

Obtaining arterial stiffness indices from simple arm cuff measurements: the holy grail?

Pierre Boutouyrie^{a,b}, Miriam Revera^{c,d} and Gianfranco Parati^{c,d}

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^aUniversité Paris Descartes; INSERM, U970, ^bDepartment of Pharmacology, Assistance Publique-Hôpitaux de Paris, Hôpital Européen Georges Pompidou, Paris, France, ^cDepartment of Clinical Medicine and Prevention, Milano-Bicocca University and ^dDepartment of Cardiology, IRCCS San Luca Hospital, Istituto Auxologico Italiano, Milan, Italy

Correspondence to Professor Gianfranco Parati, MD, Department of Cardiology, San Luca Hospital, Istituto Auxologico Italiano, Via Spagnoletto 3, 20149 Milan, Italy
Tel: +39 02 6191 12890; fax: +39 02 6191 12956;
e-mail: gianfranco.parati@unimib.it

See original paper on page 2186

Precise assessment of cardiovascular risk factors is a necessary step for the identification of patients at high risk of developing cardiovascular events. When setting the operating curve of the risk function, measurement of blood glucose and lipids, estimation of blood pressure (BP) levels, identification of smoking status, and assessment of existing organ damage represent the main determinants of the tendency to develop cardiac and vascular problems over and above the impact of nonmodifiable factors such as age and sex. Each of these classical risk factors is included in a risk function specific to a given population and aimed at yielding absolute quantitative values of cardiovascular risk [1,2]. Such an approach, in spite of its clinical usefulness, is affected by important limitations. This is because the importance of any modifiable risk factor and its ill effects is highly variable in individual patients, with most of their risk level depending on nonmodifiable characteristics and/or on the complex interaction between a variety of mechanisms. The usual and disappointing result of this classical approach to cardiovascular risk assessment is the possibility to target a very small number of patients at a very high risk only. This allows prevention of only a minority of the total burden of cardiovascular events, as most of them occur in the large majority of patients with only marginally elevated levels of risk [3].

In this context, the quest for new markers of risk offering better identification of patients worth receiving preventive intervention is intense. When focusing on patients with arterial hypertension, markers of target organ damage, such as left ventricular hypertrophy and microalbuminuria, have demonstrated their predictive value, both at baseline and following treatment [4]. More recently, large artery properties, such as intima-media thickness and arterial stiffness, have also been proposed

as useful indices of hypertension target organ damage and, thus, as clinically relevant new risk factors.

Several methods have been developed over the years to assess arterial stiffness in humans. Overall, three main groups of techniques can be identified: methods based on the analysis of arterial pressure pulse waveform, methods based on the quantification of pulse transit time, and methods based on a direct estimation of arterial stiffness through the assessment of arterial diameter and of the corresponding distending pressure [5]. The method most commonly employed in this setting is the assessment of carotid-femoral pulse wave velocity (cf-PWV), which is also the method most frequently shown to carry prognostic information. Indeed, the predictive value of arterial stiffness, measured through cf-PWV, has been demonstrated in more than 11 independent studies, being beyond and above that of the classical risk factors [6]. In particular, the prognostic value of arterial stiffness has been demonstrated in hypertension [7], type II diabetes [8], end-stage renal disease [9], and in the general population [10]. Moreover, the prediction of cardiovascular risk was shown to be improved by inclusion of cf-PWV in the risk equation [10,11]. This has led arterial stiffness through cf-PWV to be recommended in the current European Society of Hypertension (ESH) and European Society of Cardiology (ESC) guidelines for risk assessment in hypertension [4]. At the present time, the two most commonly employed noninvasive methods that allow the measurement of cf-PWV are those implemented in the Complior (Artech Medical, Pantin, France) and in the Sphygmocor (AtCor Medical, Sydney, Australia). These methods are considered as techniques of reference, although they differ according to certain aspects [12].

There are currently two major limitations for a wider use of arterial stiffness assessment in the routine management of patients, in particular, of those with high BP. First, the lack of undisputable reference values for arterial stiffness interpretation as 'being normal' or 'pathologically increased'. This subject is currently addressed by large multicenter studies, and the necessary information should be provided in the near future [13]. Second, measurement of cf-PWV is still technically demanding and not easy to implement in daily practice. The patient under evaluation has to remain still in a steady-state condition for a few minutes, whereas the two mechanosensors have to be firmly positioned on the carotid artery and the femoral artery throughout the

recording time. This is not free from difficulties, including the fact that exposure of the groin, which is necessary to detect femoral pulse waves, is considered somewhat embarrassing in many cultures. Moreover, applying a captor firmly on the carotid artery may be risky in the presence of unstable plaque (although rupture of an atherosclerotic plaque has never been described under these conditions).

