# Hemodynamic consequences of ventricular interaction as assessed by model analysis

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SANTAMORE, WILLIAM P., AND DANIEL BURKHOFF. *Hemodynamic consequences of ventricular interaction as assessed by model analysis.* Am. J. Physiol. 260 (Heart Circ. Physiol. 29): H146–H157, 1991.—Because of close anatomic association, the pressure and volume in one ventricle can directly influence the pressure and volume in the opposite ventricle. To examine the importance of ventricular interdependence in controlling the circulation, we developed a computer model in which ventricular interdependence could be turned on and off. Left ventricular chamber contractility, as judged by maximal elastance ($E_{max}$), was enhanced on the order of 10% as a result of ventricular interaction, whereas right ventricular $E_{max}$ was affected by as much as 60% under physiological conditions. With increases in systemic vascular resistance, ventricular interaction caused a smaller stroke volume (SV) decrease than with no interaction. For canine data (SV = 21.4 ml), doubling systemic vascular resistance decreased SV by 3.7 without ventricular interdependence, 3.5 with diastolic ventricular interdependence, and 3.3 ml with diastolic and systolic ventricular interdependence. In contrast, with increases in pulmonary vascular resistance, ventricular interaction caused a greater decrease in SV than with no interaction present. Decreasing left ventricular free wall elastance or right ventricular free wall elastance decreased SV. Diastolic ventricular interdependence reduced the SV changes, whereas systolic ventricular interdependence accentuated the SV changes with alterations in right and left ventricular free-wall elastance. The results of the present simulation demonstrate the importance of ventricular interdependence in the observed responses of the right ventricle to volume overload, pressure overload, and ischemia.

ventricular interdependence; right ventricle; left ventricle; ventricular mechanics; computer simulation

BECAUSE OF CLOSE ANATOMIC association, the pressure and volume in one ventricle can directly influence the pressure and volume in the opposite ventricle (3, 5, 9, 13, 26, 27). This phenomenon, known as ventricular "interdependence" or "interaction" results from the fact that some muscle bundles of the heart wrap around both ventricles and that the two chambers share a common wall, the septum. The pericardium provides additional constraints on total heart (ventricular plus atrial) volumes and thus plays an important role in modulating ventricular interaction (13, 31). Current knowledge about the physiological role of ventricular interdependence is limited to an understanding of how conditions in one ventricle influence the end-systolic and end-diastolic properties of the opposite ventricle (31). In addition, ventricular interdependence may be modified in certain disease states (5). However, the impact the ventricular interdependence has on overall cardiovascular system function (e.g., cardiac output and arterial pressure) is unknown.

Several barriers limit experimental evaluation of the consequences of ventricular interdependence on the cardiovascular system. Paramount among these barriers is the fact that ventricular interdependence is always present. To overcome such experimental problems, we developed a computer simulation of the cardiovascular system in which ventricular interdependence could be turned on and off, thereby enabling a comparison of cardiovascular function with and without interaction. Modeling of systolic and diastolic ventricular interactions was based on experimental data already in the literature (3, 5, 9, 13, 25–27). We did not include a pericardium because, in this initial study, we were interested in gaining insight into the consequences of ventricular interdependence by itself. The specific goal of the present study was to determine the extent to which ventricular interdependence influences changes in stroke volume after acute unilateral changes in vascular resistances or in ventricular contractile states.

## METHODS

*Overview of simulation.* An electric circuit representation of the model used to simulate the cardiovascular system is shown in Fig. 1. The brackets show the circuit with ventricular interaction. Both systemic and pulmonic circuits consist of inlet and outlet valves (represented by diodes), a characteristic impedance ($R_c$), arterial resistance ($R_a$), a resistance to venous return ($R_v$), and arterial and venous compliances ($C_a$, and $C_v$, respectively), in the arrangement shown in Fig. 1. Both systemic and pulmonary circuits were thus modeled as modified windkessel impedances (36).

Without interaction, the right and left ventricles act independently of each other. The model we used to represent ventricular function is an extension of the previously proposed time-varying volume-elastance model [$E(t)$], which describes the relation between instantaneous ventricular volume (V) and ventricular pressure (P) (34). The present model assumes a nonlinear end-diastolic pressure-volume relationship, a linear end-systolic pressure-volume relationship, and a smooth progression between the two during the cardiac cycle. End-

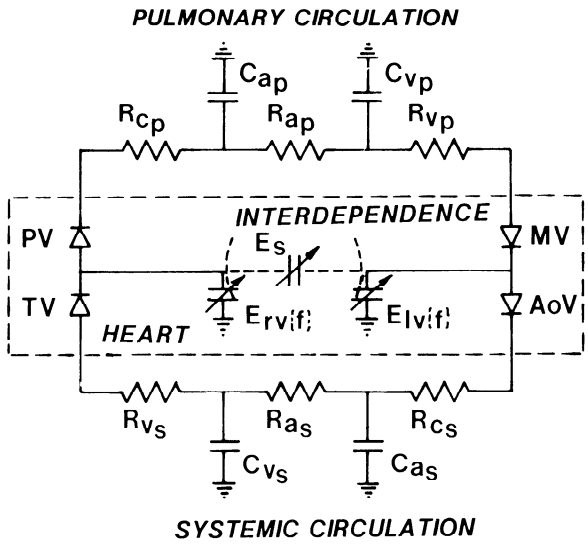


FIG. 1. Sketch of circuit used to simulate cardiovascular system. Ventricles are represented by time-varying elastances $E_{rv}$ and $E_{lv}$, respectively. Pulmonary and systemic circulations are modeled as nonlinear 4-element modified "windkessel." Both systemic and pulmonic circuits consist of inlet and outlet valves represented by diodes, a characteristic impedance ($R_c$), arterial resistance ($R_a$), resistance to venous return ($R_v$), and arterial and venous compliances ($C_a$ and $C_v$, respectively). TV, tricuspid valve; PV, pulmonary valve; MV, mitral valve; AoV, aortic valve. Braces show modification to incorporate ventricular interdependence. Heart is now represented by 3 time-varying elastances that correspond to right ventricular free wall ($E_{rvf}$), left ventricular free wall ($E_{lvf}$) and septum ($E_s$).

diastolic pressure ($P_{ed}$) and volume ($V_{ed}$) are interrelated by (11)

$$P_{ed} = B[e^{A(V_{ed}-V_0)} - 1] \quad (1)$$

where $A$ and $B$ are constants. The end-systolic pressure ($P_{es}$) and volume ($V_{es}$) are interrelated by

$$P_{es} = E_{es}(V_{es} - V_0) \quad (2)$$

where $E_{es}$ is the maximal volume elastance, and $V_0$ is the volume at which end-systolic pressure is 0 mmHg. Finally, we define a time function $e(t)$, which describes the time course of the chamber stiffness between end systole (*Eq. 2*) and end diastole (*Eq. 1*)

$$\begin{aligned} e(t) &= 0.5\,[1 - \cos(2\pi t/T_{max})] \qquad 0 < t < 2T_{max} \\ e(t) &= 0 \qquad\qquad\qquad\qquad\qquad 2T_{max} \le t \le T \end{aligned} \quad (3)$$

where $t$ is the time from the onset of systole, $T_{max}$ is the time to the end of systole, and $T$ is the duration of the cardiac cycle. Thus $e(t)$ has a value of 0 at end diastole (when $t = 0$ or when $t = T$) and a value of unity at end systole (when $t = T_{max}$). *Equations 1–3* can be combined to describe the instantaneous relationship between ventricular volume and pressure

$$P[V(t), t] = e(t)\{P_{es}[V(t)] - P_{ed}[V(t)]\} + P_{ed}[V(t)] \quad (4)$$

Accordingly, ventricular function is characterized by the parameters maximal elastance ($E_{max}$), $T_{max}$, $V_0$, $A$, $B$, and the function $e(t)$. The function $e(t)$ was considered to be the same for both ventricles (6), whereas the other parameter values were different for the right and left ventricles (see below).

