Preload-adjusted right ventricular maximal power: concept and validation

Soren Schenk,1 Zoran B. Popović,2 Yoshih Ochiai,1 Fernando Casas,1 Patrick M. McCarthy,1,3 Randall C. Starling,2 Michael W. Kopcak, Jr.,1 Raymond Dessoffy,1 Jose L. Nava,3 Neil L. Greenberg,2 James D. Thomas,2 and Kiyotaka Fukamachi1

1Department of Biomedical Engineering, 2Department of Cardiovascular Medicine, 3Department of Thoracic and Cardiovascular Surgery, The Cleveland Clinic Foundation, Cleveland, Ohio 44195

Submitted 4 February 2004; accepted in final form 7 May 2004

Schenk, Soren, Zoran B. Popovic, Yoshih Ochiai, Fernando Casas, Patrick M. McCarthy, Randall C. Starling, Michael W. Kopcak, Jr., Raymond Dessoffy, Jose L. Nava, Neil L. Greenberg, James D. Thomas, and Kiyotaka Fukamachi. Preload-adjusted right ventricular maximal power: concept and validation. Am J Physiol Heart Circ Physiol 287: H1632–H1640, 2004. First published May 20, 2004; 10.1152/ajpheart.00123.2004.—Right ventricular (RV) maximal power (PWRmax) is dependent on preload. The objective of this study was to test our hypothesis that the PWRmax, versus end-diastolic volume (EDV) relationship, analogous to the load-independent stroke work (SW) versus EDV relationship (preload-recruitable SW, PRSW), is linear, with the PWR x-axis intercept (V0PWR) corresponding to the PRSW intercept (V0SW). If our hypothesis is correct, the preload sensitivity of PWRmax could be limited by adjusting for EDV and V0PWR. Ten dogs were instrumented with a pulmonary flow probe, micromanometers, and RV conductance catheter. Data were obtained during bivacal occlusions under various conditions and fitted to PWRmax = a1(EDV − V0PWR)β, where a is the slope of the relationship. The PWRmax versus EDV relationship did not deviate from linearity (β = 1.09, P = not significant vs. 1), and V0PWR correlated with V0SW (r = 0.93, P < 0.0001). V0PWR was related to steady-state EDV and left ventricular end-diastolic pressure, allowing for estimation of V0PWR (V0Real) and single-beat PWRmax preload adjustment. Dividing PWRmax by the difference of EDV and V0PWR (PAMPV0PWR) eliminated preload dependency down to 50% of the baseline EDV. PWRmax adjustment using V0Real (PAMPV0Real) showed similar preload independence. Enhancing contractility increased PAMPV0PWR and PAMPV0Real from 176 ± 52 to 394 ± 205 W/ml × 104 and 145 ± 51 to 404 ± 261 W/ml × 104, respectively, accompanied by an increase of PRSW from 13.0 ± 4.5 to 29.7 ± 16.4 mmHg (all P < 0.01). PAMPV0PWR and PAMPV0Real correlated with PRSW (r = 0.85; r = 0.77; both P < 0.001). Numerical modeling confirmed the accuracy of our experimental data. Thus preload adjustment of PWRmax should consider a linear PWRmax versus EDV relationship with distinct V0PWR. PAMPV0PWR is a preload-independent estimate of RV contractility that may eventually be determined noninvasively.

METHODS

Preload Adjustment of PWRmax: Vo Dependency

We propose that, because power is the first derivative of SW, the PWRmax versus EDV relationship should be analogous to the relationship of SW versus EDV defined by its slope (i.e., PRSW) and volume-axis intercept (V0SW) (13). Figure 1A shows typical PWRmax versus EDV relationships during preload reduction. Dividing PWRmax by EDV raised to an exponent ≠ 1 assumes the following nonlinear relationship:

\[ PWR_{max} = a \cdot EDV^\beta \]  

(1)

where a is the slope of the relationship.

The best fit was obtained with an exponent β = 1.4, therefore, dividing PWRmax by EDV1.4 sufficed to reduce preload dependency (Fig. 1B). It is noteworthy that the nonlinear fitting forces the PWRmax versus EDV relationship through the axis origin. Obviously, if the PWRmax versus EDV relationship shifts in either direction, a different exponent β is required. Thus the value of this exponent is likely arbitrary.

