Evaluating aortic stiffness through an arm cuff oscillometric device: is validation against invasive measurements enough?

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Introduction

Following the 2006 expert consensus document of the European Network for Noninvasive Investigation of Large Arteries [1], arterial stiffness and central pressure measurements should be considered as recommended tests for the evaluation of cardiovascular risk, particularly in patients in whom target organ damage is not discovered by routine investigations. Within the area of noninvasive methods, pulse wave recording and analysis either from central (ascending aorta, carotid artery) or peripheral (radial artery) sites have become popular, particularly after the release of dedicated commercial devices [2]. Theoretically, pulse wave analysis should allow calculation of at least three parameters related to arterial wall properties: central pulse pressure, central systolic pressure and the augmentation index (Aix). There is large consensus that these parameters should not be considered as direct measures of arterial stiffness, but rather as surrogate estimates. Conversely, most investigators [1] agree that pulse wave velocity (PWV) is the more direct measure of arterial stiffness. Unfortunately there are different definitions of PWV, and different measurement sites have been proposed while, at the same time, the number of published papers on the validity and prognostic value of carotid–femoral, aortic, brachial–ankle and local PWVs is constantly increasing. Carotid–femoral PWV (PWVcf), the 'gold standard' of arterial stiffness [1], and aortic PWV (PWVao) are supported by the largest amount of epidemiological evidence on their ability to predict cardiovascular events in specific subgroups of patients and, possibly, in the population at large. However, there is also increasing evidence that central Aix predicts all-cause mortality in end-stage renal disease and cardiovascular events in hypertension and coronary artery disease [1].

Nonetheless, even the most widely applied noninvasive methodologies for the assessment of PWV and pulse wave reflections have been criticized and shown to be affected by limitations and pitfalls, as recently reviewed by the group of Segers *et al.* [3]. Among the recently released new devices trying to overcome these shortcomings the Arteriograph (TensioMed Kft, Budapest, Hungary) takes a special position as it claims a completely different working principle. The Arteriograph is an oscillometric device that simultaneously measures peripheral and aortic systolic blood pressure (SBPao), aortic Aix (Aixao) and PWVao. Basically, it is a simple upper arm cuff connected to a piezo-electronic sensor that picks up pressure signals induced by the overpressurized (35 mmHg over the actual systolic pressure) cuff [4]. The designers and the manufacturer of the Arteriograph have postulated that correct measurements of central BP and stiffness indices are conditional upon a number of hypotheses underlying the working principle of the device:

(1) Correct assessment of the parameters requires measurement under strict stop-flow conditions (Bernouilli effect). The suprasystolic overinflation stands for a totally occluded artery. This condition is unique, as it is not fulfilled for the competing devices. The Arteriograph manufacturing team further claims simultaneous measurements of all parameters (including PWVao) from one single location (brachial artery).
(2) The conduit arteries (brachial, axillary, subclavian) act as a perfect cannula (as in a catheterization laboratory) that directly transfers central aortic pressure waves to the edge-positioned sensor at the occluded brachial artery level. This postulate would obviate the use of any kind of generalized or personalized transfer function.
(3) The brachial artery wall and surrounding tissue properties (such as the elastic behaviour, stress–strain relationships) play a negligible role.
(4) The reflected waves from the lower body (aortic–iliac bifurcation) can be picked up easily at the brachial cuff level. The basic postulate is that wave reflections are not unpredictably distributed along the whole aortic tree and its side branches, but can be condensed into the region of the aortic bifurcation, theoretically allowing correct assessment of the travel time between the reflection site and the arm cuff sensor. This is a key point for the calculation of PWVao by the device. As a consequence the time

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(measured at the brachial cuff) between the first systolic wave and the second systolic wave is the time needed for a wave to travel back and forth between the arm cuff and the aortic bifurcation.

(5) The true aortic length can be approximated with sufficient precision by externally measuring the distance between the sternal jugulum and pubic symphysis. Intrinsic common problems of external measurements such as obesity, and the tortuous aorta at older age, are not taken into account.

