Left Ventricular Volume and Function During Relief of Cardiac Tamponade in Man

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With the technical assistance of Robert Bontemps, B.S.

SUMMARY To determine the causes of cardiac failure during cardiac tamponade in man, we studied left ventricular volume and function in eight patients during pericardiocentesis using gated equilibrium radionuclide ventriculography. In the seven patients with clinical and hemodynamic evidence of cardiac tamponade, end-diastolic and end-systolic volumes increased progressively as the initial 500 ml of fluid were removed; the most marked increase occurred during the removal of the first 200 ml of pericardial fluid. After removal of 500 ml of pericardial fluid, end-diastolic volume increased from 52 ± 8 ml to 111 ± 13 ml (p < 0.05) and end-systolic volume from 17 ± 5 ml to 34 ± 7 ml (p < 0.05). Additional aspiration of fluid resulted in no further changes in left ventricular volume. The ejection fraction averaged 70% before removal of fluid and was unchanged by pericardiocentesis. In the one patient who did not have hemodynamic evidence of tamponade, there were only minor changes in left ventricular volumes and ejection fraction. These data suggest that pump function of the left ventricle is well preserved in cardiac tamponade, and that the diminution in stroke volume and consequent cardiovascular collapse seen in tamponade are due to marked underfilling of the ventricle.

THE DECREASED effective filling pressures in the left and right ventricles found in cardiac tamponade may contribute significantly to depressed stroke volume also present in that condition. Several investigators have shown that left ventricular end-diastolic volume or internal diameter is diminished during experimental tamponade. However, there is a lack of agreement regarding the effect of tamponade on left ventricular end-systolic volume and contractile function. End-systolic volume or internal diameter was found to be increased, unchanged or decreased. Furthermore, left ventricular contractile function was considered to be either impaired or diminished appropriately with respect to the marked underfilling of the ventricle. How these observations apply to the clinical situation is not known. Accordingly, we evaluated left ventricular volume and function during relief of cardiac tamponade in man using multigated equilibrium radionuclide ventriculography.

Materials and Methods

Patients

The study group consisted of eight patients with significant pericardial effusions who were to undergo diagnostic or therapeutic pericardiocentesis. Informed consent was obtained from each patient. Patients who were sent directly to surgery were too unstable for adequate collection of hemodynamic data were not included. The protocol was approved by this institution’s Research Committee and Subcommittee on Research on Human Subjects.

Procedures and Recordings

Right-heart catheterization was performed at the bedside using a #7F triple-lumen thermodilution balloon catheter. Arterial pressure was obtained with a #18 or #20 Teflon catheter inserted percutaneously into a radial or brachial artery. Percutaneous pericardiocentesis was performed by puncturing the pericardial sac with a stainless-steel needle. The needle was used as an exploring electrode to achieve continuous electrocardiographic monitoring by connecting it to the V lead of a standard electrocardiograph. A 5.5-inch #19 Teflon catheter with four side holes was then advanced over the rigid needle so that all side holes were within the pericardial cavity and no damage was done to the cardiac structures. The needle was then withdrawn. There were no complications of the pericardiocentesis, and the initial insertion was performed with a single puncture in all cases. In patient 6, mechanical problems with the catheter necessitated repeat puncture after 200 ml of pericardial fluid had been withdrawn. In patient 5, withdrawal of pericardial fluid was halted after 500 ml because of unsustained ventricular tachycardia related to negative pressure applied to the pericardial catheter.

Pressures were measured with Statham P23ID transducers and recorded along with a bipolar electrocardiographic lead on an Electronics for Medicine VR6 recorder. To ensure precise linearity of response, the transducers were connected to a single manifold, which allowed them to be calibrated simultaneously. Thermodilution cardiac output was calculated by a computer from the curve generated by hand injection of 10 ml of room temperature 5% dextrose solution.
Radionuclide Determination

Red blood cells were labeled with 25 mCi of technetium-99m (\(^{99m}\)Tc) using an in vivo method. The mean percent labeling by this method was 69.8 ± 14.8% (± SD), and the effective half-life of the \(^{99m}\)Tc red blood cells was 4.5 hours. Data were acquired using a mobile standard field of view gamma camera with a high-sensitivity collimator (Picker Corporation) interfaced to a dedicated computer (Digital Equipment Corporation). With the camera placed in the modified left anterior oblique projection that best separated the left and right ventricles, 28-frame multigated studies were acquired for approximately 5 million counts. Data were acquired in zoom mode in 64 × 64 matrices. Typical data acquisition times were approximately 90 seconds per study, and depended upon body habitus and red cell labeling efficiency. For each study, end-diastolic and end-systolic regions of interest were determined using an automated edge-detection method. Ejection fraction was calculated according to the formula (ED – ES)/ED, where ED = end-diastolic counts and ES = end-systolic counts after correcting for background. The correlation between left ventricular ejection fraction determined by this method and by contrast angiography is 0.90.