To account for shifts of the PWRmax versus EDV relationship with the alteration of V0PWR, we tested this equation:

ACCURATE ASSESSMENT of right ventricular (RV) contractility is an unresolved clinical problem. Despite recent advances in the assessment of RV performance such as Doppler tissue imaging (36), indexes that express RV “output,” i.e., pressure and flow, continue to be of interest. Maximal ventricular power (PWRmax), the peak instantaneous product of pressure and flow, reflects contractility (32) and can be determined noninvasively (1, 22). Unfortunately, PWRmax is dependent on preload, i.e., end-diastolic volume (EDV). Various concepts have been proposed for preload-adjusted PWRmax (PAMP) in both ventricles (18, 29, 30). A common approach was dividing PWRmax by EDVβ, with β ≠ 1. The assumptions were that the PWRmax versus EDV relationship is nonlinear, its volume-axis intercept (V0PWR) is zero, and PAMP relates to the slope (Ees) of the end-systolic pressure-volume relationship (ESPVR), the latter being linear with a volume-axis intercept (V0Ees) near zero. Many of these assumptions have been challenged (19, 28), and PWRmax preload adjustment that is not limited to a given state remained elusive.

The aims of this study were to 1) examine the relationship between RV PWRmax and EDV, 2) test a concept of PWRmax preload adjustment that reflects the shape of this relationship, and 3) assess the sensitivity of preload-adjusted PWRmax to modulations of the contractile state under various loading conditions. We first confirmed that the RV PWRmax versus EDV relationship was linear, with a distinct V0PWR. From the understanding that PWRmax is the first derivative of stroke work (SW), the optimal preload adjustment was found to resemble the calculation of preload recruitable SW (PRSW) (13). We found that this novel power index is susceptible to modulations of the contractile state while remaining independent of preload and that it correlated with PRSW. We further provided an approach for the assessment of PAMP from a single, steady-state beat.

hemodynamics; contractility; right ventricle

Address for reprint requests and other correspondence: K. Fukamachi, Dept. of Biomedical Engineering/ND20, Cleveland Clinic Foundation, 9500 Euclid Ave., Cleveland, OH 44195 (E-mail: fukamachi@bme.rice.ccf.org).

The costs of publication of this article were defrayed in part by the payment of page charges. The article must therefore be hereby marked “advertisement” in accordance with 18 U.S.C. Section 1734 solely to indicate this fact.
PRELOAD-ADJUSTED RIGHT VENTRICULAR MAXIMAL POWER

\[ \text{PWR}_{mx} = a \cdot (\text{EDV} - V_{0\text{PWR}})^\beta \]  

(2)

Apparently, if \( \beta \) approximates 1.0, a linear \( \text{PWR}_{mx} \) versus EDV relationship can be expected, and if preload adjustment incorporates \( V_{0\text{PWR}} \), shifts of the relationship should not alter \( \beta \). The application of this concept to the example given above, optimal fit of Eq. 2 yielded \( \beta = 0.96 \), implying a linear \( \text{PWR}_{mx} \) versus EDV relationship with \( V_{0\text{PWR}} = 9 \text{ ml} \) (Fig. 1A). Moreover, dividing \( \text{PWR}_{mx} \) by the difference of EDV and \( V_{0\text{PWR}} \) eliminated preload dependency (Fig. 1B). Whether this concept can be applied to any hemodynamic state and whether \( V_{0\text{PWR}} \) can be estimated to allow for single-beat \( \text{PWR}_{mx} \) preload adjustment were examined in this study.

Experimental Preparation and Protocol

All experiments were approved in compliance with the Guide for the Care and Use of Laboratory Animals, published by National Institutes of Health. Ten mongrel dogs (19–30 kg) were anesthetized (1.0–1.5% isoflurane) and ventilated. Upon sternotomy, tapes were passed around both venae cavae for preload reduction. After the pericardium was opened, a dual-sensor micromanometer (SPC-751, Millar Instruments; Houston, TX) was inserted into the right atrium and right ventricle to measure right atrial pressure and right ventricular pressure, respectively. Single-sensor micromanometers (SPC-350, Millar Instruments) were inserted into the main pulmonary artery (PA) and left ventricle to measure PA pressure and left ventricular (LV) pressure, respectively. A conductance catheter (SPC-562-I, Millar Instruments) was inserted through the RV apex to measure RV volume (SVRP) and flow. Pacing leads were attached to the right atrium. Echocardiography was performed to calculate RV ejection fraction (EFecho) by the previously validated ellipsoid shell method (9, 12). Gain of the conductance catheter-derived RV volume was calibrated by SVRP with the offset calibrated by EFecho (14). Blood conductivity was adjusted at each data point (Lecycom, Sigma-5 DF; Stoneham, MA).

