Total arterial inerance as the fourth element of the windkessel model

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1Biomedical Engineering Laboratory, Swiss Federal Institute of Technology, Parc Scientifique d’Ecublens, 1015 Lausanne, Switzerland; 2Biomedical Instrumentation, Institute of Applied Physics, Netherlands Organisation for Applied Scientific Research, Academic Medical Centre, 1015 AZ Amsterdam; and 3Laboratory for Physiology, Institute for Cardiovascular Research, Free University of Amsterdam, 1081 BT Amsterdam, The Netherlands

Stergiopulos, Nikos, Berend E. Westerhof, and Nico Westerhof. Total arterial inerance as the fourth element of the windkessel model. Am. J. Physiol. 276 (Heart Circ. Physiol. 45): H81–H88, 1999.—In earlier studies we found that the three-element windkessel, although an almost perfect load for isolated heart studies, does not lead to accurate estimates of total arterial compliance. To overcome this problem, we introduce an inertial term in parallel with the characteristic impedance. In seven dogs we found that ascending aortic pressure could be predicted better from aortic flow by using the four-element windkessel than by using the three-element windkessel: the root-mean-square errors and the Akaike information criterion and Schwarz criterion were smaller for the four-element windkessel. The three-element windkessel overestimated total arterial compliance compared with the values derived from the area and the pulse pressure method (P = 0.0047, paired t-test), whereas the four-element windkessel compliance estimates were not different (P = 0.81). The characteristic impedance was underestimated using the three-element windkessel, whereas the four-element windkessel estimation differed marginally from the averaged impedance modulus at high frequencies (P = 0.0017 and 0.031, respectively). When applied to the human, the four-element windkessel was more accurate in these same aspects. Using a distributed model of the systemic arterial tree, we found that the inertial term results from the proper summation of all local inertial terms, and we call it total arterial inerance. We conclude that the four-element windkessel, with all its elements having a hemodynamic meaning, is superior to the three-element windkessel as a lumped-parameter model of the entire systemic tree or as a model for parameter estimation of vascular properties.

windkessels; total arterial compliance; aortic characteristic impedance; total arterial inerance; aortic pressure and flow; human; dog

LUMPED-PARAMETER OR SIMPLIFIED models of the arterial system can assist in understanding of the function of the arterial system (1, 5, 7, 22), and they may be used in cardiac studies as a load on the heart (6). In arterial models they may serve as peripheral load (3, 17), and they may be used as a means to derive arterial parameters, notably total arterial compliance (C) (11, 14–16, 18). Lumped-parameter models are also used to derive aortic flow from arterial pressure (20).

The first lumped-parameter arterial model was the two-element windkessel, introduced by Otto Frank in 1899 (7). It consisted of a peripheral resistance (R = mean pressure ÷ mean flow) and C (= dV/dP, where V is total arterial volume and P is arterial pressure). The arterial resistive properties are mainly located in the small arteries and arterioles, and C is mainly determined by the elastic properties of the large arteries, notably the aorta. The two-element windkessel thus gave insight into the contribution of the different arterial properties to the load on the heart. The two-element windkessel also formed the basis of different methods to estimate C, such as the decay time method (7), the area method (11, 14), and the pulse pressure method (16). However, the two-element windkessel model is not a good model to mimic systemic input impedance (Zin) (15). Also, when aortic flow is as an input, this model produces unrealistic aortic pressure wave shapes (15, 16). This is mainly due to the poor medium- to high-frequency representation of the aortic Zin. To overcome this apparent weakness of the two-element windkessel model, Westerhof et al. (22), on the basis of new information about Zin, introduced the three-element windkessel model. This third term, the characteristic impedance of the aorta (Zc), accounts for the local inertia and local compliance of the very proximal ascending aorta and is based on wave transmission theory. It therefore connects lumped-parameter models with transmission-line models. Zc was connected in series with the two-element windkessel. Introduction of Zc improves considerably the medium-to-high-frequency behavior of the model. As a consequence, the three-element windkessel can produce realistic pressure and flow wave shapes and can fit experimental data well (15, 18, 22). The three-element windkessel is thus based on hemodynamic principles and has become the most widely used and accepted lumped-parameter model of the systemic circulation.

