ATCOR

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Managing Cerebrovascular Disease and Cognitive Decline with Central Blood Pressure Measurement

The Role of Elevated Central Aortic Pressure in Long-Term Brain Health

Summary

- Elevated central pressures have been associated with an increased risk of vascular events and cognitive impairment.
- Monitoring of central pressures can provide information that helps treatment decisions related to cerebrovascular disease and cognitive impairment.
- Including a dual blood pressure monitoring system (measuring both central and brachial blood pressure) as part of patient care is anticipated to improve understanding of vascular physiology, add value in the determination of risk for cerebrovascular disease and cognitive impairment, and provide additional guidance for treatment decisions with the objective of improving long-term brain health.

Introduction

Hypertension is perhaps the most prominent clinical risk factor for stroke. Multi-infarct dementia (or vascular dementia) is a result of repeated, often subclinical, strokes (disruption of blood flow to an area of the brain leading to tissue destruction). In addition to direct damage to the brain due to transmission of high arterial pressures, hypertension can lead to damage through decreased blood flow to the brain from atherosclerosis and low cardiac output resulting from heart failure. Multiple publications have highlighted the association between hypertension and either dementia or cognitive impairment.[1-3] The association is mainly noted when hypertension occurs early in adult life relatively to the elderly population. As well, data exist demonstrating that lowering blood pressure in middle-age adults with hypertension can reduce the subsequent development of dementia or cognitive impairment.[4,5]

Hypertension is perhaps the most prominent clinical risk factor for stroke. Controlling hypertension improves vascular outcomes.

Lowering blood pressure in middle-age adults with hypertension can reduce the subsequent development of dementia or cognitive impairment.

Central Blood Pressure and Hypertension

Management of hypertension through cuff measurement of peripheral (brachial artery) pressures has dramatically but incompletely improved the ability of health care providers and their patients to control hypertension and reduce associated end-organ damage including the brain. Multiple issues likely contribute to the ongoing socioeconomic burden of hypertension despite the availability of multiple effective medications and widespread educational efforts. Such issues include, but are not limited to, case finding (early diagnosis), continuity and continued follow-up of care, affordability of care, medication adverse effects, medication compliance and challenges in modifying lifestyle behavior.

An underappreciated but clinically relevant area to consider is the precision and reliability of current monitoring which is based on brachial blood pressure measurements, including patient and health care provider factors. Cuff brachial blood pressure can be viewed as a surrogate for central (i.e., aortic) blood pressures, as aortic pressure represents the actual pressure that is transmitted to organs effected by hypertension (e.g., heart, brain, kidney) due to the closer proximity of the ascending aorta to these vital organs. Non-invasive pulse wave analysis (PWA) is a technique that transforms the data from peripheral arterial pressure waveforms obtained into an evaluation of central aortic pressures. Variables that can be obtained include the following:

- Central aortic systolic and diastolic pressures
- Augmentation index (ratio expressing the relationship of forward and backward traveling waves in the central aorta)
- Central aortic pulse pressure (systolic minus diastolic pressure).
- Pulse pressure amplification (the difference between the peripheral and central pulse pressure)

Peripheral (brachial) blood pressures are highly correlated to central pressures; however, significant variability exists such that central pressures cannot be reliably inferred from brachial pressures. Additionally, brachial systolic pressures are generally higher than central (aortic) pressures although diastolic pressures are similar. The ability to obtain and quantify these variables provide in-depth understanding of the vascular physiology and help determine risk and potential treatment strategies.

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The technology for non-invasive assessment of central aortic pressures through PWA is currently available and approved by the United States Food and Drug Administration (FDA). In recognition of the clinical utility of PWA, a Current Procedural Terminology (CPT) code has been established. The SphygmoCor® XCEL system is a dual arterial pressure monitoring medical device consisting of brachial blood pressure and central aortic pressures (using partial cuff inflation to record the outgoing brachial waveform), which can be obtained in the clinic in the same patient session. The SphygmoCor® XCEL is the only FDA cleared medical device for non-invasive central arterial pressure waveform analysis for all adults. The SphygmoCor® System incorporation of PWA was developed as complementary to brachial pressure measurements to help guide treatment decisions designed to prevent or reduce long-term target organ damage and cardiovascular events resulting from increased aortic pressure.

