Contribution of systemic vascular resistance and total arterial compliance to effective arterial elastance in humans

Denis Chemla,1,2 Isabelle Antony,2 Yves Lecarpentier,1 and Alain Nitenberg3

1Service de Physiologie Cardio-Respiratoire, Centre Hospitalier Universitaire de Bicêtre, Assistance Publique-Hôpitaux de Paris, 94 275 Le Kremlin-Bicêtre; 2Unité Propre de l’Enseignement Supérieur 2705, Université Paris Sud 11, 92 141 Clamart; and 3Service de Physiologie et d’Explorations Fonctionnelles, Centre Hospitalier Universitaire Jean Verdier, Assistance Publique-Hôpitaux de Paris, Université Paris 13, 93 143 Bondy, France

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Chemla, Denis, Isabelle Antony, Yves Lecarpentier, and Alain Nitenberg. Contribution of systemic vascular resistance and total arterial compliance to effective arterial elastance in humans. Am J Physiol Heart Circ Physiol 285: H614–H620, 2003. First published April 10, 2003; 10.1152/ajpheart.00823.2002.—The respective contribution of systemic vascular resistance (R) and total arterial compliance (C) to the arterial load remains to be established in humans. Effective arterial elastance (Ea), i.e., the left ventricular end-systolic pressure (LVESP)-over-stroke volume ratio, is a reliable estimate of arterial load. It is widely accepted that Ea mainly relates to mean aortic pressure (MAP) and thus to the R-to-T ratio (R/T ratio), where T is cycle length. We tested the contribution of R/T and 1/C to Ea in 20 normotensive and 46 hypertensive subjects (MAP range: 84–160 mmHg). The multilinear model applied (Ea = 1.00R/T + 0.42/C – 0.04; r2 = 0.97). The sensitivity of Ea to a change in R/T was 2.5 times higher than to a similar change in 1/C in both normotensive and hypertensive adults. The LVESP was more strongly related to systolic aortic pressure (SAP; r2 = 0.94) than to MAP (r2 = 0.83), and LVESP matched 90% SAP (bias = 0 ± 5mmHg). An alternative model of Ea is proposed, in which Ea is proportional to the heart rate × SAP-product-over-cardiac index ratio whatever the MAP.

In an attempt to simplify the assessment of Ea, the following aortic pressures have been used as surrogates for LVESP: mean aortic pressure (MAP) (38–40) and aortic notch pressure (2, 9, 15, 18), and empirical formulas based on systolic (SAP) and diastolic aortic pressures (DAP), namely, the (2SAP + DAP)/3 formula (19, 29) and the 0.9 SAP formula (6, 19). The second aim of our study was to investigate which aortic pressure was the strongest hemodynamic correlate of LVESP. Our results indicated that LVESP was most strongly related to SAP, and the physiological implications for the Ea model are discussed.

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METHODS

Study population. The study population was composed of normotensive control subjects \((n = 20)\) and hypertensive patients \((n = 46)\). Hypertensive patients had a well-established history of elevated blood pressure \(>140/90\) mmHg, with at least four sets of readings taken at 1-wk intervals. Control subjects had a systolic blood pressure \(<140\) mmHg and a diastolic blood pressure \(<90\) mmHg. All subjects were referred for the diagnosis of chest pain and evidenced an abnormal or equivocal treadmill test or single-photon emission computed tomographic stress scintigraphy. All subjects underwent coronary arteriography, and only subjects with coronary artery stenosis \(\geq 30\%\) at coronary arteriography were included in the study. Patients with valvular heart disease or diabetes mellitus were excluded from the study. The characteristics of the study population are listed in Table 1. All subjects gave informed consent, and the study was approved by our institution.