Count data were obtained in triplicate before removal of pericardial fluid and in duplicate after removal of each aliquot of pericardial fluid; the camera-patient relationship was constant. All data are reported as averages of triplicate or duplicate determinations. The coefficient of variance was 2.8% for repeat measurements of ejection fraction (n = 48) and 7.7% for repeat measurements of cardiac output (n = 48).

To determine whether tracer had leaked into the pericardial fluid, which might have influenced the absolute number of counts over the left ventricle, 2-ml aliquots from each pericardial withdrawal were counted under the camera for 3 minutes. There was no increase in counts over background in the pericardial aspirates for any patient. Additionally, there was some concern that the presence of pericardial fluid itself might cause a significant decrease in the absolute number of counts recorded. Consequently, the increases in both stroke volume (by thermodilution) and stroke counts (by radionuclide angiography) were examined after maximal withdrawal of pericardial fluid. For the group with tamponade, stroke volume increased by a factor of 2.28 ± 0.28 and stroke counts increased by a factor of 2.47 ± 0.46 (NS); the patient without tamponade had increases of 1.08 and 1.13, respectively. The similarity of the change in stroke volume and stroke counts argues strongly against any significant attenuation of counts by the pericardial effusions.

Hemodynamic Measurements and Calculations

After insertion of the catheters, recordings were obtained before withdrawal of any intrapericardial fluid (except approximately 2 ml for bacterial culture and hematocrit) and after incremental aspiration until no further fluid could be withdrawn (cumulative amounts of 50, 100, 200, 300, 500 and 1000 ml of fluid were withdrawn). Data acquisitions at each stage required approximately 10 minutes. During data acquisition, parenteral fluid administration was minimal; all patients (except patient 1) received only the dextrose solutions injected for the cardiac output determinations and a peripheral i.v. infusion of 15 ml/hour. At each level of pericardial fluid withdrawal, phasic and mean right atrial, pericardial, pulmonary arterial, pulmonary capillary wedge and systemic arterial pressure were recorded. Mean pressures were measured at end-expiration with the patient breathing quietly. Thermodilution cardiac output was obtained in triplicate and the radionuclide ventriculogram was obtained in duplicate and both were averaged.

Pulsus paradoxus was defined as the difference between peak systolic expiratory and inspiratory pressures during quiet respiration. Stroke volume was calculated by dividing the average thermodilution output by heart rate. Thermodilution stroke volume divided by the radionuclide ejection fraction yielded end-diastolic volume, and end-systolic volume was calculated as end-diastolic volume minus stroke volume.

Statistical Analysis

Seven patients had hemodynamic evidence of cardiac tamponade. For these patients, repeat-measurement analysis of variance was used to determine significant relationships between the hemodynamic and volume variables and changing intrapericardial fluid volumes. A p value of 0.05 was considered significant.

Results

Clinical Characteristics

All patients were in sinus rhythm and none had a history of myocardial infarction or valvular heart disease. Six were males and two were females, average age 55 years (range 28–76 years). The cause of the pericardial effusion was carcinoma in six patients, uremia in one patient and idiopathic in one. In seven patients, cardiac tamponade was the indication for pericardiocentesis; one patient was studied because of a large pericardial effusion and an episode of hypotension during hemodialysis. Patient 1 was studied with a constant infusion of dopamine, 250 μg/min, throughout the investigation.

Hemodynamics and Ventricular Volume

Tamponade Group

All seven patients with clinical evidence of cardiac tamponade had equalization of diastolic pressures in the right atrium, right ventricle, pulmonary artery and pulmonary wedge, superimposition of phasic right atrial, pulmonary wedge and pericardial pressure tracings, loss of right atrial “y” descent and a pulsus paradoxus of 10 mm Hg or greater. Before removal of any pericardial fluid, the heart rate averaged 106 beats/min, and arterial systolic pressure was 114 mm Hg, with an average pulsus paradoxus of 26 mm Hg. Mean pulmonary artery pressure averaged 24 mm Hg and mean right atrial, pericardial and pulmonary wedge pressures averaged 18, 18 and 19 mm Hg, respective-
The stroke volume was severely depressed (35 ml/beat) and cardiac output averaged 3.7 l/min. The radionuclide ventriculograms revealed markedly diminished cardiac chamber size (fig. 1) and end-diastolic and end-systolic volumes averaged 52 ml and 17 ml, respectively. The mean ejection fraction was normal (70%) (table 1).

