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Pericardium modulates left and right ventricular stroke volumes to compensate for sudden changes in atrial volume

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Gibbons Kroeker, Carol A., Nigel G. Shrive, Israel Belenkie, and John V. Tyberg. Pericardium modulates left and right ventricular stroke volumes to compensate for sudden changes in atrial volume. *Am J Physiol Heart Circ Physiol* 284: H2247–H2254, 2003. First published January 30, 2003; 10.1152/ajpheart.00613.2002.—The pericardium may modulate acute compensatory changes in stroke volumes seen with sudden changes in cardiac volume, but such a mechanism has never been clearly demonstrated. In eight open-chest dogs, we measured left and right ventricular pressures, diameters, stroke volumes, and pericardial pressures during rapid (~300 ms) systolic infusions or withdrawals of ~25 ml blood into and out of the left atrium and right atrium. Control beats, the infusion/withdrawal beat, and 4–10 subsequent beats were studied. With infusions, ipsilateral ventricular end-diastolic transmural pressure, diameter, and stroke volume increased. With the pericardium closed, there was a compensatory decrease in contralateral transmural pressure, diameter, and stroke volume, mediated by opposite changes in transmural end-diastolic pressures. The sum of the ipsilateral increase and contralateral decrease in stroke volume approximated the infused volume. Corresponding changes were seen with blood withdrawals. This direct ventricular interaction was diminished when pericardial pressure was <5 mmHg and absent when the pericardium was opened. Pericardial constraint appears essential for immediate biventricular compensatory responses to acute atrial volume changes.

ventricular interaction; cardiac output; orthostatic hypotension; transmural pressure

ALTHOUGH IT IS GENERALLY ACCEPTED that the pericardium plays an important role in ventricular interaction, a mechanism to compensate for sudden changes in cardiac volume has not been clearly demonstrated. Such an acute mechanism may also be important in maintaining left (LV) and right ventricular (RV) outputs because, for example, increased RV output would quickly increase pulmonary and left atrial (LA) volume. The pericardium might produce an immediate compensatory response whereby both LV (LVSV) and RV stroke volume (RVSV) change in a way that would correct the error. Based on the work of Henderson and Prince (10), Hamilton (9), and Wiggers (18), Shabetai (15) stated, "Inasmuch as the pericardium influences ventricular interaction and thereby the instantaneous dimensions of the ventricles, it may help provide the means whereby the stroke outputs of the two ventricles are continuously adjusted by operation of the Frank-Starling mechanism to provide equal left and right heart outputs." Several other investigators (5, 6, 14) have anticipated this conclusion. With the use of an isolated cat heart preparation, Elzinga et al. (7) demonstrated that injecting liquid into the LV during diastole reduced the next SV of the RV and that this effect was more pronounced with the pericardium closed.

The aim of this study was to examine how the pericardium may mediate ventricular interaction on a beat-to-beat basis. Specifically, the pericardium may modulate changes in LVSV and RVSV to compensate for sudden changes in ventricular volume. Furthermore, if the pericardium is removed, there may be little or no direct ventricular interaction, and the ability to compensate rapidly for sudden cardiac volume changes may be limited. In addition, at low filling pressures, the low pericardial pressure may be associated with a diminished pericardial effect. We therefore studied the effects of sudden changes in atrial volume on ventricular pressures, dimensions, and outputs in the presence and absence of an intact pericardium. Our results suggest that the pericardium has a critical role in mediating rapid (i.e., next beat) compensatory responses to sudden changes in ventricular volume.

MATERIALS AND METHODS

Animal preparation. Experiments were performed in eight open-chest anesthetized dogs. Anesthesia was induced with 25 mg/kg iv thiopental and maintained with an infusion of 25 mg/ml solution (100 ml/h) of fentanyl citrate. The dogs were ventilated with a constant-volume respirator (model 607; Harvard Apparatus). A single-lead ECG was used for cardiac monitoring and body temperature was maintained in the physiological range with a heating pad. All animal care and treatment protocol conformed with the principles of the Canadian Council on Animal Care, and the work had full approval from the University of Calgary Animal Care Committee.

LV, RV, atrial, and aortic pressures were measured with 8-Fr micromanometer-tipped catheters (Millar Instruments; Houston, TX). Ventricular and aortic catheters were inserted

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via peripheral vessels and atrial catheters (3-Fr) directly. Ventricular and aortic pressures were referenced using their respective fluid-filled lumens (in turn, referenced to the midplane of the LV) and atrial pressures, by comparison to ventricular pressure values during diastole. Ascending aortic and proximal pulmonary arterial flows were measured with ultrasonic flowmeters (Transonic Systems; Ithaca, NY). LV endocardial diameters (anterior-posterior and septum to free wall) and the RV diameter (septum to free wall) were measured by sonomicrometry (Sonometrics; London, ON, Canada). Two flat, fluid-filled balloon catheters were loosely attached to the epicardium to measure pericardial pressure, one on the anterolateral surface of the LV and one on the RV. Pacing leads were placed on the RA and thoracic muscle wall. The heart was repositioned and the pericardium was reapproximated with interrupted loose sutures.

A pneumatic occluder (14–16 mm; In-Vivo Metrics, Healdsburg, CA) was placed around the inferior vena cava to decrease preload transiently. A large-bore catheter attached to a reservoir was inserted into the jugular vein to allow for volume loading and subsequent phlebotomy. The dogs were paced at ~90 beats/min.

