Preload-adjusted right ventricular maximal power: concept and validation

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Schenk, Soren, Zoran B. Popovic, Yoshie Ochiai, Fernando Casas, Patrick M. McCarthy, Randall C. Starling, Michael W. Kopcak, Jr., Raymond Dessoffy, Jose L. Navia, 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 (PWRmx) is dependent on preload. The objective of this study was to test our hypothesis that the PWRmx 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 PWRmx could be eliminated under various loading conditions and fitted to PWRmx versus EDV relationship: PWRmx = a(EDV − V0PWR)β, where a is the slope of the relationship. The PWRmx 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 (V0PAM) and single-beat PWRmx preload adjustment. Dividing PWRmax by the difference of EDV and V0PWR (PAMPV0PWR) eliminated preload dependence down to 50% of the baseline EDV. PWRmx adjustment using V0PAM showed similar preload independence. Enhancing contractility increased PAMPV0PWR and PAMPV0AM from 176 ± 52 to 394 ± 205 W/ml × 10^4 and 145 ± 51 to 404 ± 261 W/ml × 10^4, respectively, accompanied by an increase of PRSW from 13.0 ± 4.5 to 29.7 ± 16.4 mmHg (all P < 0.01). PAMPV0PWR and PAMPV0AM 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 PWRmx should consider a linear PWRmx 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 PWRmx-V0 Dependency

We propose that, because power is the first derivative of SW, the PWRmx 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 PWRmx versus EDV relationships during preload reduction. Dividing PWRmx by EDV raised to an exponent ≠ 1 assumes the following nonlinear relationship:

\[
PWRmx = a \cdot EDV^\beta
\]

where \(a\) is the slope of the relationship.

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

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

\[
PWRmx = a \cdot EDV^\beta
\]

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 (PWRmx), the peak instantaneous product of pressure and flow, reflects contractility (32) and can be determined noninvasively (1, 22). Unfortunately, PWRmx is dependent on preload, i.e., end-diastolic volume (EDV). Various concepts have been proposed for preload-adjusted PWRmx (PAMP) in both ventricles (18, 29, 30). A common approach was dividing PWRmx by EDV\(^\beta\), with \(\beta \neq 1\). The assumptions were that the PWRmx 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 PWRmx 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 PWRmx and EDV, 2) test a concept of PWRmx preload adjustment that reflects the shape of this relationship, and 3) assess the sensitivity of preload-adjusted PWRmx to modulations of the contractile state under various loading conditions. We first confirmed that the RV PWRmx versus EDV relationship was linear, with a distinct V0PWR. From the understanding that PWRmx 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.

METHODS

Preload Adjustment of PWRmx-V0 Dependency

We propose that, because power is the first derivative of SW, the PWRmx 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 PWRmx versus EDV relationships during preload reduction. Dividing PWRmx by EDV raised to an exponent ≠ 1 assumes the following nonlinear relationship:

\[
PWRmx = a \cdot EDV^\beta
\]
PRELOAD-ADJUSTED RIGHT VENTRICULAR MAXIMAL POWER  

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

(2)

Apparently, if \( \beta \) approximates 1.0, a linear \( \text{PWR}_{mx} \) versus EDV relationship can be expected, and if preload adjustment incorporates \( V_{opwr} \), shifts of the relationship should not alter \( \text{PWR}_{mx} \) changes of EDV and \( V_{opwr} \) eliminated preload dependency (Fig. 1A). Moreover, dividing \( \text{PWR}_{mx} \) by the difference of EDV and \( V_{opwr} \) eliminated preload dependency (Fig. 1B). Whether this concept can be applied to any hemodynamic state and whether \( V_{opwr} \) 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 placed 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-562-1, Millar Instruments) was inserted through the RV apex to measure RV pressure, volumes, and flow through the circulation that is conceptualized as eight different chambers: the right atrium and ventricle, pulmonary arteries and right ventricular walls and interventricular septum.

Data Analysis

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

\[ \text{PWR} = \text{RVP} \cdot Q_{RV} \]  

(3)

The volume-axis intercepts of PRSW (\( V_{opsw} \)), ESPVR (\( V_{oesv} \)), and the \( \text{PWR}_{mx} \) versus EDV relationship (\( V_{opwr} \)) 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 \( \text{PRSW} \) and \( \text{EDV} \) 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.

