Right Atrial and Right Ventricular Transmural Pressures in Dogs and Humans
Effects of the Pericardium

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Background To determine the transmural pressure-dimension relations of the right atrium (RA) and right ventricle (RV) before and after pericardectomy, six open-chest dogs were instrumented with pericardial balloons placed over the RA and RV free walls.

Methods and Results RA appendage dimensions and RV free-wall segment lengths were measured using sonomicrometry. Intact-pericardium RA and RV transmural pressures were calculated by subtracting the pericardial pressures (measured using balloons) from the cavitary pressures. Pooled data from six animals with pericardium intact indicate that at RA and RV cavitary pressures of 5, 10, and 15 mm Hg, RV pericardial pressure was 4.3±0.3, 8.6±1.0, and 13.3±1.5 mm Hg, respectively, and RA pericardial pressure was 4.8±0.3, 9.6±0.6, and 14.6±0.6 mm Hg, respectively (mean±SD). With calculated unstressed dimensions, the caviy cavity data were normalized to strain (in percent). We determined that in the dog, RV strain would increase by 14% and RA by 68% to maintain cavitary pressure at 10 mm Hg on pericardiectomy. To compare these results with clinical data, RV (n=7) and RA (n=6) transmural pressures were measured using balloons in patients (age, 19 to 76 years) undergoing cardiac surgery. RA transmural pressure of six patients was 1.0±1.5 mm Hg when central venous pressures (CVPs) ranged from 3 to 16 mm Hg. RV transmural pressure equaled 1.2±1.9, 2.3±1.9, and 3.4±2.0 mm Hg when CVP was 5, 10, and 15 mm Hg, respectively.

Conclusions Pericardial constraint (as evaluated by the ratio of pericardial to intracavitary pressures when CVP is 10 mm Hg) accounted for 96% of RA cavitary pressure in the dog and 89% in humans and at least 86% of RV cavitary pressure in the dog and 77% in humans. (Circulation. 1994;90:2492-2500.)

Key Words • pericardium • pressure

The role played by the pericardium in cardiac hemodynamics has stimulated the curiosity of physiologists for many years. Almost a century ago, Barnard1 concluded that the pericardium can be a significant constraint in filling of the heart. In a simple experiment, he isolated and inflated the pericardium of a dog with a bicycle pump and observed that it did not rupture until pressures of 950 to 1330 mm Hg were obtained. Barnard further observed that while within its pericardium, a cat's heart would hold 12 mL at a filling pressure of 20 cm H2O, and this increased to 23 mL when the pericardium was removed. After pericardiectomy, he noted, “This extra quantity of blood is chiefly received by the right auricle and ventricle.” From these and other experiments, Barnard concluded, “When a relaxed heart is subject to a venous pressure of from 10 to 20 mm Hg, the pericardium takes the strain and prevents dilatation of the heart beyond a certain point. Thus the mechanical disadvantages of dilated cavities and of a thinned wall are prevented.” Barnard's observations—that the parietal pericardium exerts a significant stress on the epicardium—are undeniable, but efforts to measure this constraint directly in the absence of pericardial effusions have yielded conflicting results.2-4 The direct measurement of pericardial pressure has been attempted through the use of open-end catheters,5,8 air-filled balloons,9-12 and liquid-filled balloons2,13-15 inserted into the pericardial space. The magnitude of pericardial pressure measured by these devices has ranged from zero to nearly the magnitude of the cavitary pressure of the chamber being investigated. As Tyberg et al16 originally proposed, the magnitude of pericardial constraint may be determined by measuring the fall in cavitary pressure (ie, left ventricular end-diastolic pressure17) after pericardiectomy, measured at the same cavity volume or strain. This rationale for determining the true magnitude of pericardial constraint has been used by several other investigators.17-19 Using liquid-containing balloon transducers over a wide range of physiological end-diastolic pressures, Traboulsi et al20 found that at physiological filling pressures, the magnitude of the right ventricular (RV) transmural pressure was only slightly above zero and, because of variability in the experimental data, difficult to resolve from zero. At the RV strain observed when the pericardium-intact cavitary pressure was 20 mm Hg, RV transmural pressure measured with the pericardium removed was only 2 to 3 mm Hg. Traboulsi et al20 also showed that the RV can undergo very large strains, even when exposed to small transmural pressures. Only when the RV strains were extreme did the magnitude of these transmural pressures rise above 5 mm Hg, and these were obtained only after the constraint of the pericardium had been removed. These results show that the pericardium is primarily responsible for the RV cavitary pressure-
volume (PV) relation but do not imply that the RV transmural PV relation is flat or has a slope of zero.\textsuperscript{20}