A Plexiglas reservoir consisting of a fluid-filled compartment terminating in a 1.27-cm thin-walled metal cannula was used to infuse volume rapidly into the LA or right atrium (RA) (17). A spherical balloon inside the fluid compartment was manually inflated (20–30 ml air) to displace fluid from the compartment down the large exit tube into either chamber. Deflation of the balloon (by removing 20–30 ml of air) withdrew blood from the atria. Manual balloon inflations and deflations were timed with the ECG to occur during systole. An in-line flow probe (model 12N; Transonic Systems, Ithaca, NY) was attached to the exit tube to measure the volume withdrawn or injected.

Pressures, diameters, flows, and the ECG were amplified (model VR16; Electronics for Medicine/Honeywell), digitized at a sampling rate of 200 Hz, and recorded on a computer (Cardiosoft; Sonometrics). Sonomicrometry data were analyzed to remove the effects of skipping, and further analysis was accomplished by using CVSOFT (Odessa Computer Systems; Calgary, AL, Canada).

Experimental protocol. After instrumentation, the LV end-diastolic pressure (LVEDP) was adjusted to 6–8 mmHg and the dog was stabilized for several minutes. The reservoir was attached to either the RA or LA (the first atrium used alternated with each animal). The respirator was turned off for 20–30 s at end expiration. The reservoir balloon was then inflated for ~300 ms during systole. Hemodynamic parameters were recorded for 8–10 beats before and for 8–10 beats after inflation, and the animal was stabilized again. The balloon was then deflated to withdraw blood. Inflations and deflations were repeated 4–6 times. LVEDP was then decreased to 3–4 mmHg by vena caval occlusion and subsequently was increased to ~12 and 18 mmHg by volume loading. The inflation/deflation sequence was then repeated at each LVEDP. The full protocol was repeated with the reservoir connected to the opposite atrium and then again after the pericardium was opened widely.

Data analysis. End diastole was identified as the moment near the peak of the ECG R wave at which LV pressure began to increase rapidly. An index of the LV cross-sectional area (calculated by multiplying the two LV minor-axis diameters) was used to reflect LV end-diastolic volume. Transmural ventricular EDP was calculated by subtracting pericardial pressure from ventricular pressure. LVSV and RVSV were calculated by integrating the respective aortic and pulmonary arterial flows. SVs were related to either LV area or RV diameter at end diastole before, during, and after a volume infusion or withdrawal. Arbitrarily, during the steady-state control period, the mean value of RVSV was corrected to equal the mean value of LVSV, to compensate for differences in instrument sensitivity. Cumulative deficits or excesses in SVs were then calculated by comparing SVs after the infusion or withdrawal to those of the preceding control beats. To examine ventricular interaction further, we plotted the relationship between LV and RV diameters during infusions and withdrawals. Linear regression was performed, and the slope was plotted against pericardial pressure to show the effect of pericardial pressure and of pericardial opening on this indicator of ventricular interaction.

RESULTS

As illustrated in Fig. 1, LA infusion immediately increased peak LV systolic pressure and decreased peak RV systolic pressure. Aortic flow increased and pulmonary flow decreased.

Figure 2 shows a representative example of changes in end-diastolic ventricular, pericardial, and transmural pressures during infusion of fluid into the LA. With the infusion, LVEDP and RV end-diastolic pressure (RVEDP) increased. Pericardial pressure over both the LV and RV increased, but transmural LVEDP increased and transmural RVEDP decreased.

In Fig. 3, LVEDP, RVEDP, and transmural pressure are plotted against LV area and RV diameter during an LA infusion. LVEDP and area increased. Within 4–5 beats after the infusion, both LVEDP and LV area

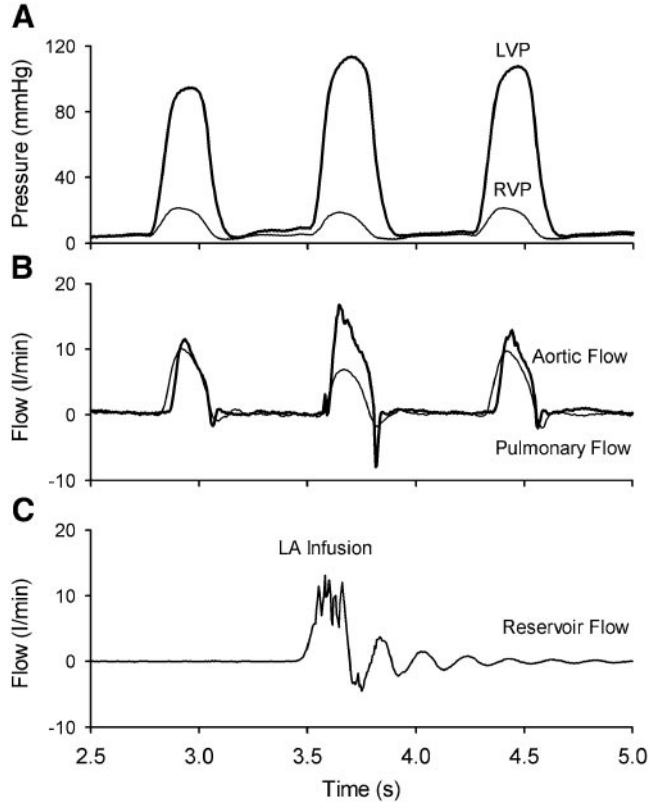

Fig. 1. Right ventricular (RV) and left ventricular (LV) pressures (RVP and LVP; *A*) and outflows (*B* and *C*) for the beat before, during, and after a left atrial (LA) infusion.