The model used to simulate the heart when ventricular interaction is present is schematized in Fig. 1 by three time-varying elastances that correspond to the right ventricular free wall ($E_{rvf}$), the left ventricular free wall ($E_{lvf}$), and the septum ($E_s$) (18). A description of how ventricular interaction was simulated is presented in the following passages. The interaction between each ventricle and its afterload is determined by numerical integration of the differential equation describing the respective circuits as shown in Fig. 1.

*Diastolic ventricular interdependence.* Although numerous studies have demonstrated diastolic ventricular interdependence (3, 5, 9, 13, 26, 27), a simple mathematical expression for diastolic ventricular interdependence has not been developed. Therefore, we developed mathematical equations to predict alterations in the diastolic pressure-volume relationship similar to the experimental data. To accomplish this, diastolic interaction was modeled by making $A$ in *Eq. 1* a function of the volume of the contralateral ventricle; $B$ was considered to be a constant. Thus for the left ventricular end-diastolic pressure-volume relation

$$A_{lv} = A_{l0} + m_{r\text{-}l} \cdot V_{rv} \quad (5)$$

where $A_{l0}$ is the left ventricular exponential coefficient with a right ventricular volume equal to zero, $m_{r\text{-}l}$ is the sensitivity of $A_{lv}$ to changes in right ventricular volume, and $V_{rv}$ is right ventricular end-diastolic volume. Similarly, the dependence of the right ventricular on left ventricular volume was simulated by

$$A_{rv} = A_{r0} + m_{l\text{-}r} \cdot V_{lv} \quad (6)$$

where $A_{r0}$ is the right ventricular exponential coefficient with left ventricular volume equal to zero, $m_{l\text{-}r}$ is the sensitivity of $A_{rv}$ to changes in left ventricular volume, and $V_{lv}$ is left ventricular end-diastolic volume. This mathematical format for modeling diastolic interactions creates changes in the end-diastolic pressure-volume relationship similar to those observed experimentally by several investigators (3, 5, 9, 13, 25–27).

Each valve was represented in the model by a diode that permitted flow in only one direction.

*Systolic ventricular interdependence.* Systolic ventricular interaction was simulated in a manner recently proposed by Maughan et al. (18), in which the heart is divided functionally into right ventricular free, left ventricular free, and septal walls. A detailed description of this model has been presented previously by Maughan et al. (18). Briefly, the systolic properties of each wall are described by its own time-varying pressure-volume relationship. These time-varying relationships are represented in Fig. 1 by $E_{lvf}(t)$, $E_{rvf}(t)$, and $E_s(t)$, for the left ventricular free wall, right ventricular free wall, and septal time-varying elastances, respectively. With this configuration, the following end-systolic pressure-volume relationships for the total left ventricle and total

right ventricle can be derived

$$P_{lv} = \frac{E_s \cdot E_{lvf}}{E_s + E_{lvf}} [V_{lv} - V_{l0}] + \frac{E_{lvf} \cdot P_{rv}}{E_S + E_{lvf}} \quad (7)$$

$$P_{rv} = \frac{E_s \cdot E_{rvf}}{E_s + E_{rvf}} [V_{rv} - V_{r0}] + \frac{E_{rvf} \cdot P_{lv}}{E_s + E_{rvf}} \quad (8)$$

where $V_{l0}$ and $V_{r0}$ are the left and right ventricular volumes, respectively, at which end-systolic pressure is equal to 0 mmHg. These $V_0$ values are calculated from the individual chamber $V_0$ values as follows

$$V_{l0} = V_{lvf0} + V_{s0} \quad (9)$$

$$V_{r0} = V_{rvf0} - V_{s0} \quad (10)$$

where $V_{lvf0}$, $V_{s0}$, and $V_{rvf0}$ are left ventricular free-wall, septal, and right ventricular free-wall $V_0$ values, respectively, when end-systolic pressure is equal to 0 mmHg. Thus pressure development in the left ventricle during systole is a function of left ventricular myocardial properties ($E_{lvf}$ and $E_s$) and right ventricular pressure. Similarly, right ventricular pressure is a function of right ventricular myocardial properties ($E_{rvf}$ and $E_s$) and left ventricular pressure. Instantaneous pressure and volume in each ventricle are calculated, as before, using *Eq. 4* with $P_{es}$ and $P_{ed}$ calculated to account for instantaneous interventricular interaction.

To quantify ventricular contractile strength we defined two different $E_{max}$ values for each ventricle. We defined the "native $E_{max}$" as the slope of the end-systolic pressure-volume relationship when the opposite ventricle was generating no systolic pressure. The native $E_{max}$ therefore represents the intrinsic pressure-generating capability of the combined septal and free wall myocardium. So, for example, the native $E_{max}$ of the left ventricle is equal to $E_s E_{lvf}/(E_s + E_{lvf})$, (from *Eq. 7*), which is simply the elastance resulting from the parallel combination of the $E_s$ and $E_{lvf}$. We defined the "effective $E_{max}$" of a ventricle as the ratio $P_{es}/(V_{es} - V_0)$. In this case, $P_{es}$ resulted not only from intrinsic septal and free wall myocardial strengths but also from the effects of pressure generation in the opposite ventricle (*Eqs. 7* and *8*). In the absence of systolic interdependence, the native and effective $E_{max}$ are identical. In the presence of systolic interdependence, the effective $E_{max}$ is the sum of the native $E_{max}$ and the effect of the opposite ventricle.

*Control parameter values and simulation interventions.* The simulation was programmed in Basic on an IBM-PC XT microcomputer. The values of all the simulation parameters under control conditions, presented in Table 1, were chosen to be appropriate for a 20-kg dog.

Total systemic $R_a$ was set at 2.7 mmHg·s·ml$^{-1}$ with $R_c$ set at slightly <10% of this total value (19). Systemic $C_a$ was set to provide a time constant of decay of arterial pressure pulse during diastole ($R_a$, $C_a$) of 1 s. Total pulmonic $R_a$ was set at roughly one-seventh that of the systemic arterial system, with pulmonic $R_c$ comprising approximately one-sixth this total value (4, 19). Pulmonic $C_a$ was also chosen to provide a 1-s decay constant for diastolic pulmonary artery pressure. Pulmonic and systemic venous compliances (and their ratio) were set according to published values (28, 29). The value of the resistance to flow between the $C_v$ and the ventricle was set the same for the pulmonic and systemic circulation and chosen to provide reasonable flow rates during filling (unpublished observations). $E_{es}$, $V_0$, and $T_{max}$ values, in the absence of ventricular interaction, were set within the range found in intact animals for the left ventricle (15) and in isolated hearts for the right ventricle (16). The parameters for the end-diastolic pressure-volume relationship were taken from published parameter values for the left ventricle (11) and estimated from published figures depicting end-diastolic pressure-volume relations for the right ventricle (18).

TABLE 1. *Control values for parameters of the simulation*

| | |
|---|---|
| Heart rate, beats/min | 80 |
| $T_{max}$, ms | 200 |
| Total effective blood volume, ml | 250 |

| | $R_v$ | $R_c$ | $R_a$ | $C_a$ | $C_v$ |
|---|---|---|---|---|---|
| Circulation | | | | | |
| Pulmonic* | 0.015 | 0.06 | 0.30 | 2.00 | 3 |
| Systemic* | 0.015 | 0.20 | 2.5 | 0.40 | 17 |

Heart without ventricular interaction

| | LV | RV |
|---|---|---|
| $E_{es}$, mmHg/ml | 7.0 | 3.0 |
| $V_0$, ml | 5.0 | 5.0 |
| $A$, ml$^{-1}$ | 0.1 | 0.09 |
| $B$, mmHg | 0.35 | 0.35 |

Heart with ventricular interaction "native" elastance

| | LV free wall | RV free wall | Septum | LV | RV |
|---|---|---|---|---|---|
| $E_{es}$, mmHg/ml | 9.4 | 2.1 | 20.0 | 6.4 | 1.9 |
| $V_0$, ml | 2.5 | 7.5 | 2.5 | 5.0 | 5.0 |

Parameters for diastolic interaction

| | |
|---|---|
| $A_{ro}$, ml$^{-1}$ | 0.06 |
| $A_{lo}$, ml$^{-1}$ | 0.08 |
| $m_{l\text{-}r}$, ml$^{-2}$ | 0.000754 |
| $m_{r\text{-}l}$, ml$^{-2}$ | 0.000568 |

* Resistance values ($R_v$, $R_c$, $R_a$) in mmHg·s·ml$^{-1}$; capacitance values ($C_a$, $C_v$) in ml/mmHg.

