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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 (E_a), 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 E_{max}, the slope of the LV end-systolic pressure-volume relation, E_a/E_{max} 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) and total arterial compliance (C; 0.5–2.0 ml/mmHg) covering the human pathophysiological range. E_a, E_a/E_{max}, LV stroke work, and hydraulic power were calculated for all conditions. Multiple-linear regression analysis revealed a linear relation between E_a, R/T (where T is cycle length), and 1/C: $E_a = -0.13 + 1.02R/T + 0.31/C$, indicating that R/T contributes about three times more to E_a than arterial stiffness (1/C). It is demonstrated that different pathophysiological combinations of R and C may lead to the same E_a and E_a/E_{max} but can result in differences of 10% in stroke work and 50% in maximal power.

arteries; heart-arterial coupling; arterial compliance; total peripheral resistance; stroke work; maximal power

EFFECTIVE ARTERIAL ELASTANCE (E_a), 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 pressure-volume data measured in the LV. As outlined by Sunagawa et al. (32), E_a can also be approximated from knowledge of total peripheral resistance (R), total arterial compliance (C), aortic characteristic impedance (Z_0), and systolic and diastolic time intervals, parameters that can be derived from pressure and flow measured in the ascending aorta. E_a thus incorporates both steady (R) and pulsatile (C, Z_0) components of the arterial load. It was later shown by Kelly and coworkers (15) that there is a good agreement between E_a calculated from pressure-volume data and E_a calculated from arterial impedance, $E_a(Z)$, 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, E_a further reduces to R/T, where T is the cardiac cycle length (15, 32).

E_a is, however, a parameter originating from studies considering mechanicoenergetic aspects of heart-arterial interaction (15, 31, 32), where it has been combined with E_{max} (i.e., the slope of the LV end-systolic pressure-volume relation; Ref. 30) to be used as the heart-arterial coupling parameter E_a/E_{max} (1, 2, 4, 6, 14, 19, 20, 22, 27, 31, 32). Analytical work based on the assumption $E_a \approx R/T$ revealed that the heart delivers maximal stroke work (SW) when $E_a/E_{max} = 1$ (4, 32), whereas optimal efficiency (ratio of SW to myocardial oxygen consumption) is obtained when $E_a/E_{max} = 0.5$ (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 E_a/E_{max} values (9).

E_a is increasingly being used as a means to quantify the properties of the arterial system (6–8, 10, 15, 20, 21). Although E_a 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). E_a 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, E_a is not—despite its dimensional units—a measure of arterial stiffness, because R and heart rate (HR) also contribute to E_a.

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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_{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 aortic pressure and flow; *3*) the relation between E_a, $E_a(Z)$, and R/T; and *4*) the impact on E_a/E_{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 inertance (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 [$E_N(t_N)$], obtained after normalization of $E(t)$ with respect to amplitude and time, remains constant under various pathophysiological conditions (25). $E_N(t_N)$ 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_{max}) and intercept (V_d) 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_P). Cardiac valves are simulated as frictionless, perfectly closing devices, allowing forward flow only.

Relation between arterial parameters R and C and E_a. E_{max} and V_d are taken as 1.7 mmHg/ml and −15 ml (6), respectively. LVEDV is chosen as 120 ml, and P_v is set to 5 mmHg. HR is 75 beats/min, and t_P is 0.3 s (38% of cardiac cycle length). Control values for Z_0 (18) and L (29) are 0.033 mmHg·ml^{-1}·s and 0.005 mmHg·ml^{-1}·s^2, respectively. These parameters are kept constant during the computations. R is varied from 0.6 to 1.8 mmHg·ml^{-1}·s (0.12 mmHg·ml^{-1}·s increments), and C is varied from 0.5 to 2 ml/mmHg (0.15 ml/mmHg increments) giving 11 values for each parameter covering the normal to pathophysiological range. Model simulations have been done for the 121 possible combinations of R and C. For each of these simulations, E_a is calculated from the data as the ratio of end-systolic pressure (P_{es}) and stroke volume (SV). E_a is then presented as a function of R and 1/C (total arterial stiffness).

