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Review Article

Arterial stiffness and cognitive impairment

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ABSTRACT

Background: Arterial stiffness is one of the earliest indicators of changes in vascular wall structure and function and may be assessed using various indicators, such as pulse-wave velocity (PWV), the cardio-ankle vascular index (CAVI), the ankle-brachial index (ABI), pulse pressure (PP), the augmentation index (AI), flow-mediated dilation (FMD), carotid intima media thickness (IMT) and arterial stiffness index-β. Arterial stiffness is generally considered an independent predictor of cardiovascular and cerebrovascular diseases. To date, a significant number of studies have focused on the relationship between arterial stiffness and cognitive impairment.

Objectives and methods: To investigate the relationships between specific arterial stiffness parameters and cognitive impairment, elucidate the pathophysiological mechanisms underlying the relationship between arterial stiffness and cognitive impairment and determine how to interfere with arterial stiffness to prevent cognitive impairment, we searched PUBMED for studies regarding the relationship between arterial stiffness and cognitive impairment that were published from 2000 to 2017. We used the following key words in our search: "arterial stiffness and cognitive impairment" and "arterial stiffness and cognitive impairment mechanism". Studies involving human subjects older than 30 years were included in the review, while irrelevant studies (i.e., studies involving subjects with comorbid kidney disease, diabetes and cardiac disease) were excluded from the review.

Results: We determined that arterial stiffness severity was positively correlated with cognitive impairment. Of the markers used to assess arterial stiffness, a higher PWV, CAVI, AI, IMT and index-β and a lower ABI and FMD were related to cognitive impairment. However, the relationship between PP and cognitive impairment remained controversial. The potential mechanisms linking arterial stiffness and cognitive impairment may be associated with arterial pulsatility, as greater arterial pulsatility damages the cerebral microcirculation, which causes various phenomena associated with cerebral small vessel diseases (CSVDs), such as white matter hyperintensities (WMHs), cerebral microbleeds (CMBs), and lacunar infarctions (LIs). The mechanisms underlying the relationship between arterial stiffness and cognitive impairment may also be associated with reductions in white matter and gray matter integrity, medial temporal lobe atrophy and Aβ protein deposition. Engaging in more frequent physical exercise; increasing flavonoid and long-chain n-3 polyunsaturated fatty acid consumption; increasing tea, nitrite, dietary calcium and vitamin D intake; losing weight and taking medications intended to improve insulin sensitivity; quitting smoking; and using antihypertensive drugs and statins are early interventions and lifestyle changes that may be effective in preventing arterial stiffness and thus preventing cognitive impairment.

Conclusion: Arterial stiffness is a sensitive predictor of cognitive impairment, and arterial stiffness severity has the potential to serve as an indicator used to facilitate treatments designed to prevent or delay the onset and progression of dementia in elderly individuals. Early treatment of arterial stiffness is beneficial and recommended.

Contents

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1. The relationship between arterial stiffness and cognitive impairment

Atherosclerotic disease is an important global disease. As the incidence of atherosclerotic disease has increased, clinicians and researchers have focused increasing amounts of attention on subclinical atherosclerosis. Structural and functional changes in the vascular wall, which may be detected by clinicians, may occur during the early stage of vascular diseases.

Arterial stiffness is characterized by decreases in arterial volume changes with pressure and is a consequence of the loss of vessel elasticity and arterial compliance. Arterial stiffness has become one of the earliest indicators of changes in vascular wall structure and function [1].

Cognitive impairment is defined as varying degrees of cognitive dysfunction attributable to deficits in a variety of domains, including learning, memory, language, executive function, orientation, attention, visuospatial reasoning and other domains. The symptoms of cognitive impairment are progressive and range from mild cognitive impairment (MCI) to dementia. Cognitive impairment may be caused by multiple diseases, such as Alzheimer's disease (AD), cerebral vascular disease-related cognitive dysfunction, lobar frontotemporal dementia, and hepatolenticular degeneration. AD and mixed dementia (AD combined with vascular disease-related cognitive dysfunction) are the two most common types of dementia.

