Hemodynamic correlates of effective arterial elastance in mitral stenosis before and after balloon valvotomy

PATRICE COLIN, MICHEL SLAMA, ALEC VAHANIAN, YVES LECARPTIE, GILBERT MOTTÉ, AND DENIS CHEMLA

Service de Cardiologie, Hôpital Antoine-Bicêtre, 92141 Clamart; Inserm U451-Loa-Ensta-Ecole Polytechnique, 91125 Palaiseau; Service de Cardiologie, Hôpital Tenon, 75970 Paris; and Service de Physiologie Cardio-Respiratoire, Hôpital de Bicêtre, 94275 Le Kremlin-Bicêtre, France

Colin, Patrice, Michel Slama, Alec Vahanian, Yves Lecarpentier, Gilbert Motté, and Denis Chemla. Hemodynamic correlates of effective arterial elastance in mitral stenosis before and after balloon valvotomy. J. Appl. Physiol. 83(4): 1083–1089, 1997.—This study had the purpose of documenting the hemodynamic correlates of effective arterial elastance (Ea; i.e., an accurate estimate of hydraulic load) in mitral stenosis (MS) patients. The main hypothesis tested was that Ea relates to the total vascular resistance (R)-to-pulse interval duration (T) ratio (R/T) in MS patients both before and after successful balloon mitral valvotomy (BMV).

High-fidelity aortic pressure recordings were obtained in 10 patients (40 ± 12 yr) before and 15 min after BMV. Ea value was calculated as the ratio of the steady-state end-systolic aortic pressure (ESAP) to stroke volume (thermodilution). Ea increased after BMV (from 1.55 ± 0.63 to 1.83 ± 0.71 mmHg/ml; P < 0.05). Throughout the procedure, there was a strong linear relationship between Ea and R/T: Ea = 1.09R/T − 0.01 mmHg/ml, r = 0.99, P = 0.0001. This ultimately depended on the powerful link between ESAP and mean aortic pressure (MAP; r = 0.99, 95% confidence interval for the difference (MAP − ESAP) from −18.5 to +4.5 mmHg). Ea was also related to total arterial compliance (area method) and to wave reflections (augmentation index), although to a lesser extent. After BMV, enhanced and anticipated wave reflections were observed, and this was likely to be explained by decreased arterial compliance. The present study indicated that Ea depended mainly on the steady component of hydraulic load (i.e., R) and on heart period (i.e., T) in MS patients.

increased afterload has been proposed as one of the causal factors of left ventricular (LV) systolic dysfunction observed in ∼30% of patients with pure mitral stenosis (MS). In this subgroup of patients, both the relatively thin-walled LV chamber and the presence of high systemic vascular resistance result in abnormally high end-systolic wall stress. Given impaired LV filling, some researchers have reported that this elevation in afterload was not offset by the Frank-Starling mechanism, thus leading to low ejection performance (5); others have suggested that decreased intrinsic contractility may also be involved (18). Given the potential role of increased arterial load in the development of systolic dysfunction in MS patients, it is important to improve the way in which arterial load is estimated in such patients.

A precise and complete description of LV afterload (i.e., hydraulic load) is provided by the input impedance of systemic circulation (17, 20, 21), but this complex approach is not always feasible in clinical practice. Sunagawa et al. (25, 26) have proposed an alternative assessment of hydraulic load, namely, effective arterial elastance (Ea). In both healthy subjects and hypertensive patients, Ea has been shown to mainly depend on 1) the R-to-T ratio (R/T) (12, 25, 26), where R is the peripheral resistance and T is heart period, and 2) the magnitude of wave reflections (4, 23). Conversely, Ea poorly depends on total arterial compliance (25, 26). The above-mentioned studies were performed under baseline conditions, and it remains to be established whether acute load manipulations modify the hemodynamic correlates of Ea. The loading conditions of the heart are dramatically modified in MS patients at both baseline and after balloon valvotomy (27, 28), and this may well modify the hemodynamic correlates of Ea. To the best of our knowledge, only one study has documented Ea values in MS patients (14), and none has examined the effects of percutaneous balloon mitral valvotomy (BMV) on arterial load, as reflected in Ea values.

