



Blood Pressure Control and Cognitive Impairment

Could recommendations for more aggressive blood pressure control worsen prognosis for vascular and neurodegenerative cognitive impairments?

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Control of Vascular Risk Factors

In the last 4 to 5 years, small vessel cerebrovascular disease in isolation or in neurodegenerative disorders (eg, Alzheimer's disease [AD], frontal temporal dementia [FTD], and Parkinson's disease or Lewy body dementia) has been increasingly recognized as having a deleterious effect.^{1,2} Because we currently don't have successful treatment for the cognitive impairment of these neurodegenerative disorders, we currently focus on reducing the rate of cognitive decline by modifying vascular risk factors of midlife hypertension, diabetes, obesity, smoking, and increased cholesterol. More aggressive treatment of these risk factors is a possible important reason why the suggested incidence of dementia has decreased in more advanced economic countries (eg, Germany, The Netherlands, the United Kingdom, and the US).³⁻⁵

Imaging Small Vessel Disease

Small vessel disease in the brain is not well visualized on MRI or MR angiography imaging. Very small lacunar infarcts and conversion of small subcortical infarcts into white matter hyperintense lesions are not always easy to see. Seeing the real consequences of small vessel disease on brain tissue depends heavily on visualizing surrounding brain tissue and is likely underestimated.

Neuropathology Correlates of Blood Pressure Changes

Results published this year showed that both high systolic blood pressure and declines in systolic blood pressure correlate with increased odds of having brain infarcts evident at autopsy in 1,288 subjects who had a mean age of 88 at death.⁶ Higher mean systolic blood pressure was associated with increased AD tangles in the brain.

In this clinicopathologic study, blood pressure data from 3 ongoing prospective studies on aging were collected at baseline and annually with self-reported history of hypertension and medications used for hypertension control (mean 8 years follow up). Postmortem evidence of cerebrovascular disease including size and location of infarcts (large and small blood vessels) and other neurologic disorders such as AD were also collected. Mean systolic/diastolic blood pressure was 134/71 mm Hg. Both having a higher mean systolic blood pressure and faster declines in systolic decline over time correlated with an increased number of brain infarcts after controlling for APOε4, blood pressure medications, and vascular risks factors. The main limit of the study was lack of access to midlife blood pressures. The study strongly suggests that blood pressure is still the most important risk factor for silent strokes.

This article is of particular interest because a faster decline in systolic blood pressure in late life has not been discussed in the past, especially as it relates to cognitive decline.

Clinical Neurology Correlates of Blood Pressure Changes

In another study of 1440 people who were Framingham offspring participants, 750 women who were free of dementia at midlife (mean age 55) attended 5 consecutive examinations every 4 years until late life (mean age 69 ± 6) and were followed for incident dementia for an average of 8 years.⁷ The study determined the effect of midlife hypertension (140/90 or higher mm Hg), lower late-life blood pressure (<100/70 mm Hg), persistence of hypertension during mid to late life, and steep decline in blood pressure from mid to late life over an 18-year period. During the follow-up period, 107 participants (71 women) developed dementia. Midlife systolic hyper-



tension and persistence of systolic hypertension into late life were associated with an increased risk of dementia. Individuals with low to normal blood pressure (less than 140/90 mm Hg) at midlife or a steep decline in systolic blood pressure during mid to late life had more than a twofold increase in dementia. The study concluded that elevated blood pressure during midlife; persistence of elevated blood pressure into late life; and among those without hypertension, a steep decline in blood pressure during mid to late life were all associated with an increased dementia risk. Hypertension predisposes people to stroke and dementia through many pathways including increasing cerebral small vessel disease by lipohyalinosis, fibrinoid necrosis, and microbleeds. Cardiac disease due to hypertension leads to cerebral hypoperfusion and reduced clearance of β -amyloid. Other studies have shown greater cortical atrophy and white matter hyperintense lesions with steep blood pressure declines over 20 to 25 years as well as impaired cognitive performance compared to those with stable blood pressure from mid to late life.^{8,9}

At the Alzheimer's Association International Conference in 2018, data from the SPRINT trial^a were presented. This trial is studying blood pressure management in adults (>50), with a therapeutic goal of systolic blood pressure less than 140 mm Hg and a more aggressive lowering of systolic blood pressure to 120 mm Hg or less. More aggressive lowering of systolic blood pressure to 120 mm Hg or less reduced the risk of cardiovascular mortality and morbidity by 30%.

In the SPRINT MIND substudy of the trial, cognitive scores were measured in both blood pressure groups along with total white matter lesions. In the 9,361 adults in the higher systolic blood pressure group (mean age 68) with increased cardiovascular risk but no diabetes, dementia, or prior strokes, cognitive assessment was done in 92% of subjects. After a year of treatment, the mean systolic blood pressure was 121 mm Hg in the intense treatment group and 136 mm Hg in the standard treatment group. Cognitive testing in the intense treatment group showed a 19% lower rate of new diagnosis of mild cognitive impairment (MCI) than in those in the standard blood pressure group.

The combined outcome of MCI plus dementia was lower in the intense blood pressure treatment group but did not meet statistical significance. The class of blood pressure medications did not affect the outcome. Hypotension, syncope, electrolyte abnormalities, and acute renal failure occurred more often in the intense treatment group. Brain imaging in 454 subjects at baseline and 4 years after randomization showed 18% fewer white matter lesions in the more aggressive treatment group

than in those in the standard care group. The study followed subjects for less than 4 years and did not include tests for amyloid positivity or AD diagnosis. Reducing the incidence of MCI however was very important.

