Direct assessment of right ventricular transmural pressure

WILLIAM P. SANTAMORE, PH.D., MARTIN CONSTANTINESCU, M.D., AND WILLIAM C. LITTLE, M.D.

ABSTRACT Although the measurement of transmural pressure is important, calculation of transmural pressure is complicated by the difficulties in measuring pericardial pressure. Recently, flat balloons have been proposed to measure pericardial pressure. Over a wide range of volumes, right ventricular diastolic pressure and pericardial balloon pressure were similar in diastole, suggesting that the right ventricle is unstressed at physiologic volumes and that right atrial pressure can be used to estimate pericardial pressure. To evaluate these concepts and to assess indirectly the accuracy of measuring pericardial pressure using flat balloons, six canine hearts were examined postmortem. The pericardium was removed and the hearts were submerged in cold cardioplegic solution. Balloons were inserted into the right and left ventricles, and right and left ventricular pressure-volume curves were obtained. Right ventricular transmural pressures of 2.6 ± 0.5, 3.9 ± 0.9, 5.9 ± 1.4, and 8.9 ± 2.4 mm Hg were required to distend the right ventricle to 10, 20, 30, and 40 ml, respectively. For the left ventricle, transmural pressures of 3.4 ± 0.7, 5.4 ± 1.2, 8.6 ± 2.1, and 14.1 ± 3.8 mm Hg were recorded at volumes of 10, 20, 30, and 40 ml, respectively. Although the right ventricular transmural pressures were less than the left ventricular transmural pressures over the physiologic range, right ventricular transmural pressures were always positive and increased with increments in ventricular volume. Thus the right ventricle is not unstressed over the entire range of physiologic volumes, suggesting that pericardial balloon pressures may overestimate pericardial pressure and that right atrial pressure cannot be used to estimate pericardial pressure.


THE FILLING PRESSURE (or transmural pressure) for the cardiac chambers is the intracavity pressure minus the pericardial pressure. The determination of filling pressures in the heart in situ has been complicated by the difficulty in measuring pericardial pressure. Fluid-filled catheters have been used to measure pericardial pressure, but Tyberg et al. have clearly demonstrated the inadequacies of fluid-filled catheters to measure pericardial pressure, especially at lower or minimal pericardial fluid volume. Catheters are designed to measure fluid pressure, whereas the pericardial cavity is a potential space under normal circumstances and thus pericardial pressure may be best described as surface pressure. Smiseth, Tyberg, and associates, using flat balloons to measure pericardial pressure, observed that the right atrial and pericardial balloon pressures were almost identical. If this balloon measurement of pericardial pressure is accurate, then right atrial pressure can be used to estimate pericardial pressure and determine transmural filling pressures. Since right atrial and right ventricular diastolic pressures are almost identical, the balloon measurements of pericardial pressure suggest that right ventricular transmural pressure is nearly zero over a wide range of right ventricular end-diastolic volumes. If this is correct, the right ventricle is unstressed at physiologic volumes; that is, large changes in ventricular volume could occur with minimal or no changes in transmural ventricular pressure, and right ventricular filling is limited only by the pericardium.

To assess the accuracy of balloon measurement of pericardial pressure independently, we examined the hypothesis of an unstressed right ventricle in a postmortem canine preparation in which the transmural pressure could be measured directly. We compared the right ventricular pressure-volume curves to the left
ventricular pressure-volume curves. Our results indicate that significant transmural right ventricular pressures are necessary to distend the right ventricle, suggesting that the pericardial balloon may overestimate pericardial pressure and thereby underestimate right ventricular transmural pressure.