Nagano et al.\textsuperscript{21} measured left atrial (LA) PV relations in patients using biplane cineangiography to determine volume and the Brockenbrough technique to measure pressure. They found the diastolic left ventricular cavity compliance to be two to three times larger than the LA compliance. However, the right atrium (RA) is a thinner structure and would be expected to be more compliant than the RV. Previous studies performed in our laboratory have shown that when the constraint of the pericardium is properly measured by a balloon transducer,\textsuperscript{2} pericardial pressure (more precisely, epicardial radial stress) accounts for the substantial difference (at a given chamber dimension) between the cavity pressure recorded when the pericardium is intact and that recorded after the pericardium has been removed (Δleft ventricular end-diastolic pressure). Since the RV transmural PV relation is mostly dependent on the pericardium\textsuperscript{20} and since the RA is an even thinner, more distensible structure, it seems reasonable to suggest that the pericardium might also be a major contributor to the RA cavity pressure-dimension relation.

Thus, our hypothesis was that it is the effect of the pericardium that dominates the intracavitary pressure-dimension relations of the RA and RV and that the pericardium tends to equalize their respective compliances, regardless of the disparity in the thicknesses of the two structures.

Methods

Animal Studies

After receiving 10 to 20 mg morphine sulfate IM, six mongrel dogs (20 to 25 kg) of either sex were anesthetized with 12.5 mg/kg sodium thiopental. Anesthesia was maintained with 30 μg·kg\textsuperscript{-1}·min\textsuperscript{-1} fentanyl while ventilation with a 2:1 ratio of nitrous oxide to oxygen mixture was delivered by a constant-volume ventilator (model 607, Harvard Apparatus). All dogs received a tidal volume of 15 ml/kg, and a positive end-expiratory pressure of 2 cm H\textsubscript{2}O was applied. The animals were maintained at 37°C using a circulating-water warming blanket and a constant-temperature heating system (model FE2, Haake). The ECC was continuously monitored throughout the experiment.

With the dog in the supine position, a midline sternotomy was performed and 100 to 200 ml of heparinized Ringer’s 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 instrumentation. RV free-wall segment length (L\textsubscript{wm}) and RA appendage diameter (D\textsubscript{a}) were measured by sonomicrometry (Triton Technology) as previously described by Smisek et al.\textsuperscript{22} Two flat liquid-containing balloon transducers were attached loosely to the epicardium with single stay sutures; one was positioned over the RV free wall adjacent to the crystals, and the other was positioned cephalad to the sonomicrometry crystals on the RA appendage. The heart was repositioned into the pericardium and the pericardial margins were reapproximated using interrupted 3-0 silk sutures spaced 1 cm apart, with care taken to avoid compromising pericardial volume.\textsuperscript{18} RV and RA cavitory pressures were measured using 8F micromanometer-tipped catheters with reference lumens (model PR279, Millar Instruments) inserted through the internal jugular and femoral veins, respectively. Aortic pressure was measured with an 8F fluid-filled catheter (Cordis Corp) introduced through the femoral artery. Inferior vena caval and pulmonary arterial pressure pulmonary vascular constrictors (In Vivo Metric Systems) were also positioned on all dogs. The RV balloon (3.0×3.0 cm) was fabricated from Silastic sheets (compound AR131, lot 0170; Dow-Corning Corp) and attached to a 70-cm 8F cardiac catheter (Cordis Corp). The RA balloon (1.2×1.4 cm) was connected directly to a pressure transducer (model P23Db, Statham-Gould) through a 20-cm length of Silastic medical grade tubing (1.0 mm ID, 2.2 mm OD; Dow-Corning Corp). Calibration curves for both balloons were described before and after each experiment using a pressurized chamber that loaded the balloons with a membrane in a way that was similar to that developed by McMahon et al.\textsuperscript{2,23} No differences between preexperiment and postexperiment calibration curves were found in any experiment. Each balloon had a 3F micromanometer-tipped catheter (model PR249, Millar Instruments) positioned internally to provide a high-fidelity measurement of balloon pressure. Intradural balloon catheter-tip pressure transducers do not sense the artifacts and oscillations generated from catheter motion and are not affected by the frequency-dependent transmission characteristics of fluid-filled tubes. The dynamic response of this high-fidelity balloon system is linear with a flat frequency response to 200 Hz.

