LABORATORY INVESTIGATION
CARDIAC TAMPOONADE

The shift in the relationship between intrapericardial fluid pressure and volume induced by acute left ventricular pressure overload during cardiac tamponade

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ABSTRACT  We hypothesized that a process leading to an acute increase in cardiac size would change the relationship between intrapericardial pressure and fluid volume during cardiac tamponade, resulting in a change in the time of onset of right ventricular diastolic collapse (RVDC) as seen on the two-dimensional echocardiogram. Five spontaneously breathing dogs were instrumented to measure ascending aortic and right atrial blood pressures and intrapericardial pressure (IPP). A hydraulic occluder was placed around the proximal descending thoracic aorta. Each animal underwent six consecutive episodes of cardiac tamponade, three in the presence alternating with three in the absence of aortic constriction. The onset of RVDC was recorded and the volume infused into the pericardial space was measured. In the presence of aortic constriction, the relationship between pericardial pressure and incremental pericardial fluid volume was shifted so that IPP was an average of 3.4 mm Hg higher at any given intrapericardial fluid volume (p < .001). At the onset of RVDC, the mean IPP was higher and the intrapericardial fluid volume was lower during aortic constriction than under control conditions (p < .001 for both comparisons). Thus, a rapid increase in left ventricular volume in the presence of an otherwise unimportant pericardial effusion may increase intrapericardial fluid pressure sufficiently to cause RVDC.


THE ACCUMULATION of a pericardial effusion under pressure results in compression of the cardiac chambers, ultimately resulting in impairment of right ventricular filling and hemodynamic deterioration. Although cardiac tamponade is a continuous hemodynamic spectrum ranging from an insignificant pericardial effusion to severe cardiac compression with circulatory collapse, some discrete events can be delineated. Early in the progression as intrapericardial pressure exceeds right atrial blood pressure during atrial diastole, there is invagination of the right atrial free wall seen on the two-dimensional echocardiogram. Later, when intrapericardial pressure exceeds right ventricular diastolic blood pressure, one can see collapse of the right ventricular free wall. Right ventricular collapse has been extensively studied and its onset in a given animal with a constant intravascular volume occurs at a predictable intrapericardial pressure and fluid volume.

In patients, diastolic collapse of the right ventricular free wall has proven to be a very sensitive and specific sign of cardiac tamponade. However, the echocardiographic observation of right ventricular diastolic collapse (RVDC) in a patient at our institution who had acute left ventricular failure but only a moderate pericardial effusion led us to ask if RVDC could be produced by an event that abruptly increased cardiac size in the presence of an otherwise insignificant pericardial effusion.

Left ventricular afterload is known to affect ventricular performance. An acute increase in left ventricular afterload induced by an aortic occluder or balloon, or phenylephrine, 15, 16 or angiotensin 17, 18 has been associated with an immediate increase in left ventricular end-diastolic pressure and in some studies with

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an increase in left ventricular chamber size. In situations of acute cardiac dilatation, the pericardium influences the ventricular pressure-dimension relationship, limiting further chamber enlargement. This restricting effect is seen during acute volume loading in canine preparations, but it is not seen in chronic volume overload states because of pericardial hypertrophy.

Several investigators have demonstrated that distention of either ventricle during diastole alters the compliance and geometry of the opposite ventricle. More specifically, an increase in left ventricular volume has been associated with an increased right ventricular end-diastolic pressure. This interdependence is mediated in part by the intact pericardium. Berglund et al. have described an apparent decrease in right ventricular function induced by acute left ventricular pressure overload caused by aortic constriction in an acute canine preparation. When the pericardium was removed, they found only a minor change in the right ventricular function curves during abrupt left ventricular pressure overload. They concluded that this apparent decrease in right ventricular function was caused by a decline in right ventricular filling mediated by pericardial constraint.