All data were recorded with temporarily stopped ventilation at 200 Hz (PowerLab, Chart v4.1.2, ADInstruments; Mountain View, CA). After autonomic reflexes were blocked by hexamethonium chloride (30 mg/kg) and atropine (0.1 mg/kg), the heart was paced at incremental rates (90, 120, and 150 beats/min) with data taken at each stage. Contractility and afterload were altered by intravenous infusion of dobutamine (5 \( \mu \)g·kg\(^{-1}\)·min\(^{-1}\)), phenylephrine (0.3 \( \mu \)g·kg\(^{-1}\)·min\(^{-1}\)), and esmolol (500 \( \mu \)g/kg bolus, followed by 50 \( \mu \)g·kg\(^{-1}\)·min\(^{-1}\)) at 120 beats/min with data taken before and at 20 min of equilibration of each condition. At all conditions (\( n = 80 \)), data were obtained at steady state and during preload reduction by occluding both venae cavae. Steady-state data were acquired over 10–15 heart cycles with a beat-to-beat variability of RV pressure, volumes, and flow of less than \( \pm 5\% \) in all experiments. Table 1 presents key hemodynamic parameters of various experimental conditions. After each experiment, the heart was harvested to weigh RV and LV free walls and interventricular septum.

Data Analysis

A custom-made program was used to calculate PRSW (13), \( E_c \) (23), and \( \text{PWR}_{mx} \) (18), the latter as the peak instantaneous product of:

\[ \text{PWR} = \text{RVP} \cdot Q_{\text{dec}}. \]  

(3)

The volume-axis intercepts of PRSW (V\(_{0\text{SW}}\)), ESPVR (V\(_{0\text{ES}}\)), and the \( \text{PWR}_{mx} \) versus EDV relationship (V\(_{0\text{PWR}}\)) were obtained by extrapolation to zero volume.

\( \text{PWR}_{mx} \) versus EDV relationship. The shape of the \( \text{PWR}_{mx} \) versus EDV relationship was examined by fitting \( \text{PWR}_{mx} \) and EDV datasets to Eq. 2 (Statistica 5.1, StatSoft; Tulsa, OK). The exponent \( \beta \) determines the shape: \( \beta > 1 \) indicates concave and \( \beta < 1 \) indicates convex relationships, respectively; if \( \beta \) approximates 1, then a linear RV \( \text{PWR}_{mx} \) versus EDV relationship is expected. The deviation of the relation during preload reduction was also examined.

\( V_0 \) estimation. Estimation of \( V_{0\text{PWR}} \) (V\(_{0\text{PWR}}\)) from a single beat was initiated by analyzing the influence of hemodynamic parameters and heart weight (invariant) by stepwise multivariable regression. The independently significant predictors of V\(_{0\text{PWR}}\) were then curve fitted to 36,000 linear and nonlinear equations (Table Curve3D 4.0, Systat Software; Richmond, CA). V\(_{0\text{PWR}}\) was calculated by the most suitable function, that is, simple model structure, low residuals and offset, and high \( r \) value. The model was derived from experiments 1–5 and subsequently validated in experiments 6–10.

Contractile sensitivity. Power indexes at baseline, at various heart rates, and before and during dobutamine, phenylephrine, and esmolol infusion were compared with \( E_c \) and PRSW as load-insensitive measures of cardiac function (13, 33).

Computer modeling. We used a lumped-parameter model of the cardiovascular system to examine the dependency of \( \text{PWR}_{mx} \) versus EDV relationships on changes of contractility, preload, afterload, and diastolic stiffness. The model has been described previously in detail (35). Briefly, it is composed of 24 coupled equations relating pressure and flow through the circulation that is conceptualized as eight different chambers: the right atrium and ventricle, pulmonary arteries

AJP-Heart Circ Physiol • VOL 287 • OCTOBER 2004 • www.ajpheart.org

Fig. 1. Maximal ventricular power (\( \text{PWR}_{mx} \)) preload adjustment: x-axis intercept \( V_0 \) dependency. A: \( \text{PWR}_{mx} \) vs. end-diastolic volume (EDV) relationship in a representative experimental condition. B: power indexes (normalized to baseline) during preload reduction in the same experiment.
and veins, left atrium and ventricle, aorta, and systemic veins. Both LV and RV activation are modeled by a cosine function, with ESPVR assumed to be linear and defined by their $E_{\text{es}}$ and $V_{0\text{es}}$. Ventricular pressure decay during relaxation is assumed to be exponential and is defined by its time constant (35). Nikolic’s equation (which defines the ventricular diastolic pressure-volume curve by its minimal slope ($E_{\text{es}}$), pressure and volume that correspond to the point of $E_{\text{es}}$, volume needed to increase $E_{\text{es}}$ by $e^{k^{-1}}$ (where $k^{-1}$ is the exponent and $V_{k^{-1}}$ is the volume required to increase ventricular stiffness by $e$), and minimal pressure and volume) is used to model both RV and LV passive properties (25, 35). The systemic and pulmonary circulations are characterized by valve area and its inertia, arterial capacitance, and minimal volume, capillary resistance and inertia, and venous capacitance, resistance, inertia, and minimal volume. Systolic pressure from the right ventricle into the pulmonary circulation is obtained by differentiating the volume signal in 5 ms resolutions (2).

