Abstract—Aortic pulse wave velocity (PWV), a measure of aortic stiffness, is an important indicator of cardiovascular risk. Derivation of PWV from uncalibrated proximal aortic or carotid pressure alone has practical advantages. However, when the time of return of the reflected wave, $\Delta t$, is used to calculate PWV, inaccurate data are obtained. With aging PWV increases but $\Delta t$ hardly decreases, suggesting that the reflection site moves toward the periphery. We hypothesized that the forward and reflected waves in the distal aorta are not in phase, leading to an undefined reflection site. We derived forward and backward waves, at the entrance and distal end of a uniform tube, with length “L.” With the tube closed at the end, forward and reflected waves are there in phase, and $\text{PWV} = \frac{2L}{\Delta t}$. When the tube is ended with the input impedance of the lower body, forward and backward waves at its end are not in phase, and $\Delta t$ is increased, suggesting that the reflection site is further away (tube seems longer), and PWV calculated from $2L/\Delta t$ is underestimated. Using an anatomically accurate model of the human arterial system, we show that the forward and backward waves in the distal aorta are not in phase. When aortic PWV increases, $\Delta t$ changes only little, and the reflection site appears to move to the periphery, similar to what is observed in humans. We conclude that to define the location of a reflection site is elusive and that PWV cannot be calculated from time of return of the reflected wave. (Hypertension. 2008;52:478-483.)

Key Words: aging ■ arteries ■ blood pressure ■ hypertension ■ vascular

It has now been recognized that arterial stiffness contributes to increased aortic systolic pressure and pulse pressure and is an important indicator of cardiovascular events.1–3 Timing and magnitude of the reflected wave contribute strongly to systolic and pulse pressure. Waveform analysis, ie, derivation of forward and reflected (backward) pressures,4–7 and the determination of the augmentation index (AIx)8,9 help us to understand the contribution of reflections to systolic pressure and pulse pressure. The reflected wave in the ascending aorta has been derived using waveform analysis,8 and the comparison between backward and forward wave has been used to estimate travel time in the aorta.10,11 The travel time has also been estimated from the time of the inflection point, ie, the start of pressure augmentation, in proximal aortic pressure.8,12–14 This time of return, derived from aortic or carotid pressure has been used to estimate aortic pulse wave velocity (PWV)10,11,13–15 as a measure of aortic stiffness. Assuming that the major reflection site is located at the lower abdominal aorta, twice this length (2L) divided by the time of return of the reflected wave (2\Delta t), ie, $2L/\Delta t$, has been taken equal to aortic PWV. However, it is now becoming clear that PWV obtained in this way is often different from the so-called carotid-femoral–derived PWV. Mitchell et al14 showed that, with aging, the aortic PWV increased but the time of return of the reflected wave decreased only little. These authors, therefore, speculated that, with aging, the reflection site is moving toward the periphery. However, Segers et al10 found that the reflection site moved closer to the heart with aging, as suggested by O’Rourke and Nichols.16

The calculations and the use of $\Delta t$, although never explicitly stated, are based on major simplifications. In essence, it is assumed that the (uniform) aorta is ended with a resistance representing the distal vascular bed. This assumption implies that reflection takes place in the lower abdominal aorta and that the reflection coefficient at that location is a real (in the mathematical sense) quantity, causing “in-phase” reflection, ie, the reflected wave is in phase with the forward wave and, thus, has the same shape and the same timing as the forward wave but may have a different amplitude (for further explanation see Methods section). By assuming in-phase reflection, an increased aortic PWV should indeed correspond with an earlier return of the reflected wave. However, the reflection coefficient at the distal aorta is not a real quantity and

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abdominal aorta. Arterial compliance (4 × 10^-5 cm^-1 s^-2) was chosen such that pulse pressure and mean pressure were similar to values found in the normal human. The characteristic impedance (178 g cm^-1 s^-2) was set equal to the characteristic impedance of the tube.

Entire Arterial System

The model of the human total arterial system is based on the original one published by Westerhof et al.20 The model consists of 121 segments of artery. The diameters of some segments of the thoracic aorta and abdominal aorta have been changed to remove the sudden change in diameter, which was leading to local reflections. Each segment is based on Womersley’s oscillatory flow theory, and the wall material is viscoelastic.21 The local peripheries are modeled with Windkessels.19,22 Pressure and flow at any location can be calculated. On the basis of the work by Murgo et al5 and Latham et al.23 we assumed the major reflection site to be located at the level of the distal abdominal aorta, 41 cm from the aortic valves.

