Ventricular coupling in constrictive pericarditis

WILLIAM P. SANTAMORE, PH.D., RICHARD BARTLETT, M.D., SUSAN J. VAN BUREN, B.S., M. KATHERINE DOWD, M.D., AND MICHAEL A. KUTCHER, M.D.

ABSTRACT Because of the close anatomic association, the volume or pressure in one ventricle can directly influence the volume and pressure in the other ventricle. Disease states that reduce pericardial compliance should accentuate this coupling between the ventricles. We examined this hypothesis in six dogs. Constrictive pericarditis was induced by injecting an irritant mixture into the pericardial cavity. Three to 4 weeks after this injection, the hearts were removed and placed in cool cardioplegic solution. Balloons were inserted into each ventricle and the pressure and volume changes caused by increasing the contralateral ventricular volume were measured. Compared with that in a control group of four dogs, the coupling between the ventricles was significantly augmented in the group with constrictive pericarditis. All the measured changes in ventricular pressure or volume caused by increasing contralateral ventricular pressure or volume were significantly greater (p < .05) in the group with constrictive pericarditis. The results of these experiments show increased coupling between the ventricles with constrictive pericarditis, which helps to explain some of the signs and symptoms of constrictive pericarditis.


THE VENTRICLES of the heart share a common septal wall, are encircled by common muscle fibers, and are enclosed with the pericardial cavity. Because of this close anatomic association, the volume or pressure in one ventricle can directly influence the volume and pressure in the other ventricle. This phenomenon, ventricular interdependence, was probably first observed by Henderson and Prince^{1} and later verified in postmortem^{2,3} and isolated heart preparations^{4-6}. These studies demonstrated that increasing right ventricular volume shifted the interventricular septum toward the left ventricle and altered left ventricular filling characteristics. Conversely, increasing left ventricular volume shifted the interventricular septum toward the right ventricle and altered right ventricular filling characteristics.

Although ventricular interdependence can occur without the pericardium, the coupling is greatly increased by the presence of the pericardium.^{7-9} Janicki and Weber^{7} observed that increasing right ventricular volume caused significantly greater changes in left ventricular end-diastolic pressure with the pericardium intact. Similarly, increasing left ventricular volume caused greater changes in right ventricular end-diastolic pressure with the pericardium intact. Using ultrasonic crystals, Glantz et al.^{10} showed that with the pericardium intact, right ventricular pressure was a more powerful predictor of left ventricular pressure than was left ventricular dimension. In postmortem canine hearts, Maruyama et al.^{11} observed that all mechanical interactions between the heart chambers were enhanced dramatically with an intact pericardium, especially when the filling pressures of all heart chambers increased simultaneously.

We therefore speculated that any disease state that decreased pericardial compliance would greatly accentuate the coupling between the ventricles. To examine this possibility, we used an animal preparation of chronic constrictive pericarditis.^{12} Three weeks after the initial experimental procedure, the hearts were removed and the coupling between the ventricles was examined.

Methods

**Experimental preparation.** Six mongrel dogs (12.7 to 16.4 kg) were anesthetized with Innovar Vet (0.2 mg/kg im) and pentobarbital (30 mg/kg iv), intubated with a cuffed endotracheal tube, and ventilated with a Harvard respirator. Under sterile conditions, the chest was entered through the right fourth inter-
costal space, and the pericardium was cannulated with a size 8 polyethylene catheter by means of a purse-string suture. A pericardial irritant mixture was used to induce constrictive pericarditis. The mixture consisted of tincture of iodine (20 ml), Dakin's solution (5 ml), sterile talcum powder (2 tablespoons), and tetracycline hydrochloride powder (1 g). Twenty milliliters of this mixture was injected into the pericardial space through the indwelling catheter and the catheter was then removed. The entry site was sutured tightly. Cyanoacrylate ester glue was placed over the suture and surrounding areas to achieve a seal. Care was taken to avoid spilling the irritant mixture outside the pericardial cavity during the procedure. The chest was closed and the dogs were allowed to recover.