Accordingly, the purpose of our preliminary study was to document the hemodynamic correlates of Ea in MS patients studied both before and after valvotomy. In our patients, we tested the hypothesis that Ea could relate to R, T, R/T, total arterial compliance, and the indexes of wave reflection.

METHODS

Patients

From November 1994 to October 1995, 10 consecutive patients who underwent BMV were included in the study after informed consent was obtained. We studied eight women and two men. Characteristics of the study population are listed in Table 1. All the included patients had MS with a narrowed mitral valve orifice (<1.5 cm² on echocardiographic examination) and were NYHA class II (8 of 10) or III (2 of 10). Echocardiography was performed the day before and between 24 and 48 h after BMV and was considered as the reference method for mitral valve area measurement. Patients were excluded from the study if they had moderate (2+) or severe (3+) mitral regurgitation, significant (>2+) aortic valve insufficiency, or any degree of aortic stenosis, significant calcification of the mitral valve, evidence of left atrial thrombus on transesophageal echography, or a previous history of coronary artery disease. Seven patients had normal sinus rhythm. Three patients were in atrial fibrillation and were given oral anticoagulant therapy (n = 3), digoxin (n = 3), furosemide (n = 1), and amiodarone (n = 1). Six patients were undergoing diuretic therapy.
Catheterization Technique and BMV Procedure

Patients were studied at baseline, at least 12 h after previous intake of their usual medication according to our routine protocol (27, 28). Patients were sedated by using clorazepate (10 mg). Aortic pressure was measured by using an 8-Fr single-lumen catheter equipped with a high-fidelity transducer (Sentron/Cordis, Roden, The Netherlands) (8). The catheter was advanced from the left femoral artery to the aortic root. Routine right-heart catheterization was performed by using the Seldinger technique through the left femoral vein. Before BMV, right heart pressures were obtained and cardiac output was measured in triplicate in all patients by using the thermodilution technique. Stroke volume (SV) was calculated as the cardiac output-to-heart rate ratio. Left ventriculography was performed in the 30° right anterior oblique projection. LV volumes were calculated by using the area-length method, taking care not to include the anterior oblique projection. LV volumes were calculated by using the area-length method, taking care not to include the anterior oblique projection.

Aortic root level. Mean aortic pressure (MAP) was defined as the area under the pressure curve divided by pulse interval duration (T). T (in ms) was defined as the time between two consecutive aortic pressure upstrokes. Aortic dicrotic notch pressure (ESAP), i.e., aortic end-systolic pressure, was defined as the trough of the incisura (dicrotic notch). We measured systolic aortic pressure (SAP), initial diastolic aortic pressure (DAP), end-diastolic aortic pressure (EDAP), and pulse aortic pressure (PAP = SAP – DAP). MAP and PAP reflect the steady and pulsed components of aortic pressure, respectively (21). We also calculated two previously proposed estimates of ESAP, namely, 0.9 SAP and 2/3 SAP + 1/3 DAP (12). Total vascular resistance (R; mmHg·ms·ml⁻¹) was calculated according to the following formula

\[ R = \frac{\text{MAP} \cdot T}{\text{SV}} \]  

(1)

Effective Ea

Theoretical background. In the Ea model, the proximal aorta is considered as an elastic chamber, the effective volume elastance Ea (mmHg/ml) of which is the slope of the relationship between ESAP and SV. This model has markedly improved the evaluation of the systemic circulation for two reasons. First, in humans, Ea provides a reasonable characterization of arterial load in the time domain (12). Second, the LV can also be considered as an elastic chamber, the end-systolic elastance (Ees; i.e., the slope of the LV end-systolic pressure-volume relationship) of which is of similar dimension to Ea (24). The operating point of the coupled equilibrium between LV and the arterial system is located at the intersection of LV end-systolic pressure-volume and ESAP-SV relationships in the pressure-volume plane (24–26). Coordinated changes in the Ees-to-Ea ratio, stroke work, and mechanical efficiency have been reported (1, 11, 25, 26).