Conditioned signals were acquired on a computer (model 2551 80286/80287 12-MHz personal computer, Compaq Computer Corp) using a 12-bit analog-to-digital converter (model 2801, Data Translation). The analog signals were scaled using gain and offset amplifiers and then filtered with a seventh-order Cauer elliptic low-pass active antialiasing filter (model 675; breakpoint, 100 Hz; Frequency Devices) before being sampled at 200 Hz. The digitized data were subsequently analyzed on a computer (model ST-1144A Packard Bell 386X 80386/80387 Personal Computer), using analytical software developed in our laboratory (CYSOFT, Odessa Computer Systems Ltd) and statistical and graphics software (SPSS Inc) running on a multiscreen computer (model VAX 11/750, Digital Equipment Corp; VMS operating system).

After preparatory surgery, all animals were stabilized for 30 minutes before data were recorded. Mean RA pressure was manipulated from 0 to 25 mm Hg by adjusting the intravascular volume (Ringer’s lactate solution was infused or blood was removed through a large-bore catheter in an external jugular vein) or by manipulating the inferior vena caval or pulmonary arterial pressure pulmonary constrictors. Hemodynamic and sonomicrometry measurements were obtained continuously for 1 minute at each volume-load state (ie, after each incremental increase of mean RA cavitory pressure); each recording interval began with a 20-second control period. The ventilator was stopped at the end-expiratory position for several cardiac cycles during each recording interval. After mean RA pressure was reduced to 4 to 5 mm Hg by hemorrhage, the pericardium was opened widely to eliminate any external constraint on the right side of the heart (the lungs were also held back from the heart). After removal of the pericardium, the animal was again allowed to stabilize for 30 minutes, and previously described methods were used to manipulate mean RA pressure.

Human Studies

Seven patients (age, 19 to 76 years) scheduled for elective cardiac surgery gave informed written consent to participate in this study. The protocol had previously been reviewed and approved by a joint university-hospital ethics committee. Patient data are given in Table 1. No patient had valvular disease or RV hypertrophy. General anesthesia was induced with an intravenous combination of 2 to 7 mg midazolam, 500 μg sufentanil, and 0.08 to 0.10 mg/kg vecuronium bromide. Anesthesia was maintained with sufentanil (8 μg/kg IV) or fentanyl (25 μg/kg IV) and isoflurane or enflurane. A median sternotomy exposed the pericardial sac. A 7F Swan-Ganz catheter (model 93A-931H-7.5F Thermodilution Paceport Catheter with Thromboshield, American Edwards Laboratories) was inserted through a peripheral vein, and the tip was positioned in a pulmonary arterial branch. A 1-cm horizontal pericardial incision was made over the RV. Through this incision, a
3×3-cm, flat, liquid-containing Silastic balloon was inserted and positioned to lie over the RV free wall. The pericardial balloons were calibrated before gas sterilization. After sterilization, the previously determined volume of saline was injected into the balloons after they had been flushed to remove all air. A calibration curve for each balloon was also described immediately after each study, using the same methods described in the animal protocol. After the study, each balloon was placed into the balloon calibration chamber and was found to calibrate linearly within 1 mm Hg of the applied pressure. The volume of saline in the balloon was measured after the experiment and compared with the amount injected preoperatively to detect any inadvertent volume changes (no such changes were found).

Stay sutures were placed at the edges of the pericardiotomy incision and secured to the balloon catheters to prevent excessive motion. No attempt was made to close or resel the pericardium. The Swan-Ganz catheter was used to measure central venous pressure (CVP), RV pressure (measured from the RV pacing port), pulmonary arterial pressure, and pulmonary capillary wedge pressure. All pressures were measured using disposable semiconductor strain-gauge transducers (Trantec Disposable Pressure Transducer, American Hospital Supply) connected to a patient-monitoring system (model 78534C, Hewlett Packard). All transducers were calibrated using internal calibration signals and then checked after surgery, using a mercury manometer, before being disconnected from the patient-monitoring system. After surgery, all transducers were found to calibrate nearly to 100 mm Hg (see “Methods, Animal Studies” for the computer analysis).