**Experimental protocol.** The dogs were studied 4 weeks after the initial procedure. If the dog developed any signs of pulmonary edema, it was studied immediately. The dogs were deeply anesthetized with pentobarbital (60 mg/kg iv). Through a left lateral thoracotomy, the hearts were removed and submerged in cool (10°C) cardioplegic solution (sodium chloride 602 mg/100 ml, calcium chloride 23.1 mg/100 ml, potassium chloride 119.3 mg/100 ml, sodium bicarbonate 37 mg/100 ml, mannitol 1250 mg/100 ml, and dextrose 300 mg/100 ml). The cool temperature retarded postmortem changes in ventricular compliance. Through a No. 7F Sones catheter, 20 to 30 ml of cardioplegic solution was infused into the left anterior descending, circumflex, and right coronary arteries, respectively. Throughout the experimental procedures, the hearts were kept submerged in the cool cardioplegic solution. Large helium balloons were inserted retrograde into each ventricle (see figure 1). Via the pulmonary artery, a No. 11 helium balloon was inserted into the right ventricle and a ligature was tied around the pulmonary artery to secure the balloon in place. Similarly, via the aorta, a No. 9 helium balloon was inserted into the left ventricle and a ligature was tied around the aorta. The balloons had an unstressed volume in excess of 45 ml. The balloons were inflated and deflated several times to ensure their proper positioning within the ventricles. This positioning was verified at the end of each experiment. The hearts were placed in an x-ray system. The balloons were filled with contrast material (meglumine diatrizoate, Renografin 76) and x-ray plate films were obtained to confirm the balloon position. The ventricular pressures, the pressures within the balloons, were measured with Statham 23Db pressure transducers connected to an Electronics for Medicine recorder (Model DR 8). The zero pressure level was set midway between the apex and the base of the heart. This level ranged from 4 to 6 cm from the surface of the cardioplegic solution.

The changes in left ventricular pressure (ΔP<sub>L</sub>) caused by increasing right ventricular pressure (ΔP<sub>R</sub>) or volume (ΔV<sub>R</sub>) were measured as follows: Left ventricular pressure was set either at a low initial value (6 mm Hg) or at a high initial value (15 mm Hg). Right ventricular pressure was initially set between 4 to 6 mm Hg. The stopcock (S<sub>1</sub>) was opened (figure 1), thereby setting left ventricular volume at a constant value. By means of a syringe pump, cool water (10°C) was infused into the right ventricular balloon. Right and left ventricular pressures were recorded during this procedure. This procedure was performed three times at each level of left ventricular pressure.

The changes in left ventricular volume caused by increasing right ventricular pressure (ΔP<sub>L</sub>/ΔP<sub>R</sub>) or volume (ΔV<sub>L</sub>/ΔV<sub>R</sub>) were measured as follows: The stopcock (S<sub>1</sub>) in figure 1 was opened, thereby setting left ventricular pressure at a fixed level. The outflow from the left ventricle fell into a weight scale. The scale consisted of Statham Green cell force transducer (+30 g, ±0.06 mm) with a lever arm. The scale was calibrated and connected to the Electronics for Medicine recorder so that the volume outflow was measured in milliliters. Right ventricular pressure was initially set between 4 to 6 mm Hg. With the syringe pump, cool water was infused into the right ventricle while right ventricular pressure and left ventricular volume outflow were recorded. This procedure was repeated three times.

By the same approach as outlined above, the ΔP<sub>L</sub>/ΔP<sub>R</sub>, ΔP<sub>L</sub>/ΔV<sub>R</sub>, ΔV<sub>L</sub>/ΔP<sub>R</sub>, and ΔV<sub>L</sub>/ΔV<sub>R</sub> measurements were obtained. To test the stability of the heart preparation, the ΔP<sub>L</sub>/ΔP<sub>R</sub>, and ΔP<sub>L</sub>/ΔV<sub>R</sub>, measurements were recorded again. The above procedure required about 75 min to complete. In half the experiments, the order of measuring was reversed: water was infused into the left ventricular balloon and the right ventricular responses were measured. Six additional mongrel dogs served as controls. Without prior surgery, the dogs were anesthetized with pentobarbital (60 mg/kg iv). The hearts with the pericardium intact were removed and studied by the techniques outlined above.