The concept of Ea is based on the Windkessel model of arterial circulation (25). Theoretical Ea values are obtained by means of a mathematical formula taking into account the intrinsic properties of circulation, namely, total peripheral resistance (R), total arterial compliance (C), and systolic and diastolic time intervals. Because the mathematical model fits with experimental (25) and clinical (12) data, Ea is currently obtained by calculating the steady-state ratio of ESAP to SV (4, 11, 12). The hemodynamic correlates of Ea have been documented in experimental studies and in studies performed on normotensive and hypertensive subjects without valve disease. In this population, Ea depends mainly on both R and heart period (i.e., T) (12, 25, 26), in such a way that R/T is a reasonable approximation of Ea (12). Although experimen-

<table>
<thead>
<tr>
<th>Subject No.</th>
<th>Age, yr</th>
<th>Gender</th>
<th>Body Surface Area, m²</th>
<th>NYHA</th>
<th>Therapy</th>
<th>MVA, cm²</th>
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<td>32</td>
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</tr>
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<td>AC</td>
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<td>II</td>
<td>F-A-AC-N</td>
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</tr>
<tr>
<td>5</td>
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<tr>
<td>6</td>
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<td>7</td>
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<td>8</td>
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<td>II</td>
<td>AC-FL</td>
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<tr>
<td>9</td>
<td>31</td>
<td>F</td>
<td>1.82</td>
<td>II</td>
<td>F</td>
<td>1.0</td>
</tr>
<tr>
<td>10</td>
<td>68</td>
<td>F</td>
<td>1.82</td>
<td>II</td>
<td>A-D-AC</td>
<td>1.0</td>
</tr>
</tbody>
</table>

Mean ± SD 40 ± 12 1.78 ± 0.29 0.92 ± 0.11 1.97 ± 0.26

M, male; F, female; NYHA, New York Heart Association classification; MVA, mitral valve area; Before, before mitral valvotomy; After, after mitral valvotomy; F, furosemide; D, digitalis; AC, anticoagulant therapy; A, amiodarone; FL, flecainide; N, nitrates. *P < 0.01.
statistical studies have shown that $E_a$ is poorly influenced by $C$ (25, 26), recent studies have demonstrated a relationship between $E_a$ and the extent of pressure wave reflection from periphery to the heart (4, 23).

Calculation of $E_a$. $E_a$ (mmHg/ml) was calculated according to the following steady-state formula

$$E_a = ESAP/SV$$

(2)

Given that ESAP is close to MAP, Sunagawa et al. (25, 26) have suggested that Eqs. 1 and 2 yield the following approximation

$$E_a = R/T$$

(3)

Estimated total arterial $C$. $C$ (ml/mmHg) was estimated by using the area method (15), assuming a two-element Windkessel model of systemic circulation and a linear pressure-volume relationship (15). This method has been proved to give reliable estimates of $C$ (15). $C$ is given by the following formula

$$C = SV/K(ESAP - EDAP)$$

(4)

where the area coefficient ($K$) is a dimensionless coefficient given by

$$K = (systolic area + diastolic area)/diastolic area$$

(5)

Systolic and diastolic areas were defined as the area under systolic and diastolic waveform, respectively. Because the area method requires zero flow in diastole, patients with $C$ were excluded from the study.

Wave reflection and augmentation index. The human aortic pressure waveform exhibits an inflection point ($P_i$), indicating the end of the forward (or incident) wave and resulting from peak flow input into the vasculature previous to the effects of wave reflection (20, 21). The relative increase in the height of the mid-to-late systolic peak pressure above the Pi shoulder ($\Delta P$) is because of arterial wave reflection and the early return of pressure waveform from the lower body (13, 16, 20). The backward or reflected wave cumulates with the incident wave, resulting in a mid-to-late increase in SAP. The ratio of $\Delta P$ to PAP defines a so-called "augmentation index" ($\Delta P/PAP$). The time from the foot of the pressure wave to $P_i$ ($\Delta t_P$) is thought to represent the travel time of the pulse wave to peripheral reflecting sites and its return. According toMurgo et al. (20), $\Delta t_P$ is a reasonable estimate of 1/2 $f_{mn}$, where $f_{mn}$ corresponds to the frequency of the minimum impedance spectra modulus. In three patients, Pi could not be clearly individualized. Thus the values of $P_i$, $\Delta P$, $\Delta P/PAP$, and $\Delta t_P$ were recorded and averaged out over 10 consecutive cycles in 7 of 10 patients only.

