

Aortic Pulse Wave Analysis Is Not a Surrogate for Central Arterial Pulse Wave Velocity

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Arterial Stiffness (AS) is a primary cardiovascular risk factor. AS increases myocardial oxygen demand and LV work and decreases coronary perfusion. Pulse Wave Velocity (PWV) is considered the gold standard for assessing AS. However, PWV testing is time consuming and impractical in the clinical setting. The purpose of this study was to determine if Pulse Wave Analysis (PWA) parameters obtained with applanation tonometry can be used to predict PWV. Radial artery PWA testing and aortic PWV measurements were performed on 77 apparently healthy subjects. A correlation matrix between all the studied variables and a stepwise multiple regression were performed. The best regression equation was obtained with central PWV as the dependent variable and Age, Height, Weight, Brachial Systolic and Diastolic Blood pressures, normalized and non-normalized Augmentation Index, Cardiac Cycle time, Ejection Duration, reflected wave round trip travel time, and time to peak pressure as independent variables. Finally, a Bland-Altman test was performed to determine the agreement between measured and predicted PWV. No significant correlations between PWV and PWA parameters were found. The resulting stepwise regression equation was $PWV = 1.76 + 0.044 \cdot \text{Age} + 0.023 \cdot \text{SBP}$ ($R = 0.544$, $\text{Adj-}R^2 = 0.28$, $P < 0.001$). No agreement between measured and predicted PWV was observed using the Bland-Altman test. Although the regression equation is significant, the adjusted coefficient of determination shows that the model could explain just 28% of PWV variability. These findings suggest that PWA should not be used as a surrogate measure for assessing aortic PWV and stiffness. *Exp Biol Med* 234:1339–1344, 2009

Key words: Arterial Stiffness; pulse wave analysis; pulse wave velocity

Introduction

Hypertension is a major public health problem for nearly 30% of the population 18 years and older (1) and is closely related to heart disease and stroke (2, 3). Chronic hypertension may produce anatomical changes to the aorta's tunica media that will progressively generate Arterial Stiffness (4). Hemodynamically, Arterial Stiffness increases myocardial work via a decreased aortic compliance and an increased reflecting pressure wave velocity (5, 6). In recent years, non-invasive techniques that assess central hemodynamics have increased in popularity (7, 8), primarily because they have proven to be better predictors of future cardiovascular events when compared to brachial blood pressure measured via sphygmomanometry (6, 7, 9–13).

Applanation Tonometry (AT) is a non-invasive and relatively inexpensive technique that is currently used in the clinical setting to assess central hemodynamics (12, 14–18). There are two main assessments derived from AT: Pulse Wave Analysis (PWA) and Central Pulse Wave Velocity (PWV). Aortic PWA is derived from the radial pulse waveform and the use of a mathematical transfer function (5, 16, 18) and is mainly used to evaluate central hemodynamics such as Aortic Pulse Pressure and Augmentation Index (AIx) (5, 11, 12, 15, 16, 19, 20).

Although some PWA parameters, such as round trip travel time of the reflecting wave (ΔT_p) and AIx (Fig. 1), provide information on aortic wave reflection and Arterial Stiffness (11, 12, 19), it is the measurement of Carotid-Femoral PWV (CF-PWV) that is recognized as the gold standard for Arterial Stiffness assessment (7, 8, 17, 19, 21). We reasoned that if a valid surrogate for complex CF-PWV could be derived from simple PWA parameters, there would be several clinical benefits. PWA can be performed in 10 to 15 minutes, while CF-PWV can require 30 to 40 minutes, is technically very demanding, and involves the combination of AT with an electrocardiogram and body landmarks measurements (7, 11, 14, 22). Several previous studies have addressed the relation between CF-PWV and some PWA parameters, but the results are conflicting and the studies