In cardiac tamponade, a pericardial effusion under pressure results in a reduction in the end-diastolic and end-systolic chamber sizes of both the left and right ventricles. Acute cardiac enlargement would increase the fraction of total intrapericardial volume occupied by the heart and thus result in a decrease in the intrapericardial fluid volume needed to cause cardiac tamponade. Since RVDC occurs when intrapericardial pressure exceeds right ventricular pressure, the intrapericardial pressure required to cause right ventricular collapse may actually increase due to an elevation in right ventricular diastolic pressure resulting from left ventricular enlargement. In this study we tested the hypothesis that rapid enlargement of the left ventricle alters the intrapericardial fluid pressure-volume relationship and results in the onset of RVDC at both a smaller accumulated pericardial effusion and a larger increase in intrapericardial pressure during cardiac tamponade. Thus, a process causing an acute increase in left ventricular end-diastolic pressure and volume in the presence of an otherwise modest pericardial effusion may result in a positive echocardiographic identification of cardiac tamponade. In such a situation diagnosis and treatment of the process causing left ventricular chamber enlargement (if reversible), rather than pericardiocentesis, would be the appropriate course.

**Methods**

Five mongrel dogs weighing from 22 to 27 kg were brought to the laboratory, anesthetized (30 mg/kg sodium pentobarbital intravenously to effect), intubated, and ventilated by a volume respirator (Harvard Apparatus Company) using air enriched with oxygen (2 to 5 liters/min). Arterial blood gases were periodically monitored and adjusted to ensure satisfactory oxygenation and acid-base balance. A left thoracotomy in the fifth intercostal space was performed and Tygon fluid-filled catheters (0.050 inch inner diameter × 0.090 inch outer diameter) were placed in the right atrium and ascending aorta as previously described. A third Tygon fluid-filled catheter was placed in the distal descending thoracic aorta through the left femoral artery.

A 3 to 4 cm longitudinal incision was made in the pericardium overlying the left anterior descending coronary artery and two fenestrated Tygon catheters were positioned in the pericardial space and secured with purse-string sutures. The tip of one catheter was adjacent to the left ventricular free wall and the other was near the diaphragmatic surface of the left ventricle. A flat, liquid-containing balloon attached to a fluid-filled catheter was positioned overlying the left ventricular free wall. This device was identical to those used by Smiseth et al. and was calibrated according to their technique. The use of this device for the measurement of intrapericardial pressure has been described in detail elsewhere. The pericardium was carefully closed with a continuous locking suture and a watertight seal was verified. A hydraulic occluder was placed around the proximal descending thoracic aorta between the two aortic fluid-filled catheters. Catheters from the hydraulic occluder and flat balloon were passed individually through the chest wall and tunnelled subcutaneously to the back. The ribs were approximated, a chest tube was placed, the wound was closed in layers to provide an airtight seal, and all air was removed from the chest.

It has been demonstrated that surface pressure plays an important role in the measurement of intrapericardial pressure at intrapericardial volumes of less than 30 ml. Pressures in that volume range are best measured with a flat balloon catheter and either method may be used at higher volumes. Although our hypothesis in this study was tested at volumes exceeding 30 ml, intrapericardial pressure was simultaneously measured with both open and flat balloon catheters to gain experience with the flat balloon device and to determine if we could corroborate the results presented by Smiseth et al.

When spontaneous respiration was adequate, the lightly anesthetized animal was removed from the ventilator, placed upright in a sling, and allowed to breath air enriched with oxygen (3 liters/min). One pericardial, the aortic, right atrial, and the flat pericardial balloon catheters were attached directly to Statham P23Db pressure transducers (Statham Instrument Company) with the zero-pressure reference point taken as one-third of the distance between the sternum and the spine. The electrocardiogram was continuously monitored.

Baseline data were recorded after the pleural and pericardial cavities were drained, the mean right atrial blood pressure was adjusted to between 0 and 4 mm Hg by intravenous infusion of normal saline, and a hemodynamic steady state had been achieved. Cardiac tamponade was induced by the continuous infusion of warmed normal saline into the pericardial space at a rate of 30 ml/min with a Masterflex infusion pump (Cole Parmer Instrument Company). Infusion began with the pericardium empty and continued until 2 min beyond the onset of RVDC. Each animal underwent three control episodes of cardiac tamponade alternating with three episodes of cardiac tamponade in the presence of acute proximal descending thoracic aortic constriction. Manually constricting the aorta with the balloon occluder increased proximal aortic blood pressure by 30 to 40 mm
TABLE 1
Hemodynamic data (mean ± SD) with the descending thoracic aorta constricted (inflated occluder) or unconstricted (deflated occluder) at baseline (empty pericardium) and during cardiac tamponade (2 min after the onset of RVDC)