Catheterization procedure. All patients were in the fasting state for \(\geq 12\) h before the procedure. All treatments were discontinued at least 3 wk before cardiac catheterization with the exception of short-acting nitrates. No premedication was administered, and 1% lidocaine was used for local anesthesia. A 15-min delay was observed after documentation of nonsignificant coronary artery stenosis to eliminate the effects of contrast material. Thereafter, simultaneous recordings of LV pressure and aortic pressure were obtained using a 7-Fr double-tipped micromanometer angiographic catheter (Sentron, Cordis Laboratory; Roden, The Netherlands) (1), as previously described (1, 25). The catheter was placed through a femoral artery with a 7-Fr sheath. The distance between the two high-fidelity transducers was 10 cm. Aortic pressure was recorded above the aortic cusps. Heart rate (HR), aortic pressures, LV end-diastolic pressure, and LVESP were calculated with the use of a catheterization data-analysis computer system (Hewlett-Packard 5600 M; Andover, MA), which performed on-line analysis on nine beats for averaging out respiratory variations. Aortic pulse pressure (PP) was calculated as SAP minus DAP. MAP (range: 84–160 mmHg) was automatically calculated as the area under the pressure curve divided by \(t\). Aortic end-ejection pressure was measured at the trough of the incisura (dicrotic notch). Aortic mean ejection pressure was defined as the systolic pressure area (from pressure upstroke to dicrotic notch) divided by the LV ejection time. LV angiography (50 frames/s) was performed in a 30° right anterior oblique projection (35 ml nonionic contrast medium, 12 ml/s) with simultaneous recording of LV pressure (paper speed 200 mm/s) and a frame marker.

Table 1. Characteristics of the study population

<table>
<thead>
<tr>
<th></th>
<th>Controls ((n = 20))</th>
<th>Hypertensives ((n = 46))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex (men/women)</td>
<td>14/6</td>
<td>30/16</td>
</tr>
<tr>
<td>Age, yr</td>
<td>56 ± 5</td>
<td>55 ± 7</td>
</tr>
<tr>
<td>Body weight, kg</td>
<td>80 ± 8</td>
<td>75 ± 11</td>
</tr>
<tr>
<td>Body height, cm</td>
<td>167 ± 10</td>
<td>165 ± 7</td>
</tr>
<tr>
<td>HR, beats/min</td>
<td>68 ± 8</td>
<td>72 ± 8</td>
</tr>
<tr>
<td>LV end-diastolic volume index, ml/m²</td>
<td>81 ± 10</td>
<td>82 ± 12</td>
</tr>
<tr>
<td>Stroke index, ml/m²</td>
<td>55 ± 7</td>
<td>55 ± 6</td>
</tr>
<tr>
<td>LV ejection fraction, %</td>
<td>68 ± 5</td>
<td>68 ± 5</td>
</tr>
<tr>
<td>Cardiac index, l/min × 1·m⁻²</td>
<td>3.73 ± 0.58</td>
<td>3.99 ± 0.63</td>
</tr>
</tbody>
</table>

Values are means ± SD; \(n\), no. of subjects. HR, heart rate; LV, left ventricular. \(P\) values were not significant (NS) between groups.

Data analysis and calculations. LV end-diastolic volume and end-systolic volume (ESV) were calculated from monoplane angiograms by means of the area-length method (11). LV SV and ejection fraction were calculated using standard formulas. The LVESP was the pressure corresponding to the separation of the aortic and LV pressure curves recorded simultaneously. \(E_a\) was calculated as LVESP divided by SV (19). The SV-to-PP ratio was calculated as an estimate of \(C\) (5, 10, 13), and its reciprocal, i.e., the PP-to-SV ratio, was calculated as an estimate of total arterial stiffness (12, 42). \(R\) was calculated as MAP divided by cardiac output (SV × HR). For comparative purposes (biological scaling), SV was normalized for body surface area in the calculation of \(E_a, R,\) and \(C\).

