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The reservoir pressure concept: the 3-element windkessel model revisited? Application to the Asklepios population study

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Abstract Traditionally the arterial system is either modeled as a lumped-parameter windkessel or a wave system. Recently, a hybrid model has been proposed in which the arterial system is considered to be a reservoir allowing for superimposed wave phenomena. This approach was applied to non-invasively obtained carotid pressure waveforms from 2019 subjects from the Asklepios population to investigate the contribution of reservoir pressure ($PP_{\mathrm{res,WS}}$) to carotid pulse pressure (PP_{car}) with age and gender. Additionally, reservoir pressures were compared to the reservoir pressure ($PP_{\mathrm{res,WK}}$) obtained from a 3-element windkessel model. $PP_{\mathrm{res,WK}}$ and $PP_{\mathrm{res,WS}}$ were determined by applying a 3-element windkessel model and the wave separation model to scaled carotid artery tonometry readings. The evolution of PP_{car}, $PP_{\mathrm{res,WK}}$ and $PP_{\mathrm{res,WS}}$ was examined for men and women after stratification into age quartiles. PP_{car} increased with age regardless of sex, but was more pronounced in women, with significant ($P < 0.001$) age–gender interaction. PP_{res} increases with age ($P < 0.001$), regardless of the model used for its determination, but more significantly for women. In men it only increases markedly in the oldest age group. Overall, the reservoir pressure concept showed large similarities to the classical 3-element windkessel model, especially in subjects characterized by a high reflection magnitude and high "windkesselness" of their arterial system. When applied to the Asklepios population, both models show the increase of pulse pressure with age to be largely due to increasing reservoir pressures.

Keywords Arterial stiffness · Arterial system · Hemodynamics · Modeling · Pulse pressure · Wave reflection

1 Introduction

Understanding the origin and nature of the pressure and flow waves generated by the heart pumping blood into the arterial system has always been of critical importance. To better understand the influence of arterial properties on

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these waveforms, several models have been proposed. Two major, well-accepted ways of looking at the arterial system co-exist. The first approach, the so-called windkessel model of the arterial system, is the oldest. This model regards the arterial system as a lumped-parameter model consisting of a resistance and compliance element placed in parallel, first mathematically described by Frank [1]. The compliance represents the buffering capacity of the large elastic vessels, while the resistance represents the summed resistance residing in the small arteries and arterioles. The alternative model views the arterial system as a wave system in which arterial pressure and flow waveforms are the result of the interaction between forward-travelling waves from the heart and backward-reflected waves originating from points of impedance mismatch at the peripheral vessels and bifurcations.

Both models have their strengths and weaknesses and neither is significantly superior over the other in predicting all aspects of the arterial pressure and flow waveforms in all types of subjects. Moreover, recent studies indicate that the ideal way in which the arterial system should be regarded may change with age, with a wave system being more appropriate for younger subjects which gradually evolves to a more windkessel-like system with ageing [2].

This somewhat ambiguous behavior of the arterial system is confusing, and efforts have been made to construct models incorporating elements of both approaches to bridge the apparent differences between these models. One such model recently proposed regards the arterial system as a classic windkessel system which still allows for wave propagation and reflection by separating the pressure waveform into a reservoir and wave component [3,4]. The major contributor to the pressure waveform in this approach is the reservoir pressure with the superimposed wave travel and reflection serving only to modulate this pressure. In essence, according to this model, the arterial pressure waveform can be regarded as the result of a combination of slow (∼low-frequency behavior in frequency domain) pressure changes due to loading and unloading of the pressure reservoir and fast-acting (∼high-frequency behavior) changes due to forward- and backward-traveling waves.

The basis of this new approach appears similar to that of the 3-element windkessel model as first introduced by Westerhof et al. [5]. This model builds upon the classic 2-element windkessel model proposed by Frank, which is able to accurately reproduce the low-frequency behavior of the arterial system, by adding a third element: the characteristic impedance. This third element was added precisely to improve the high-frequency behavior of the windkessel model.

The aims of this paper are multiple. First, we want to apply the novel wave-separation approach proposed by Aguado-Sierra et al. [3] and Wang et al. [4] to non-invasively obtained pressure data from the Asklepios population and investigate the contribution of the reservoir pressure to pulse pressure with age and gender. Second, we will compare these results to the reservoir pressure obtained by applying a 3-element windkessel model to our data to study to what extent the wave-separation approach is different from or provides added value to the classic 3-element windkessel model.