**Data analysis.** The pressure and volume displacement curves were traced on an Apple II digitizer tablet with cross-hair cursor the digitized waveforms stored in the Apple II + computer. From the calibration signals, the computer determined actual pressure and volume displacement values and calculated the derivatives of the pressure curves and the volume displacement curves. The derivatives were determined by using a sliding second-order polynomial fit to the pressure and volume displacement curves. From the derivatives, the coupling coefficients or transfer functions, ΔP<sub>L</sub>/ΔP<sub>R</sub>, ΔP<sub>L</sub>/ΔV<sub>R</sub>, etc., were calculated by dividing point-by-point one derivative by the other. For each experiment, the average values of the transfer functions were determined. For the experimental and control groups, the means, standard deviations, and standard errors of the average values of the transfer functions were calculated. At matched levels of ventricular pressures the experimental and control data were compared by a t test with significance at p < .05.

**Results**

Figure 2 shows the typical transfer of pressure and volume information between the ventricles in the control experiments. In panel A, water was infused into the right ventricular balloon as right and left ventricu-
lar pressures were recorded. In panel B, the left ventricular volume outflow caused by increasing right ventricular volume is shown. As stated above, stopcock S, in figure 1 was opened, thereby setting the left ventricular pressure at a fixed level. As right ventricular pressure and volume increased, the septum shifted toward the left and water was ejected from the left ventricle. From the same experiment, panels C and D show right ventricular pressures and volume outflow as left ventricular pressure increased.

Figure 3 presents typical results for the constrictive pericarditis experiments. Panels A and B show left ventricular pressure and volume outflow as right ventricular pressure increased. Similarly, panels C and D show right ventricular pressure and volume outflow as left ventricular pressure increased. In comparing figures 2 and 3, it is obvious that the response variables (left ventricular pressure, panel A; left ventricular volume, panel B; right ventricular pressure, panel C; right ventricular volume, panel D) changed more with constrictive pericarditis. For example, in figure 2, B, 3.7 ml of water was ejected from the left ventricle as right ventricular pressure increased by 24 mm Hg. In figure 3, B, 5.2 ml of water were ejected from the left ventricle as right ventricular pressure increased by only 14 mm Hg.

Figures 4 and 5 show the computer analysis for the data in figures 2 and 3, respectively. In each experiment, the waveforms were digitized and the computer calculated the derivative of each waveform. The derivatives were divided point-by-point to determine the transfer functions. These responses were plotted
against ventricular pressure. In these typical examples, $\Delta P/\Delta P_i$, $\Delta V/\Delta P_i$, $\Delta P/\Delta P_i$, and $\Delta V/\Delta P_i$ were all greater with constrictive pericarditis. At every level of ventricular pressure, the transfer functions were greater in the hearts with constrictive pericarditis.

Table 1 compares the control and constrictive pericarditis responses. For each experiment the average values of the transfer functions were determined. For both experimental and control groups, the mean and standard error of these average responses were calculated. Table 1 presents the mean average responses and shows that the coupling between the ventricles is increased with constrictive pericarditis. Every response is significantly greater ($p < .05$) with constrictive pericarditis.

Discussion

In this study we speculated that disease states that decreased pericardial compliance would greatly accentuate ventricular coupling. To examine this possibility, we studied postmortem hearts from dogs with constrictive pericarditis. Balloons were inserted into each ventricle. Changes in pressure or volume caused by changing the contralateral ventricular volume were measured. As speculated, ventricular coupling was greatly increased in hearts with constrictive pericarditis and every response ($\Delta P/\Delta P_i$, etc.) was significantly greater in the constrictive pericarditis group.

Clinically, chronic constrictive pericarditis is associated with a decreased pericardial compliance. Hence, ventricular filling is impaired and ventricular stroke volume is reduced. Ventricular filling is rapid in early diastole. However, as the limits of ventricular distensibility are reached, the ventricular filling is severely restricted, with little ventricular filling occurring in late diastole. The filling pattern results in a “square root” pattern of ventricular diastolic pressures. Both right and left ventricular diastolic pressures are elevated, and the ventricular pressures tend to equilibrate. The normal inspiratory increase in vena cava flow and the decrease in vena cava pressure are diminished or, more often, absent.\(^{20}\)

The results of the current study help to explain some of the clinical signs of chronic constrictive pericarditis. In our experiments, the transfer of pressure and volume information between the ventricles was measured postmortem in dogs with chronic constrictive pericarditis. As compared with control animals, the transfer functions were increased.

