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Review

Cardiovascular Comorbidities and Cognitive Impairment

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Abstract

Various grades of cognitive impairment generally occur in older adults over the age of 55, where cardiovascular risk factors such as diabetes and/or hypertension, coronary artery disease, or cerebrovascular accidents are also common. Cognitive impairment occurs in various forms, from mild or amnesia such as forgetting today's date to more ominous and progressive forms, such as frank dementia. Over 5 million people worldwide suffer from dementia, most of whom live in low- and middle-income countries. It has been envisaged from the beginning that dementia or cognitive impairment has neurodegenerative origins. However, recent studies have indicated that dementia may have a mixed origin or may be preceded by vascular insult and then neurodegenerative pathology. From a pathophysiological standpoint, one of the puzzling questions in the field of cognitive impairment and comorbidities is that it is not clear whether cardiovascular comorbidity or cognitive impairment comes first. Cognitive impairment negatively affects mobility and fitness and this can potentially contribute to development of hypertension or/and diabetes. The present review examines this perplexing situation and tries to anser whether the comorbid conditions are innocent bystanders to cognitive impairment or they play greater causative roles. The rationale of the review is that it is possible to address these

cardiovascular risk factors for dementia prevention and hence it summarizes the evidence related to cardiovascular risk factors and cognitive impairment.

Keywords
Cognitive impairment; cardiovascular comorbidities; dementia; hypertension; diabetes.

1. Introduction

Cardiovascular diseases are known to contribute to cognitive decline [1-6], but it is unclear whether the reverse is also true. It is clear that hypertension or/and diabetes are common cardiovascular conditions leading to changes in brain structure and function.

The incidence of both cognitive impairment and cardiovascular risk factors increases with age, it seems plausible question to examine the association between the two [1]. Therefore, there is a strong need to understand whether concomitant or comorbid cardiovascular risk factors contribute to cognitive decline, more importantly, the nature of the association of cardiovascular risk factors with cognitive decline.

As mentioned previously, it is clear that controlling cardiovascular risk factors may slow cognitive decline [1]. However, the nature of the association between them is unclear [2, 3]. Therefore, it is necessary to document the contribution of common cardiovascular factors such as hypertension, diabetes, overweight, dyslipidemia, etc. in cognitive decline. A simple algorithm can be proposed in terms of risk factors that may be conferred by the presence of these factors, either individually or in groups.

The purpose of this review is to collate the evidence related to cardiovascular risk factors and cognitive impairment. This has major implications in today's world, as life expectancy increases the burden of non-communicable diseases also increases. Also, the additional importance is implementation gaps that exist in the area of cognitive impairment, especially in primary care [1]. It is well known that cardiovascular risk factors can be addressed with appropriate interventions. However, there are no proven interventions to address the cognitive impairment at present. Hence this intervention aims to ensure the appropriate control of cardiovascular risk factors and compliance with the drugs that can potentially prevent cognitive impairment. It is hoped that this approach may slow or prevent the onset of dementia which is particularly relevant for low- and middle-income countries like India.

2. Association between Cardiovascular Comorbidities

Studies have indicated that cardiovascular factors (e.g. hypertension or/and diabetes, coronary artery disease, cerebrovascular accidents, arterial disease, etc) affect the development of cognition [1-6]. A recent study [7] with more than 400 participants confirmed that the presence of cardiovascular risk factors impacts mild cognitive impairment development, which is detectable in the primary care setting. It has been suggested that cardiovascular risk factors like hypercholesterolemia and hypertension are key factors in the development of mild cognitive impairment, and therefore, measures to control these two conditions in primary care should be reinforced to stop the development of dementias [7, 8]. A similar study [9] provided additional

evidence for the link between cardiovascular risk factors and cognitive dysfunction in mild cognitive impairment subjects and demonstrated that comorbid risk factors increased the degree of cognitive deficit, indicating a higher risk of developing dementia.

Vascular contributions to cognitive impairment and vascular dementia are characterized by the aging neurovascular unit facing and failing to cope with biological damages caused by systemic and cerebral vascular disease, proteinopathy including Alzheimer's biology, metabolic disease, or immune response, resulting in cognitive decline [8, 9]. Atherosclerosis has been described as a predictor of cognitive impairment [10] and has the potential as a drug target to prevent or delay the onset and progression of dementia in older adults. Hence, early identification and treatment are recommended.

3. Cardiovascular Risk Factors as Catalyst for Cognitive Decline

It is natural for a person to experience a certain degree of cognitive decline after a certain age (healthy aging). However, in those with cardiovascular risk factors, this cognitive decline may be accelerated. If someone has experienced a heart attack or angina, cognitive decline is anticipated, indicating a temporal association with biological plausibility.

Cardiovascular diseases can affect the ability of blood vessels to deliver oxygen to various parts of the brain [9, 10]. The link between cardiovascular risk factors like obesity, diabetes, hypertension and dyslipidemia, and cognitive impairment is becoming increasingly apparent. This “heart-brain” connection is important, and those with poor heart health may also have poor memory. Likewise, in patients with heart failure, poor memory can cause mental confusion.