Effective arterial elastance: theoretical background. In the two-element windkessel model, the governing equation in the frequency domain is as follows

\[
Z_{in} = R/(1 + jωRC)
\]

where \(Z_{in}\) is the input impedance, \(j = \sqrt{-1}\), and \(ω\) is the circular frequency (21). More simple, time-domain indexes of systemic vascular load have been recently proposed. Assuming that the systemic arteries can be considered an elastic chamber, the effective volume elastance \(E_a\) is the slope of the linear relationship between aortic end-systolic pressure and SV (38–40). If one assumes that end-systolic pressure can be approximated by end-ejection pressure, that end-ejection pressure matches mean ejection pressure, and that the intercept with the pressure axis is small enough to be negligible, the three-element windkessel model of arterial circulation predicts the following equations (38–40)

\[
\text{LVESP} = R_T \times \text{SV}/[(t_d + \tau(1 - e^{-t_d/τ}))]
\]

where \(R_T\) is the sum of characteristic impedance and peripheral resistance; \(t_d\) and \(t_{es}\) are the systolic and diastolic time periods, respectively; and \(τ\) is the diastolic pressure decay time constant \((\tau = RC)\). With the use of this approach, \(E_a\) is uniquely determined by arterial properties, time intervals, and SV, independently of how SV is generated, i.e., without the need to take into account the preload and intrathoracic state (30, 38–40). In cases where \(τ\) is long compared with \(t_d\) \((τ >> t_d)\), then the denominator of the LVESP reduces to \(t_d + t_{es} = T\), and thus \(E_a = R_T/τ^2\) (19).

The LV can also be considered as an elastic chamber, the end-systolic elastance \((E_{es})\) of which is the slope of the LVESP – (ESV – \(V_e\)) relationship, where \(V_e\) is the volume intercept (36, 37). Given similar dimensions for \(E_a\) and \(E_{es}\) (mmHg/ml), this framework allows rational analysis of the ventriculoarterial coupling in a concise way. Assuming similar LV and aortic pressure at end systole, the operating point of the coupled equilibrium between LV and arterial system is located at the intersection of the LVESP-ESV and LVESP-SV relationships in the pressure-volume plane (36–40).

In animals, previous studies have confirmed the linearity of the LVESP-SV relationships obtained in various experimental conditions, thus allowing the precise calculation of \(E_a\). In humans, serial SV assessment in various loading conditions is not easy to obtain without changing LV contractility. Therefore, \(E_a\) is currently calculated as the steady-state LVESP-over-SV relationship, assuming a linear LVESP-SV relationship and negligible pressure intercept (19)

\[
E_a = \frac{\text{LVESP}}{\text{SV}}
\]

Given that experimental studies have shown that MAP was close to LVESP, the following equation has been proposed (38–40)
\[ E_a = \frac{MAP}{R/T} \]

Assuming negligible downstream pressure, and consistent with the calculations based on the three-element windkessel model, Sunagawa et al. (38–40) have proposed a redundant formalism of the latter equation

\[ E_a = \frac{R}{T} \]

where \( R \) is expressed in mmHg·m²·s⁻¹·ml⁻¹. However, in humans, LVESP is usually higher than MAP. Thus Cohen-Solal et al. (7, 8) have proposed the following equation

\[ E_a = (R/T) + E_a' \]

where \( E_a' \) represents the increment of pressure above MAP at end systole divided by SV

\[ E_a' = \frac{(LVESP - MAP)}{SV} \]

The \( E_a' \) component is increased in humans with stiff vasculature (i.e., aged and hypertensive subjects) (7–9, 19), but no analytic model relating \( E_a, E_a', \) and \( C \) has been yet proposed in humans.

Very recently, Segers et al. (34) used a mathematical heart-arterial interaction model to precisely quantify the respective contribution of \( R \) and \( C \) to \( E_a \). Systemic arterial load was described by a four-element windkessel model in which 121 possible combinations of \( R \) and \( C \) were simulated, together with fixed values for total ineritance and characteristic impedance (34). The authors found that \( E_a \) was linearly related \((r^2 = 0.99)\) to \( R/T \) and \( 1/C \) according to the following equation

\[ E_a = 1.023R/T + 0.314/C - 0.127 \]

The applicability of this model remains to be demonstrated in humans.