Statistical Analysis

Data are expressed as means ± SD. Data were averaged out over 10 consecutive beats. Linear regression was obtained by using the least squares method. Comparisons between $E_a$ and $R/T$ were performed by using the Mann-Whitney U-test; we also calculated the 95% confidence intervals (CI) for the difference (2). The same was performed for comparisons between ESAP and each of three estimates of ESAP, namely, MAP, 0.9 SAP, and 2/3 SAP + 1/3 DAP. A $P < 0.05$ was considered statistically significant.

RESULTS

Hemodynamic data before and after BMV are listed in Tables 2 and 3 and in Fig. 1.

Table 2. Hemodynamic data before and after BMV

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Before BMV</th>
<th>After BMV</th>
<th>$P$ Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pulse interval, ms</td>
<td>843 ± 107</td>
<td>809 ± 149</td>
<td>0.41</td>
</tr>
<tr>
<td>Stroke volume, ml</td>
<td>67 ± 23</td>
<td>62 ± 20</td>
<td>0.17</td>
</tr>
<tr>
<td>Ejection fraction, %</td>
<td>55 ± 11</td>
<td>56 ± 13</td>
<td>0.62</td>
</tr>
<tr>
<td>Mean aortic pressure, mmHg</td>
<td>24.7 ± 7</td>
<td>22.4 ± 5</td>
<td>0.22</td>
</tr>
<tr>
<td>Total vascular resistance, mmHg·ml⁻¹</td>
<td>1.167 ± 0.35</td>
<td>1.343 ± 0.41</td>
<td>0.062</td>
</tr>
<tr>
<td>Mitral valve area, cm²</td>
<td>0.92 ± 0.11</td>
<td>1.98 ± 0.26</td>
<td>0.0001</td>
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<td>Mitral valve gradient, mmHg</td>
<td>10.2 ± 4.4</td>
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<td>Mean pulmonary artery pressure, mmHg</td>
<td>24.7 ± 7</td>
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<td>End-systolic aortic pressure, mmHg</td>
<td>93.6 ± 24.4</td>
<td>103.7 ± 24.9</td>
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<tr>
<td>Effective arterial elastance, mmHg·ml⁻¹</td>
<td>1.55 ± 0.63</td>
<td>1.83 ± 0.71</td>
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<td>$R/T$, mmHg/ml</td>
<td>1.43 ± 0.57</td>
<td>1.70 ± 0.61</td>
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<td>Estimated total arterial compliance, mmHg/ml</td>
<td>1.83 ± 0.98</td>
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Values are means ± SD; $n = 10$ subjects. BMV, balloon mitral valvotomy; $R$, total vascular resistance; $T$, pulse interval.

Hemodynamic Correlates of $E_a$ in MS Patients at Baseline

$E_a$ was 1.55 ± 0.63 mmHg/ml. There was no relationship between $E_a$ and age, MAP, ESAP, or mitral valve area. There was a negative linear relationship between $E_a$ and $T$ ($r = -0.72$, $P < 0.01$). $E_a$ was closely related to the following steady-state formula

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(4)

where the area coefficient ($K$) is a dimensionless coefficient given by

$$K = (systolic area + diastolic area)/diastolic area$$

(5)
Fig. 2. A: Ea as a function of total vascular resistance (R)-to-pulse interval duration (T) ratio (R/T) at baseline (n = 10). Ea was positively related (r = 0.99, P = 0.0001) to R/T in accordance with following equation: Ea = 1.09 R/T - 0.01 (mmHg/ml). B: R/T as an estimate of Ea at baseline. Solid line, mean difference (i.e., R/T - Ea); dashed lines, ±2 SD; dotted line, zero axis. There was a positive linear relationship (r = 0.64, P = 0.046) between difference and Ea: R/T - Ea = -0.09 Ea + 0.03.

