Left-to-right systolic and diastolic ventricular interactions are dependent on right ventricular volume

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Dickstein, Marc L., Koji Todaka, and Daniel Burkhoff. Left-to-right systolic and diastolic ventricular interactions are dependent on right ventricular volume. *Am. J. Physiol.* 272 (*Heart Circ. Physiol.* 41): H2869–H2874, 1997.— Three-compartment elastance modeling predicts that the magnitude of gain is solely dependent on the ratio of free wall and septal elastances. However, when nonlinearities in pressure-volume relationships are considered, the same model predicts that gain is load dependent. We therefore studied left-to-right ventricular interactions in the isolated cross-perfused canine heart preparation to determine whether, in fact, right ventricular volume modulates left-to-right ventricular interaction. We found that left-to-right systolic gain increased from 0.035 ± 0.022 to 0.073 ± 0.017 ($P = 0.003$) and left-to-right diastolic gain increased from 0.067 ± 0.050 to 0.186 ± 0.097 ($P = 0.03$) in response to increased right ventricular volume. This degree of volume dependency of gain is predicted by the three-compartment model when measured nonlinearities in time-varying elastance are taken into account. Future studies will need to account for changes in loading conditions when interpreting changes in systolic and diastolic interactions.

ventricular interdependence; pressure-volume relationship; cardiac mechanics; cardiovascular model

IT HAS LONG BEEN KNOWN that the function of one ventricle directly impacts on the function of the opposite ventricle. These direct ventricular interactions occur throughout the cardiac cycle but tend to have opposite effects on ventricular function during systole and diastole. During systole, a portion of the pressure of one ventricle is transmitted to the opposite ventricle (2–5, 7, 11, 12, 14). During diastole, the volume of one ventricle impinges on the volume of the opposite ventricle and thereby alters diastolic compliance and preload (5, 8, 9). The portion of pressure that is transmitted from one ventricle to the opposite ventricle is quantified by the term gain.

Using a three-compartment model, several groups theorized that gain is solely dependent on the ratio of ventricular free wall and septal end-systolic elastances (9, 10). Consequently, although gain has been considered to be a unique feature of myocardial function under conditions of a constant contractile state, this may not be the case. To test this hypothesis, we studied left (LV)-to-right ventricular (RV) interactions in the isolated cross-perfused canine heart preparation to determine whether RV volume (RVV) modulates LV-to-RV interaction. We found that left-to-right systolic gain increased with increased RVV. Additionally, left-to-right diastolic interactions were more profound at higher RVVs. These findings may be explained by nonlinearities in the end-diastolic and end-systolic pressure-volume relationships (ESPVR).

METHODS

Surgical Preparation

For each experiment, a pair of mongrel dogs (20–25 kg) was anesthetized with pentobarbital sodium, and the lungs were mechanically ventilated to maintain normoxia and normocarbia. The femoral arteries and veins of one dog ("support dog") were cannulated and connected to a perfusion system. Through a midline sternotomy, the left subclavian artery of the second dog ("donor dog") was cannulated with the arterial perfusion line, and the RV was cannulated through the right atrium with the venous return line. Coronary perfusion pressure was measured via a catheter placed in the brachiocephalic artery. Flow of filtered and warmed (37°C) blood was servo-controlled to maintain perfusion pressure at 80 mmHg in the aortic root. Once the heart was cross-perfused, the azygous vein, superior and inferior venae cavae, descending aorta, and lung hili were ligated, and the entire heart was removed from the donor dog. The heart was suspended over a collecting funnel, and both ventricles and the coronary sinus were vented to the air. Two metal rings that served to attach each ventricle to a servo-pump were sutured onto the mitral and tricuspid valve rings. The heart was positioned so that a water-filled latex balloon fit inside each of the ventricular cavities, with each balloon attached to its own calibrated and water-filled cylinder. A rotary motor controlled the piston position of a cylinder pump, thus allowing for volume control of each ventricle. A micromanometer-tipped catheter was placed inside each balloon for measurement of ventricular pressure. Pacing wires were placed in the right atrium, and the heart rate was set at 120 beats/min.

Experimental Protocol

Throughout the experiment, both ventricles contracted isovolumically. Measurement of left-to-right gain was performed at a low (~10 ml) or a high RVV (~25 ml) as follows. With the RV contracting isovolumically, LV volume (LVV) was varied between 5 and 35 ml in a gradual manner, creating a "volume ramp." RVV and LVV were chosen to provide a reasonable range of ventricular pressures. LVV ramps were repeated if arrhythmias occurred (most often this was found during LVV ramps from low to high rather than from high to low).