The parameters values for diastolic interdependence were selected first to ensure that under control conditions, the right and left ventricular diastolic pressures and volumes would be unaltered, even with varying levels of interdependence. Second, a wide range of values were examined from very low levels of interdependence to very high levels of diastolic interdependence before the final values were chosen to reproduce previously published experimental data (11, 13). Figure 2, *A* and *B*, shows the effects of these parameters on the diastolic pressure-volume relationships. The control pressures are the pressures that would be recorded without ventricular interdependence but without a change in contralateral ventricular volume. Figure 2*A* shows the effects on right ventricular diastolic pressure ($P_{rv}$) of a 5-ml increase or decrease in $V_{lv}$ from the control value (40.5 ml). Similarly, Fig. 2*B* shows the effects of a 5-ml increase or decrease in control $V_{rv}$ (34.7 ml) on left ventricular diastolic pressure ($P_{lv}$).

For systolic ventricular interaction, $E_s$ was first se-

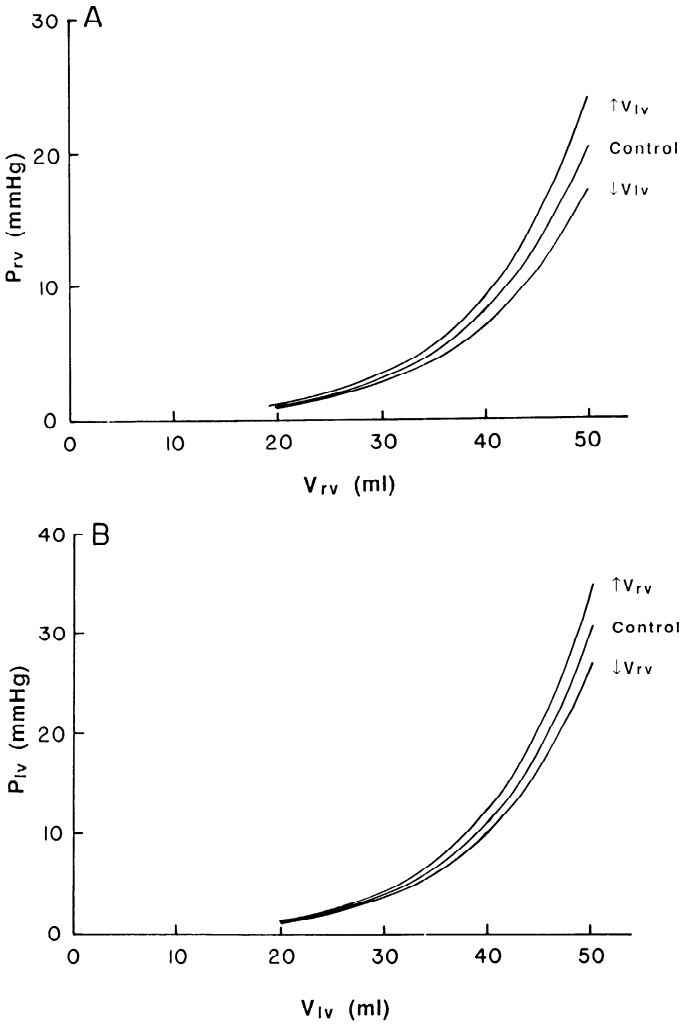


FIG. 2. *A*: right ventricular pressure ($P_{rv}$) vs. volume ($V_{rv}$). Control, right ventricular pressures; ↑$V_{lv}$, pressures obtained with 5-ml increase in left ventricular volume; ↓$V_{lv}$, pressures obtained with 5-ml decrease in left ventricular volume. *B*: left ventricular pressure ($P_{lv}$) vs. volume ($V_{lv}$). Control, left ventricular pressure; ↑$V_{rv}$, pressure obtained with 5-ml increase in right ventricular volume; ↓$V_{rv}$, pressure obtained with 5-ml decrease in right ventricular volume.

TABLE 2. *Hemodynamic variables obtained with parameters values set at control values*

| Variable | Values | |
|---|---|---|
| Stroke volume, ml | 21.4 | |
| Aortic blood pressure, mmHg | 123/60 | |
| Pulmonary blood pressure, mmHg | 36/18 | |
| Systemic blood volume, ml | 105 | |
| Pulmonary blood volume, ml | 70 | |
| | Left Ventricular | Right Ventricular |
| End-diastolic pressure, mmHg | 11.8 | 4.7 |
| End-diastolic volume, ml | 40.5 | 34.7 |
| Ejection fraction | 0.53 | 0.62 |
| Stroke work, mmHg·ml | 2,189 | 628 |
| Effective $E_{max}$ | 7.0 | 3.0 |

These control values are the same whether interaction is present or not.

lected. Based on approximately two-thirds of the total left ventricle being composed of the left ventricular free wall and one-third composed of the septum, $E_s$ would be 21 mmHg/ml. This was reduced to 20 mmHg/ml to compensate for the right ventricular contribution to left ventricular systolic pressure development. $E_{rvf}$ and $E_{lvf}$ were then adjusted to keep pressures and stroke volume at the same values obtained without ventricular interaction. Similarly, the values of $V_0$ were selected to keep total left and right ventricular $V_0$ at 5 ml.

The resulting hemodynamic variables obtained with the control parameter values (Table 1) are presented in Table 2. Again, $E_{rvf}$ and $E_{lvf}$ were adjusted appropriately to keep the effective $E_{max}$ the same with and without interaction. This meant that in the presence of systolic interaction, $E_{lvf}$ and $E_{rvf}$ were reduced to 9.4 and 2.1, respectively. If $E_{lvf}$ and $E_{rvf}$ had not been reduced with systolic ventricular interaction, then stroke volume (23.7), ejection fraction (0.56 left, 0.73 right ventricle), and effective $E_{max}$ (7.3 left, 6.1 right ventricle) would have all been substantially greater.

*Protocol.* Four interventions were examined: alterations in systemic and pulmonary resistance and changes in $E_{lvf}$ and $E_{rvf}$. For each intervention, the other parameters (Table 1) were kept constant. The systemic resistance was varied from 0.5 to 10.0 mmHg·s·ml$^{-1}$. Pulmonary $R_a$ was varied from 0.02 to 1.40 mmHg·s·ml$^{-1}$. $E_{lvf}$ and $E_{rvf}$ were varied from 20 to 250% of their control values, respectively. Thus, in the absence of systolic ventricular interaction, $E_{lvf}$ varied from 2.2 to 27 mmHg/ml and $E_{rvf}$ varied from 0.7 to 8.8 mmHg/ml, whereas in the presence of systolic ventricular interaction, $E_{lvf}$ varied from 1.9 to 23 mmHg/ml and $E_{rvf}$ varied from 0.5 to 5.2 mmHg/ml.

