Advancements in Blood Pressure Management

New technology for better management of anti-hypertension medications and improved assessment of cardiovascular risk

For over 100 years, physicians have relied on the systolic and diastolic pressures measured with a brachial cuff sphygmomanometer to manage their patients. However, blood pressure in the brachial artery can be very different from the pressure at the heart, and numerous recent studies have shown that blood pressure at the heart explains the effects of anti-hypertensive drugs and predicts clinical outcomes significantly better than brachial pressure. Today, new technology allows the noninvasive measurement of the central blood pressure with the same fidelity as a pressure catheter placed in the ascending aorta, without the associated costs and risks. The predictive superiority of central blood pressure over brachial blood pressure is primarily due to the closer proximity of the ascending aorta to important target organs such as the heart, brain, and kidney.

Three aspects of central blood pressure are especially important:

- Individual variability in the difference between central and brachial pressures can be significant and clinically important.
- Central pressures cannot be reliably inferred from brachial pressures.
- Medications may have significantly different effects on brachial blood pressure than on central blood pressure.

Noninvasive Central Blood Pressure Measurement

Central systolic blood pressure cannot be estimated from the brachial systolic value. McEniery et al. reported a study of over 10,000 adults aged 18 to 101 years whose individual brachial systolic pressures ranged from 100 to 200mmHg. They found individual variability between brachial and central systolic pressures ranged from as few as 2-3mmHg to approximately 30mmHg. The variations decreased with age, but even in the oldest adults averaged approximately 10mmHg. Central pulse pressure also showed a large degree of variability. In addition, central pulse pressure increased continually over the age range while brachial pulse pressure declined up to age 60 and then increased as individuals aged further. Because of such individual variability, central pressure cannot reliably inferred from brachial pressure measurement.

The SphygmoCor XCEL System derives the central aortic pressure waveform using a standard blood pressure cuff. The pressure oscillations in a partially-inflated cuff are analyzed to produce the central aortic pressure waveform. As in previous tonometer-based SphygmoCor systems, generalized transfer functions are used to derive the central aortic pressure waveform and corresponding indices (Figure 1). The SphygmoCor XCEL was cleared by the US Food and Drug Administration as substantially equivalent to previously validated SphygmoCor systems. The procedure can be conducted in the office setting with minimal training and is quick, easy to perform, painless and reproducible.

![Figure 1](image)

Figure 1: An example of two patients with the same brachial systolic/diastolic pressures (144/90), but significantly different central systolic pressures (122/90 and 136/90). Left panel – peripheral waveform, Right panel – central aortic waveform.
Central Blood Pressure, Cardiovascular Risk, and Hypertension
Numerous studies in both healthy and diseased subjects have consistently demonstrated that elevated central blood pressure is independently associated with increased cardiovascular events and is superior to brachial pressure as a predictor of those events. In a report from the Strong Heart Study, a multi-year NIH-funded study, Roman et al. reported that in 2,405 individuals central pulse pressures were more strongly predictive of cardiovascular events, independent of brachial pressures. Specifically, when central pulse pressure equals or exceeds 50mmHg, the risk of cardiovascular disease increases by nearly 70%; in individuals younger than 60 years, the increase was 150%. The risk for those whose central pulse pressure was less than 50mmHg was statistically the same across all lower pulse pressures. Thus, in this study, 50mmHg represents a threshold above which the risk of a cardiovascular event increases dramatically. Brachial pressure did not demonstrate the same threshold for risk. Elevated central pressure and central pressure indices are also predictive of numerous types of end-organ damage, as well as morbidity and mortality. The evidence has been reviewed by Nelson et al. in Mayo Clinic Proceedings.

Several studies have shown that central pressure and central pressure indices can distinguish those individuals who, although not hypertensive, can be found to have end-organ damage. Just as importantly, brachial pressures could not make such a distinction. In a study of 1,169 participants, Boosens et al. reported that the classes of normal vs. high normal brachial blood pressure did not distinguish those with or without end-organ damage. However, when the same group was divided according to normal vs. high normal central systolic pressure, the groups with and without such damage could be identified. Also, Kaess, in a report from the Framingham Heart Study, showed that central pressure augmentation index predicted the development of hypertension in those who were originally normotensive. Brachial pressure measurements were not predictive of the development of arterial stiffness, a major indicator of end-organ damage. Conversely, a European study of 354 young and middle age people with untreated Stage 1 hypertension showed that those with low central systolic pressure (<125mmHg) were at significantly less risk of requiring antihypertensive medication than those with high central systolic pressure.