Finally, in an attempt to simplify the calculation of \( E_a \) in humans, various LVESP estimates/surrogates have been used, namely, MAP (9, 39, 40), aortic notch pressure (2, 9, 15, 18), the \( (2SAP + DAP)/3 \) formula (19, 29), and the \( 0.9SAP \) formula (6, 19).

**Statistical analysis.** Data are expressed as means ± SD. ANOVA was used for overall comparisons between groups. Regressions were obtained using the least squares method. The following LVESP estimates were tested: MAP, aortic notch pressure, aortic mean ejection pressure, the \( (2SAP + DAP)/3 \) formula, and the \( 0.9SAP \) formula. Among the various estimates of LVESP (namely, MAP, aortic notch pressure, aortic mean ejection pressure, the \( (2SAP + DAP)/3 \) formula, and the \( 0.9SAP \) formula), please note that \( 0.9SAP \) was the most precise estimate of LVESP in the overall population. *P < 0.001 vs. controls.

**Table 2. Aortic and LV end-systolic pressures**

<table>
<thead>
<tr>
<th></th>
<th>Controls (n = 20)</th>
<th>Hypertensives (n = 46)</th>
</tr>
</thead>
<tbody>
<tr>
<td>SAP, mmHg</td>
<td>132 ± 7</td>
<td>182 ± 12*</td>
</tr>
<tr>
<td>DAP, mmHg</td>
<td>68 ± 5</td>
<td>90 ± 13*</td>
</tr>
<tr>
<td>PP, mmHg</td>
<td>64 ± 9</td>
<td>92 ± 20*</td>
</tr>
<tr>
<td>MAP, mmHg</td>
<td>94 ± 6</td>
<td>126 ± 10*</td>
</tr>
<tr>
<td>Aortic notch pressure, mmHg</td>
<td>105 ± 7</td>
<td>138 ± 12*</td>
</tr>
<tr>
<td>Aortic mean ejection pressure, mmHg</td>
<td>117 ± 7</td>
<td>152 ± 14*</td>
</tr>
<tr>
<td>( (2SAP + DAP)/3 ), mmHg</td>
<td>111 ± 5</td>
<td>151 ± 8*</td>
</tr>
<tr>
<td>0.9SAP, mmHg</td>
<td>119 ± 6</td>
<td>164 ± 11*</td>
</tr>
<tr>
<td>LVESP, mmHg</td>
<td>117 ± 10</td>
<td>164 ± 9*</td>
</tr>
</tbody>
</table>

Values are means ± SD; n, no. of subjects. SAP, systolic aortic pressure; DAP, diastolic aortic pressure; PP, aortic pulse pressure; MAP, mean aortic pressure; LVESP, LV end-systolic pressure. Among the various estimates of LVESP (namely, MAP, aortic notch pressure, aortic mean ejection pressure, the \( (2SAP + DAP)/3 \) formula, and the \( 0.9SAP \) formula), please note that \( 0.9SAP \) was the most precise estimate of LVESP in the overall population. *P < 0.001 vs. controls.

\[ R/T (E_a = 1.28R/T + 0.43, r^2 = 0.89) \text{ and } 1/C (E_a = (0.96/C + 1.28, r^2 = 0.62) \text{ (each } P < 0.001) \text{.} \]

No relationship was found between \( E_a \) and HR \((r^2 = 0.03)\) or age \((r^2 = 0.02)\).

\[ R/T \text{ as an estimate of } E_a \text{. The } R/T \text{ ratio significantly underestimated } E_a \text{ (Fig. 1, left, and Table 4). The } (E_a - R/T) \text{ difference (i.e., } E_a' \text{) was higher in hypertensive patients than in normotensive subjects (} P < 0.001 \text{) (Table 3).} \]

The steady, \( R/T \) component of arterial load accounted for a lower percentage of \( E_a \) in hypertensive patients \((77 ± 5\%) \text{ than in controls (} 81 ± 5\% \text{) (} P < 0.02; \text{ Table 3).} \)

