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Relation of effective arterial elastance to arterial system properties

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SEGERS, Patrick, Nikos Stergiopulos, and Nico Westerhof. Relation of effective arterial elastance to arterial system properties. Am J Physiol Heart Circ Physiol 282: H1041–H1046, 2002. First published November 23, 2001; 10.1152/ajpheart.00764.2001.—Effective arterial elastance (Ea), defined as the ratio of left ventricular (LV) end-systolic pressure and stroke volume, lumps the steady and pulsatile components of the arterial load in a concise way. Combined with Emax, the slope of the LV end-systolic pressure-volume relation, Ea/Emax has been used to assess heart-arterial coupling. A mathematical heart-arterial interaction model was used to study the effects of changes in peripheral resistance (R; 0.6–1.8 mmHg·ml⁻¹·s⁻¹) and total arterial compliance (C; 0.5–2.0 ml/mmHg) covering the human pathophysiological range. Ea, Ea/Emax, LV stroke work, and hydraulic power were calculated for all conditions. Multiple-linear regression analysis revealed a linear relation between Ea, R/T (where T is cycle length), and 1/C: Ea = −0.13 + 1.02R/T + 0.31/C, indicating that R/T contributes about three times more to Ea than arterial stiffness (1/C). It is demonstrated that different pathophysiological combinations of R and C may lead to the same Ea and Ea/Emax but can result in differences of 10% in stroke work and 50% in maximal power.

Effective arterial elastance (Ea), commonly known as the ratio of left ventricular (LV) end-systolic pressure and stroke volume (SV) (31, 32), is a simple and convenient way to characterize the arterial load from knowledge of total peripheral resistance (R), total arterial compliance (C), aortic characteristic impedance (Zo), and systolic and diastolic time intervals, parameters that can be derived from pressure and flow measured in the ascending aorta. Ea thus incorporates both steady (R) and pulsatile (C, Zo) components of the arterial load. It was later shown by Kelly and coworkers (15) that there is a good agreement between Ea calculated from pressure-volume data and Ea calculated from arterial impedance, Eoa(Zo), in normal and hypertensive human subjects. Provided that 1) end-systolic pressure can be approximated by mean arterial pressure, and 2) the time constant of the arterial system, RC, is large compared with the diastolic time interval, Ea further reduces to R/T, where T is the cardiac cycle length (15, 32).

Ea is, however, a parameter originating from studies considering mechanicoenergetic aspects of heart-arterial interaction (15, 31, 32), where it has been combined with Emax (i.e., the slope of the LV end-systolic pressure-volume relation; Ref. 30) to be used as the heart-arterial coupling parameter Ea/Emax (1, 2, 4, 6, 14, 19, 20, 22, 27, 31, 32). Analytical work based on the assumption Ea ≈ R/T revealed that the heart delivers maximal stroke work (SW) when Ea/Emax = 1 (4, 32), whereas optimal efficiency (ratio of SW to myocardial oxygen consumption) is obtained when Ea/Emax = 0.5 (4). This theoretical relation has been confirmed in experimental work (4, 9, 31, 32), although it has also been observed that SW remains near maximal within a relatively wide range of Ea/Emax values (9).

Ea is increasingly being used as a means to quantify the properties of the arterial system (6–8, 10, 15, 20, 21). Although Ea incorporates steady and pulsatile features of arterial impedance, it is important to realize that it is not a surrogate of impedance (31), which can only be calculated from the ratio of measured aortic pressure and flow and which is expressed in terms of complex harmonics in the frequency domain (17, 18). Ea lumps the steady and pulsatile components of the arterial load into a single number, but it does not provide any information on their relative contribution. Additional information (e.g., R) is required for an unequivocal characterization of the arterial system. Furthermore, by itself, Ea is not—despite its dimensional units—a measure of arterial stiffness, because R and heart rate (HR) also contribute to Ea.

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The aim of this study was twofold. First, we wanted to illustrate that $E_a$, by itself, contains insufficient information to fully capture the arterial system. Second, we wanted to illustrate how the finite arterial compliance interferes with the theoretical relationship between $E_a/E_{\text{max}}$ and LV SW generation. Using a previously validated heart-arterial interaction model (23, 24, 28), we calculated LV pressure-volume loops, aortic pressure and flow, and $E_a$ for a set of chosen and fixed cardiac parameters but with values for arterial resistance and compliance covering the human pathophysiological range. This allowed us to demonstrate 1) the relation between $R$ and $C$ with $E_a$; 2) the nonspecific character of $E_a$ and the impact on calculated arterial pressure and flow; 3) the relation between $E_a$, $E_0(Z)$, and $R/T$; and 4) the impact on $E_a/E_{\text{max}}$ as a determinant of LV SW and hydraulic power generation.