Removal of 500–1430 ml of pericardial fluid (mean 880 ml) from the patients with cardiac tamponade resulted in a progressive decrease in heart rate, increase in arterial systolic pressure, and loss of pulsum paradoxus (table 1). There was no significant change in mean pulmonary artery pressure. Right atrial and intrapericardial pressures both decreased continuously during removal of the first 500 ml of pericardial fluid. In all patients, equalization of the atrial and pericardial pressures continued after removal of 50 ml and 100 ml of pericardial fluid. The pericardial pressure tracing fell below right atrial pressure only after a minimum of 200 ml had been aspirated.

After removal of the maximal amount of pericardial fluid, the end-diastolic volumes fell to 424 ml (control) and 175 ml (after removal of fluid). The end-systolic volumes fell to 175 ml (control) and 71 ml (after removal of fluid). The mean ejection fraction was 42% (control) and 34% (after removal of fluid).

**TABLE 1. Hemodynamic Data**

<table>
<thead>
<tr>
<th>Pericardial fluid removed (ml)</th>
<th>0</th>
<th>50</th>
<th>100</th>
<th>200</th>
</tr>
</thead>
<tbody>
<tr>
<td>HR (beats/min)</td>
<td>106±6</td>
<td>102±6</td>
<td>100±5</td>
<td>97±5</td>
</tr>
<tr>
<td>Art P (mm Hg)</td>
<td>114±10</td>
<td>125±9</td>
<td>135±11</td>
<td>135±10</td>
</tr>
<tr>
<td>AP (mm Hg)</td>
<td>26±5</td>
<td>23±7</td>
<td>19±6</td>
<td>12±4</td>
</tr>
<tr>
<td>PA (mm Hg)</td>
<td>24±2</td>
<td>23±2</td>
<td>24±2</td>
<td>23±2</td>
</tr>
<tr>
<td>RA (mm Hg)</td>
<td>18±2</td>
<td>16±1</td>
<td>14±2</td>
<td>12±2</td>
</tr>
<tr>
<td>Peri (mm Hg)</td>
<td>18±2</td>
<td>16±2</td>
<td>14±3</td>
<td>9±2</td>
</tr>
<tr>
<td>SV (ml)</td>
<td>35±6</td>
<td>43±7</td>
<td>50±6</td>
<td>62±7</td>
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<tr>
<td>EDV (ml)</td>
<td>52±8</td>
<td>68±13</td>
<td>78±13</td>
<td>95±13</td>
</tr>
<tr>
<td>ESV (ml)</td>
<td>17±5</td>
<td>24±8</td>
<td>27±8</td>
<td>32±9</td>
</tr>
<tr>
<td>EF (%)</td>
<td>70±6</td>
<td>68±6</td>
<td>68±6</td>
<td>68±5</td>
</tr>
</tbody>
</table>

Values are mean ± SEM.

*p < 0.05 vs 0.

Abbreviations: HR = heart rate; Art P = peak arterial pressure; ΔP = pulsum paradoxus; PA = mean pulmonary artery pressure; RA = mean right atrial pressure; Peri = mean intrapericardial pressure; SV = stroke volume; EDV = end-diastolic volume; ESV = end-systolic volume; EF = ejection fraction.
fluid in each patient, relief of tamponade was indicated by a decrease in intrapericardial pressure to 0 mm Hg (range -3 to 3 mm Hg), and right atrial pressure to within the normal range (≤ 8 mm Hg, fig. 2A). The right atrial pressure was less than pulmonary wedge pressure in all patients except patient 6. The right atrial pressure contour normalized with appearance of a ‘y’ descent. The ‘x’ descent was deeper than the ‘y’ descent in all patients except patient 6, in whom the right atrial pressure remained abnormally elevated and the ‘y’ descent was deeper. Pericardial fluid reaccumulated rapidly in patient 6, and necessitated surgical intervention. At surgery, a very thickened parietal pericardium was stripped from the right side of the heart and right atrial pressure subsequently normalized.

