Pleural Effusion as a Cause of Right Ventricular DiastolicCollapse

Kevin Vaska, MD; L. Samuel Wann, MD; Kiran Sagar, MD; and H. Sidney Klopfenstein, MD, PhD

Background. We hypothesized, after seeing several suggestive clinical examples, that a process leading to a large bilateral pleural effusion in the presence of an otherwise insignificant pericardial effusion could result in right ventricular diastolic collapse (RVDC) as seen by two-dimensional echocardiography. This noninvasive marker for hemodynamically significant cardiac tamponade occurs when pericardial fluid is under pressure. Therefore, RVDC resulting from a large pleural effusion would represent a false-positive indication of cardiac tamponade caused by excessive pericardial fluid.

Methods and Results. Seven spontaneously breathing dogs were chronically instrumented to measure ascending aortic, right atrial, intrapericardial, intrapleural, left atrial, and pulmonary artery pressures and cardiac output. Intravascular volume was adjusted before each experiment to the euvolemic range with saline solution. The onset of RVDC was observed in each animal by two-dimensional echocardiography during seven paired episodes of tamponade induced by infusions of warm saline into the pericardial space alone and, after drainage of the pericardial fluid and complete recovery, into the pleural space in the presence of a small pericardial effusion. The onset of RVDC occurred at the same intrapericardial (8.17 versus 9.47 mm Hg) and right atrial (7.41 versus 7.46 mm Hg) blood pressures regardless of whether it was produced by an intrapericardial or an intrapleural effusion but began in expiration during the former and in inspiration during the latter. Intrapericardial pressure increased in the same manner as intrapleural pressure during intrapleural saline infusion. Nevertheless, cardiac output and aortic blood pressure were better preserved, and at the onset of RVDC, the pulmonary artery systolic blood pressure was higher (p<0.0001) and the degree of pulsus paradoxus lower (p<0.01) with intrapleural infusion.

Conclusions. These results indicate that a large bilateral pleural effusion can elevate intrapericardial pressure sufficiently to cause RVDC and, perhaps, lead to misdirected therapy of an otherwise insignificant pericardial effusion. (Circulation 1992;86:609–617)

KEY WORDS • transmural pressure • pulsus paradoxus • intrathoracic pressure • pericardial constraint • cardiac tamponade • pleural effusion • right ventricular collapse

Cardiac tamponade is a life-threatening hemodynamic abnormality caused by the accumulation of pericardial fluid under pressure. It is not a discrete event, but encompasses a spectrum ranging from pericardial effusions that produce trivial hemodynamic abnormalities to those that result in hemodynamic decompensation.1–3 At any point along this progression, the severity of the hemodynamic abnormality is believed to depend on the intrapericardial pressure, intracavitary filling pressures, and chamber compliances.4–7 It has been helpful to have two-dimensional echocardiographic landmarks along this progression to clinically assess the severity of the compromised cardiac function and to aid in planning therapeutic interventions before decompensation occurs. This is especially important because the treatment of hemodynamically significant cardiac tamponade (pericardiocentesis or surgery) is invasive and associated with some risk.

Right atrial and right ventricular (RV) diastolic collapse (RVDC) have been shown to be sensitive and specific markers for cardiac tamponade both in conscious animals8–10 and in human studies.11,12 In euvolemic, nonconvalescent, conscious animals and humans without RV hypertrophy or elevated RV diastolic pressures, the onset of RVDC has been shown to be associated with a 15–20% decline in cardiac output from baseline levels and a preserved systemic blood pressure.

The echocardiographic observation of RVDC in several patients who had large pleural effusions and small pericardial effusions led us to test the hypothesis that a large bilateral pleural effusion may result in RVDC in the presence of an otherwise insignificant pericardial effusion. In such a situation, removal of the pleural effusion and treatment of the process causing it, instead of a pericardial drainage procedure, would seem to be the appropriate course.