## RESULTS

*Theoretical impact of systolic interaction on chamber "contractility."* Before proceeding with the analysis outlined above, we examined quantitatively how the presence of systolic ventricular interaction influenced the contractile strength of the right and left ventricles. For this purpose, we indexed the contractile states of the right and left ventricles, as stated above, by their respective effective $E_{max}$. Thus left ventricular $E_{max}$ was obtained by dividing *Eq. 7* by [$V_{lv} - V_{l0}$] and right ventricular $E_{max}$ can be obtained by dividing *Eq. 8* by [$V_{rv} - V_{r0}$]. For illustrative purposes, the free wall and $E_s$ and $V_0$ values were those presented in Table 1. The impact of right ventricular pressure generation on effective left ventricular $E_{max}$ is shown in Fig. 3*A*, with $V_{lv}$ set at 19 ml (for values given in Table 1). Left ventricular $E_{max}$ with right ventricular $P_{es}$ set at 0 mmHg (i.e., the *y*-axis intercept) is the native $E_{max}$ as defined above and represents the intrinsic pressure-generating properties of the left ventricular chamber. The increase in effective left ventricular $E_{max}$ above this intercept value with increases in right ventricular $P_{es}$, represents the impact of systolic ventricular interaction on left ventricular contractile strength under the defined conditions. As shown, there is a linear relationship between right ventricular $P_{es}$ and effective left ventricular $E_{max}$. Within the physiological range of right ventricular $P_{es}$ values (15–30 mmHg), left ventricular $E_{max}$ was 6.8–7.0 mmHg/ml ~7 to 10% greater than the native $E_{max}$ of 6.4 mmHg/ml.

The influence of left ventricular $P_{es}$ on effective right

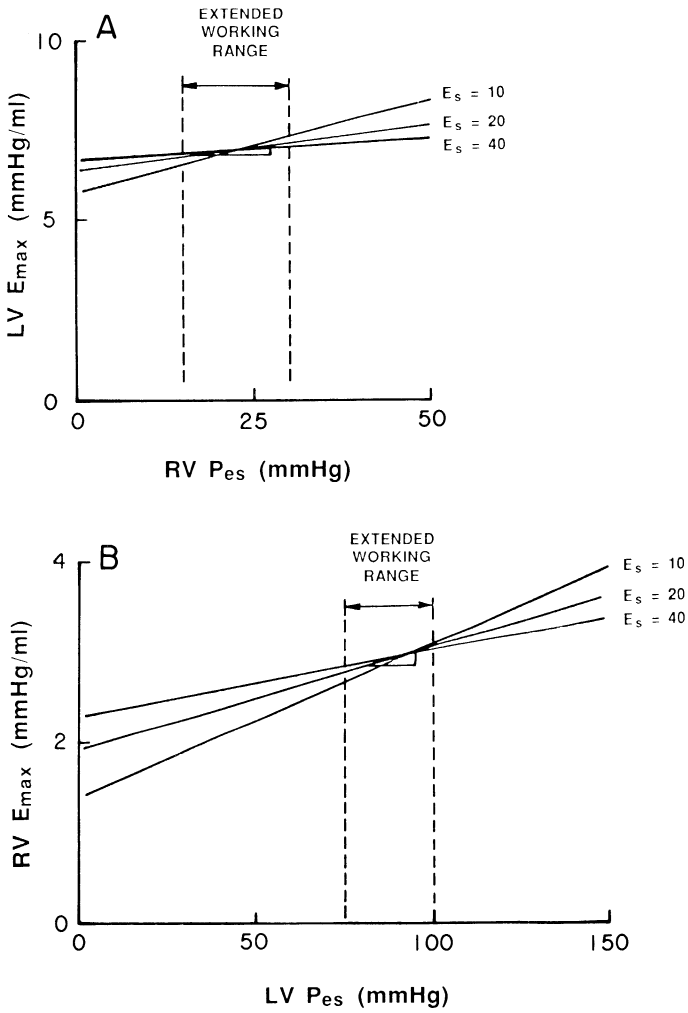


FIG. 3. *A*: effective left ventricular maximal elastance ($E_{max}$) vs. right ventricular end-systolic pressure ($P_{es}$). Effective $E_{max}$ with 0 right ventricular end-systolic pressure represents intrinsic left ventricular pressure generation. Increasing right ventricular end-systolic pressure increased slightly left ventricular effective $E_{max}$. *B*: effective right ventricular $E_{max}$ vs. left ventricular end-systolic pressure. Again, effective $E_{max}$ with 0 left ventricular end-systolic pressure represents intrinsic pressure generation property of right ventricle. Because of larger values, increasing left ventricular end-systolic pressure caused large increase in right ventricular $E_{max}$. $E_s$, septum elastance.

ventricular $E_{max}$ is shown in Fig. 3*B*, with right ventricular $V_{es}$ set at 13.2 ml (for values given in Table 1). The influence of left ventricular $P_{es}$ on effective right ventricular $E_{max}$ is significant despite the fact that the slope of the left ventricular $P_{es}$ effective-right ventricular $E_{max}$ relationship is quantitatively less than in the relationship depicted in Fig. 3*A*. The reason for this significant left ventricular influence is that left ventricular $P_{es}$ is large. Within a physiological range of left ventricular $P_{es}$, effective right ventricular $E_{max}$ (3.0 mmHg/ml) is nearly 1.6 times its value when left ventricular $P_{es}$ is 0 mmHg (i.e., the native right ventricular $E_{max}$ is 1.9 mmHg/ml). This indicates that as a consequence of ventricular interaction the right ventricular chamber (theoretically) has roughly 60% more pressure-generating capability than if the right ventricular free wall and septum had acted as an isolated organ. Over a physiological range of left ventricular $P_{es}$ values (80–100), effective right ventricular $E_{max}$ ranged from 2.8 to 3.1 mmHg/ml.

*Impact of ventricular interaction on cardiovascular hemodynamics.* In the first simulation, we examined the impact of interventricular interaction on hemodynamic responses to changes in system $R_a$. Figure 4 shows the relationship between systemic $R_a$ and stroke volume. Regardless of the level of ventricular interaction, stroke volume decreased as systemic $R_a$ increased. However, both systolic and diastolic ventricular interaction each individually reduced the influence of systemic $R_a$ on stroke volume; that is, in the presence of either systolic or diastolic ventricular interaction an increase in systemic $R_a$ from control was associated with a smaller decrease in stroke volume, and a decrease in systemic $R_a$ from control was associated with a smaller increase in stroke volume. When both systolic and diastolic ventricular interaction were present, this effect was synergistic.

Table 3 presents the values of several system variables obtained with systemic $R_a$ set at 5.0 mmHg·s·ml$^{-1}$ (double control value) with various degrees of ventricular interaction (refer to Table 2 for values obtained under control conditions). With the increase in systemic $R_a$ and without ventricular interaction, left ventricular stroke volume and ejection fraction decreased, whereas end-diastolic pressure and volume increased. For the right side of the heart, the decrease in venous return led to a primary decrease in right ventricular $P_{ed}$, $V_{ed}$, stroke volume, and ejection fraction. In the presence of diastolic ventricular interdependence, this decrease in right ventricular filling led to an increased left ventricular diastolic compliance, allowing a higher left ventricular $V_{ed}$ and resulting in a greater stroke volume than had existed with no interdependence.

With systolic ventricular interaction, the increase in pressure generation by the left ventricle significantly increased the effective contractility ($E_{max}$) of the right ventricle. Also note that as a result of reduced $P_{rv}$ gen-

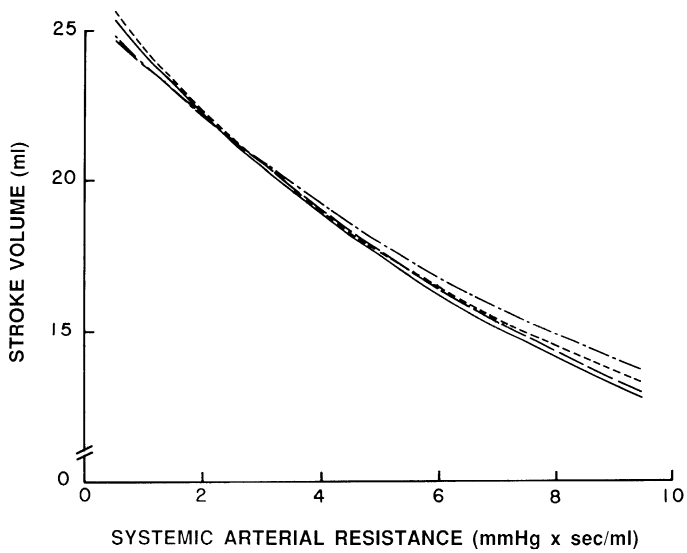


FIG. 4. Plots stroke volume vs. systemic arterial resistance. Control systemic arterial resistance was 2.5. Increasing resistance decreased stroke volume, whereas decreasing resistance increased stroke volume. Ventricular interdependence, however, reduced alterations in stroke volume. Solid line, simulation without ventricular interdependence; dot-dashed lines, diastolic ventricular interdependence only; small-dashed lines, systolic ventricular interdependence; long-dashed lines, systolic and diastolic ventricular interdependence.