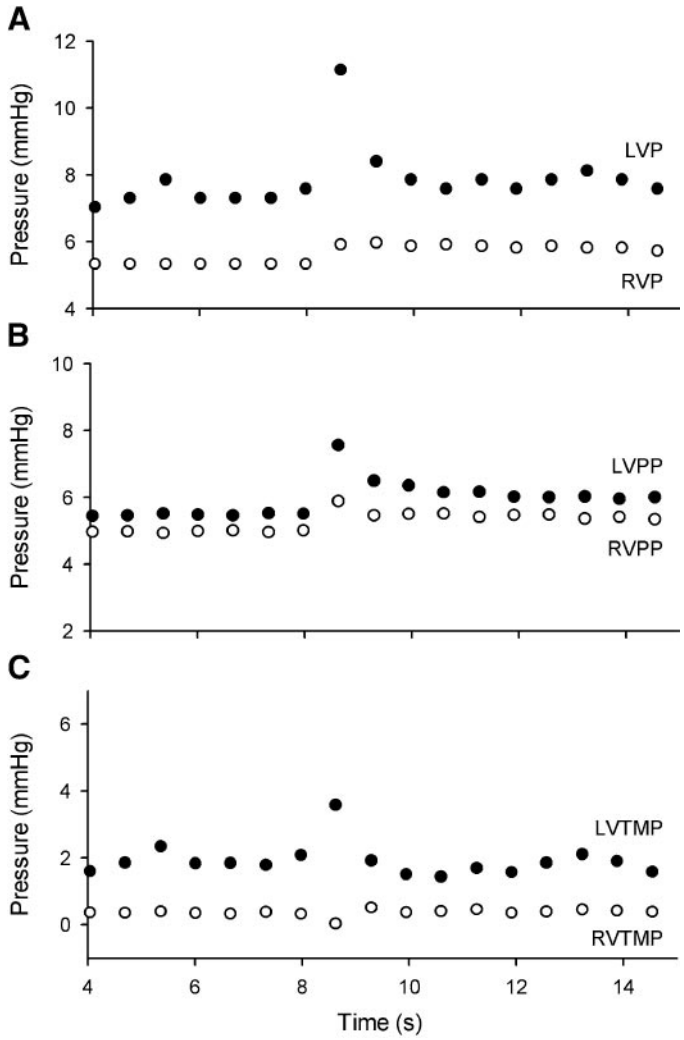

Fig. 2. Typical examples of a LA infusion. *A*: end-diastolic LVP and RVP. *B*: LV and RV pericardial pressures (LVPP and RVPP). *C*: LV and RV transmural pressures (LVTMP and RVTMP). All pressures were plotted against time. ●, LV values; ○, RV values.

returned to control values. Pericardial pressure over the left ventricle also increased, but the increase in LVEDP was greater, resulting in an increased transmural LVEDP. Right-sided changes were opposite those on the left. RVEDP changed little, but pericardial pressure over the RV increased, thereby decreasing transmural RVEDP. RV septum-to-free wall diameter also transiently decreased before returning to control values.

Figure 4, *A* and *B*, illustrates how LVSV and RVSV changed as functions of their respective dimensions during the same LA infusion. After the LA infusion, LVSV increased substantially and RVSV decreased, both returning to their control values within approximately three beats. Cumulative changes in LVSV and RVSV were calculated, compared with the infused volume, and plotted against time in Fig. 4*C*. When the cumulative excess LVSV was added to the cumulative deficit RVSV, the sum (22 ml) was similar to the infused volume (24 ml). In all cases, the response was rapid (75–85% of complete response occurred in the first postinfusion or postwithdrawal beat).

As shown in Fig. 5, when the pericardium was opened and the LA infusion was repeated, the results were markedly different. Although LVSV increased in a similar fashion to the pericardium-intact runs, there was no compensatory decrease in RVSV. In most cases, a small increase in RVSV occurred. The differences in RVSV and LVSV did not add up to equal the infused volume, as was true when the pericardium was intact. Several more beats (not shown) were required before control values were reached.

Similar results (not shown) were obtained for LA withdrawal, RA infusion, and RA withdrawal. In each case, when the pericardium was intact, the response was immediate and biventricular, and complete compensation was achieved, in that the sum of the cumulative LVSV and RVSV changes was approximately equal to the volume initially infused or withdrawn. The ipsilateral ventricle showed a compensation in the same direction as the volume change (for example, the RVSV decreased in response to a right-sided withdrawal). The contralateral ventricle showed an opposite change in SV. After the pericardium had been removed, the response of the ipsilateral ventricle was similar and in the direction to compensate for the infusion or withdrawal, but the response of the con-