Data Analysis

All data were digitally acquired at a sampling rate of 200 Hz. The data were subsequently processed off-line on a Macintosh computer with customized routines written with IGOR software (WaveMetrics, Lake Oswego, OR).

Determination of LV-to-RV end-systolic gain. During the LVV ramp, peak RV pressure (RVP) was plotted against peak LV pressure. The slope of the linear regression is defined as $G_{S,L\text{-}R}$.

Determination of LV-to-RV end-diastolic gain. The timing of end diastole was defined by the point that just preceded the rapid upstroke of ventricular pressure. RV end-diastolic pressure (RVEDP) was plotted against LV end-diastolic pressure (LVEDP) during the LVV ramp. The slope of the linear regression is defined as $G_{D,L\rightarrow R}$.

Determination of instantaneous LV-to-RV gain. Transmission of pressure from the LV to the RV was examined throughout the cardiac cycle during an LVV ramp. Pressure waveforms were divided into individual cycles with the start of the cycle ($t = 0$) defined as the time point of peak rate of RVP development. LV pressure (LVP) and RVP were thus compared at 5-ms increments from the start of each cycle, and gain was calculated as the slope of the regression line through a plot of RVP(t) vs. LVP(t).

Statistical Analysis

To determine whether RVV influences gain, values of $G_{S,L\rightarrow R}$ or $G_{D,L\rightarrow R}$ were compared under the conditions of low and high RVVs by paired t-test. A P value of 0.05 was considered significant. Linear relationships were fit to the line $RVP = E(V - V_0)$, where E is the slope of the line, V is the volume, and V_0 is the volume-axis intercept; linearity was assessed by a runs test (GraphPad Software, San Diego, CA). Nonlinear relationships were fit to the parabolic equation $RVP = E'(RVV - V_0) + A(RVV - V_0)^2$, where E' is the slope of the curve at zero effective volume ($RVV = V_0$) and A is the coefficient for the squared term, thus reflecting the degree of curvilinearity.

RESULTS

Data from a representative LVV ramp are shown in Fig. 1. Fig. 1*A* shows tracings of pressure and volume for both the RV and LV during the ramp, with the peak and end-diastolic pressures marked for each beat. In response to the reduction in LVV, peak systolic LVP decreases. Because RVV remains constant, the slight decrease in peak systolic RVP is attributed to a reduction in pressure transmitted from the LV. The plot of peak LVP vs. peak RVP is shown in Fig. 1*B*, and the slope of the regression line through those individual points defines $G_{S,L\rightarrow R}$ for this particular LVV ramp. The impact of reducing LVV on RVEDP is illustrated in Fig. 1*C*. Beats with negative end-diastolic pressures were