**MATERIALS AND METHODS**

The heart-arterial interaction model. Aortic blood pressure is computed using a previously validated heart-arterial interaction model (Refs. 23, 24, 28; Fig. 1). LV function is described by a time-varying elastance model (30) and is coupled to a four-element lumped-parameter windkessel model representing the systemic arterial load (29). The arterial model parameters are $R$, $C$, total inerance ($L$), and $Z_0$. Time-varying elastance is calculated as $E(t) = P_{LV}/(V_{LV} - V_d)$, where $P_{LV}$ and $V_{LV}$ are LV pressure and volume, respectively, and $V_d$ is the intercept of the end-systolic pressure-volume relation. It has been shown that the shape of the normalized $E(t)$ curve [$E_N(t)$], obtained after normalization of $E(t)$ with respect to amplitude and time, remains constant under various pathophysiological conditions (25). $E_N(t)$ is thus assumed to be constant and has been implemented in the model (23, 24). The actual $E(t)$ is then characterized by a limited number of cardiac parameters: the slope ($E_{\text{max}}$) and intercept ($E_0$) of the end-systolic pressure-volume relation, LV end-diastolic volume (LVEDV), venous filling pressure ($P_v$), HR, and the time to reach maximal elastance ($t_F$). Cardiac valves are simulated as frictionless, perfectly closing devices, allowing forward flow only.

Relation between arterial parameters $R$ and $C$ and $E_a$. As an illustration of our results, Fig. 2 shows P-V loops and aortic pressure and flow calculated for three different combinations of $R$ and $C$, each yielding the same $E_a$ of 1.7 mmHg/ml (R = 1.08, 1.2, and 1.32 mmHg·ml⁻¹·s, and corresponding $C = 0.8, 1.1$, and 2 ml/mmHg, respectively). For all 121 simulations, $E_a$ is plotted as a function of $R$ and $1/C$ in Fig. 3. For a given

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Fig. 1. In the heart-arterial interaction model (A), the heart function is modeled as a time-varying elastance function $E(t)$ (B). The arterial model is a lumped-parameter model consisting of total compliance ($C$), total peripheral resistance ($R$), characteristic impedance of the aorta ($Z_0$), and the inertia of blood in the systemic arteries ($L$). The model directly yields left ventricular (LV) pressure and volume and aortic pressure and flow ($C$). $R_{mv}$, mitral valve resistance, which was assumed 0 for these simulations.
compliance value, $E_a$ practically linearly increases with resistance. Although the relation of $E_a$ with compliance is nonlinear, it linearizes when $E_a$ is expressed as a function of $1/C$. The relations $E_a(R)$ or $E_a(1/C)$ shift with C and $R$, but their slopes are independent of C and $R$ and are 1.28 s$^{-1}$ and 0.31, respectively. Multiple-linear regression analysis with $E_a$ as independent and $R/T$ (with, in this case, constant $T = 0.8$ s) and $1/C$ as dependent variables yields $E_a = -0.127 + 1.023R/T + 0.314/C$ ($r^2 = 0.99$). For a given resistance, $E_a$ tends toward an asymptotic value ($R/T$) for high values of C (low values of $1/C$). It may be seen that several possible combinations of $R$ and $C$ yield the same $E_a$.

Linear regression analysis yields the following relation between $E_a(Z)$ and $E_a(P_{es}/SV)$: $E_a(Z) = 1.0E_a + 0.12$ ($r^2 = 0.99$). The difference between these is shown in Fig. 4. $E_a(Z)$ is somewhat higher than $P_{es}/SV$, with the mean difference (calculated from the 121 model simulations) being 0.113 ± 0.037 mmHg/ml. As can be expected from the multiple-linear regression analysis, $R/T$ is always lower than $P_{es}/SV$. The difference between these becomes higher with decreasing C (Fig. 4).

$E_a/E_{max}$ as determinant of LV mechanical energetics. SW and $W_{max}$ are given as a function of $E_a/E_{max}$ for constant compliance values (Fig. 5). For $C = 2$ ml/mmHg, SW is maximal when $E_a/E_{max}$ equals 1. For all other values, the relation is less clear, but maximal SW is reduced and the maximum is found for $E_a/E_{max}$ between 0.6 and 1.1. For a given $E_a/E_{max}$, maximal power increases with C. For a given C, $W_{max}$ first decays with $E_a/E_{max}$, reaches a minimum, and then increases with $E_a/E_{max}$. The value of $E_a/E_{max}$ corresponding to this minimum is a function of C.