Methods
Six mongrel dogs (13 to 24 kg), free of heart worms, were deeply anesthetized with sodium pentobarbital (60 mg/kg iv). The hearts were removed and placed in cool (10°C) cardioplegic solution (sodium chloride 602 mg/100 ml, calcium chloride 23.1 mg/100 ml, potassium chloride 199.3 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. Via a No. 7F Sones catheter, 20 to 30 ml of cool cardioplegic solution were injected into the left anterior descending, circumflex, and right coronary arteries. Throughout the experimental procedures the hearts were kept submerged in the cool cardioplegic solution. Large helium balloons were inserted retrograde into each ventricle (figure 1). Via the pulmonary artery, a No. 11 helium balloon was inserted into the right ventricle and a ligature 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 tied around the aorta. The balloons had an unstressed volume in excess of 45 ml and were inflated and deflated several times to ensure their proper positioning within the ventricles. In one experiment, to prevent the balloons from herniating into the atrium, the tricuspid valve was loosely sutured closed through an atrial approach. The ventricular pressures were measured with fluid-filled catheters positioned within the ventricular balloons. The catheters were connected to pressure transducers (Cobe Laboratories, Lakewood, CO) and the pressures recorded on a physiologic recorder (Model VR-6 Electronics for Medicine/Honeywell, White Plains, NY). The zero pressure level was set midway between the apex and the base of the heart. During the experimental procedures, the pressure signals were sampled at 0.5 sec intervals, converted by analogue-to-digital processing, and stored in an Apple II+ computer.

Ten millimeters of cool water (10°C) were injected into the right ventricular balloon. The left ventricle was filled with cool water until left ventricular pressure reached 15 mm Hg. With a syringe pump, cool water was injected into the right ventricular balloon at a rate of 38.2 ml/min while right and left ventricular pressures were recorded. The right ventricular infusion was halted when right ventricular pressure equaled or exceeded 30 mm Hg. With the same approach, left ventricular pressure-volume data were recorded.

Data analysis. Since the hearts were submerged in cardioplegic solution, the difference (in mm Hg) between the reference level and the fluid height was subtracted from the measured left and right ventricular pressures. Ventricular volume was calculated as the initial volume in the ventricle (10 ml) plus the amount that had been injected into the ventricle. The pressures needed to distend the right ventricle to volumes of 10, 20, 30, 40, and 50 ml were compared with zero by a paired Student's t test. Data were summarized as the mean ± SEM.

Results
Figure 2 shows typical pressure-volume plots for the right and left ventricles from one experiment in vitro. In this example, at every ventricular volume right ventricular pressure was less than the left ventricular pressure. However, throughout the volume range, right ventricular pressure was different from zero.

Table 1 summarizes the results from the six experiments and presents the mean transmural ventricular pressures for the right and left ventricles. Transmural pressures of 2.6 ± 0.5, 3.9 ± 0.9, 5.9 ± 1.4, and 8.9 ± 2.4 mm Hg were required to distend the right ventricle to 10, 20, 30, and 40 ml, respectively. At each of these right ventricular volumes the distending pressure was significantly (p < 0.05) different from zero.

To further investigate the concept of an unstressed
ventricle, the minimal change in pressure for any given volume increment was calculated in each experiment. For the right ventricle, the minimal pressure change per volume change was 0.13 ± 0.06 mm Hg/ml with a range of 0.06 to 0.38. For the left ventricle, the minimal pressure change per volume change was 0.24 ± 0.07 mm Hg/ml with a range of 0.19 to 0.37. These pressure increments per volume increments were significantly different (p < 0.05) between the right and left ventricles.

Discussion

End-diastolic volume is one of the primary determinants of cardiac output. In turn, transmural end-diastolic pressure determines the end-diastolic volume. Thus the measurement of transmural pressure is important in evaluating ventricular function and assessing efficacy of therapeutic interventions. However, calculation of transmural pressure in intact animals and clinical situations is complicated by the difficulties in measuring pericardial pressure. Frequently, pericardial pressure is assumed to be zero, but this assumption may be inaccurate and can produce serious errors. Esophageal pressure has been used as an estimate of pericardial pressure. However, Fewell et al. showed that pericardial pressure was significantly different from esophageal pressure. Fluid-filled catheters have been used to directly measure pericardial pressure, but they cannot accurately determine pericardial pressure in the absence of pericardial fluid. Recently, a flat balloon inserted into the pericardium has been proposed as an appropriate method to measure pericardial pressure in the absence of pericardial fluid. Data obtained in dogs suggest that pericardial pressure measured in this manner closely approximates right heart diastolic pressures. If this is so, then right atrial pressure can be substituted for pericardial pressure to determine transmural left ventricular pressure. This finding also means that the right ventricular diastolic transmural pressure is close to zero, thus the filling of the right ventricle is restrained by the pericardium, not by the right ventricle itself.

