Human Right Ventricular End-Systolic Pressure-Volume Relation Defined by Maximal Elastance

Kenneth A. Brown, MD, and Roy V. Ditchey, MD

This study was undertaken to determine 1) whether a combined radionuclide-hemodynamic technique could define the right ventricular end-systolic pressure-volume relation (RV ESPVR) in the clinical setting, 2) whether the human RV ESPVR defined by maximal elastance is linear and responsive to inotropic interventions, and 3) whether more easily measured modifications of the ESPVR are reliable substitutes as an index of RV function. Eight patients with normal RV function were studied with simultaneous micromanometer RV pressure measurements and radionuclide ventriculography to construct RV pressure-volume loops. Data were collected at baseline and after at least two alterations in loading conditions with nitroglycerin, phenylephrine, or saline. End systole was defined by maximal elastance (E(t) = P(t)/(V(t) - V0)). Data were also obtained during administration of dobutamine in four patients and after atrial pacing tachycardia in one patient. The RV ESPVR defined by maximal elastance was highly linear (r=0.988–0.999) throughout the range of pressures and volumes tested. Furthermore, the linear correlations were significantly higher (p<0.005), and the linear regression standard error of the estimate (SEE) was significantly lower (p<0.005) for the RV ESPVR defined by maximal elastance compared with modifications of the ESPVR with the ratio of pulmonary artery–dicrotic notch pressure or RV peak pressure to end-ejection volume. Dobutamine or atrial pacing tachycardia produced a leftward shift of the entire RV pressure-volume loop, and in each patient (five of five), the point of maximal elastance fell outside the 95% confidence interval defined by the baseline ESPVR. However, because of the larger SEE, the leftward shift with modifications of the ESPVR was not statistically significant in any patient by the pulmonary artery–dicrotic notch pressure: end-ejection volume ratio and was significant in only one of five patients by the RV peak pressure: end-ejection volume ratio (p<0.03). Therefore, it appears that the steady-state RV ESPVR defined by maximal elastance in patients with normal RV function is responsive to alterations in inotropic state and is more sensitive to alterations in RV function than the frequently used, more easily measured modifications of the RV ESPVR. (Circulation 1988;78:81–91)

The concept of the left ventricular (LV) end-systolic pressure-volume relation (ESPVR) has evolved substantially in complexity in recent years. However, there is a large body of experimental and clinical data showing that the LV ESPVR is relatively load independent and sensitive to changes in LV contractility and, hence, can serve as a clinically useful index of LV function.1–15 In the isolated heart, the right ventricular (RV) ESPVR also appears to be load independent and responsive to inotropic changes.16 However, there have been few studies of the RV ESPVR in humans.17–19

Although Sagawa1 has defined end systole as the point when the active contractile process peaks, identified as the time of maximal elastance, previous clinical reports of RV ESPVR17–19 have used pulmonary artery (PA)–dicrotic notch or peak RV pressure and minimum radionuclide-derived RV volume as estimates of RV end-systolic pressure and volume, respectively, because they are relatively easy to measure. For the LV, the ESPVRs derived with comparable pressure and volume surrogates correlate reasonably well with the ESPVRs determined from maximal elastance.20,21 However, there are theoretical considerations that may limit the applicability of these surrogates to the RV.
Normally, LV ejection ends shortly after end systole defined by maximal elastance, but this is not true when peripheral resistance is low,\textsuperscript{1,22} as is the case in the pulmonary circulation. Indeed, Maughan et al\textsuperscript{16} have demonstrated that RV ejection continues well beyond end systole defined by maximal elastance. The relation between RV maximal elastance and these other indexes of end systole has not been previously examined in humans. Therefore, the present study was undertaken to determine 1) whether a combined radionuclide-hemodynamic approach can be clinically applied to the study of the RV ESPVR, 2) whether the human RV ESPVR defined by maximal elastance is sensitive to changes in contractile state, and 3) whether more easily measured indexes of RV end systole are reliable substitutes when determining ESPVR as a measure of RV function.