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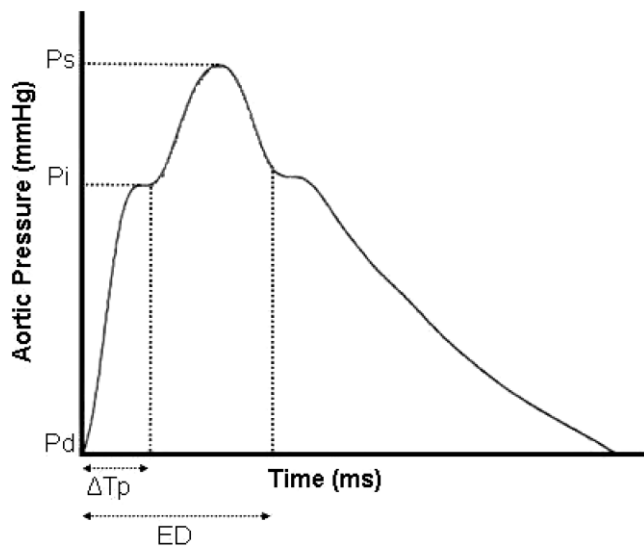


Figure 1. Aortic pressure wave synthesized from the measured radial artery pressure wave (applanation tonometry) using a generalized transfer function. ED, Ejection Duration; ΔT_p , Round trip travel time; Pd, Diastolic pressure; Ps, Systolic pressure; Pi, Inflection point indicating the beginning of the reflected pressure wave; $AIx = [(Ps - P_i) / (Ps - P_d)] \times 100$.

were not designed to answer the question regarding a surrogate measure (22–29).

This will be the first study designed specifically to determine whether CF-PWV may be obtained from PWA parameters in healthy subjects (22–25). Accordingly, the purpose of our study is to predict CF-Pulse Wave Velocity from Pulse Wave Analysis parameters using applanation tonometry. We will test the hypothesis that there exists a significant regression model to use PWA as a surrogate measure of CF-PWV and Arterial Stiffness.

Methods

Subjects. Forty-one men and thirty-six women, 18.9–63.5 years of age, were enrolled in the study. All subjects were apparently healthy, with no known cardiovascular disease or major cardiovascular risk factors, and none were receiving any prescribed medications. The study was approved by the Institutional Review Board of the University of Florida and written informed consent was obtained from all subjects. Height and weight were assessed before subjects were placed in a supine resting position on a gurney in a quiet, temperature-controlled environment. Following a 10-minute rest period, brachial blood pressure was measured in triplicate via an automated non-invasive device (BpTRU BPM-100, VSM MedTech Ltd., Vancouver, BC, Canada). Subjects remained in the same position and conditions for the duration of the measurements. All subjects were tested at the same time of day to avoid any diurnal variations following at least 8 hours of fasting and with no caffeine intake for at least 12 hours.

Pulse Wave Analysis. The assessment of arterial wave reflection characteristics was performed noninvasively

using the SphygmoCor *Pulse Wave Analysis Px* system and SCOR-2000 Version 6.31 software (AtCor Medical, Sydney, Australia). High-fidelity radial artery pressure waveforms were recorded by applanation tonometry of the radial pulse in the left wrist using a “pencil type” micromanometer (Millar Instruments, Houston, TX). The aortic pressure waveform was derived non-invasively from the radial pulse using applanation tonometry and application of a generalized transfer function, which corrects for pressure wave amplification in the upper limb (5). At least five consecutive measurements were performed per subject, and the average of the best three high-quality recordings, defined as an in-device quality index of over 80% (derived from an algorithm including average pulse height variation, diastolic variation, and the maximum rate of rise of the peripheral waveform), was used for analysis. The following PWA parameters related to the amplification and temporal characteristics of the reflecting wave were used as independent variables in the present study; for further details, consult Nichols and Singh (12):

Augmentation Index (AIx), defined as reflected wave amplitude divided by pulse pressure and is expressed as a percentage (20);

Normalized AIx (AIx@75), defined as AIx normalized to a fixed heart rate of 75 beats per minute (30),

Round trip travel time of the reflecting wave (ΔT_p), defined as the forward traveling wave from the ascending aorta to the major reflection site and back, is measured from the foot of the forward traveling pressure wave to the foot of the reflected wave (12),

Time to peak pressure (TPP), defined as the time where the aortic systolic pressure is reached,

Cardiac Cycle time (tCC), defined as the duration time of a cardiac cycle, and

Ejection Duration (ED), defined as the duration time of every cardiac systole.