<table>
<thead>
<tr>
<th>Hemodynamic measurement</th>
<th>Baseline</th>
<th>Cardiac tamponade</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Occluder deflated</td>
<td>p value</td>
</tr>
<tr>
<td>Aortic blood pressure (mm Hg)</td>
<td>150.2±13.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Right atrial blood pressure (mm Hg)</td>
<td>2.0±1.0</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intrapericardial pressure (mm Hg; open catheter)</td>
<td>-2.0±1.5</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intrapericardial pressure (mm Hg; flat balloon catheter)</td>
<td>1.2±1.3</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>

Hg. This stable elevation in mean aortic blood pressure was present for 40 to 120 sec before infusion, and the degree of constriction was maintained unchanged throughout intrapericardial infusion of saline. Hemodynamic data were continuously recorded with use of an FM tape recorder (A. R. Vetter Company) and a Gould strip-chart recorder (Model No. 2800, Gould, Inc.). Short-axis two-dimensional echocardiograms were obtained with a hand-held transducer in the right fourth or fifth intercostal space with an Irex HSP-1 phased-array ultrasonoscope (Johnson and Johnson). The echocardiograms were viewed by two observers in real time and right ventricular collapse was considered to be present if there was indentation or abnormal inward motion of the right ventricular free wall during diastole. After cessation of infusion, steady-state hemodynamic data were recorded before the fluid was manually removed.

When cardiac tamponade was induced during aortic constriction, a steady state before and after occluder release was obtained before draining the pericardial space. At the completion of six episodes of cardiac tamponade, all transducers were recalibrated and the animal was killed.

All data were transferred to a digital computer (DEC LSI 11/23). Mean hemodynamic data were acquired for each 20 sec interval and the volume infused into the pericardium to that point was determined. The volume infused was calculated by multiplying the time to the midpoint of the 20 sec file by the infusion rate of the pump. A 20 sec file length was chosen so that several complete respiratory cycles were recorded, thereby obviating any error caused by sampling a subset of a single cycle. The point of onset of RVDC was noted and a final file for statistical analysis was created.

For the purpose of statistical analysis, data recorded during each control intrapericardial infusion were paired with data recorded during the aortic constriction run that immediately followed it. A two-factor repeated-measures analysis of covariance was used to evaluate the effect of constriction on the relationship between intrapericardial pressure and percent of control volume infused while adjusting for dog.36 Since each dog underwent studies in both the constricted and unconstricted states, a test for interaction between intrapericardial pressure and percent constriction was used to test whether or not the curves were parallel.36 Comparisons between occluder-inflated (constriction) and deflated (control) conditions (tables 1 and 2) were made with a two-factor repeated-measures analysis of variance. The Waller-Duncan multiple comparisons procedure was used to compare aortic constriction and control at baseline, RVDC, and steady-state cardiac tamponade.37

Results

Thirteen paired episodes of cardiac tamponade with and without aortic constriction were analyzed in five dogs. Two paired episodes had to be excluded when ventricular ectopy during aortic constriction made data analysis unreliable. Table 1 illustrates the effects of acute constriction of the descending thoracic aorta at baseline (empty pericardium) and of rapid release of aortic constriction in the presence of a steady-state pericardial effusion (2 min after the onset of RVDC). Predictably, aortic constriction resulted in an increase of mean aortic blood pressure of 33 mm Hg, while rapid release of constriction in the presence of a pericardial effusion reduced mean aortic blood pressure by 45 mm Hg. Aortic constriction at baseline raised the mean right atrial blood pressure by 3.0 mm Hg compared with normal (p < .001) and raised the mean intrapericardial pressure by 2.2 mm Hg (2.8 mm Hg with flat balloon catheter) compared with normal (p <

TABLE 2
Hemodynamic data (mean ± SD) at the point of onset of RVDC during episodes of cardiac tamponade in the presence and absence (control) of acute constriction of the descending thoracic aorta