TABLE 3. *Hemodynamic variables obtained with systemic vascular resistance increased to 5.0 mmHg·s·ml$^{-1}$ and various modes of interaction*

| Modes of Interaction | End-Diastolic | | Peak Pressure | Stroke Volume | Ejection Fraction | Effective $E_{max}$ | Stroke Work |
|---|---|---|---|---|---|---|---|
| | Pressure | Volume | | | | | |
| No interaction | | | | | | | |
| LV | 14.1 | 42.2 | 158.9 | 17.5 | 0.41 | 7.0 | 2,430 |
| RV | 3.2 | 30.8 | 34.2 | 17.5 | 0.57 | 3.0 | 515 |
| Diastolic only | | | | | | | |
| LV | 13.3 | 42.6 | 160.8 | 17.7 | 0.41 | 7.0 | 2,498 |
| RV | 3.4 | 30.7 | 33.5 | 17.7 | 0.57 | 3.0 | 504 |
| Systolic only | | | | | | | |
| LV | 15.4 | 42.9 | 161.1 | 17.7 | 0.41 | 6.8 | 2,475 |
| RV | 2.8 | 29.5 | 36.1 | 17.7 | 0.60 | 3.8 | 546 |
| Systolic + diastolic | | | | | | | |
| LV | 14.5 | 43.8 | 164.1 | 18.0 | 0.41 | 6.8 | 2,580 |
| RV | 3.0 | 29.3 | 35.5 | 18.0 | 0.61 | 3.9 | 553 |

LV, left ventricle; RV, right ventricle; $E_{max}$, maximal elastance. Units of measure: pressures, mmHg; volumes, ml; stroke work, mmHg·ml.

TABLE 4. *Hemodynamic variables obtained with pulmonary vascular resistance increased to 0.9 mmHg·s·ml$^{-1}$ and various modes of interaction*

| Modes of Interaction | End-Diastolic | | Peak Pressure | Stroke Volume | Ejection Fraction | Effective $E_{max}$ | Stroke Work |
|---|---|---|---|---|---|---|---|
| | Pressure | Volume | | | | | |
| No interaction | | | | | | | |
| LV | 7.4 | 35.9 | 106.9 | 18.6 | 0.52 | 7.0 | 1,730 |
| RV | 4.8 | 34.9 | 43.6 | 18.6 | 0.53 | 3.0 | 696 |
| Diastolic only | | | | | | | |
| LV | 7.7 | 36.3 | 108.0 | 18.9 | 0.52 | 7.0 | 1,767 |
| RV | 4.6 | 35.4 | 44.5 | 18.9 | 0.53 | 3.0 | 724 |
| Systolic only | | | | | | | |
| LV | 6.4 | 34.5 | 105.9 | 18.1 | 0.52 | 7.3 | 1,665 |
| RV | 5.2 | 35.7 | 41.4 | 18.1 | 0.51 | 2.6 | 634 |
| Systolic + diastolic | | | | | | | |
| LV | 6.8 | 35.0 | 107.3 | 18.4 | 0.53 | 7.3 | 1,712 |
| RV | 4.9 | 36.5 | 42.5 | 18.4 | 0.51 | 2.5 | 668 |

See Table 3 for abbreviations and units of measure.

eration during systole (secondary to decreased right ventricular filling), effective left ventricular $E_{max}$ decreased slightly. Overall, despite the drop of right ventricular $V_{ed}$ and slight decrease in left ventricular $E_{max}$, both ventricles were able to maintain a higher stroke volume compared with that existing without systolic interaction. When both systolic and diastolic ventricular interaction were present, both factors discussed above (increased left ventricular diastolic compliance and increased effective right ventricular contractility) played a role in potentiating stroke volume. Furthermore, the effect was synergistic; that is, the increase in stroke volume achieved in the presence of both systolic and diastolic interdependence was greater than the sum of the increases obtained with either alone.

The impact of ventricular interaction on the hemodynamic response to an increase in pulmonary $R_a$ is somewhat different from the response to an increase in systemic $R_a$ (Fig. 5 and Table 4), in that systemic and diastolic interaction had opposite effects when present separately. In the presence of diastolic interaction the increased pulmonary $R_a$ resulted in a primary decrease in left ventricular $V_{ed}$, causing an increase in right ventricular end-diastolic compliance and thus an increase in right ventricular $V_{ed}$ and stroke volume. With systolic interaction, the decrease in left ventricular $V_{ed}$ associated

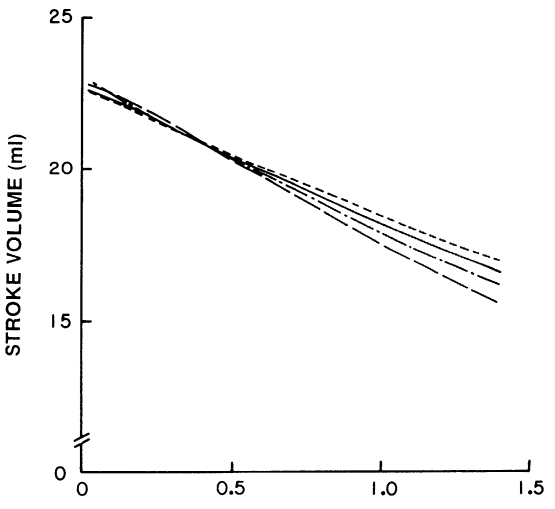


FIG. 5. Plots stroke volume vs. pulmonary arterial resistance. Control pulmonary arterial resistance was 0.3. Stroke volume changes were less with only diastolic ventricular interdependence and were greatest with systolic ventricular interdependence. Line descriptions as in Fig. 4.

TABLE 5. *Hemodynamic variables obtained with left ventricular free wall contractility decreased by 50%*

| Modes of Interaction | End-Diastolic | | Peak Pressure | Stroke Volume | Ejection Fraction | Effective $E_{max}$ | Stroke Work |
|---|---|---|---|---|---|---|---|
| | Pressure | Volume | | | | | |
| No interaction | | | | | | | |
| LV | 16.3 | 43.6 | 18.1 | 100.0 | 0.42 | 4.2 | 1,413 |
| RV | 3.7 | 32.2 | 18.1 | 37.0 | 0.56 | 3.0 | 576 |
| Diastolic only | | | | | | | |
| LV | 15.4 | 43.8 | 18.2 | 100.6 | 0.41 | 4.2 | 1,440 |
| RV | 4.0 | 32.0 | 18.2 | 36.0 | 0.57 | 3.0 | 557 |
| Systolic only | | | | | | | |
| LV | 15.8 | 43.3 | 17.6 | 98.2 | 0.41 | 4.1 | 1,342 |
| RV | 4.8 | 34.9 | 17.6 | 35.6 | 0.50 | 2.7 | 534 |
| Systolic + diastolic | | | | | | | |
| LV | 15.2 | 43.6 | 17.7 | 98.7 | 0.41 | 4.0 | 1,373 |
| RV | 4.0 | 32.2 | 17.7 | 34.9 | 0.55 | 2.8 | 525 |

See Table 3 for abbreviations and units of measure.

with an increased pulmonary $R_a$ led to a decrease in left ventricular pressure generation, which in turn had a deleterious effect on effective right ventricular contractility (effective $E_{max}$), with an overall effect of decreasing stroke volume. When both systolic and diastolic interaction are present, right ventricular $V_{ed}$ increased. However, despite the greater value for right ventricular $V_{ed}$, stroke volume was still below the values obtained without interdependence because of the decrease in the effective right ventricular $E_{max}$.