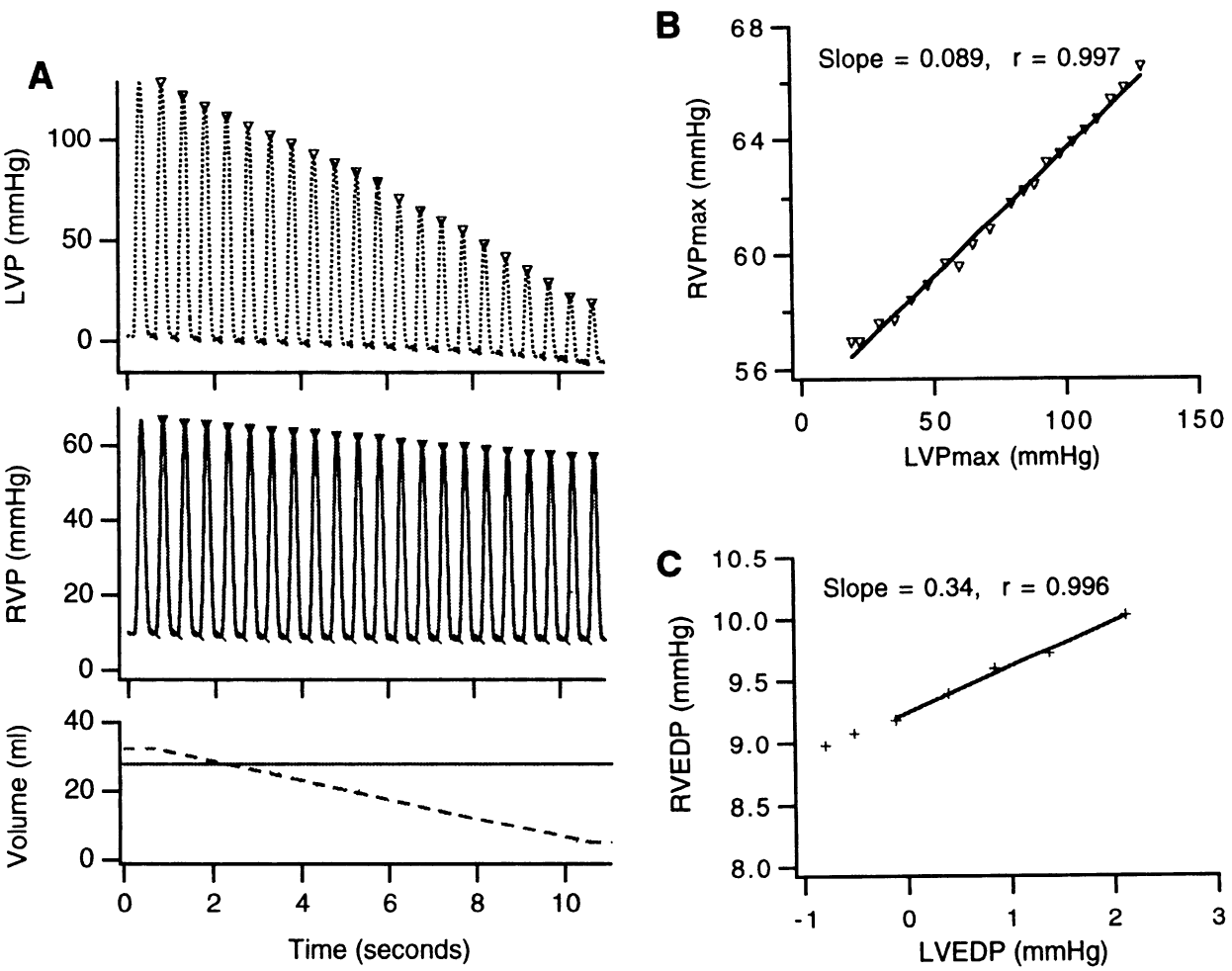

Fig. 1. *A*: representative data recorded during a left ventricular (LV) volume ramp. *Top* and *middle*: responses of LV pressure (LVP) and RV pressure (RVP) to reduction in LV volume. Peak pressures and end-diastolic pressure of each cycle are identified on the pressure waveforms. *Bottom*: right ventricular (RV) volume (solid line) is held constant while LV volume is gradually reduced (dashed line). *B*: peak RVP (RVP_{max}) plotted against peak LVP (LVP_{max}). Slope of regression line defines left-to-right systolic gain. *C*: RV end-diastolic pressure (RVEDP) plotted against LV end-diastolic pressure (LVEDP). This relationship exhibits an LVEDP threshold point beneath which there was no transmission of pressure to RV. Therefore, linear regression was performed in range of points above this threshold.

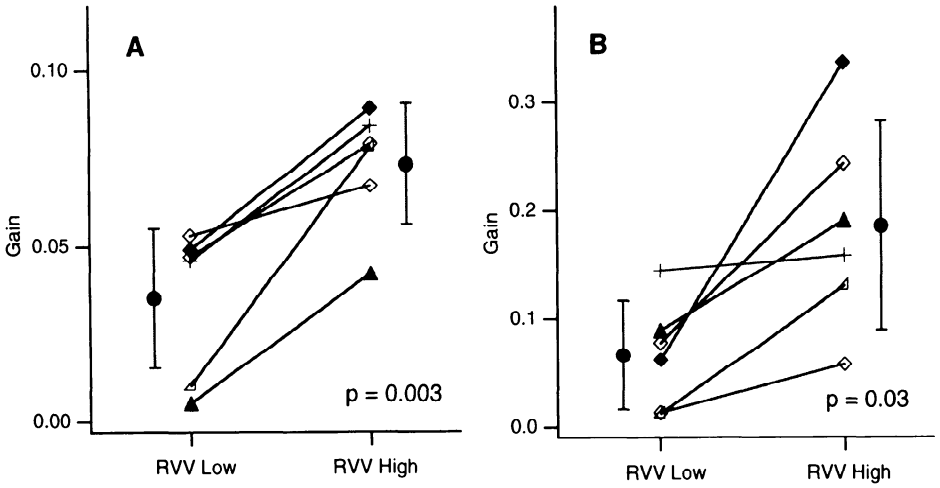

Fig. 2. Left-to-right end-systolic (*A*) and end-diastolic (*B*) gain measured at a low and a high RV volume (RVV) in 6 hearts. Each symbol represents a different heart; ● and vertical bars, means ± SD.

excluded from the diastolic calculations because of the possibility of balloon separation from the LV wall.

