Right Ventricular Preload Recroutable Stroke Work, End-Systolic Pressure–Volume, and $dP/dt_{max}$–End-Diastolic Volume Relations Compared as Indexes of Right Ventricular Contractile Performance in Conscious Dogs

Mohanraj K. Karunanithi, Jerzy Michniewicz, Susan E. Copeland, and Michael P. Feneley

Three indexes developed originally to assess left ventricular contractile performance were applied instead to the right ventricle (RV) in 11 conscious dogs: the relation between stroke work and end-diastolic volume (EDV), termed the preload recruitable stroke work (PRSW) relation; the end-systolic pressure–volume (ESPV) relation; and the maximum $dP/dt$ ($dP/dt_{max}$)–EDV relation. The reproducibility, inotropic sensitivity, chronotropic sensitivity, and afterload sensitivity of these RV relations were compared. RV volume was determined with an ellipsoidal shell subtraction model from orthogonal dimensions measured by sonomicrometry. RV transmural pressure was measured with micromanometers. After autonomic blockade, preload was varied by repeated, transient vena caval occlusions before and during partial occlusion of the main pulmonary artery, after release of the pulmonary arterial occlusion, after calcium infusion, and over a range of heart rates induced by atrial pacing. The slope and volume–axis intercept of the PRSW relation were more reproducible (SD/mean, 7.8±3.3% and 6.2±4.1%, respectively) than the slope and volume–axis intercept of the ESPV relation (10.1±6.7% and 23.0±31.3%, both $p<0.05$) or the slope and volume–axis intercept of the $dP/dt_{max}$–EDV relation (43.4±70.4% and 153.8±184.6%, both $p<0.05$). The slope of the PRSW relation increased 32±17% ($p<0.05$) after calcium infusion, but the volume–axis intercept did not change significantly. In contrast, the slopes of the ESPV and $dP/dt_{max}$–EDV relations did not change significantly after calcium infusion, but the volume–axis intercepts decreased significantly (both $p<0.05$). Despite a 71±26% increase in mean RV ejection pressure during partial occlusion of the main pulmonary artery, the slopes and volume–axis intercepts of both the PRSW and $dP/dt_{max}$–EDV relations did not change significantly, but the slope of the ESPV relation increased 45±22% ($p<0.05$) without significant change in the volume–axis intercept. None of the relations demonstrated significant chronotropic sensitivity. The PRSW relation is the preferred index of RV contractile performance because 1) it is the most reproducible, 2) its slope alone sensitively detects changes in contractile state, and 3) unlike the ESPV relation, it is relatively insensitive to afterload. (Circulation Research 1992;70:1169–1179)

Key Words • right ventricle • contractility • pressure–volume relations • stroke work

Right ventricular (RV) contractile performance remains poorly characterized, particularly in vivo, when compared with that of the left ventricle (LV). Estimation of dynamic LV volume by application of an ellipsoidal geometric algorithm to LV dimensions measured continuously by sonomicrometry has facilitated the investigation of LV function in vivo.1–4 The lack of a geometric algorithm for determination of RV volume by sonomicrometry has impeded similar studies of RV function in vivo. Recently, however, an ellipsoidal shell subtraction model for determining RV volume by sonomicrometry was described.5 The availability of this model permitted the investigation of RV contractile performance described in this report.

Three relations derived from LV pressure–volume loops have been proposed as linear and relatively load-independent indexes of LV contractile performance: the end-systolic pressure–volume (ESPV) relation; the relation between stroke work and end-diastolic volume (EDV), termed the preload recruitable stroke work (PRSW) relation; and the maximum $dP/dt$ ($dP/dt_{max}$)–EDV relation.7 Recent evidence suggests that the ESPV relation of the LV is subject to significant variability,8,9 nonlinearity,5,10–11 and afterload sensitivity in vivo.8,12–16 The PRSW and $dP/dt_{max}$–EDV relations of the LV are relatively afterload insensitive in vivo;3,16 but the PRSW relation has been found recently to be the most strictly linear and most reproducible of the three indexes of LV contractile performance in vivo.16
The purpose of this study was to characterize RV contractile performance by deriving simultaneously the ESPV, PRSW, and\( \frac{dP}{dt}_{\text{max}} \text{-EDV} \) relations of the RV from RV pressure-volume loops in conscious dogs. The reproducibility, inotropic sensitivity, chronotropic sensitivity, and afterload sensitivity of these three RV relations were compared.

Materials and Methods

Experimental Preparation

Eleven healthy adult dogs (22–42 kg) were anesthetized with halothane (1–2%) and succinylcholine (0.3 mg/kg i.v.) after induction with thiamylal sodium (20 mg/kg i.v.). A left lateral thoracotomy was performed. The pericardium was opened wide. Pulse-transit ultrasonic dimension transducers were positioned across the base–apex major axis (a) and anteroposterior minor axis (b) diameters of the LV and also across the septal-free wall minor axis diameters of both the LV (c) and the RV (d). The positioning of this biventricular orthogonal array of crystals has been described in detail previously.\(^{5,6} \) The septal crystal (1.5 mm o.d. cylinder) was placed through the tract of a 19-gauge needle that was introduced into the septum just to the right of the left anterior descending coronary artery, and the crystal was positioned near the RV endocardial surface midway between the anterior and posterior crystals. The remaining crystals (5 mm o.d. hemispheres) were sutured to the epicardium under direct vision. Silicone rubber pneumatic occluders were positioned around the inferior vena cava and the main pulmonary artery. A heparin-filled silicone catheter (2.6 mm i.d.) was secured in the apex of the RV. A similar catheter (3.2 mm i.d.) was secured in the base of the left atrial appendage. Another catheter (2.6 mm i.d.) with multiple side holes was positioned adjacent to the ventricular epicardium. Pacing wires were sewn to the right atrial appendage. The pericardium was left wide open. The transducer leads, catheters, and occluder tubing were tunneled into a subcutaneous pouch dorsal to the thoracotomy, which was repaired in multiple layers. Buprenorphine (10 \( \mu \)g/kg i.v.) and/or pethidine (2–3.5 mg/kg i.m.) were given as required for postoperative analgesia. After a recovery period of 7–10 days, the hardware was exteriorized from the pouch under 1% lidocaine local anesthesia. Each animal, lying quietly on its right side, was studied in the conscious state 1 hour after light sedation (morphine sulfate, 10 mg i.m.).