2 Materials and methods

2.1 Study population

Data for the present study were drawn from the first round of the Asklepios study, completed between October 2002 and September 2004. The Asklepios study is a large-scale, longitudinal population study designed to focus on the interplay between aging, cardiovascular disease and inflammation in (pre-clinical) cardiovascular disease. The complete database comprises 2524 apparently healthy subjects (1301 female, 1223 male) constituting a representative cohort of 35–55 year old subjects randomly sampled from the twinned Belgian communities of Erpe-Mere and Nieuwerkerken. For the purpose of the present study, subjects were excluded if they were on current antihypertensive or lipid-lowering therapy. A complete description of the rationale, methods and baseline characteristics of the Asklepios-study population can be found in [6]. This section will briefly discuss the collection of basic clinical data and measurement of local carotid pressure and aortic outflow.

2.2 Basic clinical data

Basic clinical data was gathered by a study nurse. Subjects were allowed a 10–15 min period of rest in a temperature-controlled environment prior to all measurements. Blood-pressure measurements were performed using a validated [7] oscillometric Omron HEM-907 blood-pressure device with cuff sizes individually chosen based on arm circumference. Subjects were blinded to blood-pressure results during measurements. Blood-pressure values reported are distinct from baseline and were recorded before the tonometry measurements.

2.3 Measurement of local carotid pressure

Applanation tonometry was performed consecutively at the left brachial and carotid arteries using a Millar pen type tonometer (SPT-301, Millar Instruments, Houston, Texas, USA) and a custom-built hard- and software platform [8]. Applanation tonometry is a non-invasive approach for measuring local pressures that is performed by placing a micromanometer tipped probe (tonometer) on a superficial artery. By applying slight pressure to the artery, the arterial wall is flattened (applanated), allowing the micromanometer to record relative pressure changes in the artery. Absolute pressure changes are obtained by properly calibrating the measured pressure waveforms. A more detailed description of the setup, processing and calibration process used in the Asklepios-study protocol was previously published [6]. Briefly, brachial artery tonometry readings were first calibrated by identifying the peak and trough of the waveform to oscillometric brachial artery systolic (SBP_{bra}) and diastolic (DBP_{bra}) blood pressure. These calibrated brachial artery waveforms were subsequently used to calibrate the carotid-artery tonometry readings by identifying the mean and trough values of the carotid-artery tonometry waveform to the calibrated brachial artery tonometry waveform. Mean values were determined by calculating the arithmetic mean of the tonometry waveforms. This approach is based on the validated [9,10] assumption that the difference between mean and diastolic blood pressure remain relatively constant in the large arteries. In 417 subjects brachial artery waveforms could not be obtained with sufficient quality within a reasonable amount of time. For these subjects, the carotid tonometry reading was scaled using a calibrated radial-artery waveform. The radial-artery waveform was scaled using DBP_{bra} and an estimated value for the radial-artery systolic blood pressure (SBP_{rad}) obtained from a population based model:

$$SBP_{ra} = 4.974 + 1.11\ SBP_{bra} - 0.178\ DBP$$

This model was derived from a linear regression analysis on a subset of 1863 subjects in the Asklepios study in which both brachial and radial-artery tonometry readings were available ($r^2 = 0.91$). This approach was previously detailed and takes into account the brachial to radial amplification of systolic blood pressure [11].

2.4 Measurement of aortic outflow

Subjects underwent a resting echocardiographic examination using a commercially available ultrasound system (Vivid7, GE Vingmed Ultrasound, Horten, Norway) equipped with a cardiac (M3S) probe. Measurements were ECG gated and consisted of cineloops of at least 5 and up to 30 cardiac cycles during normal breathing. The internal diameter of the left ventricular outflow tract (LVOT) was measured and the LVOT area was calculated assuming circularity. Flow velocities were obtained in the LVOT. All images were exported for off-line processing within a dedicated software platform running in a Matlab environment (The Mathworks Inc, Natick, MA, USA) in order to determine the maximal velocities. The obtained maximal velocities were multiplied by the LVOT cross-sectional area to obtain the aorta outflow waveform (Q).

2.5 Determination of reservoir pressure by pressure wave separation ($P_{res,WS}$)

A mathematical framework for the separation of pressure and flow waves in a reservoir ($P_{res,WS}$) and wave component was recently published [3] based on the work of Wang et al. [4]. Briefly, the reservoir pressure at an arbitrary location can be determined from:

$$\frac{\mathrm{d}P_{\mathrm{res,WS}}}{\mathrm{d}t} = a\left(P - P_{\mathrm{res,WS}}\right) - b\left(P_{\mathrm{res,WS}} - P_v\right) \tag{1}$$

where, a, b: rate constants of the system; P_v: venous pressure; P: blood pressure; $P_{\mathrm{res,WS}}$: reservoir pressure.