Ea was related to R (r = 0.96, P = 0.0001). There was a strong linear relationship between Ea and R/T (Ea = 1.09 R/T - 0.01 mmHg/ml, r = 0.99, P = 0.0001) (Fig. 2). R/T slightly but significantly underestimated Ea (Table 2, Fig. 2), especially at high Ea values. There was also a negative linear relationship between Ea and C (r = -0.85, P < 0.01). After the influence of SV was taken into account, Ea and C were still significantly related [partial correlation coefficient (r') = -0.66, P < 0.05]. There was no relationship between Ea and ΔP/PAP (r = 0.61, P = 0.15).

Hemodynamic Correlates of Ea After BMV

Ea was positively related to R (r = 0.94, P = 0.0001) but not to heart period (r = -0.30). There was a strong linear relationship between Ea and R/T (Fig. 3), and R/T underestimated Ea (Table 2, Fig. 3). There was a negative linear relationship between Ea and C (r = -0.85, P < 0.01). After the influence of SV was taken into account, Ea and C were no longer related (r' = -0.56, P = NS). Increases in Ea were not related to changes in mitral valve area as induced by BMV (r = -0.42, P = NS). There was a positive relationship between Ea and ΔP/PAP (r = 0.82, P = 0.025).

Evaluation of MAP as an Estimate of ESAP

There was a powerful linear relationship between ESAP and MAP both before and after BMV in patients either in sinus rhythm or in atrial fibrillation (Fig. 4). When MAP was taken as an estimate of ESAP, MAP underestimated ESAP (P < 0.001) (Fig. 4). There was a negative linear relationship between the MAP-ESAP difference and ESAP, such that the higher the ESAP, the more negative the difference. Table 4 indicates the accuracy of the two empirical formulas (ESAP = 2/3 SAP + 1/3 DAP; and ESAP = 0.9 SAP), both of which significantly overestimated ESAP.
Table 4. Accuracy of the two empirical formulas previously proposed in estimation of end-systolic aortic pressure

<table>
<thead>
<tr>
<th>(2/3 SAP + 1/3 DAP) – ESAP</th>
<th>0.9 SAP – ESAP</th>
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</thead>
<tbody>
<tr>
<td>Before</td>
<td>After</td>
</tr>
<tr>
<td>Mean error, mmHg</td>
<td>2.7</td>
</tr>
<tr>
<td>SD</td>
<td>2.6</td>
</tr>
<tr>
<td>95% CI, mmHg</td>
<td>-2.5/+7.9</td>
</tr>
<tr>
<td>r</td>
<td>0.994</td>
</tr>
<tr>
<td>P</td>
<td>0.0001</td>
</tr>
</tbody>
</table>

Values are means ± SD; n = 10 subjects. DAP, diastolic aortic pressure; ESAP, end-systolic aortic pressure; CI, confidence interval. Mean error, standard deviation, and CI of estimation of ESAP by each formula are calculated over 100 beats (i.e., 10 consecutive beats in each patient) at basal state before BMV, 100 beats 15 minutes after BMV, and 200 beats before and after BMV. P and r are calculated by using a linear regression between ESAP and each formula.
The increase in $E_a$ was not related to the increase in mitral valve area as induced by BMV. Because BMV did not modify SV, the increase in $E_a$ was mainly explained by the significant increase in both ESAP and MAP in all patients. In two previous studies (6, 29), MAP was not significantly modified by BMV, but it must be noted that patients were premedicated with atenolol in the study of Wisenbaugh et al. (29), and this may have minimized reflex changes in aortic pressure.

Although the $E_a$ concept is based on the Windkessel model, which also takes $C$ into account, experimental studies have shown that $E_a$ is poorly influenced by $C$ (25, 26). In our MS patients studied at baseline, there was a negative linear relationship between $E_a$ and $C$ both before and after BMV. After the effects of SV were taken into account, this relationship was no longer observed after BMV. Furthermore, the increase in $E_a$ induced by BMV and the decrease in $C$ were not related.

A positive relationship between $E_a$ and $\Delta P/PAP$ has been previously reported in normotensive and hypertensive patients (23), a finding also observed in our MS patients after but not before BMV.