\( V_{estimation} \). Estimation of \( V_{opwr} \) (\( V_{oesv} \)) from a single beat was initiated by analyzing the influence of hemodynamic parameters and heart weight (invariant) stepwise multivariable regression. The independently significant predictors of \( V_{oesv} \) were then curve fitted to 36,000 linear and nonlinear equations (Table Curve3D 4.0, Systat Software; Richmond, CA). \( V_{oesv} \) 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 \( E_a \) 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
and veins, left atrium and ventricle, aorta, and systemic veins. Both LV and RV activation are modeled by a raised cosine function, with ESPVR assumed to be linear and defined by their $E_0$ and $V_0_{PWR}$. 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 ($E_0$), pressure and volume that correspond to the point of $E_0$, volume needed to increase $E_0$ by $e^kV_0$ (where $k$ is the exponent and $V_0$ 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 inertance, and venous capacitance, resistance, inertance and minimal volume. Systolic volume 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 $E_0$, $V_0_{PWR}$, 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, $E_0$ and $V_0_{PWR}$ 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 $E_0$ 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 obtain the $PWR_{mx}$ versus EDV relationship and PRSW. We separately altered contractility ($E_{es}$; 0.8, 0.4, and 1.6 mmHg/ml), ESPVR x-axis intercept ($V_0_{es}$; 2.4, −4, 8, and 14 ml), afterload (PVR; 239, 120, and 600 dyn·s·cm$^{-5}$), and diastolic stiffness ($E_d$; 0.06, 0.03, and 0.12 mmHg/ml). Results are presented in a modified Jacobian matrix, showing the change of normalized average index divided by change of normalized average parameter. Thus, for index $y$ and parameter $x$, the Jacobian matrix yields $(dy/xy)/(dx/xy)$. Ideally, a systolic index has sensitivity to $E_0$ equal to 1 but sensitivity to other input parameters equal to 0.

**Statistical Analysis**

Data are reported as means ± SD or as medians (25% and 75% quartiles). The shape of the $PWR_{mx}$ versus EDV relationship was determined by nonlinear fitting of Eq. 2. The average exponent $β$ was compared with a value of 1 using a single-sample $t$-test. We further examined individual slopes of two adjacent pairs of $PWR_{mx}$ 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 $PWR_{mx}$ versus EDV relationship was assumed 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 pressure 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 inotropic state (dobutamine, phenylephrine, and esmolol) were compared by Wilcoxon matched-pairs tests. $P < 0.05$ indicated statistical significance.

**RESULTS**

**Shape of $PWR_{mx}$ Versus EDV Relationship and $V_0$ Interrelationship**

The median exponent $β$ 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 $β$ in various experimental conditions, demonstrating that median $β$ was close to 1 in every experimental condition ($P$ not significant vs. 1 in each condition) and that the 95% confidence interval of mean $β$ always overlapped with 1. Furthermore, there was no relationship between exponent $β$ and PRSW or PVR ($r = 0.19$, $P$ not significant; $r = 0.03$, $P$ not significant, respectively), further suggesting that the shape of the $PWR_{mx}$ versus EDV relationship was independent of the contractile state and afterload condition. Moreover, the grand average of codes determining the shape of the $PWR_{mx}$ versus EDV relationship was 0.009 (95% confidence interval, −0.057 and 0.075), demonstrating that $β$ did not deviate in any direction during preload reduction. Together, these results confirm our hypothesis of a linear $PWR_{mx}$ versus EDV relationship in the right ventricle with existence of $V_{0PWPR}$.

We next examined the interrelationship of $V_{0PWPR}$, $V_0_{es}$, and $V_0_{SW}$. Strong correlations existed between $V_{0PWPR}$ and $V_0_{SW}$ ($r = 0.93$, $P < 0.0001$; Fig. 2B). The relationship between $V_{0PWPR}$ and $V_0_{es}$ ($r = 0.79$, $P < 0.0001$) was significantly less strong than that between $V_{0PWPR}$ and $V_0_{SW}$ ($P < 0.0001$).

