CONNEQT Health

Precision Hypertension Management Guided by Central Aortic Pressures

Clinical Insights

- Elevated central aortic pressure (central BP) serves as a robust predictor of cardiovascular events and mortality, offering valuable insights into cardiovascular structural changes and cardiovascular dysfunction.
- Despite a high correlation with brachial blood pressures (BP), central BP cannot be reliably extrapolated from brachial BP, emphasizing the distinct and essential nature of central BP measurements.
- Clear threshold values for diagnosing elevated central BP have been defined and endorsed by professional and national societies, providing a standardized approach for healthcare practitioners.
- The integration of central BP into the hypertension diagnosis and treatment paradigm yields dual benefits for both health outcomes and economics:
  - ✓ It reduces additional costs associated with confirming white coat hypertension.
  - ✓ It helps avoid unnecessary medication costs for treating hypertension when white coat hypertension is identified, consequently minimizing costs related to medication side effects.
  - ✓ The potential for earlier aggressive treatment, following confirmed hypertension, contributes to a subsequent reduction in socioeconomic costs due to decreased morbidity.
  - ✓ It provides guidance for attempting trials of medication reduction in treated patients with low or low-normal central pressures and normal brachial pressures.
- FDA-cleared BP monitors capable of measuring both brachial and central BP are now commercially available. This technological advancement enhances accessibility and underscores the ease of adopting central BP measurements in everyday clinical practice.

"[Central aortic] pressures should be the most relevant blood pressure relating to vascular events. Cuff blood pressure is not so much a surrogate, but a compromised measure that is recorded because of technical limitations.[13]"

Background

Hypertension remains a common disorder responsible for substantial vascular morbidity and mortality despite the availability of multiple effective medications and widespread educational efforts. An underappreciated but clinically relevant area to consider is the precision and reliability of current monitoring based on brachial blood pressure (BP) measurements.

BP is a continuous pressure wave made up of the summation of the pressure generated by the heart's contraction and the pressure reflected toward the heart from the peripheral arterial tree. The pressure wave changes shape and size as it traverses the arterial tree, impacted by the distensibility of each arterial branch. An elastic artery, such as the aorta, is made up of elastin fibers and permits significant distension. Whereas a muscular artery, such as the brachial or the radial, have a higher proportion of collagen fibers, making them less distensible. The change in arterial structure is quantified in terms of pressure, which is characterized in terms of simply a maximum (systolic) and a minimum (diastolic).

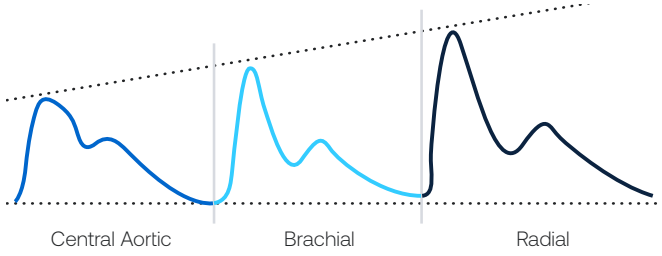

Figure 1: Illustration of 'amplification phenomenon', where the amplitude of the pressure waveform increases the further away from the heart. Published from Nichols et al.[1]

The stiffness of the arteries increases with the distance from the heart and results in higher pressure amplitude in peripheral arteries. Known as 'amplification phenomenon', brachial systolic and pulse pressure are significantly higher than central pressures in young individuals, whereas diastolic blood pressure is roughly constant.[2] Interestingly, the difference in arterial stiffness between central and peripheral arteries falls and even reverses with aging, leading to a progressive fall in pressure amplification in older individuals.[3]

As an example, in a young, healthy man, the difference in systolic pressure at the proximal aorta compared with the brachial artery may be more than 25 mmHg, while in an elderly healthy woman it may be as little as 4 mmHg to 6 mm Hg.[4] The differences in the amplification of systolic BP are not readily apparent from the brachial systolic and diastolic BPs, as shown in Figure 2.