Arterial stiffness is generally considered an independent predictor of cardiovascular and cerebrovascular diseases, as well as other fatal diseases [2,3]. Numerous recent studies have demonstrated that an independent relationship exists between arterial stiffness and cognitive impairment [4]. Those studies assessed arterial stiffness using various parameters, such as pulse-wave velocity (PWV), the cardio-ankle vascular index (CAVI), the ankle-brachial index (ABI), pulse pressure (PP), the augmentation index (AI), flow-mediated dilation (FMD), intima media thickness (IMT) and arterial stiffness index-β.

To investigate the relationships between each of the above arterial stiffness parameters and cognitive impairment, elucidate the pathophysiological mechanisms underlying the relationships and determine how to interfere with arterial stiffness to prevent cognitive impairment, we searched PUBMED for studies regarding the relationship between arterial stiffness and cognitive impairment that were published from 2000 to 2017. We used the following key words in our initial search: "arterial stiffness and cognitive impairment". We subsequently performed a second search using the key words "pulse-wave velocity and cognitive impairment", "cardiac-ankle vascular index and cognitive impairment", "ankle-brachial index and cognitive impairment", "pulse pressure and cognitive impairment", "augmentation index and cognitive impairment", "flow-mediated dilation and cognitive impairment", "intima media thickness and cognitive impairment", "arterial stiffness index-β and cognitive impairment", "arterial stiffness and cognitive impairment mechanism", and "arterial stiffness treatment". We then reviewed the two sets of search results and screened them to identify relevant studies. Studies involving human research subjects older than 30 years were included in the study, while irrelevant studies (i.e., studies involving subjects with other comorbid diseases, such as kidney disease, diabetes and cardiac disease) were excluded from the review. We identified ninety-seven papers, including 41 papers (including 32 cross-sectional studies, 10 longitudinal studies and 1 combined cross-sectional/longitudinal study) regarding the relationship between arterial stiffness and cognitive impairment (Table 1 summarizes the longitudinal studies, Table 2.1 summarizes the cross-sectional studies with positive results, and Table 2.2 summarizes the cross-sectional studies with neutral or negative results), 15 papers regarding the pathophysiological mechanisms underlying the relationship between arterial stiffness and cognitive impairment, and 41 papers regarding arterial stiffness prevention and treatment.

1.1. PWV

PWV, a non-invasive measure of vascular wall elasticity, is defined as the propagation speed of pulse waves traveling between two points in an arterial system. A higher PWV is indicative of poor vessel wall elasticity and compliance, which contribute to increases in blood vessel stiffness [5]. PWV includes carotid-femoral pulse-wave velocity (cfPWV) and brachial-ankle pulse-wave velocity (baPWV). cfPWV is defined as the propagation speed of pulse waves traveling from the carotid arteries to the femoral arteries, whereas baPWV is defined as the propagation speed of pulse waves traveling between the brachial and ankle arteries. cfPWV is currently considered the gold standard method for measuring arterial stiffness [6]. A previous review of twelve studies involving >6000 individuals that was published in 2012 noted the existence of a significant association between increased arterial stiffness and cognitive impairment via multivariate analysis following adjustments for age, education level, and other factors that influence cognition. Moreover, the review determined that arterial stiffness is related to the longitudinal progression of cognitive decline and that a higher PWV is a significant predictor of subsequent cognitive decline [7]. We reviewed 11 clinical studies (6 cross-sectional studies, 4 longitudinal studies and 1 combined cross-sectional/longitudinal study) that were published from 2000 to the present day. Eight of these studies (3 cross-sectional studies, 4 longitudinal studies and 1 combined cross-sectional/longitudinal study) provided evidence supporting the idea that a higher PWV is linked to cognitive impairment and the longitudinal progression of cognitive decline [8–15]. In the indicated studies, a higher PWV was confirmed to be related to memory loss [8], poorer processing speeds [11] and declines in executive function [8,11,12]. Moreover, a higher continuous cfPWV was determined to predict an increased 10-year risk of MCI in dementia-free elderly Framingham individuals with a mean age of