In this context, the emergence of new techniques allowing measurement of PWV by considering a single site of measurement and making use of a simple oscillometric arm cuff represents a very interesting novelty. A system based on this approach is now commercially available known as Arteriograph (TensioMed Ltd., Budapest, Hungary). This is a recently developed, computerized device using an oscillometric method to determine PWV, augmentation index (AIx) and central systolic blood pressure (SBPao). In the study by Jatoi *et al.* [14], published in the present issue of the journal, the clinical performance of the Arteriograph is evaluated against the Sphygmocor and the Complior devices. The elegant technique implemented in the Arteriograph takes advantage of a cuff measure of BP by using a high fidelity pressure sensor giving good quality pressure traces. The inventors of the technique noticed that during suprasystolic (+35 mmHg) cuff inflation,

the late systolic peak on the BP waveform, corresponding to the reflection of BP waves from the aortic bifurcation point, appeared more clearly. The time delay between the peak of the pressure wave and the late systolic peak represents twice the time taken by the pressure wave from the heart to the main reflection site (usually considered to be at the aortic bifurcation, the distance between heart and aortic bifurcation being approximated by distance between the sternal notch and pubian symphysis). An additional fascinating feature of this technique is the possibility of its easy future adaptation to ambulatory measurements of arterial stiffness.

Two previous studies [15,16], recently published in this journal, have evaluated the relationship between data taken from the Arteriograph and the two 'classical methods' for the assessment of PWV. The interest of the present study by Jatoi *et al.* [14] is that the study was done in a large population of 254 untreated hypertensive patients, and that the authors also analyzed the determinants of PWV and AIx, when recorded by the different devices. The results are similar to those of the two previous studies published on this issue, confirming a close agreement between the arterial stiffness parameters provided by Arteriograph, Complior, and Sphygmocor. Similar results were also obtained when assessing the

Table 1 Summary of main advantages and limitations of three different techniques for arterial stiffness evaluation

Device	Advantages	Limitations
Complior	<ul style="list-style-type: none"> The delay in pulse transit time between two arteries sites is taken simultaneously using a 'foot to foot' waveform method Numerous data on the prognostic value of cf-PWV so obtained are available 	<ul style="list-style-type: none"> Operator's skill dependency Carotid tonometry is difficult Necessity to undress 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	<ul style="list-style-type: none"> PWA is available allowing assessment of augmentation index and central BP through a transfer function application Numerous data on the prognostic value of the parameters so obtained are available 	<ul style="list-style-type: none"> Operator's skill dependency Carotid tonometry is difficult Necessity to undress 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	<ul style="list-style-type: none"> The technique only needs access to the patient's upper arm (no need to undress) It is based on an easy methodology (largely operator-independent method) It is a time-saving method. This fast assessment of arterial stiffness parameters is particularly suitable to population studies Higher reproducibility of parameters, as compared with the other two methods Potentially adaptable to ambulatory arterial stiffness assessment 	<ul style="list-style-type: none"> Scarce data on its validation and on the prognostic value of parameters so obtained are available Patients with atrial fibrillation or marked bradycardia cannot be evaluated

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

determinants of PWV and AIx making use of any of these three devices. However, at least in the population of the study by Jatoi *et al.* [14], the limits of agreement when comparing the data provided by the three devices were quite wide. This indicates that these techniques for arterial stiffness assessment are not interchangeable. In Table 1, the main advantages and limitations of each of these three techniques are summarized. The results also indicate that the 'gold standard' in this field still needs to be identified, an issue that deserves to be addressed in a specific study.

It has to be emphasized that this study raises a number of questions. First, it is still unknown what the minimal level of agreement between techniques, for them to be used interchangeably, might be. Second, it needs to be clarified whether we need data illustrating prediction of morbidity and mortality for each new technique, even when they are assessing a parameter, which has previously been shown to have an independent prognostic value. Finally, and most importantly, the biggest question is 'How and when should we use any measure of arterial stiffness in clinical decision-making?'. This question has yet to be addressed properly.

To our knowledge, the demonstration of a better risk stratification, leading to better care of patients by using arterial stiffness indices, has only been shown in a small group of patients with end-stage renal disease [17]. Similar studies are needed in more general populations.

Moreover, for a meaningful risk stratification, we need to have undisputable reference values for a patient to be classified as having elevated arterial stiffness. We also need to know which therapeutic interventions might be beneficial in patients with elevated arterial stiffness. Needless to say, the availability of a simple, affordable, and easy to apply technique will be of great help in this regard.

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John Feely died in June 2009 at the untimely age of 61 years. As Professor of Pharmacology and Therapeutics at Trinity College and St. James's Hospital, Dublin, for 25 years, he led a department with a reputation for excellence in teaching, research, and health service delivery. John leaves a legacy of greater than 300 original published articles describing important findings concerning drug metabolism, pharmacoepidemiology, pharmacoeconomics, cardiovascular medicine, and hypertension.

Most recently, as illustrated by the article published in this issue of the journal, arterial stiffness had been a particular interest. John, a distinguished clinician, educator, and researcher, will not only be sadly missed by his family and friends but also his absence will be mourned by patients and students, and by medical and scientific colleagues in Ireland and abroad.

Alice Stanton is a member of the Molecular and Cellular Therapeutics and RCSI Research Institute, Royal College of Surgeons in Ireland, Dublin, Ireland.

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