Methods
Seven healthy and acclimated adult mongrel dogs of either sex (weight, 26–30 kg) were anesthetized with thiamylal sodium (20 mg/kg i.v.), intubated, and venti-
Table 1. Hemodynamic Data During Pericardial Effusion and Pleural Effusion

<table>
<thead>
<tr>
<th></th>
<th>Baseline</th>
<th>Mean</th>
<th>End inspiration</th>
<th>End expiration</th>
<th>Pericardial effusion</th>
<th>End point (DCT)</th>
<th>End expiration</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPP (mm Hg)</td>
<td>0.45±0.09</td>
<td>8.17±0.20*</td>
<td>6.91±0.17</td>
<td>8.88±0.24</td>
<td>17.00±0.37*</td>
<td>16.12±0.36</td>
<td>17.39±0.25</td>
</tr>
<tr>
<td>IPIP (mm Hg)</td>
<td>-3.45±0.31</td>
<td>-0.96±0.29</td>
<td>-7.86±0.37</td>
<td>-0.10±0.32</td>
<td>-0.57±0.13</td>
<td>-7.22±0.29</td>
<td>-0.04±0.11</td>
</tr>
<tr>
<td>TMP (mm Hg)</td>
<td>3.9±0.22</td>
<td>9.13±0.30</td>
<td>14.77±0.41</td>
<td>8.98±0.33</td>
<td>17.57±0.33</td>
<td>23.34±0.40</td>
<td>17.43±0.27</td>
</tr>
<tr>
<td>RABP (mm Hg)</td>
<td>1.58±0.08</td>
<td>7.41±0.10*</td>
<td>7.06±0.19</td>
<td>7.73±0.15</td>
<td>15.13±0.39*</td>
<td>15.01±0.30</td>
<td>15.37±0.21</td>
</tr>
<tr>
<td>TMPIPP (mm Hg)</td>
<td>1.13±0.11</td>
<td>-0.76±0.13*</td>
<td>0.15±0.11</td>
<td>-1.15±0.17</td>
<td>-1.88±0.06*</td>
<td>-1.11±0.14</td>
<td>-2.02±0.19</td>
</tr>
<tr>
<td>CO (l/min)</td>
<td>3.5±0.2</td>
<td>3.0±0.1*</td>
<td>2.5±0.3</td>
<td>3.6±0.3</td>
<td>1.2±0.1*</td>
<td>0.4±0.2</td>
<td>2.4±0.6</td>
</tr>
<tr>
<td>AoBP (mm Hg)</td>
<td>102.9±1.1</td>
<td>84.7±1.1*</td>
<td>79.2±1.3</td>
<td>88.7±1.5</td>
<td>69.5±0.4*</td>
<td>62.8±1.5</td>
<td>76.7±2.1</td>
</tr>
<tr>
<td>HR (bpm)</td>
<td>104±4</td>
<td>131±5*</td>
<td>126±7</td>
<td>135±6</td>
<td>159±4*</td>
<td>128±5</td>
<td>170±5</td>
</tr>
<tr>
<td>LABP (mm Hg)</td>
<td>6.72±0.25</td>
<td>11.80±0.48*</td>
<td>9.58±0.24</td>
<td>14.07±0.27</td>
<td>14.73±0.41*</td>
<td>11.53±0.32</td>
<td>17.65±0.44</td>
</tr>
<tr>
<td>TMPVA (mm Hg)</td>
<td>6.27±0.28</td>
<td>3.63±0.24*</td>
<td>2.67±0.20</td>
<td>5.19±0.22</td>
<td>-2.27±0.35*</td>
<td>-4.59±0.41</td>
<td>0.26±0.39</td>
</tr>
<tr>
<td>PASP (mm Hg)</td>
<td>22.09±0.98</td>
<td>23.29±0.94*</td>
<td>21.84±0.69</td>
<td>25.11±0.77</td>
<td>13.45±0.80*</td>
<td>12.02±0.44</td>
<td>14.07±0.56</td>
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<tr>
<td>TMPASAP (mm Hg)</td>
<td>25.54±0.72</td>
<td>24.25±0.72*</td>
<td>29.70±0.55</td>
<td>25.21±0.49</td>
<td>14.02±0.77*</td>
<td>19.24±0.39</td>
<td>14.11±0.37</td>
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<tr>
<td>PP (mm Hg)</td>
<td>4.0±0.1</td>
<td>8.0±0.2*</td>
<td>...</td>
<td>...</td>
<td>12.1±0.2*</td>
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<td>...</td>
</tr>
<tr>
<td>SVR (Woods)</td>
<td>29.0±1.4</td>
<td>25.9±1.2*</td>
<td>...</td>
<td>...</td>
<td>47.4±4.0*</td>
<td>...</td>
<td>...</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>34±2</td>
<td>23±1*</td>
<td>20±2</td>
<td>27±2</td>
<td>8±1*</td>
<td>4±1</td>
<td>13±2</td>
</tr>
</tbody>
</table>

