Cognitive Decline and Dementia
Are We Getting to the Vascular Heart of the Matter?

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See related article, pp 651–661

H uman lifespan has increased linearly during the past 170 years. Not only do we live to an older age but also we do so in better health and with less disability. Healthcare advances have turned previously fatal or crippling diseases into chronic comorbidities. Especially in the field of cardiovascular medicine, medical advances have shifted the age of onset of common disorders, such as myocardial infarction, to higher age, together with improved functional outcome after treatment. This has led to what is known as compression of morbidity: serious disability caused by chronic diseases occurs only in the last years of life.

Looming over this prospect of a long life in good functional status is the threat of cognitive decline. Rough estimates of the prevalence of dementia show a strong increase with age from 5% at the age of years 65 to 20% at the age of 80 years and 40% at the age of 90 years. The majority (>70%) of these dementia cases results from Alzheimer disease. A distressing note is that, despite tremendous research efforts, all (mainly antiamyloid) Alzheimer drugs that have been developed since the cholinesterase-inhibitors (1996–2001) have failed to produce clinical benefit. For other prominent causes of dementia (vascular dementia, Lewy body dementia, and frontotemporal dementia), there is an equal lack of effective treatment.

However, hopeful news emerges from a previously unforeseen corner: the cardiovascular field. Recent population cohort studies have found that the relative prevalence of all-cause dementia has declined (absolute numbers continue to rise because of the growing number of elderly), and this decline has been attributed to the improved cardiovascular care that has been available in the lifetimes of these cohorts.1

In this issue of Hypertension, Böhm et al1 have analyzed ≈25,000 patients at high risk for cardiovascular disease, who had participated in hypertension trials. Patients with cognitive impairment at baseline were excluded, as were patients with uncontrolled hypertension (on-treatment blood pressure [BP] >160/100 mm Hg). This excluded group contained mainly older elderly with more severe comorbidity. Cognitive function was assessed at baseline, after 2 years (100%) and at study end (=90% of patients), which was between 3 and 5.5 years. BP and heart rate were recorded at regular intervals (6 months), with an average of 11 recordings during a period of 4.5 years. These patients provide a wealth of data that are highly welcome in a field that is obscured by cross-sectional studies, short follow-up studies with only a single measurement of BP or cognition, and underpowered intervention studies.

Critics will scrutinize the use of the Mini Mental State Examination as the sole determinant of cognitive function, and the absence of clinical, imaging, or pathological confirmation of diagnosis. The Mini Mental State Examination is insensitive to dementia in patients with higher education and those with vascular dementia and is sensitive to confounding (eg, depression). However, the power here is in the large numbers and repeated assessments. The patterns of decline in Mini Mental State Examination that emerge in this study, taking into account what we have learned from other studies, most likely truly reflect trends of cognitive decline in this population. Approximately 5% of patients developed cognitive impairment (suggesting that they were somewhere on the continuum of mild cognitive impairment and dementia), which is consistent with what would have been expected based on population studies of dementia in this age group.1 Because of this, and because the Mini Mental State Examination is more sensitive to cognitive decline because of Alzheimer disease than to vascular dementia, we can postulate that the causes of cognitive decline in these patients reflect the causes observed in the larger population (ie, mostly Alzheimer, mixed Alzheimer/vascular pathology followed by vascular dementia). This is supported by the fact that exclusion of patients with stroke did not alter the results.4

Before moving to the major and new findings, an important confirmatory finding is that high systolic BP (>145 mm Hg) was associated with incident cognitive impairment (although not as an independent predictor), and that low-normal BP (<124 mm Hg) was not, the latter contradicting conclusions from cross-sectional studies that a low BP may be detrimental for cognitive function. However, the oldest and most frail patients were not included in this analysis, and specifically in this group, optimal BP levels remain unknown.
Thinking outside the box, beyond the supply of oxygen and glucose, the brain’s vasculature may play an important role in clearance of toxic waste from the brain, including Alzheimer amyloid-β (Aβ). The paravascular circulation of brain interstitial fluid and cerebrospinal fluid along penetrating arterioles is dependent on adequate pulsatile flow. Could high BP variation or high heart rate be causes or markers of a reduced vascular clearance?

All in all, the observations by Böhm et al should stimulate a strong research effort, unifying the cardiovascular and neuroscience fields, aimed at elucidating the links between vascular disease and onset and progression of cognitive decline.

Disclosures

None.

References


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