To examine the concept of an unstressed right ventricle, we directly measured right ventricular pressure-volume curves in vitro. To circumvent any potential problems in measuring transmural pressure, the pericardium was removed so that the intracavity and transmural pressures were identical. A transmural pressure significantly different from zero (p < .05) was always required to distend the right ventricle to physiologic volumes. For small dogs (10 to 15 kg) the normal right ventricular end-diastolic volumes are in the range of 30 to 40 ml. We found that a substantial transmural pressure of 4 to 9 mm Hg was required to distend the right ventricle to a size of 20 to 40 ml. Thus, even in the low volume range, we observed right ventricular transmural pressures significantly different from zero. Furthermore, the right ventricular pressure always increased as right ventricular volume increased. Thus the right ventricle did not behave as unstressed ventricle. These results are in agreement with those of other experimental studies that directly examined ventricular interdependence and indirectly assessed right ventricular pressure-volume relationship. The findings showed positive transmural pressure and increasing transmural pressure with increasing ventricular volume.

The findings of our study are in conflict with the concept of an unstressed right ventricular and zero transmural diastolic pressure. Why do the results of our study conflict with the results reported by Smiseth, Tyberg, and associates, using the pericardial balloon to measure transmural pressure? First, their studies were performed in intact dogs, while our data were obtained from excised hearts. We used this preparation so that transmural right ventricular pressure could be determined directly and right ventricular volume measured accurately. We do not believe that these experimental differences explain the conflicting results, since fresh cardioplegic preserved hearts have pre-

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**TABLE 1**

<table>
<thead>
<tr>
<th>Right and left ventricular pressure-volume data</th>
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<tbody>
<tr>
<td></td>
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<tr>
<td>Right ventricular pressure (mm Hg)</td>
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<tr>
<td>10</td>
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<tr>
<td>2.6 ± 0.5*</td>
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<tr>
<td>Left ventricular pressure (mm Hg)</td>
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<tr>
<td>3.4 ± 0.7*</td>
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All data expressed as mean ± SE.

*p < .05, value significantly greater than zero.
viously been shown to accurately reflect diastolic properties of the intact heart. Furthermore, we excluded dogs with heart worms, whose right ventricles may be abnormally stiff.

Another possible explanation for the difference in our results and those obtained with the pericardial balloon is that the pericardial balloon overestimates pericardial pressure, thus underestimating right ventricular transmural pressure. This might occur for several reasons. Under normal circumstances, with little pericardial fluid the pericardial cavity is a potential space only a few microns thick. Thus the flat pericardial balloon that is several hundred microns thick may cause local distortion of the pericardial space. Based on physical principles, the flat balloons might systematically overestimate pericardial pressure, thereby systematically underestimating transmural cavity pressure.

The calibration of the flat balloons is also a potential problem since small variations in balloon volume may greatly affect the recorded pressure. Tyberg et al. have minimized this problem by carefully calibrating the balloons before and immediately after each experiment, using a special chamber. However, even with pre- and postcalibration the recorded pressures may still be uncertain because the fluid within the balloon may be distributed unevenly during the experimental procedure. This uneven distribution could cause measurement errors. Mann et al. have recently measured pericardial pressures using an air-filled balloon of a different design. In agreement with our observations, they found that right atrial pressure exceeded pericardial pressure by 2 to 7 mm Hg.

In summary, although the measurement of transmural pressure is important, calculation of transmural pressure is complicated by the difficulties in measuring pericardial pressure. The inadequacies of fluid-filled catheters to measure pericardial pressure have been clearly demonstrated. From flat balloon measurements, nearly identical pericardial and right ventricular diastolic pressure have been reported, suggesting that right ventricular transmural pressure is near zero. However, we found that a right ventricular transmural pressure other than zero is needed to distend the right ventricle to its normal size. This suggests that use of the flat balloon may overestimate pericardial pressure and that right atrial pressure cannot be accurately substituted for pericardial pressure in determining left ventricular transmural pressure. Since a fluid-filled catheter is not adequate to measure pericardial pressure, further investigation into methods of determining pericardial pressure is needed.

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