Pulse Wave Velocity. CF-PWV was measured in triplicate from the left common carotid pulse to the left femoral pulse using applanation tonometry, as described elsewhere (17, 22, 31, 32). In general, pressure waveforms were gated with simultaneous electrocardiographs and were used to calculate the PWV between the two sites (Carotid-Femoral). Foot-to-foot PWV was calculated by determining the delay between the appearance of the pressure waveform foot in the carotid and femoral sites (Δt). The measurement of the tonometry transit distance (TTD) was made using a measuring tape on the surface of the body connecting the carotid measuring site with the suprasternal notch and the suprasternal notch with the femoral measuring site, respectively. The aortic or central transit distance (CTD) was estimated subtracting two times the suprasternal notch-carotid distance to TTD, to account for parallel transmission in the aorta and common carotid (33). Finally, CF-PWV was estimated dividing CTD by Δt , using SphygmoCor *Pulse Wave Velocity Vx* system and SCOR-2000 Version 6.31 software.

Table 1. Subject Characteristics and Descriptive Statistics ($n = 77$)

	Minimum	Maximum	Mean	SD
Age (years)	18.90	63.52	26.44	9.33
Height (cm)	146.00	195.00	172.83	10.81
Weight (Kg)	44.00	121.00	70.59	15.03
BMI (Kg/m ²)	17.36	33.52	23.46	3.38
SBP (mmHg)	96.00	138.00	116.19	10.47
DBP (mmHg)	60.00	88.00	72.74	6.77
MAP (mmHg)	71.00	106.00	86.27	7.66
AIx (%)	-25.33	36.33	7.55	12.47
AIx@75 (%)	-31.67	29.00	0.48	12.79
Δ Tp (ms)	105.33	208.33	157.17	19.03
TPP (ms)	170.00	276.67	227.55	21.61
tCC (ms)	612.00	1434.67	1030.80	171.42
ED (ms)	246.00	386.00	336.35	22.86
PWV (m/s)	3.69	9.10	5.61	0.93

BMI, Body Mass Index; SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; MAP, Mean Arterial Pressure; AIx, Augmentation Index; AIx@75, normalized AIx; Δ Tp, Round trip travel time; TPP, time to peak pressure; tCC, Cardiac Cycle time; ED, Ejection Duration; PWV, Pulse Wave Velocity.

Statistical Analysis. Data analysis was performed in three steps using SPSS software (version 16.0, Chicago, IL). A correlation matrix was produced using all the study variables (Age, Height, Weight, AIx, AIx@75, Δ Tp, TPP, tCC, ED, and PWV) to look for significant associations at $P < 0.05$. Then, a stepwise multiple regression was performed to obtain the best regression equation, including aortic PWV as the dependent variable and the remaining variables as independent. The stepwise multiple regression uses the highest regression coefficients between PWV and the independent variables, without significant collinearity between these variables or predictors. It adds them up until no additional predictors contribute significantly to the model, based on the adjusted determination coefficient ($\text{Adj-}R^2$). Finally, a Bland-Altman test for agreement between CF-PWV and the best regression equation was performed, with 0.35 m/s as the maximal tolerated differ-

ence (34), a value that approximates a 5% error in normal subjects (7).

Results

Table 1 shows subject characteristics and descriptive statistics of the variables used in the study.

The correlation matrix between all the variables used in the study is shown in Table 2. Within the matrix, it is possible to observe that PWV is significantly correlated with three different variables (Age $r = 0.479$, Weight $r = 0.272$, and SBP $r = 0.324$), with no significant correlation with any PWA parameter (AIx, AIx@75, Δ Tp, TPP, tCC, or ED). Age, Height, and Weight are the variables with more numbers of significant correlations within the variables. Especially relevant is the finding of a significant correlation between PWV and Age, while no significant correlation is represented between Δ Tp and Age ($r = -0.038$, $P > 0.05$).

