Increased Arterial Stiffness Trumps on Blood Pressure in Predicting Cognitive Decline in Low-Risk Populations

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See related article, pp 171–175

Cognitive impairment and dementia have become serious human, social, and economic burdens. WHO and the G8 Dementia Summit (2013) emphasized prevention as a key element to counteract the dementia epidemic. Thus, identifying risk factors that predict cognitive decline and dementia has been the holy grail of epidemiologists. Identifying such risk factors can be used to target individuals in whom modifiable risk factor should be mitigated. There is increasing evidence that cardiovascular disease and its risk factors contribute to the development of cognitive impairment.

With its rich vascularization and low resistance to flow, the brain is particularly susceptible to cardiovascular dynamics. Thus, the relation of high blood pressure (BP) with cognitive function and dementia has, in recent years, received much attention from epidemiological research, resulting in inconsistent observations. Multiple factors may be contributing to these inconsistent observations, including the wide use of antihypertensive medications and the inherent variability of BP measurements. In this context, Ihab Hajjar et al fill this important gap in our knowledge by demonstrating that the increased arterial stiffness is superior to BP in predicting cognitive decline in all domains and in explaining the hypertension–executive function association in healthy subjects.

As stated by Pase et al in their important article: Increased stiffness of central arteries causes an increase in the speed of arterial wave propagation so that reflected waves arrive back at the aorta earlier, during the systolic part of the cardiac cycle. As a consequence, the systolic BP is augmented, whereas the diastolic BP is reduced, creating an increase in arterial pulse pressure. As a result of increased arterial stiffness, the cerebral vasculature is exposed to the potentially damaging forces of augmented arterial pulse pressures.

Many noninvasive methods have been developed to quantify arterial stiffness. Pulse wave velocity (PWV) measures the speed of a pulse wave travelling between 2 selected sites of measurement; this increases as arterial stiffness increases. The measurement of PWV between the carotid and femoral sites reflects arterial stiffness along the aorta, the primary site of age-associated arterial stiffening. This approach is considered to be the gold standard in the noninvasive assessment of large artery stiffness.

In this article of Hypertension, a prospective cohort study was conducted from several hundred participants to evaluate the usefulness of BP and arterial stiffness in predicting cognitive decline and explaining the hypertension–executive decline association. The major results of the study are as follows. At the population level, the authors found that higher arterial stiffness, measured as PWV, but not BP levels predicts a greater decline in cognitive function across multiple domains for healthy adults. Although hypertension is traditionally associated with a greater decline in executive function, this relationship was better explained by higher PWV rather than elevated BP. Finally, the authors identified a significant interaction between a history of hypertension and PWV such that subjects with hypertension and higher PWV had the greatest 4-year risk for decline in executive function. Thus, higher PWV, predicting hypertension, may be responsible for impaired cognition predicting cognitive decline.

Despite our understanding of the epidemiological evidences that suggest a role of arterial stiffness in cognitive decline, the pathophysiologic mechanisms remain unclear and relatively unexplored. Several pathways linking arterial stiffness and cognitive decline have been postulated (Figure). First, when arteries undergo stiffness, they often result in damages to pressure pulsatility. The increase in central pulse pressure results in hemodynamic stress in the heart, as well as in high-flow end-organs to which it is transmitted, such as the brain. High local blood flow is associated with low microvascular impedance, which facilitates penetration of excessive pulsatile energy into the microvascular bed. This may contribute to repeated episodes of microvascular ischemia and tissue damage and manifests as white matter hyperintensities, clinically unrecognized focal brain infarcts, and tissue atrophy, each of which contributes to cognitive impairment and frank dementia. Moreover, the high levels of central pulse pressure in the brain result in structural changes and dysfunction to its microcirculation, increasing inflammation and oxidative stress. Second, high pulse pressures may result in structural changes to cerebral blood vessels, which may in turn interfere with the transport of important nutrients to the brain, as well as interfere with the clearance of toxic byproducts out of the brain. Third, recent brain imaging studies have increasingly linked arterial stiffness to cerebral microvascular disease and changes in the functioning of the frontal-subcortical regions of the brain, such as white matter hyperintensities, which in turn are associated with cognitive impairment. Finally, arterial stiffness has also been demonstrated as an independent...
predictor of CVD events and CVD risk factors, which in turn are important predictors of cognitive decline. The cellular/molecular proinflammatory mechanisms underlying the relationship between arterial stiffness and cognition, including inflammation, oxidative stress, cerebral hypoperfusion, or impaired cerebral vasoreactivity, are novel putative candidates to be targeted by interventions aimed at attenuating cognitive disorders. As the cognitive consequences of central arterial stiffening continue to emerge, strategies to combat this covert degenerative process of arterial aging should emphasize the long-term control of modifiable vascular risk factors. Thus, this study for the first time clearly identified a prevention intervention time in the time course toward cognitive dysfunction and dementia. However, the data from Hajjar et al.7 open new horizons in clinical research of the cognitive decline. As correctly pointed out by Qiu et al.4: The following research questions need to be addressed in the future: (1) Is there any modifying effect of genetic factors (eg, family dyslipidemia and diabetes mellitus) and environmental factors (eg, educational attainment and lifestyle) on the relation between increased arterial stiffness and cognition and dementia? (2) What are the optimum arterial stiffness levels required to maintain cognitive function? (3) What is the most effective antihypertensive treatment regimen? (4) Finally, long-term community-based prospective studies that integrate epidemiological and clinical data with neuropathological and neuroimaging information are needed to better understand the mechanisms that link increased arterial stiffness to neurodegeneration. Further clarification of these questions will eventually contribute to the development of preventive strategies against cognitive decline.

Disclosures

None.

References

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In the article by Marfella and Paolisso (Marfella R, Paolisso G. Increased arterial stiffness trumps on blood pressure in predicting cognitive decline in low-risk populations. Hypertension. 2016;67:30–31. doi: 10.1161/HYPERTENSIONAHA.115.06450), which published online ahead of print November 2, 2015, and appeared in the January 2016 issue of the journal, corrections were needed.

Two citations and a reference have been added. On page 30, left column, line 23, the text “As stated by Pase et al in their important article8:” was added as a source for the remaining paragraph, citing Pase et al, which was added in the reference list:


Subsequent citation numbers in text were updated to reflect the added reference.

On page 31, left column, line 13, “As correctly pointed out by Qiu et al4:” was added as a source for the remaining paragraph, citing Qiu et al in the reference list.

The authors regret the errors.

These corrections have been made to the current online version of the article, which is available at http://hyper.ahajournals.org/content/67/1/30.