Equation parameters of the model were obtained as follows. For RV $E_{\text{es}}$, $V_{0\text{es}}$, time constant of relaxation, pulmonary systemic vascular resistance (PVR), systemic vascular resistance, and heart rate, we used the average of experimental data collected at baseline. To obtain RV diastolic parameters, $E_d$ and $V_{0\text{es}}$ were estimated from the experimental data using Nikolic’s equation (25), whereas the other equation parameters were adjusted to obtain realistic end-diastolic data. Finally, LV $E_{\text{es}}$ and $V_0$ were supplemented from previous canine studies (14).

After computation of steady-state pressure-volume loops, we simulated preload reduction by decreasing model circulatory volume to estimated preload reduction by decreasing model circulatory volume to 42% of baseline preload. Similarly, the other vascular resistance (PVR), systemic vascular resistance, and heart rate parameters were estimated from previous canine studies (25).

### Statistical Analysis

Data are reported as means ± SD or as medians (25% and 75% quartiles). The shape of the PWR max versus EDV relationship was determined by nonlinear fitting of Eq. 2. The average exponent $\beta$ was compared with a value of 1 using a single-sample $t$-test. We further examined individual slopes of two adjacent pairs of PWR max versus EDV; a code of 1 indicated that the preceding slope was steeper, whereas −1 indicated that the subsequent slope was steeper. The grand average of all codes with 95% confidence interval was calculated. The PWR max versus EDV relationship was assessed linear if the grand average was not different from zero. Deviations toward −1 or 1 indicated a predominantly concave or convex relationship, respectively (39).

Preload dependency was assessed by normalizing power indexes and EDV to initial (baseline) values before preload reduction. Comparisons were made by one-way ANOVA followed by Bonferroni post hoc testing.

Data obtained before and during modulations of the isotropic state (dobutamine, phenylephrine, and esmolol) were compared by Wilcoxon matched-pairs tests. $P < 0.05$ indicated statistical significance.

### RESULTS

**Shape of PWR max Versus EDV Relationship and $V_0$ Interrelationship**

The median exponent $\beta$ in Eq. 2 of the entire dataset was 1.09 (25% and 75% quartiles of 0.84 and 1.37; $P$ not significant vs. 1; $P < 0.01$ vs. 2). Figure 2A depicts the variation of exponent $\beta$ in various experimental conditions, demonstrating that median $\beta$ was close to 1 in every experimental condition ($P$ not significant vs. 1 in each condition) and that the 95% confidence interval of mean $\beta$ always overlapped with 1. Furthermore, there was no relationship between exponent $\beta$ and PRSW or PVR ($r = 0.19$, $P$ not significant; $r = 0.03$, $P$ not significant, respectively), further suggesting that the shape of the PWR max versus EDV relationship was independent of the contractile state and afterload condition. Moreover, the grand average of codes determining the shape of the PWR max versus EDV relationship was 0.009 (95% confidence interval, −0.057 and 0.075), demonstrating that $\beta$ did not deviate in any direction during preload reduction. Together, these results confirm our hypothesis of a linear PWR max versus EDV relationship in the right ventricle with existence of $V_{0\text{PWR}}$.

We next examined the interrelationship of $V_{0\text{PWR}}$, $V_{0\text{es}}$, and $V_{0\text{SW}}$. Strong correlations existed between $V_{0\text{PWR}}$ and $V_{0\text{SW}}$ ($r = 0.93$, $P < 0.0001$; Fig. 2B). The relationship between $V_{0\text{PWR}}$ and $V_{0\text{es}}$ ($r = 0.79$, $P < 0.0001$) was significantly less strong than that between $V_{0\text{PWR}}$ and $V_{0\text{SW}}$ ($P < 0.0001$).
To estimate $V_{0\text{PWR}} (V_{0\text{Est}})$ from a single beat, we examined the influence of baseline hemodynamic parameters and invariant factors, i.e., RV weight. The strongest influences were observed for EDV and SV (both $P < 0.0001$) and LV end-diastolic pressure (LVEDP; $P = 0.01$). There was no evidence of an influence of any other factor. Because EDV and SV highly cross-correlated ($r = 0.83, P < 0.0001$), only EDV and LVEDP were entered into the curve-fitting analysis. With the use of the data of experiments 1–5, the best suitable equation was

$$V_{0\text{Est}} (\text{ml}) = 0.43 \cdot \text{EDV (ml)} - 1.2 \cdot \text{LVEDP (mmHg)} - 0.2 \cdot \text{LVEDP}^{-1} (\text{mmHg}) - 2.6 \text{ ml} \quad (4)$$