We recently showed, however, that when a three-element windkessel is used to fit aortic pressure (with aortic flow as input), the estimates of C and Zc deviate significantly from their values obtained with standard methods used in the literature (15). C tends to be overestimated and Zc underestimated. This means that the three-element windkessel can produce realistic aortic pressures and flows, but only with parameter values that quantitatively differ from the vascular properties. The same conclusion had been drawn earlier by Latson et al. (10) but, for unknown reasons, had largely escaped the attention of the scientific community.
We have therefore set out to resolve the limitations of the two- and three-element windkessel models. For very low frequencies the whole blood mass is accelerated apparently simultaneously. We therefore hypothesized that an inertial term is missing from the three-element windkessel model. With realization that \( Z_c \) is based on wave transmission phenomena and should not contribute to the relation between mean pressure and mean flow, it seems logical therefore to include an inertial element in parallel with \( Z_c \), a model that was first proposed by Burattini and Gnudi in 1982 (2) and later applied by Campbell et al. (4). This four-element model indeed offers the advantages that we have expected: it accounts for the inertia of the whole arterial system, contributes to the low frequencies only, and permits \( Z_c \) to come into play at medium-to-high frequencies.

The main objective of the present study was to investigate whether the four-element windkessel, including an inertia term, describes the relations between aortic pressure and flow better than the three-element windkessel. The second objective was to assess the physiological meaning of the inertia term.

**METHODS**

Animal data. Ascending aortic pressure and flow as a function of time in seven dogs with closed chests under anesthesia were obtained from earlier studies (19, 24). Pressure was determined using a catheter-tipped sensor and flow using an electromagnetic sensor around the ascending aorta; the sensors were implanted ~7–10 days before the experiments. Details of the animal experiments can be found in the original studies (19, 24). From aortic pressure and flow, the windkessel parameters of the three- and four-element windkessels were determined and compared with the “actual” values as described in Data analysis.

Human data. Human ascending aortic pressure and flow waves were taken from a previous study (12). We have analyzed a “type A” and a “type C” beat. The type A beat is characteristic of a subject with augmented wave reflections; the type C beat is typical of a subject with small or late reflections. Comparison with the actual parameter values of \( Z_c \) and C was done as for the dog data (see Data analysis).

Distributed model of the systemic arterial tree. A distributed model of the human systemic circulation (17) was used to derive the physical meaning of the inertia term. Aortic pressure and flow waves produced by this distributed model are used as a basis for the calculations. Details of the model have been presented earlier (15–17). The pressure and flow in the root of the ascending aorta will be referred to as “model aortic pressure” and “model aortic flow” to distinguish them from the in vivo aortic pressure and flow. Total \( R_p \) of the distributed model was obtained by addition of the (parallel) \( R_p \) of the organs. \( C \) of the distributed model was calculated by summing the volume compliances of all arterial segments. \( Z_c \) of the distributed model was calculated from the iner- tance and compliance per length of the most proximal ascending aortic segment. Total systemic iner- tance \( L \) was calculated as follows. The iner- tance of a tapered arterial segment \( L_x \) was evaluated as

\[
L_x = \int_0^{l_x} c_x \frac{\rho}{A(x)} dx
\]  

where \( \rho \) is blood density, \( l_x \) is segment length, \( A \) is cross-

sectional area, and \( c_x \) is a coefficient that accounts for a nonflat velocity profile as given by Womersley’s theory (26). For low frequencies, Jager et al. (8) showed that \( c_x \) equals 4/3 (8). The iner- tance of an artery is calculated as the sum of all segmental arterial iner- tances, and for arteries in parallel the sum is obtained as follows: \(1/L_1 = 1/L_{11} + 1/L_2 \). This sum- mation gives \( L \) of the distributed model.