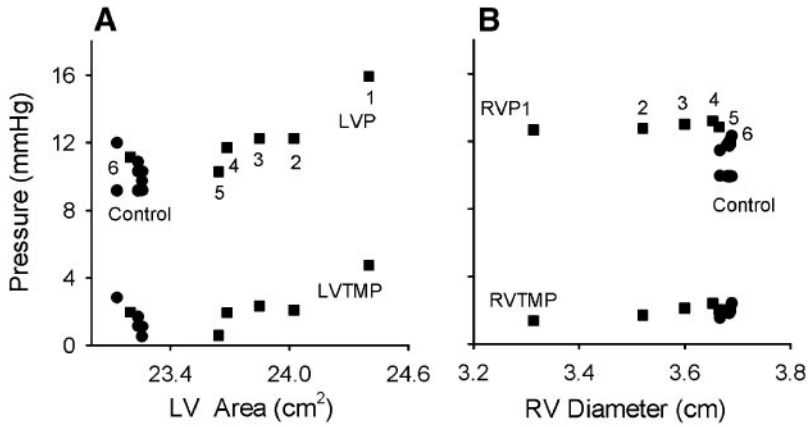

Fig. 3. *A*: LV end-diastolic pressure and transmural pressure plotted against LV area for an LA infusion. *B*: RV end-diastolic pressure and transmural pressure plotted against RV diameter. ●, Control beats before infusion; ■, control beats after infusion. Numbers indicate the beats after the infusion.

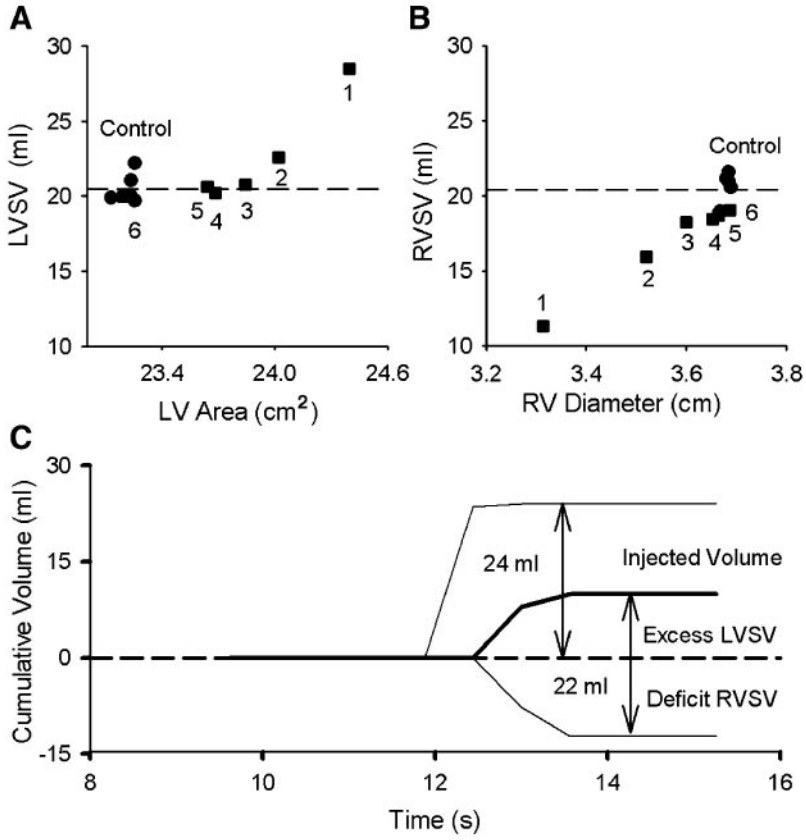

Fig. 4. *A* and *B*: changes in stroke volume (SV) against LV area and RV diameter, respectively, for an LA infusion. ●, Control SV before infusion; ■, control beats after infusion. Numbers indicate the beats after infusion. *C*: cumulative changes in SV plotted against time. Note that the sum of the excess LVSV and the deficit RVSV is approximately equal to the injected volume.

