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Research Progress on Cognitive Frailty in Elderly Patients with Heart Failure

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Abstract

With the deepening of aging in our country, frailty, as a common elderly syndrome, has become a new prominent public health problem. Cognitive frailty, as a component of frailty, often coexists with heart failure, leading to a variety of adverse clinical outcomes. However, most of the current studies are devoted to cross-sectional investigation of the incidence of cognitive frailty in patients with heart failure and discussion of the correlation between the two, and the studies on its pathogenesis and intervention measures are scattered, and the review literature is relatively lacking. Moreover, in-depth study of the pathogenesis of such patients and exploration of effective intervention measures are extremely necessary to improve the quality of life and prognosis of patients. Therefore, this paper expounds the pathophysiological mechanism and summarizes the intervention measures in combination with relevant recent research, aiming to provide reference for the development of intervention programs for people with heart failure combined with cognitive frailty.

Keywords: heart failure, cognitive frailty, assessment, prevalence, prognosis, mechanisms, management, systematic review

1. Introduction

Heart failure is the final stage of cardiovascular disease, which seriously endangers human life and is characterized by high fatality rate, high hospitalization rate and poor quality of life of patients (Tsutsui H, IsobeM, Ito H et al, 2019). It has been reported (Wang H, Chai K, Du M, et al, 2021) that the prevalence of heart failure in people aged 65-79 and ≥80 years in China is 3.86% and 7.55%, respectively, which has caused serious impact on the health of our people and increased the economic burden. Cognitive frailty was specifically defined by the International Society of Nutrition and Aging and the International Association of Gerontology and Geriatrics in 2013 as a heterogeneous clinical syndrome characterized by simultaneous physical frailty and cognitive impairment. The key conditions to be met include simultaneous physical frailty and cognitive impairment, but not clinical diagnosis of Alzheimer's disease or other dementias (Kelaiditi E, Cesari M, Canevelli M, et al, 2013). The incidence of adverse clinical outcomes such as fall, disability, re-hospitalization and death after cognitive frailty in patients with heart failure has increased significantly, seriously affecting the prognosis and quality of life of patients (Beltrami M, Fumagalli C & Milli M, 2021). Early identification and timely intervention can provide a new target for the prevention and intervention of pathological aging and its adverse consequences (Bu Z, Huang A, Xue M, et al, 2021). This paper intends to systematically summarize the criteria, epidemiology, adverse consequences and intervention measures of cognitive frailty in patients with heart failure, so as to provide theoretical basis for early identification and formulation of preventive measures.

2. Concept

2.1 Cognitive Frailty

As a heterogeneous clinical manifestation, cognitive frailty is characterized by both physical frailty and cognitive impairment; Key factors defining the condition include the presence of physical frailty and cognitive impairment (assessed at 0.5 on the Clinical Dementia Rating Scale (CDR)) and the exclusion of Alzheimer's disease (AD) or other types of dementia. These two defining criteria mean that cognitive decline is characterized by reduced cognitive reserve, which is distinct from physiological brain aging, but may be a precursor to neurodegenerative processes (Kelaiditi E, Cesari M, Canevelli M, et al, 2013).

2.2 Cognitive Impairment

Cognitive impairment is divided into three types: subjective cognitive decline (SCD), MCI and dementia.

1) SCD refers to a state in which an individual's subjective sensory, memory, and cognitive functions decline while the objective neuropsychological test results are within the normal range (Sachdev P, Andrews G, Hobbs MJ, et al, 2009).

2) MCI is defined as impairment of memory or other cognitive functions, but the ability to live daily lives is not significantly affected and does not meet the criteria for dementia diagnosis. MCI can be divided into two categories: amnestic MCI and non-amnestic MCI, and non-amnestic MCI is the most common in patients with cardiovascular disease. Amnestic MCI is an early stage of Alzheimer's disease (AD), and it is highly likely to be converted into AD (Chinese Dementia and Cognitive Impairment Guidelines Writing Group, Cognitive Disorders Professional Committee of Neurology Branch of Chinese Medical Doctor Association, 2018).

3) Dementia refers to the syndrome with acquired cognitive dysfunction as the core, and causes the patient's daily living ability to decline and mental behavior abnormalities (Chinese Dementia and Cognitive Impairment Guidelines Writing Group, Cognitive Disorders Professional Committee of Neurology Branch of Chinese Medical Doctor Association, 2018).