The unsteady, \( E_a' \) component of arterial load accounted for a higher percentage of \( E_a \) in hypertensive patients \((19 ± 5\%) \text{ than in controls (} 23 ± 5\%) \text{ (} P < 0.02; \text{ Table 3).} \)

Among all the clinical and hemodynamic variables studied, \( 1/C \text{ was the one most strongly related to } E_a \text{ (} r^2 = 0.82 \text{), such that } R/T \text{ closely approximated } E_a \text{ for large } C \text{ values only (Fig. 1, right).} \)

\[ \text{The respective contribution of } R/T \text{ and } 1/C \text{ to } E_a \text{ and to } E_a'. \text{ After the inclusion of } 1/C \text{ in the model, multiple linear regression analysis yielded the following relation} \]

\[ E_a = 1.00(R/T) + 0.42(1/C) - 0.04 \]

\((r^2 = 0.97, P < 0.001)\)

A similar regression line was obtained when raw data were used instead of body surface area-normalized values of \( E_a, R, \) and \( C \). Thus, in the overall population, the combined influences of \( R/T \) and \( 1/C \text{ explained 97\% of the variability of } E_a. \text{ The sensitivity of } E_a \text{ to a change in } R/T \text{ was 2.5 times higher than to a similar change in } 1/C. \text{ The true } E_a \text{ was precisely estimated using the multilinear model (Fig. 2, left,} \text{ and the bias (i.e., formula - true } E_a \text{) was similar in controls and hypertensive patients (Table 4). Assuming that } (-0.04) \text{ is small enough to be negligible, the multilinear model implies that } E_a' \text{ can be described by the following equation in resting humans and over a wide } MAP \text{ range} \]

\[ E_a' = 0.42/C \]
The LVESP was strongly related to SAP (LVESP = 0.91SAP - 2 mmHg, $r^2 = 0.94$, $P < 0.001$), and the equation line was close to the 0.9SAP empirical estimate of LVESP previously proposed (19). The LVESP was related to MAP (LVESP = 1.22MAP + 7 mmHg, $r^2 = 0.83$, $P < 0.001$), to aortic notch pressure (LVESP = 0.67aortic notch pressure + 28 mmHg, $r^2 = 0.71$, $P < 0.001$), and to aortic mean ejection pressure (LVESP = 1.07mean ejection pressure - 1 mmHg, $r^2 = 0.85$, $P < 0.001$). The LVESP was also positively related to DAP ($r^2 = 0.41$) and PP ($r^2 = 0.48$) (each $P < 0.001$).

Empirical estimates of LVESP. The empirical formula (LVESP = 0.9SAP) gave an accurate estimate of LVESP [bias = 0 ± 5 mmHg, $P$ = not significant (NS)], and the bias was similar in normotensive subjects (bias = 2 ± 5 mmHg) and in hypertensive patients (bias = 0 ± 6 mmHg; $P$ = NS). All other empirical estimates significantly underestimated LVESP (each $P < 0.001$). The bias was higher in hypertensive patients than in normotensive subjects for MAP (−37 ± 9 vs. −23 ± 11 mmHg), aortic notch pressure (−26 ± 13 vs. −12 ± 5 mmHg), aortic mean ejection pressure (−12 ± 8 vs. 0 ± 6 mmHg), and the empirical formula

$$\text{LVESP} = \frac{2SAP + DAP}{3} (-13 \pm 4 \text{ vs. } -6 \pm 7 \text{ mmHg})$$

(Each $P < 0.001$).

Implications for the $E_a$ model. The following estimate was shown to be accurate over a wide pressure range

$$\text{LVESP} = 0.9\text{SAP}$$

By dividing both sides of this equation by the SV index (SVI), we obtain

$$E_a = 0.9\text{SAP}/\text{SVI}$$

By multiplying the numerator and denominator by HR, we obtain

$$E_a = 0.9(\text{HR} \times \text{SAP})/\text{CI}$$

where HR × SAP is the rate-pressure product and CI is the cardiac index. The true $E_a$ was precisely estimated using this formula (Fig. 2, right), and the bias (i.e., formula − true $E_a$) was similar in controls and hypertensive patients (Table 4). Thus, in the study population, and over a wide MAP range (84–160 mmHg), there was a simple, proportional relation between the effective $E_a$ and the ratio of the rate-pressure product divided by the cardiac index.

