Comment on Association between Coronary Heart Disease, Heart Failure and Risk of Alzheimer's Disease

The authors[1] have attempted to evaluate the association between cardiovascular diseases (CVD) and the risk of Alzheimer's disease (AD). They came up with the results that coronary heart disease (CHD) and heart failure (HF) were associated with 22% and 53% elevated risk of AD, respectively. We believe this is a valuable topic to explore, but the results should be further analyzed to reach a stable conclusion.

AD is the leading cause of dementia. The prevalence of dementia will triple worldwide by 2050 and that estimate will be three times higher when based on a biological (rather than clinical) definition of AD.[2] CVD and AD are both common in aging populations. *Dementia in Europe Yearbook 2019* has suggested that the strong push on public health messaging on cardiovascular health and smoking cessation might be vital for reducing the prevalence of dementia.[3] In addition, cardiovascular risk factors were suggested to be associated with an increased risk of dementia.[2] The currently available treatments for AD are mainly treatments of symptoms but not curative therapies; hence, the prevention or reducing AD risk aroused great attention.[4] Identifying and managing risk factors is vital for AD prevention strategies. Previous studies suggested that early identification and correct medical treatment of cardiovascular conditions may reduce the prevalence of AD.[5] However, the relationship between CVD and AD remains unclear. The exploration of the association between CVD and AD in this study is of great clinical significance.

This study concluded that CHD and HF are associated with an increased risk of developing AD. However, the high heterogeneity (I^2 = 96.8% ~ 97.2%) of this study indicates that the conclusion is unstable. The authors also mentioned the result of the association between HF and AD inconsistent with a previous research,[6] which has lower but still high heterogeneity (I^2 = 74.8%). The reasons for this inconsistency have not been fully explored in the article. One possible reason could be the difference in the population, as this study included patients with AD, while the previous study included patients with all-cause dementia. In addition, the improper meta-regression and subgroup analysis lead to unclear sources of heterogeneity. Only publication year, age, gender, follow-up time, population, and type of studies are considered as the heterogeneity factors. The results of meta-regression and subgroup analysis indicated none of the above factors were responsible for the heterogeneity between included studies. However, the diagnosis of AD, education level, smoking, hypertension, and body mass index, which are the factors closely related to AD[7] and CVD,[8,9] has not been analyzed as possible heterogeneity source. Further meta-regression and subgroup analysis should be conducted to reduce the heterogeneity, thereby reaching stable conclusions.

In addition, the summary and discussion of the included studies investigating the association between CVD and the risk of AD are insufficient. We noticed that most included cohort and case-control studies have mostly adjusted the currently known risk factors for AD, such as education, APOE4 status, age, gender, hypertension, body mass index, and diabetes. However, more attention should be paid to modifiable risk factors in clinical research, especially lifestyle-related factors. Previous studies have suggested that intervention of lifestyle-related factors, including physical exercise, mentally stimulating activities, social activities, smoking, diet, and alcohol use, to individuals at risk of dementia could effectively prevent cognitive impairment.[10] Particularly, cigarette smoking status, a modifiable risk factor for both CHD[9] and AD,[4] should be paid more attention to in future relevant cohort and case-control studies. The improvement of relevant clinical studies quality is vital for clarifying the relationship between CVD and AD.

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