The comparison of $G_{S,L\rightarrow R}$ measured at low RVV vs. high RVV for all six hearts is depicted in Fig. 2*A*. $G_{S,L\rightarrow R}$ was 0.035 ± 0.022 at a low RVV and increased to 0.073 ± 0.017 at a high RVV (P = 0.003); peak RVP increased from 22 ± 2 to 48 ± 14 mmHg (P = 0.006) with the change from a low to a high RVV. A similar comparison of $G_{D,L\rightarrow R}$ is depicted in Fig. 2*B*. $G_{D,L\rightarrow R}$ increased from 0.067 ± 0.050 to 0.186 ± 0.097 (P = 0.03); RVEDP increased from 1.8 ± 4.3 to 11.5 ± 4.4 mmHg (P = 0.01) with the change from a low to a high RVV. LVV ramps were associated with peak LVPs that ranged from 111 ± 22 to 29.7 ± 9.2 mmHg and LVEDP values that ranged from 6 ± 4 to −3 ± 2 mmHg.

Instantaneous gain measured throughout the cardiac cycle at three RVV values is shown for a representative heart in Fig. 3. A normalized RVP waveform is superimposed on these tracings to visualize the timing of the cardiac cycle. There is a smooth increase in gain as ventricular relaxation occurs. Although the absolute values of gain at each part of the cardiac cycle increase with RVV, the difference between systolic and diastolic gain is more pronounced at high RVVs.

To explore one possible reason for load dependence of left-to-right gain, we focused on the linearity of the pressure-volume relationships. A tracing of RVP during a reduction in RVV measured in the same representative heart is shown in Fig. 4. Despite the fact that the linear regression correlation coefficient for the ESPVR is close to unity (r = 0.995), the relationship is better described by a second-order polynomial function (RVP = 0.70 + 0.97·RVV + 0.023·RVV²); A is significantly different from zero (P < 0.001), thus confirming that the ESPVR is curvilinear. In fact, in all six hearts, the ESPVR was found to be nonlinear (P < 0.01), although A varied considerably among the hearts tested, ranging from −0.006 to 0.09 (0.024 ± 0.033). The same data depicted in Fig. 4 are shown as a family of isochronal pressure-volume relationships in Fig. 5. It is apparent from Fig. 5 that the convexity of the pressure-volume relationship decreases during systole and is most pro-

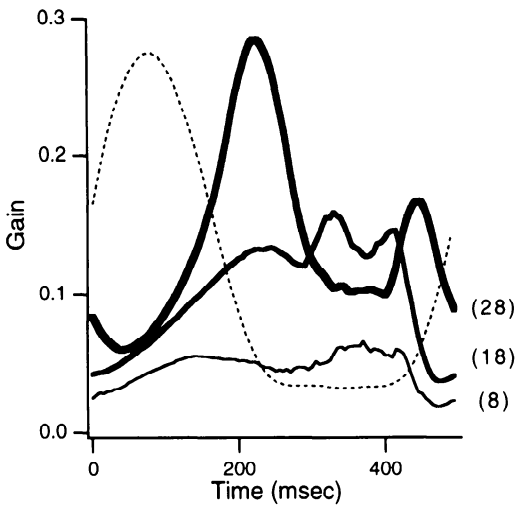

Fig. 3. Representative tracings of instantaneous gain throughout cardiac cycle at 3 RVVs (nos. in parentheses). Time is measured from point of peak rate of RVP development, and a normalized RVP tracing (dashed line) is provided to help interpret cycle timing. Instantaneous gain tends to increase during ventricular relaxation, and greatest volume dependency of gain is found during ventricular relaxation. Gain tends to increase at all portions of cardiac cycle with increased RVV.

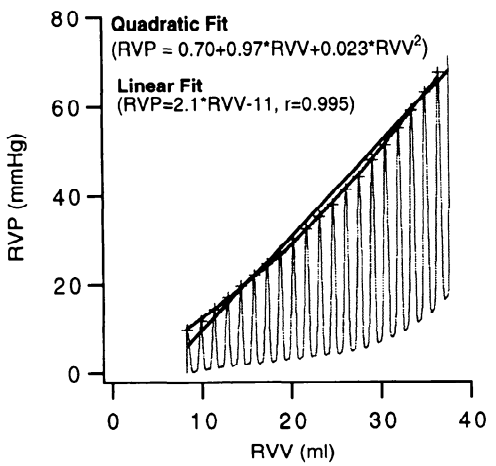

Fig. 4. Representative tracing of RVP vs. RVV during an RVV ramp. End-systolic pressure-volume points are marked, and this set of points was fit to both a linear and quadratic equation. It is apparent that despite a high linear correlation coefficient, RV end-systolic pressure-volume relationship exhibits significant convexity.