From pressure and flow in the proximal ascending aorta of the distributed model, the values of \( R_p \), \( C \), \( Z_c \), and total arterial iner- tance \( L \) were estimated using the three- and four-element windkessels, as for the dog and human data. These windkessel-estimated parameters were compared with the lumped parameters derived from the distributed model as described above.

Data analysis. From mean pressure and mean flow, \( R_p \) was calculated by division. From Fourier analysis of pressure and flow, the systemic \( Z \) was derived according to standard methods (23). For each harmonic the pressure modulus is divided by the flow modulus, and the phases are subtracted. \( Z \) was estimated from the average of the modulus of the \( Z \)s between the 3rd and 10th harmonics (12, 23). \( C \) was estimated using the area method (11, 14) and the pulse pressure method (16). The estimated values of \( Z_c \) and \( C \) determined by these standard methods are called actual values.

The three- and four-element windkessels were fitted in the time domain with use of aortic flow as input and adjustment of the model parameters to minimize the root-mean-square deviation between measured pressure and windkessel-predicted pressure. The residual sum of squares (RSS) between windkessel-predicted \( (P_p) \) and measured \( (P_m) \) pressure was calculated as follows: \( RSS = \sum (P_p - P_m)^2 \), where \( N \) is the number of samples in the heart cycle studied. The root-mean-square error (RMSE) of the pressure deviations was calculated as follows: \( RMSE = \sqrt{RSS}/N \).

To compare fits of models with a different number of parameters, we have used the Akaike information criterion (AIC) and the Schwarz criterion (SC), because there is some controversy about the interpretation of these criteria (9). These criteria account for the fact that with a greater number of parameters the fit will always be better. Thus a model with more parameters is only better when the AIC and SC are smaller. AIC and SC are defined as follows

\[
AIC = N \ln(RSS) + 2P
\]  

\[
SC = N \ln(RSS) + P \ln(N)
\]

where \( P \) is the number of parameters and \( N \) is the number of samples.

\( R_p \) (mean pressure = mean flow) was given so that only two parameters of the three-element windkessel \( (Z_c \) and \( C \)) and three parameters of the four-element windkessel \( (L, Z_c \), and \( C \)) had to be estimated. Initial values for \( C \) and \( Z_c \) were obtained from standard methods. Variations in the initial values did not influence the final fit. Details of the fitting procedure can be found in earlier publications (15, 18).

The windkessel parameters obtained by the fits, with the exception of inertia for the dog and human data, were compared with their actual values. A paired t-test (significance level \( p = 0.05 \)) on the dog data was used to determine whether the windkessel-predicted \( Z_c \) and \( C \) differed from the actual values.

We performed a sensitivity analysis by calculating the change in RMSE values when \( Z_c \), \( C \), and \( L \) were increased by 10%.

RESULTS

Animal data. Figure 1 shows an example of flow and pressure measured in the ascending aorta of dog 71 and...
the fit of pressure using the three- and four-element windkessel models. Both fits are close, but it may be noticed that the diastolic pressure decay in diastole is not correctly described by the three-element windkessel. Also, the incisura is less pronounced in the three-element windkessel. The RMSE is smaller for the four-than for the three-element windkessel model. The data for all dogs are presented in Table 1. In all dogs the RMSE of the four-element windkessel fit is smaller than that of the three-element windkessel. Also, all values of the AIC and SC are smaller when the four-element windkessel is used. The estimate of C by the four-element windkessel is not statistically different from the actual values (P = 0.81). Zc is slightly underestimated by the four-element windkessel (P = 0.031). The three-element windkessel significantly underesti-

Table 1. Dog arterial parameters and their estimates with use of three- and four-element windkessel models