Calculations

The tube model and the model of the entire systemic arterial tree were both programmed on a personal computer using Mathematica (version 4.0, Wolfram Research, Inc). Aortic flow, as measured in the human ascending aorta,24 was used as input. The same flow was used in the entire study to avoid differences in the contribution of the heart.

Using the model of the entire arterial system, waveform analysis was performed for 3 conditions. First, in the normal system, the arterial tree distal of the abdominal aorta was occluded in analogy to Murgo et al.5 In the original experiment, the femoral arteries were manually occluded, whereas in the model, we occluded the aorta at the bifurcation. Second, we analyzed the normal arterial system with its distal arterial tree present. Third, the stiffness of the aorta alone was increased such that PWV was doubled, leaving all of the other vessels unchanged.

Waveform analysis was performed on pressure and flow at the entrance (“ascending aorta”) and at the end of the tube model. This analysis was also performed in the human arterial model at the ascending aorta and lower abdominal aorta of the model (the major reflection site taken at 41 cm). Waveform analysis was carried out using standard calculations (Westerhof et al21 and Murgo et al). Although measured pressures were given in full calibration, the mean value of forward and reflected waves had no meaning; their amplitudes were, therefore, given only; and their diastolic values were set at the same level.

Times of return were estimated from the foot of the waves. Another estimate of the time of return of the reflected wave was obtained from the inflection point of aortic pressure.

The reflection magnitude (RM) is the ratio of the backward (Pb) and forward pressure (Pf) amplitudes, RM=Pb/Pf, and the reflection index (RI) is defined as RI=Pb/(Pf + Pb), with RI=RM/(1 + RM), as measures of the amount of reflection.6 The AIx, ΔP/PP, with ΔP as the augmentation in pressure and PP as pulse pressure, was used as a measure of amount of reflection, to be compared with the RI.

Results

Uniform Tube

Figure 2A shows the forward and backward waves at the entrance and end of the uniform tube when the tube is occluded. The forward wave arrived at the end of the tube after 55 ms; thus, the wave speed was 41.055 = 745 cm/s. The wave was reflected in phase, i.e., there was no time difference between backward and forward waves at end of tube, and their amplitudes were equal. The backward wave traveled back with the same speed arriving after 110 ms, which gave a wave speed of 820/11 = 745 cm/s. Thus, the time of return gave the correct wave speed.

In Figure 2B, the tube was loaded with the Windkessel. The forward wave arrived again after 55 ms at the end. However, as a result of the different phase shifts of all of the tube and its distal arterial tree present. Third, the stiffness of the aorta alone was increased such that PWV was doubled, leaving all of the other vessels unchanged.

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In Figure 2B, the tube was loaded with the Windkessel. The forward wave arrived again after 55 ms at the end. However, as a result of the different phase shifts of all of the
individual sine waves, the distal reflected wave exhibited a time delay with respect to the forward distal wave, here ≈30 ms. Also, the reflected wave had a different, much smoother, wave shape and had smaller amplitude than the forward wave. The backward wave returned to the entrance after ≈140 ms, and the wave speed calculated was 82/0.14 = 586 cm/s, an underestimation of the actual wave speed.

In Figure 2C, the wave speed in the aorta was doubled to 1490 cm/s. Again the complex reflection affected the timing of the reflected wave (compare P^f da and P^b da). This backward wave then traveled back to arrive at the aorta after 92 ms. The wave speed calculated was now 82/0.092 = 891 cm/s, lower than the actual wave speed of 1490 cm/s.

The data were also used to calculate the apparent site of reflection. The wave speed and the time of return of the backward wave, Δt, gave the following distances of the reflection site from the entrance of the tube, for the 3 cases:
1. length = 745×0.11/2 = 41 cm;
2. length = 745×0.14/2 = 52 cm;
3. length = 1490×0.092/2 = 69 cm.
With increased wave speed, the apparent reflection site appeared to be further away. Using Δt thus gave inconsistent estimates of length, which are explained in the Discussion section.