The solution of Eq. 1 is given by:

$$P_{\mathrm{res,WS}} - P_v = \left(P_{\mathrm{res,WS}}\left(T_N\right) - P_v\right)\exp\left(-b\left(t - T_N\right)\right), \quad T_N \le t \le T, \tag{2}$$

$$P_{\mathrm{res,WS}} = \frac{b}{a+b}P_v + \exp\left(-\left(a+b\right)t\right)\left[\int_0^t a\,P\left(t'\right)\exp\left(\left(a+b\right)t'\right)\mathrm{d}t' + P_{\mathrm{res,WS}}\left(t=0\right) - \frac{b}{a+b}P_v\right], \quad 0 \le t \le T_N \tag{3}$$

with T time when heart beat ends, and T_N time when aortic valve shuts at end of systole–dicrotic notch.

The venous pressure (P_v) was assumed to be zero. The dicrotic notch was visually identified on the carotid pressure waveforms.

$P_{\mathrm{res,WS}}(T_N)$, a and b were determined by fitting Eq. 2 and requiring continuity at $P_{\mathrm{res,WS}}(T_N)$ using an unconstrained nonlinear optimization routine (fminsearch in Matlab), minimizing the sum of squares of the error between fitted and measured pressure data. Finally, $P_{\mathrm{res,WS}}$ was determined for the entire period using Eqs. 2 and 3. As free fitting of P_v resulted in unphysiological values for P_v in many cases, it was decided to set P_v to 0 mmHg for the entire dataset.

2.6 Determination of reservoir pressure using a 3-element windkessel model

We fitted the 3-element windkessel model to the available data. The analysis was performed in Matlab (version 7.0, The Mathworks, Natick, MA) using the fminsearch (Nelder–Mead simplex) algorithm with default convergence settings and without any constraints on the model parameter values [12]. We used measured flow, Q, as an input to the model, and minimized the difference between the model response (P_{model}) and the measured pressure, P.

The model response was calculated in the frequency domain through the impedance of the model (Z_{model}). As such, flow was decomposed into a Fourier series ($\sum Q_n$), the response for each harmonic (index n) was calculated, and these were recomposed ($\sum P_n$) to obtain P_{model}. For each harmonic, the following applies:

$$P_n = Z_{\mathrm{model}}\,Q_n \tag{4}$$

For the 3-element windkessel model, Z_{model} becomes (with f frequency, i the complex constant, R vascular resistance, C total arterial compliance and Z_c characteristic impedance):

$$Z_{\mathrm{wk3}} = Z_c + R/(1 + \mathrm{i}.2\omega\mathrm{f}.\mathrm{RC}) \tag{5}$$

Windkessel pressure in the 3-element windkessel model configuration, $P_{\mathrm{res,WK3}}$ was calculated as

$$P_{\mathrm{res,wk3}} = P_{\mathrm{model}} - Q^{*}Z_c \tag{6}$$

2.7 Application of the reservoir-wave and windkessel concepts to the Asklepios-study database

Pressure and flow data obtained from the Asklepios-study population were used to calculate reservoir pressures using the wave separation and windkessel models. The contribution of the reservoir pulse pressures obtained using either model to carotid pulse pressures was examined for men and women per age half-decade and differences between reservoir pulse pressures were examined. To quantify wave reflection, the reflection magnitude (the ratio of the amplitude of the backward to the forward pressure wave) was calculated from carotid pressure and aortic flow as previously described [2].

Table 1 Overview of general population parameters of the study population

Age (years)	45 (6)
Gender (F/M)	1017/922
Weight (kg)	72.4 (13.7)
Height (cm)	169.3 (8.8)
SBP_{bra} (mmHg)	126 (13)
DBP_{bra} (mmHg)	79 (10)
PP_{bra} (mmHg)	46 (8)
Smoking (active/ex/never)	391/525/1023
Total cholesterol (mg/dl)	216.3 (36.7)
HDL cholesterol (mg/dl)	64.8 (17.2)
LDL cholesterol (mg/dl)	130.5 (34.3)
Triglycerides (mg/dl)	104.5 (71.7)
Glycemia (mg/dl)	90.4 (8.9)

Values are mean (SD)

Table 2 Overview of fitting parameters for the wave-separation and 3-element windkessel model obtained by fitting the models to the measured carotid-pressure data

	Parameters	Mean (SD)
Reservoir pressure concept	a (s^{-1})	10.5 (22.3)
	b (s^{-1})	0.64 (0.15)
	$P_{res,WS}(T_N)$ (mmHg)	108 (14)
3-Element windkessel model	R (mmHg/ml s)	1.18 (0.29)
	C (ml/mmHg)	1.66 (0.59)
	Z_c (mmHg/ml s)	0.10 (0.03)

2.8 Statistical analysis

Subjects were divided into 4 age categories (35–40 years, 41–45 years, 46–50 years, 51–56 years). Comparison between groups was performed using analysis of variance (ANOVA). All statistical analyses were performed in R 2.8.1 (The R Project for Statistical Computing, http://www.r-project.org). Values reported are mean (standard deviation). Statistical significance is indicated by P-values < 0.05 unless indicated otherwise.