Figure A: Patient 1

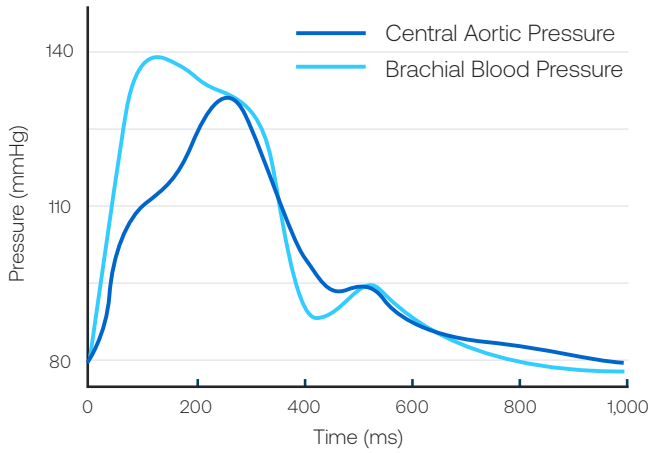

Figure B: Patient 2

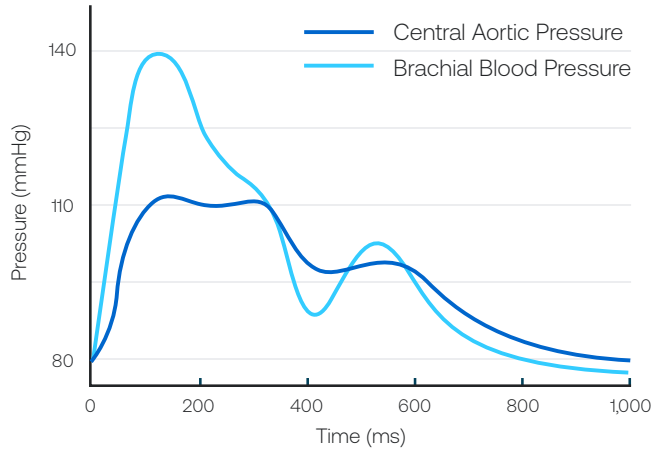

Figure 2: Two patients with equivalent brachial pressures but with significantly different central arterial pressure waveforms. The difference in waveform shapes, due to differences in arterial stiffness and the effects of wave reflections.

Central BP can be determined through the analysis of the peripheral arterial waveform obtained from the brachial artery using an oscillometric cuff or the radial artery using a tonometer. Both methods produce a waveform that is then subjected to a general transfer algorithm to produce a central pressure profile and extract central BP.

Several devices are available for the measurement of central BP. These devices have, in general, been validated in catheterization laboratories and when accurately calibrated have been shown to be within 1 mmHg to 2 mmHg of the actual pressure in the proximal aorta.[5] This use of these devices at the point-of-care is in line with the CPT code issued in 2016 (93050) "arterial pressure waveform analysis for assessment of central arterial pressures" to provide additional information to physicians managing BP beyond current brachial BP goals.

Utility of Central Aortic Pressure

While BP measured at the brachial artery plays a central role in our understanding and management of cardiovascular risk, there is an increasing recognition on the importance of central blood pressure as that is the pressure directly affecting the major organs.

Importance of Isolated Central Hypertension

A critically important role of central BP is in identifying individuals with isolated central systolic hypertension (i.e., elevated central pressure with normal brachial pressure). A person-level meta-analysis of the International Database of Central Arterial Properties for Risk Stratification (IDCARS) (n=5,576; 54.1% women; mean age 54.2 years) determined that the hazard ratios for adverse cardiovascular and cerebrovascular outcomes when compared to concordant normotension were 1.30 for isolated brachial hypertension, 2.02 for concordant hypertension, and 2.28 in isolated central hypertension, the highest risk group.[6] This signals the need to identify and manage individuals with central hypertension with greater precision irrespective of the brachial blood pressure status.

