Atrioventricular nonuniformity of pericardial constraint

Douglas R. Hamilton,1,2 Rozsa Sas,2 and John V. Tyberg2

1Baylor College of Medicine, Department of Family and Community Medicine, Texas Medical Center, Houston, Texas 77098; and 2Department of Medicine and Department of Physiology and Biophysics and the Cardiovascular Research Group, The University of Calgary, Calgary, Alberta, Canada T2N 4N1

Submitted 4 February 2004; accepted in final form 30 April 2004

Hamilton, Douglas R., Rozsa Sas, and John V. Tyberg. Atrioventricular nonuniformity of pericardial constraint. Am J Physiol Heart Circ Physiol 287: H1700–H1704, 2004.—Physiologists and clinicians commonly refer to “pressure” as a measure of the constraining effects of the pericardium; however, “pericardial pressure” is really a local measurement of epicardial radial stress. During diastole, from the effects of the pericardium; however, “pericardial pressure” is really a local measurement of epicardial radial stress. During diastole, from the bottom of the y descent to the beginning of the a wave, pericardial pressure over the right atrium (PpRA) is approximately equal to that over the right ventricle (PpRV). However, in systole, during the interval between the bottom of the y descent and the peak of the y wave, these two pericardial pressures appear to be completely decoupled in that PpRV decreases, whereas PpRA remains constant or increases. This decoupling indicates considerable mechanical independence between the RA and RV during systole. That is, RV systolic emptying lowers PpRV, but PpRA continues to increase, suggesting that the relation of the pericardium to the RA must allow effective constraint, even though the pericardium over the RV is simultaneously slack. In conclusion, we measured the pericardial pressure responsible for the previously reported nonuniformity of pericardial strain. PpRA and PpRV are closely coupled during diastole, but during systole they become decoupled. Systolic nonuniformity of pericardial constraint may augment the atrioventricular valve-opening pressure gradient in early diastole and, so, affect ventricular filling.

dogs; diastole physiology; systole physiology; pericardium physiology; ventricular function; ventricular pressure; atrial function; atrial pressure

THE PERICARDIUM HAS A DISTINCTLY NONLINEAR STRESS-STRAIN RELATIONSHIP AND, WHEN ACTUALLY STRAINED BEYOND A CERTAIN LEVEL, IS EFFECTIVELY NONDISTENSIBLE (10–12, 19). THIS IMPLIES THAT SMALL CHANGES IN PERICARDIAL VOLUME WILL CREATE LARGE CHANGES IN PERICARDIAL CONSTRAINT (8). THIS LOW PERICARDIAL COMPLIANCE IS SIGNIFICANT WHEN THE MAGNITUDE OF PERICARDIAL CONSTRAINT IS CONSIDERED (16). SCALAR TERMS SUCH AS “PERICARDIAL PRESSURE” HAVE BEEN USED TO DESCRIBE PERICARDIAL CONSTRAINT; HOWEVER, THE FORCES BETWEEN THE PERICARDIUM AND THE EPICARDIUM ARE ACTUALLY AN EXCHANGE OF INHOMOGENEOUS, NONHYDROSTATIC RADIAL STRESSES. THESE FORCES DO NOT BEHAVE IN A HYDROSTATIC MANNER (2, 3, 14) EXCEPT IN THE PRESENCE OF A SEALED PERICARDIUM AND AN EXCESS OF PERICARDIAL FLUID (16, 22, 23).

IMMEDIATELY BEFORE ATRIAL CONTRACTION, BOTH THE ATRIUM AND VENTRICLE ARE RELAXED AND THE PRESSURE GRADIENTS AND FLOWS ACROSS THE ATRIOVENTRICULAR VALVES ARE SMALL. BECAUSE THE MOVEMENT OF THE HEART AT END DIASTOLE IS MINIMAL, MEASUREMENT OF PERICARDIAL PRESSURE IS NOT AFFECTED BY THE MOTION OF BLOOD OR MYOCARDIAL ACTIVATION. IT HAS BEEN SHOWN THAT PERICARDIAL PRESSURE IS RELATIVELY UNIFORM THROUGHOUT THE HEART AT END DIASTOLE (15, 16, 21). RECENT INVESTIGATIONS IN THIS LABORATORY HAVE SHOWN THAT THE MYOCARDIUM PLAYS A RELATIVELY MINOR ROLE IN THE DEVELOPMENT OF RIGHT ATRIAL (RA) AND RIGHT VENTRICULAR (RV) END-DIASTOLIC CAVITARY PRESSURE (PRA AND PRV, RESPECTIVELY), WITH LOCAL PERICARDIAL PRESSURE BEING DOMINANT (16, 26). MEASUREMENTS OF EARLY DIASTOLIC AND PANSYSTOLIC PERICARDIAL PRESSURE HAVE NOT BEEN REPORTED TO DATE, PERHAPS DUE TO LIMITATIONS IN TRANSDUCER TECHNOLOGY.

