

Frailty, heart failure, and cognitive impairment: a triangle in elderly people

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Abstract

Considering the high incidence of heart failure (HF) in elderly individuals, more attention should be given to geriatric conditions, especially frailty and cognitive impairment. These conditions significantly affect the course of HF, its management, and its prognosis in the elderly. The recently developed concept of frailty includes both the decline in physical function and cognition. The prevalence of physical frailty and cognitive impairment ranges between 15% and 74% and between 25% and 80%, respectively, depending on the criteria used for the diagnosis and on the study population. It is estimated that, in at least one-quarter of elderly patients, HF is complicated with both physical frailty and cognitive impairment. To date, there are no standardized screening tools for cognitive impairment in patients with HF, but the Montreal Cognitive Assessment seems to be better than the Mini-Mental Status Examination. The mechanistic relationships between HF and cognitive impairment are complex and have not been fully elucidated. One of the most important factors is cerebral perfusion abnormalities in patients with HF; therefore, specific interventions that can increase cardiac output may improve cognitive impairment in patients with HF. Increasing evidence demonstrates that cognitive function significantly improves following, among other possible treatments, exercise in patients with HF. Further investigations regarding the pathophysiological interaction among physical frailty, HF, and cognitive impairment are needed to implement strategies to treat or prevent frailty in elderly patients with HF. ■ *Heart Metab.* 2018;76:8-12

Keywords: cognitive impairment; elderly; physical frailty

Elderly patients with heart failure: high risk for frailty and cognitive impairment

Along with the robust increase in the elderly population, the increasing incidence of heart failure (HF) in older people has become the most challenging problem in developed countries due to the

associated high mortality rates and economic costs.^{1,2} Considering the advanced age of individuals with HF, we should pay more attention to geriatric conditions, including multiple morbidities, polypharmacy, disability, malnutrition, frailty, and cognitive impairment.^{1,3-5} Each of these conditions significantly affects the course of HF, its management, and its prognosis in the elderly.

Abbreviations

ADL: activities of daily living; **CBF:** cerebral blood flow; **HF:** heart failure; **IADL:** instrumental ADL; **LVAD:** left ventricular assist device; **MMSE:** Mini-Mental Status Examination; **MoCA:** Montreal Cognitive Assessment

Frailty represents a complex clinical syndrome characterized by decreased physiological reserve, increased vulnerability to stressors, and most importantly, reversibility by appropriate interventions.²⁻⁵ Frailty was mainly considered from the perspective of decline in physical function, the so-called physical frailty. Recently, neuropsychiatric status, including cognitive impairment and depression, as well as social conditions, such as solitude, have been shown to contribute to frailty.^{5,6} A consensus group consisting of the International Academy on Nutrition and Aging and the International Association of Gerontology and Geriatrics defined cognitive frailty as “a syndrome in older adults with evidence of both physical frailty and cognitive impairment without a clinical diagnosis of Alzheimer’s disease or another dementia.”⁷

Among patients with HF, the prevalence of frailty ranged from 15% to 74%, depending on the criteria used for diagnosis and on the study population.^{3,5} The pathophysiology of HF directly contributes to frailty by reducing exercise capacity and skeletal muscle function. Furthermore, patients with HF are more susceptible to cognitive impairment, which accelerates the development of physical frailty and HF, resulting in a vicious cycle.¹⁻⁴

This review discusses the pathophysiology and clinical implications of and therapeutic strategies for cognitive impairment in elderly patients with HF.

Definitions, assessment, and epidemiology

Cognition is a superior cortical function involving multiple brain processes that allow an individual to perceive information, learn, and remember specific knowledge and use this to solve problems and plan actions in daily life.^{8,9} Cognitive function covers different specific aspects, known as cognitive domains, including memory, attention/working memory, psychomotor speed, executive function, language/speech, and visuospatial/constructional function.^{8,9}

Cognitive impairment in elderly patients with HF indicates impairment of one or more of the above-

mentioned cognitive domains, and presents acutely as delirium or chronically as dementia or mild cognitive impairment.^{2,3,10} Dementia is a chronic condition characterized by severe cognitive impairment that interferes with an individual’s ability to perform basic activities of daily living (ADL) and instrumental ADL (IADL), social activities, and occupational responsibilities. Dementia is progressive and generally irreversible. In contrast, mild cognitive impairment is defined as chronic cognitive deficits that make any performance of IADL more difficult than usual, but which are not severe enough to impair the ability to perform most IADL and basic ADL. Despite the observed constant rate of mild cognitive impairment progressing to dementia, mild cognitive impairment is thought to be a reversible condition, similar to physical frailty.^{2,3,6,10}