Over the past two decades, a growing body of evidence has shown that central BP to be useful in medication selection and titration for hypertension treatment.[7] While brachial BP threshold values have been defined that represent the targets for initiation of antihypertensive treatment, and values have been defined for the goals of treatment, there is limited published data on how and what target values should be used for recommending modification in pharmacotherapy.

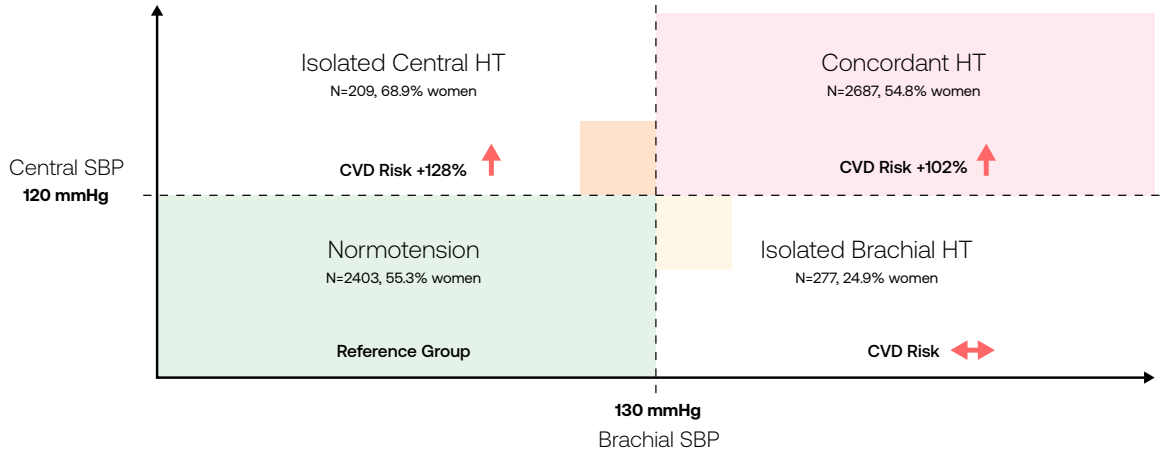

Figure 3: CVD Risk of Brachial & Central Hypertension from IDCARS.[6]

Nuances of clinical pharmacodynamics within antihypertensive agents, particularly with the beta-blocking drugs, will drive heterogeneity of effects.[8] Therefore, it is important to measure the central changes after an intervention to provide assurance that the results are in the direction expected. Figure 4 presents the expected direction of changes, and their magnitude, on brachial and central pressure profile.

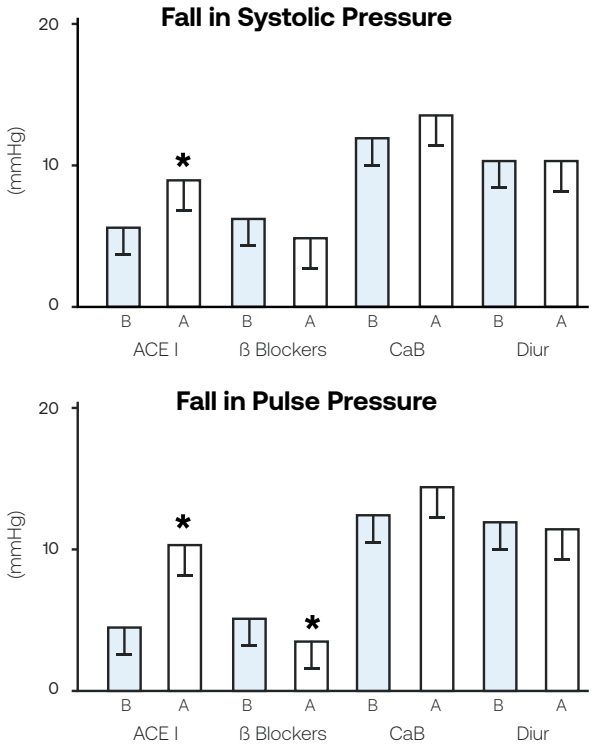

Figure 4: Fall in systolic and pulse blood pressure in the brachial artery (B) and central aortic artery (A) with the different drug classes. ACE I = angiotensin-converting enzyme inhibitors; CaB = calcium blockers; Diur = diuretics. *P < .05 compared with brachial artery values.