<table>
<thead>
<tr>
<th>Hemodynamic measurement</th>
<th>Control</th>
<th>Aortic constriction</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Aortic blood pressure (mm Hg)</td>
<td>142.2±20.9</td>
<td>178.2±19.8</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Right atrial blood pressure (mm Hg)</td>
<td>6.3±2.3</td>
<td>7.9±1.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intrapericardial pressure (mm Hg; open catheter)</td>
<td>5.7±2.3</td>
<td>7.1±1.7</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Intrapericardial pressure (mm Hg; flat balloon catheter)</td>
<td>5.4±2.3</td>
<td>7.5±1.4</td>
<td>&lt;.001</td>
</tr>
<tr>
<td>Volume infused (%)</td>
<td>60.2±10.0</td>
<td>44.9±9.8</td>
<td>&lt;.001</td>
</tr>
</tbody>
</table>
Table 2 compares the mean hemodynamic variables at the point of onset of RVDC in the presence and absence of descending thoracic aortic constriction during cardiac tamponade. RVDC occurred at a higher mean right atrial blood pressure during aortic constriction than in its absence (p < .001). Moreover, the mean intrapericardial pressure at the onset of RVDC was higher with acute left ventricular pressure overload than without it (p < .001), and the percent of total control volume infused into the pericardial space at the point of onset of RVDC was lower in the presence of aortic constriction than in its absence (p < .001).

Figure 2 displays the relationship between intrapericardial pressure and volume infused into the pericardial space during cardiac tamponade in a representative animal. Data collected during the three episodes of cardiac tamponade in the presence of aortic constriction were tightly grouped, as were those from episodes without constriction. In this animal, aortic constriction shifted the curve by an amount equal to approximately 3.5 mm Hg of intrapericardial pressure or 40 ml of intrapericardial fluid volume.

Figure 3 illustrates the pooled data for all episodes of cardiac tamponade in the five animals in the absence (control) and in the presence of descending thoracic aortic constriction. Each episode of cardiac tamponade without aortic constriction has been paired with the
FIGURE 2. The relationship between the intrapericardial pressure measured with an open catheter and the total volume infused into the pericardial space in a representative animal during three episodes of cardiac tamponade in the presence of aortic constriction and three episodes in its absence (control).

FIGURE 3. The relationship between intrapericardial pressure (open catheter) and the volume infused into the pericardial space during all episodes of cardiac tamponade in the presence of aortic constriction and in its absence (control) for all animals. Each infusion during aortic constriction has been paired with the infusion without aortic constriction that immediately preceded it. All volumes are expressed as a percent of the total volume infused during each control intrapericardial infusion. All related mean values are connected and standard deviations are shown. The curves are different (p < .001) but have the same slopes. The point of onset of RVDC under each condition is indicated by an arrow and occurs at significantly different intrapericardial pressures (p < .001) and volumes (p < .001).
episode during aortic constriction that immediately followed it. The volume infused for each episode of cardiac tamponade has been adjusted to the percent of total volume infused during each control run of the pair. The curve for aortic constriction was extended to the highest mean percent of total volume infused (78.6%) for such runs. The slopes of these two curves were not statistically different, but the curves significantly differed from each other (p < .001). The parallel regression lines for the control and aortic constriction episodes of cardiac tamponade suggest that aortic constriction did not alter the compliance characteristics of the pericardia studied. Our end point for volume infusion (2 min beyond onset of RVDC) was early enough in the progression of tamponade so that all data collected were on a relatively flat portion of the pericardial compliance curve. Thus, in the presence of acute left ventricular pressure overload, the relationship between intrapericardial pressure and percent volume infused during cardiac tamponade was shifted upward and to the left. The average magnitude of this shift at any given intrapericardial pressure was approximately 30% of infused volume. For a given volume infused during cardiac tamponade, aortic constriction shifted the curve by an intrapericardial pressure of about 3.4 mm Hg.

Discussion

Collapse of the right ventricle occurs in diastole when intrapericardial pressure exceeds right ventricular diastolic pressure.1 This anatomic consequence of pressure changes clearly marks a specific point in the progression of hemodynamic events that occur during cardiac tamponade. RVDC is known to be both a sensitive and specific sign of significant cardiac compression in cardiac tamponade.8, 9 We have demonstrated that this sign first occurs early in the hemodynamic progression of cardiac tamponade when cardiac output has declined about 20% from baseline levels but before any change in aortic blood pressure.3 In general, this noninvasive marker complements the other traditional clinical signs of cardiac compression.