Data Acquisition and Experimental Protocol

The ultrasonic dimension transducers were coupled to a sonomicrometer.\(^{5} \) Micromanometer-tipped catheters (model MPC-500, Millar Instruments, Inc., Houston, Tex.), which had been balanced and calibrated simultaneously against a water column, were passed via the implanted silicone catheters to obtain RV, LV, and pleural pressures. Pharmacological attenuation of autonomic reflexes was achieved by intravenous administration of propranolol (1 mg/kg) and atropine (0.2 mg/kg).

Data were recorded under steady-state conditions and during transient vena caval occlusion induced by inflation of the implanted occluder for approximately 10 seconds. After all parameters had returned to their baseline level, transient vena caval occlusion was repeated. After restabilization, the pulmonary artery occluder was partially inflated to achieve a stable increase in RV systolic pressure of at least 50%. After stabilization of all parameters at their new levels, transient vena caval occlusion was repeated while the partial pulmonary arterial occlusion was maintained. After release of both the caval and pulmonary arterial occlusions, time was allowed for all parameters to return to their baseline levels. Caval occlusion was then repeated on two additional occasions. Atrial pacing was commenced at the lowest rate at which capture could be maintained during caval occlusion. The pacing rate was increased in steps of 10 beats per minute up to 170 beats per minute, and caval occlusion was repeated at each step. After cessation of pacing and a further period of restabilization, transient caval occlusion was performed before and after intravenous infusion of calcium gluconate (15 mg/kg).

At the conclusion of the study, each animal was killed by intravenous injection of potassium chloride under deep barbiturate anesthesia. The heart was excised, and the satisfactory position of implanted hardware was confirmed. After excision of the atria and valve tissue, the RV free wall was separated from the LV, and the volume of each was determined by water displacement.

Data Analysis

Analog data were digitized in real time at 200 Hz (model 1012 A/D converter, ADAC) and analyzed on a microprocessor (model PDP 11/23, Digital Equipment Corp., Marlboro, Mass.). The volume of the RV chamber was calculated from the ultrasonic cardiac dimension measurements according to an ellipsoidal shell subtraction method.\(^{5} \) With this model, RV chamber volume is calculated by subtracting the volume of the RV free wall (FWV) and the volume within the epicardial (outer) shell of the LV from the total epicardial (outer) shell volume of both ventricles. The volume within the epicardial shell of the LV was calculated by fitting its three axial diameters (a, b, and c) to the formula for a general ellipsoid \( \frac{\pi}{6} a \cdot b \cdot c \). Similarly, the total epicardial shell volume of both ventricles was calculated by fitting its three axial diameters (a, b, and [c+d]) to the formula for a general ellipsoid \( \frac{\pi}{6} a \cdot b \cdot [c+d] \). FWV was determined postmortem, as described above. Consequently, RV chamber volume (RVV) was given by the formula:\(^{5} \)

\[
RVV = \frac{\pi}{6} a \cdot b \cdot (c+d) - \frac{\pi}{6} a \cdot b \cdot c - FWV
\]

RV and LV transmural pressures were calculated as the difference between the respective chamber pressure and pleural pressure. RV \( \frac{dP}{dt} \) was computed from the digital pressure waveform as a running five-point polyorthogonal transformation.\(^{7} \) For the purpose of determining the RV ESPV relation, end systole was defined as the time at which the instantaneous ratio of pressure to volume was maximal during each cardiac cycle, in accordance with the definition originally used to determine the LV ESPV relation.\(^{6,17,18} \) The time from end diastole to end systole, according to this definition, was compared with the time from end diastole to the achievement of the minimum calculated RV volume and
peak negative dP/dt to document the temporal relation between maximal RV elastance and end ejection. Stroke work (SW) was calculated as the integral of transmural pressure and chamber volume.

The RV PRSW, ESPV, and dP/dt_{max}-EDV relations were determined by linear regression analyses, according to the following equations, respectively

\[ SW = M_a(EDV - V_w) \]  
\[ ESP = E_{sv}(ESV - V_0) \]  
\[ dP/dt_{max} = M_{dP/dt}(EDV - V_{dP/dt}) \]

where ESP and ESV are the end-systolic pressure and volume, respectively; \( M_a, E_{sv} \) and \( M_{dP/dt} \) are the slopes of the respective relations; and \( V_w, V_0 \) and \( V_{dP/dt} \) are the volume-axis intercepts of the respective relations. Linear regression analyses were used because significant nonlinearity of the RV PRSW and ESPV relations had been excluded in a previous investigation.

The ESPV relation defined by Equation 3 was described initially as a convenient approximation to the instantaneous pressure-volume relation of the LV at the time (\( t_{max} \)) when the slope of that relation reached its maximum value. Because the temporal behavior of the instantaneous pressure-volume relation of the RV has been shown previously to differ significantly from that of the LV, the instantaneous pressure-volume relation of the RV was also determined by linear regression analyses of isochronal data points at 20-msec intervals throughout contraction to determine \( t_{max} \) its temporal relation to end systole defined by the maximal instantaneous ratio of pressure to volume, and any differences between the instantaneous pressure-volume relation at \( t_{max} \) and the ESPV relation defined by Equation 3.