Before each set of measurements was made, the pressure transducers were zeroed at the midplane of the left ventricle. Volume loading was achieved by an intravenous infusion of 1 to 2 L of Ringer’s lactate or normal saline. In two cases, 100 mL of 25% albumin was given in addition to the crystalloid solutions. Depending on the patient’s status during the surgical procedure, the mean CVP was increased 5 to 10 mm Hg from baseline during volume loading. In all except the first patient, the pericardial balloon was initially placed over the RA to measure RA pericardial pressure and then repositioned over the RV during volume loading. This balloon then remained over the RV throughout the volume loading. When the CVP had stabilized at its highest value after the volume loading, the balloon was moved back over the RA. This protocol allowed measurement of RA pericardial pressures at the lowest and highest CVPs obtained. RV pericardial pressure was measured continuously throughout volume loading.

### Data Analysis

#### Animal Studies

Only data collected at end expiration were analyzed. All high-fidelity micromanometer-tipped catheter signals were corrected to equal their corresponding pressures recorded via the fluid-filled catheters. This correction was performed using software that automatically adjusted the mean pressure of the micromanometer-tipped catheter to equal the mean of its fluid-filled counterpart. This method was completely automatic and therefore eliminated operator input; nevertheless, all pressure tracing corrections were inspected to ensure validity, although no retrospective adjustments were made. With the pericardium intact, transmural pressure was calculated as cavitary pressure minus pericardial balloon pressure. On pericardiectomy and retraction of the lungs, epicardial radial stress (ie, pericardial pressure) was reduced to zero, and therefore transmural pressure became equal to cavitary pressure.

All data were collected over 60-second intervals. The post-experiment analysis involved the extraction from the sampled data file of the last three late-diastolic data points (5-millisecond sampling interval) immediately preceding atrial contraction.

Unstressed cavitary dimensions were determined to provide a means of comparing the pericardiectomy-affected changes in dimensions between both chambers and among animal studies. Due to the asymptotic behavior of the RA and RV transmural pressure-dimension relations with respect to the dimension axis (ie, at low transmural pressures, the slopes approached zero), determination of the unstressed dimensions was difficult, and no single type of regression equation seemed satisfactory for analysis of all the data. Therefore, using transmural pressure-cavity-dimension (X) data before (ie, calculated transmural pressure) and after pericardiectomy, the unstressed cavitary dimension (X0) for each dog was calculated using three different least-squares regression techniques.

First, the natural logarithm of the transmural pressure (Ptrans) was used as the dependent variable in a linear regression analysis:

(1) \[ \ln(P_{\text{trans}}) = Mx + b \]

The 0.1 mm Hg and 1.0 mm Hg intercepts and slope of this linear regression equation were used to determine the unstressed cavitary dimension. The technique could not be used for data sets that contained negative pressures. (When the transmural pressures approached zero, the noise in the transducer systems occasionally produced individual negative values, even though the mean value of several nearby points was zero or slightly positive.)

Second, a three-parameter exponential function was used to determine the unstressed cavitary dimension:

(2) \[ P_{\text{trans}} = Ae^{bX} + C \]

Inspection of the raw data points and the corresponding three-parameter exponential regression line indicated that this regression technique followed the cavitary pressure-dimension relation quite convincingly. Furthermore, this regression method is capable of handling negative-pressure data points.

Third, a cubic equation was used:

(3) \[ P_{\text{trans}} = Ax^3 + Bx^2 + Cx + D \]

This regression equation was very effective at creating solutions that intersected the Ptrans=0 mm Hg line and thereby defined the unstressed dimension, but depending on the distribution of individual data points, in some animals the derived cavitary pressure-dimension relation did not model the behavior of a simple elastic vessel (ie, pressure did not always increase monotonically with dimension).

For RV and RA data from each dog, the value of the unstressed dimension defined by each regression equation was compared with the distribution of the pericardium-intact cavitary pressure-dimension data to determine which technique was best. To avoid any model-based bias, a pericardium-intact cavitary pressure-dimension relation was described by connecting the successive raw data points with straight lines as pressure increased. The unstressed dimension was chosen.
using the following rules. (1) If the pericardium-intact cavi-
tary pressure-dimension relation and the transmural regres-
sion curve intersected, this point of intersection was taken
as the unstressed dimension. (2) If the pericardium-intact cavi-
tary pressure-dimension relation and transmural pressure-dimen-
sion curve did not intersect, but the pericardium-intact cavi-
tary pressure-dimension relation came within 2 mm Hg of the
transmural pressure regression curve, that point (at which the
difference was less than 2 mm Hg) was taken as the unstressed
length. (3) If the pericardium-intact caviatory pressure-dimen-
sion relation and transmural pressure-dimension curve did not
intersect or approach within 2 mm Hg of each other, then the
smallest caviatory dimension measured was taken to be the
unstressed dimension.