3 Results

3.1 Fitting performance

Table1 summarizes the main descriptives of the study population. From the 2524 Asklepios-study subjects, 374 were excluded due to current antihypertensive or lipids treatment therapy. The required pressure and flow data were available in 2019 subjects. The fitting procedure as outlined in [3] for determination of the wave separation model parameters was successful in 1712 subjects (84.8%). For the remaining 307 subjects a modified fitting algorithm was used in which the diastolic part of the pressure waveform was defined as the last two thirds of the heart cycle past the occurrence of the dicrotic notch (as opposed to the part of the cycle from the dicrotic notch on). This modified algorithm was successful in determining the model parameters in an additional 227 subjects (11.2%). In 80 subjects (4.0%) the fitting algorithm did not converge to a solution. These subjects were discarded from further analysis. The parameters of the 3-element windkessel model were successfully determined in all subjects where the parameters of the wave separation model had been determined. Table 2 summarizes the average values for the fitted parameters for the wave separation and 3-element windkessel models. Figure 1 shows a representative example of the fittings using the reservoir pressure and windkessel model approach.

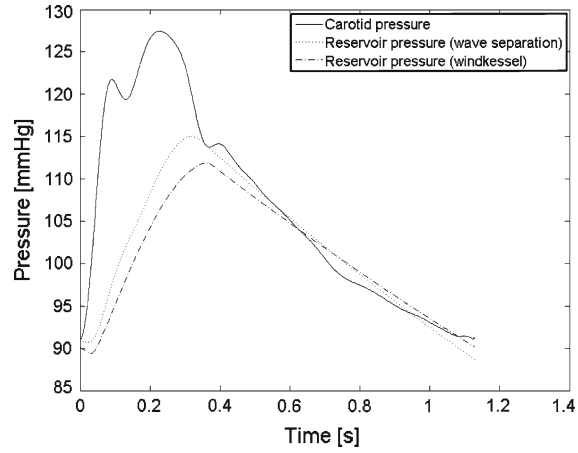

Fig. 1 Representative example of the fittings to a carotid-pressure waveform using the reservoir pressure and windkessel-model approach

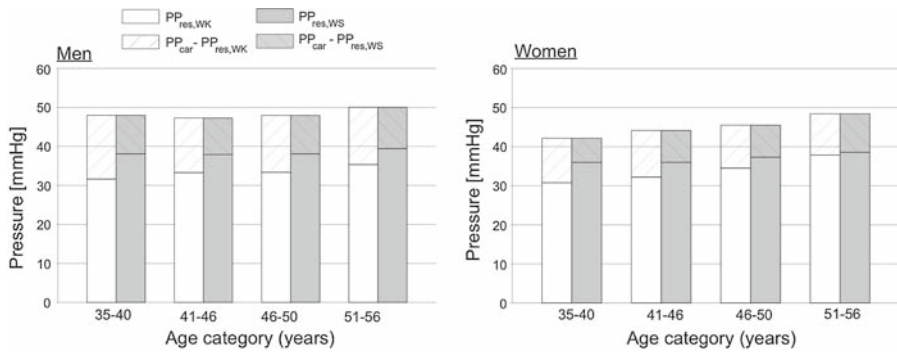

Fig. 2 Stacked bar representation of the evolution of carotid pulse pressure and the contribution of the reservoir pressure determined by the wave separation model (*white bars*, $PP_{\mathrm{res,WS}}$) and 3-element windkessel model (*grey bars*, $PP_{\mathrm{res,WK}}$). *Left*: data for men; *right*: data for women

3.2 Evolution of carotid pulse pressure and reservoir pressure with age in men and women and model comparisons

The change of carotid pulse pressure (PP_{car}) according to age quartiles for men and women is graphically represented in Fig. 2. Carotid pulse pressure increased with age regardless of gender. (ANOVA, $P < 0.001$), but did so in a more pronounced way for women. ANOVA analysis showed a significant age–gender interaction ($P < 0.001$).

Figure 2 also shows the evolution of the reservoir pressure obtained from the wave separation model ($PP_{\mathrm{res,WS}}$) and by applying a 3-element windkessel model ($PP_{\mathrm{res,WK}}$). Reservoir pulse pressures increase with age ($P < 0.001$), regardless of the model used for their determination. Both models show the evolution of PP_{res} with age to be different for men and women. Furthermore, Fig. 2 shows a good qualitative agreement between the way in which the evolution with age differs. In both cases, PP_{res} increases more significantly in women. In men it only increases markedly in the oldest age group, whereas PP_{res} remains fairly constant in the first three age groups.