### Patients and Methods

#### Patient Population

The study group consisted of eight patients (six male and two female) scheduled to undergo diagnostic cardiac catheterization for suspected coronary artery or valvular heart disease. At catheterization, four patients had normal findings, two had isolated left anterior descending coronary artery disease (50% and 80% luminal diameter narrowing), one had mild aortic stenosis (mean gradient=10 mm Hg), and one had moderate aortic insufficiency (Table 1). All patients had normal baseline right heart hemodynamics and normal RV contraction by radionuclide ventriculography (see below). The mean age was 55±11 (± SD) years. Cardiac medications at the time of admission included nitrates (one of eight), \(\beta\)-blockers (two of eight), and diuretics (one of

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CAD, coronary artery disease; HR, heart rate; RVEF, right ventricular ejection fraction; EDVI, end-diastolic volume index; ESP, end-systolic pressure; ESVI, end-systolic volume index; PA-DN, pulmonary artery-dicrotic notch pressure; RV-PP, right ventricular peak pressure; EEVI, end-ejection volume index; PVR, pulmonary vascular resistance; AS, aortic stenosis; LAD, left anterior descending artery stenosis; AI, aortic insufficiency.
eight). At the time of study, no patient had evidence of recent acute myocardial infarction, unstable angina pectoris, congestive heart failure, ventricular ectopy, cardiomyopathy, or right heart valvular pathology. Specifically, there was no evidence in any patient of tricuspid regurgitation by physical examination or by hemodynamic criteria. The research study was approved by the University of Vermont, Medical Center Hospital of Vermont Committee on Human Research, and each patient gave written, informed consent after receiving details of the protocol, its purpose, and potential risks. There were no complications as a result of this study.

**Cardiac Catheterization and Coronary Angiography**

Coronary angiography and left ventriculography were performed in a standard manner. After routine catheterization, a 7F thermoloculation Swan-Ganz catheter (American Edwards, Irvine, California) was inserted percutaneously and advanced to the pulmonary artery. In addition, a 5F temporary atrial pacing electrode catheter was placed in a stable position within the right atrium. Finally, a specially made 8F thin-wall balloon flotation guiding catheter (Kimal, Indian Mills, New Jersey) was inserted percutaneously through a femoral vein and advanced into the RV. A 3F high-fidelity micromanometer-tipped Millar catheter (Houston, Texas) was then passed within the 8F guiding catheter to its end.

All study pressure measurements were made at least 25 minutes after the last contrast injection. The RV micromanometer-tipped catheter was calibrated with a mercury manometer before insertion. The slow-filling phase of the high-fidelity RV pressure tracings were matched to the RV pressures measured within the fluid-filled guiding catheter (with a Tooeby-Borst adapter) before each set of pressure recordings to correct for any baseline drift. The fluid-filled Swan-Ganz catheter was used to measure pulmonary capillary wedge, pulmonary artery, and right atrial pressures. Systemic pressures were measured with a fluid-filled pigtail catheter in the proximal aorta. Zero reference for all pressure measurements was the midchest level. All data were recorded on a Honeywell-Electronics for Medicine recorder (model VR-16, Waltham, Massachusetts).

A square-wave pulse signal timed to the end-diastolic gating signal of the nuclear medicine gamma camera was superimposed on the pressure tracings to allow synchronization of pressure and radionuclide data to end diastole.

**Radionuclide Techniques**

Gated blood pool radionuclide ventriculography was performed according to a previously described technique. Autologous red blood cells were labeled with 20 mCi technetium-99m with an in vitro technique, and equilibrium was established. With the patient supine, a standard Anger gamma camera (Technicare 420, Solon, Ohio) equipped with a 30° slant-hole collimator was positioned over the heart in the left anterior oblique view that best separated the RV and LV as well as the right atrium and RV. Gated images were collected with a 64 × 64-matrix in 32 frames/cycle for 3–8 minutes. The exact time of each collection was recorded, and a blood sample was obtained at the midpoint of each study. Radionuclide ventriculograms and simultaneous pressure measurements were recorded at baseline and after sequential alterations in loading conditions (see below).