Results are summarized as mean±SD. Variation of the slopes or volume-axis intercepts of the three relations on repeated determinations was assessed by calculating the coefficient of variation (SD/mean) for the four venae cavae occlusions performed under control conditions (two before and two after the pulmonary arterial occlusion protocol). The coefficient of variation was expressed as a percentage. Multiple comparisons were performed by analysis of variance, including analysis of variance for repeated measures for the heart rate data. Intergroup comparisons were made with paired \( t \) tests with the Bonferroni correction for multiple comparisons. The level at which statistical significance was accepted was \( p<0.05 \).

Results

Representative dynamic data recordings obtained under baseline conditions and during one vena cavae occlusion are shown in Figure 1. Data recordings selected from runs of vena cavae occlusion before and during partial pulmonary arterial occlusion at matched RV end-diastolic volumes are shown in Figure 2. The RV pressure-volume loops obtained during these runs are shown in Figure 3 (panels A and B), together with the corresponding PRSW, ESPV, and dP/dt_{max}-EDV relations (panels C, D, and E, respectively). Note that peak RV pressure occurs early during ejection and that the pressure then falls as ejection proceeds. The PRSW

![Figure 1. Recordings showing representative cardiac dimensions and pressures recorded under baseline conditions and during a transient vena caval occlusion. LV, left ventricular; RV, right ventricular.](http://circres.ahajournals.org/)

and ESPV relations were highly linear (both \( r=0.96±0.03 \)), but linear regression coefficients for the dP/dt_{max}-EDV relation were consistently lower (\( r=0.82±0.16 \)). This appeared to be due mainly to the much greater beat-to-beat variation in dP/dt_{max} than in stroke work or end-systolic pressure during vena caval occlusion (Figure 3). RV dP/dt_{max} preceded the onset of RV ejection (defined as the onset of the reduction in calculated RV volume) by 38±20 msec.

A representative example of the instantaneous RV pressure-volume relations obtained by linear regression analyses of isochronal data points at 20-msec intervals from end diastole to \( t_{max} \) is shown in Figure 4. The slopes of the isochronal lines tended to increase during contraction, as originally described for the LV, but variation in the slopes of the isochronal lines after the first 60–80 msec from end diastole was quite small. Moreover, the temporal behavior of the volume-axis intercepts differed considerably from the tendency to convergence on a single value reported for the LV. The overall trend was for the volume-axis intercepts to move leftward as a function of time, as observed previously in the RV, but this trend was very erratic. Consequently, the most consistent temporal definition of \( t_{max} \) was provided by
selecting the most upward/leftward isochronal line, which was not always the line with the highest slope.

In Table 1, the mean time delay between end diastole and \( t_{\text{max}} \), defined in this way is given, together with the time delays between end diastole and end systole defined as the time at which the instantaneous ratio of pressure to volume was maximal, the time at minimum RV volume, and the time at peak negative dP/dt, respectively. There was no significant difference between \( t_{\text{max}} \) and the time to the maximal instantaneous ratio of pressure to volume, but both occurred significantly earlier than end ejection, whether indexed by the minimum RV volume or peak negative dP/dt (both \( p<0.05 \)). There was no significant temporal discrepancy between the two indexes of end ejection. The mean slope of the instantaneous pressure–volume relation at \( t_{\text{max}} \) was 1.32±0.51 mm Hg · ml⁻¹, and the corresponding mean volume–axis intercept was 10.1±19.3 ml. These data did not differ significantly from the mean values for \( E_{\text{es}} \) (1.20±0.45 mm Hg · ml⁻¹) and \( V_0 \) (9.2±18.3 ml), respectively.

When the four control vena caval occlusion runs were compared to assess the reproducibility of the PRSW, ESPV, and dP/dt\(_{\text{max}}\)–EDV relations (\( n=7 \) dogs) (Table 2), \( M_c \) proved to be less variable (SD/mean, 7.8±3.3%) than either \( E_{\text{es}} \) (10.1±6.7%, \( p<0.05 \)) or \( M_{dP/dt} \) (43.4±70.4%, \( p<0.05 \)). Vena caval occlusion produced a much larger reduction in stroke work relative to control values (78±7%) than in end-systolic pressure (52±16%, \( p<0.05 \)) or dP/dt\(_{\text{max}} \) (43±14%, \( p<0.05 \)). Consequently, determination of the volume–axis intercept of the PRSW relation required far less extrapolation from the measured data than did determination of the volume–axis intercepts of the ESPV and dP/dt\(_{\text{max}}\)–EDV relations, particularly when RV afterload was increased (Figure 3). On repeated determinations (Table 2), there was much less variation in \( V_w \) (6.2±4.1%) than in \( V_0 \) (23.0±31.3%, \( p<0.05 \)) or \( V_{dP/dt} \) (153.8±184.6%, \( p<0.05 \)). \( V_w \) exceeded \( V_0 \) by 15.3±15.4 ml (\( p<0.05 \)), and \( V_0 \) exceeded \( V_{dP/dt} \) by 37.3±38.3 ml (\( p<0.05 \)). Unlike \( V_w \) and \( V_0 \) values, \( V_{dP/dt} \) values were negative often.

The effects of partial pulmonary arterial occlusion (\( n=8 \) dogs) on steady-state hemodynamic parameters and the linear regression data for all three relations are summarized in Tables 3 and 4, respectively. Partial pulmonary arterial occlusion increased RV mean ejection pressure by 71±26%, increased end-diastolic volume, and decreased stroke volume, without changing heart rate significantly. Despite this large increment in RV afterload and consequent reduction in RV ejection fraction from 34±16% to 21±6% (\( p<0.05 \)), neither the slope, \( M_c \), nor the volume–axis intercept, \( V_w \), of the PRSW relation changed significantly. Similarly, \( M_{dP/dt} \) did not change significantly with increased RV afterload, and the change in \( V_{dP/dt} \) did not achieve statistical significance, although \( V_{dP/dt} \) values were subject to great variability. In contrast to these findings, the slope of the ESPV relation, \( E_{\text{es}} \), increased significantly by 45±22% with increased RV afterload (\( p<0.05 \)), but \( V_0 \) did not change significantly (Figure 3).