GOTO ET AL. (4) FOUND THAT PERICARDIAL STRAINS OVER THE RV AND RA DIFFERED SIGNIFICANTLY DURING SYSTOLE AND THAT CHANGES IN STRAIN OVER THE RV PARALLELED CHANGES IN RV VOLUME, WHEREAS CHANGES IN STRAIN OVER THE RA VARIED RECIPROCALLY WITH RV VOLUME. THESE FINDINGS SUGGESTED THAT RA AND RV PERICARDIAL PRESSURE (PpRA AND PpRV, RESPECTIVELY) MIGHT ALSO BE DIFFERENT. THE NONLINEAR STRESS-STRAIN AND CREEP CHARACTERISTICS OF THE PERICARDIUM (10–12, 19) WOULD MAKE ESTIMATION OF THE EXACT MAGNITUDE OF THESE TRANSPERICARDIAL STRESSES FROM MEASUREMENTS OF STRAIN DIFFICULT. ACCORDINGLY, WITH RECENT ADVANCES IN PERICARDIAL PRESSURE MEASUREMENT TECHNOLOGY (7), WE undertook to quantify the cycle-specific nonuniformity of pericardial constraint (4).

METHODS

THE PROTOCOL FOR THE ANIMAL EXPERIMENTS CONFORMED TO THE “GUIDING PRINCIPLES OF RESEARCH INVOLVING ANIMALS AND HUMAN BEINGS” OF THE AMERICAN PHYSIOLOGICAL SOCIETY AND WAS APPROVED BY THE INSTITUTIONAL ANIMAL CARE COMMITTEE.

AFTER RECEIVING 10–20 mg morphine sulfate (im), five mongrel dogs (20–25 kg) of both sexes were anesthetized with 12.5 mg/kg thiopental sodium. Anesthesia was maintained with 30 μg·kg–1·min–1 fentanyl while a 2:1 nitrous oxide-oxygen mixture was delivered by a constant-volume ventilator (model 607, Harvard Apparatus; Millis, MA). All dogs received a tidal volume of 15 ml/kg; a positive end-expiratory pressure of 2 cmH2O was applied. The animals were maintained at 37°C using a circulating-water warming blanket and a constant-temperature bath (model FE2, Haake; Berlin, Germany). The ECG was continuously monitored throughout the experiment.

With the dog in the supine position, a midline sternotomy was performed, and 100–200 ml of heparinized Ringer lactate solution was infused to maintain normal aortic pressure. The left lateral surface of the pericardium was opened, and the ventricles were delivered through this incision for purposes of instrumentation. The RV free wall segment length (Lrv) and RA appendage diameter (Ord) were measured by sonomicrometry (Triton Technology; San Diego, CA), as previously described (14). Two flat liquid-containing balloon transducers (7) were attached loosely to the epicardium with single stay sutures; one was positioned over the RV free wall, and the other was positioned just cephalad to the RA appendage. The RV balloon (3.0 × 3.0 cm) was fabricated from Silastic sheets (compound

Address for reprints and other correspondence: J. V. Tyberg, Faculty of Medicine, 3330 Hospital Dr, NW, Calgary, Alberta, Canada T2N 4N1 (E-mail: jtyberg@ucalgary.ca).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
We studied the diastolic interval from the bottom of the \( y \) descent (i.e., the early diastolic minimum in RA pressure) to the beginning of the \( a \) wave (pre-\( a \) wave) and the systolic interval from the bottom of the \( x \) descent (i.e., the early systolic minimum immediately after the \( c \) wave) to the peak of the \( v \) wave (see Fig. 1).

The regional difference in epicardial radial stress (pericardial pressure) was calculated by subtracting \( P_{\text{pRV}} \) from \( P_{\text{pRA}} \) during systole (until the beginning of the \( a \) wave) and diastole (until the beginning of the \( a \) wave). These \( P_{\text{pRA}}-P_{\text{pRV}} \) differences in pericardial pressure during systole and diastole were measured over a wide range of \( P_{\text{RA}} \) (i.e., hemorrhage through volume loading).