**Analysis**

RV time-activity curves from serial background-corrected radionuclide ventriculograms were analyzed in each patient with an operator-drawn fixed end-diastolic RV region of interest. The end-diastolic image was used to identify the septal border of the ventricle, while the stroke volume image and isocontour fitting were used to identify the inferior and free walls of the RV. A fixed region of interest was chosen because it minimizes operator error and variability for frame-by-frame analysis of ventricular counts. Baseline absolute RV end-diastolic volume (EDV) was calculated from baseline radionuclide ejection fraction (EF) and thermoloculation stroke volume (SV = cardiac output/heart rate): RVEDV = SV/EF. Relative changes in RV volumes between baseline and postloading radionuclide ventriculograms were determined by correcting RV counts for acquisition time, physical decay, and biological clearance. Acquisition time was calculated as the product of frame duration and number of cardiac cycles that were counted. Physical decay was corrected by recording the duration of time between each study. Biological clearance of the tracer was determined, with a well counter, from changes in counts per second per 100 microliters sample of blood obtained at the midpoint of each study.

**Experimental Protocol**

**Baseline data collection.** Before data collection, the temporary atrial pacemaker was set to capture approximately 5 beats/min above resting rate to minimize changes in heart rate during load changes. After baseline radionuclide and hemodynamic measurements were obtained, loading conditions were altered with intravenous infusion of nitroglycerin or phenylephrine (starting at 10 μg/min) or 0.9% saline boluses of 250–300 ml infused intravenously during 2–3 minutes. Infusions were titrated to produce changes in RV systolic pressure of 4–8 mm Hg or at least a 15% change from baseline. In four patients, more than one type of intervention was used to change load (Table 1).

At the new steady-state loading condition, a radionuclide ventriculogram with simultaneous hemodynamic measurements was recorded. In this
manner, resting data were collected during three or four steady-state loading conditions in each patient. With atrial pacemaker capture (described above), heart rate showed no change in six patients and less than 6% change in two patients in response to load alterations (Table 1).

After completion of the resting data collections, a subgroup of four patients (all with normal coronary arteries) received an intravenous infusion of dobutamine (10 μg/kg/min), and repeat radionuclide and hemodynamic data were again collected. In one additional patient (with isolated left coronary disease), atrial pacing tachycardia was produced to 85% of age-predicted maximal heart rate (132 beats/min), and repeat radionuclide and hemodynamic data were collected. In this patient, no chest pain or ischemic ST depression developed at peak pacing. In all cases, neither the patient nor gamma camera was moved between data collections.

Pressure-Volume Relations

Calculation of \( E_{\text{max}} \) and \( V_0 \) from analysis of maximal elastance. Pressure-volume loops were generated for each radionuclide ventriculogram. RV pressure tracings encompassing one respiratory cycle (usually 6–9 beats) were digitized to 128 points/cardiac cycle. End diastole for each cardiac cycle was defined as the onset of the gating signal of the nuclear medicine cardiology camera/computer that was superimposed upon the pressure tracings. The gating signal represents the moment when the imaging computer recognizes the electrocardiographic QRS signal and begins collecting data for that cardiac cycle. The serial RV pressure tracings were then averaged point by point for each of the 128 points per cardiac cycle by computer (Endeco Medical, Marion, Massachusetts), resulting in a single signal-averaged RV pressure tracing for a given data acquisition. The 32-frame RV radionuclide ventriculogram time-activity curve was digitized, with linear interpolation, to 128 points. The average RV pressure and time-activity curves were then smoothed with a five-point weighted low-pass filter. After the curves were synchronized to end diastole, pressure-volume loops were plotted from 128 pressure-volume coordinates throughout the cardiac cycle. The time interval between data points depended upon the cardiac cycle duration and varied between 3.5 and 6.6 msec. The slope (\( E_{\text{max}} \)) and volume intercept (\( V_0 \)) of the ESPVR were determined from the baseline and postloading pressure-volume loops. End systole was defined as the time of maximal elastance, that is, the point in time (t) in a given cardiac cycle at which the elastance was maximal according to the formula: 

\[
E(t) = P(t)/[V(t) - V_0],
\]

where \( V_0 \) = volume axis intercept of the ESPVR. To determine the end-systolic pressure-volume line, the method of Kono and colleagues was used: \( V_0 \) was first assumed to be zero, and the maximal pressure-volume ratio was calculated for each loading condition. A least-squares linear regression was then applied, and an initial estimate of \( V_0 \) was defined as the volume intercept of this regression line. With the initial \( V_0 \), the maximal pressure-volume ratio was recalculated for each loading condition, and a new linear regression and \( V_0 \) were obtained. This procedure was iterated until \( V_0 \) changed less than 1%.