While there is certainly an agreement in the overall averaged tendencies in windkessel and reservoir pressure in men and women, Fig. 2 also reveals that the magnitude of the two differs, especially in the younger subjects, where $PP_{\mathrm{res,WS}}$ tends to higher values than $PP_{\mathrm{res,WK}}$. These results are further illustrated in the left panel of Fig. 3, showing a scatter plot of $PP_{\mathrm{res,W}}$ and $PP_{\mathrm{res,WK}}$. While a relatively good correlation was found between $PP_{\mathrm{res,WS}}$ and $PP_{\mathrm{res,WK}}$ ($R = 0.78$, $P < 0.001$), as illustrated in the left hand panel of Fig.3, there is a significant bias with $PP_{\mathrm{res,WS}}$ on average higher than $PP_{\mathrm{res,WK}}$, the difference being slightly more pronounced for higher PP values. The right-hand panel of Fig. 3 finally, shows the Bland–Altman plot of $PP_{\mathrm{res,WS}}$ and $PP_{\mathrm{res,WK}}$.

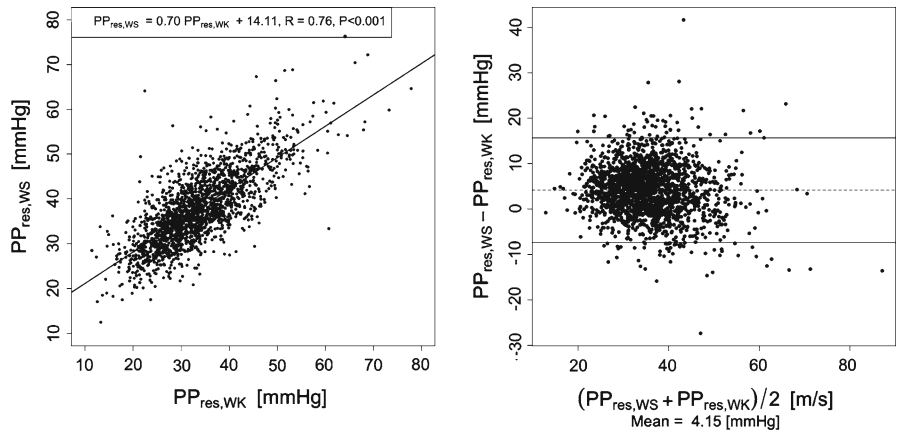

Fig. 3 Left panel: regression of $PP_{\mathrm{res,WS}}$ and PP_{res}, WK. *Right panel*: Bland–Altman plot of $PP_{\mathrm{res,WS}}$ and $PP_{\mathrm{res,WK}}$

4 Discussion

The 2-element windkessel model as originally introduced by Frank [1] is probably still the most widely used model of the arterial system. Its elements are readily identified to physiological reality and it successfully explains the pressure drop in diastole as the uniformly decreasing outflow of a pressure reservoir in time. The 2-element windkessel model is virtually always the core element of more elaborate lumped-parameter models [13] and the model is often the basis of methods used to determine total arterial compliance [14]. Nevertheless, it has its obvious shortcomings. It fails to accurately predict complete arterial waveforms, especially during systole, it does not take into account the wave-propagation properties of the arterial tree and inherently assumes an infinite wave speed throughout the arteries [15,16].

The value of considering the arterial tree as a wave system in which forward and backward travelling waves determine the shape of the arterial waveform in a complex interaction of constructive and destructive interference has long been demonstrated [17–19]. Models considering the arteries as a wave system have been proposed and yield relatively good predictions of arterial waveforms [5,20–23]. They lack, however, the conceptual simplicity of linking a limited number of model parameters directly to physiological parameters as in the windkessel model. These models are most suitable to study "forward" hemodynamic problems, i.e., the effect of changing arterial system properties on pressure and flow waves [21,23], but they are too complex to be used in reverse engineering applications, i.e., estimating arterial properties from measured pressure and flow. Another potential problem with pure wave models is that the strict application of the wave-separation theory to physiological pressure and flow profiles necessarily leads to the existence of relatively large, self-cancelling forward and backwards waves during diastole. Though mathematically sound, these waves are difficult to explain from a physiological point of view as the arterial system is cut off from the left ventricle by the closure of the aortic valve during diastole [4].

Attempts have been made to improve both types of models. Westerhof et al. [16,24] improved on the original windkessel model by adding a third component, the characteristic impedance, in an effort to improve the high-frequency behavior, most obvious in systole. Although this model is capable of closely mimicking arterial input impedance, it strictly does not take into account wave propagation and again implies an infinite wave speed through the arteries. Nevertheless, the introduction of the characteristic impedance can be seen as a link between the 2-element windkessel model, and the intrinsic wave system properties of the arterial tree [16,24]. Quick et al. [25] further elaborated on reconciling the 3-element windkessel model and a wave model and introduced the concept of a frequency-dependent "apparent arterial compliance", which allows to incorporate transmission-line theory within the concept of the 3-element windkessel model.