The biggest difference between cognitive frailty and cognitive impairment is that cognitive frailty has both physical frailty and cognitive damage, while the latter only refers to the decline of intelligence.

3. Assessment

According to the assessment criteria of cognitive frailty formulated by the International Frailty Consensus Group (Kelaiditi E, Cesari M, Canevelli M, et al, 2013) and the assessment criteria of mild cognitive impairment in the guidelines (Chinese Guidelines for the diagnosis and treatment of dementia and cognitive Impairment, 2018), the judgment criteria are: 1) the patients themselves or their family members complain that the patients' cognitive ability has declined; 2) FP score was 3-5; 3) In the score of Mo CA scale, the score of patients with junior high school education or above was ≤24, the score of patients with primary school education was ≤19, and the score of illiterate patients was ≤13. A CDR scale score of 0.5 and no diagnosis of dementia. The above criteria must be met simultaneously.

4. Prevalence

There are limited epidemiological data on heart failure combined with cognitive frailty. Matsue Y (Matsue Y, Kamiya K, Saito H, et al, 2020) conducted a survey on 1180 heart failure patients aged ≥65 years, and the prevalence of cognitive frailty was 37.1%. Yamamoto S (Yamamoto S, Yamasaki S, Higuchi S, et al, 2022) conducted a survey on heart failure patients aged ≥65 years who were hospitalized for HF. It was found that 279 patients (23.0%) had cognitive frailty; Warraich HJ (Warraich HJ, Kitzman DW, Whellan DJ, et al, 2018) investigated 202 elderly inpatients with acute decompensated heart failure (HF) and found that the detection rate of cognitive frailty was as high as 75%.

5. Prognosis

Simple cognitive frailty (without other diseases) has a poor prognosis. Solfrizzi (Solfrizzi V, Scafato E, Seripa D, et al, 2017) found that the risk of death in patients with cognitive frailty was 75% higher than that in healthy elderly people during 3.5 years of follow-up. Feng (Feng L, Zin NM, Gao Q, et al, 2017) also pointed out that cognitive frailty has a higher risk of death than physical frailty or cognitive impairment. Yamamoto S (Yamamoto S, Yamasaki S, Higuchi S, et al, 2022) conducted a prospective multicenter observational study to evaluate 1215 patients who were enrolled in the study using the Mini-Cog and Fried criteria, and found that 279 of them (23.0%) had cognitive frailty. They were followed up for 1 year after discharge, and 398 combined events were observed. Cognitive frailty was significantly associated with a higher incidence of all-cause mortality and HF rehospitalization combined events.

6. Mechanisms

Cognitive frailty is a component of frailty syndrome. The mechanism of heart failure combined with frailty is also applicable to heart failure combined with cognitive frailty.

6.1 Inflammatory Response

The occurrence of elderly cardiovascular disease with frailty is considered to be inseparable from inflammatory response, and heart failure and frailty may have a common origin. Under the action of chronic low levels of pro-inflammatory cytokines and inflammatory cells, vascular endothelial damage, vascular remodeling, arteriosclerosis and insulin resistance can lead to a higher risk of cardiovascular disease and frailty in the elderly. Matrix metalloproteinases, angiotensin II, human monocyte chemoattractant protein-1, interleukin-6, and tumor necrosis factor-α may be inflammatory factors that promote the occurrence of elderly heart failure with frailty (Bellumkonda, L., et al, 2017). In conclusion, inflammatory response is considered to be one of the pathological mechanisms of elderly cardiovascular disease with frailty.

6.2 Apoptosis

Apoptosis is an active cell death process regulated by specific genes. During this process, the expression and secretion of "senescence-associated secretory phenotypes" (SASP) such as chemokines, cytokines, matrix proteases and extracellular vesicles are increased. In heart failure, insufficient blood supply to the heart, increased oxygen consumption, increased vascular load, accelerated cell aging and apoptosis (WU Q Q, YAO Q, HU T T, et al, 2022), and the accumulation of aged cells is one of the reasons leading to cognitive frailty (XU T, JI M H, CHEN Y M, et al, 2023).

6.3 Testosterone Changes

Abnormal testosterone secretion in the endocrine system is associated with frailty (IELLAMO F, VOLTERRANI M, CAMINITI G, et al, 2010). Hormone levels change with age and disease, and testosterone levels are significantly decreased in patients with heart failure compared to healthy individuals of the same age. The decrease of testosterone level will cause muscle mass loss and energy disorder, which will aggravate the symptoms of heart failure in patients (JONES T H, 2010). In addition, subnormal testosterone can also affect cognitive function (He Xueyou & Jin Zhe, 2012).