The hemodynamic changes accompanying changes in $E_{lvf}$ are presented in Fig. 6 where we show the relationship between $E_{lvf}$ and stroke volume. $E_{lvf}$ is expressed as a percent of the control value, since $E_{lvs}$ equaled 10.8 without interdependence and 9.4 with systolic interdependence. Without systolic ventricular interdependence, $E_{lvf}$ initially equaled 10.8 mmHg/ml and was varied from 2.2 to 27 mmHg/ml. With systolic ventricular interdependence, $E_{lvf}$ was set to 9.4 mmHg/ml and varied from 1.9 to 23 mmHg/ml. Decreasing $E_{lvf}$ decreased stroke volume, whereas increasing $E_{lvf}$ increased stroke volume. The presence of diastolic interaction had very little influence on the relationship when $E_{lvf}$ was decreased below control conditions. With diastolic interaction, however, the increase in stroke volume with increased $E_{lvf}$ was greater than under control conditions. With systolic interaction the increase in stroke volume accompanying increased $E_{lvf}$ was slightly greater and the decrease in stroke volume accompanying decreases in $E_{lvf}$ was also greater than the responses without systolic ventricular interdependence. The net effect of simultaneous diastolic and systolic interaction was roughly the sum of the effects of each alone. Table 5 summarizes the circulatory hemodynamics when $E_{lvf}$ was decreased by 50%. Without ventricular interdependence, stroke volume decreased as left ventricular effective $E_{max}$ and ejection fraction decreased and left ventricular end-diastolic pressure and volume increased. Incorporating diastolic ventricular interdependence increased stroke volume slightly as left ventricular end-diastolic volume increased. In the presence of systolic ventricular interdependence, the stroke volume decrease was greater as left and right ventricular effective $E_{max}$ decreased.

Figure 7 and Table 6 summarize the response to a decrease in $E_{rvf}$. Here again $E_{rvf}$ is expressed at a percent

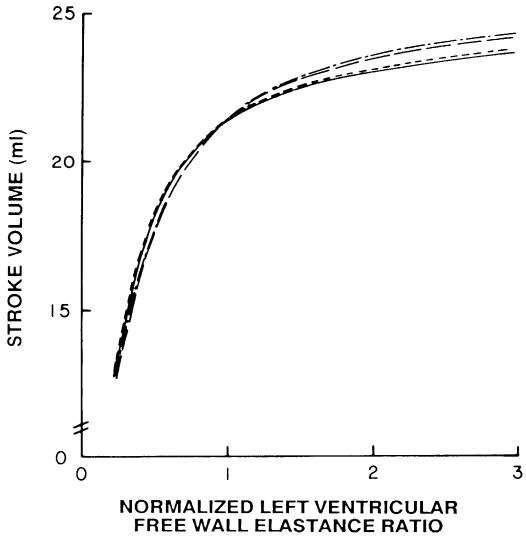


FIG. 6. Plots stroke volume vs. normalized left ventricular free wall elastance. Elastance was normalized by dividing by 10.77 for simulations without ventricular interdependence and with only diastolic ventricular interdependence and by 9.4 for simulations incorporating systolic ventricular interdependence. See Fig. 4 for line descriptions.

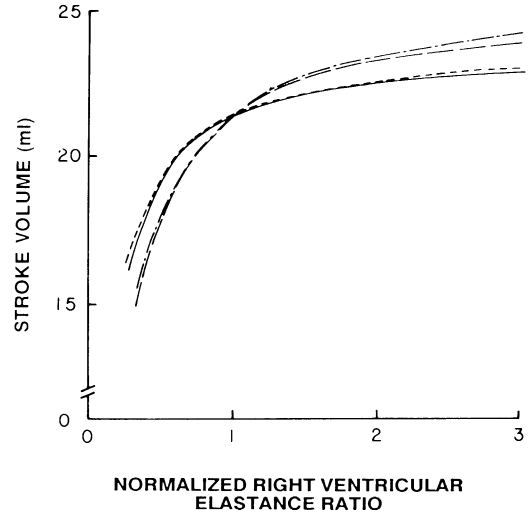


FIG. 7. Plots stroke vs. right ventricular elastance. Elastance was normalized by dividing by 3.53 for simulations without ventricular interdependence and with only diastolic ventricular interdependence, and by 2.4 for simulations incorporating systolic ventricular interdependence. See Fig. 4 for line descriptions.

TABLE 6. *Hemodynamic variables obtained with right ventricular free wall contractility decreased by 50%*

| Modes of Interaction | End-Diastolic Pressure | End-Diastolic Volume | Peak Pressure | Stroke Volume | Ejection Fraction | Effective $E_{max}$ | Stroke Work |
|---|---|---|---|---|---|---|---|
| No interaction | | | | | | | |
| LV | 8.2 | 36.9 | 110.8 | 19.1 | 0.52 | 7.0 | 1,831 |
| RV | 6.0 | 37.3 | 27.4 | 19.1 | 0.51 | 1.6 | 398 |
| Diastolic only | | | | | | | |
| LV | 8.7 | 37.1 | 110.9 | 19.2 | 0.52 | 7.0 | 1,834 |
| RV | 5.8 | 37.7 | 28.1 | 19.2 | 0.51 | 1.6 | 414 |
| Systolic only | | | | | | | |
| LV | 7.1 | 35.5 | 106.7 | 18.2 | 0.51 | 6.9 | 1,683 |
| RV | 6.5 | 38.0 | 25.3 | 18.2 | 0.48 | 1.3 | 334 |
| Systolic + diastolic | | | | | | | |
| LV | 7.7 | 35.7 | 107.1 | 18.3 | 0.51 | 7.0 | 1,694 |
| RV | 6.2 | 38.7 | 26.1 | 18.3 | 0.47 | 1.3 | 355 |

See Table 3 for abbreviations and units of measure.

of the control value. Without systolic ventricular interdependence, $E_{rvf}$ initially equaled 3.5 and was varied from 0.7 to 8.8 mmHg/ml. With systolic interdependence, $E_{rvf}$ was reduced to 2.1 and was varied from 0.5 to 5.2 mmHg/ml. Diastolic interaction had very little impact on the relationship between stroke volume and $E_{rvf}$ (Fig. 7). With systolic interaction, increases in stroke volume with increased $E_{rvf}$ were greater than under control conditions, whereas decreases in stroke volume were greater when $E_{rvf}$ was decreased. The $E_{rvf}$ stroke volume relationship with both systolic and diastolic interaction was nearly the same as just described for systolic interaction. In Table 6, we show the hemodynamic variables with $E_{rvf}$ decreased by 50% from control. With systolic interaction, the primary decrease in $E_{rvf}$ results in a greater decrease in left ventricular $V_{ed}$ than under control conditions, which results in less pressure generation by the left ventricle which, as a consequence of systolic interaction, leads to even less effective strength of the right ventricle as evidenced by the lower effective right ventricular $E_{max}$ and right ventricular ejection fraction.