Table 2. Correlation Matrix Between All Variables

	Height (m)	Weight (Kg)	SBP (mmHg)	DBP (mmHg)	AIx (%)	AIx@75 (%)	Δ Tp (ms)	TPP (ms)	tCC (ms)	ED (ms)	PWV (m/s)
Age (years)	.164	.271*	.142	.097	.501**	.376**	-.038	.265*	.252*	.295**	.479**
Height (m)		.722**	.513**	.078	-.371**	-.480**	.443**	-.041	.305**	.152	.171
Weight (Kg)			.564**	.175	-.242*	-.332**	.237*	-.148	.215	.044	.272*
SBP (mmHg)				.464**	-.074	-.041	.032	-.156	-.047	-.178	.324**
DBP (mmHg)					.223	.252*	-.208	.054	-.078	-.144	.045
AIx (%)						.904**	-.291*	.501**	.145	.389**	.154
AIx@75 (%)							-.432**	.216	-.251*	.135	.117
Δ Tp (ms)								.133	.319**	.348**	-.060
TPP (ms)									.636**	.645**	.016
tCC (ms)										.606**	.092
ED (ms)											.083

SBP, Systolic Blood Pressure; DBP, Diastolic Blood Pressure; AIx, Augmentation Index; AIx@75, normalized AIx; Δ Tp, Round trip travel time; TPP, time to peak pressure; tCC, Cardiac Cycle time; ED, Ejection Duration; PWV, Pulse Wave Velocity.

* $P < 0.05$.

** $P < 0.01$.

The best regression equation after performing a stepwise analysis is:

$$\text{PWV} = 1.76 + 0.044 * \text{Age} + 0.023 * \text{SBP}$$

$$(R = 0.544, \text{Adj-}R^2 = 0.28, P < 0.001).$$

Although this equation resulted in a highly significant P value ($P < 0.001$), the variability of the dependent variable can be explained by just 28% of the model ($\text{Adj-}R^2 = 0.28$). In addition, it is possible to observe that no PWA parameter is included in the equation, mainly because no significant correlation was seen between PWV and PWA parameters.

The agreement analysis of the best regression equation is represented in Figure 2, where the mean of the differences between the measured and the predicted PWV is 0 m/s and the standard deviation is 0.78 m/s. The range established by mean ± 2 SD (0.0 ± 1.56 m/s) is three-fold greater than the range established a priori as the maximal tolerated difference (± 0.35 m/s) and 50% of the sample is out-of-range.

Discussion

This study was designed to elucidate a possible surrogate measurement for Carotid-Femoral PWV using PWA. Our findings are three-fold: first, no significant correlations were found between CF-PWV and PWA parameters; second, the best regression equation to estimate CF-PWV included Age and Systolic Blood Pressure as independent variables, with just 28% of the variability explained by the model; and third, the Bland-Altman agreement analysis did not confirm the best regression equation as a surrogate of CF-PWV. Based on these results, we reject our hypothesis and conclude that PWA cannot be used as a surrogate measurement for CF-PWV in apparently healthy, normal subjects.

Arterial Stiffness has been linked to hypertension and is an independent risk factor for cardiac disease (5, 6). Indeed, Arterial Stiffness is a better predictor of future cardiac events when compared to brachial blood pressure (6, 7, 10–13). Pulse Wave Velocity (PWV) is considered the gold standard for determining Arterial Stiffness (7, 8). Unfortunately, measurement of CF-PWV using AT is time consuming, must be coupled with electrocardiogram monitoring, requires precise body landmark measurements, and is technically demanding. Alternatively, Pulse Wave Analysis (PWA) has been proposed as a surrogate method to assess Arterial Stiffness (11, 12, 19). Indeed, if PWA could be used as a valid surrogate for Arterial Stiffness, clinical screening for cardiovascular disease could be simplified and significantly shortened.

Previous investigations have yielded conflicting results (22–25). London *et al.* (23) were the first to report a significant relationship between PWV and ΔTp ($r = -0.598$, $P < 0.001$). Subsequently, others have erroneously cited that study as evidence that PWA data can be used as a surrogate measurement for Arterial Stiffness (7, 9, 35, 36). However, London *et al.* (23) used a different method

(Transcutaneous Doppler flow velocity vs. AT) to assess PWV and their study was further confounded by using a mixed sample of healthy subjects and end-stage renal disease patients, including both normotensive and hypertensive subjects. Moreover, only 36% of PWV variability was explained by their model and no statistical agreement test was performed (23). Interestingly, McEniery *et al.* (29), in a large sample of normal subjects, reported that a direct relation exists between ΔTp and CF-PWV ($r = 0.34$, $P < 0.001$), suggesting that the reflecting wave returned more slowly from the periphery when central stiffness is increased. The authors do not explain their paradoxical finding (29).