The effects of calcium infusion on steady-state hemodynamic parameters (\( n=7 \) dogs) are summarized in Table 5. Representative RV pressure–volume loops obtained under control conditions and after calcium infusion are shown in Figure 5 (panels A and B), together with the corresponding PRSW, ESPV, and dP/dt\(_{\text{max}}\)–EDV relations (panels C, D, and E). Regression data for these interventions are summarized in Table 6. Calcium infusion increased RV stroke volume, mean ejection pressure, and dP/dt\(_{\text{max}} \), but the average ejection fraction did not change significantly because of a small concomitant increase in end-diastolic volume in

**Figure 2.** Recordings of selected right ventricular (RV) and left ventricular (LV) dimensional and pressure data obtained during vena caval occlusion before (VCO) and during (PAO+VCO) partial pulmonary arterial occlusion at matched RV end-diastolic volumes. Partial pulmonary arterial occlusion increases RV systolic pressure and RV septal-free wall dimension and decreases LV systolic pressure and the anteroposterior, base–apex, and LV septal–free wall dimensions.
some dogs, although the average end-diastolic volume did not change significantly. Thus, as conventionally measured, the inotropic effect of calcium infusion was relatively mild. Nevertheless, the PRSW slope, $M_w$, increased significantly from $23.6 \pm 10.5$ to $31.4 \pm 16.1$ $\text{erg} \cdot \text{cm}^{-3} \cdot 10^3$, an average increase of $32 \pm 17\%$.

**FIGURE 3.** Right ventricular (RV) pressure–volume loops recorded during vena caval occlusions before (panel A) and during (panel B) partial pulmonary arterial occlusion. Graphs of the corresponding preload recruitable stroke work (panel C), end-systolic pressure (ESP)–end-systolic volume (ESV) (panel D), and maximum $dP/dt$ (dP/dt$_{max}$)–end-diastolic volume (EDV) (panel E) relations derived from these loops are also shown. Open circles indicate data obtained before pulmonary arterial occlusion, and closed circles indicate data obtained during pulmonary arterial occlusion.

**FIGURE 4.** Graph showing instantaneous right ventricular (RV) pressure–volume relations obtained by linear regression analyses of isochronal data points at 20-msec intervals from end diastole to the time ($t_{max}$) when the most upward/leftward position of the relation was attained. $E_{max}$, slope at $t_{max}$; $V_{0,t_{max}}$, volume–axis intercept at $t_{max}$. 

$E_{max} = 0.94 \text{ mmHg} \cdot \text{ml}^{-1}$
$V_{0,t_{max}} = 6.6 \text{ ml}$
TABLE 1. Time From End Diastole to Various Definitions of Right Ventricular End Systole

<table>
<thead>
<tr>
<th>t max (msec)</th>
<th>(P/V) max (msec)</th>
<th>−dP/dt max (msec)</th>
<th>End ejection (msec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>160±19</td>
<td>162±31</td>
<td>220±13</td>
<td>246±26</td>
</tr>
</tbody>
</table>

Values are mean±SD. t max. Time when the most upward/leftward position of the end-systolic pressure-volume relation was attained; (P/V) max maximal instantaneous ratio of pressure to volume; −dP/dt max peak negative dP/dt.

(p<0.05), but V w did not change significantly. In contrast, the slopes of the ESPV and dP/dt max–EDV relations did not change significantly after calcium infusion, but the volume–axis intercepts of both relations decreased significantly (Table 6, both p<0.05), indicating parallel leftward shifts of both relations with inotropic stimulation.

The effects of altered heart rate on the three relations are summarized in Table 7, and representative examples are shown in Figure 6. Increments in heart rate from 130 to 170 beats per minute induced by atrial pacing did not exert any systematic effect on any of the three relations. It should be noted that an apparent trend for the average slopes of the three relations to increase with increasing heart rate in Table 7 is due largely to the smaller number of dogs paced at rates of 130 beats per minute (n=4) and 140 beats per minute (n=8) when compared with higher pacing rates (n=9). The absence of chronotropic sensitivity is more readily apparent in the case of the PRSW relation (Figure 6), however, because of the much greater inherent variability of the slopes and volume–axis intercepts of the ESPV and dP/dt max–EDV relations on repeated determinations (Table 2).

Discussion

The investigation of LV contractile performance based on interpretation of the pressure–volume diagram has been a fertile field of research over the last 20 years. The ESPV relation, an offspring of the time-varying elastance model of ventricular contraction, has been the dominant index of LV contractile performance during this period, having been proposed initially as a linear and load-independent index. More recently, however, attention has been focused on both the nonlinear and afterload-dependent behavior of the ESPV relation of the LV.\cite{ref1,ref2,ref3,ref4,ref5} The PRSW and dP/dt max–EDV relations were proposed as alternative linear and relatively afterload-independent indexes of LV contractile performance that could be derived from the same pressure–volume data used to determine the ESPV relation.\cite{ref6} Recently, Little and colleagues\cite{ref7} determined all three LV relations simultaneously in conscious dogs and compared their variability and sensitivity to changes in inotropic state and afterload. Of these three relations, only the PRSW relation demonstrated no significant nonlinearity. The PRSW relation also was the least variable but least sensitive index of the LV contractile state, whereas the dP/dt max–EDV relation was the most sensitive but also the most variable index. While the slopes of all three relations increased when the contractile state was increased with dobutamine, the volume–axis intercepts of both the dP/dt max–EDV and ESPV relations increased also; only the volume–axis intercept of the PRSW relation remained constant. Like many others,\cite{ref8,ref9,ref10,ref11,ref12,ref13} Little and colleagues \cite{ref14} found that the LV ESPV relation was significantly afterload dependent, shifting leftward after phenylephrine administration. In contrast, there was no significant change in the position of either the PRSW or the dP/dt max–EDV relation with increased LV afterload. When linearity, reproducibility, afterload sensitivity, and stability of the volume–axis intercept were considered, therefore, the PRSW relation appeared to provide the most reliable index of the LV contractile state.\cite{ref15}