There was a significant increase in stroke volume after removal of the first 100 ml of pericardial fluid. After removal of 200 ml, stroke volume increased by an average of 77% over control. An average additional increase of 40% occurred after aspiration of the next 300 ml of pericardial fluid. End-diastolic volume changes paralleled changes in stroke volume (table 1, fig. 2B). In each case, end-diastolic volume increased dramatically early in the course of pericardial fluid removal and then leveled off; for the group, the change in end-diastolic volume was significant after removal of the first 100 ml of pericardial fluid. End-systolic volume (fig. 2C) increased gradually, but because of the variability in response, the increase was significant only after 500 ml of pericardial fluid had been removed. The average end-diastolic volume increased by 113% and end-systolic volume by 100% when 500 ml of fluid had been aspirated. Ejection fraction (fig. 2D) did not change significantly during relief of cardiac tamponade. The marked changes in volumes are illustrated qualitatively in the end-systolic and end-diastolic frames of a representative radionuclide ventriculogram in figure 1.

**Effusion Without Tamponade**

Patient 8, who had effusion without tamponade, had a significant pulsus paradoxus of 15 mm Hg at rest, but pericardial and atrial pressures did not equalize, and there was no loss of the right atrial ‘y’ descent. There was a resting tachycardia of 108 beats/min. The arterial systolic pressure was 150 mm Hg and cardiac output was 5.8 l/min. Removal of 500 ml of pericardial fluid did not change pulmonary capillary wedge pressure, but produced a decrease in intrapericardial pressure from 7 mm Hg to 2 mm Hg and right atrial pressure from 10 mm Hg to 9 mm Hg. Arterial systolic pressure decreased from 150 mm Hg to 135 mm Hg, but the 15-mm Hg pulsus paradoxus remained. There were minor increases in stroke volume (13%) and end-diastolic volume (33%) after drainage of the pericardial effusion.

**Discussion**

Although there have been a number of experimental animal studies of ventricular volume and function during cardiac tamponade, the present report appears to be the first such study in man. Effusions in man often accumulate over days or weeks, as opposed to minutes in experimental tamponade. Intrapericardial pressures are usually 15–20 mm Hg in man and only 8–10 mm Hg in animals, and animals are studied in a sedated state or immediately after thoracotomy. Thus, it would not be surprising if observations in man differed from those in experimental animals. Nevertheless, our data concerning end-diastolic volume are remarkably similar to the observations in animal studies and the limited observations with M-mode echocardiography in man. We found a marked step-wise increase in left ventricular diastolic volume during relief of cardiac tamponade. This incremental increase in end-diastolic volume paralleled the increase in stroke volume demonstrated by us and others. The most marked increases in stroke volume and end-diastolic volume occurred during withdrawal of the first few hundred milliliters of pericardial fluid. During this initial removal of fluid, there was a concomitant decrease in right atrial, pulmonary wedge and pericardial pressures, but all pressures remained superimposed. In every patient with tamponade, when 200–400 ml of pericardial fluid had been removed, pericardial pressure decreased below right atrial pressure and the right atrial ‘y’ descent reappeared. These later changes were accompanied by a leveling off of the end-diastolic volume (fig. 2B). These data support the concept that while the atrial and pericardial pressures remain equal, there is significant compression of the ventricles. Because of the steep slope of the pericardial pressure-volume curve during severe tamponade, initial removal of only small amounts of pericardial fluid causes significant changes in left ventricular filling, while subsequent removal of large quantities of fluid causes little change in atrial pressure or left ventricular diastolic volume.

Experimental studies have reported conflicting results concerning the effect of cardiac tamponade on left ventricular end-systolic volume and ejection fraction. Using aortic thermodilution curves to calculate left ventricular volume, Ferguson et al. found an increase in the ratio of end-systolic volume to end-diastolic volume and a decrease in the end-systolic force-circumference ratio. They thought these data implied a decrease in pump function during tamponade. Using a similar model and indocyanine green dye curves, Frank et al. reported a decrease in both end-systolic volume and ejection fraction during tamponade but no change in other indexes of contractile function. They concluded that the decrease in pump performance was appropriate to the decrease in loading conditions produced by the tamponade. Craig et al. measured angiographic left ventricular volumes and reported an insignificant decrease in end-systolic volume but a significant decrease in ejection fraction and mean systolic ejection rate during tamponade. However, these authors thought that deterioration of contractile function during tamponade was not proved, as there were marked changes in loading conditions. Pegram et al. measured left ventricular diameter with ultrasonic crystals and reported a decrease in left ventricular end-
FIGURE 2. Individual data during relief of tamponade: (A) right atrial (RA) pressure, (B) end-diastolic volume (EDV), (C) end-systolic volume (ESV), and (D) ejection fraction (EF). The mean values for the seven patients during removal of the first 500 ml of fluid are represented by the open circles connected by the heavy dotted lines; asterisk indicates significant difference compared with the value before pericardiocentesis. The most dramatic decreases in RA pressures and increases in EDV and ESV were during removal of the first 200 ml of pericardial fluid. There was no significant change in EF during relief of tamponade.
systolic diameter during tamponade in all animals at intrapericardial pressures of 8 mm Hg and 10 mm Hg. In our patients, the average end-systolic volume doubled during relief of tamponade, an increase similar to that for end-diastolic volume. The average ejection fraction was normal in our patients during tamponade, and was unchanged after pericardiocentesis.