The raw data for dog 1 are displayed in Fig 1 with a
reference line indicating the chosen unstressed dimension, X₀.
The percent strain for each cavity was calculated using the
unstressed dimension, X₀, in the following formula:

\[ \text{Strain (\%) = } \frac{(X - X₀)}{X₀} \times 100\% \] (4)

The RA and RV pericardium-intact caviatory pressure and
transmural pressure-strain curves for all dogs were compared,
using two methods designed to quantitate the horizontal and
vertical differences between these respective curves: (1) the
estimated increase in strain that would have been observed on
removal of the pericardium, had caviatory pressures of 5, 10,
and 15 mm Hg been maintained (see Fig 2A); strain was
determined by linearly interpolating between the pressure
values closest to the nominal caviatory pressure; and (2) the
estimated decrease in caviatory pressure that would have been
observed when the pericardium was removed had strain
remained constant (ie, \( \Delta \)end-diastolic pressure) was deter-
mimed at strains corresponding to caviatory pressures of 5, 10,
and 15 mm Hg (measured with an intact pericardium, see Fig
2B). The decrease in pressure was calculated by linearly
interpolating between pericardium-intact intracavitary pres-
sure closest to the nominal pressures (ie, 5, 10, or 15 mm Hg)
and subtracting the transmural pressure at the same strain.
The transmural pressure was calculated using the three-
parameter exponential regression equation.

**Human Studies**

RV end-diastolic transmural pressure was calculated as RV
caviatory pressure (measured from the pacing port of the
Swan-Ganz catheter) minus pericardial pressure. RA transmu-
ral pressure was calculated as CVP minus pericardial pressure.
Both pressures were measured just before the a wave for the
purpose of comparing simultaneous diastolic transmural pres-
sures. The pericardial balloon was connected to its respective
transducer via a 100-cm length of extension tubing. All data
were collected over 60-second intervals. All the transducers
were mounted on a rack to ensure that their zero-reference
ports remained at the same level. The absolute error in each
pressure measurement was found to be less than 1 mm Hg
when the automatic-balancing and gain-adjustment features of
the patient-monitoring system were calibrated against a mer-
cury manometer. Therefore, the error in the calculated trans-
mural pressures could have been no more than ±2 mm Hg.
These errors should have been random and should not have
affected the mean values of the pooled data. The postexperi-
ment analysis involved the extraction of the last three late-di-
astolic data points (5-millisecond sampling interval) immedi-
ately preceding atrial contraction. To compensate for the delay
introduced by the extension tubing, a correction of 50 milli-
seconds was used to temporally align the pericardial pressures
to those obtained from the Swan-Ganz catheter (the time shift
from the different Swan-Ganz ports was negligible). Any
significant motion-induced artifacts in the pressure tracings
were filtered using a 101-term, finite impulse-response, linear-
phase, digital, low-pass, time-corrected filter (breakpoint, 20
Hz; attenuation of 80 dB in a 5-Hz band; Remez exchange
algorithm; Signal Technology Inc).

**Results**

**Animal Studies**

The results from the six animals consistently showed
large changes in the chamber pressure-dimension relations
on the removal of the pericardium (see Fig 3). When the pericardium was intact, the transmural pres-
sures of both chambers were calculated using the dif-
ference between caviatory pressure and pericardial pres-
sure. After the pericardium had been removed, transmural pressure was equal to the intracavitary pres-
sure, assuming no constraint by other structure (eg, the
lungs). As is evident in Fig 3, the transmural pressure
calculated with the pericardium intact and the intracavi-
atory pressure after pericardectomy tended to form a
single curvilinear relation (with respect to strain) for all
dogs.