<table>
<thead>
<tr>
<th>Dog No.</th>
<th>Body Mass, kg</th>
<th>Heart Rate, beats/min</th>
<th>Parameters Estimated With Standard Techniques*</th>
<th>Three-Element Windkessel</th>
<th>Four-Element Windkessel</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td></td>
<td>Rp</td>
<td>Rc</td>
<td>Cppm</td>
</tr>
<tr>
<td>71</td>
<td>20.0</td>
<td>2.38</td>
<td>4.54</td>
<td>0.275</td>
<td>0.208</td>
</tr>
<tr>
<td>72</td>
<td>19.0</td>
<td>1.92</td>
<td>2.70</td>
<td>0.255</td>
<td>0.207</td>
</tr>
<tr>
<td>74</td>
<td>22.7</td>
<td>1.58</td>
<td>3.63</td>
<td>0.327</td>
<td>0.134</td>
</tr>
<tr>
<td>76</td>
<td>16.3</td>
<td>2.25</td>
<td>3.44</td>
<td>0.426</td>
<td>0.143</td>
</tr>
<tr>
<td>77</td>
<td>17.0</td>
<td>2.53</td>
<td>6.31</td>
<td>0.536</td>
<td>0.109</td>
</tr>
<tr>
<td>78</td>
<td>20.7</td>
<td>1.56</td>
<td>3.77</td>
<td>0.176</td>
<td>0.243</td>
</tr>
<tr>
<td>79</td>
<td>17.5</td>
<td>1.80</td>
<td>5.46</td>
<td>0.597</td>
<td>0.114</td>
</tr>
</tbody>
</table>

Rp and Rc, peripheral and characteristic resistance (mmHg·ml⁻¹·s); Cppm and Carr, compliance (ml/mmHg) derived from pulse pressure method and area method; RMSE, root mean square error (mmHg); AIC, Akaike information criterion; SC, Schwarz criterion; L, total arterial inertance (mmHg·s²·ml⁻¹). *See METHODS.
mated $Z_c$ ($P = 0.0014$) and overestimated $C$ ($P = 0.0029$) in all dogs. Mean values and standard errors for $Z_c$ and $C$ are shown in Fig. 2.

Alternatively, when we use the actual values of $Z_c$ and $C$ together with the best estimate of inertia, the aortic pressures predicted by the three- and four-element windkessels compare with the measured pressure (Fig. 3). We note a good overall prediction by the four-element windkessel, whereas the three-element windkessel predicts pulse pressure that is much too high and a poor diastolic wave.

Sensitivity analysis on the data of dog 71 showed that a 10% increase in $Z_c$, $C$, and $L$ led to an increase in the RMSE by 11, 20, and 5%, respectively.

Human data. The type A and type C aortic flow and pressure waves used in the analysis are shown in Fig. 4, A and B. Figure 4, C and D, shows the fit of the three- and four-element windkessel models to the type A and type C pulses. The estimated lumped-model parameters, the RMSE values, and the AIC and SC are given in Table 2. Table 2 also gives the actual parameters of the systemic arterial tree ($R_p$, $C$, and $Z_c$) estimated by standard techniques as explained in METHODS.

The estimates of the lumped-parameter values given by the four-element windkessel model are closer to the actual values than the estimates of the three-element windkessel. For $C$ the deviations are <4% for the four-element windkessel compared with 36% (type A) and 108% (type C) for the three-element windkessel. The four-element windkessel underestimates $Z_c$ by 22%, whereas the three-element model has an error of ~50%. The estimates of $L$ are similar for the type A and type C beats ($L = 0.0051$ and $0.0054$ mmHg·s²·ml⁻¹, respectively).

From Fig. 4 we see that the quality of the fit, notably the dicrotic notch and diastolic pressure decay, is better predicted by the four- than by the three-element windkessel.

Analysis using the distributed model. Using the three- and four-element windkessels to fit model aortic pressure from model aortic flow yielded essentially the same results as for the human data. Again the four-element windkessel describes the pressure wave shape better.