Assuming a three-element windkessel model (33) for the arterial circulation (consisting of R, C, and Z_0), Sunagawa et al. (31, 32) showed that E_a can be calculated from arterial system properties as $E_a(Z) = (R + Z_0)/\{t_s + RC[1 - \exp(-t_d/RC)]\}$, where t_s and t_d are systolic and diastolic time intervals, respectively. In this study, t_s is calculated from the period of forward aortic flow and $t_d = 0.8 - t_s$. The relation between $E_a(Z)$ and P_{es}/SV is studied by linear regression and by plotting $E_a(Z) - P_{es}/SV$ as a function of P_{es}/SV. In addition, the difference between P_{es}/SV and R/T was calculated for the 121 simulated cases.

Linear regression analysis was done with SigmaStat 2.0 (Jandel Scientific). Multiple-regression analysis was performed with E_a as dependent and R/T and 1/C as independent variables (SigmaStat 2.0)

E_a/E_{max} as determinant of LV mechanical energetics. Hydraulic power ($\dot{W}$) is calculated as the product of instantaneous aortic pressure (P_{Ao}) and flow (Q_{Ao}), and its maximum yields maximal power ($\dot{W}_{max}$). LVSW is calculated as the area contained within each of the P-V loops for the combinations of R and C studied. SW and $\dot{W}_{max}$ are presented as a function of E_a/E_{max}.

RESULTS

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

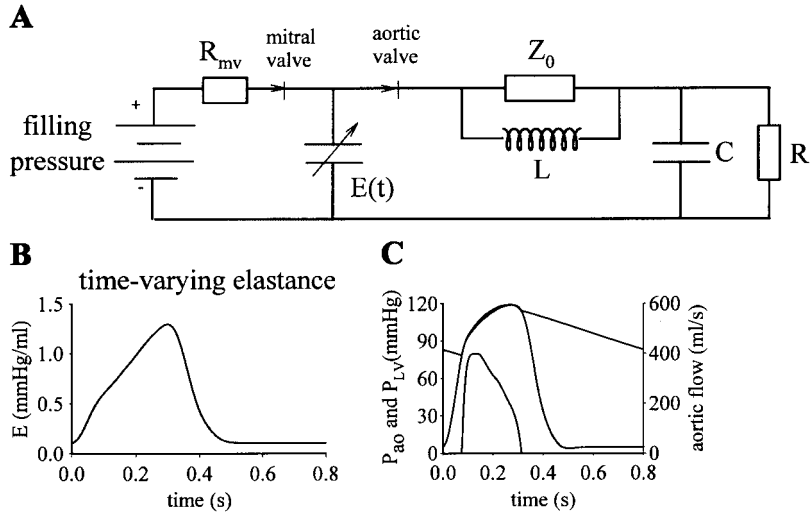

Fig. 1. In the heart-arterial interaction model (*A*), the heart function is modeled as a time-varying elastance function $E(t)$ (*B*). The arterial model is a lumped-parameter model consisting of total compliance (C), total peripheral resistance (R), characteristic impedance of the aorta (Z_0), and 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.