Figure 2C shows the residuals of $V_0$ (estimated minus observed value) in relation to the measured value ($V_{0\text{PWR}}$). The majority of the data fell within 10 ml of residuals ($r = 0.84, P < 0.0001$), indicating adequate fit. The model was subsequently validated in experiments 6–10, demonstrating adequate prediction capabilities ($r = 0.83, P < 0.0001$) with a consistent trend of the residuals.

**Preload Dependency**

Figure 3 depicts grouped data from the entire dataset. Power indexes and EDV were normalized to baseline allowing combined illustration. Dividing $PWR_{mx}$ by the difference of EDV and $V_{0\text{PWR}}$ (i.e., preload-adjusted $PWR$ through $V_{0\text{PWR}}$, $PAMP_{V0PWR}$) eliminated preload dependency down to 50% of baseline EDV without significant deviation in any direction (Table 2). Likewise, adjusting $PWR_{mx}$ by the difference of EDV and $V_{0\text{Est}}$ ($PAMP_{V0Est}$) reduced preload dependency, however, with somewhat higher data variability and significant deviation from baseline beginning at 60% preload reduction (Fig. 3 and Table 2).

**Contractility Sensitivity**

Tables 1 and 3 summarize the effect of modulations of the inotropic state on key hemodynamic parameters, power indexes, $E_{es}$, and PRSW. $PAMP_{VOPWR}$ and $PAMP_{V0Est}$ significantly increased in response to dobutamine, accompanied by significant increases of $E_{es}$ and PRSW. Phenylephrine caused significant increases of power indexes and PRSW. However, $E_{es}$ did not change significantly. Finally, both power indexes significantly decreased with esmolol. In contrast, the decrease of $E_{es}$ and PRSW did not reach statistical significance (Table 3).

The relationship of both power indexes with PRSW is shown in Fig. 4A. $PAMP_{VOPWR}$ and $PAMP_{V0Est}$ correlated closely with PRSW ($r = 0.85, P < 0.001; r = 0.77, P < 0.001$). However, the correlation of both power indexes with $E_{es}$ was only modest ($r = 0.64, P < 0.001; r = 0.54, P < 0.001$; Fig. 4B).

**Computer Modeling**

Computer simulations are compared with representative experimental data in Fig. 5; the physiological model matched satisfactorily with the observed data. Applying Eq. 2, 10 simulations yielded an exponent $\beta$ of $1.33 \pm 0.14$, that is, comparable to the median exponent $\beta$ as obtained directly from
the experimental data (not significantly different compared with experimental data; \( P < 0.01 \) compared with \( P/H_11021 \)). Noteworthy, when equation SW = \( a \cdot (EDV - V_{OSW})^b \) was applied, exponent \( \beta \) was 1.44 ± 0.13 (\( P < 0.001 \) compared with 1), indicating that a slight concavity of ESPVR is neglected by our computer model.

\( V_{OPWR} \) correlated closely with \( V_{OSW} \) (\( r = 0.92, P < 0.0001 \)) with an average difference of 0.7 ml (range −1.7 to 4.1 ml). In contrast, the average difference between \( V_{OPWR} \) and \( V_{Oes} \) was 20.5 ml (range 18.3–23.5 ml), confirming our experimental data showing that \( V_{OPWR} \) correlated more closely with \( V_{OSW} \) than with \( V_{Oes} \).

The influence of alterations in \( E_{es} \), \( V_{Oes} \), PVR, and \( E_d \) on \( V_{OPWR} \), \( V_{OPSW} \), PRSW, and \( V_{OSW} \) are displayed in Table 4. \( PAMP_{VOPWR} \) and PRSW showed optimal correlation with \( E_{es} \). As expected, \( E_d \) was inversely correlated with \( PAMP_{VOPWR} \) and PRSW.

**DISCUSSION**

We found that the \( PWR_{mx} \) versus EDV relationship is linear with a distinct volume-axis intercept. There were strong correlations between \( V_{OPWR} \) and \( V_{OSW} \), as well as between PAMP and PRSW. In addition, \( V_{OPWR} \) correlated with baseline EDV and LVEDP, potentially allowing single-beat preload adjustment. Dividing \( PWR_{mx} \) by the difference of EDV and \( V_{OPWR} \) eliminated preload dependency yet did not abolish its sensitivity to modulations of the contractile state. Computer simulations confirmed findings from our experimental data.