The recently introduced hybrid conceptual model of the arterial system as a reservoir on top of which there is wave travel and reflection is another expression (in the time domain) of the urge to reconcile the two conceptual

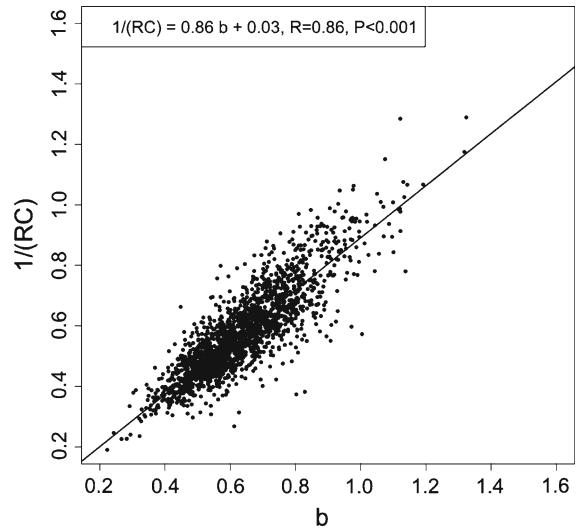

Fig. 4 Regression of parameters *b* (from wave separation model) and 1/RC (from windkessel model). The *dotted line* represents the identity line

views of the arterial system [3,4] and to solve the difficulty of the self-cancelling forward and backward waves during diastole found when applying a pure wave separation model.

One may ask which of the two modelling approaches is the most accurate. The description of the arterial tree as a branching network with wave travel and reflection is certainly the most general in nature. Based on measured patterns of input impedance in middle-aged subjects, Segers et al. [2] recently reported that treating the arterial tree as a wave system is probably more appropriate in younger subjects, while it gradually evolves to a more windkessel like system with ageing. This observation is in accordance with a theoretical study of Mohiuddin et al. [26] who demonstrated that the systemic arterial tree degenerates into a windkessel with increase in pulse wavelength. With ageing and associated vessel stiffening, pulse-wave velocity indeed increases, and so does the pulse wavelength, supporting our observations. Given these observations, the question as to which approach is the most appropriate is moot and hence the potential interest of hybrid models incorporating both windkessel and wave concepts. In theory, the hybrid reservoir-wave model might be able to capture both the windkessel-like arterial behavior of older subjects as well as the more wave-like aspects of the arterial tree in younger subjects.

In spite of its outward appearance, the wave-separation model has a lot in common with the more established 3-element windkessel model. Both view the arterial waveform as the result of an interaction between fast and slow acting phenomena, and both define a reservoir pressure driving the pressure drop during diastole. The main difference between the models lies in the way the fast-acting phenomena are modelled: the 3-element windkessel adds a third component, disregarding wave phenomena, whereas the wave-separation model seeks to model the fast-acting phenomena by accounting for wave-propagation effects. The former is applied in the frequency domain, while the latter is applied in the time domain. Nevertheless, in both models, the RC-element and the reservoir functionally acts as filter, separating slow (low-frequency) and fast (high-frequency) wave phenomena. We therefore hypothesized that the reservoir pressures derived from either model should in theory agree relatively well. Our results indeed show that $PP_{\mathrm{res,WS}}$ agrees well with $PP_{\mathrm{res,WK}}$, with a relatively strong correlation between the two. A further point of similarity between the two models is found when examining the model parameters influencing the exponential decrease in diastole. For the wave-separation model, the model parameter *b* is a measure of the exponential decrease in pressure in diastole. For the 3-element windkessel model, the parameter 1/RC is indicative of the steepness of exponential decrease during diastole. A linear regression performed on 1/RC and *b* found an excellent correlation between both parameters ($R = 0.86$, $P < 0.001$), as illustrated in Fig. 4. This further supports our view that the reservoir pressure concept is very similar to the concept of the arterial tree as a 3-element windkessel model.

The fitting of the wave-separation model was, in our population, less evident than the fitting of the windkessel-model parameters. For the calculation of our wave-separation models we had to assume the venous pressure to be