In contrast, Nakae *et al.* (24) did not find a significant correlation between radial AIx and brachial-ankle PWV in treated hypertensive subjects using a tonometry device. Using the same methodology as applied in the present study, Yasmin and Brown (25) and Wimmer *et al.* (22) found significant correlations between AIx and central PWV ($r = 0.29$, $P < 0.005$), and AIx@75 and central PWV ($r = 0.31$, $P < 0.0001$), respectively, in offspring hypertensive siblings (25) and subjects with chronic kidney disease (22). Although Yasmin and Brown (25) and Wimmer *et al.* (22) designed their studies to determine possible PWV measurements using PWA, they found only modest correlations. More importantly, their models explained only 8.4 and 9.6% of PWV variability. Lastly, neither study tested for statistical agreement between both techniques (34).

Our results showed no statistically significant correlations, but our correlation coefficient between AIx and PWV was comparable to the r values observed between AIx and PWV in previous studies ($r = 0.15$ vs. $r = 0.29$ (25) and $r = 0.25$ (22)). Comparable r values across studies confirms that the behavior of the different AIx/PWV regression functions are similar and, despite the statistical significance shown elsewhere (22, 25), the overall PWV variability is poorly explained by the different models. From a statistical perspective, the appropriate interpretation of these r values is that AIx cannot be used as a surrogate of PWV.

Another reason, in our opinion, for the somewhat disparate conclusions across studies is that entirely different populations were tested. While Yasmin and Brown (25) and Wimmer *et al.* (22) tested clinical populations, and London *et al.* (23) tested a mixed sample, as described above, we tested apparently healthy subjects with no known cardiovascular disease or risk factors. We believe that this is a very important factor because vascular diseases alter dispersion and reflection of the pressure wave (5, 12, 16, 20, 23, 37). Consequently, an increase in the relationship between PWV and AIx or ΔTp is to be expected.

Our study is not without limitations. A larger sample size and more subjects 50 years of age and older would strengthen our results, though no change in the general outcomes would be expected. A second possible limitation of the present study is the use of indirect non-invasive assessment for PWV and PWA. However, Sakurai *et al.*