**PWR\textsubscript{mx} Preload Adjustment: Previous Studies**

Preload adjustment of \( PWR_{mx} \) was previously sought by dividing the square of EDV (18). The rationale was substantiated by an association with \( E_{es} \) (18). However, \( E_{es} \) is an end-systolic measure of contractility, yet \( PWR_{mx} \) occurs early during ejection. Ejection-derived parameters do not always correlate with end systole-derived contractile parameters (10, 16). Furthermore, ESPVR can show curvilinear features and considerable shifts of \( V_{Oes} \) with varying load (19, 28), both making \( E_{es} \) calculation by linear regression less accurate a correlate of PAMP. Accordingly, we found that \( PAMP_{VOPWR} \) and \( V_{OPWR} \) correlated modestly with \( E_{es} \) and \( V_{Oes} \), respectively.

It recently became apparent that dividing \( PWR_{mx} \) by EDV\(^2\) does not suffice to reduce preload dependency in either LV or RV (15, 29, 30). The “optimal” exponent \( \beta \) in \( PWR_{mx}/EDV^\beta \) varied with cardiac chamber size and volume-axis intercept of ESPVR (24, 29, 30). In agreement with the aforementioned studies, applying \( PWR_{mx}/EDV^2 \) to our experimental data also showed dependency of this index on preload conditions, and our computer model further confirmed this observation (see Table 4).
Table 3. Contractile response

<table>
<thead>
<tr>
<th></th>
<th>PAMP_{Vopwr}</th>
<th>V_{opwr}</th>
<th>PAMP_{Vest}</th>
<th>V_{est}</th>
<th>E_{es}</th>
<th>V_{est}</th>
<th>PRSW</th>
<th>V_{osw}</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>176±52</td>
<td>3 (−8;15)</td>
<td>145±51</td>
<td>4 (−2;10)</td>
<td>1.4±1.5</td>
<td>−4 (−14;6)</td>
<td>13.0±4.5</td>
<td>10 (0;19)</td>
</tr>
<tr>
<td>Dobutamine</td>
<td>394±205</td>
<td>6 (−5;16)</td>
<td>404±261</td>
<td>4 (−1;10)</td>
<td>2.9±2.6</td>
<td>−2 (−11;8)</td>
<td>29.7±16.4</td>
<td>9 (0;18)</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>143±57</td>
<td>13 (0;25)</td>
<td>129±55</td>
<td>15 (0;29)</td>
<td>1.3±1.6</td>
<td>0 (−7;8)</td>
<td>12.2±4.2</td>
<td>20 (4;36)</td>
</tr>
<tr>
<td>Esmolol</td>
<td>280±118</td>
<td>15 (−6;36)</td>
<td>224±86</td>
<td>11 (0;23)</td>
<td>1.7±0.8</td>
<td>−2 (−11;16)</td>
<td>25.7±8.1</td>
<td>19 (−4;43)</td>
</tr>
<tr>
<td>P</td>
<td>0.007</td>
<td>NS</td>
<td>0.004</td>
<td>NS</td>
<td>0.005</td>
<td>NS</td>
<td>0.005</td>
<td>NS</td>
</tr>
<tr>
<td>Baseline</td>
<td>158±93</td>
<td>6 (−1;13)</td>
<td>146±57</td>
<td>5 (−1;12)</td>
<td>1.0±0.6</td>
<td>−5 (−10;0)</td>
<td>9.8±3.3</td>
<td>10 (1;18)</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>116±51</td>
<td>12 (3;20)</td>
<td>108±31</td>
<td>6 (0;12)</td>
<td>0.9±0.3</td>
<td>1 (−5;7)</td>
<td>9.0±2.9</td>
<td>17 (7;26)</td>
</tr>
<tr>
<td>P</td>
<td>0.025</td>
<td>0.036</td>
<td>0.027</td>
<td>NS</td>
<td>0.036</td>
<td>NS</td>
<td>0.036</td>
<td>NS</td>
</tr>
</tbody>
</table>

PAMP_{Vopwr} preload-adjusted maximal power (adjusted with observed volume-axis intercept of maximal power vs. EDV relationship); V_{opwr}, measured volume-axis intercept of maximal power vs. EDV relationship; PAMP_{Vest}, preload-adjusted maximal power (adjusted with estimated volume-axis intercept of pressure vs. EDV relationship); V_{est}, estimated volume-axis intercept of pressure vs. EDV relationship; E_{es}, slope of the end-systolic pressure-volume relationship; V_{osw}, volume-axis intercept of stroke work vs. EDV; PRSW, preload recruitable stroke work; V_{osw}, volume-axis intercept of stroke work vs. EDV; numbers in parentheses represent 25% and 75% quartile values.