The prevalence of cognitive impairment in patients with HF ranged from 25% to 80%, depending on the measures used and the characteristics of the HF sample studied.^{4,9-15} Patients with HF have a higher risk for cognitive impairment than people without HF, after controlling for other factors, such as age, sex, and comorbidities.¹⁶ In patients of similar age with or without HF, patients with HF had worse cognition in the domains of memory, attention, psychomotor speed, and executive function.^{8,9} In contrast, language and visuospatial ability are less affected in patients with HF, although only a few studies assessed them in patients with HF. Interestingly, Athilingam et al showed that the pattern of impaired cognitive domains was different between patients with HF with reduced ejection fraction and patients with HF with preserved ejection fraction.¹⁷ This finding might be associated with the pathophysiology of cognitive impairment in patients with HF.

Despite the higher prevalence of cognitive impairment, there are no standardized tools recommended to screen for cognitive impairment in patients with HF. The Mini-Mental State Examination (MMSE) is a widely used instrument for cognitive testing in older people, with or without HF^{10,11,13,18}; however, it seems to lack sensitivity for detecting mild cognitive impairment.^{10,11,18} Patients with HF and mild cognitive impairment will often score within the normal range on the MMSE, meaning that mild cognitive impairment may be underestimated. A recent study demonstrated that the observed prevalence of cognitive impairment by the MMSE score corrected by age and

education were 27.6% in patients with HF (mean age, 71 ± 11 years).¹³ The Montreal Cognitive Assessment (MoCA) is being increasingly used in patients with HF because the MoCA covers numerous cognitive domains and is sensitive for detecting cognitive deficits in older patients with HF.^{9-12,18} A recent study demonstrated that physical frailty was identified in 49% of patients with HF and that 58% of them had cognitive impairment detected by the MoCA.¹² In contrast, the complication of cognitive impairment in nonfrail patients with HF was only 8%, although the mean age of the sample in this study was 57 ± 10 years. Therefore, it is expected that at least one-quarter of patients with HF are suffering from cognitive frailty. A recent systematic review and meta-analysis indicated that the odds ratio for cognitive impairment in the HF population was 1.67 (95% CI, 1.15-2.42) in case control studies involving those with and without HF (1414 participants).¹⁶ This study also revealed that the prevalence of cognitive impairment in HF cohorts (4175 participants) was 43% (95% CI, 30-55).

Pathophysiology

The mechanistic relationships between HF and cognitive impairment are complex and not fully elucidated; however, there are several emerging themes within the literature that provide mechanistic insight into this relationship (Figure 1).^{2,3,6,9,11,19} Risk factors are independently associated with both HF and cognitive impairment.^{2,3,6} For example, coronary artery disease, hypertension, and diabetes mellitus are independent risk factors for cognitive impairment, which is also frequently observed in patients with HF. In addition, depression, atrial fibrillation, and sleep apnea are more common in patients with HF than in the general population, and each of these conditions is independently associated with cognitive impairment.^{2,3,6}

One of the most important factors for cognitive impairment is hemodynamic stress in patients with HF.^{2,9,19} Reduction in cerebral blood flow (CBF) is often considered a determinant in brain changes affecting

patients with HF. CBF depends on several variables, such as cardiac output, blood pressure, and cerebrovascular reactivity.⁹ Cerebral microvascular architecture in older patients is disrupted by a combination of age-associated changes and vascular risk factors.² Therefore, it is difficult to maintain adequate CBF in response to hemodynamic disturbances. The capacity of cerebral vascular autoregulation is further reduced in older patients with HF. In addition, disruption in cerebral perfusion may result from abnormal blood viscosity that contributes to the development of microemboli in patients with HF.^{2,19} Cardiac output is an important determinant of CBF.^{9,19} Evidence from large observational studies showed that reduced cardiac output is linked to cognitive impairment.^{9,19} A recent study by Suzuki et al demonstrated that reduced CBF in the posterior hippocampus was significantly associated with the severity of cognitive impairment in patients with HF.²⁰ The posterior hippocampus plays a major role in cognitive function and its hypoxic vulnerability has been confirmed in patients being resuscitated after cardiac arrest.²⁰