RVDC, right ventricular diastolic collapse; DCT, decompenated cardiac tamponade; IPP, change in intrapericardial pressure from baseline; IPIP, change in intrapleural pressure from baseline; TMP, calculated transmural pressure, change in intrapericardial pressure from baseline; RABP, right atrial blood pressure; TMPIPP, calculated transmural pressure, right atrial; CO, cardiac output; AoBP, aortic blood pressure; HR, heart rate; bpm, beats per minute; LABC, left atrial blood pressure; TMPLA, calculated transmural pressure, left atrial; PASP, pulmonary artery systolic blood pressure; TMPASAP, calculated transmural pressure, pulmonary artery systolic blood pressure; PP, pulse paradoxus; SVR, systemic vascular resistance; SV, stroke volume.

Data are mean±SEM.
*p<0.001 compared with baseline values.
†Not significant.
‡p<0.01 compared with baseline values
§p<0.05 compared with baseline values.

lathed with a volume-cycled respirator (LKB Medical AB, Engstrom 311). Anesthesia was maintained with an in-line halothane vaporizer (1–1.5% by volume in oxygen). Arterial blood gases were monitored hourly, and adequate oxygenation and acid–base status were maintained. A left thoracotomy was performed in the fifth intercostal space using aseptic technique, and Tygon fluid-filled catheters (Tygon microbore tubing, 0.05-in. i.d.×0.09-in. o.d., Norton Plastics) were placed into the ascending aorta (via the left internal mammary artery), right atrium (via the right internal mammary vein), main pulmonary artery (retrograde through an extrapericardial branch), and left atrium (retrograde through an extrapericardial pulmonary vein).

The pericardial sac was entered through a 4–5-cm longitudinal incision beginning near the base of the heart, and an electromagnetic flowprobe was placed around the aortic root (Howell Instruments; used with a Narcomatic flowmeter, Model RT 500, Healthdyne Cardiovascular, Inc.). Two fenestrated Tygon fluid-filled catheters were positioned in the pericardial space over the posterior and diaphragmatic surfaces of the left ventricle (avoiding the RV free wall) and were secured with purse-string sutures. The pericardium was closed with a continuous locking suture, and a watertight seal was verified by infusion of warm saline solution sufficient to cause a 30% reduction in mean aortic blood pressure. The intrapericardial fluid was removed, and 20–25 ml of sterile saline was returned to the pericardial space. All catheters were passed individually through the chest wall and exteriorized near the scapulae. The anterior mediastinum was opened wide to allow communication of right and left pleural cavities. A separate Tygon fluid-filled catheter was positioned in the anterior thorax, and a 14F sump tube (Argyle, Sherwood Medical Co.) was passed through the seventh intercostal space and its tip positioned in the anterior left pleural space. After brief hyperexpansion of the lungs, the ribs were approximated with umbilical tape, and the wound was closed in layers to provide an airtight seal. All pleural fluid and air were evacuated, and all intravascular catheters were aspirated, filled with a heparin solution, and sealed.

The animal was extubated after spontaneous respirations and reflexes had returned and allowed to recover overnight in an incubator with controlled temperature and supplemental oxygen (5 l/min). Xylocaine (1–2 mg/kg i.m. every 8 hours) was administered as needed for analgesia, and intramuscular injections of penicillin and streptomycin were given prophylactically. The pericardial space was irrigated with saline after surgery and daily thereafter for 2 or 3 days; integrity of the space was confirmed by recovery of all irrigating fluid.

On day 2 or 3 after surgery, before thoracic adhesions had formed between the parietal pericardium and visceral pleura, the conscious animal was returned to the laboratory and allowed to stand comfortably in a sling. The fluid-filled catheters were attached directly to pressure transducers (Deseret Medical, Inc.) with the zero-
pressure reference point adjusted to be one third of the vertical distance between the sternum and spine. Respirations were measured with a Whitney gauge placed around the thorax.