Clinical Utility of Central BP – Understanding Whitecoat Hypertension

Central BP is also useful ruling out whitecoat hypertension during diagnosis[9], a condition with prevalence between 10 and 50% based on national and international registries.[10] A 2019 study found that normal central blood pressure was present in 100% in patients with white coat hypertension. Furthermore, an investigation of the diagnostic performance of central BP devices showed a sensitivity of 93% and specificity of 95% for detecting hypertension in a sample with a prevalence of 52%, dramatically outperforming that of brachial BP devices with a sensitivity of 49% and specificity of 94%.[11]

Clinical Application of Central Aortic Pressures

Some patients may have high brachial BP and central BP, and others may have elevated brachial BP with normal central BP. By providing different, and complementary, information to a single brachial BP measurement, central BP adds an extra dimension of physiological insights that give clinicians the ability to assess patents' hypertension and cardiovascular status.

In 2015, the North American Artery Society, a professional society dedicated to the understanding of the role of vascular structure & function in human health and disease, recommends using a value of 124 mmHg as a reasonable upper limit of normal for central systolic pressure based on longitudinal studies.[4] In 2019, the Taiwan Hypertension Society issued a consensus statement recommending <110 mmHg as optimal central systolic pressure, with 110-129 mmHg defined as prehypertension and >130 mmHg defined as hypertension.[12,13]

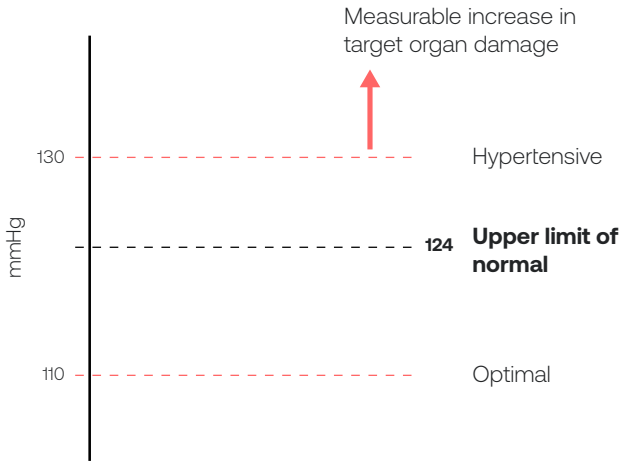

Figure 5: Recommended targets for central BP.

A thoughtful and practical example of how to incorporate central pressure monitoring in clinical practice can be found in the BP GUIDE study.[7] The

study was a prospective randomized trial (n=286) evaluating the use of central aortic blood pressure compared with best-practice care without central pressure measurements to guide hypertension management. Best-practice usual care included office, home, and 24-h ambulatory blood pressure. The group that had the addition of central aortic blood pressure guided management had a significant reduction in the amount of medication they required to achieve blood pressure control. This important result of reducing the amount and dose of medications resulted in favorable patient level outcomes such as high adherence to medication changes when they were suggested and no adverse effects during dose reduction or medication cessation.

By incorporating central blood pressure evaluation into routine clinical visits, healthcare professionals can differentiate between genuine hypertension and the transient elevation caused by situational stress. This not only refines diagnostic precision but also guides more targeted treatment plans, ensuring that interventions are tailored to the actual cardiovascular health of the individual. As such, routine central blood pressure assessment can significantly improve the quality of hypertension care, foster more informed decision-making, and ultimately optimize patient outcomes

Central BP assessment in routine clinical visits can enhance the accuracy of diagnosing and managing hypertension by providing a more reliable indicator of true cardiovascular risk.