Table 2A shows the percentage increase in caviatory
strain after the pericardium was removed, compared at
various end-diastolic pressures (see Fig 2A). The RV
distended much less than the RA after pericardectomy.
Although the pericardium-on and pericardium-off pres-
sure-strain curves continued to diverge somewhat as
pressures increased (Fig 3), most of the increase in
strain with pericardiectomy was achieved at low pressures (ie, ≤5 mm Hg).

Table 2B shows the reduction in cavitary pressure (Δend-diastolic pressure) required to maintain the same strain after the removal of the pericardium (see Fig 2B). These reductions indicate that for both the RA and the RV, pericardial pressure was substantively greater than transmural pressure; thus, pericardial pressure is the major determinant of cavitary pressure of both chambers. Furthermore, over the range of strains normally observed with an intact pericardium (ie, pericardium-on

cavitary pressure <15 mm Hg), the transmural pressure-strain relation of the RV is almost flat, and because of the variability in these physiological measurements, we are unable to distinguish the RA transmural pressure from zero.

Fig 4 shows the balloon-measured RA (top) and RV (bottom) pericardial pressures, each plotted against their respective intracavitary pressures (data from all dogs). These plots show that for both the RA and the RV, intracavitary pressures at any volume are mostly accounted for by pericardial constraint.

Fig 5 represents the pooled data of all dogs and shows the respective RV and RA transmural pressures (both before and after pericardiectomy) plotted against cavitary strain. The RA is much more distensible than the RV. As is evident from a comparison of the data shown in Table 2B (see Fig 2B), both these plots show the nonphysiological behavior of the greatly dilated unconstrained RA and RV. Even the plot with the expanded normalized scale (Fig 5, bottom) greatly exceeds the physiological range because, for example at intracavitary pressures as high as 15 mm Hg, RA transmural pressure is only approximately 1 mm Hg and RV transmural pressure is only approximately 2 mm Hg (Table 2B).

**Human Studies**

The RA transmural and cavitary pressures measured in six patients are plotted versus CVP in Fig 6. The RA pericardial pressure rises almost equally with CVP, almost describing a line of identity. The slope (1.10) and intercept (−1.85) of the regression line (r = .95, P < .0005) describing this relation indicates that the RA transmural pressure is very small and, given the variability of the data, cannot be distinguished from zero. The calculated RA transmural pressure (CVP minus RA pericardial pressure) was 1.0 ± 1.5 mm Hg over CVPs ranging from 3 to 16 mm Hg. From these data, we cannot characterize the relation between RA transmu-
the whole range of CVPs obtained during the volume load (Fig 7). Table 3 gives pooled results of the calculated RV cavity, pericardial, and transmural pressures at CVPs of 5, 10, and 15 mm Hg.

**Discussion**

In this study of canine and human subjects, we find that the transmural pressure-dimension relations for both the RA and RV are relatively flat; that is, transmural pressures increase only minimally in the ranges of strains observed when the pericardium was intact. When intracavitary RA and RV pressures were less than 15 mm Hg, the measured and calculated transmural pressures were found to be small compared with pericardial pressure. Pericardial constraint, as evaluated by the ratio of pericardial to cavitory pressures when CVP equals 10 mm Hg, accounted for 96% of RA cavitory pressure in the dog and 89% in humans and at least 86% of RV cavitory pressure in the dog and 77% in humans. Our results imply that the normal heart (ie, with pericardium intact), with high RV end-diastolic pressures of 15 mm Hg, operates at no more than 5% to 7% strain.