During each infusion, pressures in the right and left atria, aorta, pulmonary artery, pericardial space, and pleural space as well as cardiac output, heart rate, and respirations were continuously recorded on an FM tape recorder (A.R. Vetter Co.) and an eight-channel strip-chart recorder (Gould series 2800). A maximum of one pericardial infusion and one pleural infusion were performed in a single day, with sufficient time allowed for recovery between runs. No animal underwent more than two sets of infusion runs. Necropsy and in vitro electromagnetic flowprobe calibration were performed on all animals as previously described.\(^\text{13}\)

Short-axis two-dimensional echocardiograms were obtained with a hand-held transducer in the right fourth or fifth intercostal space and an Irex HSP-1 phased-array ultrasonoscope (Johnson and Johnson) and were recorded on videotape with a Sony Betamax videocassette recorder (Sony Corp.). The echocardiograms were reviewed by two independent observers, and RVDC was considered present if there was an inward motion of the RV outflow tract or free wall endocardial surface in diastole that varied with the respiratory cycle. The reversal of curvature of the RV wall always began after the mitral valve opened (as judged in the left atrial pressure tracing) and was sustained for at least 40% of the diastolic interval. It has been shown in clinical studies that right and left atrial collapse occur very early in the progression of cardiac tamponade and are present before RV collapse. Unfortunately, we were not able to reliably obtain a true apical four-chamber view of the heart in this conscious canine model; therefore, we were unable to investigate these very early signs of increased intrapericardial pressure.

The pericardial and pleural spaces were drained, and 30 ml of saline was instilled into the pericardial space so that open-ended catheters would provide a valid measure of intrapericardial pressure.\(^\text{14}\) Mean right atrial blood pressure was adjusted to between 1 and 2 mm Hg by intravenous infusion of normal saline, and baseline data were collected when a hemodynamic steady state had been achieved. Warmed normal saline solution was then continuously infused into the pericardial space at a rate of 10 ml/min with a Masterflex infusion pump (Cole Parmer Instrument Co.). The infusion continued until the time of hemodynamic decompensation, which is defined as a 30% decline in mean aortic blood pressure from baseline levels. The pericardial fluid was immediately removed, and the mean right atrial blood pressure was measured to ensure that intravascular volume had remained stable. The volume infused and the pressures present at the onset of RVDC and hemodynamic decompensation were noted.

The dog was allowed to recover for \(\approx 1\) hour. Absence of fluid in the pleural space was confirmed, and a volume of saline equal to 50% of the volume that resulted in the onset of RVDC in the preceding pericardial infusion run was instilled into the pericardial space. Therefore, each dog's individual physiology, size, and pericardial compliance were able to influence the specific volume of fluid chosen. The actual mean volume of fluid instilled into the pericardium, 63±3 ml, resulted in only a slightly elevated intrapericardial fluid pressure (1.73±0.04 mm Hg). This method caused an equivalent small, hemodynamically unimportant pericardial effusion in all dogs and allowed us to monitor the pericardial pressure with open catheters. Steady-state data again were collected as the baseline for a pleural effusion run. The pleural effusion was produced by rapid manual instillation of 1.5 l of warm saline into the pleural space, which was followed by a continuous intrapleural infusion at a rate of 50 ml/min with the Masterflex infusion pump. Data were continuously recorded as before, and the intrapleural infusion was stopped when the increase in intrapericardial pressure equaled that present at the time of hemodynamic