Fig. 4. Correlation between PAMP and load-independent parameters of contractility. A: PWR_{mx} adjusted by EDV and V_{opwr} (top) or V_{est} (bottom) vs. PRSW. B: PWR_{mx} adjusted by EDV and V_{opwr} (top) or V_{est} (bottom) vs. slope of end-systolic pressure (E_{es}). Open squares, data obtained with inotropic infusion (dobutamine, phenylephrine). Closed diamonds, data obtained without inotropic infusion.
Table 5). Although the sensitivity to changes in contractility and afterload was similar to the sensitivity of the power index proposed in the current study (see Table 4 for comparison), a decrease of the "circulating volume in the model by 10% resulted in an increase of PWR_{mx}/EDV by 65% (Jacobian matrix in Table 5). More recently, PWR_{mx} preload adjustment was sought under incorporation of the volume-axis intercept of ESPVR (29, 30), and this index \[ \text{PWR}_{mx} (\text{EDV} - V_{0Es})^2 \] demonstrated reduced preload dependency in both our experimental data and computer model (see Fig. 6).

The current study examined the PWR_{mx} versus EDV relationship with its own volume-axis intercept (i.e., V_{0PWR}). PAMPV_{0PWR} resembles PRSW (13), a load-insensitive parameter of contractility with least curvilinearity, yet highest reproducibility, in the RV (16). Our observation of a correlation between PRSW and PWR_{mx}/(\text{EDV} - V_{0PWR}) is also supported by power being the derivative of instantaneous cumulative work from the beginning of ejection. We therefore propose that optimal preload adjustment of PWR_{mx} should be based on the PWR_{mx} versus EDV relationship with consideration of V_{0PWR}.

**Afterload Dependency**

Ventricular power has been regarded as little influenced by acute afterload changes; the increase of LV PWR_{mx} after gradual aortic occlusion was attributed to increases of EDV (18), and RV PWR_{mx} did not change with partial PA occlusion (20). Others (32) noted increases of LV PWR_{mx} with prolonged augmentation of afterload. We observed PWR_{mx} increases in response to pharmacological modulation of RV afterload. The observation that α-adrenergic agonists (phenylephrine) increased parameters of RV contractility was expected (3). Afterload increases in and of themselves also affect the ESPVR by homeometric autoregulation (8, 27). Therefore, the intrinsic inotropic effect of phenylephrine infusion cannot be separated from the adaptation at cell level resulting in in-

---

**Table 4. Jacobian matrix**

<table>
<thead>
<tr>
<th></th>
<th>PAMP_{0PWR}</th>
<th>V_{0PWR}</th>
<th>PRSW</th>
<th>V_{0Sw}</th>
</tr>
</thead>
<tbody>
<tr>
<td>E_{es}</td>
<td>1.99</td>
<td>-0.13</td>
<td>0.98</td>
<td>-0.04</td>
</tr>
<tr>
<td>V_{0Es}</td>
<td>-0.09</td>
<td>0.16</td>
<td>-0.09</td>
<td>0.14</td>
</tr>
<tr>
<td>PVR</td>
<td>0.14</td>
<td>-0.08</td>
<td>0.01</td>
<td>0.09</td>
</tr>
<tr>
<td>E_{d}</td>
<td>-0.36</td>
<td>-0.16</td>
<td>-0.34</td>
<td>-0.20</td>
</tr>
</tbody>
</table>

\(E_{es}\), minimal diastolic elastance; \(E_{es}\), slope of end-systolic pressure-volume relationship; \(V_{0Es}\), volume-axis intercept of end-systolic pressure-volume relationship.

