Why do we need to measure more than central blood pressure alone?

While the prognostic value of brachial blood pressure is well established, there is now ample evidence of the pathophysiological importance of central haemodynamic measurements. Central (aortic) systolic and diastolic pressures are determinants of cardiac loading and coronary perfusion and are significant in identifying and understanding the development of cardiovascular disease. Central blood pressure and measurements taken from the central arterial pulse wave have been shown to be powerful predictors of major cardiovascular events, independent of the traditional risk factors, including brachial blood pressure. Furthermore, they are important markers for evaluating the effect of treatment.

The European Society of Hypertension\(^1\), as well as leading clinicians and researchers have recognized the importance of these values, specifically central SBP, PP and Aix. These measures of arterial wave reflection indices and central pressure (along with aortic PWV) provide a comprehensive and integrated approach to total cardiovascular assessment of a patient \([1, 2, 3, 4, 5]\).

**PWA and central blood pressure**

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 resulting in the pressure waves travelling faster and the reflected pressure wave returning during the systolic phase. This increases aortic systolic pressure, widens pulse pressure and increases left ventricular load \([6]\).

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), as shown in Figure 1. 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). Aix represents a complex measure of wave reflection and includes a component of arterial stiffness.

![Figure 1. Central pressure waveform.](image)

A salient feature of the arterial pressure waveform is that it changes shape as it travels away from the heart. The diastolic and mean pressure change little across the arterial tree, but the systolic pressure is amplified as it travels from the aorta to the periphery \([7]\). This pulse pressure amplification is important

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when considering the relationship between brachial and central blood pressure as the pulsatile components may vary significantly. 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 [8].

The most widely used device in clinical studies for PWA, the SphygmoCor, measures the arterial pressure waveform at the radial artery and applies a validated generalised transfer function to provide the central pressure waveform [2, 9, 10]. Along with central systolic blood pressure, a number of PWA indices provided have been shown to have clinical relevance.

**Predictors of disease and events**

Central blood pressure and Alx have been shown to be a significant predictor of all-cause mortality and or major cardiovascular events in observational studies and over a range of diseases, such as coronary artery disease, end stage renal disease and diabetes as well as in the elderly [11, 12, 13, 14, 15, 16, 17, 18, 19, 20, 21, 22]. Moreover, these measurements have been shown to be independent of brachial blood pressure.

Pulse pressure (PP), and in particular central PP have been shown to better predict cardiovascular events than brachial blood pressure [11]. Data from the Strong Heart Study found that central pulse pressure predicted cardiovascular events more strongly than brachial pulse pressure, independently of traditional risk factors, such as age, smoking, gender and cholesterol [11]. 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 [12], as shown in Figure 2.

Central pressure has also been shown to be more closely related to other important cardiovascular intermediate endpoints such as left ventricular hypertrophy (LVH). LVH is commonly seen in hypertension and increases the risk for cardiac events, mostly as a result of increased left ventricular mass due to an increase in afterload of the left ventricle [23]. Recent work from the Strong Heart Study has shown that central systolic pressure has a stronger association with LVH than brachial or pulse pressure [24, 25].

Central Alx has also been shown to have a significant correlation with LVH, as seen in end stage renal patients [26]. In a group of renal patients on haemodialysis, an increased Alx was associated with the development of LVH, independent of other factors known to influence cardiac structure in ESRD patients, as shown in Figure 3. Furthermore, Alx is a strong independent predictor of cardiovascular (and all-cause) mortality in end stage renal failure. For each 10% increase in Alx, the risk of cardiovascular events or all-cause mortality increases by approximately 50% (RR of 1.51 and 1.48, respectively) [20].

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2 The Strong Heart Study is an observational study of prevalent and incident cardiovascular disease and their risk factors in American Indians.
Similarly, central AIX has been shown to be an independent predictor of severe cardiovascular events in patients with coronary artery disease [17, 18] and even in males in the general population without a history of cardiovascular disease [13].