### Table 1. Continued.

<table>
<thead>
<tr>
<th>Pleural effusion</th>
<th>Onset of RVDC</th>
<th>End point</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean</td>
<td>End inspiration</td>
</tr>
<tr>
<td>Baseline</td>
<td>Mean</td>
<td>End inspiration</td>
</tr>
<tr>
<td>1.73±0.14</td>
<td>9.47±0.20(^*)</td>
<td>4.81±0.29</td>
</tr>
<tr>
<td>−3.33±0.26</td>
<td>4.69±0.16(^*)</td>
<td>−0.37±0.19</td>
</tr>
<tr>
<td>5.06±0.23</td>
<td>4.78±0.16(^*)</td>
<td>5.18±0.32</td>
</tr>
<tr>
<td>1.69±0.08</td>
<td>0.96±0.11(^*)</td>
<td>0.95±0.33</td>
</tr>
<tr>
<td>−0.04±0.18</td>
<td>2.01±0.57(^*)</td>
<td>−3.86±0.0</td>
</tr>
<tr>
<td>3.6±0.1</td>
<td>3.3±0.1(^*)</td>
<td>3.0±0.2</td>
</tr>
<tr>
<td>105.1±1.7</td>
<td>109.0±2.0(^*)</td>
<td>107.5±2.1</td>
</tr>
<tr>
<td>123±2</td>
<td>141±4(^*)</td>
<td>137±5</td>
</tr>
<tr>
<td>6.82±0.28</td>
<td>11.73±0.46(^*)</td>
<td>7.69±0.37</td>
</tr>
<tr>
<td>5.09±0.16</td>
<td>2.26±0.29(^*)</td>
<td>2.88±0.43</td>
</tr>
<tr>
<td>21.31±0.90</td>
<td>38.74±1.25(^*)</td>
<td>37.49±1.07</td>
</tr>
<tr>
<td>19.58±0.86</td>
<td>34.05±0.64(^*)</td>
<td>37.86±0.95</td>
</tr>
<tr>
<td>4.1±0.1</td>
<td>5.5±0.2(^*)</td>
<td>...</td>
</tr>
<tr>
<td>29.2±1.2</td>
<td>31.0±1.0(^*)</td>
<td>...</td>
</tr>
<tr>
<td>29±1</td>
<td>23±1(^*)</td>
<td>22±2</td>
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</tbody>
</table>
FIGURE 1. Graphs showing relations between mean intrapericardial pressure and hemodynamic indexes during intrapleural infusion (dashed lines) and during intrapericardial infusion (solid lines). Panel A: The curves are significantly different from each other (p<0.001), but the point of onset (circle) of right ventricular diastolic collapse (RVDC) is the same. Panel B: The curves differ significantly from each other (p<0.01), but the cardiac output at the onset of RVDC (circle) during each infusion is the same. Panel C: The curves are different from each other (p<0.001), and the aortic blood pressure is preserved during intrapleural infusion (p<0.0001). Panel D: The curves differ significantly from each other (p<0.01), but the stroke volume at the onset of RVDC (circle) during each infusion is the same. Panel E: The curves are different from each other (p<0.001), and the pulmonary artery systolic blood pressure at the onset of RVDC (circle) is higher during intrapleural infusion (p<0.0001). Panel F: The curves differ significantly from each other (p<0.01), and pulsatil paradoxa at the onset of RVDC (circle) is greater during intrapericardial infusion (p<0.01).

decompensation during the preceding pericardial infusion run. The pleural fluid was removed immediately, and the mean right atrial blood pressure was checked to ensure a stable intravascular volume. Arterial blood gas samples were measured at baseline and at the completion of each type of infusion.
Data Analysis

All data were stored on analog magnetic tape and transferred to a digital personal computer (Compaq, Inc.). By use of sequential interactive programs, individual beats in a 30-second file were defined at the baseline, at each 2-mm Hg increment in intrapericardial pressure above baseline, at the onset of RVDC, and at the time of decompensated cardiac tamponade or the termination of the pleural infusion. Each file included several complete respiratory cycles. Respiratory phases were noted, and mean pressures for each data file were calculated. The volumes infused into the pericardial or pleural spaces were calculated by multiplying the time to the midpoint of the 30-second data file by the infusion rate of the pump and adding the baseline amount of pericardial fluid.

Statistical Analysis

Mean data recorded during each intrapericardial infusion were paired with data recorded during the pleural infusion run that followed it. Paired t tests were used to compare baseline values with values at the onset of RVDC and at the termination of each run. Differences between pericardial and pleural infusions at baseline, at the onset of RVDC, and at termination were tested with a two-way repeated-measures ANOVA with the dog as the block effect. Multivariate regression analysis was used to analyze the relation between increases in intrapericardial pressure from baseline versus increases in intrapleural pressure from baseline, calculated transmural pressure, mean aortic blood pressure, mean pulmonary artery systolic blood pressure, left atrial blood pressure, mean cardiac output, mean heart rate, and mean pulsus paradoxus. A multiple comparison procedure was used to compare pleural infusion and pericardial infusion at baseline, at RVDC, and at decompensation or the termination of the pleural infusion as defined previously.

Results

Seven matched pairs of pericardial and pleural infusion runs were analyzed in seven conscious unanesthetized dogs. Table 1 shows the mean, end-inspiration, and end-expiration hemodynamic data (mean ± 1 SEM) for each intervention at baseline, at the onset of RVDC, and at the termination of each run.