### Effects of BMV on C and Wave Reflections

Estimated $C$ significantly decreased after BMV. Even though MAP significantly increased, relative changes in $C$ were not related to relative increases in MAP. The decrease in $C$ was not related to the increase in mitral valve area induced by BMV. After BMV, $PAP$ significantly increased, and this was consistent with the observed decrease in $C$ (21). The values of $PAP$, $Pi$, $SAP – Pi$, and $(SAP – Pi)/PAP$ significantly increased, thus attesting to enhanced wave reflection, whereas the decreased $Pi$ suggested anticipated timing of wave reflection. A similar hemodynamic pattern has been attributed to decreased $C$ in aged and hypertensive subjects (12, 16, 20, 21). Thus increased and anticipated wave reflection are probably explained by decreased $C$.

### Clinical Implications: End-Systolic Pressure

**Estimated From Peripheral Arterial Pressure Recordings in MS Patients**

Systolic arterial pressure increases from aorta to periphery, according to the so-called “pulse wave amplification” phenomenon. The magnitude of the pulse wave amplification phenomenon varies markedly from one individual to another, depending on body size, sex, age, arterial pressure, and arterial compliance (13, 16, 20). Thus the two formulas previously proposed (12) as estimates of ESAP, namely, $0.9 SAP$ and $2/3 SAP + 1/3 DAP$, are more relevant to central pressure recordings than to noninvasive peripheral pressure recordings. Furthermore, these formulas significantly overestimated ESAP in MS patients (Table 4).

Effective $E_a$ has also been estimated indirectly after having replaced end-systolic pressure by 1) intrabronchial dicrotic notch pressure recorded invasively (1); 2) carotid dicrotic notch pressure measured by using external tonometry (23); and 3) cuff-determined systolic blood pressure (10). The cannulation of the brachial artery is an invasive procedure and therefore not routinely repeatable. The external tonometry technique is not available in all research laboratories, and the accuracy of carotid dicrotic notch pressure as an estimate of central end-systolic pressure, although probable, remains to be validated (23).

Numerous studies and physiological textbooks have reported that one key property of systemic circulation is that mean arterial pressure remains almost constant along the arterial tree, the drop in mean pressure between the ascending aorta and a large peripheral artery being $< 3$ mmHg (21). We have found a powerful relationship between ESAP and MAP in MS patients, as also recently observed in children (22) and in adults without valve diseases (8). Thus, in patients with MS at baseline, one implication of our study is that ESAP could be reasonably estimated by using cuff-determined mean arterial pressure, rather than systolic arterial pressure, according to the following formula: $ESAP = 1.09$ mean peripheral arterial pressure. Further studies are needed to confirm this.

### Limitations of the Study

The limitations of our study need to be discussed. First, given our invasive study design, clinical implications are limited by its short-term aspect. We judged it unethical to perform a left-sided catheterization in MS patients 1 mo after BMV, such that the long-term effects of valvotomy on $E_a$ were not documented in our study. Further studies are needed to document the chronic effects of BMV on $E_a$. Second, we studied a limited sample size of MS patients. Despite this, we found an unusually powerful relationship both between $E_a$ and $R/T$, and between ESAP and MAP, and this tends to strengthen the relevance of our results.

### Conclusions

$E_a$ depends mainly on $R$ and $T$ in patients with MS studied at baseline or after BMV. The powerful relationship between $E_a$ and $R/T$ observed in our study extends to MS patients the primary results of Sunagawa et al. (25, 26) and Kelly et al. (12). The $E_a$ vs. $R/T$ relationship ultimately depends on the powerful link between MAP and ESAP in MS patients. Given that mean arterial pressure remains constant along the arterial tree, this result may have clinical implications for the noninvasive assessment of $E_a$ in populations similar to ours. Last, in patients with MS, and for a given $T$, our study indicates that $E_a$ depends mainly on the steady rather than the pulsatile component of arterial load ($R$), whether before or after BMV.

The authors thank John Kenneth Hylton for helpful discussions. Address for reprint requests: P. Colin, Service de Cardiologie, 157 rue de la porte de Trivaux, Hôpital Antoine-Béclère, 92141 Clamart, France (E-mail: chemla@enstay.ensta.fr).

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