To determine the effect of changing epicardial radial stress on the pressure-dimension properties of the RA and RV, local pericardial pressures were subtracted from intracavitary pressures to produce transmural pressure (TM)-dimension relationships (see Figs. 3 and 4). The \( P_{\text{RA}-TM} \) loop was calculated by subtracting \( P_{\text{pRA}} \) from \( P_{\text{RA}} \) and the \( P_{\text{RV}-TM} \) loop was calculated by subtracting \( P_{\text{pRV}} \) from \( P_{\text{RV}} \).

RESULTS

A typical time-domain plot of the pressure and dimension signals (Fig. 1) shows that there is a significant difference between \( P_{\text{pRA}} \) and \( P_{\text{pRV}} \) during systole. This systolic increase in \( P_{\text{pRA}} \) while \( P_{\text{pRV}} \) decreases, thereby increasing the difference between the two pressures, suggests that the structure of the pericardium prevents the decrease in \( P_{\text{pRV}} \) from being communicated to the RA. Figure 2 shows \( P_{\text{pRA}} \) plotted against \( P_{\text{pRV}} \) for each animal. The plots illustrate two portions of the cardiac cycle, diastole (from the bottom of the \( y \) descent to the beginning of the \( a \) wave) and systole (from the bottom of the \( x \) descent to the peak of the \( v \) wave), at mean values of \( P_{\text{RA}} \) ranging from 2 to 20 mmHg. In all five animals, the results are consistent in that, during diastole, \( P_{\text{pRA}} \) and \( P_{\text{pRV}} \) rose, approximately in a 1:1 fashion, describing a line of identity. During systole, however, \( P_{\text{pRV}} \) decreased, whereas the \( P_{\text{pRA}} \) remained approximately the same or increased slightly (see Fig. 1 for an example of a time-domain plot).

In Fig. 2, systolic data from dogs 3–5 show \( P_{\text{pRV}} \) falling from a higher value than is true in dogs 1 and 2, thus shifting the systolic relationship rightward and causing it to intersect...
the diastolic relationship. However, systolic uncoupling is clearly demonstrated in these animals also, as evidenced by the systolic increase in the pericardial pressure difference (PpRA - PpRV; see Fig. 1). The regional difference in pericardial pressure, during systole, between the RV and the RA increased with volume loading (i.e., increasing PRA).

Figure 3 shows typical RA pressure-dimension loops showing PRA-dimension (top), PpRA-dimension (middle), and PRA-TM-dimension (bottom) relationships (mean PRA equaled 5 mmHg). The PRA-TM-dimension loop is counterclockwise (positive work) for the a loop (atrial contraction) and clockwise for the v loop (ventricular contraction).

Figure 4 shows typical RV cavitary pressure-dimension (top), pericardial pressure-dimension (middle), and transmural pressure-dimension (bottom) relationships with a mean PRA of 10 mmHg. Each plot consists of three consecutive superimposed cardiac cycles all going counterclockwise (i.e., performing positive work).

**DISCUSSION**

During diastole, from the bottom of the y descent to the beginning of the a wave, the pericardial pressure over the RA tracks the pericardial pressure over the RV, thus describing a 1:1 relationship between the two pressures. However, in systole, from the bottom of the x descent to the peak of the v wave, these two pericardial pressures are decoupled, with PpRV falling, whereas PpRA remaining constant or increasing. This systolic decoupling indicates a considerable independence between the RA and RV. That is, the systolic emptying of the RV lowers PpRV but PpRA continues to increase. This suggests that the relation of the pericardium to the RA must allow effective constraint even though the RV pericardium is momentarily slack and that the pericardial volume evacuated by the ejecting RV is not entirely available to the RA. This phenomenon is probably due to a combination of factors, among which are the rigidity of the cardiac exoskeleton that resists descent toward the RV and RA pericardial constraint.

