Measurement of Arterial Stiffness: Why should I measure both PWA and PWV?

Central blood pressure and measures of arterial stiffness have been shown to be powerful predictors of major cardiovascular events, independent of the traditional risk factors. Furthermore, they have also become important targets for examining the effect of different types of treatment.

Arterial stiffening is typically observed in a number of conditions including hypertension, diabetes, and renal disease. With the significant morbidity and mortality rate worldwide for cardiovascular diseases and related conditions, the ability to improve the assessment of cardiovascular function and cardiovascular risk and therapeutic treatment is of paramount importance.

The two most frequently used methods for measurement of arterial stiffness are PWV and aortic (or central) PWA. The values obtained from these measurements are not interchangeable, but instead coupled together provide a comprehensive approach to the assessment of cardiovascular risk.

What is arterial stiffness and why should it be measured?

In healthy and compliant arteries the pressure waves (generated by the left ventricle) travel through the arterial tree and are reflected at multiple peripheral sites. As a result, the arterial pressure waveform at any site is a combination of the forward travelling waveform and the backward (or reflection) waveform. The two waveforms merge during diastole and augment coronary perfusion. With ageing, the arterial wall thickens and the arteries get stiffer. As a result, the pressure waves travel faster and the reflected pressure wave returns during the systolic phase, increasing systolic pressure and thus increasing left ventricular load [1].

Conventional brachial cuff blood pressure measurements are commonly used to measure arterial pressure and do not measure reflected waves, or the additional pressure exerted on the heart from stiff arteries. More recently, it has been acknowledged that central pressure may not be the same as that measured at the arm [2, 3]. This was demonstrated in the Anglo-Cardiff Collaborative Trial II where data from 10,600 individuals showed that central pressure cannot be reliably inferred from peripheral pressure due to the variation in the gradient between central and peripheral pressures [4].

How is arterial stiffness measured?

In addition to the systolic and diastolic blood pressure values, additional information can be provided by examining the morphology and timing of the pressure waveform itself. The most widely used device in clinical studies is the SphygmoCor device [3] which allows for both PWA and PWV to be performed non-invasively using the gold standard techniques [3, 5, 6].

Pulse Wave Velocity (PWV)

Aortic PWV is a direct measurement of aortic stiffness and is considered to be the gold standard of arterial stiffness measurements [7]. PWV is a measure of the speed of the arterial pressure waves travelling along the aortic and aorto-iliac pathway. Higher arterial pressure wave velocity is indicative of stiffer arteries.

The most common technique for measuring PWV is through the non-invasive method of applanation tonometry [8]. In general, measurements are performed by recording pressure waveforms at the carotid artery followed by the femoral artery, with an ECG signal being recorded simultaneously. PWV is calculated using the mean time difference and the arterial path length between the two recording sites.
**Pulse Wave Analysis (PWA)**

The most widely used device in clinical studies for PWA measures the arterial pressure waveform at the radial artery and applies a validated generalised transfer function to provide the central pressure waveform [3, 9, 10]. Analysis of the aortic pressure waveform provides a measure of central blood pressure and indices of systemic arterial stiffness, such as Augmentation Pressure (AP) and Augmentation Index (AIx). These indices are related to the reflected pressure waves from the peripheral arterial system, either as a direct increase in pressure at the heart from the reflected wave (AP) or as a percentage of pulse pressure (AIx).

**Clinical relevance of Arterial Stiffness measurement.**

PWA and PWV have been performed extensively in healthy individuals and in clinical populations with a variety of diseases. These studies have shown that PWA and PWV are different in various clinical populations compared to healthy individuals and can be changed by therapeutic treatments.

**Effect of ageing**

While central pressure measurements (PP, AP and AIx) and aortic PWV all increase significantly with age, AIx and PWV follow different patterns [11]. Changes in AIx have been shown to be more prominent in people below 50 years of age, whereas changes in aortic PWV are more marked in individuals over 50 years of age, as shown in Figure 1.

![Figure 1](image)

Therefore, it has been suggested that AIx should be used to determine risk in patients below the age of 50, and that PWV used in patients over the age of 50, when the changes in aortic stiffness are likely to be more prevalent [11].

**Predictors of Cardiovascular disease and events**

Central blood pressure has been shown to be a significant predictor of cardiovascular events in observational studies [12, 13] and over a range of diseases, such as coronary artery disease [14, 15, 16, 17], end stage renal disease [18] and diabetes [19] as well as in the elderly [20]. Importantly, pulse pressure (PP), and in particular central PP have been shown to better predict cardiovascular events than brachial blood pressure [12]. Data from the Strong Heart Study\(^1\) found that central pulse pressure predicted cardiovascular events more strongly than brachial pulse pressure, independently

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\(^1\) The Strong Heart Study is an observational study of prevalent and incident cardiovascular disease and their risk factors in American Indians.
of traditional risk factors, such as age, smoking, gender and cholesterol [12]. Furthermore, data from the same study showed in a 5-year follow-up that quartiles of central PP predicted cardiovascular outcomes more strongly than quartiles of brachial PP. Having a central PP, ≥ 50 mmHg, doubled the risk of heart attack or stroke in both men and women, in the presence or absence of diabetes, and in people younger or older than 60 years of age [13], as shown in Figure 2.