Mean Hemodynamic Measurements During Pericardial and Pleural Infusions

By design, a small amount of pericardial fluid was present at baseline for both pericardial infusion runs (30 ml saline) and pleural infusion runs (63 ± 3 ml saline). Mean absolute intrapericardial pressures were similar statistically at 0.45 ± 0.09 and 1.73 ± 0.14 mm Hg, respectively. Therefore, the animals were operating on the flat portion of their pericardial pressure-volume curves in both baseline situations. Furthermore, the mean absolute intrapleural pressures (−3.45 ± 0.31 versus −3.33 ± 0.26 mm Hg, respectively) were not different at that time. At baseline, the mean initial right atrial blood pressure, cardiac output, aortic blood pressure, left atrial blood pressure, pulmonary artery systolic blood pressure, calculated transmural pressure, degree of pulsus paradoxus, systemic vascular resistance, and stroke volume did not differ statistically between the two conditions. At the onset of RV diastolic collapse, the mean absolute intrapericardial pressure was statistically the same regardless of treatment (8.17 ± 0.20 mm Hg for pericardial infusion versus 9.47 ± 0.20 mm Hg for pleural infusion). In addition, the increase in intrapleural pressure paralleled that of intrapericardial pressure during the intrapleural fluid infusion. At the time of onset of RVDC, the mean right atrial blood pressure, cardiac output, heart rate, left atrial blood pressure, calculated transmural pressures, systemic vascular resistance, and stroke volume were the same for both types of infusion. Mean aortic blood pressure, however, was 84.7 ± 1.1 mm Hg during pericardial infusion and 109.0 ± 2.0 mm Hg during pleural infusion (p < 0.0001). Similarly, mean pulmonary artery systolic blood pressure varied by intervention (pericardial infusion, 23.29 ± 0.94 mm Hg and pleural infusion, 38.74 ± 1.25 mm Hg, p < 0.0001), as did calculated transmural pressure (24.25 ± 0.72 and 34.05 ± 0.64 mm Hg, respectively;
The magnitude of pulsus paradoxus at the onset of RVDC also varied by intervention \((p<0.01)\). At the termination of each type of infusion (i.e., hemodynamic decompensation for pericardial infusion and an equivalent increase in intrapericardial pressure during pleural infusion), the increase in intrapleural pressure continued to parallel the increase in intrapericardial pressure only during the intrapleural infusion. Figure 1A graphically displays this continuous relation between mean intrapleural pressure and mean intrapericardial pressure for both interventions. As for all values in this study, the curves represent the mean±SEM (at 2–mm Hg increments in intrapericardial pressure) for both intrapericardial (solid curves) and intrapleural infusions (dashed curves) and only extend to the end points of each condition. These two curves differ significantly \((p<0.001)\). Although not illustrated, the curves for mean right atrial blood pressure, calculated mean transmural right atrial pressure, and heart rate did not differ statistically between the two treatments. Hemodynamic decompensation during pericardial infusion was marked by a reduction compared with baseline in mean cardiac output (Figure 1B, curves significantly different; \(p<0.01\)), aortic blood pressure (Figure 1C, curves significantly different; \(p<0.001\)), and stroke volume (Figure 1D, curves significantly different; \(p<0.01\)). These values during decompensated cardiac tamponade were significantly less than at the end point during pleural infusion \((p<0.0001\) in all cases). At the same time, the final systemic vascular resistance was higher during intrapericardial infusion \((p<0.01)\). Therefore, at similar increases in intrapericardial pressure during each type of infusion in these euvolemic animals, hemodynamic decompensation occurred only with intrapericardial infusion. Whereas the initial mean and calculated transmural pulmonary artery systolic blood pressures were similar for both treatments, they fell during decompensation because of intrapericardial infusion and actually increased to hypertensive levels during pleural infusion (Table 1, \(p<0.0001\)); the curves were significantly different (Figure 1E, \(p<0.001\)). The magnitude of pulsus paradoxus also varied by intervention between the two end points \((p<0.0001\), and the curves were significantly different (Figure 1F, \(p<0.01\)). Left atrial blood pressure had increased at the end point of both interventions but to a lesser extent with intrapericardial infusion \((p<0.05\) versus pleural infusion); calculated transmural left atrial blood pressures were similar.
dogs without RV hypertrophy, this occurs when cardiac output has declined about 20% from baseline but before significant changes in aortic blood pressure have occurred. RVDC has been shown to be sensitive and specific for the early detection of a hemodynamically important pericardial effusion and has been used as an indication that a pericardial drainage procedure is needed. We have reported that RVDC may be absent despite elevated intrapericardial pressures and significant hemodynamic impairment in the presence of RV hypertrophy or during acute elevations of RV pressure. Conversely, we found RVDC to occur in the presence of an otherwise insignificant pericardial effusion if cardiac size were abruptly increased. If the process leading to the acute increase in cardiac size was reversible, we would suggest that therapy be directed to that end and RVDC be considered a false-negative indication that a drainage procedure was indicated.