In addition to hemodynamic stress and hypercoagulation in patients with HF, systemic inflammation may contribute to the development of cognitive impairment by inducing neuroinflammation and disrupting neurovascular coupling in the blood-brain barrier.^{6,11,19} The coexistence of systemic inflammation is also associated with the development of physical frailty in patients with HF.⁵ Furthermore, the changes in the neurohormonal axis of patients with HF may have a role in the relationship between HF, cognitive impairment, and structural brain changes,^{6,11} includ-

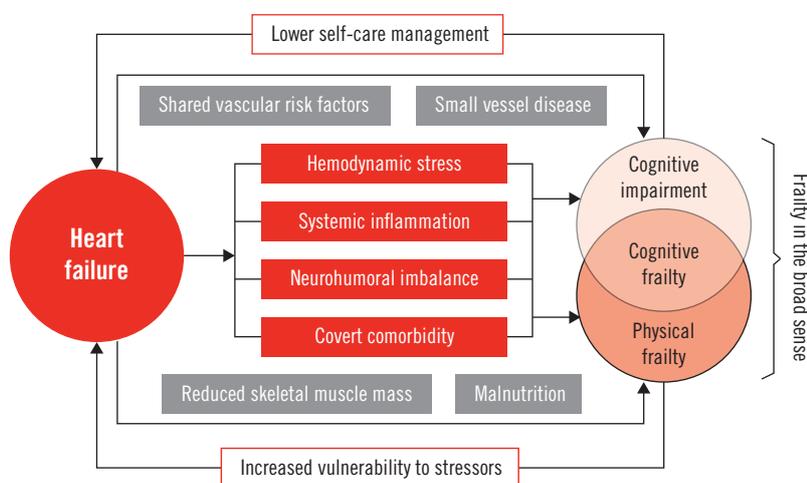


Fig. 1 Pathophysiology and the impact between heart failure, cognitive impairment, and frailty.

ing elevated serum levels of cortisol and catecholamines and activation of the renin-angiotensin-aldosterone system.

Clinical impact and therapeutic strategies

Cognitive impairment can affect the ability of elderly patients with HF to manage their disease, recognize worsening of symptoms, make appropriate decisions about their health, and adhere to specific and complex therapeutic regimens, meaning that they have a significantly lower self-care management.^{9,10} The co-existence of cognitive impairment in patients with HF is very important in determining mortality, hospital admission, poor quality of life, and functional decline.¹⁻³ At worst, patients with HF and cognitive impairment exhibited almost a five-fold increase in mortality.¹⁵

The course of cognitive changes in patients with HF was examined in the context of HF treatments and the length of follow-up periods vs a control group.¹⁴ Hajduk et al reported that a significant decline in cognitive function was observed in patients with HF followed-up after more than 1 year.¹⁴ In contrast, cognitive function in patients with HF improved over a short time period (<1 year) when they underwent interventions to ameliorate cardiac function. In the studies using a comparison group without HF, cognitive function in patients with HF decreased or stabilized over time, suggesting that patients with HF are at risk for cognitive decline, but this risk seems to be modified by appropriate cardiac treatment.

While cognitive function improved after cardiac transplantation and following left ventricular assist device (LVAD) implantation,^{21,22} recent studies showed that LVAD implantation did not improve cognitive function significantly, although it improved the frailty status.^{23,24} Cardiac resynchronization therapy is reported to not only improve cardiac function, but also cognitive function in selected patients with symptomatic HF.^{25,26} These interventions might improve cardiac output and reduce cerebral hypoperfusion, but are not applicable in all patients with HF.

Other possible treatments include exercise, increasing physical activity, and treatment for comorbidities, such as hypothyroidism, vitamin B12 deficiency, sleep apnea, anticholinergic medication use, depression, infections, and visual and hearing disturbances.^{2,9-11} Taking measures to minimize polypharmacy and malnutrition in patients with HF are useful

to prevent cognitive decline.^{1,2} Treatment with angiotensin-converting enzyme inhibitors²⁷ or digoxin²⁸ may improve neuropsychological functions. Increasing evidence demonstrates that cognitive function significantly improves following exercise in patients with HF.^{2,11,29,30} Exercise and cardiac rehabilitation are also effective to prevent the development of physical frailty.^{1,5}

Unfortunately, no definitive consensus on the optimal method to avoid changes in cognitive function in patients with HF has been achieved. Further investigations regarding the pathophysiological interactions among physical frailty, HF, and cognitive impairment are needed to identify strategies to treat or prevent cognitive impairment in elderly patients with HF. ■

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