Although left ventricular size increases after aortic constriction, as documented in this study, the intervention chosen would be expected to enlarge the size of the right heart chambers as well since other investigators have reported augmented right heart filling pressures and venous return after this maneuver.13, 14, 40, 41 Acute left ventricular pressure overload such as that induced by acute descending thoracic aortic constriction initially results in a fall in stroke volume followed by a rise in left ventricular end-diastolic pressure and volume.12-18 These compensatory measures and increased venous return eventually result in elevated stroke volume and cardiac output by means of the Frank-Starling mechanism. Taylor et al.26 demonstrated that the magnitude of dilatation of one ventricle affects the pressure-volume relationship of the opposite ventricle and this effect becomes more significant at abnormally elevated end-diastolic volumes.

In addition, the intact pericardium may play a role in limiting acute cardiac dilatation by influencing the ventricular pressure-dimension relationship.10-22 Indeed, in studies using volume loading to raise the left ventricular end-diastolic pressure, as pressure rose and the heart expanded, the pericardium moved to a steeper part of its pressure-volume curve, producing even tighter coupling between right and left ventricular pressures.20 Shirato et al.21 have postulated a contribution of pericardial restriction to elevation of left ventricular diastolic pressure in acute dilatation of the heart. With these considerations in mind, we examined the effects of acute increases in left ventricular pressure and volume on the relationship between pericardial fluid pressure and volume and on the appearance of right ventricular collapse during cardiac tamponade.

Initially, aortic constriction with the pericardial space empty results in an increase in the mean right atrial blood pressure (of 3.0 mm Hg; as expected physiologically) and in the mean intrapericardial pressure (of 2.1 mm Hg for open or 2.8 mm Hg for flat balloon). At the point of onset of RVDC, the mean right atrial blood pressure and mean intrapericardial pressure were higher in the presence of descending aortic constriction than in its absence. Moreover, a consistently smaller volume of accumulated pericardial fluid was required to produce right ventricular collapse in the presence of left ventricular pressure overload. Thus, acute left ventricular pressure overload during cardiac tamponade resulted in an increase in pericardial pressure of about 3.4 mm Hg for any given intrapericardial fluid volume, regardless of how the intrapericardial pressure was measured. Over the range of intrapericardial pressures and volumes sampled, the slope of the relationship with and without descending thoracic aortic constriction remained constant. We and others have reported evidence suggesting that RVDC results when intrapericardial pressure exceeds diastolic right ventricular cavitary pressure.3, 5 Since this is a transmural pressure phenomenon, we can comment on its mechanism in the context of the current study.

Several investigators have postulated an increase in right ventricular filling pressure in the presence of acute left ventricular pressure overload.13, 14, 39, 40
Ilebekk et al. demonstrated that acute constriction of the descending thoracic aorta resulted in partial collapse of the vascular bed beyond the constriction and redistribution of blood volume to the upper body. In further studies, these investigators and others showed an increase in superior vena caval blood flow during descending aortic constriction, while vascular beds in the lower body were depleted. Others have reported that increases in left ventricular pressure at a constant right ventricular input are associated with direct elevation in right ventricular end-diastolic pressure. In isolated rabbit heart preparations, rapid increases in left ventricular volume led to a rise in right ventricular pressure, the magnitude of which was approximately one-quarter of the increase in left ventricular pressure.

We have demonstrated in our laboratory that an increase in right ventricular filling pressure results in the occurrence of RVDC later in the hemodynamic progression of cardiac tamponade. In the present study, the close correlation between the increase in mean right atrial blood pressure and the increase in intrapericardial pressure (measured with both open and flat balloon catheters) during aortic constriction when the pericardial space was empty suggests that an elevation in right ventricular filling pressure during left ventricular pressure overload may be responsible for the higher intrapericardial pressures needed to cause RVDC during cardiac tamponade. The smaller percent volume infused before the onset of RVDC during aortic constriction is probably due to the larger portion of total intrapericardial volume being occupied by the heart.

This investigation documents coupling between the chambers of the heart by the intact pericardium. This interdependence may be enhanced during cardiac tamponade when the pericardium is stretched and less compliant. Acute constriction of the descending thoracic aorta significantly alters the relationship between pericardial pressure and incremental intrapericardial fluid volume during cardiac tamponade. In the presence of acute left ventricular pressure overload, right ventricular collapse occurs at a higher intrapericardial pressure and at a smaller intrapericardial fluid volume. Thus, we conclude that a process leading to a rapid increase in left ventricular pressure and volume, in the presence of an otherwise unimportant pericardial effusion, may increase the intrapericardial fluid pressure sufficiently to cause the appearance of RVDC.

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