**DISCUSSION**

Our study shows that $E_a$ can be precisely described by a multilinear function of $R/T$ and $1/C$ in humans. In both normotensive subjects and hypertensive patients, the sensitivity of $E_a$ to a change in $R/T$ was 2.5 times higher than to a similar change in $1/C$. It was also demonstrated that the most accurate estimate of LVESP was 0.9SAP. This implies that $E_a$ is proportional to the rate-pressure product-over-cardiac index ratio whatever the prevailing aortic pressure.

The $R/T$ ratio significantly underestimated $E_a$ in hypertensive subjects because of an important additional influence of pulsatile impedance load related to decreased arterial compliance (7, 8, 19). The ($E_a - R/T$) difference, namely, $E_a'$, reflects the pulsatile component of $E_a$ (7–9, 19). In hypertensive patients, Cohen-Solal

![Fig. 1. Influence of $R/T$ (where $R$ is systemic vascular resistance and $T$ is cycle length) and $1/C$ (where $C$ is total arterial compliance) on effective arterial elastance ($E_a$) in normotensive subjects ($n = 20$) and hypertensive patients ($n = 46$). Left: linear relationship between $R/T$ and $E_a$ in normotensive subjects and hypertensive patients. $E_a = 1.28R/T + 0.01 (r^2 = 0.89, P < 0.001)$. The $R/T$ ratio significantly underestimated $E_a$, especially in hypertensive patients. Right: the ($E_a - R/T$) bias (termed $E_a''$) was most strongly related to arterial stiffness ($1/C$) according to the equation ($R/T - E_a''$) = $-0.42/C + 0.04 (r^2 = 0.82, P < 0.001)$.

Table 3. Indexes of arterial load and time intervals

<table>
<thead>
<tr>
<th></th>
<th>Controls ($n = 20$)</th>
<th>Hypertensives ($n = 46$)</th>
<th>$P$ Values</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R$, mmHg·m$^{-2}$·s·m$^{-1}$</td>
<td>1.54 ± 0.24</td>
<td>1.95 ± 0.35</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>$C$, ml·mmHg$^{-1}$·m$^{-2}$</td>
<td>0.88 ± 0.21</td>
<td>0.64 ± 0.18</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>$1/C$, mmHg·m$^2$·ml$^{-1}$</td>
<td>1.19 ± 0.22</td>
<td>1.69 ± 0.45</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>$T$, ms</td>
<td>892 ± 97</td>
<td>841 ± 98</td>
<td>0.054</td>
</tr>
<tr>
<td>$RC$, ms</td>
<td>1,315 ± 123</td>
<td>1,218 ± 339</td>
<td>NS</td>
</tr>
<tr>
<td>$E_a$, mmHg·m$^2$·ml$^{-1}$</td>
<td>2.17 ± 0.38</td>
<td>3.01 ± 0.42</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>$R/T$, mmHg·m$^2$·ml$^{-1}$</td>
<td>1.74 ± 0.28</td>
<td>2.32 ± 0.33</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>$E_a' = E_a - R/T$, mmHg·m$^2$·ml$^{-1}$</td>
<td>0.43 ± 0.14</td>
<td>0.69 ± 0.19</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>$R/T$, %$E_a$</td>
<td>81 ± 5</td>
<td>77 ± 5</td>
<td>&lt;0.02</td>
</tr>
<tr>
<td>$E_a'$, %$E_a$</td>
<td>19 ± 5</td>
<td>23 ± 5</td>
<td>&lt;0.02</td>
</tr>
</tbody>
</table>

Values are means ± SD; $n$, no. of subjects. $R$, systemic vascular resistance; $C$, total arterial compliance; $T$, cardiac cycle length; $E_a$, effective arterial elastance; $E_a'$, pulsatile component of $E_a$. **Adapted from http://ajpheart.physiology.org by 10:22:33 AM on October 23, 2017**

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et al. (7) have reported that $E_a$ is augmented proportionally more than $R/T$, although the latter largely predominates in determining $E_a$ quantitatively, and our findings are fairly consistent with their results (Table 3). However, partitioning $E_a$ into a steady ($R/T$) and a pulsatile ($E_a^p$) component does not allow us to precisely quantify the respective contribution of $R$ and $C$ to $E_a$.