Figure 8 shows the effects of varying the degree of systolic ventricular interdependence on the response to changes in $E_{rvf}$. A high level of systolic ventricular interdependence was simulated by setting $E_s$ to 10 mmHg/ml and then adjusting $E_{rvf}$ (1.6 mmHg/ml) and $E_{lvf}$ (13.8 mmHg/ml) until ventricular pressures and volumes returned to control values (Table 2). Similarly, a low level of systolic ventricular interdependence was simulated by setting $E_s$ to 40 mmHg/ml and adjusting $E_{rvf}$ (2.4 mmHg/ml) and $E_{lvf}$ (8.1 mmHg/ml) to return ventricular pressures and volumes to control values. A change in the degree of systolic ventricular interdependence alters the sensitivity to changes in $E_{rvf}$. Increasing systolic ventricular interdependence increased the changes in stroke volume with changes in $E_{rvf}$, while decreasing systolic ventricular interdependence decreased the changes in stroke volume with changes in $E_{rvs}$.

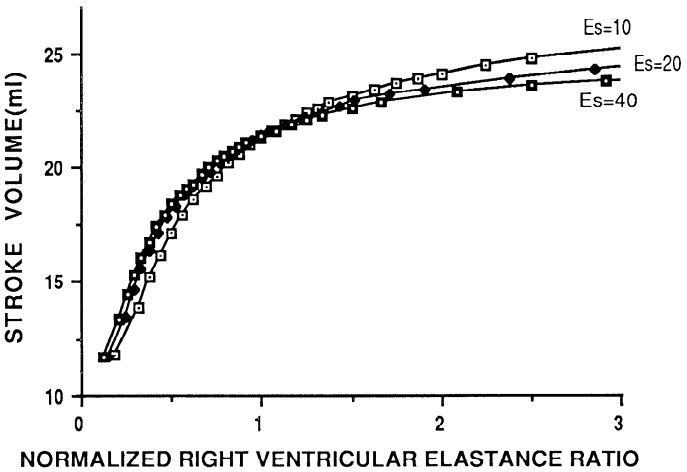


FIG. 8. Plots stroke volume vs. normalized right ventricular elastance. Systolic interdependence was set to three levels, high ($E_s$ = 10), normal ($E_s$ = 20), or low ($E_s$ = 40). Increasing systolic interdependence increased changes in stroke volume associated with changes in right ventricular free wall elastance.

## DISCUSSION

On a moment-to-moment basis, the pressure and volume in one ventricle can directly influence the pressure and volume in the other ventricle. This interaction occurs through the myocardium and is augmented by the pericardium. Because ventricular interdependence is always present and cannot be abolished in the working heart, the impact that ventricular interdependence has on overall cardiovascular system function has been difficult to ascertain. To overcome such experimental problems, we developed a computer simulation of the cardiovascular system in which ventricular interdependence could be turned on and off. Using the computer simulation, we examined the steady-state cardiovascular response to unilateral alterations in vascular resistance and ventricular contractility. The effects of ventricular interaction were different if the primary change in a system parameter was made to the systemic circulation or to the pulmonic circulation. With increases in systemic $R_a$ the presence of ventricular interaction caused less of a decrease in stroke volume than without interaction. In contrast with increases in pulmonary $R_a$ the presence of ventricular interaction caused a greater decrease in stroke volume than with no interaction present. Diastolic ventricular interdependence decreased slightly the stroke volume changes associated with alterations in $E_{rvf}$ and $E_{lvf}$, whereas systolic ventricular interdependence accentuated the stroke volume changes with alterations in $E_{rvf}$ and $E_{lvf}$.

*Comparison to literature.* To ascertain the validity of our model, we compared our simulation results with those obtained in working isolated heart preparations, whole animal studies, and clinical studies that have had direct quantitative measurements of ventricular interdependence.

In a working isolated heart preparation, Elzinga and colleagues (9) examined ventricular interdependence. The circulatory connections between the left and right ventricles were broken, allowing the aortic resistance, pulmonary artery resistance, and left and right atrial filling pressures to be controlled independently. While the right atrial pressure was maintained constant, increasing left atrial pressure led to an increase in left ventricular systolic pressure and a decrease in right ventricular systolic pressure. To simulate Elzinga's study, we modified our simulation to allow right atrial pressure to remain constant. Similar to Elzinga's study, an increase in left atrial pressure caused right ventricular systolic pressure to decrease slightly.

Several studies (8, 14, 18, 31) have measured the systolic gain or cross-talk between the ventricles. In general, these studies have measured the changes in systolic pressure caused by abrupt changes in afterload of the opposite ventricle. Table 7 summarizes the results of these studies. The studies show that the right-to-left ventricular gain is larger than the left-to-right ventricular gain. Elzinga et al. (8) report a very low right-to-left ventricular gain. However, they did not try to directly measure this gain and right ventricular pressure was only varied by 10 mmHg. Discounting this gain, right-to-left ventricular systolic gains ranged from 13.6 to 34.5%, whereas left-to-right ventricular systolic gains ranged from 8.6 to 14%. In the present study, *Eqs. 7* and *8* give the cross-talk gains between the ventricles. The gain for left-to-right ventricular pressure is $E_r/(E_r + E_s)$ or 9.5%, and the gain for right-to-left ventricular pressure is $E_l/(E_l + E_s)$, or 32%. These values are within the reported normal physiological range, with the right-to-left ventricular systolic gain on the high side of normal.

On a philosophical point, systolic gains do not directly indicate the relative importance of interdependence. For example, if the left-to-right gain was 10% and the right-to-left gain was 30%, one might assume that systolic ventricular interdependence is more important for left ventricular systolic function. However, if one examines the absolute magnitude of this cross-talk, the conclusions are totally different. This is because left ventricular systolic pressure is much greater than right ventricular systolic pressure. If we assume that all the left ventricular systolic pressure (100 mmHg, for example) is transmitted (10%) to the right ventricle then 10 mmHg (or ~50%) of the total measured right ventricular pressure was generated by the left ventricle. Thus the systolic gains, while providing a direct measure of ventricular interdependence, can be misleading in regard to the relative importance of ventricular interdependence.

TABLE 7. *Comparison of model and experimental results*

| Study | Ref. No. | Systolic Gain, % | |
|---|---|---|---|
| | | RV-to-LV | LV-to-RV |
| Theoretical | 18 | $E_l/(E_l + E_s)$ | $E_r/(E_r + E_s)$ |
| Elzinga et al.* | 8 | <5 | 14 |
| Langille and Jones | 14 | 34.5 | 8.6 |
| Maughan et al. | 18 | 14.6 | 8.0 |
| Slinker and Glantz | 31 | | |
| Pericardium on | | 33.3 | NM |
| Pericardium off | | 16.7 | NM |
| Slinker et al. | 32 | 13.6 | NM |
| Present study | | 32 | 9.5 |

* Estimated from Figs. 6 and 8. NM, not measured. $E_l$, left ventricular elastance; $E_s$, septal elastance; $E_r$, right ventricular elastance.

Slinker and colleagues (30) observed that chronic pressure overload hypertrophy decrease ventricular interaction. For our simulation to show the same phenomena, hypertrophy would have to increase septal elastance more than free wall elastance; this would decrease the relative ratios of the elastances, and thereby decreasing the cross-talk between the two ventricles.

Moulopoulos et al. (20) observed depression of left ventricular systolic function caused by either right ventricular bypass or overdistension of the right ventricle. These observations would also be consistent with the observations of the present study. Right ventricular bypass by decreasing right ventricular systolic pressure development should cause a mild reduction in left ventricular systolic function, similar to the results reported by Moulopoulos et al. Right ventricular overdistension by theoretical analysis should not cause an immediate depression in left ventricular systolic function. However, Moulopoulos et al. (20) did not measure left ventricular volume but rather plotted the indexes of left ventricular systolic pressure vs. left ventricular end-diastolic pressure. These results could be explained by diastolic ventricular interdependence; the large increase in right ventricular diastolic volume decreases left ventricular compliance.

Several clinical studies report results consistent with the concept of ventricular interdependence. Feneley et al. (10) observed that when right ventricular contraction either preceded or followed left ventricular contraction, right ventricular change in pressure over time waved form was double peaked. One peak corresponded to the peak rise in left ventricular change in pressure over time. These clinical data suggest the direct effect of right and left ventricular systolic pressure on right ventricular pressure development. However, these clinical studies give no indication of the magnitude of this interaction.