Similarly, aortic PWV [21, 22, 23] and AIx [22] have been shown to be independent predictors of cardiovascular (and all-cause) mortality in chronic kidney disease. In end stage renal failure patients for each increase in AIx (%) of 10, the risk of cardiovascular and all-cause mortality is increased by around 50% and that for any increase of PWV of 1 m/s there was a 39% increase in adjusted overall mortality, independent of other factors known to affect the outcome of on haemodialysis [22], as shown in Figure 3.

In diabetic patients, aortic PWV has also been identified as an independent predictor of mortality [24]. The risk of mortality doubled for patients with diabetes or glucose intolerance in a study with a 10 year follow-up period. For each increase in PWV of 1 m/s there was an 8% increase in the risk of mortality.
An increase in Alx and aortic PWV have also been shown to be independent predictors of cardiovascular events in the general population and in patients with cardiac disease, hypertension and diabetes [12,13,25,26,27,28,29,30,31,32].

As PWA is measures the CV risk of stiff peripheral arteries, and aortic PWV is measures the CV risk from central aortic stiffness, it is important that both PWA and PWV are measured, as increases in both indexes have been shown to be predictors of cardiovascular risk.

**Precursor to Hypertension**

Measures of aortic stiffness and pressure wave reflection have recently been shown to be related to future incident hypertension. As part of a community-based study, around 1700 participants with normal BP (from the Framingham Offspring cohort\(^2\)) were examined over a 7 year period to examine the relationship of arterial stiffness and progression to High BP. Aortic PWV, Alx and amplification of the forward wave were found to be related to development of high Systolic Blood pressure in the future. This study demonstrated that higher arterial stiffness was predictive of incident hypertension [33] rather than a result of hypertension.

**Response to treatment**

Over the last decade there has been an increasing awareness that beneficial effects of various therapies may be from improvements in central blood pressure and/or arterial stiffness, and these beneficial cardiovascular outcomes may be observed beyond brachial blood pressure. Furthermore, indices of arterial stiffness can be influenced independently of each other and therefore should not be considered interchangeable.

In the largest prospective evaluation of cardiovascular drugs on central blood pressure and haemodynamics to date, the CAFÉ study\(^3\), differential effects of treatment can be seen in central blood pressure despite a similar effect on brachial blood pressure. The improvement in central systolic and pulse pressures following amlodipine/perindopril therapy are considered to have played a role in the superior cardiovascular outcomes observed in the larger ASCOT trial and would not have been detected if only brachial blood pressure was measured [34].

The results of this trial were consistent to that of a similar study, REASON project [35], and with a number of smaller short term studies in hypertension [36, 37, 38, 39, 40, 41, 42, 43].

Like central blood pressure, improvement in aortic PWV has also been shown to be independent of brachial BP. In a group of end stage renal patients treated with an ACE inhibitor patient survival was significantly better for those patients whose aortic PWV was lowered with the blood pressure lowering treatment, as shown in Figure 4.

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\(^2\) The Framingham Heart study has followed three generation of participants since 1948 to identify common factors or characteristics that contribute to cardiovascular disease. The Original Cohort consisted of 5209 participants aged 30-62 years. In 1971 the Offspring Cohort Study commenced and included 5124 men and women consisting of offspring from the Original Cohort and their spouses. Participants have undergone cardiovascular examinations every 4-6 years and PWA and PWV measurements have been included since cycle 7 (1998-2001).

\(^3\) CAFÉ study – Conduit Artery Function Evaluation study was a makor sub-study within the Anglo-Scandinavian Cardiac Outcome Trial (ASCOT) conducted across 5 centres in the UK and Ireland. Over 2000 patients with either untreated or treated hypertension participated in the study for up to 4 years, during which time multiple blood pressure measurements were made.
In the REASON\(^4\) study, a large trial that extended over 12 months, PWV was equally reduced with both drug regimes, (perindopril/indapamide combination compared with atenolol), but a greater reduction was observed in AIx with the combination therapy [44]. More recently the effects on both AIx and PWV were examined using drugs from 4 different major antihypertensive classes and while some of the antihypertensive agents had a beneficial effect on AIx, aortic PWV was not changed by any of the drugs [36].

The effects of antihypertensive drugs on arterial stiffness are complex. Many drugs have different actions and measures of wave reflection from PWA, such as AIx can change independently of PWV, and vice versa. Together they provide information on the effects on large artery tone as well as small artery tone and function (which influences wave reflection). Arterial stiffness can be used a target for treatment as well as a measure for how effective a treatment is.

**PERSPECTIVE**

Pulse wave analysis and pulse wave velocity are two measurements for assessment of cardiovascular risk and evaluation of treatment. Although PWA and PWV are measures of arterial stiffness, they can differ based on the age of the patient and the medication that the patient may be taking, and thus together they offer a deeper assessment of cardiovascular risk and subsequent treatment options, and it is important to note that these measurements are not interchangeable.

When selecting a device to measure arterial stiffness, it is important that the device measures both PWA and PWV using validated methods. The SphygmoCor device is the most widely used device in clinical trials and offers both measurements using gold standard techniques.

References


\(^{4}\) REASON project – pREterax in regression of Arterial Stiffness in a controlled double blind study was a multicentre trial conducted across 13 countries.