Arterial System

Figure 3 shows in the model of the arterial system the forward and backward waves at the ascending aorta and distal abdominal aorta, 41 cm away. Figure 3A shows the results when the distal aorta is occluded. In Figure 4, the aortic pressure wave shapes are shown in the model with distal aorta occlusion ("measured" aortic pressures of Figure 3A and 3B), in comparison with occlusion of both femoral arteries in the human (redrawn from Murgo et al).

The forward wave arrived at the location of the distal aorta after 50 ms. Thus, the PWV = 41/0.050 = 820 cm/s. The distal forward and reflected waves were in phase, and the reflected wave returned to the ascending aorta after 100 ms, giving a PWV of 82/0.100 = 820 cm/s. The moment of the inflection point was close to 100 ms. In the ascending aorta, the RM was ≈0.70, the RI was ≈0.40, and the AIX was ≈0.31.

Figure 3B shows the situation of the normal arterial tree. The times happened to be the same as those of the occluded distal aorta. The amount of reflection was smaller. In the ascending aorta, the RM was ≈0.5, RI was ≈0.33, and AIX was ≈0.17.

Figure 3C shows the effect of an increase of aortic PWV by a factor 2. The forward wave ran toward the periphery in ≈25 ms, ie, a wave speed of ≈1640 cm/s. The reflected returned after ≈75 ms in the ascending aorta, giving a calculated wave speed of 82/0.075 = 1090 cm/s, whereas the actual wave speed was 1640 cm/s.

When we calculated the distance of the apparent reflection site, it was at a distance of 1640×0.075/2 = 62 cm and, thus, was considerably moved to the periphery. The inflection point was again found at ≈100 ms, not different from in Figure 3A or 3B. The RM was 0.43, the RI was 0.30, and the AIX was ≈0.10.

It should be noted that the reflected wave at the reflection site was much smoother than the distal forward wave, because RM at that location was small for the higher harmonics in the signal.

Discussion

We found that the reflected wave does not necessarily return at the travel time from the aorta and back. The time of return of the reflected wave, the so-called "travel time," Δt, is determined by the phase ("time delay") between forward and reflected waves at the chosen reflection site plus the travel times from entrance to reflection site and back. Thus, the moment of return of the reflected wave is not only determined by the wave speed and distance of travel but also by the time shift at the reflection site. As a result, with an assumed location of the reflection site, the PWV cannot be derived.
Inversely, the time of return of the backward wave does not allow estimation of the location of the reflection site when PWV is known. Thus, the reflection site is an elusive quantity that depends on the reflection coefficient at the site.

In Figure 5, the problem in defining reflection site location is elucidated. The tennis player will, with an equally powerful serve, observe a later return of the ball when the reflection site is elastic (Figure 5B) and conclude that the reflection site is further away. This return time will depend on the material of the reflection site and the speed of the ball.

Therefore, the calculation of wave speed from proximal measurements of pressure (and flow) is not possible, neither from the inflection point on the pressure wave nor from the methods to derive forward and backward pressure waves, such as wave form analysis, the triangulation method, and wave intensity analysis. However, calculation of forward and reflected waves by all of these methods is still correct and gives valuable information about magnitude, timing, and duration of the forward and reflected waves and, thus, gives information on the genesis of systolic pressure, pulse pressure, and load on the heart. The only problem is that the moment of return of the reflected wave depends not only on wave speed and distance of the reflection site but also the time delay introduced by the reflection site.

The reflection coefficient gives the relation between backward and forward waves, at any chosen location. The reflection coefficient depends on the input impedance of the arterial bed distal of the chosen reflection site and on the wave speed (or, more accurately, on the characteristic impedance) of the aorta. Thus, the phase difference of each harmonic of forward and backward pressure depends on both of these quantities. Because the forward and backward waves consist of series of sine waves, each with its own phase shift, a very complex relation between these waves exists. We can, therefore, in practice, only estimate the time shift (eg, foot-foot) between these waves. Also, each harmonic is reflected with a different magnitude. In the distal aorta, as a consequence of better impedance matching for higher frequencies, higher harmonics are reflected less than the lower harmonics so that the reflected wave is quite different in shape; it is smoothed and may approach a single sine wave (see Figure 2B and 2C and Figure 3B and 3C). Only when the reflection coefficient is a real number, as in complete occlusion, is the reflection site not elusive (Figures 2A and 3A).