### Table 1: Comparative Effects of Antihypertensive Medications on Central Hemodynamic Indices

<table>
<thead>
<tr>
<th>Class</th>
<th>Central Systolic Pressure</th>
<th>Augmentation Index</th>
<th>Arterial Stiffness</th>
</tr>
</thead>
<tbody>
<tr>
<td>ACE inhibitors</td>
<td>↓↓</td>
<td>↓↓</td>
<td>↓</td>
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<tr>
<td>Angiotension-receptor blockers</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
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<tr>
<td>Beta-blockers (non-vasoactive)</td>
<td>↑</td>
<td>↑</td>
<td>↓</td>
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<tr>
<td>Calcium-channel blockers</td>
<td>↓</td>
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<tr>
<td>Diuretics</td>
<td>↔</td>
<td>↔</td>
<td>↔</td>
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<tr>
<td>Nitrates</td>
<td>↓↓</td>
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Waveform physiology overview
While blood pressure is most often characterized in terms of simply a maximum (systolic) and a minimum (diastolic) pressure, it is actually a continuous wave made up of the summation of pressure waves generated by the heart’s contraction and the pressure reflected back toward the heart from the peripheral arterial tree as the outgoing wave meets branches or other sources of impedance mismatch. The interaction of these two waves is strongly affected by the speed of the transmitted and reflected waves – the faster the wave travels, the less separation there is between the two. The primary determinant of the wave speed is arterial stiffness. The central pressure waveform, especially during systole, differs in various parts of the arterial tree if, for example, the reflected wave occurs earlier or later in the cardiac cycle (Figure 2).

Central Pressure Indices
A number of clinically important central pressure indices can be derived from the central pressure waveform captured using the SphygmoCor System, including central systolic, central diastolic and central pulse pressure (Figure 3). Additionally, augmentation pressure (AP), the increase in systolic pressure due to early return of the reflected wave, and augmentation index (Alx), the ratio of augmentation pressure to the central pulse pressure expressed as a percentage, are also provided. The SphygmoCor System provides age and gender-specific reference ranges based on over 4000 healthy, normotensive adults, ages 18 – 90 years old.

Reports generated by the SphygmoCor System display patient demographic data, quality control criteria, measures of central blood pressure, AP, and Alx (Figure 4). Additionally, central systolic pressure, CPP, AP and Alx parameters are displayed on the continuum of normal reference range values based on age and gender. The patient’s SphygmoCor Reference Age, an estimate of the patient’s vascular age based on values derived during the assessment, is also displayed.

Using Pulse Wave Analysis to Guide Therapy
Analysis of the central pulse waveform, along with corresponding central blood pressure measurements, provides valuable information as to the choice and effectiveness of anti-hypertensive medications. Since augmentation index is a measure of the contribution of the reflected wave for central systolic pressure, it provides an indication of the efficacy of vasoactive drugs intended to reduce the size of the reflected wave.

In patients with elevated augmentation pressure and/or augmentation index, vasodilating drugs may have a greater efficacy than non-vasodilating drugs. Patients with a lower augmentation pressure and/or augmentation index indicate hypertension due to factors other than arterial stiffness (e.g., high cardiac output). A general guide to the relative effectiveness of different anti-hypertensive medications in reducing central pressure compared to brachial pressure is shown in Table 1.
The Role of Central Blood Pressure in Clinical Management

As previously described, central blood pressure provides clinicians with better prognostic and diagnostic information to determine the need for and type of interventions.

Hypertension

Measurement of central blood pressure can provide improved management in a variety of clinical conditions to potentially prevent incidence or progression of target organ damage. As previously noted, certain antihypertensive medications have a more profound effect on central blood pressure than on brachial blood pressure. Measurement of central blood pressure may provide improved therapy guidance for borderline hypertensive patients or those near blood pressure goal, (e.g., brachial systolic blood pressure of 130-140mmHg), as well as improve therapy guidance in resistant hypertensive patients.