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The following sections highlight data that is indicative of the value of incorporating PWA into the care of all patients with hypertension, particularly for the objective of reducing the risk of damage to the brain.

Structural Changes to the Brain and Elevated Central Blood Pressure

Radiographic evaluation of the brain through magnetic resonance imaging (MRI) can identify brain abnormalities that may be present even in the absence of overt focal neurologic signs and symptoms. Specifically, white matter hyperintensities (abnormalities in the brain that show up as areas of increased brightness on MRI) and silent strokes (also referred to as silent brain infarcts) on MRI have been associated with cognitive impairment, dementia, depression, and an increased risk of stroke.[6,7] Hypertension has consistently been documented as a risk factor for both white matter hyperintensities and silent brain infarcts.[6] Central pressures represent the direct pressures that are transmitted to the brain and monitoring of central pressures provides additional risk data. The risk of vascular events is associated with elevated central pressures and the risks are at least as high, and in some studies, higher than that associated with brachial pressures.

The risk of vascular events is associated with elevated central pressures.

In a population based study of elderly subjects, approximately 11% had silent brain infarcts on MRI.[8] The presence of silent brain infarcts more than doubles the risk of future strokes and the development of dementia.[8,9] Studies that have identified a relationship between the severity of white matter hyperintensities and dementia, include the Cardiovascular Health Cognitive Study (significant risk for dementia and Alzheimer's disease), the Rotterdam Scan Study (dementia), Osaki-Tajiri Project (vascular dementia), and the Framingham Offspring Study (dementia).[10-13]

A study of 993 subjects older than 55 years sought to determine the associations of central and brachial blood pressure and subclinical (i.e., silent) cerebrovascular disease.[14] Brachial and central pulse pressure were independently associated with silent brain infarctions. Central systolic BP and central pulse pressure were associated with increased white matter hyperintensities, even after adjustment for brachial BP. Both brachial and central pulse pressure were independently associated with silent brain infarction. The investigators concluded that higher central systolic BP and central pulse pressure, but not brachial BP, were significantly associated with silent cerebrovascular disease.[14]

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The study highlights the value of monitoring central pressure variables to determine risk of cerebrovascular disease.

Clinical Brain Consequences Associated with Elevated Central Blood Pressure

Elevation of central blood pressure has clinical consequences in terms of cognition. A cross-sectional study of 50 patients was performed to evaluate the association between central blood pressure variables and mild cognitive impairment in subjects over 50 years of age.[15] Mild cognitive impairment was assessed using the Montreal Cognitive Assessment instrument and by the European Consortium Criteria. In total, 67% had hypertension and 52% were diagnosed as having mild cognitive impairment. No significant association was found between any of the measured blood pressure variables and global cognition. Significant associations were noted between augmentation index and a test of cognition (abnormal clock-drawing and language) and between pulse pressure amplification and language; however, no associations were present based on brachial pressures. Although the number of subjects in the study was small, the study documented that central blood pressure markers were associated with tests indicative of cognitive impairment.

In a clinical study, central blood pressure markers were associated with tests indicative of cognitive impairment.

Another area not readily acknowledged is repeated episodes of decreased blood flow (hypoperfusion) from relative low blood pressure (hypotension) due to medication overtreatment of hypertension. Indeed, authors have described a bimodal distribution of vascular events including effects on the brain, heart, kidneys and survival whereby high blood pressure and low blood pressure substantially increase risk of adverse outcomes.[17-19] Therefore, while treatment of hypertension is clearly warranted, careful and prudent treatment to ensure that adverse effects do not have long-term consequences is also necessary.

Monitoring of central pressures can provide information that helps treatment decisions.