In a clinical study, Nunez et al. (21) used M-mode echocardiography to assess right ventricular wall thickness in normal tensive and essential hypertensive subjects. Right ventricular wall thickness was increased almost twofold in the hypertensive patients with hypertrophy. The results of the present simulation would be consistent with this observation. With hypertrophy, the elastance of the septum and left ventricular free wall would increase, thereby decreasing the systolic cross-talk between the ventricles. In effect, the left ventricular contribution to right ventricular performance would be lessened greatly. The right ventricle would have to compensate by increasing its intrinsic pumping ability to result in an increase in right ventricular wall thickness. Using our model, we simulated hypertension and hypertrophy, by increasing septal elastance to 40 $mmHg \cdot ml^{-1}$.

min and increasing systemic arterial to 4.0. With systolic ventricular interdependence, right ventricular free wall elastance had to be increased from 2.1 to 3.3. Thus the results and logic in the present simulation are consistent with this clinical observation, but obviously other interpretations of these clinical data are very possible and plausible.

*Critique of methods.* Because of the underlying assumptions the calculated results of this study should not be considered quantitative. Rather, the results should be viewed as a qualitative demonstration of the potential physiological importance of ventricular interdependence. Also, because of the length of the paper, an advantage of a computer simulation was only briefly presented. In a computer simulation, one is able to vary from very low to very high values a large number of parameters. The examination of the extremes can sometimes provide additional insights. Figures 3 and 8 provide an example of this where elastance is varied from very low to very high values. Again, due to the length of the paper, we only presented the values that probably represent normal ranges for diastolic and systolic interdependence.

Diastolic ventricular interdependence (3, 5, 25, 27, 35) was simulated by first approximating the diastolic pressure-volume characteristic of each ventricle by an exponential relation, the parameters of which were modified by the volume in the contralateral ventricle. With this simulation, the changes in ventricular diastolic pressure caused by changing contralateral volume were set to be similar to the reported literature (3, 5, 9, 13, 25–27).

Simulating systolic ventricular interdependence was more problematic. We selected the approach of Maughan and colleagues (18). The heart was viewed as three walls composing two chambers. With this approach, the systolic pressure developed in one ventricle as partially a function of the contralateral systolic ventricular pressure. The values for septal and left ventricular free-wall elastance were selected based on the approximate relative size of these walls. Right ventricular free-wall elastance was adjusted until the effective right ventricular elastance was 3.0.

This simulation studied only direct myocardial effects of interaction without including the pericardium. The pericardium is generally believed to accentuate this coupling between the ventricles (35). Thus we anticipated that the responses would have been greater if we had included the pericardium. Also, the stimulation did not model transient changes in ventricular input or arterial resistance. Amoore (1) simulated transient changes in ventricular input that would occur with respirations. Incorporation of ventricular interdependence caused greater changes in left ventricular end-diastolic volume and stroke volume. By design the stimulation does not incorporate neurological reflexes and humoral responses that could modulate ventricular function. Finally, this simulation does not attempt to account for chronic adaptations of the heart observed with long-term altered afterloads or altered contractile states.

*Implications.* Examination of the models we used to simulate ventricular interaction and the results we obtained from the simulation offer several physiological insights. However, as with all simulations, these insights are speculative and need to be interpreted cautiously. With the model used, a significant proportion of the pressure-generating capacity of each ventricle can be attributed to the contralateral ventricle. Left ventricular chamber contractility, as judged by maximal elastance, was enhanced on the order of 10% as a result of ventricular interaction, whereas right ventricular maximal elastance was affected by as much as 60%. This augmentation of maximal elastance is a direct consequence of *Eqs. 7* and *8*, which were derived and experimentally verified by Maughan and colleagues (18). The general prediction of these equations support earlier (3, 25, 27, 33) and more recent observations (31, 37). The effects of systolic ventricular interdependence on effective maximal elastance are explicitly presented in Fig. 3. These equations imply that less total heart mass is required for the same total work. For example, in the presence of systolic ventricular interdependence, left ventricular free-wall elastance was only 9.4 and right ventricular free-wall elastance was only 2.1 to achieve effective left ventricular maximal elastance of 7.0 and right ventricular maximal elastance of 3.0, respectively. Without interdependence, left ventricular free-wall elastance was 10.77 and right ventricular free-wall elastance was 3.53. If elastance is directly related to muscle mass then, without interdependence, the left ventricular free wall would have to be 15% greater and the right ventricular free wall would have to be ~50% greater to provide the same pumping ability.

The model also implies that right ventricular volume can influence our estimations of left ventricular function. For example, the end-systolic pressure-volume relationship is often used to assess left ventricular function. In experimental studies, both the inferior and superior vena cava are occluded to reduce inflow into the left ventricle, thereby obtaining left ventricular pressure-volume data over a wide range of ventricular volumes. This method of assessing left ventricular function probably minimizes the effects of right ventricular pressure on left ventricular systolic pressure. Conversely, if left ventricular function was assessed on releasing the vena cava, the left ventricular end-systolic pressure-volume relationship would be steeper, implying augmented left ventricular systolic function. The right ventricle has often been considered to respond adequately to increased stroke volume demands, but to respond poorly to increased pressure demands (22). This has generally been attributed to the bellows pattern of right ventricular contraction. The results of the present study reinforce this concept and suggest that ventricular interaction may be an underlying mechanism. With an increase in pulmonary resistance (Fig. 5 and Table 4), right ventricular stroke volume decreased. Without other compensating mechanisms (i.e., reflex responses), left ventricular preload decreased with a resulting decrease in left ventricular systolic pressure. With systolic ventricular interaction the shift downward in stroke volume is worsened, according to *Eq. 8*, since the decrease in left ventricular pressure, in turn, decreases the left ventricular contribution to right ventricular function. The calculated systolic indexes of right ventricular function (ejection fraction and effective contractility) decreased. Thus the present study suggests

that the poor response of the right ventricle to increased pressure demands may be related to ventricular interdependence. The converse would happen with a reduction in pulmonary resistance: left ventricular pressure would increase and, thereby, indexes of right ventricular systolic function, ejection fraction, and effective contractility would increase.

Similarly, the response to altered right ventricular free wall contractility was accentuated with the inclusion of systolic ventricular interdependence. With a decrease in right ventricular free wall contractility, cardiac output decreased further in the presence of systolic ventricular interdependence. Conversely, with an increase in right ventricular free wall contractility, cardiac output increased further with systolic ventricular interdependence. These predictions at first appear to conflict with earlier studies that demonstrated minimal changes in cardiac output after severe damages to the right ventricular free wall (2, 7, 33). However, these earlier studies damaged the right ventricular free wall by cauterization or by injections of liquid plastic that later solidified. Both techniques probably stiffened the right ventricular free wall and thereby increased right ventricular free-wall elastance. By *Eq. 8*, the increase in right ventricular free-wall elastance could accentuate systolic ventricular interaction, thereby explaining the preservation of function. Without excessively stiffening the right ventricular free wall, more recent studies have clearly demonstrated right ventricular dysfunction after right ventricular free wall ischemia and/or damage (12), similar to the predictions of the current study.

*Summary.* Because ventricular interdependence is always present, the hemodynamic consequences of ventricular interdependence have been difficult to ascertain for the closed-loop cardiovascular system. To overcome these problems, we developed a computer simulation of the cardiovascular system in which ventricular interdependence could be turned on and off. A major impact of ventricular interaction appears to be simply that pressure generation in one ventricle impacts on the pumping performance of the opposite ventricle. Ventricular interdependence decreased the hemodynamic effects of increasing systemic vascular resistance, while accentuating the effects of increasing pulmonary vascular resistance. The effects of regional decreases in elastance were accentuated by ventricular interdependence. In all cases, however, the magnitude of these effects were relatively small. This analysis may help to explain the right ventricular responses to elevated pulmonary artery pressure and regional ischemia.

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