Apart from poor memory and blurred consciousness, impaired thinking and disorientation can occur in severe cases as well. In the same manner, cardiovascular risk factors can cause cognitive impairment due to their association with small vessel disease. Small vessel disease could affect cerebral blood flow by disrupting the blood-brain barrier and increasing susceptibility to neurological injuries (Figure 1).

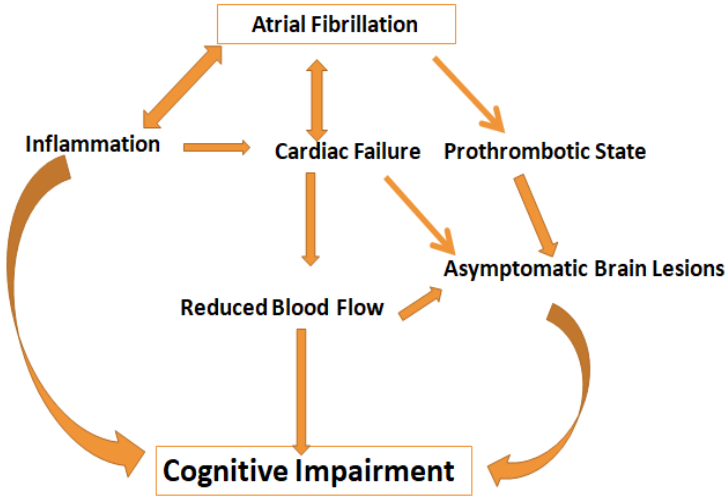

Figure 1 Heart diseases can cause poor memory or/and cognitive decline. Poor tissue perfusion can potentiate asymptomatic brain lesions that may later contribute to the development of cognitive impairment or/and dementia.

A recent large study [11] was done to evaluate the impacts of cognitive impairment and systemic vascular comorbidities on hazards of all-cause and cardiovascular mortality in a representative United States population (subjects ≥60 years of age).

The study concluded that the confluence of cognitive impairment with other systemic vascular comorbidities predicted further increased risks of mortality. Hence, more extensive assessments and management of cognitive function and systemic vascular comorbidities are warranted [11]. It is logical to assume that a combination of mild cognitive impairment with cardiovascular risk factors may increase mortality and it is suspected that hypertension plays a lead role in most such cases in this regard [12]. The relationship between cardiovascular risk factors and cognitive decline is explained in Figure 2.

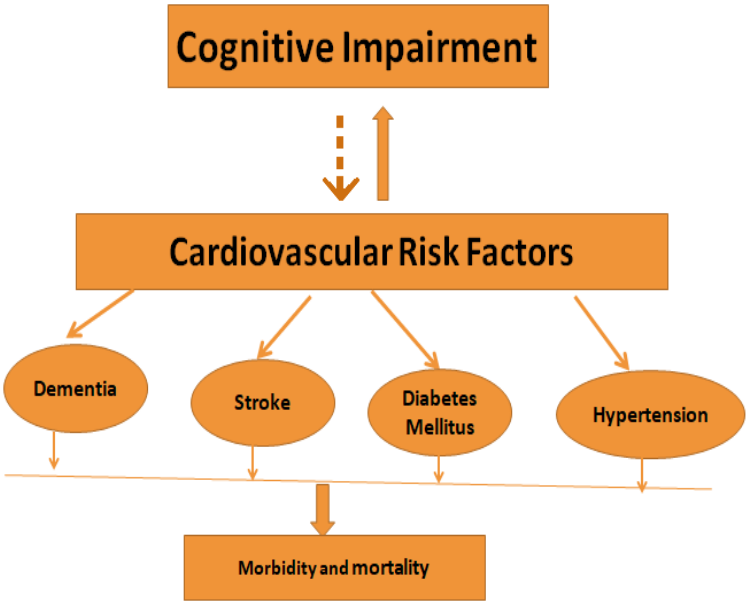

Figure 2 Relationship between cognitive impairment and cardiovascular factors. Note that cardiovascular factors are well-known risk factors for several noncommunicable diseases such as stroke, hypertension and diabetes in addition to cognitive impairment. Hence, addressing the comorbidities with cognitive impairment not only has the potential to slow cognitive decline or contribute towards better cognitive health but addressing them can also prevent other catastrophic cardiovascular events.

4. Treating Cardiovascular Risk Factors Associated with Cognitive Impairment

While it is clear that cardiovascular risk factors are associated in patients with cognitive impairment, what is not clear is whether addressing these risk factors will lead to a slowing down or even reversal of cognitive impairment in specific patients. In terms of association, it seems to be considered important to systematically address these risk factors. The main issue seems to be adherence to long-term treatment, and a study done by our group almost a decade ago showed poor compliance to drugs that have the potential to slow cognitive decline or prevent dementia, even among those who received the medicines for free [13]. Consider that studies have shown that incipient cognitive impairment may be common [1, 14].