We found (Figure 3) that the inflection point in the ascending aortic pressure changes little in time, even for a change in PWV by a factor 2. This is in accordance with the findings in humans where PWV increased by about a factor 2 and the transmission time decreased on the order of 10%. These studies and our present analysis show that, with increased aortic stiffening, as in aging, the reflection site, although actually not changing in location, appears to move away from the heart. Recently, it has been shown that wave separation into forward and backward waves and their time difference is the best way to estimate travel time. Using this analysis, Segers et al found that, with age, the reflection site moved closer to the heart. Qasem and Avolio, using wave separation and calculating transit times, found estimates of PWV close to the values obtained from carotid-femoral pulse delay times, implying a real reflection site at the distal aorta.

We have studied either a change in the distal load or a change in aortic PWV only; in reality, both may change, leading to a more complex situation, and in principle any change in apparent distance of the reflection site may occur. Although Hashimoto et al found that RM is an independent determinant of left ventricular mass regression during anti-hypertensive treatment, there is no association between regression in ventricular mass and round-trip travel time.

Figure 3. Pressure in a model of the entire human arterial tree. Each panel shows measured pressure in the ascending aorta (entrance) and the forward and backward waves at the entrance and at the lower abdominal aorta. A, Waves when the distal aorta is occluded (Murgo et al), to represent a real reflection coefficient with a modulus of 1. The forward and reflected waves in the distal aorta are equal and in phase. Wave speed is 820 cm/s. B, Waves when the arterial model is used. Return time happens to be close to that in A, C, As B but with a doubled PWV of the aorta only. Calculated wave speed is 1090 cm/s, whereas actual wave speed is 1640 cm/s. P_{aa} and P_{da} are the measured pressures at ascending aorta and the distal abdominal aorta; P_{aa} and P_{da} are the forward and backward pressures at the ascending aorta; and P_{aa} and P_{da} are the forward and backward pressures at the distal abdominal aorta.
The concept of effective length has been the subject of earlier studies. Otto Frank (see Campbell et al.) identified a principal reflection site at the iliac bifurcation and an additional one where the carotid arteries enter the head, leading to the asymmetrical T-tube model. However, the literature remained unclear and reported effective lengths of 50 cm to >2 m. Sipkema and Westerhof showed in 1975 that a reflection site is elusive and hampers the calculation of cardiac output. Latham et al. suggested 2 reflection sites in series: in the aorta at the level of the renal arteries and a second one distal to the aortic bifurcation. These authors clearly struggled with the determination of the site of reflection. Pythoud et al. studied, using a sophisticated technique, the relation between the location of reflection site obtained by aortic occlusion and its prediction by means of a calculated reflection profile. These distances correlated well, supporting the concept that, with total occlusion, the reflection coefficient is a real number and no phase shift takes place. Burattini and Campbell showed that identification of effective length meets with problems when a tube is ended with a complex load, and/or blood viscosity or wall viscosity play a role. Thus, the literature reports many problems with effective length, but none of these studies addressed the errors in the estimation of wave speed using the time of return of the reflected wave.

**Perspectives**

Aortic PWV is an important independent predictor of systolic blood pressure and, therefore, its accurate determination is mandatory. However, return time of the reflected wave, as we show here and as reported by Mitchell et al., is not closely related to PWV. Therefore, PWV data based on analysis of proximal (aortic or carotid) pressure alone should be reconsidered. Although PWV increases with age, the return time is reported to change little with (higher) age. It was also found that the RM, ie, P/P, decreases (increased P and little change in P) or increases significantly but minimally (a few percent). Thus, the timing and magnitude of the reflected wave, now considered to form the basis of the increase in systolic blood pressure with age, can only be part of the explanation. It is, therefore, mandatory that we search for other parameters. Increased PWV implies a decrease in total arterial compliance and decreased compliance relates to increased pulse pressure. The suggestion by Mitchell et al. that characteristic impedance increases and, therefore, forward pressure increases is also a possibility but assumes that forward flow is little changed in hypertension, implying a contribution of cardiac pump function. To understand the effects of age on (systolic) blood pressure, comprehensive studies are needed that quantitatively compare the arterial and cardiac parameters that contribute.

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Location of a Reflection Site Is Elusive: Consequences for the Calculation of Aortic Pulse Wave Velocity
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