Advancements in Hypertension Management

**New technology for better management of anti-hypertension medications and improved assessment of target organ damage**

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 studies have shown that analysis of the central arterial pressure waveform explains the effects of anti-hypertensive drugs and predicts clinical outcomes significantly better than brachial pressure. The predictive superiority of central blood pressure over brachial blood pressure is primarily due to the closer proximity of the ascending aorta to target organs such as the heart, brain, and kidney.

The SphygmoCor System provides noninvasive measurement of the central aortic pressure waveform with the same fidelity as a pressure catheter placed in the ascending aorta, without the associated costs and risks.

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 aortic pressures and arterial stiffness indices cannot be reliably inferred from brachial pressures.
- Medications may have significantly different effects on the central arterial pressure waveform than on brachial blood pressure.

**Noninvasive Central Arterial Pressure Waveform Analysis**

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 200 mmHg. They found individual variability between brachial and central systolic pressures ranged from as few as 2-3 mmHg to approximately 30 mmHg. Because of such individual variability, central pressure cannot be 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 system 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 and is easy to perform, painless and reproducible. The AMA assigned a Category I CPT Code, 93050, for use in reporting noninvasive central arterial pressure waveform analysis.

**Figure 1:** An example of two patients with significantly different central systolic pressures (122/90 and 136/90), but the same brachial systolic/diastolic pressures (144/90).

Left panel – peripheral waveform

Right panel – central aortic waveform
Central Hemodynamics and Medication Effectiveness

Numerous studies have demonstrated that individuals with the same brachial blood pressure can have significantly different central aortic pressure waveforms and that differential clinical outcomes can be explained by these differences in central aortic pressures. The Conduit Artery Function Evaluation (CAFE) Study, a substudy of the ASCOT trial, demonstrated that elevated central systolic and pulse pressure are associated with a higher risk of cardiovascular events and renal impairment, even though brachial pressures were the same in the different study cohorts. Kampus et al. showed that individuals treated to the same target brachial pressure had different central systolic and pulse pressures and different left ventricular mass effects.

Different classes of anti-hypertensive medications can have different effects on the central hemodynamics. In general, vasoactive medications have a more beneficial impact on central aortic waveforms than non-vasoactive drugs. Arterial vasodilators promote relaxation of vascular smooth muscle cells, delaying the return of the reflected wave and reducing systolic pressure augmentation. As can be seen from Table 1, the effect on central aortic waveform indices of different classes of vasoactive drugs varies by class. In addition, an individual’s response can vary, even within the same class of drugs.

Table 1: Comparative Effects of Anti-hypertensive 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>
</tr>
<tr>
<td>Angiotension-receptor blockers</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Beta-blockers (non-vasoactive)</td>
<td>⇔</td>
<td>↑</td>
<td>↓</td>
</tr>
<tr>
<td>Beta-blockers (vasoactive)</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Calcium-channel blockers</td>
<td>↓</td>
<td>↓</td>
<td>↓</td>
</tr>
<tr>
<td>Diuretics</td>
<td>⇔</td>
<td>⇔</td>
<td>⇔</td>
</tr>
<tr>
<td>Nitrates</td>
<td>↓↓</td>
<td>↓↓</td>
<td>⇔</td>
</tr>
</tbody>
</table>

Central Arterial Pressure Waveforms, Target Organ Damage, and Hypertension

Numerous studies in both healthy and diseased subjects have consistently demonstrated that elevated central aortic blood pressure is independently associated with increased cardiovascular events and is superior to brachial pressure as a predictor of those events. In the Strong Heart Study, Roman et al. reported that central pulse pressures were more strongly predictive of cardiovascular events, independent of brachial pressures. Specifically, when the central pulse pressure equals or exceeds 50mmHg, the risk of cardiovascular disease increases by nearly 70%; brachial pressure did not demonstrate any such threshold. Elevated central aortic pressure and arterial stiffness 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.

Studies have also shown that analysis of the central aortic waveform and corresponding indices can distinguish those individuals who, even if not hypertensive, can be found to have target organ damage. Roman and Devereux reviewed numerous longitudinal studies demonstrating that changes in central aortic blood pressure are more significant than decreases in brachial blood pressure with respect to target organ damage in hypertensives.
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. 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 arterial 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).