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**Table 1. Hemodynamics**

<table>
<thead>
<tr>
<th>Condition</th>
<th>HR, beats/min</th>
<th>EDV, ml</th>
<th>SV, ml</th>
<th>$PWR_{mx}$, mW</th>
<th>RVP, mmHg</th>
<th>PAP, mmHg</th>
<th>PAP, mmHg</th>
<th>PVR, dyn·cm$^{-5}$·m$^{-2}$</th>
<th>LVP, mmHg</th>
<th>LVP, mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Baseline</td>
<td>112 ± 18</td>
<td>66 ± 42</td>
<td>21 ± 12</td>
<td>536 ± 295</td>
<td>4 ± 1</td>
<td>20 ± 5</td>
<td>7 ± 3</td>
<td>13 ± 3</td>
<td>342 ± 176</td>
<td>90 ± 35</td>
</tr>
<tr>
<td>RA pacing at 120 beats/min</td>
<td>119 ± 0.2</td>
<td>55 ± 44</td>
<td>23 ± 17</td>
<td>565 ± 419</td>
<td>4 ± 1</td>
<td>20 ± 5</td>
<td>8 ± 2</td>
<td>13 ± 3</td>
<td>313 ± 170</td>
<td>85 ± 16</td>
</tr>
<tr>
<td>Phenylephrine</td>
<td>119 ± 0.1</td>
<td>42 ± 26</td>
<td>18 ± 9</td>
<td>763 ± 413</td>
<td>4 ± 1</td>
<td>23 ± 10</td>
<td>17 ± 8</td>
<td>24 ± 9</td>
<td>496 ± 276</td>
<td>183 ± 47</td>
</tr>
<tr>
<td>$P$ value</td>
<td>NS</td>
<td>0.051</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>0.012</td>
<td>0.012</td>
<td>0.011</td>
<td>0.008</td>
<td>0.011</td>
</tr>
<tr>
<td>Pre-dobutamine</td>
<td>117 ± 10</td>
<td>30 ± 20</td>
<td>14 ± 7</td>
<td>308 ± 131</td>
<td>4 ± 1</td>
<td>19 ± 3</td>
<td>8 ± 2</td>
<td>13 ± 3</td>
<td>505 ± 184</td>
<td>87 ± 20</td>
</tr>
<tr>
<td>Post-dobutamine</td>
<td>120 ± 12</td>
<td>34 ± 25</td>
<td>20 ± 12</td>
<td>852 ± 680</td>
<td>4 ± 2</td>
<td>23 ± 7</td>
<td>9 ± 2</td>
<td>15 ± 4</td>
<td>446 ± 178</td>
<td>109 ± 45</td>
</tr>
<tr>
<td>$P$ value</td>
<td>NS</td>
<td>NS</td>
<td>0.007</td>
<td>NS</td>
<td>0.005</td>
<td>0.011</td>
<td>0.013</td>
<td>0.022</td>
<td>0.059</td>
<td>0.007</td>
</tr>
<tr>
<td>Pre-epinephrine</td>
<td>115 ± 10</td>
<td>33 ± 20</td>
<td>16 ± 8</td>
<td>350 ± 269</td>
<td>5 ± 1</td>
<td>19 ± 2</td>
<td>9 ± 2</td>
<td>14 ± 2</td>
<td>439 ± 179</td>
<td>79 ± 34</td>
</tr>
<tr>
<td>Post-epinephrine</td>
<td>116 ± 10</td>
<td>38 ± 22</td>
<td>11 ± 6</td>
<td>280 ± 151</td>
<td>5 ± 1</td>
<td>17 ± 3</td>
<td>8 ± 2</td>
<td>12 ± 3</td>
<td>669 ± 584</td>
<td>68 ± 32</td>
</tr>
</tbody>
</table>

Values are means ± SD. Additional data were acquired at 90 and 150 beats/min in some dogs, resulting in 80 data points. HR, heart rate; EDV, right ventricular end-diastolic volume; SV, right ventricular stroke volume; $PWR_{mx}$, right ventricular maximal power; RVP, right ventricular end-diastolic pressure; PAP, pulmonary vascular resistance; LVP, pulmonary vascular resistance; $LVP_{es}$, and $LVP_{mx}$, systolic and end-diastolic left ventricular pressure, respectively; NS, not significant; RA, right atrial.
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 PWRmax by the difference of EDV and $V_{0\text{PWR}}$ (i.e., preload-adjusted PWR through $V_{0\text{PWR}}$, PAMPV$_{0\text{PWR}}$) eliminated preload dependency down to 50% of baseline EDV without significant deviation in any direction (Table 2). Likewise, adjusting PWRmax by the difference of EDV and $V_{0\text{est}}$ (PAMPV$_{0\text{est}}$) 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, $E_s$, and PRSW. PAMPV$_{0\text{PWR}}$ and PAMPV$_{0\text{est}}$ significantly increased in response to dobutamine, accompanied by significant increases of $E_s$ and PRSW. Phenylephrine caused significant increases of power indexes and PRSW. However, $E_s$ did not change significantly. Finally, both power indexes significantly decreased with esmolol. In contrast, the decrease of $E_s$ and PRSW did not reach statistical significance (Table 3).