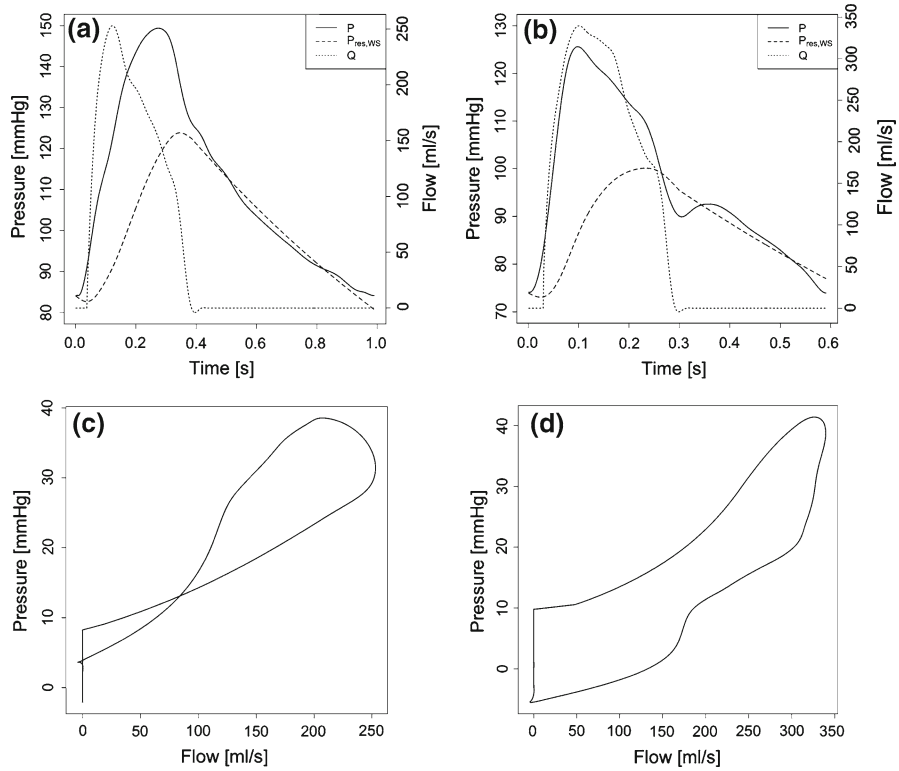

Fig. 5 Case study for A-type (*left panels*) and C-type (*right panels*) waveform showing (*top panels*) measured pressure (*solid line*), flow (Q; *dotted line*) and reservoir pressure ($P_{\mathrm{res,WS}}$, *dashed line*) and (*bottom panels*) the relation between Q versus P_{ex} (excess pressure: the difference between measured pressure and $P_{\mathrm{res,WS}}$)

zero. In the fitting algorithm as outlined by Aguado-Sierra et al., the venous pressure is a parameter, which is to be estimated in the optimization routine. We found that including the venous pressure as a parameter in the model, however, yielded a large number of cases with values for the venous pressure that were not physiological. Even after assuming the venous pressure to be zero, which is a de facto simplification of the model valid in our particular case, we found the original fitting procedure to yield unrealistic values in 15% of our subjects, which we managed to decrease to 4% by slightly modifying the fitting algorithm. In contrast, we had no such problems in determining the model parameters for the 3-element windkessel model.

The problem associated with the fitting is related to the diastolic part of the waveform, which is not always a true exponential. To illustrate our case, we make use of two exemplary pressure waveforms (see Fig. 5), which one may encounter in humans, one of the so-called A-type, and one of the C-type. As one might expect, the reflection magnitude (ratio of backward to forward pressure-wave amplitude) was relatively high (0.68) for the A-type wave, while reflection magnitude was much lower for the C-type wave (0.33). The A-type waveform is characterized by an early return of the reflected wave (early inflection point). More importantly, the diastolic part shows a clear exponential decay, and this wave could be ascribed to a system with a high "windkesselness". The C-type wave, on the other hand, shows a late systolic inflection point and it can be appreciated that there is no clear exponential pressure decay in diastole. One could consider this system as having a low "windkesselness". This waveform is clearly more determined by wave phenomena, despite the fact that the reflection magnitude in itself is rather low. As one might expect, given the absence of the exponential decay in diastole, fitting the reservoir component to C-type waveforms is challenging. The fitting is relatively poor and a low reservoir-pressure component is found, in contrast to the case of the A-type wave.

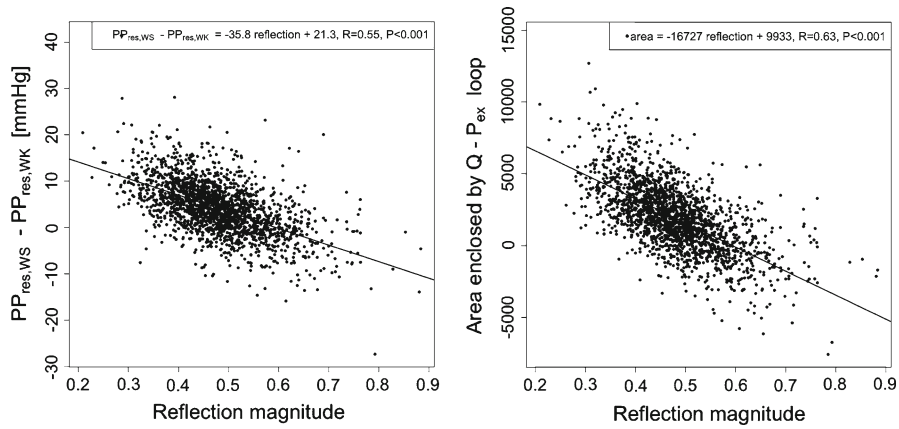

Fig. 6 *Left panel*: Difference between reservoir pulse pressures derived using the wave separation ($PP_{res,WS}$) and windkessel ($PP_{res,WK}$) models versus reflection magnitude. *Right panel*: area enclosed by Q-P_{ex} versus reflection magnitude. P_{ex} (excess pressure) is found by subtracting the reservoir pressure ($P_{res,WS}$) from the measured pressure (P_{car}). Q: measured flow. The area is counted positive for loops running clockwise; negative for loops running counter clockwise, explaining the negative values in the graph