Recently, using a mathematical heart-arterial interaction model in which the systemic circulation was described by a four-element windkessel model, Segers et al. (34) reported that $E_a$ was linearly related to $R/T$ and to $1/C$ according to the following equation: $E_a = 1.023R/T + 0.314/C - 0.127$ ($r^2 = 0.99$). In our study, by use of a two-element windkessel model of the systemic arterial circulation in humans and over a wide MAP range (84–160 mmHg), $E_a$ was accurately described according to the following equation: $E_a = 1.00R/T + 0.42/C - 0.04$ (in mmHg·m²·ml⁻¹, $r^2 = 0.97$). The consistency between our clinical study and previous theoretical results (34) is thus excellent, and we feel that this strengthens the clinical relevance of the model.

Considering that aortic pressure is a continuous variable, we found that a single multilinear function of $R/T$ and $1/C$ meaningfully described $E_a$ in both normotensive and hypertensive patients. Thus, the sensitivity of $E_a$ to a change in $R/T$ was 2.5 times higher than to a similar change in $1/C$ whatever the prevailing MAP in humans. Assuming that the ($-0.04$) factor was small enough to be negligible, we also found that $E_a$ matched ($0.42/C$) in both normotensive and hypertensive subjects. As $C$ is lower (the $1/C$ ratio is higher) in hypertensives than in normotensive subjects, our model was consistent with higher $E_a$ and higher impedance load related to decreased $C$ in hypertensives (Refs. 7, 8, and 19and Table 3).

The two-element ($RC$) windkessel model is a linear model that does not incorporate the influences of wave transmission characteristics and implies an absence of wave reflection. This may be a limitation in hypertensive patients, in whom a weak but significant relationship has been previously reported between $E_a$ and the extent of wave reflections (32). Conversely, a previous theoretical study (34) has shown that $E_a$ is not necessarily related to the characteristics of wave reflections. Furthermore, the ability of the $RC$ model to accurately describe the mechanical properties of the arterial system with a limited number of parameters and in various pathophysiological conditions has been stressed (24, 28, 35).

It is widely accepted that $E_a$ mainly depends on MAP and SV, and thus the $R/T$ ratio, given obvious redundancy in hemodynamic formulas. This implies that LVESP must be strongly related to MAP. However, in our study, LVESP was more strongly related to SAP ($r^2 = 0.94$) than to MAP ($r^2 = 0.83$). The advantage of relating arterial load to SAP rather than to MAP is that SAP incorporates the influences of peripheral resistance, arterial compliance, and wave reflections (27). Several studies, including the present one, have documented a strong linear relationship between MAP and SAP, thus suggesting the major role of increased peripheral resistance and small artery vascular tone on the increased SAP in hypertensive patients (14). Furthermore, in patients with stiff vasculature, both reduced arterial compliance and increased wave reflections result in a rise in late-peaking systolic pressure that may unfavorably load the still-ejecting LV (22, 27).