6.4 Oxidative Stress

Reactive oxygen species (ROS) are highly reactive oxygen-containing compounds produced by body metabolism (Senoner T & Dichtl W, 2019). When ROS is present in normal concentration, it helps to maintain cell homeostasis. Excessive ROS can induce oxidative stress in cells, leading to the damage of cellular macromolecules (such as nucleic acids and proteins), causing irreversible cell damage and death (van der Pol A, et al, 2019). The accumulation of ROS is the main cause of frailty in elderly patients with heart failure. During the development of heart failure, cellular oxidative damage leads to the accumulation of ROS. When the accumulation of ROS exceeds the body's clearance capacity, the risk of frailty increases (Rech DA, Silveira LSD, Martins EM, et al, 2022). Revel (Revel F, Gilbert T, Roche S, et al, 2015) found that oxidative stress biomarkers, especially glutathione peroxidase and glutathione, can predict the process of cognitive decline in patients with AD or other neurodegenerative diseases. Oxidative stress can also trigger inflammatory responses through the production of oxidative cellular components, which in turn can link frailty with cognitive decline.

7. Management

At present, there is a lack of intervention studies on cognitive frailty in patients with heart failure at home and abroad. There are few interventions for this population, which are mainly divided into:

7.1 Multidisciplinary Team

Multidisciplinary team (MDT) management refers to a multidisciplinary team composed of specialists, anesthesiologists, rehabilitation therapists, nutritionists and nurses to construct an inter-departmental management model from multiple perspectives, which can effectively identify and communicate problems, mobilize the subjective initiative of doctors, nurses and patients, formulate comprehensive treatment plans, and achieve the most ideal intervention effect (Wagner EH, Austin BT & von Korff M, 1996). Edward H Wagne (Wagner EH, 2000) proposed in 2000 that effective chronic disease management relies on a multidisciplinary team, so it is speculated that such management mode is also effective for patients with heart failure and cognitive frailty. It is recommended that general practitioners take the lead and establish a multidisciplinary team to formulate diagnosis and treatment plans. Diagnosis and treatment plans should comprehensively consider individual and disease factors, reasonably refer to relevant guidelines, assess the impact of comorbidity and frailty on treatment and prognosis, and whether the benefits of diagnosis and treatment plans outweigh the risks, so as to effectively improve the overall management level of such patients (Xu Hu, Fan Li & Cao Feng, 2019). However, most of the current studies focus on elderly patients with frailty, and there are few studies on the multidisciplinary team of patients with heart failure combined with cognitive frailty, which lacks targeted multidisciplinary teams.

7.2 Cardiac Rehabilitation

cardiac rehabilitation (CR) contains five prescriptions — drug prescription, exercise prescription, nutrition prescription, psychological prescription, smoking cessation and alcohol reduction prescription. Cr is a standardized secondary prevention and health care model, which is mainly composed of risk factor management, structured exercise, patient education and psychosocial counseling. The main goals include improving risk factors, increasing functional reserve and peak oxygen consumption VO2, and improving balance and flexibility (Grace SL, Turk-Adawi KI, Contractor A, et al, 2016). The results of existing studies have shown that traditional rehabilitation department/center-based CR can significantly reduce morbidity, rehospitalization, and mortality of patients suffering from cardiovascular disease, improve the quality of life of patients, and reduce the cost of treatment (Taylor RS, Dalal HM & McDonagh STJ, 2022; Francis T, Kabboul N, Rac V, et al, 2019; Kabboul NN, Tomlinson G, Francis TA, et al, 2018). Cardiac rehabilitation evaluation indicators focus on frailty itself or changes in physical function, such as grip strength, gait speed, 6-minute walking test, peak oxygen uptake, etc., which can significantly improve physical frailty, but whether the improvement of cognitive frailty needs to be further explored.

7.3 Exercise Intervention

Exercise has been shown to effectively improve physical frailty (Macdonald SH, Travers J, Shé ÉN, et al, 2020), but there is a lack of exercise intervention studies for patients with heart failure and cognitive frailty. The physical condition of the frail elderly has individual differences. In the future, the safety, simplicity and acceptance of the elderly should be considered while exploring the best exercise program and tracking the long-term efficacy of exercise. Therefore, more high-quality and multi-type studies are needed to determine the personalized exercise intervention program in the future.