Because only one data collection, and hence only one pressure-volume loop, was generated from radionuclide-hemodynamic data obtained during dobutamine infusion or atrial pacing tachycardia, maximal elastance was calculated as the maximal instantaneous pressure-volume ratio for that loop (i.e., assuming \( V_0 = 0 \)).

Calculation of estimates of \( E_{\text{max}} \) and \( V_0 \) from modifications of RV ESPVR. For each patient, \( E_{\text{max}} \) and \( V_0 \) were estimated with the linear regression of pressure-volume points from each data collection determined by the ratio of PA-dicrotic notch pressure to end-ejection (minimum) RV volume and by the ratio of RV peak pressure to end-ejection volume. In addition, for each patient, a single maximal instantaneous pressure-volume ratio was derived from the baseline pressure-volume loop before altering loading conditions. By definition, in this case \( V_0 = 0 \).

Statistical Analysis

Reproducibility of volume calculations from end-diastolic and end-systolic counts was analyzed by correlating duplicate measurements and by computing a coefficient of variability (defined as the ratio of the mean difference between these duplicate measurements to the mean end-diastolic or end-systolic volume, expressed as a percentage).

As a further assessment of the accuracy of our radionuclide RV volume calculations, we used linear regression analysis to relate radionuclide-derived RV stroke volume to thermodilution-derived RV stroke volume. The data collected during baseline conditions (before loading conditions were altered) for each patient were omitted from analysis of RV stroke volume regression since the baseline thermodilution and radionuclide stroke volumes were defined to be equal to calculate the baseline absolute RV end-diastolic volume.

To compare the goodness of fit of the ESPVR defined by different methods, the correlation coefficient (r value) and the standard error of the estimate (SEE) for each linear ESPVR defined by maximal elastance and by modifications of the ESPVR were compared with repeated-measures analysis of variance followed by paired t tests with Bonferroni’s corrections. A similar analysis was used to compare end-systolic RV pressures and volumes determined from maximal elastance with estimates with modifications of the ESPVR. Finally, linear regression was used to correlate \( E_{\text{max}} \) and \( V_0 \) with the slope and volume-intercepts defined by modifications of the RV ESPVR.
In patients receiving dobutamine or undergoing atrial pacing tachycardia, a significant change in the RV ESPVR was defined as a shift in the point of maximal elastance (or estimate of maximal elastance) beyond the 95% confidence interval defined by the resting linear ESPVR (determined from baseline and postloading data). Differences in sensitivity for detecting significant changes in the ESPVR defined by the different methods were compared by $\chi^2$ analysis.

**Results**

**Reproducibility and Accuracy of RV Volume Determination**

For duplicate measures of end-diastolic and end-systolic volumes, the coefficient of variability was 1.4% and 1.2%, respectively, with both correlation coefficients ($r$) equal to 0.99. Radionuclide-derived and thermodilution-derived RV stroke volumes were highly correlated ($r=0.97, \text{SEE}=3.8 \text{ ml}, p<0.0001$) (Figure 1). The slope and volume intercept of this relation did not significantly differ from 1 and 0, respectively ($p>0.50$).

**RV Pressure-Volume Diagram: Configuration of Loops and Calculation of $E_{\text{max}}$ and $V_0$**

RV pressure-volume loops were generally triangular in shape with early peaking of pressure (Figures 2 and 3). In one patient, some loops showed late peaking of RV pressures toward the point of maximal elastance (Figure 4). The relation between the point of maximal elastance and end-ejection (i.e., the time of minimum volume) was variable. In two patients (1 and 7), ejection continued well beyond end systole defined by maximal elastance (Figure 2), while in patient 4 end ejection coincided with end systole. In others, the relation varied even within the same patient as loading conditions were altered. Overall, the RV end-ejection volume was significantly smaller than end-systolic volume defined by maximal elastance ($\Delta=2\pm2 \text{ ml/m}^2$, $p<0.001$) (Table 1). This difference between RV end-systolic and end-ejection volume showed a weak but significant negative correlation with pulmonary vascular resistance ($r=-0.50, p<0.01$) and RV peak systolic pressure ($r=-0.36, p<0.05$). In addition, the PA-dicrotic notch pressure was significantly lower ($\Delta=3\pm3 \text{ mm Hg}, p<0.001$), and the RV peak pressure was significantly higher ($\Delta=4\pm3 \text{ mm Hg}, p<0.001$) than end-systolic pressure defined by maximal elastance (Table 1). The difference between RV end-systolic pressure and PA-dicrotic notch pressure or RV peak pressure showed no significant correlation with either pulmonary vascular resistance or RV peak systolic pressure.