DISCUSSION

Our results demonstrate that for a given condition of the heart (HR, contractility, and end-diastolic volume), $E_a$ is linearly related to $R$ and to $1/C$. There is an excellent correlation and good agreement between $R/T$, cardiac cycle length.

Fig. 2. LV pressure-volume loops (A), aortic pressure (B), and aortic flow (C) for 3 combinations of $R$ and $C$, each giving effective arterial elastance ($E_a$) = 1.7 mmHg/ml ($E_a/E_{max} = 1$, where $E_{max}$ is slope of LV end-systolic pressure-volume relation). $V_a$, intercept of end-systolic pressure-volume relation.

Fig. 3. The heart-arterial model was loaded with values for $R$ (0.6–1.8 mmHg·ml$^{-1}·s$) and C (0.5–2 ml/mmHg) covering the human pathophysiological range. $E_a$ was then calculated as the ratio of LV end-systolic pressure and stroke volume (SV). A: data are organized to show the variation of $E_a$ with $R$ for fixed values of C. B: the variation of $E_a$ with $1/C$ for fixed values of $R$. C: the quasi-perfect agreement (solid line) between $E_a$ calculated as the ratio of end-systolic pressure and SV and $E_a$ predicted from $R$ and $1/C$ with the multiple-linear regression equation. $T$, cardiac cycle length.
$E_a(Z)$ calculated from vascular system properties and $E_a$ calculated as $P_{es}/SV$. The sensitivity of $E_a$ to $1/C$ is three times lower than to $R/T$. For large compliance values (>2 ml/mmHg), $E_a$ approximates $R/T$. $E_a$, by itself, cannot be used to quantify the arterial system, because there are different combinations of $R$ and $C$, yielding the same $E_a$ but representing totally different arterial loads. This limitation becomes obvious when SW is plotted as a function of $E_a/E_{max}$. For large $C$ values, we find the theoretical relation with maximal SW at $E_a/E_{max} = 1$. For $C$ values within the normal pathophysiological range, however, maximal SW is reduced, and this maximal SW value occurs within a wider range of $E_a/E_{max}$ values.

We varied $R$ and $C$ over what we consider the pathophysiological range in the adult human. There is, however, a large variability in reported values for $R$ and $C$, both in control and pathological conditions, because of different flow measuring techniques and different methods to estimate $C$. Aortic pulse wave velocity, independent of flow measuring techniques, can change by a factor of 2 in aging and in hypertension (3). $C$ is proportional to the square of pulse wave velocity (17) and may thus change by a factor of 4. We varied $C$ from 0.5 to 2 ml/mmHg, thereby covering the reported range of values in normal and pathological conditions in humans (5, 13, 16, 26). Changes in $R$ were between 0.6 and 1.8 mmHg·ml$^{-1}$·s$^{-1}$ (12, 13, 26).

Because $E_a$ depends both on $R$ and $C$, it is clear that it cannot represent a unique arterial load. The question is whether different combinations of $R$ and $C$, giving the same $E_a$, actually occur in humans, because in aging and in hypertension both $R$ and arterial stiffness tend to increase. However, the data in the literature show that, within healthy or pathological populations, there is considerable biological diversity in both $R$ and $C$ (3, 5, 12, 13, 16, 20, 26). Figure 2 also illustrates that despite identical $E_a$, markedly different pressure and flow wave profiles are found, each with physiological values for blood pressure and SV. These simulations thus show that it is reasonable to assume that combinations of $R$ and $C$ presenting the same $E_a$ actually occur. Figure 2 also shows that $E_a$ is not necessarily related to indexes characterizing the arterial wave shape or wave reflection such as the augmentation index. This may explain why in a recent study, despite different values for $E_a$, the augmentation index was similar in two groups of hypertensive patients (20).

The agreement between $E_a(Z)$ and $P_{es}/SV$ was previously demonstrated in humans (15). Our computer simulation data confirm the excellent correlation be-
between $E_a(Z)$ and $P_{\text{es}}/SV$, but $E_a(Z)$ is, on average, 0.13 mmHg/ml higher than $P_{\text{es}}/SV$ (although Kelly et al. (15) found a small underestimation of $E_a(Z)$ compared with $P_{\text{es}}/SV$). We believe the discrepancy is because we calculated $E_a(Z)$ by using the parameters of the four-element windkessel model that was used as arterial load, whereas the expression for $E_a(Z)$ is based on a three-element windkessel model. It is known that the latter characterizes the impedance spectrum with higher values for C and lower values for $Z_0$ than the four-element windkessel model (29). Our multiple-linear regression analysis results indicate that the relation between $P_{\text{es}}/SV$ and arterial system properties can be further simplified as a linear relation with $R/T$ and $1/C$. However, this relation requires further validation in vivo, where, besides arterial system properties, HR, $t_s$ and $t_d$ also vary.