This result—that the transmural pressures of the right heart chambers are normally very low—has been the most controversial implication of the observation that pericardial pressure is very similar to RV filling pressure. Controversy has sometimes focused on whether RV transmural pressure is or is not zero and whether there is a finite slope to the transmural PV relation (the implication being that if the slope is zero, the Frank-Starling law cannot apply and some new basis of cardiac mechanics must be found for the right heart). Our present results confirm our earlier observations that in the range of strains corresponding to normal intracavitary pressures, the transmural pressures that we measure are not different from zero. However, this is only a carefully circumscribed statistical statement that implicitly acknowledges the limited accuracy and/or precision of physiological experimental technique and is different from the positive statement that transmural pressure is zero. Much more important than the absolute level of transmural pressure is the question of the slope of the relation. Again, if only the range of strains corresponding to normal intracavitary pressures is considered, it cannot be claimed that the slopes are different from zero. However, if the much-wider open-pericardium range of strains is considered (see Figs 1, 3, and 5), it is obvious that the values of the RA and RV transmural slopes are not zero. The slope of the RA transmural relation is that of a very distensible chamber (transmural pressure increases approximately 3 mm Hg for a 30% increase in strain [see Fig 5, bottom]); however, from that fact it cannot be inferred that this slope is so small that the Frank-Starling mechanism is inoperable. Furthermore, using a simple expression to relate wall stress (\(\sigma\)) to transmural pressure (\(P_{\text{trans}}\)) in the RV outflow tract (ie, the law of Laplace for a sphere: \(\sigma P_{\text{trans}} = r/2t\), where \(t\) is thickness [mm] and \(r\) is radius [mm]), our data agree impressively with those of de Tombe and ter Keurs. At a strain of 15%, which corresponds to a rat trabeculae sarcomere length of 2.19 \(\mu\)m, de Tombe and ter Keurs determined that stress equaled 4.5 mN/mm\(^2\). Our data show transmural pressure to be 0.15 Mn/mm\(^2\) (1.1 mm Hg) and 0.77 Mn/mm\(^2\) (5.8 mm Hg) for the RA and RV, respectively. Using
these data, one can derive the ratio $\sigma/P_{\text{trans}}$ at a strain of 15% for the RA (4.5/0.15 = 30) and RV (4.5/0.77 = 5.8). In the case of the RA, a thickness of 1 mm and a radius of curvature of 40 mm produces a ratio $(r/2t)$ of 20. In the case of the RV, a thickness of 5 mm and a radius of curvature of 40 mm produces a ratio of 4. These $\sigma/P_{\text{trans}}$ ratios (calculated using de Tombe's data $\sigma$ with ours $P_{\text{trans}}$) is well within an order of magnitude of the $r/2t$ ratio (based on estimates of chamber dimensions). Therefore, we conclude that our estimates of both the RV and RA distensibilities agree very closely with the force-resting sarcomere length relations measured in rat trabeculae.\(^\text{31}\)

In each dog after pericardiectomy, RA end-diastolic cavitary pressure would have needed to have been reduced to 1 mm Hg or less to achieve the values of strain that had been observed when the pericardium was intact. Because marked hypotension frequently made this impossible, the calculated transmural pressure (ie, intracavitary pressure minus local pericardial pressure)-dimension data have been combined with directly measured pressure-dimension data (ie, those data recorded after

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**FIG 7.** Right ventricular (RV) end-diastolic pressure (A, open triangles), RV pericardial pressure (B, open diamonds), and RV transmural pressure (C, open circles) plotted against central venous pressure (CVP). Patient numbers are indicated. Lines indicate the results of linear regression analysis.
the pericardium had been opened widely). The fact that there is no discontinuity between the two sets of data strongly supports the validity of the balloon-transducer measurements of pericardial pressure.

We submit that it is the presence of the pericardium that tends to equalize the compliance of the two chambers. In the absence of the pericardium, both chambers dilate greatly. At a moderate RV filling pressure (eg, 10 mm Hg), our data predict that the RA would be dilated by a factor of 1.7 and the RV by a factor of 1.4, without a pericardium (or any other constraining structure [see Table 2A]).

Regarding the effects of pericardieotomy on atrial dimensions, it of course matters whether the chest is closed. In the experimental laboratory, when the dog's chest is opened via a median sternotomy and retracted and when the pericardium is opened widely, "normal" cardiac filling pressures result in markedly distended atria and right ventricles. These chambers distend so greatly that it is obvious that they could not be contained within a normal pericardium. Perhaps this simple laboratory observation continues to be the most persuasive argument for the conclusion that pericardial pressure is sometimes much more than ≈0 mm Hg, as early data appeared to suggest.

When the chest is closed, as in the postoperative patient, the situation is more complex. Although the pericardium is seldom completely reclosed at the end of cardiac surgery, the pericardium may not be completely removed from the atria, for example, and so could continue to constrain those chambers. Also, we suggest that the constraint exerted by the mediastinum and pleural surfaces about the heart could be significant.

It may be useful to consider why under tamponade conditions diastolic pressures in all four chambers appear to be equal. That during tamponade the pressures in left ventricle are not different from those in the other chambers implies to us that tamponade conditions reduce the volume of the left ventricle to the point that its transmural pressure is very low. If it were not so, even though pericardial pressures during tamponage are uniform, left ventricular pressure would have to be greater since caviatory pressure is always the sum of transmural pressure plus pericardial pressure. Therefore, with a normal pericardium (no excess fluid), left ventricular diastolic pressure is greater than the diastolic pressures in the other chambers by the amount of its transmural pressure (5 to 10 mm Hg), assuming that pericardial pressure is low and, at low to normal blood volumes, approximately uniform over the surface of each chamber.