In the present study, we have identified yet another cause for RVDC in the absence of a hemodynamically significant pericardial effusion. Although little has been written about the hemodynamic significance of large bilateral pleural effusions under pressure, this intervention would be expected to contribute to overall extracardiac pressure, given a compliant pericardium. Indeed, our data (Figure 1A, Table 1) show that intrapleural and intrapericardial pressures rise uniformly during intrapleural fluid infusion. Most importantly, the onset of RVDC for both interventions occurred at similar intrapericardial pressures.

There were three unexpected and provocative findings. First, the same intrapericardial pressure is better tolerated when caused by pleural effusion in the presence of a small pericardial effusion than when caused solely by increased pericardial fluid. For example, the same intrapericardial pressure that produced hemodynamic decompensation during isolated cardiac tamponade was associated with a smaller reduction in stroke volume, no significant change from baseline in mean aortic blood pressure, less pulsa
d paradoxus, and an increase in pulmonary artery blood pressure during intrapleural fluid infusion. Increasing intrapericardial pressure during intrapericardial saline infusion in these dogs was associated with a continuous decrease in mean aortic blood pressure. This response is typical of convalescent conscious dogs and differs from that seen on day 4 or 5 after surgery and thereafter, when mean arterial blood pressure is well preserved during acute cardiac tamponade until late in the progression. It was necessary to study these dogs on day 2 or 3 after surgery to ensure that the pleural surface overlying the parietal pericardium was not affected by adhesions or fibrosis.

The major cause of hemodynamic deterioration during intrapericardial infusion appears to be the greater fall in stroke volume at similar elevated heart rates. This was associated with a greater elevation in systemic vascular resistance than occurred during intrapleural infusion. Perhaps the enhanced ability to tolerate increased intrapericardial pressure during intrapleural infusion in these euvolemic convalescent dogs is related to the better-preserved respiratory variation of intrapericardial pressure (as evidenced by comparison of the end-inspiratory and end-expiratory pressures) with brief inspiratory improvement in chamber compliance.
left heart filling gradient,\textsuperscript{18-23} and reduced left ventricular afterload.\textsuperscript{4,21,24,25} As with the less severe extent of pulsatls paradoxus, a smaller degree of pulmonary vascular pooling (caused by relatively smaller lung volumes) and adverse ventricular interactions may have also played a role.\textsuperscript{23,24} In addition, contractility may have been supported more vigorously by neurohumoral responses to this stress. The mechanism(s) responsible for these observations and other possible reasons for the smaller increase in pulsatls paradoxus during intrapleural infusion require further study.

The second unexpected finding was that the onset of RVDC occurred during expiration during intrapericardial infusion and inspiration during intrapleural infu-

sion. During intrapericardial infusion, the cause of RVDC, much like that of pulsatls paradoxus, has been related in part to the inspiratory augmentation of venous return, RV volume, and right-sided pressures.\textsuperscript{1,2,4,24-26} As a result, elevated intrapericardial pressure exceeded elevated RV diastolic pressure only in expiration (i.e., transmural pressure became negative) and led to the initiation of RVDC during this respiratory phase.\textsuperscript{12,27} In contrast to the observations of Shabetai et al.,\textsuperscript{26} we found that the inspiratory augmentation of RV volume in acute cardiac tamponade did not further increase intrapericardial pressure, although the transpericardial pressure did rise as a result of negative intrathoracic pressure. This difference may have occurred because we used a chronically instrumented, unanesthetized, convalescent canine model instead of the acute model they studied. Our data are consistent with theories on the changing relation of right-sided diastolic and intrapericardial pressures.\textsuperscript{28,29} In the present study, intrapericardial infusion was associated with minimal respiratory variation in both intrapericardial and right atrial blood pressures (Figure 2), with a constant and minimal varying difference between these two pressures throughout the respiratory cycle. Intrapercardial pressure showed enough variation to exceed right atrial blood pressure only in expiration, thereby creating the negative RV transmural pressure that led to RVDC. During intrapleural infusion, negative swings in intrathoracic pressure were followed by both intrapericardial and right atrial blood pressures, but right atrial blood pressure fell to a lower level, leading to a negative transmural pressure and RVDC. Apparently, the inspiratory augmentation of venous return was insufficient to offset the fall in right atrial blood pressure created by the negative intrathoracic pressure, perhaps because of a reduced extrathoracic-to-intrathoracic venous pressure gradient.\textsuperscript{4,6,21,30}

