Subjects aged >80 years (the so called old-old subjects) are the fastest growing segment of the population, contributing to the aging of an aging population. In this age group, the prevalence of clinical overt dementia is 30% (when compared with 7% in subjects >65 years of age),\(^1\) representing a great burden to family and caregivers and to healthcare costs.

In the current issue of *Hypertension*, Cooper et al\(^2\) reported that elevated carotid-femoral pulse wave velocity (PWV) was associated with higher cerebral white matter hyperintensities (WMH) volume and vascular resistance and higher odds for the presence of subcortical infarcts in a large population of old old subjects. PWV has also been confirmed to be associated with more impaired memory function. When peripheral vascular resistance and cerebral WMH were introduced in the model as the only mediator candidates related to both carotid-femoral PWV and memory score,\(^2\) PWV effect on memory remained significant, but decreased by 41%.

The study confirmed that arterial stiffness, indexed as PWV, is an independent and significant determinant of cognitive function. It is remarkable that this association is consistently reported in both population studies and patients.\(^3\)

Notably, WMH and peripheral vascular resistance—separately and jointly—impacted on memory function. Alteration in white matter structure has been recognized to play a relevant role in cognitive function. Changes in peripheral vascular resistance indicate that cerebral microcirculation is undergoing vascular remodeling that, in turn, reduces vasodilator responses (hyperemic flow reserve) because even at full vasorelaxation, the remodeled small artery lumen area is reduced.\(^4\) Consequently, older subject are more susceptible to intermittent hypotension and relative ischemia, with the onset and progression of WMH.\(^5\) Indeed, the simultaneous occurrence of WMH, higher PWV, and hypotension has been reported to dramatically accelerate the progression to dementia in subjects with subjective complaints of memory loss.\(^6\)

All these findings taken together should results in a positive attitude in clinical practice. In fact, aortic stiffening and cerebral microvascular damage are partly reversible, also—but not exclusively—through an accurate control of established cardiovascular risk factors.\(^7\) Prevention of dementia by slowing the progression of cognitive impairment should be routinely pursued as a primary therapeutic goal in older subjects\(^8\) by targeting the cross talk between large and small (cerebral) arteries.\(^9\)

The study by Cooper et al\(^2\) leaves at least 2 relevant open questions. The first one is the complexity of the parameter PWV, routinely measurable in a reproducible manner even in clinical practice. In fact, a reduction in the elastic components of arterial wall,\(^10\) an increased impedance mismatch between elastic and muscular arteries,\(^11\) and microvascular damage with increased peripheral resistance\(^12\) are all major contributors to arterial aging and PWV increase. The in-depth characterization of this complexity may facilitate identification and discovery of novel therapeutic agents capable to decrease age-associated increase in PWV and, thus, to facilitate prevention of cognitive impairment and dementia.

The second open question relates to the recognition of cognitive impairment as a target-organ-damage in hypertension, primarily in older subjects.\(^12\) The major identified issue in pursuing routine assessment of cognitive organ is the availability of a reliable marker for cerebral/cognitive damage and its costs. For instance, 2013 Guidelines of the European Society of Hypertension and European Society of Cardiology\(^13\) proposed brain magnetic resonance imaging as the potentially more relevant mean to evaluate cerebral damage related to hypertension, but wisely considered its (unsustainable) high cost for screening purpose. If PWV remain a significant and strong determinant of cognitive function independently of brain WMH (and cerebral peripheral vascular resistance), we can envision (and suggest) a broader diffusion of PWV routine assessment in clinical practice.

**Disclosures**

None.

**References**


Are Hemodynamic Factors Involved in Cognitive Impairment?
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