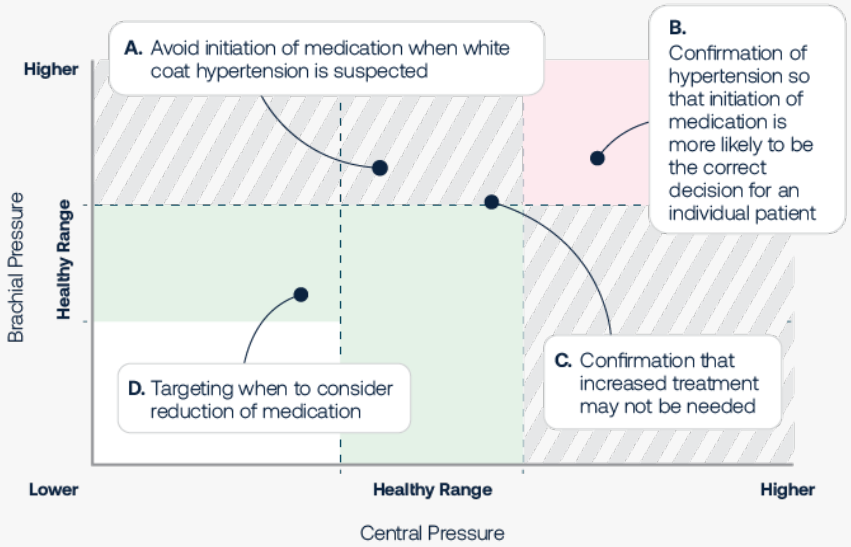

Figure 6: Central BP provides an extra dimension of physiological insights that give clinicians the ability to assess patents' hypertension status.

Four common clinical scenarios are presented below, and depicted in the figure above, to demonstrate the application of central BP in clinical decision-making.[14]

Scenario A: A patient without previous hypertension diagnosis presents with elevated brachial pressure and normal central pressure. A case of white coat hypertension is suspected and initiation of antihypertensives is avoided.

Scenario B: A patient without previous hypertension diagnosis presents with concurrent elevation in brachial and central pressures. This confirms hypertension and the initiation of

Scenario C: A patient currently undergoing antihypertensive medication treatment presents with borderline high BP and normal central BP. This indicates that the antihypertensive regimen is effective, and an increased treatment is not needed.

Scenario D: A patient currently undergoing antihypertensive medication treatment presents with normal BP and low central BP, or extended period of normal brachial and central BP. This

antihypertensives is the correct treatment decision.

indicates the patient may be over-medicated and should be considered for a reduction in antihypertensives.

Clinical and Economic Benefits

Embracing advancing medical technologies requires careful consideration of replacement costs and a compelling demonstration that the innovation not only enhances patient outcomes and safety but also optimizes operational efficiency and cost-effectiveness within the healthcare ecosystem. A collaborative effort involving physicians and health economists affiliated with the Taiwan Hypertension Society undertook an evaluation of the costs and benefits associated with central BP versus brachial BP in diagnosing hypertension.

Utilizing a well-established model that compares ambulatory BP monitoring to clinic and home brachial BP monitoring, the team scrutinized a hypothetical primary care population aged 35 years or older, comparing central BP to brachial BP. The evaluation, which assessed quality-adjusted life years (QALY), revealed that the use of central BP had an incremental cost-effectiveness ratio (ICER) ranging from £226 to £2,750 (US$287 to $3,490) for each QALY gained. Applying the threshold value of £20,000 per QALY gained, as defined by the UK's National Institute for Health and Clinical Excellence (NICE), central BP emerged as highly cost-effective in the diagnosis of hypertension.