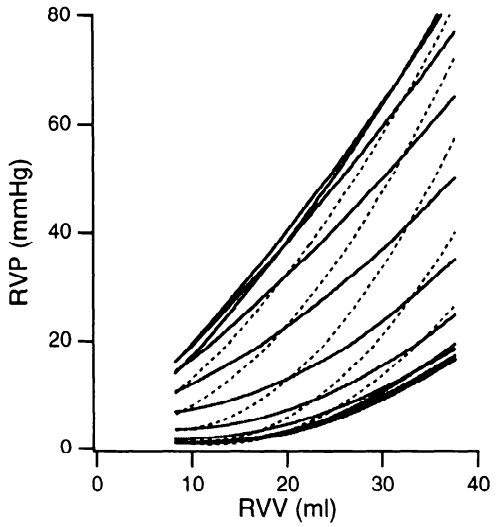

Fig. 5. Isochronal RVP-RVV relationships extracted from data presented in Fig. 4. Data were collected at 5-ms intervals but are displayed in 25-ms intervals for clarity. End-diastolic pressure-volume relationship is lowest curve shown and has classic shape of a compliance curve, with a flat initial portion and a steeper slope at higher volumes. As ventricular contraction progresses (solid lines), pressure-volume relationships are elevated and become more linear. End-systolic pressure-volume relationship is topmost curve and corresponds to family of points identified in Fig. 4. Notice that as ventricle relaxes, pressure-volume relationships (dashed lines) are steeper and more convex than during contraction.

nounced during ventricular relaxation. Similarly, left-to-right gain (Fig. 3) is most volume dependent during ventricular relaxation.

In the APPENDIX, we show that incorporation of a curvilinear pressure-volume relationship into the three-compartment elastance model can explain why left-to-right gain is load dependent. In brief, curvilinearity in the pressure-volume relationship causes volume dependency of elastance that then translates into volume dependency of gain. We used the equations detailed in the APPENDIX to plot the relationship of $G_{S,L\rightarrow R}$ and RVV at different values of A (Fig. 6). Notice that when A is zero (i.e., the pressure-volume relationship is linear), $G_{S,L\rightarrow R}$ does not vary with RVV. However, as A increases (denoted by the increasingly thick lines and representing increased convexity), the volume dependency of $G_{S,L\rightarrow R}$ increases. When A is negative (representing increased concavity), $G_{S,L\rightarrow R}$ decreases with RVV. It is apparent that the seemingly small nonlinearity in the ESPVR results in significant volume dependency of gain with the three-compartment model.

DISCUSSION

Results of this study demonstrate that the magnitude of LV-to-RV interaction is dependent on RVV. We have shown that both systolic and diastolic left-to-right gains are enhanced by RVV and have proposed that these volume dependencies of gain may be explained by nonlinearities in pressure-volume relationships. The implication is that studies of the parameters that modify ventricular interactions need to examine ventricular interactions over a range of RV loading conditions and to consider the impact of nonlinearities in pressure-volume relationships on the findings.

A number of researchers have explored factors that influence the magnitude of ventricular interactions. Maughan et al. (10) developed a three-compartment model that quantifies left-to-right gain by the ratio of RV free-wall elastance (E_{RVF}) to the sum of E_{RVF} and septal elastance (E_S). In other words, the transmission of pressure is decreased as the E_S is decreased relative to E_{RVF}. Conceptually, if the E_{RVF} values were low relative to the E_S, a change in LVP would cause a large deformation of the septum and a great increase in RVP. Conversely, if the E_{RVF} were low, the septal deformation would result in a small increase in RVP. In their model, the ratio of E_{RVF} to E_S is the sole determinant of gain; the implication is that gain is a unique feature of a heart at a constant contractile state.