It is still a matter of debate whether these postulates and the working principle of the device hold true. The necessity of stop-flow conditions, the 'unique' reflection site at the aortic bifurcation, the assumption that PWVao can be derived from one single measurement and the assumption that the brachial sensor only picks up reflected waves from the lower body are among the most criticized items. In a first seminal paper, the group of Segers *et al.* [3] evaluated the working principle of the Arteriograph. In a numerical model of the arterial tree they simulated pressure and flow in a configuration with a fully occluded brachial artery and were able to produce the late reflected systolic peak at the site of the occluded brachial artery. The existence of that second peak was compatible with a forward compression wave. Initially they confirmed the working principle of the device; however, their work raised considerable concern on the magnitude of the unique late reflected second systolic peak. Moreover, the model failed to pinpoint the exact location of the source of the reflected waves. They were, in the end, unable to confirm the statement of a unique reflection site. One year earlier Westerhof *et al.* [5] in a more general paper already warned the scientific community that accurate location of reflection sites within the arterial tree would be elusive and that it is questionable that there would be one single location that generates the majority of reflections. The group of Segers *et al.* [6] very recently refined their analyses, suggested alternative explanations and even questioned the working principle of the Arteriograph based on theoretical computer model simulations. Using more in-depth wave intensity analysis, they suggested that it is more likely that the second systolic peak of the Arteriograph is the forward compression wave caused by a re-re-re-reflection of the first incidence wave, thus an alternative explanation would be a wave that is travelling back and forth several times between the occlusion at the brachial cuff and a branching point between the brachial artery and the aorta (in the subclavian–axillary region?). Thus, the Arteriograph essentially would pick up wave reflection phenomena confined to the stiffness of the brachial artery (axillo-brachial stiffness). Trachet *et al.* [6] further hypothesized that the good correlation of the PWV of the Arteriograph with established techniques might be owing to an intrinsic good correlation between brachial and central aortic stiffness. No doubt these suggestions are, in their turn, highly speculative and there is no need to emphasize that these data are model simulations and have not been validated against in-vivo catheterization data.

Invasive evaluation of the Arteriograph

In this issue of the Journal, Horváth *et al.* [7] evaluated the accuracy of the key parameters (Aixao, SBPao and PWVao) of the Arteriograph versus invasive measurements (by fluid-filled catheters) obtained during cardiac catheterization procedures in a limited (16–55) number of patients. Assessing the validity of the working principle of the Arteriograph or the physiology behind it was clearly out of the scope of the paper. Essentially, the authors report correlations and Bland–Altman plots supporting 'acceptable agreement' between the Arteriograph and invasive measurements. It should be realized that the agreement was far from optimal and that good agreement does not imply a proof of concept of the proposed methodology. It should be realized as well, in fairness, that the working principles and the methodology of the most important competing devices (Complior based on piezo-electronic detection and SphygmoCor based on applanation tonometry and a generalized transfer function) have also been the subject of a heavy controversy between several research groups. Among the many debated issues, most controversies related to the methodology of the assessment of central SBPao, Aix and PWV by commercially available devices focussed on topics such as need of a generalized transfer function, calibration of BP, pulse pressure augmentation in the upper arm versus the forearm, calculation of fiducial points on the pulse wave curve by nth derivatives, estimation of the path length in the calculation of PWV, 'gold standard' carotid–femoral versus regional PWV and many more [8–12]. Further discussion of all applications, implications, merits and limitations of the competing SphygmoCor and Complior devices is out of the scope of this editorial comment, however.

During the last 2 years, at least 3 important papers [13–15] presented head-to-head comparisons between the Arteriograph and the more widespread and more often evaluated commercially available devices. Baulmann *et al.* [13] showed excellent correlations between Aix of the SphygmoCor and Arteriograph. Correlations between the PWVs of the SphygmoCor, Complior and Arteriograph were only moderate, however. Rajzer *et al.* [14] described higher PWV by Complior than by SphygmoCor and Arteriograph, the latter being comparable. They attributed the differences primarily to differences in algorithms to measure travelled distance. The most recent paper by Jatoi *et al.* [15] emphasizes that although values for Aix and PWV are closely related between the devices and the determinants of Aix and PWV of the Arteriograph mirror the corresponding determinants for the two other devices, the three techniques are not interchangeable, as also discussed by Boutouyrie *et al.* [4] (Table 1).