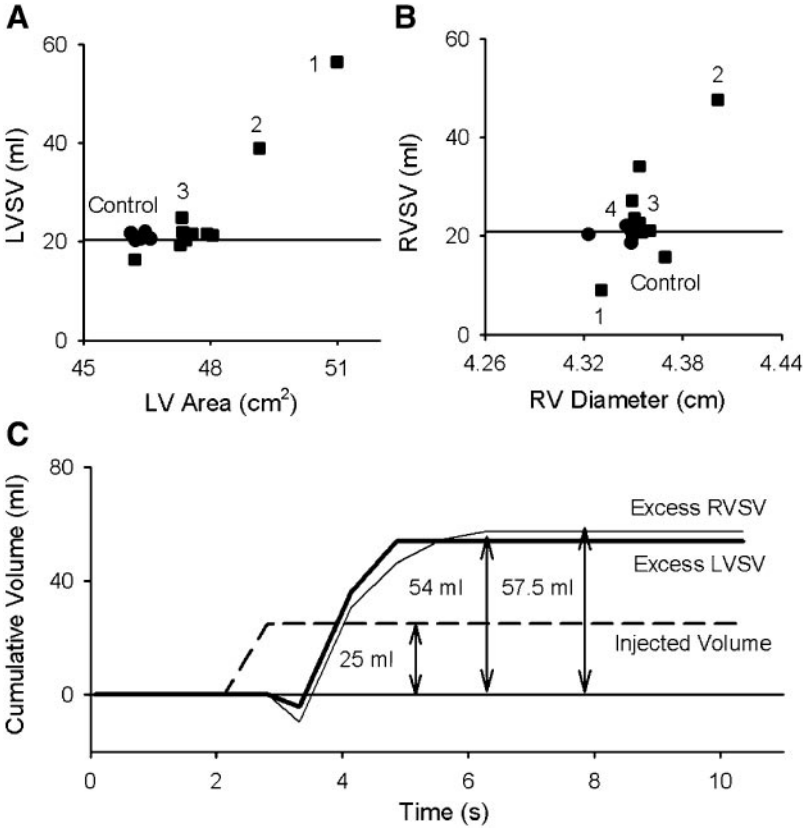

Fig. 5. LA infusion after removal of the pericardium. *A* and *B*: changes in SV plotted against LV area or RV diameter. Symbols and numbering are the same as in Fig. 3. *C*: cumulative changes in SV for a LA infusion with the pericardium removed. Note that the contralateral (i.e., RV) response is not compensatory and that the injected volume (25 ml) is not removed (57.5 − 54 = 3.5 ml) during the time of observation.

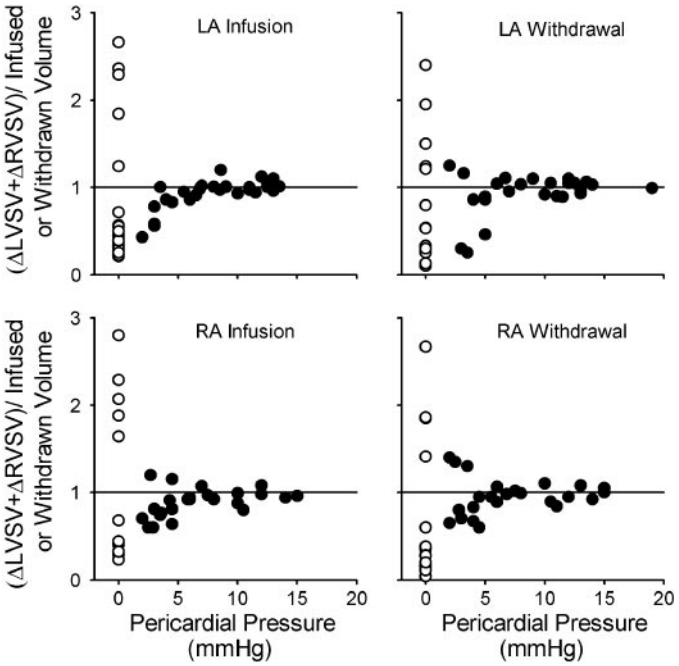

Fig. 6. Effect of pericardial pressure on the accuracy of the biventricular compensatory response [(ΔLVSV + ΔRVSV)/infused or withdrawn volume]. ●, Pericardium closed; ○, pericardium open. Data shown are combined from all 8 dogs. Note that compensation equals ~1.0 when the pericardium is closed and pericardial pressure exceeds ~5 mmHg.

tralateral ventricle was unpredictable and not compensatory, as illustrated for LA infusion in Fig. 5.

To assess the degree of the biventricular compensatory response, with and without the pericardium, we plotted the sum of the cumulative changes in LVSV and RVSV as a fraction of the infused or withdrawn volume (Fig. 6). Compensatory SV changes were added. For example, for the LA infusion data, the cumulative excess in LVSV was added to the cumulative deficit in RVSV; with precise compensation, the sum of the cumulative excess in LVSV and the deficit in RVSV would be equal to the infused volume and the ratio would equal 1. These ratios were plotted against ipsilateral (with respect to the infusion or withdrawal) end-diastolic pericardial pressure, which was varied by volume loading and vena caval occlusion. When the pericardium was intact and pericardial pressure exceeded ~5 mmHg, the ratio was ~1, indicating excellent equalization of LV and RV outputs and compensation for the initial infusion or withdrawal. When pericardial pressure was less than ~5 mmHg, compensation was less precise. Once the pericardium was opened (pericardial pressure = 0 mmHg), compensation did not occur.

To evaluate the possibility that most of the compensation was brought about by the ipsilateral ventricle, we plotted, in a similar way, the change in the SV of just that ventricle as a fraction of the infused or withdrawn volume (results not shown). With the pericardium intact, the values of the ratio are much less than l, indicating that the compensatory response of the contralateral ventricle was substantial (see Fig. 6). With the pericardium opened, compensation remained poor (i.e., the ratio did not approach 1).

With the view that the essence of direct ventricular interaction is complementary between ventricular volumes and to explore the role of the pericardium further, we plotted the relationship between left and right septum-to-free wall diameters. With the pericardium intact, an inverse relationship was seen. Because of the constraint imposed by the pericardium, as the left side diameter increased, the RV diameter decreased (Fig. 7*A*). This is compared with an example with the pericardium removed (Fig. 7*B*). Data with the pericardium opened also tended to show more scatter (lower R values), which suggests that the complementary relationship seen with direct ventricular interaction is lost when the pericardium was opened. After linear regression, the slopes of these relationships were plotted against pericardial pressure for all four interventions (Fig. 8). When pericardial pressure exceeded ~5 mmHg, the slopes were negative, indicating an inverse relationship between left and right diameters. When pericardial pressure was <5 mmHg or when the pericardium was opened, the inverse linear (i.e., complementary) relationship between left and right diameters was lost.