Chow and Farrar (2) reported that $G_{S,L\rightarrow R}$ increased from 0.04 ± 0.01 in normal hearts to 0.10 ± 0.02 in a pacing-induced dilated cardiomyopathy. Woodard et al. (14) demonstrated that left-to-right gain varied during systole, with gain reaching a minimum in late systole and increasing until the point of end ejection. In a subsequent study, Farrar et al. (6) found that left-to-right gain is influenced by volume loading (both systolic and diastolic gain), the presence of the pericardium

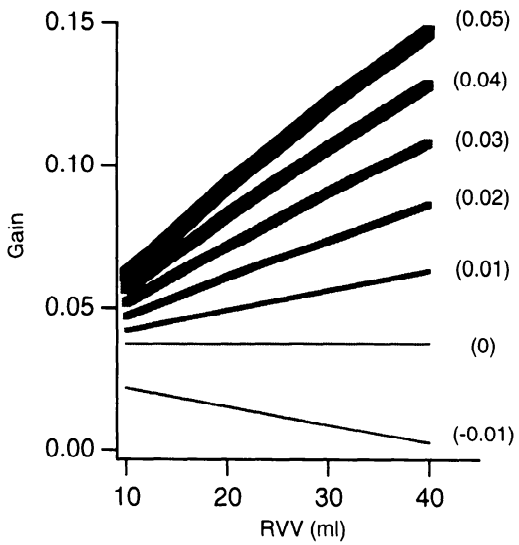

Fig. 6. Results of 3-compartment model of ventricular interactions controlling for nonlinearities in RV free-wall pressure-volume relationship. See APPENDIX for details of model. Parameters necessary to solve for gain include total RVV, total RVV-axis intercept ($V_{o,R}$), elastance value at zero effective volume for RV free wall (E'_{RVF}) and septum (E'_S), and coefficient of curvilinearity for RV free wall (A_{RVF}) and septum (A_S). Gain was determined for 7 values of A_{RVF} (nos. in parentheses), each over range of RVV shown. A_S was assumed to be zero (0.0001 was used to avoid zero in denominator of *Eq. A10* in APPENDIX), and E'_S was 45 mmHg/ml [taken from original description of 3-compartment model (9)]. E'_{RVF} was 0.88 mmHg/ml, calculated as $1/[(1/E'_{tot}) - (1/E'_S)]$, where E'_{tot} is average value of RV end-systolic elastance at zero effective volume measured in the 6 hearts. Increasing convexity of pressure-volume relationship is associated with increased volume dependency of gain. Notice that when $A_{RVF} = 0$ (indicating a linear pressure-volume relationship), there is no volume dependency of gain. When pressure-volume relationship is concave ($A_{RVF} = -0.01$), increased volume reduces gain.

(diastolic gain), and a pacing-induced model of dilated cardiomyopathy (systolic gain). Slinker et al. (13) showed that chronic pressure-overload hypertophy reduces direct ventricular interaction. However, the mechanisms by which these parameters modulate gain is unknown.

The results of the present study suggest that curvilinearities in pressure-volume relationships can explain why left-to-right gain varies with load, contractile state, and the cardiac cycle. Our data illustrate that the pressure-volume relationship is highly convex with respect to the volume axis (i.e., A is high) at end diastole and becomes more linear as the cardiac cycle approaches end systole. In addition, the pressure-volume relationship tends to be more convex during isovolumic relaxation than during isovolumic contraction. It has been previously shown that the value of A at end systole is related to the ventricular contractile state (1). For example, in the ischemic LV, A is high and the ESPVR is convex with respect to the volume axis. In contrast, positive inotropes have been shown to cause A to become negative, resulting in an ESPVR that is concave with respect to the volume axis. When these nonlinearities are factored into the three-compartment elastance model, it is apparent that alterations in contractility, RVV, and contraction phase alter ventricular interactions and the measurement of gain.

The incorporation of curvilinear pressure-volume relationships into the three-compartment model were restricted to the RV free wall. Because the pressure-volume relationship of the septal volume compartment was not measured, it was assumed to be linear. Further testing of the model with nonlinear septal ESPVR had a negligible effect on the calculated values of gain. This was due to the fact that the modeled E_S is very high, and, therefore, the operational volume range is very narrow; nonlinearities have less impact over a limited volume range. However, results from the modeling should be used to demonstrate that nonlinearities in pressure-volume relationships result in volume dependency of gain, whereas the calculated values are only approximate and limited by the assumptions of the model.

The isolated heart preparation used in the present study allows for control of many parameters of ventricular function so that the independent effects of a reduction in LVP may be assessed; however, limitations of this preparation should be considered. Artifacts introduced by balloon properties may have impacted on the results; however, balloons were overstretched such that their compliance would be very high compared with the ventricular compliance. Truncation of negative end-diastolic values may have altered the absolute values of the diastolic gain results; however, these effects would be expected to be slight. The pericardium was not present in this preparation; it is expected that the pericardium would accentuate curvilinearities in pressure-volume relationships and thus increase the volume dependency of gain.