The ESPVR defined by points of maximal elastance was highly linear throughout the range of pressures and volumes tested with $r$ values ranging from 0.988 to 0.999 (Figures 2–5). Furthermore, for individual patients, the point of maximal elastance during steady-state alterations in loading conditions produced by nitroglycerin appeared to lie on the same ESPVR line defined by load alterations produced by phenylephrine (Figure 3) or saline loading (Figure 4). The mean $E_{\text{max}}$ was $0.84\pm0.32 \text{ mm Hg/ml/m}^2$ and showed a fairly wide range from 0.32 to 1.23 mm Hg/ml/m$^2$. The mean $V_0$ was $8\pm12$
ml/m² and ranged from −8 to 28 ml/m². The difference between end-systolic volume (defined by maximal elastance) and the volume at the point of maximal instantaneous pressure:volume ratio for each loop was 2 ± 3 ml/m².

**RV ESPVR: Comparison of Maximal Elastance to Modifications of ESPVR**

The linear correlations were significantly higher (p<0.005), and the linear regression SEE significantly lower (p<0.005) for the ESPVR defined by maximal elastance compared with modifications with the ratio of PA-dicrotic notch or RV peak pressure to end-ejection volume (Table 2). Furthermore, the r values were statistically significant in seven of eight patients when defined by maximal elastance compared with zero of eight patients when defined by the alternative methods (p<0.0001). There were no significant correlations between Emax (determined by maximal elastance) and the slope of the RV ESPVR defined by these modifications (Table 3). Similarly, there was no significant correlation between V0 calculated with maximal elastance and the volume intercepts defined by modifications of the ESPVR.

**Effect of Inotropic Interventions**

When the RV ESPVR was defined by maximal elastance, dobutamine caused a significant leftward shift (Figure 4) in each of the four patients (i.e., the point of maximal elastance lay outside of the 95% confidence interval of the resting linear ESPVR, Figure 5A). In fact, the entire loop was shifted leftward in each patient such that the pressure-volume coordinates for at least the last third of ejection lay outside the 95% confidence interval of the resting linear ESPVR defined by maximal elastance. However, when the RV ESPVR was defined with PA-dicrotic notch pressure:end-ejection volume or RV peak pressure:end-ejection volume ratios, the leftward shift was not significant in any patient (Figures 5B and 5C) because of the larger SEE (see above; Table 2).

Compared with the resting ESPVR, tachycardia caused the point of maximal elastance to be significantly shifted leftward (Figure 6). Similar to dobutamine, the entire loop during pacing tachycardia was shifted leftward such that the pressure-volume coordinates of the last third of ejection were beyond the 95% confidence interval of the resting ESPVR. When analysis was performed with RV peak pressure:end-ejection volume ratio, rather than maximal elastance, the leftward shift remained significant. However, a significant shift was not observed with the PA-dicrotic notch pressure:end-ejection volume ratio relation.

The sensitivity for detecting a change in RV function during dobutamine or pacing tachycardia was significantly greater (p<0.03) when analysis was performed with maximal elastance (five of five) compared with either PA-dicrotic notch pressure: end-ejection volume ratio (zero of five) or peak RV pressure:end-ejection volume ratio (one of five).

**Discussion**

This study demonstrates that a combined radionuclide-hemodynamic technique can be used in humans to analyze the RV ESPVR derived from
full RV pressure-volume loops. With this technique, the ESPVR defined by maximal elastance is highly linear over a physiological range of pressures and volumes in patients with normal RV function and is responsive to changes in RV function produced by positive inotropic interventions with dobutamine or atrial pacing tachycardia. Furthermore, the linear regression used to determine the RV ESPVR has a higher correlation coefficient and lower SEE when defined by maximal elastance than when surrogates derived from modifications of the ESPVR are used. This results in a greater sensitivity to changes in RV function produced by inotropic alterations.