It is extremely difficult to compare left ventricular contractile state during tamponade to that without tamponade because of the marked difference in loading conditions and the higher level of catecholamine stimulation during tamponade.6,20 Nevertheless, the small end-systolic volumes and normal ejection fractions in our patients with tamponade suggest that the contractile state of the compressed left ventricle is increased or normal. Ejection fraction is influenced by loading conditions, but the effect of a decrease in preload with tamponade, which would decrease ejection fraction, would tend to be offset by the effect of a decrease in left ventricular ejection pressure, which would increase ejection fraction. Thus, the severe diminution in stroke volume in cardiac tamponade is secondary to the marked underfilling of the ventricles,13,17,18 and not to decreased left ventricular function caused by decreased coronary flow.5,21–23 or some other factor.

Our data might additionally explain a recent report by Martins et al.,24 who found that dopamine and isoproterenol given to patients with tamponade produced only minor increases in stroke volume (19% and 24%, respectively), in contrast to the large increases caused by isoproterenol in experimental animals.25,26 This small increase in stroke volume in man probably occurs because isoproterenol and dopamine were unable to significantly decrease the already extremely small end-systolic volumes demonstrated here in clinical tamponade.

Although the group reported here was relatively small, the patients were representative of those with cardiac tamponade seen on the medical service at this institution and reported elsewhere14 (excluding patients with penetrating trauma or aortic dissection). The hemodynamic and ventricular volume changes were uniform and of sufficient magnitude to be statistically significant. Although most of the patients had a malignancy, the one patient with idiopathic pericarditis behaved similarly to those with carcinoma. In patient 6, the high right atrial pressure after relief of tamponade and subsequent normalization of pressure after pericardiectomy suggest that an element of "effusive-constrictive" disease27 was present. However, the constriction in this case did not change the marked increase in stroke volume and end-diastolic volume during relief of tamponade. The changes reported here all occurred during relief of cardiac tamponade. One can always question whether directionally opposite changes would occur during the creation of cardiac tamponade; they probably would. There is only one report of cardiac tamponade being intentionally induced in man28 and practical and ethical considerations make it unlikely that additional cases will be reported.

For statistical purposes, tamponade patients were grouped according to how many milliliters of pericardial fluid were removed. It is unclear whether patients with different volumes of intrapericardial fluid have the same degree of relief of cardiac compression after withdrawal of equal amounts of pericardial fluid. The level of cardiac tamponade involves a complex interaction of numerous factors, including the amount of intrapericardial fluid,14,17,19 the pericardial compliance and rate of fluid accumulation,24 the intravascular volume status of the patient,17,29 inotropic state of the heart,2,20 and peripheral vascular resistance. Therefore, although the groupings were somewhat arbitrary, the uniformity of response supports the validity of these comparisons.

In conclusion, left ventricular end-diastolic and end-systolic volumes increased significantly while ejection fraction remained unchanged during relief of cardiac tamponade in man. These findings suggest that pump function of the left ventricle is well preserved during tamponade, and that the cardiovascular collapse seen in this condition is due to marked underfilling of the ventricle.

Acknowledgment

We gratefully acknowledge the inspiration and assistance provided by Tada Yipintosis, M.D., Ph.D., during the initial part of this study, the support of James Scheuer, M.D., and the secretarial assistance of Eleanor T. Schley and Janet Ellen Holwell.

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Left ventricular volume and function during relief of cardiac tamponade in man.
R Grose, M Greenberg, R Steingart and M V Cohen

Circulation. 1982;66:149-155
doi: 10.1161/01.CIR.66.1.149
Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
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Print ISSN: 0009-7322. Online ISSN: 1524-4539

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