The LVESP-to-SV ratio is a hemodynamic parameter per se, and therefore $E_a$ may not necessarily relate to the windkessel model. Thus we tested the possibility

![Fig. 2. Left: $E_a$ as a multilinear function of $R/T$ and $1/C$ in normotensive subjects ($n = 20$) and hypertensive patients ($n = 46$; $r^2 = 0.97$, $P < 0.001$). Right: redundant formalism of $E_a$, relating arterial load to the rate-pressure product (heart rate (HR) × systolic arterial pressure (SAP)-over-cardiac index (CI) ratio ($r^2 = 0.98$, $P < 0.001$).](http://ajpheart.physiology.org/10.1152/ajpheart.00352.2002)
that an alternative model may be proposed to describe $E_a$. Taking advantage of certain redundancy in hemodynamic formulas, we demonstrated that $E_a$ is proportional to the rate-pressure product-over-cardiac index ratio whatever the prevailing aortic pressure (Fig. 2, right). For a given level of cardiac contractility, the rate-pressure product reflects the myocardial oxygen demand (4, 16, 41), and our results thus argue in favor of a fixed relationship among the arterial load, cardiac index, and myocardial oxygen demand, a point that deserves confirmation.

Several aortic pressures have been proposed as surrogates for LVESP in an attempt to simplify the clinical assessment of $E_a$ and $E_{es}$. To the best of our knowledge, our study is the first to critically evaluate these pressure surrogates in a significant number of subjects ($n = 66$) and over a wide pressure range. Mean pressure, notch pressure, mean ejection pressure, and the $(2SAP + DAP)/3$ formula significantly underestimated LVESP, the bias being higher in hypertensive patients than in normotensive subjects in all cases. Conversely, 0.9SAP gave a reliable estimate of LVESP whatever the prevailing aortic pressure. The 0.9SAP formula has been previously shown to give an accurate estimate of LVESP in four young normotensive and six older hypertensive subjects studied at rest and after preload reduction and pharmacological interventions (19). Given that the subjects in the present study were free of aortic stenosis and hypertrophic cardiomyopathy, our finding is also in keeping with previous results showing that 1) peak LV pressure is usually achieved close to the volume point of minimal LV volume (11, 37); 2) peak LV pressure and LVESP are close in magnitude, although they occur at different points in time (17, 31); and 3) LV peak systolic pressure can be used instead of LVESP to calculate LV $E_{es}$ with reasonably good accuracy (20, 26).

The main clinical implication is that 0.9SAP may provide the most accurate estimate of LVESP, and this may improve the noninvasive calculation of $E_a$ and $E_{es}$ by aplanation tonometry. Conversely, other empirical LVESP estimates must not be used, especially in hypertensive patients. Importantly, the 0.9SAP approximation applies strictly to central pressure recordings and not to brachial artery pressure, given the physiological increases in systolic pressure observed from the aorta to periphery (pulse wave amplification phenomenon) (27).

The limitations of our study must be discussed. Although some authors have suggested that the SV-to-PP ratio overestimates $C$ (for a review, see Ref. 5), we (5) have recently reported that the bias between the SV-to-PP ratio and $C$ (calculated using the so-called area method) was $0.03 \pm 0.15$ ml/mmHg in 31 subjects. In the present study, $R$, $C$, and $E_a$ were calculated using widely used, standard formulas, in which the influences of downstream (zero flow) pressure were not taken into account. Further studies are needed to test the potential effects of changes in downstream pressure on the relationship among $R$, $C$, and $E_a$. For an invasive, high-fidelity pressure study, the number of normotensive and hypertensive subjects was likely to be sufficient to justify the conclusions drawn from the data. Finally, the results pertain strictly to the population under study, and data were obtained at rest. Improving our understanding of resting hemodynamics is an important goal of clinical research, because hypertension is a risk factor for increased morbidity and mortality (23). Further studies are needed to confirm our study in dynamic conditions and after pharmacological interventions.

In conclusion, in normotensive subjects and hypertensive patients, $E_a$ can be precisely described by a multilinear function of $R/T$ and $1/C$. The sensitivity of $E_a$ to a change in $R/T$ was 2.5 times higher than to a similar change in $1/C$. This confirms previous theoretical modeling and gives a valuable representation of the function of the arterial circulation as a mechanical load. Furthermore, the most accurate estimate of LVESP was 0.9SAP. This implies that a complementary aspect of the ventriculoarterial coupling might be proposed, in which $E_a$ is proportional to the HR $\times$ SAP product-over-cardiac index ratio whatever the prevailing aortic pressure.

REFERENCES