The parameter estimates of the four-element windkessel are much closer to those obtained directly from the distributed model than the parameters estimated from the three-element windkessel (Table 3). We see that the three-element windkessel again underestimates $Z_c$ by 42% and overestimates $C$ by 19%. The four-element windkessel accurately predicts $L$ (Table 3). Its value is indeed within 4% of the sum of all local inertances of the distributed model. The estimate of $C$ is 7% lower and the estimate of $Z_c$ is 19% lower than the actual values.

**DISCUSSION**

We have shown that the four-element windkessel model is able to fit ascending aortic pressure from flow well and that the fit is better than that based on the three-element windkessel. We made this decision on the basis of the AIC and SC. The three-element windkessel can also fit pressure and flow rather well, but the parameter values obtained are different from the ac-
tual parameter values. The four-element windkessel estimates the parameters of the systemic arterial tree accurately (Tables 1–3). We concluded this from comparison with the actual values of $Z_c$ and $C$ obtained through accepted methods in the dog and the human. Using the distributed model, for which the true arterial parameters are known a priori, we came to the same conclusion.

Table 2. Human arterial parameters and their estimates with use of three- and four-element windkessel models

<table>
<thead>
<tr>
<th>Parameters Estimated With Standard Techniques*</th>
<th>Three-Element Windkessel</th>
<th>Four-Element Windkessel</th>
</tr>
</thead>
<tbody>
<tr>
<td>$R_p$</td>
<td>$R_c$</td>
<td>$C_{PPM}$</td>
</tr>
<tr>
<td>--------</td>
<td>--------</td>
<td>-----------</td>
</tr>
<tr>
<td>Type A</td>
<td>0.79</td>
<td>0.070</td>
</tr>
<tr>
<td>Type C</td>
<td>0.63</td>
<td>0.058</td>
</tr>
</tbody>
</table>

See Table 1 footnote for definition of abbreviations. *See METHODS.

Fig. 4. Fit of 3- and 4-element windkessel models to type A and type C human aortic pressure and flow waves. A: measured flow; B: measured pressure; C: pressure fitted by a 3-element windkessel model; D: pressure fitted by a 4-element windkessel model.
Using the distributed model, we could find the meaning of the inertance term. We found that it is the summation of all local inertances of the arterial system. In the dogs, inertance appears to decrease with increasing body mass (Table 1). The inertance of the human was much smaller than that of the dog (Tables 1 and 2), corroborating this negative correlation. This can be understood by keeping in mind that inertance is inversely proportional to arterial cross-sectional area (Eq. 1). Inertial effects are included in all transmission-line models for all frequencies (17, 21). In the three-element windkessel the aortic $Z_c$ was introduced to partially bridge the gap between wave travel phenomena as known from distributed models (17, 21) and the lumped-parameter or windkessel models. This $Z_c$ relates to the local inertia and compliance of the very proximal ascending aorta. When all individual segmental compliances are added, $C$ is obtained, and similarly a proper summation of all local inertances results in $L$.

From an analytic standpoint, it is interesting to note that the four-element windkessel contains all characteristics of the two- and three-element windkessels. When the impedance of $L$ is very small with respect to the impedance of $Z_c$, the first will short circuit the latter, and the two-element windkessel results. When the inertance is very large, its influence with respect to $Z_c$ is negligible, and the three-element windkessel is obtained. Also, the decay of aortic pressure in diastole is given by the product of $R_p$ and $C$ in all three models. Because the ratio of mean pressure to mean flow in the three-element windkessel gives the sum of $Z_c$ and $R_p$, the $R_p$ is smaller and the diastolic decay of aortic pressure is more rapid.