In conclusion, we have shown that left-to-right ventricular interactions are influenced by nonlinearities in pressure-volume relationships. The volume dependency of gain is predicted by the three-compartment model when nonlinearities in instantaneous pressure-volume relationships are taken into account. Alterations in nonlinearities may also explain how other parameters, such as contractility and pericardial influences, modulate gain. Future studies will need to account for nonlinearities in pressure-volume relationships when interpreting changes in systolic and diastolic interactions.

APPENDIX

The three-compartment elastance model divides the heart into three compartments: RV free wall, septal, and LV free wall. Each compartment is described by its own pressure-volume relationship. For the case of a linear pressure-volume relationship [as assumed in the original paper by Maughan et al. (10)], the volume of the RV free-wall compartment (V_{RVF}) is described by the formula

$$V_{RVF} = (RVP/E_{RVF}) + V_{o,R} \quad (A1)$$

where $V_{o,R}$ is the volume-axis intercept of the RVP-V_{RVF} relationship, and E_{RVF} is RV free-wall elastance. Septal volume (V_S) is similarly described

$$V_S = (LVP - RVP)/E_S \quad (A2)$$

where E_S is septal elastance. There is no volume-axis intercept by definition so that the V_S is zero when in the neutral position. Because total RVV is defined as

$$RVV = V_{RVF} - V_S \quad (A3)$$

it follows that

$$RVP = \frac{E_S \cdot E_{RVF}}{E_S + E_{RVF}}(RVV - V_{o,R}) + \frac{E_{RVF}}{E_S + E_{RVF}} LVP \quad (A4)$$

Hence Maughan et al. (10) expressed gain (the slope of the relationship between LVP and RVP) as the ratio of E_{RVF} to ($E_s + E_{RVF}$). Importantly, the only condition under which this ratio expresses gain is when E_s and E_{RVF} are independent of LVP. However, this condition is not satisfied when the pressure-volume relationship is nonlinear. Because a change in LVP causes a redistribution of volume between V_s and V_{RVF}, volume-dependent alterations in the individual elastance terms render the relationship between LVP and RVP far more complex.

The pressure-volume relationship for the RV free-wall and septal compartments are better described by second-order polynomial equations

$$RVP = E'_{RVF}(V_{RVF} - V_{o,R}) + A_{RVF}(V_{RVF} - V_{o,R})^2 \quad (A5)$$

$$LVP - RVP = E'_S V_S + (A_S V_S)^2 \quad (A6)$$

where A_{RVF} and A_S are the coefficients for the RV free wall and the septum, respectively. In these expressions, E' is the value of elastance when the effective compartment volume is zero. A reflects the amount that the pressure-volume relationship deviates from a straight line: positive values result in a

concave curve, whereas negative values result in a convex curve.

Substituting *Eq. 5* for RVP in *Eq. 6* yields

$$\mathrm{LVP} - E'_{\mathrm{RVF}}(\mathrm{V_{RVF}} - \mathrm{V_{o,R}}) + A_{\mathrm{RVF}}(\mathrm{V_{RVF}} - \mathrm{V_{o,R}})^2 = E'_{\mathrm{S}}\mathrm{V_S} + (A_{\mathrm{S}}\mathrm{V_S})^2 \quad (A7)$$

and substituting *Eq. 3* for $\mathrm{V_S}$ yields

$$\mathrm{LVP} - E'_{\mathrm{RVF}}(\mathrm{V_{RVF}} - \mathrm{V_{o,R}}) - A_{\mathrm{RVF}}(\mathrm{V_{RVF}} - \mathrm{V_{o,R}})^2 = E'_{\mathrm{S}}(\mathrm{V_{RVF}} - \mathrm{RVV}) + A_{\mathrm{S}}(\mathrm{V_{RVF}} - \mathrm{RVV})^2 \quad (A8)$$

that may be rearranged to form

$$\begin{aligned} 0 = {} & \mathrm{V_{RVF}^2}\,(A_{\mathrm{S}} - A_{\mathrm{RVF}}) \\ & + \mathrm{V_{RVF}}[2(\mathrm{RVV}\cdot A_{\mathrm{S}}) - E'_{\mathrm{S}} - E'_{\mathrm{RVF}} + 2(\mathrm{V_{o,R}}A_{\mathrm{RVF}})] \\ & + \mathrm{LVP} + (E'_{\mathrm{S}}\cdot\mathrm{RVV}) \\ & + (A_{\mathrm{S}}\cdot\mathrm{RVV}) + E'_{\mathrm{RVF}}\mathrm{V_{o,R}} - (A_{\mathrm{RVF}}\mathrm{V_{o,R}})^2 \end{aligned} \quad (A9)$$