In an editorial regarding assessment of hypertension related brain insults using central pulse pressure, King highlighted that study results[14] suggest that central BP monitoring in addition to traditional cuff peripheral BP can provide a more accurate marker of risk for cerebral microvascular disease.[16] He also noted that the American Heart Association has recommended identifying and reducing vascular risk factors such as hypertension as a means to mitigate the risk for development of dementia and cognitive impairment.

Using Central Blood Pressure Monitoring to Improve Management of Hypertension

Incorporation of PWA into the treatment paradigm for hypertension has the following advantages and can be considered in the following situations to improve blood pressure management:

1. Confirmation of hypertension so that initiation of medication is more likely to be the correct decision for a patient.
   Scenario: Concurrent elevation in brachial and central pressures
2. Avoiding initiation of medication when white coat hypertension is suspected.
   Scenario: Elevated brachial pressure and normal central pressures
3. Confirmation that increased treatment may not be needed.
   Scenario: Borderline high peripheral pressures and normal central pressures

4. Targeting when to consider reduction of medication.
   Scenario: Normal peripheral and low central pressures, or extended period of normal peripheral and normal central pressures (particularly in the setting of medication tolerance issues)

Optimizing Brain Health

The focus of medical publications including the above brief review is directed to disease (e.g., cerebrovascular disease, dementia). Although in many respects the objectives are the same, health care professionals and the population at large should provide time towards the concept of health or maintaining health. For the brain, one can refer to brain health. The Centers for Disease Control and Prevention (CDC) define a healthy brain as "one that can perform all the mental processes of cognition, including the ability to learn new things, intuition, judgement, language, and remembering."[20] The American Heart Association/American Stroke Association (AHA/ASA) reported brain health as "average performance levels among all people at that age who are free of known brain or other organ system diseases in terms of decline from function levels, or as adequacy to perform all activities that the individual wishes to undertake.[21]

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The AHA/ASA Presidential Advisory recommended metrics to define optimal brain health based on "factors that could be measured, monitored and modified". The factors were non-smoking, physical activity, healthy diet, appropriate body mass index, blood pressure, total cholesterol, and blood glucose to maintain optimal brain health.[21] It is inherent within the recommendations that prevention and monitoring is key to maintaining brain health. While the Presidential Advisory referred to a brachial blood pressure target, sufficient data has been published that indicate monitoring of brachial BP alone is likely suboptimal for controlling the vascular effects of elevated blood pressure on brain health. The SphygmoCor® XCEL system provides both brachial BP as well as central BP variables such as aortic systolic pressure, aortic diastolic pressure, pulse pressures and augmentation index. Including a dual blood pressure monitoring system as part of patient care is anticipated to improve understanding of vascular physiology, determination of risk to a healthy brain and provide additional guidance for treatment decisions with the objective of improving brain health.

Conclusion

Measuring central blood pressure provides clinicians and patients additional information about the possibility of experiencing end organ damage, cerebrovascular disease, cognitive impairment, and other complications associated with high blood pressure that will increase the possibility of interventions (lifestyle and medical) that improve health, including brain health.

Key Take-Away Messages

- Hypertension is perhaps the most prominent clinical risk factor for stroke. Controlling hypertension improves vascular outcomes.
- Lowering blood pressure in middle-age adults with hypertension can reduce the subsequent development of dementia or cognitive impairment.
- Elevated central pressures have been associated with an increased risk of vascular events and cognitive impairment.
- Monitoring of central pressures can provide information that helps treatment decisions.
- The SphygmoCor® XCEL system is a dual arterial pressure monitoring medical device consisting of brachial blood pressure and central aortic pressures, which can be obtained in the clinic in the same visit. The SphygmoCor® XCEL is the only FDA cleared medical device for non-invasive central arterial pressure waveform analysis for all adults.
- Including a dual arterial blood pressure monitoring system as part of patient care is anticipated to improve understanding of vascular physiology, determination of risk to a healthy brain and provide additional guidance for treatment decisions with the objective of improving brain health.

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