The present report provides a comparison of the ESPV, PRSW, and dP/dt max–EDV relations of the RV in conscious dogs. This was made possible by the recent development of the ellipsoidal shell subtraction model,\cite{ref16} which is the only method described to date for recording continuously instantaneous RV volume in vivo. Alternative, noncontinuous methods of measuring RV volume are limited by relatively low sampling frequencies.\cite{ref17,ref18,ref19,ref20} Consequently, studies of the RV pressure–volume diagram in vivo have been very limited, although a linear RV ESPV relation has been reported in both the isolated and intact canine heart\cite{ref21,ref22,ref23} and in the human heart in vivo.\cite{ref24,ref25} Recently, with the aid of the shell subtraction model, it was demonstrated that the RV ESPV relation is indeed linear in conscious dogs, unlike the LV relation, and that the RV PRSW relation also is highly linear, like its LV counterpart.\cite{ref26} The present investigation confirms these observations, but linear correlation coefficients for the RV dP/dt max–EDV relation were consistently lower than for the PRSW and ESPV relations and were also lower than those reported for the LV dP/dt max–EDV relation.\cite{ref27} The PRSW relation was the most reproducible of the three RV relations, and the dP/dt max–EDV relation was the least reproducible, in agreement with findings for the LV.\cite{ref28}

Three previous studies have cast doubt on the applicability of the time-varying elastance model of ventricular contraction to the RV.\cite{ref29,ref30,ref31} Elzinga and Westerhof\cite{ref32} found that isochronal “pressure–volume” relations derived by geometric extrapolation from force–length relations of isolated feline RV trabeculae shifted progressively leftward during the contraction

<table>
<thead>
<tr>
<th>PRSW</th>
<th>ESPV</th>
<th>dP/dt max–EDV</th>
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<tbody>
<tr>
<td>M w (%)</td>
<td>V w (%)</td>
<td>E w (%)</td>
</tr>
<tr>
<td>Mean±SD</td>
<td>7.8±3.3</td>
<td>6.2±4.1</td>
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</table>

Variation is measured as SD/mean. PRSW, preload recruitable stroke work relation; ESPV, end-systolic pressure–volume relation; dP/dt max–EDV, maximum dP/dt–end-diastolic volume relation; M w, slope of PRSW; V w, volume intercept of PRSW, expressed as a percentage; E w, slope of ESPV; V 0, volume intercept of ESPV; M dP/dt, slope of dP/dt max–EDV; V dP/dt, volume intercept of dP/dt max–EDV.
cycle rather than rotating around an approximately constant "volume–axis" intercept as described for the LV. Although the authors interpreted this finding as evidence that the time-varying elastance behavior of the LV reflected the complex organization of the muscle fibers in the intact ventricle rather than a fundamental muscle property, they noted that RV myocardium might differ from LV myocardium. Qualitatively identical findings of a time-dependent, parallel leftward shift of the human RV instantaneous pressure–volume relation during contraction were subsequently reported. In the latter study, however, the angiographic determination of RV volume and linear regression analyses of only three data points obtained under widely different afterload conditions may have influenced the results obtained, particularly in view of the afterload sensitivity of the RV ESPV relation demonstrated in the present study. In an isolated canine heart preparation, Maughan and colleagues also demonstrated a time-dependent leftward shift of the RV instantaneous pressure–volume relation during contraction, but the slope of the relation also increased as a function of time.

The findings of the present study with regard to the RV instantaneous pressure–volume relation are qualitatively similar to those of Maughan and colleagues in that we observed both an increase in the slope of the relation and a tendency for the volume–axis intercept to decrease during contraction. In the intact heart, however, variations in the slope of the relation were quite small after the first 60–80 msec of contraction and the behavior of the volume–axis intercept was too erratic to be described by the simple time-dependent function proposed by Maughan and colleagues (Figure 4).

There is considerable evidence, therefore, to support the conclusion that RV contraction cannot accurately be described by the simple time-varying elastance model proposed initially for the LV. Nevertheless, we found that \( t_{\text{max}} \) defined by the most upward/leftward position of the RV instantaneous pressure–volume relation was concordant with the time at which the maximal RV pressure–volume ratio was obtained during each contraction, and the RV ESPV relation closely approximated the instantaneous pressure–volume relation at \( t_{\text{max}} \). Like other investigators, we found that both \( t_{\text{max}} \) and the time of the maximal RV pressure–volume ratio occurred well before the termination of RV ejection (Table 1). This temporal discrepancy between maximal elastance and end ejection greatly exceeded that reported for the LV and may be appreciated qualitatively by the less rectilinear shape of RV pressure–volume loops (Figure 3).