4.1 Non-pharmacological Prevention

It is well known that cognitive impairment is common among older adults and is associated with factors known to be linked to a higher risk of cognitive decline and dementia. Identifying cognitive impairment in those with cardiovascular risk is important and several scales have been described for the same. The clock-drawing test may be valuable for identifying high-risk individuals who may then benefit from targeted non-pharmacological prevention (Mediterranean diet, exercise, cognitive training, and vascular risk factor management) [14]. Community education is an essential part of re-integrating the patient into the social setting. Reducing social isolation and increasing community engagement are important to maintain the patient's independence in their own homes [15]. A host of non-pharmacological preventive measures have been described, which can address cardiovascular risk factors contributing potentially or actually to cognitive impairment [16].

4.2 Pharmacological Prevention

Unfortunately, at present, there is no drug for preventing dementia. However, drugs such as antihypertensives, anti-diabetes, and lipid-lowering can address risk factors and hence may be useful for dementia prevention. Though, there may be compliance-related issues regarding the same [13]. The field of pharmacological prevention of dementia is vast at present.

5. Cardiovascular Risk Factors in Other Neurodegenerative Diseases

Cardiovascular factors have been reported in other neurodegenerative diseases as well, such as Parkinson's disease [17, 18]. These have also been associated with behavioral and psychological symptoms of dementias [19] and hippocampal atrophy, one of the earliest and most severely affected structures [19-27]. Perhaps hormones such as glucocorticoids synergize with vascular factors in causing vascular damage [28]. Hypersensitive/vulnerable individuals could be prone to the development of vascular components inside the brain, which may contribute to cognitive impairment [29]. Affected neural structures such as the hippocampus could undergo atrophy which could invite other pathologies such as seizures [30]. Since the pharmacological management of dementia is still limited [31], other options are being searched [32]. Cognitive impairment, regardless of the cause, predisposes individuals to abuse available medications such as benzodiazepines [33]. Hence early screening of dementias, even in primary care appears to be a feasible and acceptable option [34].

6. Prognosis Based on Cardiovascular Comorbidities in Cognitive Impairment

It has been envisaged that mortalities [11] in patients with cognitive impairment are likely to be higher if they have cardiovascular comorbidities. Hence, predicting prognosis based on cardiovascular comorbidities has been suggested [35]. Modifiable risk factors for Mild Cognitive Impairment (MCI) should be sought (at the very latest) in persons who already have MCI, as their optimal treatment may improve these patients' cognitive performance or keep the existing deficits from progressing [36]. Modifiable comorbidities should always be addressed in cognitive impairment [37]. Indeed, addressing comorbid conditions could help identify patients with

cognitive impairment in the community [34, 38]. This will help screen out the patients with mild cognitive impairment at the earliest stage from the community [39].

Geriatric cardiology is an emerging subject [40], where along with cardiac conditions, cognitive impairment can be screened at the earliest. Measures of cardiovascular risk have been associated with cognitive impairment across various populations [41]. Control of cardiovascular risk factors has been linked to beneficial effects on cognition in cross-sectional and prospective follow-up studies, but the results of interventional trials have been disappointing [42]. However, there seems to be a plausible biological basis in terms of disturbed cerebral hemodynamics in patients with cognitive impairment and cardiovascular comorbidities [43-49] and appears to be an area of research. Change in cognitive performance has been associated with treatable vascular risk in people over 35 years of age [46]. Evidence indicated that in those with stable coronary artery disease, cognitive performance [47-50] has been linked with modifiable [51] cardiovascular risk factors. It has also been shown that having a cardiovascular condition (e.g. heart disease) is associated with lower cognitive impairment-free life expectancy [52]. Hence, minimizing exposure to multiple cardiovascular risk factors may be useful in helping to improve the cognitive health expectancy in specific populations.

7. Conclusions

Comorbid cardiovascular conditions with cognitive impairment are common and appear to be important therapeutic targets along with managing cognitive impairment itself. This may not only reduce the excess mortality but may also slow/manage cognitive decline due to the potential concomitant adverse effects of cardiovascular risk factors (e.g. hypertension and diabetes) on cognitive performance.

Author Contributions

Dr Vikas Dhikav convceived the idea, drafted the manuscript, did proof reading, and addressed the pre-publication comments. Pankaj Kumar made figures in the paper and helped in proof reading and addressing the comments prior to publication. Dr Praveen Kumar Anand did editorial corrections in the manuscript before final publication.

Competing Interests

The authors have declared that no competing interests exist.

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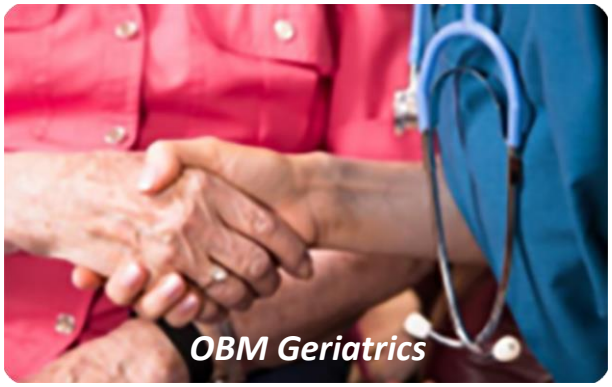

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