Figure 9 shows the change in pericardial pressure (see Fig. 2*B*) after either an LA or RA infusion or withdrawal, plotted against initial pericardial pres-

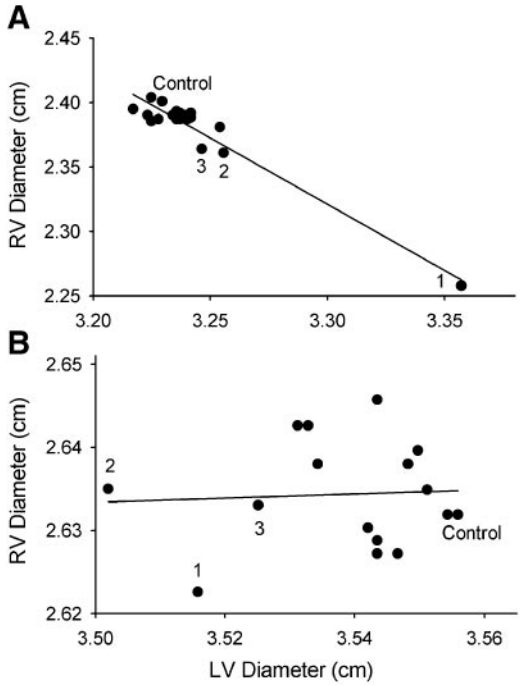

Fig. 7. *A*: typical example of the inverse, complementary relationship seen between left and right septum-to-free wall diameters (D_{LV} and D_{RV}) for a right-sided withdrawal with the pericardium intact. Note that an increase in one diameter causes a corresponding decrease in the second diameter. *B*: typical example of the same intervention with the pericardium removed. Note that the inverse relationship is lost. In both cases, control points are labeled and the first 3 beats after the withdrawal are numbered.

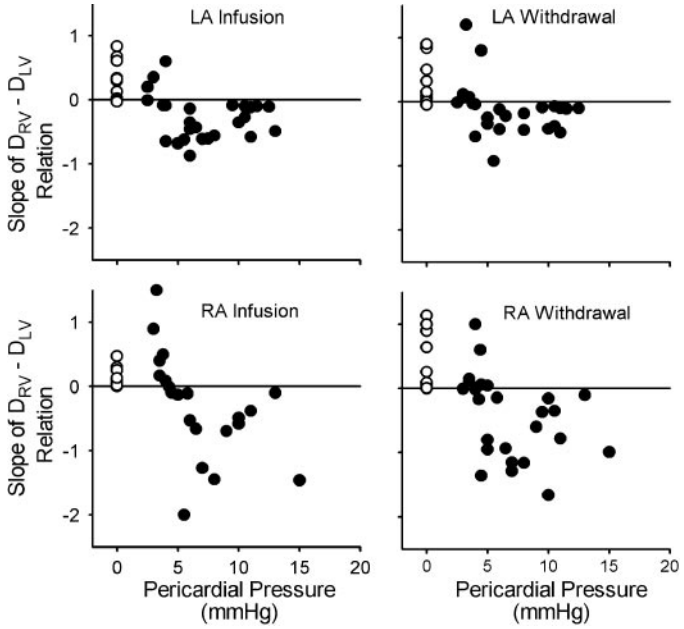

Fig. 8. Slope of the relationship between D_{LV} and D_{RV} (see Fig. 7) plotted as a function of pericardial pressure for the 4 interventions. ●, Pericardium on; ○, pericardium off. Data shown are combined from all 8 dogs. Note that when the pericardium is removed or when pericardial pressures are low, the inverse relationship (negative slope) between the diameters (i.e., the ventricular interaction) is diminished or lost.

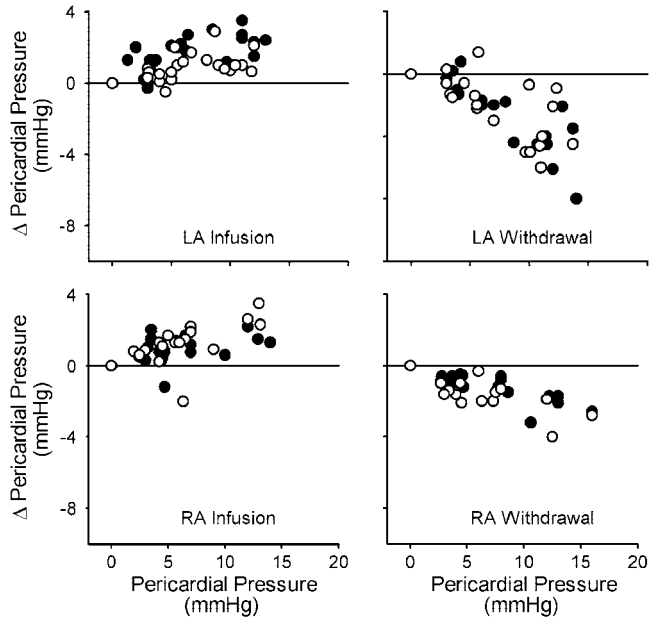

Fig. 9. Plots showing the change in pericardial pressure after either a LA or right atrial (RA) infusion or withdrawal (see Fig. 3) plotted against initial pericardial pressure. ●, LVPP; ○, RVPP. Data shown are combined from all 8 dogs. In almost all infusion cases, both the LVPP and RVPP increased, whereas in almost all withdrawal cases, both the LVPP and RVPP decreased.