We can now explain the function of the four-element windkessel as follows. For mean pressure and flow (0 Hz), wave transmission is of no importance, and only $R_p$, determined by the very distal parts of the arterial tree, i.e., arterioles and small arteries, contributes. For very low frequencies (below the 1st harmonic), the wavelengths of the pressure and flow waves are large with respect to the length of the arterial tree, and thus the whole arterial blood mass is accelerated simultaneously; i.e., inertia importantly contributes to the hemodynamics for these low frequencies. For medium frequencies (~2–4 times heart rate), the impedance of the compliance becomes so small that it plays an overriding role, and the $Z_i$ modulus decreases strongly with frequency, whereas its phase angle is negative. Arterial compliance is mainly located in the large conduit arteries. For high frequencies, reflections return to the aorta with random phases and cancel, so that the aorta behaves as a reflectionless tube with an impedance equal to aortic $Z_c$ (21).

On the basis of the above reasoning and on our knowledge of $Z_{in}$, it is logical to have the inertial term in parallel with $Z_c$. This parallel arrangement means that at very low frequencies, where the local properties of the aorta ($Z_c$) play a negligible role, it is the total arterial inertia that dominates, whereas at high frequencies it is $Z_c$ that determines the arterial impedance. We did consider the series $Z_c$-$L$ connection; however, the main problem with this configuration is that $L$ in series with $Z_c$ always gives a higher impedance modulus than $Z_c$ alone. Thus this series arrangement increases the impedance modulus at all frequencies, and, as shown previously, it is the large impedance modulus at low frequencies that makes the three-element windkessel a poor model (15). Therefore, the
addition of $L$ in series to the $Z_c$ results in a model that behaves even less well than the three-element windkessel. It is clear also that at high frequencies the $Z_c$ becomes very large if the inertance term is placed in series with $Z_c$ and the $Z_m$ modulus will differ strongly from the physiological values. A constant level of the modulus of aortic $Z_m$ at high and very high frequencies has been reported for the dog (13).

The $Z_m$ of the three- and four-element windkessel derived from the actual parameters is compared with the $Z_m$ derived from Fourier analysis of pressure and flow of dog 71 in Fig. 5. It is especially the very low and low-to-medium frequencies of the impedance modulus where the difference between the two models becomes apparent. The three-element windkessel impedance modulus is always larger than the $Z_c$. This represents a severe limitation in the low- to medium-frequency range. The differences in impedance show that with the correct compliance value the pulse pressure, which is mainly determined by the first few harmonics (16), will be too large (Fig. 3) or, inversely, for the best time domain fit, compliance will be overestimated. The presence of the inertance term in the four-element windkessel, however, permits the modulus to be lower than the $Z_c$ at low frequencies, and therefore its impedance modulus follows the true impedance. The phase angle is also rather well represented by the four-element windkessel.

Frank’s (7) two-element windkessel was the first lumped-parameter model of the entire arterial tree with the two elements related to the properties of the arterial system: $R_a$ and $C$. Subsequently, in the German literature (25) this model was extended in many ways. However, the extra terms introduced were obtained by intuition rather than understanding their contribution in relation to arterial function. Burattini and Gnudi (2) were the first to introduce the here proposed form of the four-element windkessel in the modern literature. However, Burattini and Gnudi stated that they “were unable to give a precise physical interpretation to $L$ and therefore it can be considered only a further degree of freedom.” Campbell et al. (4) used the same four-element windkessel model, but they thought that $Z_c$ and $L$ “combine to determine the characteristic impedance” and “do not, in themselves, represent physiologic entities.” In later papers this type of four-element windkessel was forgotten and was not considered in studies that compared different lumped models (1).

We conclude that the introduction of $L$ produces a fourth element in the windkessel with physiological meaning. The four-element windkessel model yields excellent wave shapes of pressure and flow with the correct parameters. All four parameters have their basis in arterial properties. The four-element windkessel can be used as a lumped-parameter model of the entire systemic tree or as a model for parameter estimation of vascular properties.

REFERENCES

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Received 31 March 1998; accepted in final form 9 September 1998.

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