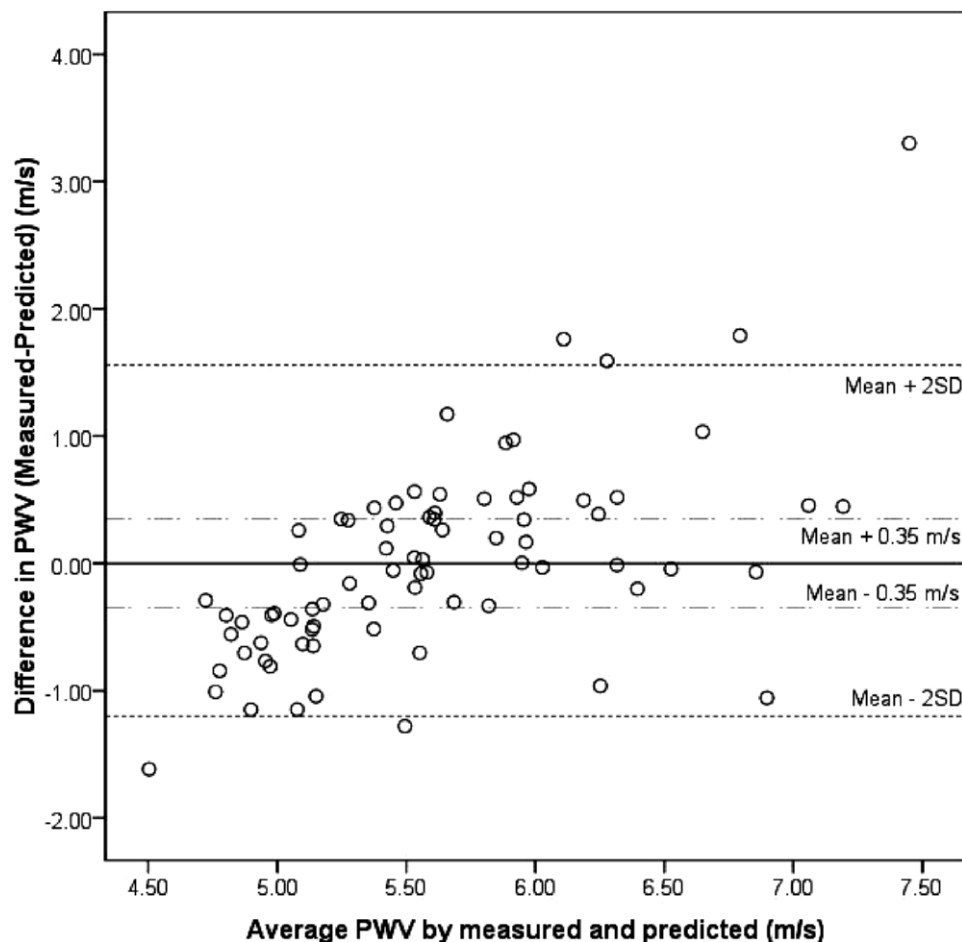


Figure 2. Bland-Altman plot of difference against mean PWV data.

(38) measured PWA and PWV invasively via aortic catheterization and observed no statistical relation between AIx and PWV ($r = 0.28$, $P > 0.05$), supporting the same general outcome observed with non-invasive measurements in the present study (38).

To date, this is the first study designed specifically to determine whether PWA parameters can be used as surrogates for CF-PWV measurement. The best regression equation found within the present study did not use any of the PWA parameters and did not pass the statistical test for agreement (34), which shows PWV should not be replaced by PWA to assess Arterial Stiffness. Our finding is further supported by Kelly *et al.* (39), who reported different and contradictory AIx and PWV responses to vasoactive drugs, confirming that a strong relationship does not exist between AIx (eq. PWA parameter) and central PWV. Finally, it should be noted that the European Society of Cardiology, in its “Expert Consensus Document on Arterial Stiffness,” correctly argues that: “Central pressure, AIx, and PWV cannot be used interchangeably as indexes of Arterial Stiffness” (8).

Although PWA is a validated assessment for central aortic pressure (12), increased myocardial work (40, 41),

and cardiovascular risk, we conclude that PWA cannot be used as a surrogate measure of Carotid-Femoral PWV in apparently healthy, normal subjects.

1. Chobanian AV, Bakris GL, Black HR, Cushman WC, Green LA, Izzo JL Jr., Jones DW, Materson BJ, Oparil S, Wright JT Jr, Roccella EJ. Seventh report of the Joint National Committee on Prevention, Detection, Evaluation, and Treatment of High Blood Pressure. *Hypertension* 42:1206–1252, 2003.
2. Pescatello LS, Franklin BA, Fagard R, Farquhar WB, Kelley GA, Ray CA. American College of Sports Medicine position stand. Exercise and hypertension. *Med Sci Sports Exercise* 36:533–553, 2004.
3. Rosamond W, Flegal K, Friday G, Furie K, Go A, Greenlund K, Haase N, Ho M, Howard V, Kissela B, Kittner S, Lloyd-Jones D, McDermott M, Meigs J, Moy C, Nichol G, O'Donnell CJ, Roger V, Rumsfeld J, Sorlie P, Steinberger J, Thom T, Wasserthiel-Smoller S, Hong Y. Heart disease and stroke statistics—2007 update: a report from the American Heart Association Statistics Committee and Stroke Statistics Subcommittee. *Circulation* 115:e69–171, 2007.
4. Safar ME, O'Rourke MF. *Handbook of Hypertension: Arterial Stiffness in Hypertension*. Edinburgh, Scotland: Elsevier, 2006.
5. Nichols WW, O'Rourke MF. *McDonald's Blood Flow in Arteries*. London: Hodder Arnold, 2005.
6. Weber T, Auer J, Lamm G, O'Rourke MF, Eber B. Arterial stiffness, central blood pressures, and wave reflections in cardiomyopathy—implications for risk stratification. *J Cardiac Failure* 13:353–359, 2007.