sure. For LA and RA infusions, pericardial pressure over both ventricles increased by approximately the same amount. For LA or RA withdrawals, pericardial pressures decreased similarly over both ventricles. However, these uniform changes in pericardial pressures produce opposite changes in transmural LVEDP and RVEDP, as illustrated by the example in Fig. 2*C* and as summarized in Fig. 10. For infusions at pericardial pressures of 5 mmHg and higher, the ipsilateral transmural pressure increased, whereas the contralateral transmural pressure decreased. When pericardial pressures were <5 mmHg, the responses were less predictable. When the pericardium was opened, both LV and RV transmural pressures increased. Similar trends were seen with withdrawals. When pericardial pressure was >5 mmHg, ipsilateral transmural pressure decreased, whereas contralateral transmural pressure increased. When pericardial pressures were <5 mmHg, this compensatory response was less predictable. When the pericardium was opened, both LV and RV transmural pressures decreased.

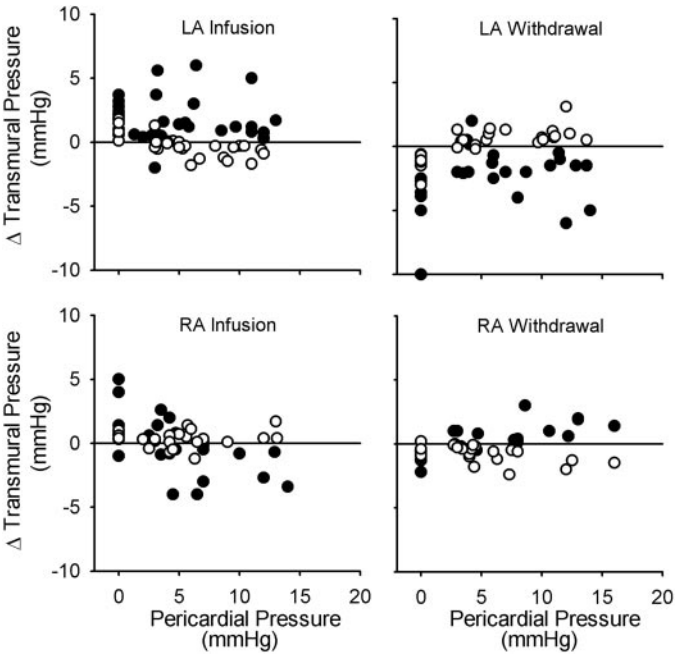

Fig. 10. Plots showing the change in transmural pressure after either a LA or RA infusion or withdrawal (see Fig. 3) plotted against initial pericardial pressure. ●, LVTMP; ○, RVTMP. Data shown are combined from all 8 dogs. In almost all infusions with initial pericardial pressures above 5 mmHg, the ipsilateral transmural pressure increased and the contralateral transmural pressure decreased. For almost all withdrawals (>5 mmHg), the ipsilateral transmural pressure decreased and the contralateral transmural pressure increased. When the pericardium was removed, this compensatory relationship was lost. When pericardial pressures were <5 mmHg, this relationship was less precise.

DISCUSSION

The present study clearly demonstrates the important role the pericardium plays in the responses to sudden changes in volume of one or the other atrium. When the pericardium was intact, a sudden increase in the volume of one atrium caused an increase in output of the ipsilateral ventricle and a compensatory decrease in that of the contralateral ventricle. Conversely, a decrease in the volume of one atrium caused

a decrease in the output of the ipsilateral ventricle and a compensatory increase in that of the contralateral ventricle. The sum of the excesses and deficits in SVs closely matched the infused and withdrawn volumes. These responses were mediated by opposite changes in RV and LV transmural EDPs. This direct ventricular interaction was diminished when pericardial pressure was <5 mmHg and was absent when the pericardium was opened. In addition, complementarily between LV and RV dimensions, the salient characteristic of direct ventricular interaction was shown to be dependent on the presence of the pericardium and the value of pericardial pressure. Thus via a mechanism that is sometimes termed feedforward control (14a), the pericardium provides a direct mechanical link that produces immediate compensatory changes in the SV of each ventricle.

Results of this study can best be interpreted by emphasizing the similarity of the pulmonary and systemic circulations. Reasoning from teleology, an increase in LV output and a decrease in RV output both compensate for an increase in LA volume, as RV output represents the input to the LA. Similarly, an increase in RV output and a decrease in LV output both compensate for an increase in RA volume, as LV output ultimately represents the input to the RA.

The mechanisms we have demonstrated may pertain to orthostatic hypotension, the symptomatic decrease in aortic blood pressure that occurs immediately after a person assumes an upright position, having been seated or supine. (We do not intend to suggest that our results pertain in any way to syncopal or presyncopal episodes that occur minutes after the initiation of head-up tilt, sometimes potentiated by pharmacological intervention, or to the classic faint of the guardsman standing under the hot sun.) In our study, RA withdrawal simulated the abrupt reduction in venous return caused by standing up and the compensatory response of the LV was to increase its SV immediately. In people whose pericardial pressure was sufficiently high, such an increase in LVSV would tend to minimize any decrease in aortic pressure. Our findings in the presence of low pericardial pressure may also help to explain the observation that endurance athletes are particularly susceptible to orthostatic hypotension (12). We might stipulate that endurance training causes the heart and pericardium to enlarge and that athletes' hearts become smaller at rest. Therefore, we suggest that their pericardia are relatively slack and pericardial pressures are low. If so, the compensatory response of the athlete at rest may be less effective than that of the untrained resting individual. Although Levine et al. (13) explained their observations by a shift in the Starling curves (pressure-volume curves), it can now be suggested that these athletes had slacker pericardia and thus less effective pericardium-mediated compensation to the sudden decrease in venous return, because their pericardial pressures were too low, with little pericardial constraint to produce effective coupling. If pericardial pressure is already near zero, a reduction in right heart volume cannot decrease pressure much further, so LV transmural pressure cannot increase substantially. Thus endurance athletes might lack the mechanism that results in an immediate increase in LVSV. Cardiac output would increase only later, after reflex mechanisms decrease venous capacitance and increase heart rate.