The relationship of both power indexes with PRSW is shown in Fig. 4A. PAMPV$_{0\text{PWR}}$ and PAMPV$_{0\text{est}}$ correlated closely with PRSW ($r = 0.85, P < 0.001; r = 0.77, P < 0.001$). However, the correlation of both power indexes with $E_s$ 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 \( \beta = 2 \)). Noteworthy, when equation \( SW = a \cdot (EDV - V_{OSW})^\beta \) was applied, exponent \( \beta \) was \( 1.44 \pm 0.13 \) (\( P < 0.001 \) 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 \( V_{O_Es} \) 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 \( V_{O_Es} \).

The influence of alterations in \( E_{es} \), \( V_{O_Es} \), PVR, and \( E_d \) on \( PAMP_{VOPWR} \), \( V_{OPWR} \), \( PRSW \), 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_{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 \( V_{O_Es} \) 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 \( V_{O_Es} \), 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 3. Contractile response

<table>
<thead>
<tr>
<th></th>
<th>PAMP V0PWR, W/ml × 10^4</th>
<th>PAMP V0Est, W/ml × 10^4</th>
<th>V0PWR, ml</th>
<th>V0Est, ml</th>
<th>Ees, mm Hg/ml</th>
<th>V0Ees, ml</th>
<th>PRSW, mmHg</th>
<th>V0SW, ml</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>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>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>p</td>
<td>0.021</td>
<td>NS</td>
<td>0.004</td>
<td>NS</td>
<td>NS</td>
<td>NS</td>
<td>0.017</td>
<td>NS</td>
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<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>Esmolol</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>NS</td>
<td>NS</td>
</tr>
</tbody>
</table>

PAMP V0PWR: preload-adjusted maximal power (adjusted with observed volume-axis intercept of maximal power vs. EDV relationship); V0PWR, measured volume-axis intercept of maximal power vs. EDV relationship; PAMP V0Est, preload-adjusted maximal power (adjusted with estimated volume-axis intercept of pressure vs. EDV relationship); V0Est, estimated volume-axis intercept of pressure vs. EDV relationship; Ees, slope of the end-systolic pressure-volume relationship; V0Ees, volume-axis intercept of Ees relationship; PRSW, preload recruitable stroke work; V0SW, 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: PWRmx adjusted by EDV and V0PWR (top) or V0Est (bottom) vs. PRSW. B: PWRmx adjusted by EDV and V0PWR (top) or V0Est (bottom) vs. slope of end-systolic pressure (Ees). Open squares, data obtained with inotropic infusion (dobutamine, phenylephrine). Closed diamonds, data obtained without inotropic infusion.
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 PWRmx/EDV by 65% (Jacobian matrix in Table 5). More recently, PWRmx preload adjustment was sought under incorporation of the volume-axis intercept of ESPVR (29, 30), and this index \[\text{PWR}_{\text{mx}}/(\text{EDV} - V_{\text{oes}})^2\] demonstrated reduced preload dependency in both our experimental data and computer model (see Fig. 6).

The current study examined the PWRmx versus EDV relationship with its own volume-axis intercept (i.e., \(V_{\text{OPWR}}\)). PAMPV_{OPWR} 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 PWRmx/(EDV – \(V_{\text{OPWR}}\))^2 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 PWRmx should be based on the PWRmx versus EDV relationship with consideration of \(V_{\text{OPWR}}\).

### Afterload Dependency

Ventricular power has been regarded as little influenced by acute afterload changes; the increase of LV PWRmx after gradual aortic occlusion was attributed to increases of EDV (18), and RV PWRmx did not change with partial PA occlusion (20). Others (32) noted increases of LV PWRmx with prolonged augmentation of afterload. We observed PWRmx increases in response to pharmacological modulation of RV afterload. The observation that \(\alpha\)-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-
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 \( E_{cs} \) (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 \( PWR_{\text{max}} \) 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 \( V_{0PWR} \) but also LVEDP. 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, cardia 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 \( PWR_{\text{max}} \) 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 \( PWR_{\text{max}} \) 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 \( PWR_{\text{max}} \) 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 \( PWR_{\text{max}} \) preload adjustment would also apply to the left ventricle.

In conclusion, we found that the RV \( PWR_{\text{max}} \) versus EDV relationship was linear, with a distinct volume-axis intercept. Dividing \( PWR_{\text{max}} \) by EDV minus \( V_{0PWR} \) eliminated preload dependency. \( V_{0PWR} \) 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 \( V_0 \) 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.

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**REFERENCES**