**RV Pressure-Volume Diagram**

Previous studies have shown that the LV pressure-volume diagram has a rectangular shape with pressure peaking late during ejection. In contrast, we found that RV pressure-volume loops were generally more triangular with early peaking of pressure. This is consistent with observations of Maughan and colleagues using an isolated heart preparation. These investigators also reported that RV volume continued to decrease well beyond end systole defined by maximal elastance. We found a variable relation between end-systolic and end-ejection volume, not only between patients, but even within individual patients. This variability in part may be related to interpatient and intrapatient differences in RV loading conditions since the difference between end-systolic and end-ejection volume tended to be inversely related to pulmonary vascular resistance and RV peak systolic pressure.

** Modifications of RV ESPVR**

Previous studies of RV pressure-volume relations have used PA-dicrotic notch (or RV peak pressure) and end-ejection volume as surrogates of RV end-systolic pressure and volume, respectively, because of the relative ease in making such measurements. However, in the present study, the ESPVR defined by these estimates of RV end systole had an inferior goodness of fit and consequently had less statistical power to detect changes in RV function produced by inotropic interventions compared with the ESPVR defined by maximal elastance.

There are probably several reasons for this observation. First, PA-dicrotic notch pressure (or RV peak pressure) and end-ejection volume do not faithfully reflect end-systolic pressure and volume defined by maximal elastance that, as conceived by Sagawa, more accurately reflects the peak active contractile process. Although in an analogous study of the LV, the ESPVR defined by aortic-dicrotic notch pressure and LV end-ejection volume corresponded well to the ESPVR derived from maximal elastance, this observation is not directly applicable to the RV. While LV ejection usually ends shortly after end systole defined by maximal elastance, Sagawa has pointed out that this relation is coincidental, dependent upon ambient loading conditions, and is not maintained when peripheral resistance is low as is the case in the normal pulmonary circulation. It is not surprising, therefore, that we found that PA-dicrotic notch pressure and end-ejection volume significantly underestimated RV end-systolic pressure and volume, respectively. The volume differences were exaggerated at lower pulmonary vascular resistances and RV sys-
TABLE 2. Correlations Between Right Ventricular End-Systolic Pressure and Volume With Different Definitions of End Systole

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<td>SEE</td>
<td>0.470 ± 0.294</td>
<td>1.715 ± 1.000*</td>
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PA-DN, pulmonary artery–dicrotic notch pressure; EEVI, end-ejection volume index; RV-PP, right ventricular peak pressure; SEE, standard error of the estimate.

*p < 0.01 compared with maximal elastance.

Inotropic pressures. Furthermore, in contrast to maximal elastance relations, PA-dicrotic notch pressure (or RV peak pressure) and end-ejection volume do not necessarily occur at the same moment in time. Finally, our data indicate that the discrepancy between alternative estimates of end systole and end systole defined by maximal elastance varies considerably even within an individual patient under different loading conditions.

Nevertheless, it should be noted that the width of the 95% confidence interval for any of the relations depends upon several factors, including the extent of true linearity of the theoretical relation, noise inherent in the measurements, and the number of observations made. Although the reasons why the RV ESPVR defined by maximal elastance has a lower SEE than relations defined with PA-dicrotic notch or by peak RV pressures and end-ejection volume have been discussed, it is possible that by obtaining more data points, the 95% confidence interval of the RV ESPVR defined by estimates of maximal elastance may become sufficiently small to be clinically useful as an empiric means of detecting changes in RV function.

Inotropic Interventions

Dobutamine caused a significant leftward shift in RV maximal elastance compared with the resting ESPVR. Because only one loop was obtained during the inotropic intervention, this could reflect an increase in the slope of the RV ESPVR or a parallel leftward shift with a decrease in \( V_0 \). Either effect is consistent with an increase in intrinsic contractility as described for the LV.3–5,7,9,13–15 In addition, a similar response to atrial pacing tachycardia was observed, suggesting a positive inotropic Treppe effect.24 This sensitivity to inotropic interventions suggests that the combined radionuclide-hemodynamic technique may be useful for studying RV function in response to various pharmacological or therapeutic interventions in pathophysiological states where changes in loading conditions might otherwise confound results.