RV \( dP/dt_{\text{max}} \) consistently preceded the onset of RV ejection in this study, which is a necessary condition for the theoretical derivation of the \( dP/dt_{\text{max}}-EDV \) relation from the time-varying elastance model of ventricular contraction. Over the range examined, the \( dP/dt_{\text{max}}-EDV \) relation did not appear to be significantly nonlinear, but there was much greater beat-to-beat variability in \( dP/dt_{\text{max}} \) than in stroke work or end-systolic pressure (Figures 3, 5, and 6). This reflects the magnification of the beat-to-beat variability of the pressure signal caused by differentiation. Given that the LV \( dP/dt_{\text{max}}-EDV \) relation is actually slightly concave toward the volume axis, the RV relation might also have been demonstrably concave if more data had been available in the lower range of \( dP/dt_{\text{max}} \) values. This and the lower linear correlation coefficients for the RV relation might explain why \( V_{\text{dprb}} \) values, which should be equivalent to \( V_o \) values theoretically, were consistently lower and frequently negative when determined by linear extrapolation. The lower linear correlation coefficients for the RV relation when compared with reported values for the LV relation may be related to the fact that LV contraction contributes significantly to the generation of RV systolic pressure, and this contribution is more evident when the pressure signal is differentiated. This duality of the RV \( dP/dt \) signal may confound the assumptions inherent in the derivation of a relation between RV \( dP/dt_{\text{max}} \) and RV end-diastolic volume from the time-varying elastance model. In any case, the inherent variability of the \( dP/dt_{\text{max}}-EDV \) relation is so great as to limit its practical application as an index of RV contractile performance because multiple determinations of the relation would be required before and

### Table 3. Effect of Partial Pulmonary Arterial Occlusion on Steady-State Hemodynamic Parameters

<table>
<thead>
<tr>
<th>Condition</th>
<th>HR (bpm)</th>
<th>EDV (ml)</th>
<th>SV (ml)</th>
<th>EF (%)</th>
<th>MEP (mm Hg)</th>
<th>SW (erg · 10^6)</th>
<th>dP/dt_{max} (mm Hg · sec⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>140±7</td>
<td>53±18</td>
<td>17±8</td>
<td>34±17</td>
<td>35±5</td>
<td>65±37</td>
<td>756±122</td>
</tr>
<tr>
<td>Pulmonary arterial occlusion</td>
<td>141±8</td>
<td>64±19*</td>
<td>13±6*</td>
<td>21±7*</td>
<td>59±6*</td>
<td>93±45*</td>
<td>924±106*</td>
</tr>
</tbody>
</table>

Values are mean±SD. HR, heart rate; bpm, beats per minute; EDV, end-diastolic volume; SV, stroke volume; EF, ejection fraction; MEP, mean ejection pressure; SW, stroke work; dP/dt_{max}, maximum dP/dt.

*\( p<0.05 \) vs. control.

<table>
<thead>
<tr>
<th>Condition</th>
<th>MEP ((\text{erg} · \text{cm}⁻² · 10^6))</th>
<th>( V_{\text{dprb}} ) (ml)</th>
<th>( E_{\text{max}} ) (mm Hg · ml⁻¹)</th>
<th>( V_o ) (ml)</th>
<th>( dP/dt_{\text{max}}-EDV ) ((\text{mm Hg} · \text{sec}⁻¹ · \text{ml}⁻¹))</th>
<th>( V_{\text{dprb}} ) (ml)</th>
<th>( r )</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>25.0±10.2</td>
<td>24.4±11.3</td>
<td>0.96±0.03</td>
<td>1.20±0.45</td>
<td>9.2±18.3</td>
<td>12.35±6.09</td>
<td>0.82±0.16</td>
</tr>
<tr>
<td>Pulmonary arterial occlusion</td>
<td>25.5±8.0</td>
<td>27.8±14.0</td>
<td>0.94±0.03</td>
<td>1.74±0.76*</td>
<td>10.9±14.0</td>
<td>11.88±3.76</td>
<td>-0.20±0.4</td>
</tr>
</tbody>
</table>

Values are mean±SD. PRSW, preload recruitable stroke work relation; ESPV, end-systolic pressure–volume relation; dP/dt_{max}-EDV, maximum dP/dt–end-diastolic volume relation; \( M_{\text{dprb}} \), slope of PRSW; \( V_{\text{dprb}} \), volume intercept of PRSW relation; \( E_{\text{max}} \), slope of ESPV; \( V_o \), volume intercept of ESPV; \( M_{\text{dprb}} \), slope of dP/dt_{max}-EDV; \( V_{\text{dprb}} \), volume intercept of dP/dt_{max}-EDV.

*\( p<0.05 \) vs. control.
TABLE 5. Effect of Calcium Infusion on Steady-State Hemodynamic Parameters

<table>
<thead>
<tr>
<th></th>
<th>HR (bpm)</th>
<th>EDV (ml)</th>
<th>SV (ml)</th>
<th>EF (%)</th>
<th>MEP (mm Hg)</th>
<th>SW (erg · 10⁻⁶)</th>
<th>dP/dt max (mm Hg · sec⁻¹)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>130±20</td>
<td>49±20</td>
<td>16±9</td>
<td>40±21</td>
<td>30±7</td>
<td>67±41</td>
<td>701±134</td>
</tr>
<tr>
<td>Calcium</td>
<td>123±20</td>
<td>52±22</td>
<td>19±10*</td>
<td>39±20</td>
<td>36±10*</td>
<td>100±56*</td>
<td>833±173*</td>
</tr>
</tbody>
</table>

Values are mean±SD. HR, heart rate; bpm, beats per minute; EDV, end-diastolic volume; SV, stroke volume; EF, ejection fraction; MEP, mean ejection pressure; SW, stroke work; dP/dt max, maximum dP/dt.

*p<0.05 vs. control.

after any intervention in a given subject to be certain of the effect exerted by the intervention.

The superior reproducibility of the RV PRSW relation, like the LV relation,²⁶,²⁹ derives from the fact that the ordinate (stroke work) is determined by integration over the whole cardiac cycle and diminishes at a much faster rate with preload reduction than either end-systolic pressure or dP/dt max, resulting in a wider data range for linear regression analysis and necessitating less extrapolation from the measured data to determine the volume–axis intercept (Figure 3). Similar observations have been made recently concerning the confidence with which the LV PRSW, ESPV, and dP/dt max–EDV relations can be determined in human subjects over a more limited data range.³⁰ The advantage of the superior reproducibility of the RV PRSW relation was demonstrated during the atrial pacing protocol, in which the absence of chronotropic sensitivity of the PRSW relation was readily apparent (Figure 6). Chronotropic insensitivity of the LV PRSW relation has been documented previously.³ In contrast, the greater variability of the RV ESPV and dP/dt max–EDV relations on repeated determinations may have contributed to the absence of a statistically demonstrable effect of altered heart rate on these relations.