7. O'Rourke MF, Staessen JA, Vlachopoulos C, Duprez D, Plante GE. Clinical applications of Arterial Stiffness: definitions and reference values. *Am J Hypertens* 15:426–444, 2002.
8. Laurent S, Cockcroft J, Van Bortel L, Boutouyrie P, Giannattasio C, Hayoz D, Pannier B, Vlachopoulos C, Wilkinson I, Struijker-Boudier H. Expert consensus document on Arterial Stiffness: methodological issues and clinical applications. *Eur Heart J* 27:2588–2605, 2006.
9. Pannier B, Guerin AP, Marchais SJ, Safar ME, London GM. Stiffness of capacitive and conduit arteries: prognostic significance for end-stage renal disease patients. *Hypertension* 45:592–596, 2005.
10. Meaume S, Rudnichi A, Lynch A, Bussy C, Sebban C, Benetos A, Safar ME. Aortic pulse wave velocity as a marker of cardiovascular disease in subjects over 70 years old. *J Hypertens* 19:871–877, 2001.
11. Nichols WW. Clinical measurement of Arterial Stiffness obtained from noninvasive pressure waveforms. *Am J Hypertens* 18:3S–10S, 2005.
12. Nichols WW, Singh BM. Augmentation index as a measure of peripheral vascular disease state. *Curr Opin Cardiol* 17:543–551, 2002.
13. Laurent S, Boutouyrie P, Asmar R, Gautier I, Laloux B, Guize L, Ducimetiere P, Benetos A. Aortic stiffness is an independent predictor of all-cause and cardiovascular mortality in hypertensive patients. *Hypertension* 37:1236–1241, 2001.
14. Mackenzie IS, Wilkinson IB, Cockcroft JR. Assessment of Arterial Stiffness in clinical practice. *Q J Med* 95:67–74, 2002.
15. O'Rourke MF, Gallagher DE. Pulse wave analysis. *J Hypertens Suppl* 14:S147–S157, 1996.
16. O'Rourke MF, Pauca A, Jiang XJ. Pulse wave analysis. *Br J Clin Pharmacol* 51:507–522, 2001.
17. Davies JJ, Struthers AD. Pulse wave analysis and pulse wave velocity: a critical review of their strengths and weaknesses. *J Hypertens* 21:463–472, 2003.
18. Soderstrom S, Nyberg G, O'Rourke MF, Sellgren J, Ponten J. Can a clinically useful aortic pressure wave be derived from a radial pressure wave? *Br J Anaesth* 88:481–488, 2002.
19. Laurent S. Surrogate measures of Arterial Stiffness: do they have additive predictive value or are they only surrogates of a surrogate? *Hypertension* 47:325–326, 2006.
20. Murgo JP, Westerhof N, Giolma JP, Altobelli SA. Aortic input impedance in normal man: relationship to pressure wave forms. *Circulation* 62:105–116, 1980.
21. Jerrard-Dunne P, Mahmud A, Feely J. Ambulatory Arterial Stiffness index, pulse wave velocity and augmentation index—interchangeable or mutually exclusive measures? *J Hypertens* 26:529–534, 2008.
22. Wimmer NJ, Townsend RR, Joffe MM, Lash JP, Go AS. Correlation between pulse wave velocity and other measures of Arterial Stiffness in chronic kidney disease. *Clin Nephrol* 68:133–143, 2007.
23. London G, Guerin A, Pannier B, Marchais S, Benetos A, Safar M. Increased systolic pressure in chronic uremia. Role of arterial wave reflections. *Hypertension* 20:10–19, 1992.
24. Nakae I, Matsuo S, Matsumoto T, Mitsunami K, Horie M. Augmentation index and pulse wave velocity as indicators of cardiovascular stiffness. *Angiology* 2008.
25. Yasmin, Brown MJ. Similarities and differences between augmentation index and pulse wave velocity in the assessment of Arterial Stiffness. *Q J Med* 92:595–600, 1999.