Because only single pressure-volume loops were obtained, true \( V_0 \) could not be calculated during inotropic interventions. Instead, \( V_0 \) was assumed to be zero, and the point of maximal instantaneous pressure:volume ratio was used. At rest, before interventions, the point of the maximal instantaneous pressure:volume ratio (assuming \( V_0 = 0 \)) differed little from the point of maximal elastance defined by determining true \( V_0 \). (\( \Delta \) volume = \( 2 \pm 3 \) m\(^3\)/m\(^2\), see above). Furthermore, the large leftward shift in the entire RV pressure-volume loop produced by inotropic interventions caused the pressure-volume coordinates of at least the entire last third of ejection to lie outside the 95% confidence interval of the resting ESPVR. Therefore, it is highly likely that the point of true maximal elastance (based on true \( V_0 \)) was significantly shifted leftward during the inotropic intervention.

**Different Load Interventions and RV ESPVR**

It was observed that for an individual patient, all points of maximal elastance appeared to lie on the same line, whether loading conditions were changed with nitroglycerin, phenylephrine, or saline (Figures 3 and 4). Previous investigators25,26 have reported that in the dog the beat-to-beat LV ESPVR produced during inferior vena caval occlusion was shifted to the left (smaller \( V_0 \)) with a vasopressor and to the right (larger \( V_0 \)) with a vasodilator without a change in slope. Slinker and Glantz27 have suggested that these parallel changes may be due in part to direct systolic ventricular interaction. It is not known whether changes in LV systolic function

TABLE 3. Comparison of Slopes and Volume Intercepts of Right Ventricular End-Systolic Pressure-Volume Relation With Different Definitions of End Systole

<table>
<thead>
<tr>
<th>Patient</th>
<th>Slope (mm Hg/ml/m(^2))</th>
<th>( V_0 ) (ml/m(^2))</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>( E_{max} )</td>
<td>PA-DN: EEVI</td>
</tr>
<tr>
<td>1</td>
<td>0.32</td>
<td>0.25</td>
</tr>
<tr>
<td>2</td>
<td>0.76</td>
<td>0.38</td>
</tr>
<tr>
<td>3</td>
<td>0.66</td>
<td>0.47</td>
</tr>
<tr>
<td>4</td>
<td>1.19</td>
<td>0.40</td>
</tr>
<tr>
<td>5</td>
<td>1.00</td>
<td>0.59</td>
</tr>
<tr>
<td>6</td>
<td>0.90</td>
<td>0.90</td>
</tr>
<tr>
<td>7</td>
<td>1.23</td>
<td>0.44</td>
</tr>
<tr>
<td>8</td>
<td>0.57</td>
<td>0.25</td>
</tr>
</tbody>
</table>

\( V_0 \), volume intercept of the end-systolic pressure-volume relation; \( E_{max} \), slope of the end-systolic pressure-volume relation; PA-DN, pulmonary artery–dicrotic notch pressure; EEVI, end-ejection volume index; RV-PP, right ventricular peak pressure.
and volume can similarly affect the beat-to-beat RV ESPVR. However, even if this were the case, such effects would not be directly relevant to our study that used steady-state alterations in loading conditions. The resting end-systolic pressure-volume points during steady-state changes in load may be influenced in part by ventricular interaction. However, based on our data and previous studies, the set of end-systolic pressure-volume points obtained at baseline and during altered steady-state loading conditions achieved through a variety of interventions appears to define a single line. Most importantly, these data suggest that, at least empirically, changes in the ESPVR are useful as an index of ventricular function.