The inotropic sensitivity of the three RV relations was determined in this study by intravenous infusion of a dose of calcium gluconate that was sufficient to cause significant increments in RV stroke volume, mean ejection pressure, stroke work, and dP/dt max yet not sufficient to increase RV ejection fraction significantly (Table 5). Consequently, it can be concluded that all three RV relations are more sensitive indexes of the RV inotropic state than the ejection fraction because all three relations were altered significantly by this inotropic stimulus (Table 6). Calcium gluconate was used in

![Figure 5](http://circres.ahajournals.org/)

**Figure 5.** Right ventricular (RV) pressure–volume loops recorded during vena caval occlusions before (panel A) and after (panel B) calcium infusion. Graphs of the corresponding preload recruitable stroke work (panel C), end-systolic pressure (ESP)–end-systolic volume (ESV) (panel D), and maximum dP/dt (dP/dt max)–end-diastolic volume (EDV) relations derived from these loops. Open circles indicate data obtained before calcium infusion, and closed circles indicate data obtained after calcium infusion.
TABLE 6. Linear Regression Data for Control State and Calcium Infusion

<table>
<thead>
<tr>
<th></th>
<th>PRSW</th>
<th>ESPV</th>
<th>dP/dt max-EDV</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>M&lt;sub&gt;n&lt;/sub&gt;</td>
<td>V&lt;sub&gt;n&lt;/sub&gt;</td>
<td>E&lt;sub&gt;es&lt;/sub&gt;</td>
</tr>
<tr>
<td>Control</td>
<td>23.6±10.5</td>
<td>22.9±13.3</td>
<td>12.7±0.59</td>
</tr>
<tr>
<td>Calcium</td>
<td>31.4±16.1</td>
<td>21.2±12.5</td>
<td>1.33±0.69</td>
</tr>
</tbody>
</table>

Values are mean±SD. PRSW, preload recruitable stroke work relation; ESPV, end-systolic pressure–volume relation; dP/dt max-EDV, maximum dP/dt–end-diastolic volume relation; M<sub>n</sub>, slope of PRSW; V<sub>n</sub>, volume intercept of PRSW; E<sub>es</sub>, slope of ESPV; V<sub>0</sub>, volume intercept of ESPV; M<sub>dP/dt</sub>, slope of dP/dt max-EDV; V<sub>dP/dt</sub>, volume intercept of dP/dt max-EDV.

*<i>p</i><0.05 vs. control.

preference to dobutamine or epinephrine, for example, because the potent vasoactive properties of the latter agents might have confounded the interpretation of the inotropic responses of the relations examined, particularly in view of the demonstrated afterload sensitivity of the ESPV relation.

As in the LV, inotropic stimulation increased the slope of the RV PRSW relation, without change in the volume–axis intercept; thus, the PRSW slope alone is an index of the contractile state in both ventricles. The inotropic responses of the RV ESPV and dP/dt max-EDV relations differed from that of the PRSW relation in that both shifted leftward, without significant change in their slopes. Unfortunately, the potential value of this shift in the volume–axis intercept of either relation as an index of contractile state is diminished by their poor reproducibility (Table 2). Maughan and colleagues also observed that the volume–axis intercept of the RV instantaneous pressure–volume relation of the isolated canine heart decreased significantly with inotropic stimulation, although this was accompanied by an increase in the slope of the relation. The leftward shift of the RV ESPV relation with inotropic stimulation provides further evidence that RV contractile behavior is not adequately described by the simple time-varying elastance model. A similar leftward shift of the LV ESPV relation with inotropic stimulation was reported by Crottogini and colleagues, but this differed from the findings of Little and colleagues.

As observed in the LV, increased RV afterload did not significantly shift the position of either the RV PRSW relation or the RV dP/dt max-EDV relation, despite the fact that RV mean ejection pressure increased by 71%, on average, during partial pulmonary arterial occlusion. It should be noted, however, that the inherent variability of the dP/dt max-EDV relation may have obscured the effects of afterload on the relation.

In contrast to the PRSW relation, the RV ESPV relation was afterload sensitive: the slope increased by 45±22%, without significant change in the volume–axis intercept. A leftward shift of the LV ESPV relation with increased LV afterload in situ, whether caused by an increase in the slope or a decrease in the linearly extrapolated volume–axis intercept, or both, has been noted by many investigators in recent years. Given the evidence that the normal LV ESPV relation in situ is actually parabolic (concave to the volume axis), both sets of observations may be consistent with counterclockwise rotation of the parabolic LV ESPV relation around a relatively constant volume–axis intercept, akin to the increase in the slope of the linear RV ESPV relation without change in the volume–axis intercept.