7.4 Nutritional Intervention

Nutritional support for frail patients aims to address many nutritional deficiencies. Common micronutrient deficiencies in frailty include vitamins A, B12, D, E, thiamine, iron, and folate (Sciatti E, Lombardi C, Ravera A, et al, 2016). The role of micronutrients (calcium, magnesium, zinc, copper, selenium, thiamine, riboflavin, folic acid, vitamins A, B6, B12, C, E, D, and coenzyme Q10) supplementation in elderly patients with heart failure has not been established (Salmon T, Essa H, Tajik B, Isanejad M, Akpan A & Sankaranarayanan R, 2022). Macronutrient, high-calorie, high-protein diets supplemented with essential amino acids have been shown to improve significant weight loss and muscle loss and improve quality of life in patients with heart failure (Rozentryt P, von Haehling S, Lainscak M, et al, 2010). In conclusion, nutritional therapy for HF patients with cognitive frailty should be tailored to the nutritional needs of the patients, and whether micronutrient supplementation is needed for further study.

7.5 Drug Intervention

Heart failure requires a combination of multiple drugs, and the golden triangle drug treatment of ACEI/ARB+ β-blockers + MRA recommended by guidelines is commonly used in clinical practice (Heart Failure Group, Chinese Society of Cardiology, Heart Failure Professional Committee, Chinese Medical Doctor Association, Editorial Committee of Chinese Journal of Cardiology, 2018). However, the effects of ACEI/ARB, β-blockers, and MRA on frailty remain to be proved. Studies have shown that sacubitril-valsartan can improve cardiac function but not frailty in elderly heart failure patients with reduced ejection fraction and frailty, but this evidence is limited (Zhao Zhiying, Jin Jing & Yu Rong, 2022).

Polypharmacy can promote the development of frailty, so it is necessary to reduce repeated drug use and inappropriate drug use on the premise of ensuring the therapeutic effect on the disease. At present, the evidence of the effectiveness of drugs on patients with heart failure and cognitive frailty is insufficient, and the benefits and possible adverse consequences of drug intervention cannot be accurately evaluated, which needs to be proved by further research.

7.6 Psychological Intervention

Patients with heart failure are prone to psychological problems, which not only aggravate the symptoms of heart failure, but also promote the occurrence and development of cognitive frailty (Wen Xue-mei, Lu Ren-Quan & Guo Lin, 2014). Gale (Gale CR, Westbury L & Cooper C, 2018) found that elderly people living alone, having less contact with friends, family and children, and less participation in community group activities have an increased risk of cognitive frailty. Therefore, in order to reduce patients' negative emotions and reduce the occurrence of psychological problems, psychological intervention should be carried out for elderly patients with heart failure to help them increase contact with friends, family and children. Encourage participation in community group activities.

Cognitive frailty increases the complexity of the management of elderly patients with heart failure, and the management of patients with heart failure combined with cognitive frailty should involve more pragmatism. Individuals with cognitive frailty can benefit from preventive interventions rather than dementia treatment

(Kelaiditi E, Cesari M, Canevelli M, et al, 2013). Some treatments for dementia may increase frailty.

8. Summary and Prospect

8.1 Summary

Heart failure and cognitive frailty usually coexist, which increases the incidence of adverse clinical outcomes and has a negative impact on the quality of life and prognosis of patients. The pathogenesis of these patients may be related to inflammatory response, oxidative stress, apoptosis, and changes in testosterone. At present, there is a lack of intervention studies on cognitive frailty in patients with heart failure at home and abroad. Through multidisciplinary team management, cardiac rehabilitation, exercise, nutrition, drug and psychological intervention, the disease performance of patients has been improved to a certain extent.

8.2 Outlook

1) In-depth study of the pathophysiological mechanism of heart failure combined with cognitive frailty. This article summarizes the possible pathogenesis of heart failure combined with cognitive frailty, but the pathogenesis of heart failure combined with cognitive frailty is still unclear. In the future, more research is needed to study the pathogenesis of heart failure combined with cognitive frailty from different levels to help better understand such diseases and develop the best rehabilitation plan.

2) Exploring the best rehabilitation program for such patients and tracking the long-term efficacy. In the existing studies, there are no intervention studies specifically for patients with heart failure and cognitive frailty. Therefore, more high-quality studies are needed to identify effective interventions to clarify their role and establish a safe and operable personalized optimal rehabilitation program.

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