Why might blood pressure decline lead to increased dementia risk?

The association between declines in blood pressure and dementia is multifactorial.⁷ With advancing age, arterial elasticity declines leading to impaired autoregulation and ability to maintain adequate cerebral perfusion in the setting of blood pressure fluctuations.¹⁰ This predisposes those of advanced age to cerebral ischemia from episodes of hypotension as well as reduction in amyloid clearance.

A decline in blood pressure has been observed in the early stages of dementia; this is proposed to be because of neurodegenerative effects on brainstem and hypothalamic nuclei controlling blood pressure and the coexistent development of weight loss and cardiovascular disease (including heart failure and myocardial infarction) in the age group that reduces blood pressure and cerebral perfusion.^{11,12} More work regarding the association of cognitive decline and dementia with aggressive blood pressure treatment is needed. Careful blood pressure monitoring, especially home based and observing pulse pressure during monitoring, can provide more accuracy and insight related to aggressive blood pressure control in patients in later life.

Blood Pressure Monitoring and Control

This information makes blood pressure monitoring in elderly patients more complicated because most neurologists don't monitor or treat blood pressure. Many patients do not monitor their own blood pressure and primary care physicians may only see many of their elderly patients a few times per year. Many patients presume their blood pressure is fine because it was apparently normal at their last visit. There are some patients who take their own blood pressure 3 to 4 times a week and keep a record of these pressures and let their doctor know when it is consistently elevated so adjustments can be made.

To add fuel to the fire that suggests rapid blood pressure decline is common in elderly patients, the American College of Cardiology this year published new recommended blood pressure levels based on literature review and meta-analysis. They stated that blood pressure levels should be equal or less than 130/80 mm Hg, preferably closer to 120/80 mm Hg, regardless of age, or medical conditions including secondary stroke prevention, stable ischemic heart disease, diabetes, and ischemic kidney disease.¹³

a. Systolic blood pressure intervention trial (NCT01206062).



Clinical Recommendations for Neurologists

Fortunately, the November 6, 2018 issue of the *Journal of the American Medical Association* was entirely devoted to hypertension. Qamar et al stated that the lower recommended blood pressure of 130/80 mm Hg and preferable 120 to 129/80 mm Hg identifies more than 18 million more adults in the US at an elevated risk of cerebrovascular disease than recognized by previous blood pressure cutoffs.¹⁴ Wang et al stated that measuring office blood pressures is still very important because if the patient has elevated blood pressure, he or she needs to be told that home blood pressure monitoring should be done with results reported to the physician who is treating the hypertension.¹⁵ For patients who take required blood pressure medication, it is essential to reinforce that it should be taken as directed, that is, daily. It is recommended that the physician tell the patient to take her or his blood pressure twice in the morning and twice in the evening for 3 to 5 days consecutively and report the results to the blood pressure treating physician who can then adjust blood pressure medications as needed. Patients should continue to take their home blood pressure 2 times a week, notifying the physician if it is higher or lower than expected. Strategies involving blood pressure measurements in pharmacies, barbershops, hair salons, and grocery stores should be encouraged to give patients more feedback on their blood pressure with or without symptoms.

These new blood pressure guidelines are very important for neurologists who see patients on a regular basis for dizziness, vertigo, cognitive impairment, and transient ischemic attack (TIA). A blood pressure measurement should be taken while the patient is lying down, sitting, and standing.

If the blood pressure is elevated but there is no positional significant drop, then be sure the patient is taking any blood pressure medications, keeping track of home blood pressure, and reporting results to the treating doctor. If the patient has postural hypotension with or without symptoms at the time of blood pressure measurement, the blood pressure medications may require adjustment and should be reported to the treating physician to make changes. This is very important in patients over age 65 who were treated for a target blood pressure less than 130/80 mm Hg, which could possibly lead to further small symptomatic or silent strokes as previously discussed.

The neurologist should contact the treating blood pressure physician to briefly discuss this problem and concern, communicate these to the patient and their caregivers, and follow them closely. Such communication will increase the role of the neurologist to help in blood pressure control, but our responsibility is to help patients with increased risk of potential cerebrovascular disease.

Conclusion

Clinicians have known for a long time that hypertension is a major cause of multiple medical and neurologic disorders and death. Although it can be difficult, the persistence of this silent killer should be more aggressively treated, and the new recommended blood pressure treatment guidelines are a step in the right direction. However, the current literature provides some evidence that, in some patients, because lower blood pressure occurs in aging and by requiring blood pressure lower than 130/80 mm Hg and closer to 120/80, patients in later life may develop more symptomatic and silent small strokes.

As neurologists, we need to look more carefully at our patients' blood pressure and ask if they are taking their blood pressure medication (especially for those with possible symptomatic cerebral vascular disorders such as "dizziness, cognitive decline, and TIAs"), and increase communication to our patients' primary blood pressure therapist (primary care physician, cardiologist etc.).

More clinical and pathological studies are needed to be sure that our more aggressive blood pressure guidelines are not leading to more silent and symptomatic small strokes and predisposing patients to neurodegenerative cognitive disorders. ■

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