During hemodynamic decompensation caused by intrapericardial saline infusion, pulmonary artery systolic blood pressure fell below mean left atrial blood pressure (Figure 4). Cardiac output at this time was 1.2 l/min. This decline in pulmonary artery systolic pressure (i.e., narrowing of pulse pressure) has been described previously,\textsuperscript{1,3,21} as have the “reversed gradients” between intrapericardial and extrapericardial structures,\textsuperscript{25,28,29,32} at least during inspiration. Furthermore, extreme cardiac tamponade has been characterized by pericardial pressure exceeding pulmonary artery systolic blood pressure, and it has been suggested that elastic recoil (i.e., diastolic suction) associated with a negative transmural pressure gradient is responsible for left ventricul-

lar filling,\textsuperscript{33,34} as evidenced by the negative left atrial transmural pressure. The reduction in left ventricular filling gradient we observed could, at least in part, represent a reason for the precipitous drop in stroke volume seen with decompensation during intrapericardial infusion. This mechanism could not be effective if the chambers of the heart function as Starling resistors during cardiac tamponade. Another provocative theory would be that blood flow through the pulmonary vascu-

lar bed during decompensated cardiac tamponade in this conscious euvolemic model is dependent on changes in pulmonary vascular capacitance induced by respiratory activity instead of on energy derived from right heart contraction. Therefore, there would be pres-

ervation of pulmonary venous—left atrial blood flow only in expiration.\textsuperscript{25} The data in Figure 4 were recorded during hemodynamic decompensation (same dog as Figure 2) and demonstrate that inspiratory excursions are present. More importantly, the intrapleural pressure at decompensation revealed markedly increased respiratory excursions compared to baseline during the intrapericardial infusion run. This suggests an increasing dependence on the mechanical energy of respiration to transport blood from the right to the left heart and a tight coupling of right and left heart function to the phase of respiration. These observations are consistent with those of Burwell,\textsuperscript{35} who noted that the loss of effective RV pumping caused by excessive intrapericardial pressure did not signal the end of left ventricular filling. The RV/pulmonary artery pressure was reduced to a nonpulsatile curve that faithfully followed intrapleural pressure. In subsequent experiments using a similar conscious canine model studied 5-14 days after surgery when the dogs had completely recovered, we found the pressure gradient across the pulmonary vascular bed to decrease to very low levels, but we never observed a reversal of the gradient as we did in these convalescent dogs.

Clinical Implications

We have seen several patients with large bilateral pleural effusions and small pericardial effusions who underwent echocardiography for evaluation of deteriorating hemodynamic status and were found to have RVDC. A number of investigations have shown that RVDC reflects a hemodynamically significant increase in intrapericardial fluid pressure\textsuperscript{6,5,12,17} and implies that appropriate treatment strategies for pericardial tamponade should be undertaken. A previous study from our laboratory has shown that RVDC occurs at a higher intrapericardial pressure and lower intrapericardial fluid volume in the presence of acute left ventricular pressure overload, thus representing a potential false-positive indication of significant pericardial effusion.\textsuperscript{7} In our canine model, the onset of RVDC occurred at similar intrapericardial and right atrial blood pressures during both pericardial and pleural infusions. Therefore, large pleural effusions can cause cardiac chamber compression in a manner analogous to that caused by intrapericardial fluid infusion.

Conclusions

A process leading to a large bilateral pleural effusion, in the presence of an otherwise unimportant pericardial effusion, may increase intrapericardial fluid pressure
sufficiently to cause RVDC. We suggest that in this situation, RVDC is a false-positive indication of a pericardial effusion in need of drainage and that the appropriate therapeutic maneuver is drainage of the pleural effusion(s).

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