The prominent afterload sensitivity of the LV ESPV relation in situ contrasts with the relative afterload insensitivity of the LV ESPV relation reported in an isolated heart preparation. One possible explanation for this difference is that coronary perfusion pressure increases with increased LV afterload in situ but was held constant in the isolated heart preparation. Abel and Reis demonstrated that increased coronary perfusion pressure increased LV systolic elastance in the isovolumically beating isolated canine heart. On the other hand, Miller and colleagues demonstrated more recently that although increased coronary perfusion pressure enhanced peak left ventricular pressure generation in isovolumically contracting pig hearts, it did not significantly influence left ventricular pressure generation, peak dP/dt, or myocardial oxygen consumption in the intact circulation. The results of the present investigation also cast doubt on the validity of the coronary perfusion pressure hypothesis because partial occlusion of the pulmonary artery not only does not increase coronary perfusion pressure but decreases it by reducing LV preload. Thus, unless the very similar

Table 7. Linear Regression Data for Atrial Pacing Protocol

<table>
<thead>
<tr>
<th>HR (bpm) n</th>
<th>M&lt;sub&gt;n&lt;/sub&gt;</th>
<th>V&lt;sub&gt;n&lt;/sub&gt;</th>
<th>E&lt;sub&gt;es&lt;/sub&gt;</th>
<th>V&lt;sub&gt;0&lt;/sub&gt;</th>
<th>M&lt;sub&gt;dP/dt&lt;/sub&gt;</th>
<th>V&lt;sub&gt;dP/dt&lt;/sub&gt;</th>
<th>r</th>
</tr>
</thead>
<tbody>
<tr>
<td>130 4</td>
<td>18.5±3.2</td>
<td>24.6±9.0</td>
<td>1.21±0.71</td>
<td>17.7±6.7</td>
<td>0.97±0.03</td>
<td>14.55±4.08</td>
<td>0.2±19.6</td>
</tr>
<tr>
<td>140 8</td>
<td>22.6±9.7</td>
<td>26.6±15.3</td>
<td>1.34±0.76</td>
<td>16.4±11.5</td>
<td>0.96±0.03</td>
<td>13.19±8.70</td>
<td>27.0±81.2</td>
</tr>
<tr>
<td>150 10</td>
<td>24.6±10.0</td>
<td>26.5±15.8</td>
<td>1.45±0.70</td>
<td>17.0±11.3</td>
<td>0.94±0.04</td>
<td>16.78±7.66</td>
<td>-5.2±23.9</td>
</tr>
<tr>
<td>160 9</td>
<td>24.9±12.7</td>
<td>26.2±15.6</td>
<td>1.58±0.76</td>
<td>18.1±12.5</td>
<td>0.95±0.02</td>
<td>21.96±11.27</td>
<td>-0.8±33.5</td>
</tr>
<tr>
<td>170 9</td>
<td>25.4±11.7</td>
<td>26.9±15.2</td>
<td>1.63±0.78</td>
<td>18.8±11.7</td>
<td>0.96±0.02</td>
<td>20.93±7.71</td>
<td>7.5±15.3</td>
</tr>
</tbody>
</table>

Values are mean±SD. HR, heart rate; bpm, beats per minute; n, number of dogs at each rate; PRSW, preload recruitable stroke work relation; ESPV, end-systolic pressure–volume relation; dP/dt max-EDV, maximum dP/dt–end-diastolic volume relation; M<sub>n</sub>, slope of PRSW; V<sub>n</sub>, volume intercept of PRSW; E<sub>es</sub>, slope of ESPV; V<sub>0</sub>, volume intercept of ESPV; M<sub>dP/dt</sub>, slope of dP/dt max-EDV; V<sub>dP/dt</sub>, volume intercept of dP/dt max-EDV.
responses of the RV and LV systolic elastances to increased afterload in situ are to be attributed to different mechanisms, which seems unlikely, the coronary perfusion pressure hypothesis is not adequate to explain the different afterload responses of isolated and in situ canine hearts.

A potential criticism of the investigation of the effects of increased RV afterload on RV performance in this study is that the distortion of biventricular geometry induced by pulmonary arterial constriction might have altered the relation between RV volumes calculated with the ellipsoidal shell subtraction model and actual RV volumes. In a previous validation study of the shell subtraction model, however, it was demonstrated that the relation between calculated and actual RV volumes was insensitive to LV volume when the volumes of both ventricles were varied independently over the range from 0 to 60 ml in the canine heart. This validation protocol involved much greater distortions of biventricular geometry (including complete inversion of the interventricular septum when LV chamber volume was zero) than observed in the present study or in two previous detailed studies of the effects of pulmonary arterial constriction on biventricular geometry. In one of those previous studies, for example, peak RV systolic pressure was increased by 140%, on average, during pulmonary arterial constriction, yet the average ratio of the LV septal–free wall dimension/antecorpo- prior dimension during this intervention (0.80) was not much less than the average ratio observed during venacaval occlusion at matched LV volumes (0.87). Given the lesser magnitude of pulmonary arterial constriction used in the present study (RV mean ejection pressure increased by 71%, on average), it is unlikely that the distortion of biventricular geometry induced would have influenced the calculation of RV volume significantly.

One current limitation of the ellipsoidal shell subtraction model is the necessity to measure RV free wall volume postmortem (see “Materials and Methods”). Although this did not present a problem in the present study, it would prevent application of the model in serial studies of RV function in vivo if changes in RV free wall mass were anticipated. Accurate echocardiographic methods for determining LV wall volume in vivo have been developed, however, and similar strategies, although more technically demanding, are potentially applicable to the measurement of RV free wall volume.

In summary, the PRSW relation of the RV, like that of the LV, is the most reproducible linear index of the contractile state and is afterload insensitive over a wide range. Because the volume–axis intercept of the PRSW relation is highly reproducible and is not altered significantly by changes in either the contractile state or afterload, its slope alone is an index of the RV contractile state. The time-varying elastance model does not provide an accurate description of RV contractile behavior. The RV ESPV relation derived from this model is significantly afterload sensitive and is less reproducible than the RV PRSW relation. Consequently, the ESPV relation is not a reliable index of the RV contractile state. The dP/dt max–EDV relation, though not demonstrably afterload sensitive, is the least reproducible index of the RV contractile state.

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References


Right ventricular preload recruitable stroke work, end-systolic pressure-volume, and dP/dtmax-end-diastolic volume relations compared as indexes of right ventricular contractile performance in conscious dogs.

M K Karunanithi, J Michniewicz, S E Copeland and M P Feneley

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