Several publications indicate that a central systolic pressure above approximately 125mmHg significantly increases cardiovascular risk:

- In the CAFE study, a CSP of 125mmHg was associated with a 10-30% increase in CV risk compared to 121mmHg
- In the McEniery study, 126mmHg represents the central systolic pressure equivalent to a brachial systolic pressure of 140mmHg, the threshold for Stage 1 hypertension\(^1\)
- Saladini’s study of young to middle age subjects showed a threshold of 125mmHg for developing hypertension requiring medications\(^13\)

While the risk threshold for central systolic pressure needs to be further defined, the literature suggests that if:

- Central systolic pressure exceeds approximately 125mmHg, or
- Central pulse pressure is equal to or exceeds 50mmHg, more aggressive management of the patient’s blood pressure should be considered
Case Study 1
A 45-year-old African American man presents with a history of difficult-to-control hypertension and left ventricular hypertrophy despite use of a beta blocker, an ACE inhibitor and a diuretic. Change in therapy or addition of a fourth drug is contemplated.

Analysis of his central pressure shows a moderately elevated central systolic pressure of 127 mmHg, and a central pulse pressure of 51 mmHg, above the threshold of 50 mmHg for significantly increased CV risk. An elevated augmentation pressure of 15 mmHg (above the 95 percentile value of 7 mmHg for a 45 year old male) indicates a significantly elevated ventricular afterload. Based on this central pressure analysis, the patient was treated to reduce the ventricular afterload and central systolic pressure including changing to a vasoactive Beta blocker and increasing the ACE inhibitor dosage. A follow-up examination revealed a brachial pressure of 128/76 mmHg and a central pressure of 114/78 mmHg, with a central pulse pressure of 36 mmHg and an augmentation pressure of 9 mmHg. Central and brachial systolic and pulse pressure are now well within normal limits as is the augmentation pressure.

Case Study 2
A 55-year-old woman presents with untreated blood pressure values of 139/77 mmHg, hyperlipidemia, mild hyperglycemia, and obstructive sleep apnea. Carotid ultrasound exam shows absence of carotid plaque but a moderately increased composite carotid intimal-medial thickness. The patient previously refused medications.

The central pressure analysis shows an elevated central systolic pressure of 130 mmHg (>95th percentile) and elevated central pulse pressure of 53 mmHg (>50 mmHg threshold for increased CV risk), but with a moderately elevated augmentation pressure of 14 mmHg, indicating only a moderately elevated ventricular afterload. Based on this central pressure analysis, antihypertensive medication is not recommended, however, the patient is recommended for a sleep study and subsequently placed on CPAP therapy. Niacin and omega-3 fatty acid are prescribed for lipid therapy due to the patient’s aversion to statin therapy. Follow-up examination revealed a brachial pressure of 113/71 mmHg and a central pressure of 104/71 mmHg, with a central pulse pressure of 33 mmHg and an augmentation pressure of 8 mmHg. Central and brachial pressure are now within normal limits as is the augmentation pressure (<30th percentile).

Conclusion
While sound clinical judgment cannot be replaced in the management of patients, the scientific literature and case studies suggest a general approach for using central pressure:

- Patients with a central pulse pressure > 50 mmHg or central systolic > 125 mmHg are at higher risk for cardiovascular disease and may benefit from more aggressive management
- In patients with elevated augmentation pressure and/or augmentation index, vasodilating drugs (e.g., ACEIs, ARBs, CCBs, vasoactive beta blockers) may have a greater efficacy than non-vasodilating drugs (e.g., beta blockers, thiazide diuretics)
- Patients with a lower augmentation pressure and/or augmentation index indicate hypertension due to factors other than arterial stiffness

Central blood pressure measurement can aid in reducing central systolic blood pressure and central pulse pressure, thereby preventing or improving target organ damage and cardiovascular events. It also provides valuable information not available from standard brachial cuff measurements as to the efficacy of antihypertensive medications.
References

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