Table 1 Summary of main advantages and limitations of three different techniques for arterial stiffness evaluation. Reproduced with changes from [4]

	Advantages	Limitations
Complior	The delay in pulse transit time between two arterial sites is taken simultaneously using a 'foot to foot' waveform method.	Operator's skill dependency.
	Numerous data on the prognostic value of cf-PWV so obtained are available.	Carotid tonometry is difficult.
		Necessity to undress the patient and expose the groin.
		Possibility of technical errors in obese patients.
		Uncertainty and approximation in measurement of distance between the two arterial sites.
		Theoretical risk of carotid plaque rupture by probe (never reported).
		Patients with atrial fibrillation cannot be evaluated.
		Unable to allow PWA.
		Underestimation of elevated PWV by built-in algorithm.
SphygmoCor	PWA is available allowing assessment of augmentation index and central BP through a transfer function application.	Operator's skill dependency.
	Numerous data on the prognostic value of the parameters so obtained are available.	Carotid tonometry is difficult.
		Necessity to undress the patient and expose the groin.
		Possibility of technical errors in obese patients.
		Uncertainty and approximation in measurement of distance between the two arterial sites.
		Theoretical risk of carotid plaque rupture by probe (never reported).
		Patients with atrial fibrillation cannot be evaluated.
		Debate regarding the validity of the generic transfer function used.
		Need of a precise BP calibration for PWA, currently not available.
		The PWV transit time delay is calculated using reference ECG signals obtained at different times respectively for carotid and femoral pulse waveforms sequentially recorded.
Arteriograph	The technique needs only access to the patient's upper arm (no need to undress).	Scarce data on its validation and on the prognostic value of parameters so obtained is available.
	It is based on an easy methodology (largely operator-independent method).	Patients with atrial fibrillation or marked bradycardia cannot be evaluated.
	It is a timesaving method. This fast assessment of arterial stiffness parameters is particularly suitable to population studies.	Working principle of the device yet not validated (measurements of brachial or of aortic stiffness?).
	Higher reproducibility of parameters, as compared with the two other methods.	
	Potentially adaptable to ambulatory arterial stiffness assessment.	

BP, blood pressure; Cf-PWV, carotid–femoral pulse wave velocity; PWA, pulse wave analysis; PWV, pulse wave velocity.

The critical issue is whether one positive state-of-the-art evaluation by invasive measurements is enough to recommend the Arteriograph as a peer competitor of the multi-evaluated Complior and SphygmoCor and sufficient to overrule the criticisms mentioned above. It has to be clarified, on the other hand, whether numerical models or method comparisons without an invasive counterpart can be regarded to be at least as convincing as invasive measurements are. It should be remembered that there are also invasive data available to support the validity of the competing commercial devices. For instance, recently Weber *et al.* [16] demonstrated an 'acceptable' correspondence between PWVcf (SphygmoCor) and invasive PWV in 135 patients, particularly for the method of subtracting carotid–suprasternal notch distance from suprasternal notch–femoral distance. Another recent example is the excellent accuracy, with an exception for the lower BP range, of the second systolic peak of the SphygmoCor versus invasive measurements [17].

Perspectives for the future

The Arteriograph is a relatively new oscilllometry-based device that is easy to use and allows simultaneous assessment of central BP, Aix and PWV independently of radial artery tonometry or generalized transfer functions and without the need to obtain measures at two different sites to generate PWV values. Notwithstanding sound criticisms questioning its working principle, recent publications showed 'acceptable' agreement between PWV and Aix of the Arteriograph and the SphygmoCor and the Complior. The paper of Horváth *et al.* [7] in this issue of the Journal adds an important piece of information to the puzzle: that is the demonstration of an 'acceptable' agreement between the parameters delivered by the Arteriograph and invasive data from the catheterization laboratory. At the time being, it is still uncertain whether the paper of Horváth *et al.* [7] will be enough to convince the medical society to introduce the device in clinical practice. Certainly, further investigations are still needed, among which studies aimed at providing an invasive validation of the working principle of the Arteriograph, which, at this point, probably represents the most controversial issue.

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