Orthostatic hypotension is common after donating blood, excessive diuresis, or returning from space travel (16), interventions that decrease blood volume. Our data suggest that orthostatic hypotension might be aggravated in conditions associated with low pericardial pressure and those in which the pericardium is enlarged, relative to the heart. Orthostatic hypotension is common in patients with treated heart failure but, because there are many potential causes of hypotension including excessive vasodilation, no pericardial mechanism has yet been identified. Orthostatic hypotension is usually alleviated by interventions that increase blood volume (which tend to increase cardiac volume and pericardial pressure), consistent with our speculation that pericardium-modulated interaction may play a role.

Before this study, direct ventricular interaction may have been best illustrated by the observation that, after pulmonary embolization in the presence of a closed pericardium, volume loading increased RV volume, which caused pericardial pressure to increase and transmural LVEDP to decrease (2). Consistent with the decrease in transmural LVEDP, LV end-diastolic volume and performance (i.e., stroke work) decreased. Thus the increase in RV volume was met with a complementary decrease in LV volume. In marked contrast, after the pericardium had been removed, volume loading increased (transmural) LVEDP, and end-diastolic volume and performance, as would have been expected in the absence of ventricular interaction (3). In the present study, we were able to demonstrate a more rapid response than those demonstrated by previous studies (2, 3).

The mechanism of this pericardium-mediated (3) direct ventricular interaction may be implicit in the mechanical properties of pericardial tissue as demonstrated by Lee and Boughner (11). The stress-strain curve of the pericardium is approximately bilinear. At low strains, the curve is quite flat, but past a certain strain, the curve becomes quite steep, with significant stress. Thus, at low heart volumes (and low pericardial pressures), there is little constraint by the pericardium, and it is easy to increase cardiac volume. However, when the pericardium becomes taut (at pericardial pressures of ~5 mmHg and higher), it forms a relatively unyielding band around the minor axis of the heart. The pericardium will then tend to fix the cross-sectional area of the heart and cause direct ventricular interaction. Thus an increase in the cross-sectional area (i.e., volume) in one ventricle necessarily causes an increase in pericardial pressure and a decrease in the transmural pressure and the area of the opposite ventricle. This was seen when pericardial pressure exceeded ~5 mmHg. Below this pressure, when the pericardium was relatively slack, this complementary

response was not seen. As pericardial pressure approached zero, the response became similar to that seen with the pericardium removed; the changes in transmural pressures were no longer opposite, there was no complementary change in dimensions, and the sum of the excess and deficit in SVs did not equal the infused or withdrawn volume. If the pericardium modulates compensation and equalization, one would predict that this compensation would be less complete when pericardial pressure is low.

It will be recalled that some people are born without pericardia and that their cardiovascular function seems to be normal. Against this implicit objection, two points must be made. First, we do not suggest that the inferior performance of the open-pericardium heart would be fatal or even dangerous in that the ipsilateral ventricle would, in time, minimize the excess or deficit by using its own intrinsic Frank-Starling mechanisms. An individual without a pericardium might rather simply lack the rapid, biventricular, exquisitely precise compensation that the presence of the pericardium seems to afford. Furthermore, such an individual might develop other adaptive mechanisms or become inured to the deficiency. Second, different from in the dog, the human mediastinum seems to effect considerable constraint, even when the pericardium is open. In studies of ventilated patients during heart surgery, we have data to show that estimated transmural LVEDP is a better measure of preload, even after the pericardium has been opened, implying that external constraint and coupling remain after pericardiectomy (4).

The purpose of this study was to clarify the mechanism of ventricle-ventricle interaction in response to acute changes in atrial volumes. We did not, however, attempt to define the contribution of atrium-ventricle interaction, which we previously demonstrated to be important and may have had a contribution in this study (14).

In conclusion, this study has demonstrated a significant role for the pericardium in compensating for sudden perturbations in cardiac volume. Although this is a role that has been attributed to the pericardium by other investigators, the mechanism has been difficult to demonstrate until now, particularly under nonpathological conditions. In this study, by using rapid volume infusion or withdrawal, we were able to demonstrate direct ventricular interaction on a beat-to-beat basis under circumstances that might occur normally. Infusion increased pericardial pressure and withdrawal decreased it. We demonstrated that these changes in pericardial pressure brought about compensatory changes in the end-diastolic transmural pressure of the contralateral ventricles, which changed their SVs by the Frank-Starling mechanism. This direct ventricular interaction was lost when the pericardium was removed and was diminished when pericardial pressure was low.

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