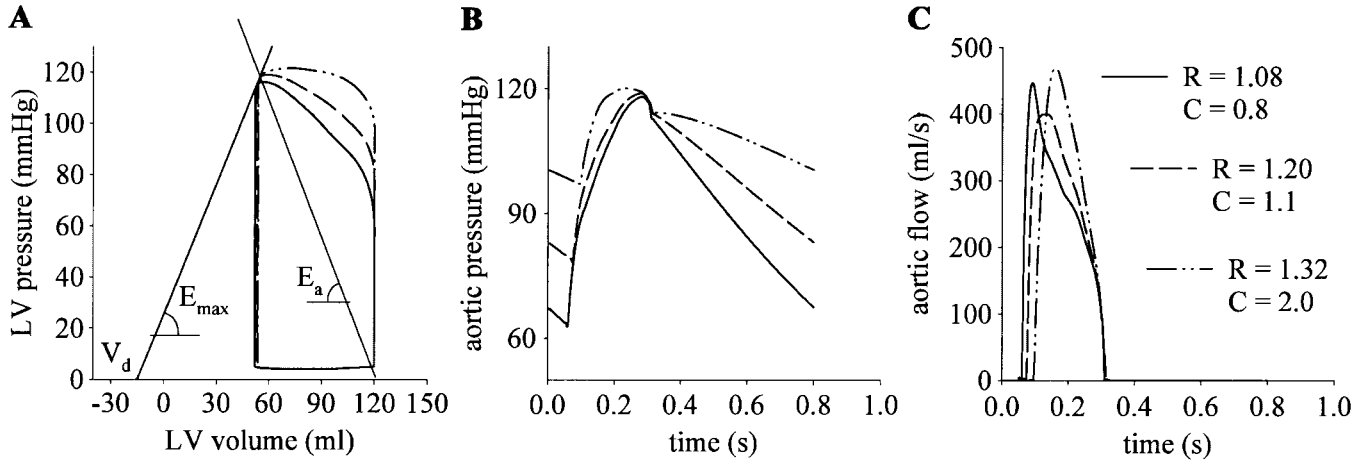

Fig. 2. LV pressure-volume loops (*A*), aortic pressure (*B*), and aortic flow (*C*) for 3 combinations of R and C, each giving effective arterial elastance (E_a) = 1.7 mmHg/ml (E_a/E_{max} = 1, where E_{max} is slope of LV end-systolic pressure-volume relation). V_d, intercept of end-systolic pressure-volume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

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

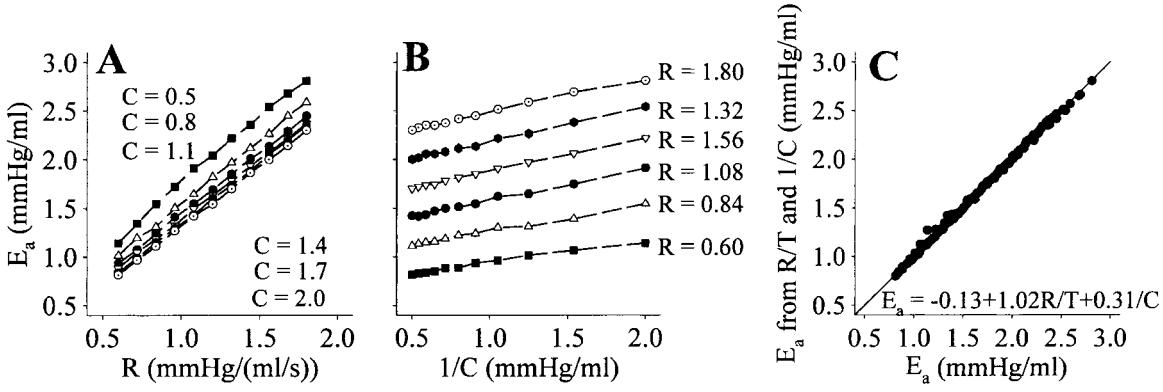

Fig. 3. The heart-arterial model was loaded with values for R (0.6–1.8 mmHg·ml^{-1}·s) and C (0.5–2 ml/mmHg) covering the human pathophysiological range. E_a was then calculated as the ratio of LV end-systolic pressure and stroke volume (SV). *A*: data are organized to show the variation of E_a with 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.

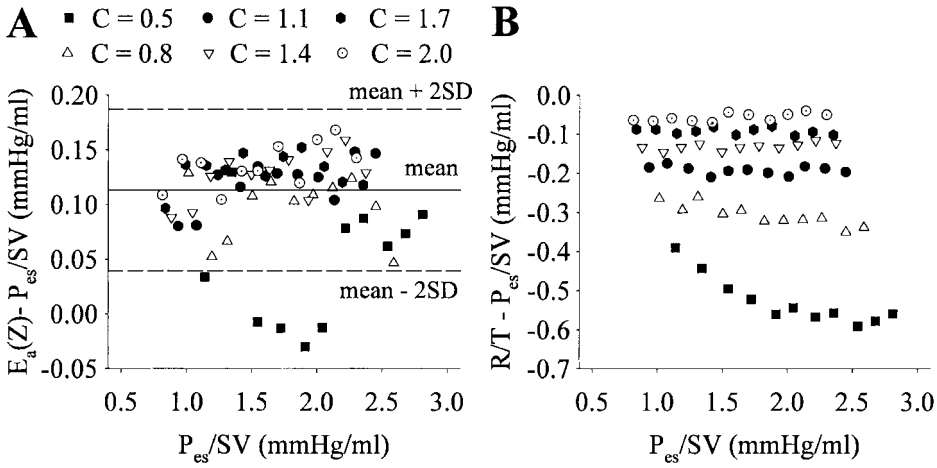

Fig. 4. *A*: the difference between $E_a(Z)$, calculated from arterial system properties, and E_a, calculated as P_{es}/SV, is given as a function of P_{es}/SV. The solid line is the mean difference; the dashed lines represent mean difference ± 2SD. *B*: the difference between E_a and R/T.