26. Lacy PS, O'Brien DG, Stanley AG, Dewar MM, Swales PP, Williams B. Increased pulse wave velocity is not associated with elevated augmentation index in patients with diabetes. *J Hypertens* 22:1937–1944, 2004.
27. Lemogoum D, Flores G, Van den Abeele W, Ciarka A, Leeman M, Degaute JP, van de Borne P, Van Bortel L. Validity of pulse pressure and augmentation index as surrogate measures of Arterial Stiffness during beta-adrenergic stimulation. *J Hypertens* 22:511–517, 2004.
28. Vyas M, Izzo JL Jr, Lacourciere Y, Arnold JM, Dunlap ME, Amato JL, Pfeffer MA, Mitchell GF. Augmentation index and central aortic stiffness in middle-aged to elderly individuals. *Am J Hypertens* 20:642–647, 2007.
29. McEniery CM, Yasmin, Hall IR, Qasem A, Wilkinson IB, Cockcroft JR. Normal vascular aging: differential effects on wave reflection and aortic pulse wave velocity: the Anglo-Cardiff Collaborative Trial (ACCT). *J Am Coll Cardiol* 46:1753–1760, 2005.
30. Wilkinson IB, MacCallum H, Flint L, Cockcroft JR, Newby DE, Webb DJ. The influence of heart rate on augmentation index and central arterial pressure in humans. *J Physiol* 525 Pt 1:263–270, 2000.
31. Casey DP, Beck DT, Braith RW. Progressive resistance training without volume increases does not alter Arterial Stiffness and aortic wave reflection. *Exp Biol Med* (Maywood, NJ) 232:1228–1235, 2007.
32. Chiu YC, Arand PW, Shroff SG, Feldman T, Carroll JD. Determination of pulse wave velocities with computerized algorithms. *Am Heart J* 121:1460–1470, 1991.
33. Mitchell GF, Izzo JL Jr., Lacourciere Y, Ouellet JP, Neutel J, Qian C, Kerwin LJ, Block AJ, Pfeffer MA. Omapatrilat reduces pulse pressure and proximal aortic stiffness in patients with systolic hypertension: results of the conduit hemodynamics of omapatrilat international research study. *Circulation* 105:2955–2961, 2002.
34. Bland JM, Altman DG. Statistical methods for assessing agreement between two methods of clinical measurement. *Lancet* 1:307–310, 1986.
35. Weber T, Auer J, O'Rourke MF, Kvas E, Lassnig E, Berent R, Eber B. Arterial stiffness, wave reflections, and the risk of coronary artery disease. *Circulation* 109:184–189, 2004.
36. Pauca AL, Kon ND, O'Rourke MF. Benefit of glyceryl trinitrate on Arterial Stiffness is directly due to effects on peripheral arteries. *Heart (British Cardiac Society)* 91:1428–1432, 2005.
37. Mitchell GF, Conlin PR, Dunlap ME, Lacourciere Y, Arnold JM, Ogilvie RI, Neutel J, Izzo JL Jr., Pfeffer MA. Aortic diameter, wall stiffness, and wave reflection in systolic hypertension. *Hypertension* 51:105–111, 2008.
38. Sakurai M, Yamakado T, Kurachi H, Kato T, Kuroda K, Ishisu R, Okamoto S, Isaka N, Nakano T, Ito M. The relationship between aortic augmentation index and pulse wave velocity: an invasive study. *J Hypertens* 25:391–397, 2007.
39. Kelly RP, Millasseau SC, Ritter JM, Chowienczyk PJ. Vasoactive drugs influence aortic augmentation index independently of pulse-wave velocity in healthy men. *Hypertension* 37:1429–1433, 2001.
40. Hashimoto J, Nichols WW, O'Rourke MF, Imai Y. Association between wasted pressure effort and left ventricular hypertrophy in hypertension: influence of arterial wave reflection. *Am J Hypertens* 21:329–333, 2008.
41. Nichols WW, Estrada JC, Braith RW, Owens K, Conti CR. Enhanced external counterpulsation treatment improves arterial wall properties and wave reflection characteristics in patients with refractory angina. *J Am Coll Cardiol* 48:1208–1214, 2006.