**Diastolic Changes**

In several patients, a parallel upward or downward shift in the diastolic pressure-volume curve was seen during load alterations (Figures 3, 4, and 6), suggesting a possible change in external pressure because of altered levels of ventricular interaction or pericardial restraint. However, for several reasons, it is unlikely that a change in external forces influenced our findings at end systole. First, while ventricular interaction and pericardial constraint are important determinants of both normal and abnormal end-diastolic pressure-volume relations, the parallel shifts observed in the current study were primarily early diastolic. These shifts are more likely the result of viscous effects, which are more prominent at higher volumes, causing greater deviation of early diastolic pressure-volume points from the end-diastolic relation at higher levels of filling. These considerations predict the type of early diastolic deviation seen in Figures 3, 4, and 6. Second, and more importantly, even if a change in external forces did occur during diastole as a result of the interventions performed in our study, such effects are much less important during systole since measured pericardial pressure over the ventricles is very small at end systole and since transseptal pressure influences are minimal in the absence of pericardial constraint. Finally, it is of interest to note that during atrial pacing tachycardia, in contrast to dobutamine stimulation, the entire diastolic pressure-volume curve was shifted upward (Figure 6). The cause of this change is unclear but may be due to impaired relaxation.

**E\text{max} as an Index of RV Function**

Experimental and clinical studies of the LV ESPVR suggest that the slope (E\text{max}) reflects the contractile state. If a similar relation holds for the RV, E\text{max} might be a useful index to separate normal from abnormal RV function. However, a fairly wide range of values for resting RV E\text{max} was observed in a population of patients with apparently normal contraction and hemodynamics. The variability of resting E\text{max} may preclude its use for studying differences in RV function across patient groups. Furthermore, although we found the RV ESPVR to be linear in the range of end-systolic volumes and pressures studied in this patient population, recent observations suggest that the ESPVR, at least of the isolated LV, may be curvilinear under conditions of augmented or depressed contractility, especially at high or low end-systolic volumes. Consequently, misleading estimates of E\text{max} or V\text{0} may result, depending on the pressure-volume range sampled. Therefore, E\text{max} may have theoretical limitations as an index of ventricular function when used to compare different patients or patient groups. Similarly, the size dependence of V\text{0} may also limit its usefulness for comparing different patient groups. But regardless of whether the RV ESPVR is truly linear or not, our data (supported by previous studies of the LV) show that for an individual patient, the ESPVR does reflect RV function and does generally support its use as a means of detecting acute changes in RV function. Although Kass et al recently concluded that the ESPVR is less sensitive to changes in contractile function than are some other indexes of performance, they pointed out that the ESPVR has the advantage of relative load insensitivity throughout a wider range of loading conditions. To our knowledge, similar comparisons of performance indexes have not been made for the RV. However, as indicated previously, our data suggest that the ESPVR based on maximal elastance has a greater sensitivity for detecting changes in RV contractile function than do similar relations based on surrogates for RV end-systolic pressure and volume.

**Radionuclide Methods**

Absolute RV volumes were not determined directly from radionuclide data. Although possible, this requires
complicated calculations and estimates of attenuation factors to correct for differences in body constitution as well as the distance between the RV center of mass and the camera. However, since each patient served as his own control, obviating the need for absolute volumes, only relative changes in RV volumes (determined from corrected count-based data) were determined for each patient. Absolute RV volumes under each altered loading condition were created with the baseline thermodilution stroke volume and radionuclide ejection fraction, and subsequent relative changes in corrected RV counts.

In addition, a fixed region of interest was used to generate RV time-activity curves to eliminate variance and error introduced when separate regions of interest are chosen for each frame of the cardiac cycle. This theoretically could lead to a systematic underestimation of stroke volume because of overlying right atrial activity. However, a slant-hole collimator was used to view the heart cranially and greatly reduce the potential for overlap. Although a slight tendency toward underestimation of stroke volume by radionuclide ventriculography (Figure 1) was found, this was not a statistically significant effect since the slope and y-intercept of the regression relating radionuclide to thermodilution stroke volume were not different from 1 and 0, respectively.

Conclusions

The human RV ESPVR defined by maximal elastance, with a combined radionuclide-hemodynamic technique, is linear over a physiological range of pressures and volumes in patients with normal RV function and is responsive to changes in RV function produced by inotropic interventions. Modifications of the ESPVR with PA-dicrotic notch pressure or end-ejection volume underestimate end-systolic pressure and volume, respectively, as determined from maximal elastance. Finally, the RV ESPVR defined by maximal elastance is more sensitive to alterations in RV function than modifications of the ESPVR with the ratio of PA-dicrotic notch pressure or RV peak pressure to end-ejection volume.

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