---

**Table 5. Jacobian matrix**

<table>
<thead>
<tr>
<th></th>
<th>PWR_{mx}/EDV</th>
<th>PWR_{mx}/EDV^2</th>
<th>PWR_{mx}/(EDV - V_{0Es})^2</th>
</tr>
</thead>
<tbody>
<tr>
<td>(E_{es})</td>
<td>1.06</td>
<td>1.20</td>
<td>1.21</td>
</tr>
<tr>
<td>(V_{0Es})</td>
<td>-0.17</td>
<td>-0.20</td>
<td>-0.04</td>
</tr>
<tr>
<td>PVR</td>
<td>0.25</td>
<td>0.17</td>
<td>0.16</td>
</tr>
<tr>
<td>(E_{d})</td>
<td>-0.37</td>
<td>-0.19</td>
<td>-0.18</td>
</tr>
<tr>
<td>Circulating volume</td>
<td>1.91</td>
<td>-6.51</td>
<td>-3.51</td>
</tr>
</tbody>
</table>

PWR_{mx}/EDV, preload adjusted maximal power (adjusted with EDV); PWR_{mx}/EDV^2, preload adjusted maximal power (adjusted with square EDV); PWR_{mx}/(EDV - V_{0Es})^2, preload adjusted maximal power (adjusted with square EDV minus volume-axis intercept of end-systolic pressure volume relationship); PVR, pulmonary vascular resistance. Circulating volume, circulating volume in the computer model. See Table 4 for comparison.

---

**Fig. 5.** Computer simulation (top) vs. experimental data (bottom). Corresponding pressure-volume loops are marked bold.

**Fig. 6.** Previously proposed PWR_{mx} indexes (18, 29, 30) applied to the experimental data. All parameters were normalized to baseline. See Fig. 3 for comparison.
creased force-generating capacity in response to higher afterload. Distinguishing between both mechanisms, however, is of modest significance, because clinically relevant, prolonged afterload changes inevitably result in changes of the contractile state, thus PRSW and $E_{es}$ (13, 17, 21, 37, 38). Importantly, although there was a wide range of pulmonary vascular resistance in the current study (see Table 1), adjusting RV PWR$_{max}$ for EDV and $V_{0PWR}$ eliminated preload dependency regardless of the afterload condition, yet maintained its high sensitivity to changes in contractility.

$V_{0PWR}$ Estimation

Apparently, PAMP can be computed from a single beat only if $V_{0PWR}$ was known. Previous studies indicated that the volume-axis intercept of LV PRSW can be estimated by LV mass and EDV (15). In the right ventricle, ventricular interdependences should be considered also, i.e., change of the septal curvature and LV contraction (5, 6, 40). Accordingly, we found that not only EDV influenced $V_{opWR}$ but also LVEDP. However, there was no evidence for the influence of invariant factors such as weight of the RV free wall. Although not the objective of this study, the approach of $V_0$ estimation should be validated in various acute and chronic hemodynamic conditions, including pulmonary and systemic arterial hypertension, cardiac hypertrophy and/or dilation, and congestive heart failure.

Implications

The need for estimation of contractility from a single beat has fostered considerable efforts by the research community (4, 15). We and others (15) observed that various indexes do not always correlate to a high degree. Obviously, those indexes may capture the interest of clinicians if they are based on rational theoretical considerations and easy-to-measure parameters. Preload-adjusted PWR$_{max}$ may fulfill these criteria because all parameters can be estimated by Doppler echocardiography, i.e., RV volume (9, 12), RV systolic pressure and pulmonary artery flow (31), and LVEDP (11, 26, 34). Study Limitations

This study was conducted in an open-chest model due to the necessary extensive instrumentation. The effects of opening the pericardium and/or hemodynamic interventions on the left ventricle may have altered RV function. Thus the linearity of the RV PWR$_{max}$ versus EDV relationship with distinct volume-axis intercept should be confirmed under closed-chest conditions. In addition, all experiments were performed on healthy animals; the applicability of this power index should be validated in pathological states with altered cardiac geometry. Furthermore, it remains to be analyzed how PWR$_{max}$ responds to an acute afterload increase (PA occlusion over a few beats) as opposed to the prolonged afterload modulations in this study, which resulted in an adjustment of the contractile state. Finally, this report focuses on parameters of RV contractility; it remains to be shown if our concept of PWR$_{max}$ preload adjustment would also apply to the left ventricle.

In conclusion, we found that the RV PWR$_{max}$ versus EDV relationship was linear, with a distinct volume-axis intercept. Dividing PWR$_{max}$ by EDV minus $V_{opWR}$ eliminated preload dependency. $V_{opWR}$ was estimated from baseline EDV and LVEDP, potentially allowing single-beat assessment of PAMP without the need for preload reductions. Power indexes based on measured or estimated V0 were sensitive to modulations of contractility and strongly correlated with PRSW. These results may encourage further studies on feasibility and usefulness in the clinical setting.

ACKNOWLEDGMENTS

The authors thank Adelaide Jaffe and Christine Kassuba for editorial advice.

GRANTS

This study was supported by the George M. and Linda H. Kaufman Center for Heart Failure and the Department of Thoracic and Cardiovascular Surgery at the Cleveland Clinic Foundation.

REFERENCES