While there isn't a nationally established ICER threshold for healthcare decision-making bodies in the United States, it is frequently employed in economic evaluations submitted to health technology assessment bodies and payers. The American College of Cardiology (ACC) and the American Heart Association (AHA) classifies interventions into three categories based on ICER:[15]

- High Value: ICER < US$50,000/QALY;
- Intermediate Value: ICER US$50,000–150,000/QALY;
- Low Value: ICER >US$150,000/QALY.

With an ICER ranging from US$287 to $3,490, the use of central BP for hypertension diagnosis falls into the High Value category according to the ACC/AHA methodology, reinforcing its cost-effectiveness and potential to provide substantial value in clinical practice.

To enhance healthcare providers' ability to acquire the essential technologies for central BP assessment, the Renal Physicians Association proactively advocated for the reimbursement of central BP monitoring. Their efforts resulted in the American Medical Association's approval of a Category I CPT reimbursement code 93050 which was officially implemented by the Centers for Medicare & Medicaid Services (CMS) in 2016.

CPT Code 93050: Arterial pressure waveform analysis for assessment of central arterial pressures, includes 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.

CPT 93050 is now used by healthcare providers throughout the US to perform central BP assessments.†

Conclusion

The accumulated evidence regarding the diagnostic and economic advantages associated with central BP measurements in the diagnosis of hypertension presents a compelling argument for their integration into routine clinical care. The assessment of central BP, which reflects the pressure in the arteries close to the heart, is positioned as having substantial value in both diagnostic accuracy and cost-effectiveness. There is robust evidence that suggests incorporating central BP assessments into standard clinical protocols could significantly enhance the overall quality of patient care.

The additional insights gained from central BP assessments contribute significantly to a more comprehensive understanding of a patient's cardiovascular health. By offering a nuanced perspective on blood pressure dynamics, central BP measurements empower healthcare professionals to make more informed decisions in tailoring treatment plans and interventions. This heightened precision in patient care has the potential to positively impact health outcomes.

Moreover, the attractiveness of integrating central BP assessments lies in their seamless provision without necessitating disruptive changes to existing clinical workflows. The advent of commercially available devices capable of measuring both brachial and central BP from a single cuff facilitates the integration of central hemodynamics into routine care. The streamlined approach offered by these devices simplifies the process, making it as straightforward as replacing a traditional blood pressure monitor. This non-disruptive incorporation is particularly noteworthy as it ensures that healthcare professionals can readily adopt central hemodynamic insights into their routine practices.

Such technological advancement not only enhances accessibility but also promotes the widespread adoption of central BP assessments as a routine component of clinical care. The diagnostic evidence, economic advantages, and the seamless integration of central BP assessments into existing clinical workflows forms a persuasive rationale for incorporating this valuable diagnostic tool into routine clinical care. This paradigm shift represents a step toward more personalized and effective healthcare practices, ultimately benefiting both healthcare providers and patients.

† Medicare claims data, 2016-2023.

About CONNEQT Health

CONNEQT Health pioneered a biosensing technology that has been clinically validated and FDA-cleared to noninvasively measure vascular biomarkers representing key indicators of vascular health. The indicators include, but not limited to, central BP, vascular stiffness, vascular age, and heart stress. Named SphygmoCor®, the technology has been deployed in healthcare systems and clinical trials to measure arterial health.

The SphygmoCor technology enables a new paradigm in the diagnosis and management of hypertension and cardiovascular diseases that is increasingly decentralized and personalized. Incorporation of non-invasive measurements of vascular biomarkers can improve hypertension management in the following areas:

- Refine monitoring requirements;
- Reduce over-treatment;
- Improve under-treatment; and
- Reduce costs of management (e.g. medication costs, monitoring such as ambulatory blood pressure monitoring (ABPM))

When combined with cloud-based data analytics, our suite of FDA-cleared medical devices enables key stakeholders throughout the healthcare ecosystem to obtain valuable health information not accessible from standard brachial blood pressure monitors.

Learn more at conneqthealth.com.

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