![Figure 4](image-url)

**FIGURE 4.** Computer analysis of the data in figure 2. The pressure and volume curves were digitized and the computer calculated the derivative of each curve. The derivatives of the pressure and volume curves were divided by each other to calculate $\Delta P/\Delta P_i$ (panel A), $\Delta V/\Delta P_i$ (panel B), $\Delta P/\Delta P_i$ (panel C), and $\Delta V/\Delta P_i$ (panel D). These responses are plotted against ventricular pressure. The numbers on top are the average response values.

### TABLE 1

Comparison of control and constrictive pericarditis responses

<table>
<thead>
<tr>
<th>Response</th>
<th>Control</th>
<th>Constrictive pericarditis</th>
</tr>
</thead>
<tbody>
<tr>
<td>$\Delta P/\Delta P_i$</td>
<td>0.29±0.03</td>
<td>0.58±0.04(^{\text{A}})</td>
</tr>
<tr>
<td>$\Delta P/\Delta V_i$</td>
<td>0.46±0.05</td>
<td>1.44±0.21(^{\text{A}})</td>
</tr>
<tr>
<td>$\Delta V/\Delta P_i$</td>
<td>0.19±0.02</td>
<td>0.41±0.08(^{\text{A}})</td>
</tr>
<tr>
<td>$\Delta V/\Delta V_i$</td>
<td>0.30±0.03</td>
<td>0.52±0.02(^{\text{A}})</td>
</tr>
<tr>
<td>$\Delta P/\Delta P_i$</td>
<td>0.34±0.02</td>
<td>0.55±0.04(^{\text{A}})</td>
</tr>
<tr>
<td>$\Delta P/\Delta V_i$</td>
<td>0.46±0.04</td>
<td>1.25±0.14(^{\text{A}})</td>
</tr>
<tr>
<td>$\Delta V/\Delta P_i$</td>
<td>0.16±0.01</td>
<td>0.37±0.05(^{\text{A}})</td>
</tr>
<tr>
<td>$\Delta V/\Delta V_i$</td>
<td>0.20±0.02</td>
<td>0.56±0.05(^{\text{A}})</td>
</tr>
</tbody>
</table>

Data expressed as mean ± SE.\(^{\text{A}}p < .05\) compared with control value.
fer of pressure and volume information between the ventricles was greatly accentuated with constrictive pericarditis. This accentuated coupling between the ventricles certainly helps to explain the observed equilibration of ventricular diastolic pressures. $\Delta P/\Delta P_r$ and $\Delta V/\Delta P$, were greater than 0.55. With this high level of pressure transfer, right and left ventricular end-diastolic pressures would tend to equilibrate.

Another consequence of this increased coupling between the ventricles is that there would be little, if any, transseptal pressure gradient during diastole. In normal subjects, mean transseptal diastolic pressure gradients in the range of 10 mm Hg have been reported. In two patients with constrictive pericarditis, Gibson et al. measured simultaneously right and left ventricular pressures. No mean transseptal pressure gradients were observed in diastole. Other studies have shown alterations in septal motion caused by changing the transseptal pressure gradient. Whether or not abnormal septal motion occurs in constrictive pericarditis is controversial. Pandian et al. did not observe abnormal septal motion, whereas Gibson et al. and Candell-Riera et al., using echocardiography, did observe abnormal septal motion.

The results of the current study imply that the normal fluctuations in right ventricular volume with respiration should greatly affect left ventricular volume. In turn, the left ventricular volume changes could cause pulsus paradoxus. Clinically, however, little or no fluctuations in aortic pressure are observed in patients with constrictive pericarditis. This discrepancy might be explained by the fact that the left ventricle is stiffer and working at a higher diastolic pressure. With a high diastolic pressure and a stiff ventricle, small changes in diastolic pressure would have minimal or no effect on right or left ventricular filling.

In summary, we examined the coupling between the ventricles in a canine preparation of constrictive pericarditis. The dogs' hearts were removed and studied postmortem. Balloons were inserted into each ventricle and changes in pressure or volume caused by changing the contralateral ventricular volume were measured. The coupling between the ventricles was significantly greater in the hearts with constrictive pericarditis.

We thank Maxine Blob and Sheree Icenhower for their careful preparation of this manuscript.

References
Ventricular coupling in constrictive pericarditis.
W P Santamore, R Bartlett, S J Van Buren, M K Dowd and M A Kutcher

Circulation. 1986;74:597-602
doi: 10.1161/01.CIR.74.3.597

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1986 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/74/3/597