

The Association of Cognitive Function and Cerebrovascular Health with the Risk of Future Cardiovascular Events and Mortality: A Mini-Review

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Human lifespans are prolonged today than in the immediate past around the world. Overall, life expectancy has been gradually increasing for many years and has more than doubled in the past two centuries [1]. The growing elderly populations are associated with several challenges of the medical and economic policies due to the increased number of care-needed dependent older people limited by age-associated cognitive impairment [2]. The human brain deteriorates with age; however, the rate and the paths of declines among the brain regions and between individuals are not indistinguishable [3]. Age-associated cognitive decline is a relevant experience that happens over the lifespan. However, there are considerable heterogeneities among elderly populations both inter- and intra-individually [4,5]. Changes in brain structure are dependent on many factors but are mostly related to age, sex, and vascular health [6]. Vascular health is a significant factor associated with cognitive brain ageing and cardiovascular events. Several studies have shown that a decline in vascular health has substantial impacts on the brain health [7]. Although the brain comprises only about 2% of body mass, it receives nearly 20% of total cardiac output. Cerebral microcirculation is responsible for delivering oxygen and nutrients needed for metabolism and the deterring of toxic products. Therefore, cerebral microcirculation is essential in preserving brain health and is associated with normal and pathological cognitive brain ageing in terms of age-related structural and functional brain abnormalities [8]. Vascular risk factors, including hypertension, hyperlipidemia, obesity, smoking, and diabetes mellitus, are all independently associated with structural brain abnormalities before the clinical manifestation of cardiovascular or cerebrovascular diseases [9]. Moreover, regardless of their roles in overt vascular events, vascular risk factors are related to pathological brain changes and accelerate the risk of cognitive impairment, dementia, and mortality [10-12].

In addition, research has demonstrated that poor cognitive function and dementia prior to the onset of cerebrovascular accidents and cardiovascular events are associated with a greater risk of such events [13,14]. The lower cognitive function might

reflect the previous exposure to cardiovascular risk factors and substantial covert vascular damages that can predispose a person to clinically recognized cardiovascular events in the future. Therefore, poor cognitive function performance might be considered as an early manifestation of clinically unrecognized cerebral and systemic vascular pathologies, which signals the future risk of cardiovascular events and mortality [15].

Neuroimaging studies have shown that existing structural brain abnormalities, including infarcts, microbleeds, white matter hyperintensities, and low cerebral blood flow, are robustly related to worse cognitive performance [16-18]. Additionally, it has been presented that impaired brain structural integrity and insufficient cerebral blood flow are associated with a greater risk of cardiovascular and non-cardiovascular mortality in older adults [19,20]. Thus, brain lesions and impaired cerebrovascular hemodynamics have been proposed as major mechanisms behind the link between cognitive impairment and mortality. Briefly, cognitive impairment and abnormalities in brain structures reflect the lack of brain integrity and may put elderly individuals at an increased risk of mortality [21]. Moreover, findings from several studies have indicated that certain domains of cognition might be more vulnerable to the adverse effects of cardiovascular risk factors [22]. Impaired executive function and attention is a major clinical presentation in patients with vascular cognitive impairment, whereas memory deficit is mainly associated with Alzheimer's type of dementia [23,24].

The association between cognitive function and the risk of vascular injuries can be explained in different ways. Cardiovascular risk factors such as obesity, smoking, hypertension, diabetes mellitus, and arterial fibrillation are associated with both cognitive impairment and cardiovascular diseases [25-28]. Besides, lower socioeconomic status and risky lifestyle behaviors, such as lower educational attainment, unhealthy diet, sedentary behavior, and pattern of alcohol intake, which indirectly increase the risk of coronary heart disease and stroke, could be considered as risk factors for cognitive impairment [29-

31]. Health literacy is the other prominent possible mechanism underlying this association. People with poor health literacy are less likely to seek preventive strategies before the onset of diseases, have less ability to recognize the symptom of the disease, and less tendency to stick to the treatment procedure [32,33]. Moreover, such risk factors affect the brain's neural plasticity and integrity, which are needed for optimal brain and body functioning [34]. Study findings have suggested that evaluating different domains of cognitive function may identify participants at higher risk of cardiovascular diseases, and it can be used, alone or in combination with other predictors, to detect individuals at increased risk of vascular events and improve the prevention strategies [35].

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