In that RA and RV diastolic compliances are similar before atrial contraction, the fundamental “advantage” of atrial systole is that it decreases atrial compliance, thus redistributing blood toward the ventricle, completing ventricular filling (1, 16).
This end-diastolic increase in RV transmural pressure is partially achieved by the reduction in ventricular external constraint (i.e., $P_{pRV}$) because of the pericardial volume made available by the ejecting atrium (5, 9, 13). If the end-diastolic ventricular constraint was allowed to persist into early diastole, the early filling of the ventricle would not be so rapid, as is the case with pericardial effusions or restrictive cardiac disease (4, 22, 23). This may also be the case in some forms of atrial systolic dysfunction where early diastolic ventricular pericardial constraint is embarrassed by a pathologically distended atrium. It seems interesting that the atrial pericardial constraint is embarrassed by a pathologically distended atrium. The atrium makes its ejected volume (i.e., pericardial volume) available to the ventricle, yet the converse seems not to be true: in this study, the ejecting atrium permits almost-continuous venous return to the heart (9, 24). The increase in RA volume (1) with a commensurate decrease in RV epicardial constraint ($P_{pRV}$) permits the atrial storage of blood during systole and facilitates the rapid filling of the RV during early diastole. The atrium is permitted to act as a reservoir during systole, but apparently without impeding early diastolic filling, because $P_{pRV}$ is not increased. Recently, Kilner et al. (9) elegantly described how momentum is conserved during systole as blood accumulates in the atrium. Minimizing ventricular pericardial constraint while maximizing atrial pericardial constraint would seem to maximize the early diastolic atrioventricular valve gradient, as Goto and Le Winter (4) suggested earlier. Without this systolic atrioventricular decoupling, a high $P_{RV}$ at early diastole could embarrass ventricular filling, as seen with pericardial tamponade.

Goto and Le Winter (4) found that atrial pericardial stress-strain areas were almost invariant throughout the cardiac cycle with high $P_{RA}$. This seems to contrast with our findings showing that the largest fluctuations of pericardial pressure (both during diastole and during systole) occur with maximum volume load. This discrepancy is most probably due to the pericardium being loaded to the noncompliant (high volume) portion of its distinctly nonlinear stress-strain relationship, and therefore large strain fluctuations would not be expected with large stress fluctuations. This suggests that pericardial strain may not be a good indicator of transpericardial radial stress because of the nonlinear stress-strain characteristics of the pericardium (11, 12). Regardless, we find substantial RA systolic cavity strains with normal mean cavitary pressures (Fig. 3); therefore, pericardial strain is a poor indicator of cavitary volume.

As shown in Fig. 3, the $P_{RA}$-dimension loops measured in dogs are similar to those found in humans by Nagano et al. (18). In contrast, however, the RA transmural pressure ($P_{RA} - P_{pRA}$)-dimension loop (Fig. 3, bottom) shows the extremely small transmural pressures developed during the $v$ loop. These small transmural pressures during systole and early diastole were consistent throughout all volume states and all animals. (Among animals, the shapes of the $a$ loops were somewhat different, but systolic decoupling was always seen.) These small transmural pressures are notable when one considers the magnitude and range of cavitary pressures and dimension measured during this interval. Nagano et al. (18) and Arakawa et al. (1) measured left atrial compliance using biplane cineangiography to determine volume and the Brockenbrough technique to measure pressure. They found the diastolic left ventricular cavitary compliance to be two to three times larger than the left atrial compliance. We have previously shown that the end-diastolic transmural compliance of the RA in dogs and humans was significantly greater than its RV counterpart (16), which is consistent with the data shown here. To date, this difference in cavitary and transmural pressure-volume relationships has never been examined over the whole cardiac cycle.

Figure 4 demonstrates the importance of accounting for pericardial pressure when assessing the work that the RV does on the blood. Pericardial pressure can be a substantial fraction of RV intracavitary pressure during systole as well as during diastole (6). Furthermore, any attempt to measure RV end-systolic elastance (25) from the intracavitary pressure-dimension loop would be significantly affected by the upward displacement of the loop due to pericardial pressure. Figure 4 also illustrates the value of using high-fidelity pericardial balloons to calculate the transmural pressure of any cardiac cavity in that motion artifacts are absent.
In conclusion, $P_{\text{BRA}}$ and $P_{\text{BRV}}$ are closely coupled during diastole; however, during RV systole, they become decoupled in that $P_{\text{BRA}}$ rises even though $P_{\text{BRV}}$ decreases. This regional difference in pericardial constraint during systole becomes more pronounced with increasing $P_{\text{RA}}$.

The end-systolic decrease in ventricular pericardial constraint with concurrent increases in atrial pericardial constraint promotes the early diastolic filling of the ventricle.

REFERENCES