A recent systematic review of pooled data of over 5500 patients confirms that central AIX is predictive of cardiovascular events and all cause mortality in a range of populations [3]. For an absolute increase in AIX of 10% the risk for cardiovascular events increased by 31.8% and the risk for all cause mortality increased by 38.4%.

The ability to measure central blood pressure and indices of wave reflection, such as AIX contributes valuable information on the cardiovascular risk of a patient.

**Precursor to hypertension**

Recent findings from a large a comprehensive longitudinal study have found that central AIX and forward wave amplitude are related to future systolic blood pressure, PP and incident hypertension. The community-based study of around 1700 normotensive participants (from the Framingham Offspring cohort) examined over a 7-year period showed that an increase in arterial stiffness was predictive of developing hypertension [27]. Treatments targeting arterial stiffness and function may play a significant role in prevention of incident hypertension. Arterial stiffness, as measured by AIX, may become a treatment target in the future.

**Response to treatment**

Over the last decade there has been an increasing awareness that beneficial effect of pharmacological therapies beyond brachial blood pressure. As such, it is considered that the additional effects antihypertensive drugs have on central haemodynamics is associated with their ability to modify arterial properties, such as stiffness of large vessels (via pulse wave velocity) and pressure wave reflections via AIX. Although the current antihypertensive drugs have not been specifically designed to lower arterial stiffness, it is possible to assess the effect they have had either directly or indirectly on these arterial properties.

In the largest prospective evaluation of cardiovascular drugs on central blood pressure and haemodynamics to date, the CAFÉ study, differential effects of treatment can be seen in central blood pressure despite a

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3 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).

4 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
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 [28].

In a similar study of high risk patients with essential hypertension that extended over 12 months (REASON trial) brachial and central SBP, PP and AIx were all significantly lower in patients on combination therapy (perindopril/indapamide), with central changes being more pronounced than brachial changes [29]. These results are consistent with a number of smaller short term studies in hypertension [30, 31, 32, 33, 34, 35, 36, 37].

A recent study has also shown that an individual class of hypertensive drug should not be considered as a homogenous group and differences in hemodynamics can be observed. In this study, a relatively new beta blocker, Nebivolol, which is considered to have ancillary vasodilatory properties, provided a significantly greater reduction in central PP, AIx and PP amplification compared with atenolol, a standard beta blocker, in patients with essential hypertension [32].

Atenolol has also been shown to significantly increase central AIx, while still being able to reduce both brachial and central SBP.

These studies highlight the importance of measuring central haemodynamic measures including AIx and central pulse pressure in patient treatment. This may help to explain why some drugs with a similar effect on brachial pressure but a different affect on central blood pressure and significantly different cardiovascular outcomes.

**Perspective**

Central arterial blood pressure and measures of arterial stiffness and wave reflection are important measures for assessment of cardiovascular risk and evaluation of treatment. Central SBP, PP and AIx have all been shown to be powerful predictors of major cardiovascular events across a range of diseases. Central SBP has consistently been shown to be better than brachial blood pressure in the determination of cardiovascular risk and the measurement of central PP, AP and AIx provide additional information on the arterial stiffness of a patient, known to be a risk factor for the development of hypertension. As a result, all of these measurements should be measured and taken together to develop an accurate assessment of the patient’s cardiovascular risk. These measurements have also become significant markers in the evaluation of, as well as potential targets for treatment.

When selecting a device to measure arterial stiffness, it is imperative that the device measures central SBP as well as central PP, AP and AIx using validated methods. The SphygmoCor device is the most widely used device in clinical trials and provides this information easily using gold standard techniques.

**References**


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treated hypertension participated in the study for up to 4 years, during which time multiple blood pressure measurements were made.

5 REASON project – pREterax in regression of Arterial Stiffness in a controlled double blind study was a multicentre trial conducted across 13 countries.


23. Kaplan NM and Douglas PS. Clinical implications and treatment of left ventricular hypertrophy in hypertension. 2011,


Note alternative picture to Figure 1.