$E_a(Z)$ 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 (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-

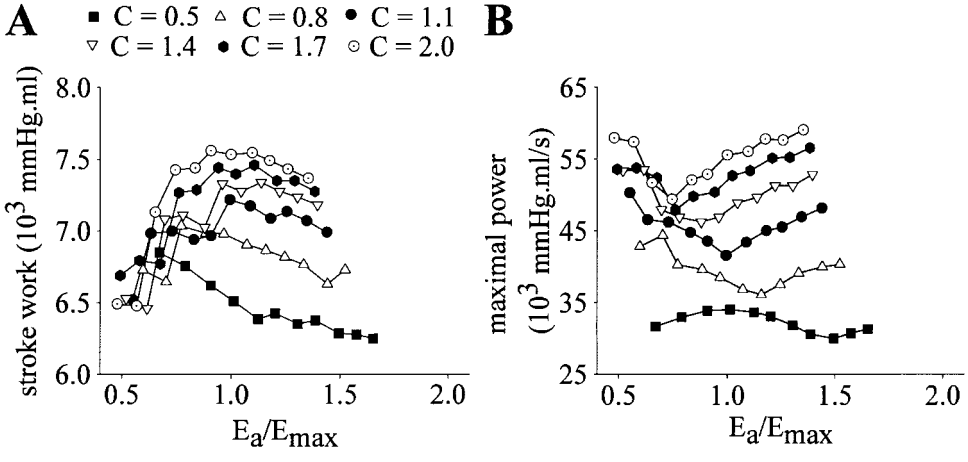

Fig. 5. Stroke work (*A*) and maximal power (*B*) as a function of E_a/E_{max}. For each curve, C is constant and R varies. For fixed E_a/E_{max}, higher C yields higher stroke work and maximal power.

tween $E_a(Z)$ and P_{es}/SV, but $E_a(Z)$ is, on average, 0.13 mmHg/ml higher than P_{es}/SV [although Kelly et al. (15) found a small underestimation of $E_a(Z)$ compared with P_{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_{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_{max} and V_d) of the heart, SW is determined only by E_a/E_{max} and SW is maximal when $E_a/E_{max} = 1$ (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_{es}. In experimental studies, the E_a/E_{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_{max} values (0.3–1.3) (9). We found that a single value of E_a may correspond to different values for SW and $\dot{W}$ (Fig. 4). E_a/E_{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_{max} and SW approximates the theoretical prediction, with SW being maximal for $E_a/E_{max} = 1$. For lower C values, maximal SW is reduced and is reached for $E_a/E_{max} < 1$ and maximal SW can be achieved for a wider E_a/E_{max} range. We also plotted the relation between E_a/E_{max} and $\dot{W}_{max}$, a parameter frequently used to characterize cardiac performance. Again, a single value for E_a/E_{max} corresponds to very distinct values of $\dot{W}_{max}$. Because E_{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_{max} is not a specific measure for heart-arterial interaction.

The use of E_a and E_a/E_{max} has been promoted by theoretical and experimental studies linking E_a/E_{max} to LV mechanicoenergetics (1, 2, 4, 6, 14, 22, 27, 32). It has been shown in humans that E_a/E_{max} is ~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_{max}) is impaired, whereas E_a generally increases and E_a/E_{max} increases progressively (14, 22). Note, however, that E_a/E_{max} is mainly a parameter related to LV volumes. With $E_a = P_{es}$/SV and $E_{max} = P_{es}$/(LVEDV − SV − V_d) and assuming V_d to be small enough that it can be neglected, E_a/E_{max} = LVEDV/SV − 1 or E_a/E_{max} = 1/EF − 1, where EF is ejection fraction. In normal hearts, where EF is ~0.5, E_a/E_{max} is indeed 1. In failing, dilated hearts, EF decreases and E_a/E_{max} thus increases. Why LVEF is ~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_a/E_{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_{max} and SW.

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