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# Elevated Central Aortic Pressure Contribution to Cerebrovascular Disease and Cognitive Decline


## 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.*

## 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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Two additional studies corroborate the value of measuring central pressures for assessment of risk of cognitive impairment. Chetouina and colleagues performed brain imaging studies in 60 older patients (mean age 75 + 5 years) with cognitive decline.[15] White matter abnormalities consistent with Alzheimer's Disease had higher correlations with central aortic systolic pressures compared to brachial systolic blood pressures.

Barnes et al investigated the relationship of aortic hemodynamics WMH in postmenopausal women (n=53) as hormonal shifts at menopause alter vascular function, which can increase the risk for both hypertension and WMH.[16] WMH as a fraction of total white matter volume was positively associated with aortic systolic BP (regression coefficient = 0.018; p = 0.046) and with AIx (regression coefficient = 0.025; p = 0.04). Brachial systolic BP was also associated with WMH fraction (regression coefficient = 0.018; p = 0.07). The % change in WMH fraction for a 1-unit increase in each variable was highest for AIx (aortic systolic BP = 1.8, brachial systolic BP = 1.8, AIx = 2.5). These investigators concluded that that "assessing aortic hemodynamics may identify individuals at risk for accelerated development of WMH and guide early treatment to reduce WMH burden and cognitive impairment in the future."

The aforementioned published reports highlight 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.[17] 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.[18-20] 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.*

Pase and colleagues sought to determine the association between central blood pressure and cognitive function in independently living adults aged 20 to 82 years (n = 493).[21] In adjusted regression models, higher central systolic pressure and higher central pulse pressure were each associated with poorer processing speed, Stroop processing, and recognition memory. Stroop processing assesses the reaction time between congruent and incongruent stimuli. The Stroop effect is a phenomenon that occurs when you must say the color of a word but not the name of the word. For example, blue might be printed in red, and you must say the color rather than the word. Higher brachial systolic pressure and brachial pulse pressure were associated with poorer Stroop processing but was not associated with poorer outcomes for processing speed and recognition memory. Based on the results, central pressures were sensitive indicators of cognitive aging, predicting aspects of cognitive performance not predicted by brachial blood pressure.

Cognitive impairment commonly occurs in hemodialysis patients, with vascular disease potentially implicated in its pathogenesis. Kim et al reported the results from 585 adult patients starting hemodialysis who were evaluated with a series of cognitive tests (Trail making test A (TMTA), Trail making test B (TMTB), and the modified Mini-Mental State Exam (3MS)) and non-invasive measurement of central aortic pressures.[22] Of the total, 157 patients remained on hemodialysis and have baseline and 1 year test results. Mean baseline age

was 55 ± 13 years, 58% were male, 72% were African American, 35% had coronary artery disease, 55% had diabetes, and 10% had cognitive impairment. At 1 year, unadjusted and adjusted analyses (systolic BP was included in the model) revealed every 10% increase in AIx and 10 mm Hg increase in central pulse pressure (cPP) were associated with longer TMTB and global cognitive impairment. The authors proposed that higher AIx and cPP might contribute to declining cognitive function in patients starting hemodialysis.

In an editorial regarding assessment of hypertension related brain insults using central pulse pressure, King highlighted that study results[23] 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

Hypertension management through the addition of non-invasive measurements of central aortic pressures has the potential to improve care through: (a) refining requirements for BP monitoring, (b) decreasing over-treatment, (c) early identification for earlier or more aggressive treatment, and (d) decreasing the overall cost of care (e.g., use of tools such as ambulatory blood pressure monitoring (ABPM), drug costs).

Identifying the requirements and amount of medication is critical to controlling gestational hypertension.

The following table provides examples where central aortic blood pressure monitoring may positively impact the treatment of gestational hypertension:

**Table 1**: Examples of clinical utility of measuring both brachial and central aortic blood pressure.

| CLINICAL USE | BRACHIAL BP | CENTRAL BP |
|---|---|---|
| Confirming hypertension (drug prescription is optimized) | Elevated | Elevated |
| Suspicion of white coat hypertension | Elevated | Normal or Low |
| Avoidance of increased drug prescription | Borderline high | Normal or Low |
| Consideration of reducing drug prescription (patients receiving at least one anti-hypertensive medication | Normal (particularly when there is suspected medication adverse effects) | Low (or extended period of normal) |

## 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.[24]

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*The AHA/ASA Presidential Advisory recommended metrics to define optimal brain health, which include hypertension.*

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.[25] 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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