It has been shown theoretically that, for a given preload (LVEDV) and inotropic state ($E_{\text{max}}$ and $V_a$) of the heart, SW is determined only by $E_a/E_{\text{max}}$ and SW is maximal when $E_a/E_{\text{max}} = 1$ (4). This relation was derived under the assumptions that $E_a \approx R/T$ and that SW can be approximated by the product of SV and $P_{\text{es}}$. In experimental studies, the $E_a/E_{\text{max}}$ value corresponding to maximal SW has been reported to be $<1$, with SW remaining close to maximal (>$90\%$ of optimal value) for a wide range of $E_a/E_{\text{max}}$ values (0.3–1.3) (9). We found that a single value of $E_a$ may correspond to different values for $E_a/E_{\text{max}}$ and $W$ (Fig. 4). $E_a/E_{\text{max}}$ corresponding to maximal SW as well as the range over which SW remains maximal change with C. For large C values ($C = 2$ ml/mmHg), the relation between $E_a/E_{\text{max}}$ and SW approximates the theoretical prediction, with SW being maximal for $E_a/E_{\text{max}} = 1$. For lower C values, maximal SW is reduced and is reached for $E_a/E_{\text{max}} < 1$ and maximal SW can be achieved for a wider $E_a/E_{\text{max}}$ range. We also plotted the relation between $E_a/E_{\text{max}}$ and $W_{\text{max}}$, a parameter frequently used to characterize cardiac performance. Again, a single value for $E_a/E_{\text{max}}$ corresponds to very distinct values of $W_{\text{max}}$. Because $E_{\text{max}}$ was constant for all simulations, this further demonstrates that $E_a$ is not an unequivocal measure for arterial load and, therefore, $E_a/E_{\text{max}}$ is not a specific measure for heart-artrial interaction.

The use of $E_a$ and $E_a/E_{\text{max}}$ has been promoted by theoretical and experimental studies linking $E_a/E_{\text{max}}$ to LV mechanicoenergetics (1, 2, 4, 6, 14, 22, 27, 32). It has been shown in humans that $E_a/E_{\text{max}}$ is $\approx 1$ in the normal heart and that the LV operates close to optimal efficiency or SW (2, 6). This optimal energetic coupling of the heart and arterial system seems to be preserved in normal aging (6, 8) and in hypertension (7). In contrast, in heart failure, cardiac contractility ($E_{\text{max}}$) is impaired, whereas $E_a$ generally increases and $E_a/E_{\text{max}}$ increases progressively (14, 22). Note, however, that $E_a/E_{\text{max}}$ is mainly a parameter related to LV volumes. With $E_a = P_{\text{es}}/SV$ and $E_{\text{max}} = P_{\text{es}}/(\text{LVEDV} − SV − V_a)$ and assuming $V_a$ to be small enough that it can be neglected, $E_a/E_{\text{max}} = \text{LVEDV} − SV − 1$ or $E_a/E_{\text{max}} = 1/EF − 1$, where EF is ejection fraction. In normal hearts, where EF is $\approx 0.5$, $E_a/E_{\text{max}}$ is indeed 1. In failing, dilated hearts, EF decreases and $E_a/E_{\text{max}}$ thus increases. Why LVEF is $\approx 0.5$ in the normal heart can be argued on mechanical-energetic grounds, but it has also been shown that this value is explicable on basis of evolutionary arguments (11). Also, the human body has no sensors or receptors sensitive to SW or power output. It is therefore unlikely that there are control mechanisms maintaining constant $E_{\text{max}}$ to operate at maximal power or maximal efficiency.

In conclusion, we have shown that $E_a$ is related to $R/T$ and arterial elastance, i.e., $1/C$, in a linear way, but the sensitivity of $E_a$ to a change in $R/T$ is about three times higher than to a similar change in arterial stiffness. $E_a$ is a convenient parameter, lumping pulsatile and steady components of the arterial load in a concise way, but it does not unequivocally characterize arterial system properties. The nonspecific character of $E_a$ and the fact that $E_a$ can be approximated as $R/T$ only for high C values contribute to the discrepancy between the observed and theoretical relationship between $E_a/E_{\text{max}}$ and SW.

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