intracavitary pressure) for P-V loop analysis would have demonstrated similar results. In the closed pericardium setting, subtracting pericardial pressure would vertically shift the P-V loop downward and should produce a substantial change in shape because the pericardium bears a variable amount of the total stress (interatrial pressure) throughout the cardiac cycle (16). Presumably, however, the shape of this transmural P-V loop would have a similar end-diastolic stiffness to a transmural P-V loop obtained with the pericardium open. In addition, whereas regional differences likely exist, pericardial constraint was considered to be uniform throughout the atrium and ventricle for simplicity (19). Finally, although the techniques reported herein incorporated the effects of an intact pericardium attempting to mimic the natural in vivo state, data obtained from an open-chest anesthetized animal surely differ to some degree from the closed-chest, human clinical setting.

In summary, this study demonstrated that the right atrium can produce a significant compensatory response to increased RV afterload, presumably to maintain RV preload and right heart output. However, baseline RA mechanics and the ability of the right atrium to respond to changes in RV hemodynamics are intimately dependent on pericardial integrity. Pericar-

![Fig. 5. Typical sequence of RA P-V loops in the following conditions: with the pericardium intact during partial PA occlusion (A), with the pericardium open during the baseline state (B), and with the pericardium open and partial PA occlusion (C). In this animal (same as depicted in previous figures), there was a substantial increase in RA stiffness (decrease in compliance) with partial PA occlusion (0.15 mmHg/ml). RA elastance also rose to 0.25 mmHg/ml with the acute rise in RV afterload. However, with the pericardium open, RA stiffness and RA elastance both fell (0.07 and 0.11 mmHg/ml) and remained low with partial PA occlusion (0.06 and 0.07 mmHg/ml).]
drial restraint is critical to maximize the RA compensatory response to physiological stress. In addition, the current investigation supports the use of load-indepen-dent indices for the evaluation of RA mechanics. These variables have the potential to enhance our knowledge of RA systolic and diastolic function and improve our understanding of RA mechanics in health and disease. While this study examined only subjects with acute pulmonary hypertension, we anticipate that subjects exposed to chronic pulmonary hypertension may be even more dependent on pericardial integrity, because RA function likely plays an increased role in maintain-ing RV output when the ventricle begins to fail (13, 15, 18). Further experimentation employing these tech-niques will be essential to elucidate the pathophysi-ology of acute and chronic diseases that intimately affect the right side of the heart.

The authors gratefully acknowledge Martha L. Lester for assistance with the surgical preparations as well as the technical assistance of Diane Toensinketter, Kathy Fore, and Dennis Gordon. This study was supported by National Heart, Lung, and Blood Institute NHLBI Grant HL-69949 and by a Foundation Research Grant from the Thoracic Surgery Foundation for Research and Education. H. S. Maniar was also supported in part by NHLBI Grant HL-69949 and by a Foundation Research Grant from the Thoracic Surgery Foundation for Research and Education. H. S. Maniar was also supported in part by NHLBI Grant T32-HL-07776.

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