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EDITORIAL

Vascular prevention and dementia

M. Muller,* Y.M. Smulders

Department of Internal Medicine, VU University Medical Center Amsterdam, the Netherlands,
*corresponding author: e-mail: m.muller@vumc.nl

The prevalence of dementia, including Alzheimer's disease, is expected to increase several-fold in the coming decades to an expected global prevalence of more than 100 million by 2050. This anticipated rise in prevalence can largely be attributed to increasing longevity and ageing of the baby boomer generation. The incidence of all-cause dementia nearly doubles every five years of age.

Given the expected dramatic increase in the incidence and prevalence of dementia, the identification of successful prevention and treatment strategies is critical. Current pharmaceutical options only modestly improve symptoms and cannot cure or prevent dementia. As a result, prevention of dementia through risk factor identification and modification is of the utmost importance until disease-modifying agents prove efficacious.

Although Alzheimer's disease and vascular dementia have traditionally been viewed as distinct disorders, it is now generally agreed that the two rarely occur in isolation. Both types of dementia share risk factors and histopathological features with atherosclerosis.[1] In addition, the presence and severity of cerebrovascular disease parallels the presence and severity of Alzheimer's disease. Thus, it is intuitively tempting to speculate that modification of vascular risk might reduce the risk of dementia.

In this issue, Richard *et al.*[2] discuss the current knowledge of the relation between vascular risk factors and dementia, and address the effect of treatment of vascular risk factors on incident dementia. Over the last decades epidemiological evidence has accumulated that increased vascular risk, especially during midlife, increases the risk of incident dementia. However, as the authors appropriately discuss, results of randomised clinical trials aiming at treatment of a single vascular risk factor in preventing cognitive decline or dementia are inconsistent. This lack of convincing trial results is only partly due to the relative lack of studies. Rather, it is the design of most cardiovascular studies that precludes firm conclusions on dementia prevention. Firstly, a long follow-up may be needed to assess the effects on dementia, which is both by nature and by definition a slowly evolving disease. In addition, a secure diagnosis of dementia is not as easy as diagnosing for example a heart attack, and usually requires cognitive decline of some magnitude before satisfying diagnostic criteria. Consequentially, a problem in the design of cardiovascular dementia prevention studies is that effects of risk modification on cardiovascular endpoints will often precede effects on clearly identifiable dementia. Any study thus runs the risk of early termination by data safety monitoring boards before the effect on dementia incidence can be firmly established. In terms of dementia prevention, it is thus possible that we will remain dependent on indirect evidence from suboptimally designed trials. Hopefully, ongoing studies particularly aimed at dementia prevention will provide a further basis for clinical recommendations.

Another important issue is cardiovascular risk modification in those already affected by dementia or earlier degrees of cognitive impairment. Conceivably, this may not be an issue for lipid lowering or platelet inhibition. For blood pressure lowering, however, the dilemma is complex.[3] In elderly individuals, in particular those with cerebrovascular pathology, cerebral autoregulation may be impaired, leaving vital brain tissue unprotected against the potentially harmful effect of lower perfusion pressure.[4] Low or even normal systemic blood pressure levels may be inadequate for optimal cerebral perfusion, causing a decline in brain function. Since many elderly subjects with dementia suffer from cerebrovascular pathology, higher blood pressure levels may be required in these patients to prevent further cognitive decline.[5] Preliminary evidence indeed suggests that lower blood pressure in combination with cerebrovascular pathology may have detrimental effects on the brain and consequently may aggravate existing cognitive impairment.[6,7] However, the level of blood pressure associated with such detrimental effects, as well as the determinants of inter-individual differences in this level, are unknown.

Meanwhile, the clinician is faced with the dilemma how to treat older patients with increased vascular risk. We believe it is prudent to start primary cardiovascular

prevention based on the conventional criteria, which include global cardiovascular event risk, comorbidity, and patient preference. Such a policy is supported by strong epidemiological evidence, but requires good clinical judgment just the same. In our view, fear of dementia, however justified, should not guide pharmacological cardiovascular risk factor management. In those who already have dementia or milder forms of cognitive impairment, clinicians should be careful. Antihypertensive therapy, if it is decided to be appropriate, should include proper follow-up with attention given to the hazard of cognitive deterioration, particularly if blood pressure drops significantly or reaches levels considered 'normal' by usual standards.

Many questions remain regarding the use of cardiovascular prevention regimens with advancing age especially in the older patient with complex diseases. Competing risks, comorbid conditions, polypharmacy and drug interactions, tolerability, and safety may alter the benefit/harm balance in older patients. In addition, applying these prevention regimens to older patients with multiple chronic diseases, a group that includes half of the population older than 65 years, may present the patient with an unsustainable treatment burden, making independent self-management and adherence difficult. Applying pharmacological cardiovascular prevention regimens in patients late in life should therefore build on principles of appropriate prescribing and includes a consideration of remaining life expectancy, goals of care, and potential benefits of medication.[8]

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