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EDITORIAL COMMENT

Heart and Brain Failure*

The Vicious Cycle of the Heart-Brain Interaction

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The prevalence of heart failure is increasing in aging populations. Furthermore, dementia is more prevalent in patients with heart failure.[1] Dementia is detected 10 years earlier in patients with heart failure in Asian countries, particularly low-income countries, than in Western countries.[2] Heart failure and dementia share similar cardiovascular risk factors, such as age, hypertension, diabetes, dyslipidemia, and increased arterial stiffness,[3] which explains their overlap in elderly patients. In this issue of JACC: Asia, Ren et al[4] report that in a large database of patients with heart failure in Hong Kong (mean age 75.3 years, 51.3% women) that 11.0% developed dementia during an average follow-up period of 4.1 years. Heart failure patients with dementia were at a 4.5-fold higher risk of all-cause mortality, 5.4-fold higher risk of cardiovascular death, and 3.8-fold higher risk of noncardiovascular death. An analysis of a longitudinal dataset indicated a causal relationship between decreased cardiac function and cognitive decline.

Although the mechanisms linking heart failure to dementia (the heart-brain interaction) have not yet been elucidated in detail,[3] deceases in the left ventricular ejection fraction and stroke volume[5] in heart failure patients have been proposed to contribute to this relationship. A reduced stroke volume may decrease cerebral blood flow. Inflammation, autonomic nerve dysregulation, and hypercoagulability may play a role in the pathogenesis of dementia in patients with heart failure. In the ARIC study,[6] left atrial reservoir strain, conduit strain, contractile strain, emptying fraction, and active emptying fraction were identified as predictors of the development of dementia, whereas left atrial volume was not. Atrial fibrillation was reported to be associated with cognitive decline,[7] and direct oral anticoagulants[8] and catheter ablation[9] for atrial fibrillation was reported to suppress cognitive decline. An increase in edema, measured as the extracellular water per total body water ratio, associated with diastolic dysfunction was recently implicated in cognitive dysfunction in elderly patients with heart failure.[10] Edema in the brain has been suggested to affect the metabolism and washout of amyloid beta and/or tau protein from the cerebrospinal fluid of patients with heart failure and thus warrants further study.

The risk of cardiovascular and noncardiovascular mortality was reported to increase following the development of dementia in elderly patients with heart failure.[4] Heart failure patients with dementia often have sarcopenia and cachexia. Nutritional changes caused by hypoperfusion and edema in skeletal muscles, the intestines, and visceral organs may contribute to the risk of cardiovascular and noncardiovascular mortality.[11] Autonomic nerve dysregulation has been detected in some patients with dementia, particularly those with Lewy body disease. Elderly patients with heart failure are also more susceptible to infections owing to a decreased lymphocyte count, which s a parameter in the Controlling Nutritional Status score and results in worsening heart failure and increased mortality.

Heart failure patients that develop dementia enter a vicious cycle of heart failure, dementia, malnutrition, sarcopenia, and cachexia, which is associated with an increased risk of all-cause mortality. Therefore, the prevention of cognitive decline is important in elderly patients with heart failure. Meta-analyses of antihypertensive medications showed that renin-angiotensin drug that crossed the blood-brain barrier[12] and angiotensin II receptor blockers were

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predictive of cognitive decline.[13] Sodium-glucose cotransporter 2 inhibitors, which are prescribed to patients with heart failure, reduced cognitive decline in diabetic patients.[14] A clinical trial to evaluate the efficacy of sacubitril/valsartan for prevention of cognitive decline and amyloid beta deposition in chronic heart failure patients with a preserved ejection fraction is awaited. However, the efficacy of diuretics to reduce cognitive decline in patients with heart failure remains unclear. After elderly patients with heart failure develop severe dementia and cachexia, the discontinuation of cardioprotective agents may be required because of low blood pressure and renal dysfunction. Elderly patients with heart failure and dementia sometimes require social support to improve adherence to medication. Therefore, heart failure may ultimately cause brain failure in elderly patients. Based on these findings, brain function needs to be considered in the management of elderly patients with heart failure.

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REFERENCES

1. Li J, Wu Y, Zhang D, Nie J. Associations between heart failure and risk of dementia: a PRISMA-compliant meta-analysis. *Medicine*. 2020;99:e18492.

2. Lam CS, Teng TK, Tay WT, et al. Regional and ethnic differences among patients with heart failure in asia: the Asian Sudden Cardiac Death in Heart Failure Registry. *Eur Heart J*. 2016;37:3141–3153.

3. Doehner W, Ural D, Haeusler KG, et al. Heart and brain interaction in patients with heart failure: overview and proposal for a taxonomy. A position paper from the Study Group on Heart and Brain Interaction of the Heart Failure Association. *Eur J Heart Fail*. 2018;20:199–215.

4. Ren Q-w, Teng T-HK, Tse Y-K, et al. Incidence, clinical correlates, and prognostic impact of dementia in heart failure: a population-based cohort study. *JACC: Asia*. 2023;3(1):108–119.

5. Jefferson AL, Himali JJ, Au R, et al. Relation of left ventricular ejection fraction to cognitive aging (from the Framingham Heart Study). *Am J Cardiol*. 2011;108:1346–1351.

6. Wang W, Zhang MJ, Inciardi RM, et al. Association of echocardiographic measures of left atrial function and size with incident dementia. *JAMA*. 2022;327:1138–1148.

7. Bunch TJ. Atrial fibrillation and dementia. *Circulation*. 2020;142:618–620.

8. Friberg L, Andersson T, Rosenqvist M. Less dementia and stroke in low-risk patients with atrial fibrillation taking oral anticoagulation. *Eur Heart J*. 2019;40:2327–2335.

9. Jin M-N, Kim T-H, Kang K-W, et al. Atrial fibrillation catheter ablation improves 1-year follow-up cognitive function, especially in patients with impaired cognitive function. *Circ Arrhythm Electrophysiol*. 2019;12:e007197.

10. Futami S, Ishikawa J, Jubishi C, et al. Prevalence and determinants of cognitive impairment in elderly patients with heart failure—pilot study in a geriatric hospital. *Circ Rep*. 2020;2:265–270.

11. von Haehling S. The wasting continuum in heart failure: From sarcopenia to cachexia. *Proc Nutr Soc*. 2015;74:367–377.

12. Ho JK, Moriarty F, Manly JJ, et al. Blood-brain barrier crossing renin-angiotensin drugs and cognition in the elderly: a meta-analysis. *Hypertension*. 2021;78:629–643.

13. Scotti L, Bassi L, Soranna D, et al. Association between renin-angiotensin-aldosterone system inhibitors and risk of dementia: a meta-analysis. *Pharmacol Res*. 2021;166:105515.

14. Pawlos A, Broncel M, Woźniak E, Gorzelak-Pabiś P. Neuroprotective effect of SGLT2 inhibitors. *Molecules*. 2021;26.

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