Analysis of the Central Arterial Pressure Waveform

A number of clinically important central aortic pressure indices can be derived from the central arterial pressure waveform captured using the SphygmoCor System, including measures of wave reflection, 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.

$$PP = \text{Pulse Pressure}$$

$$AP = \text{Augmentation Pressure, the contribution of the reflected wave to the pulse pressure}$$

$$Alx = \text{Augmentation Index, the percentage of the pulse pressure due to the AP}$$

Figure 3. The central pressure waveform indices include central systolic pressure (SP), central pulse pressure (PP), Augmentation Pressure (AP), and Augmentation Index (Alx).
The Role of Central Arterial Pressure Waveform Analysis in Clinical Management

As previously described, central arterial pressure waveform analysis provides clinicians with better prognostic and diagnostic information to determine the need for and type of interventions. A panel of researchers and clinicians from leading U.S. medical centers has published recommendations on the use of noninvasive central arterial pressure waveforms in clinical practice. The panel concluded that analysis of the central pressure waveform provided valuable information when added to traditional brachial blood pressure measurement. Central arterial pressure waveform analysis, in addition to brachial blood pressure measurement, allows physicians to assess the effects of arterial stiffening and pressure wave reflection, which can increase the blood pressure actually exerted on the heart, brain and kidneys.

The panel focused their recommendations on three areas where pulse wave analysis can make a significant difference in patient care:

- Deciding whether to initiate, intensify or change therapy in younger patients.
- Deciding which anti-hypertensive medication to prescribe and when to add additional medications.
- Determining whether drug therapy or lifestyle changes that have reduced brachial pressure have equally reduced central blood pressure.

Using Arterial Pressure Waveform Analysis to Guide Therapy

Analysis of the central arterial pressure waveform, along with corresponding indices of arterial stiffness and wave reflection, provides valuable information as to the choice and effectiveness of anti-hypertensive medications. In a randomized controlled trial of 286 patients, Sharman et al. found that use of central arterial pressure waveform analysis to guide care, in addition to best-practice usual care including office, home and 24-hour ABPM, resulted in a step-wise decrease in medication, with cessation of medication in 16% of patients, (with no difference in LV mass, quality of life or other measures).

Since augmentation index is a measure of the contribution of the reflected wave to central systolic pressure, it provides an indication of the efficacy of vasoactive drugs intended to reduce wave reflection. 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).

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Reimbursement for Arterial Pressure Waveform Analysis

The AMA CPT Editorial Panel assigned CPT code 93050 for use in reporting noninvasive arterial pressure waveform analysis, which the SphygmoCor System provides.

93050 Arterial pressure waveform analysis for assessment of central arterial pressures, including obtaining waveform(s), digitization and application of nonlinear mathematical transformations to determine central arterial pressures and augmentation index, with interpretation and report, upper extremity artery, non-invasive. (Do not report 93050 in conjunction with diagnostic or interventional intra-arterial procedures).

The code is effective for use as of January 1, 2016.

Conclusions

While sound clinical judgment cannot be replaced in the management of patients, scientific literature, as well as positions taken by leading physicians, provides an approach for implementing central arterial pressure waveform analysis as an adjunct to traditional brachial pressures in patient management.

• The SphygmoCor System provides the ability to noninvasively obtain central arterial pressure waveforms in the office without the risks associated with invasive procedures.

• Analysis of the central aortic waveform provides important and valuable information related to wave reflection and central hemodynamics that is not available from standard brachial cuff measurements.

• 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).

• Central arterial pressure waveform analysis is more closely tied to target organ damage and cardiovascular outcomes.

Central arterial pressure waveform analysis can aid in individualizing care. By reducing the harmful effects of the early return of the reflected wave, central arterial pressure waveform analysis can help prevent or reduce target organ damage and cardiovascular events.
References

1. McEniery et al., Central pressure: variability and impact on cardiovascular risk factors, Hypertension, 2008; 51:1475-82.


5. Kelly et al., Nitroglycerin has more favourable effects on left ventricular afterload than apparent from measurement of pressure in a peripheral artery, European Heart Journal, 1990; 11(2):138-44.