The result is also that, when plotting the excess pressure (P_{ex}; the difference between the total pressure and the reservoir pressure) as a function of flow, the relation between both much more adheres to a straight, linear relation for the A-type wave than for the C-type wave. This can be nicely illustrated when plotting the relation between the reflection magnitude and the area enclosed by the Q-P_{ex} loop (Fig. 6, right panel). The finding that the relation between excess pressure and flow tends to linearize with increasing reflection magnitude is intriguing: in arterial hemodynamics, a linear relation between pressure and flow is indicative for a wave system free of reflected waves. Wang et al. [4] used this observation as an argument to state that, when subtracting the reservoir component, the excess pressure component is in phase with the aortic flow, suggesting that there is hardly any effect of reflected waves in systole. In our opinion, this interpretation might be too simplistic, as the flow waveform is not a single forward wave, but is in itself affected by reflected pressure waves [19] and is therefore a composite waveform. It is our feeling that the fact that the relation between pressure and flow linearizes provides additional indirect evidence that the reservoir pressure concept is not (so) different from the 3-element windkessel model.

These observations also imply that the more important the wave-reflection magnitude becomes, the better the reservoir-pressure concept seems to hold. This is, in our opinion, due to the interplay between wave reflection and the "windkesselness" of the system in the systemic circulation. In order to "recruit" the buffer capacity of the arterial system and to load the windkessel, vascular resistance needs to be high enough, which leads to more important wave reflections and waveforms of the A-type exhibiting a clear exponential decay. When resistance is low (vasodilatation), the arterial buffer is far less recruited and there is no clear exponential decay (C-type waveform). As the reservoir component is more difficult to assess (without prolonging the diastolic phase), it becomes much more difficult to apply the reservoir-pressure concept. As such, it is our feeling that the arterial system should display sufficient "windkesselness" for the reservoir-pressure concept to be applicable. This is to some extent counter-intuitive, as the potential benefit of the reservoir pressure concept over windkessel models is that it aims to reconcile the windkessel and the co-existence of pressure waves.

In a previous study performed in the Asklepios population it was found that local carotid stiffness indices, though gradually increasing with age regardless of gender, increase differently in men and women [27]. Since pulse-pressure levels are related, amongst other things, to arterial stiffness, the difference in behavior of carotid pulse pressure with age is as expected. Our results show this increase in pulse pressure to be mostly due to the increase in reservoir pressure with age due to arterial stiffening of the vessels, and to a lesser extent due to the increase in reflections. When looking at the evolution of PP_{res} with age in men and women to a certain degree, there is also a relatively good qualitative agreement between the wave-separation and windkessel-model approaches. In both cases, reservoir pressure is fairly constant in men in the first three age quartiles, rising only in the fourth age group, whereas in

women a constant, quicker increase in reservoir is found over all age quartiles. As anticipated, given the discussion above, the difference between both approaches is most clear in the younger age groups, where the contribution of reservoir pressure to total pressure is larger for the wave-separation model than for the windkessel model. The difference gradually becomes smaller in the older age groups, which appears be another reflection of the fact that with increasing age, the "windkesselness" of the arterial system increases [2,26]. These results are illustrated in Fig. 6 (left panel), which show the difference between $PP_{\mathrm{res,WS}}$ and $PP_{\mathrm{res,WK}}$ to decrease with increasing reflection magnitude.

Finally, it should be stressed that the data we used in this study were obtained non-invasively, implying some methodological limitations. We used hand-held carotid applanation tonometry recordings as surrogate for central pressure curves, and combined these with flow waveforms measured at the left ventricular outflow tract. Although both curves were carefully re-aligned in time, the contours of central and carotid pressure are not entirely equal. Also, the age range in our study is rather narrow. This has the advantage of focussed analysis over this specific age range, but precludes thorough analysis of effects of aging.

5 Conclusions

We have shown that the recently proposed (time domain) reservoir pressure concept shows large similarities to the classical (frequency domain) 3-element windkessel model, especially in subjects characterized by a high reflection magnitude and high "windkesselness" of their arterial system. When both models are applied to the Asklepios population, both show the increase of pulse pressure with age to be largely due to increasing reservoir pressures.

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