$\mathrm{V_{RVF}}$ may be solved for with the quadratic formula

$$\mathrm{V_{RVF}} = \frac{-y \pm (y^2 - 4xz)^{1/2}}{2x} \quad (A10)$$

where

$$x = A_{\mathrm{S}} - A_{\mathrm{RVF}}$$

$$y = 2(\mathrm{RVV}\cdot A_{\mathrm{S}}) - E'_{\mathrm{S}} - E'_{\mathrm{RVF}} + 2(\mathrm{V_{o,R}}A_{\mathrm{RVF}})$$

$$z = \mathrm{LVP} + (E'_{\mathrm{S}}\cdot\mathrm{RVV}) + (A_{\mathrm{S}}\cdot\mathrm{RVV}) + E'_{\mathrm{RVF}}\mathrm{V_{o,R}} - (A_{\mathrm{RVF}}\mathrm{V_{o,R}})^2$$

Once $\mathrm{V_{RVF}}$ is known, RVP is solved by the RV free-wall pressure-volume relationship (*Eq. 5*).

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REFERENCES

1. **Burkhoff, D., S. Sugiura, D. T. Yue, and K. Sagawa.** Contractility-dependent curvilinearity of end-systolic pressure-volume relations. *Am. J. Physiol.* 252 (*Heart Circ. Physiol.* 21): H1218–H1227, 1987.
2. **Chow, E., and D. J. Farrar.** Effects of left ventricular pressure reductions on right ventricular systolic performance. *Am. J. Physiol.* 257 (*Heart Circ. Physiol.* 26): H1878–H1885, 1989.
3. **Damiano, R. J., Jr., P. La Follette, Jr., J. L. Cox, J. E. Lowe, and W. P. Santamore.** Significant left ventricular contribution to right ventricular systolic function. *Am. J. Physiol.* 261 (*Heart Circ. Physiol.* 30): H1514–H1524, 1991.
4. **Elzinga, G., H. Piene, and J. P. De Jong.** Left and right ventricular pump function and consequences of having two pumps in one heart. *Circ. Res.* 46: 564–574, 1980.
5. **Elzinga, G., R. Van Grondelle, N. Westerhof, and G. C. Van Den Bos.** Ventricular interference. *Am. J. Physiol.* 226: 941–947, 1974.
6. **Farrar, D. J., E. Chow, and C. D. Brown.** Isolated systolic and diastolic ventricular interaction in pacing-induced dilated cardiomyopathy and effects of volume loading and pericardium. *Circulation* 92: 1284–1290, 1995.
7. **Feneley, M. P., T. P. Gavaghan, D. W. Baron, J. A. Branson, P. R. Roy, and J. J. Morgan.** Contribution of left ventricular contraction to the generation of right ventricular systolic pressure in the human heart. *Circulation* 71: 473–480, 1985.
8. **Janicki, J. S., and K. T. Weber.** The pericardium and ventricular interaction, distensibility, and function. *Am. J. Physiol.* 238 (*Heart Circ. Physiol.* 7): H494–H503, 1980.
9. **Little, W. C., F. R. Badke, and R. A. O'Rourke.** Effect of right ventricular pressure on the end-diastolic left ventricular pressure-volume relationship before and after chronic right ventricular pressure overload in dogs without pericardia. *Circ. Res.* 54: 719–730, 1984.
10. **Maughan, W. L., K. Sunagawa, and K. Sagawa.** Ventricular systolic interdependence: volume elastance model in isolated canine hearts. *Am. J. Physiol.* 253 (*Heart Circ. Physiol.* 22): H1381–H1390, 1987.
11. **Santamore, W. P., P. R. Lynch, J. L. Heckman, A. A. Bove, and G. D. Meier.** Left ventricular effects on right ventricular developed pressure. *J. Appl. Physiol.* 41: 925–930, 1976.
12. **Santamore, W. P., P. R. Lynch, G. D. Meier, J. L. Heckman, and A. A. Bove.** Myocardial interaction between the ventricles. *J. Appl. Physiol.* 41: 362–368, 1976.
13. **Slinker, B. K., C. P. Chagas, and S. A. Glantz.** Chronic pressure overload hypertrophy decreases direct ventricular interaction. *Am. J. Physiol.* 253 (*Heart Circ. Physiol.* 22): H347–H357, 1987.
14. **Woodard, J. C., E. Chow, and D. J. Farrar.** Isolated ventricular systolic interaction during transient reductions in left ventricular pressure. *Circ. Res.* 70: 944–951, 1992.