In terms of fiber orientation, the atrium is a complicated structure and the distensibility of the base of the appendage may be quite different than the wall of the atrial chamber. The presence of trabeculae in the RA appendage may increase its stiffness relative to that of the RA free wall and may help explain the wide variability in atrial stiffness between animals (see Fig 5, top). This phenomenon requires further investigation.

The use of three different types of regression techniques to describe the transmural pressure-dimension relation resulted in differences in the unstressed dimensions. In all cases the regression equations modeled the caviatory stiffness quite well, in that the pressure increased monotonically with dimension and the raw data points were symmetrically distributed around the regression curves. The three-parameter exponential regression equation consistently converged onto solutions describing the transmural pressure-dimension relation with correlation coefficients greater than .83 and .92 for RA and RV, respectively. This equation was used to estimate RA and RV transmural pressure for later analysis. The parameters for the regression techniques (ie, logarithmic, exponential, and cubic) and the unstressed dimensions obtained by each technique are available on request.

This study has again shown that a small Silastic liquid-containing balloon can be used to estimate the epicardial radial stress imposed by the pericardium on the heart. The techniques used to measure epicardial radial stress (ie, "pericardial pressure") continue to be controversial. This is true despite the fact that there is almost unanimous acceptance of the proposition that the true value of "pericardial pressure" is equal to the isovolumic difference in end-diastolic pressures (Δend-diastolic pressure), before and after the removal of the pericardium. Furthermore, the controversy has persisted despite the fact that Smiseth et al showed that the pressure measured by a liquid-containing balloon transducer was equal to Δend-diastolic pressure, regardless of the volume of fluid in the pericardial space.

In conclusion, we find that during diastole, the pericardium influences the RA and RV in a major way. When the pericardium is intact, the transmural pressure of both chambers is quite small, but the pericardial constraint can be measured accurately with a small

### Table 3. Human Right Ventricular Pressures at Central Venous Pressures of 5, 10, and 15 mm Hg

<table>
<thead>
<tr>
<th>Central Venous Pressure</th>
<th>Transmural</th>
<th>Cavitary</th>
<th>Pericardial</th>
</tr>
</thead>
<tbody>
<tr>
<td>5 mm Hg</td>
<td>3.9±2.8</td>
<td>9.7±0.9</td>
<td>7.7±2.7</td>
</tr>
<tr>
<td>10 mm Hg</td>
<td>4.7±2.7</td>
<td>14.5±1.1</td>
<td>11.4±3.3</td>
</tr>
<tr>
<td>15 mm Hg</td>
<td>5.4±3.1</td>
<td>13.6±2.5</td>
<td>14.5±1.3</td>
</tr>
</tbody>
</table>

Mean right ventricular transmural, pericardial, and cavitary pressures calculated at central venous pressures of 5, 10, and 15 mm Hg using the regression equations of the data shown in Fig 7.

### Table 4. Comparison of Cavitary and Transmural Compliance Change In Percent Strain With Pressure Increase From 0 to 10 mm Hg

<table>
<thead>
<tr>
<th></th>
<th>RAtrans</th>
<th>RVtrans</th>
<th>(RA/RV)trans</th>
<th>RACav</th>
<th>RVcav</th>
<th>(RA/RV)cav</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean</td>
<td>118</td>
<td>28</td>
<td>5.2</td>
<td>21</td>
<td>6</td>
<td>6.4</td>
</tr>
<tr>
<td>SD</td>
<td>42</td>
<td>9</td>
<td>2.2</td>
<td>20</td>
<td>4</td>
<td>8.6</td>
</tr>
</tbody>
</table>

RA indicates right atrial; RV, right ventricular.

Linear cavity and chamber compliances were estimated by measuring the increase in percent strain caused by a pressure increase from 0 to 10 mm Hg.
Silastic liquid-containing balloon. Our animal data demonstrate that the unconstrained RA is much more compliant than the RV.

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Right atrial and right ventricular transmural pressures in dogs and humans. Effects of the pericardium.

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