The Affect of Frailty on Cardiac Function in Senior Citizen with Chronic Cardiac Failure

Xinran He[1], Rong Li[2*]

[1] Master of Geriatrics, Affiliated Hospital of Qinghai University, Xining 810000, Qinghai, China

[2] Second Ward of Geriatrics, Affiliated Hospital of Qinghai University, Xining 810000, Qinghai, China

[*] Corresponding author

Abstract: Amidst the accelerating global demographic shift towards an aging populace, the construct of multimorbidity has commanded escalating scholarly focus in recent years. Particular emphasis centers on frailty a pathophysiological state precipitating progressive multisystem deterioration and a concomitant escalation in deleterious clinical sequelae. Frailty exhibits a robust correlation with adverse prognostic trajectories in chronic cardiac failure and numerous cardiovascular pathologies, and permeates thechronic cardiac failure patient cohort with high prevalence. Crucially, frailty not merely potentiates the incidence of chronic heart failure, but substantially augments the propensity for adverse cardiovascular events.

***Keywords*:** chronic cardiac failure, frailty, elderly, co-morbidities

1. Introduction

Frailty has long been recognized as a manifestation of accelerated aging involving various physiological systems simultaneously leading to increased susceptibility to negative outcomes. In addition debility is a serious and common co-morbidity, and debility is strongly associated with chronic heart failure, with a higher incidence and prevalence in the elderly population. The impact of debility on chronic heart failure outcomes may influence treatment choices for chronic heart failure. The prevalence of debilitating co-morbidities in patients with chronic heart failure is increasing, and it has been suggested that there is a correlation between chronic heart failure and debilitation, with patients with chronic heart failure having six times the risk of developing debilitation compared to the normal population [1], and patients with debilitation being at higher risk of new-onset heart failure, and that a combination of the two conditions can lead to a more complex condition. In this paper, we will explore the impact of frailty on patients with chronic heart failure and the current status of co-morbidities.

2. Definition and overview

Frailty is defined as a multidimensional physiological syndrome of dysregulation, impaired homeostasis, and reduced physiological reserve caused by multiple systems that leads to an increased risk of various adverse outcomes, such as death, major cardiovascular events, hospitalization, falls, and fractures. Its predominant occurrence is in people over 65 years of age. It is associated with significant reductions in physiologic reserve function due to many co-morbidities, the effects of stressors, and general homeostatic dysregulation. It is the result of processes occurring within the body and the effects of the external environment on the human organism. This ultimately leads to impairment of energy, physical and cognitive abilities, and health. One of the important factors determining the manifestation of the syndrome is the reduction of the body's physiologic reserve function. [2]

Chronic heart failure is an abnormal change in the structure and/or function of the heart due to a variety of causes, which results in impaired ventricular systolic and/or diastolic function, causing a decrease in ventricular filling and ejection function, and insufficient perfusion of blood flow to vital organs and tissues, and is a common condition in the elderly. About 80% of patients with chronic heart failure are older than 65 years old, and the clinical manifestations are dyspnea, decreased exercise tolerance, and may be accompanied by peripheral edema, jugular venous rage, and pulmonary rales. [3]

3. Epidemiologic association between debility and heart failure

Chronic heart failure is becoming a global health challenge as well as a major cause of the global burden of disease due to aging populations and increasing survival rates [4]. The prevalence of chronic heart failure among adults in developed countries ranges from 1% to 2% [5], while the prevalence in European countries is as high as 13% according to the 2019 European Society of Cardiology Heart Failure Association ATLAS program report [6]. In China, the prevalence of chronic heart failure is equally grim, with epidemiologic surveys showing that there are approximately 12.1 million patients (1.10%

of the total population) in China, with an annual incidence rate of 275/100,000 people [7]. Patients with chronic heart failure usually have a decreased functional reserve, also known as frailty, making them more vulnerable to adverse factors, which in turn further increases the risk of falls, disability, hospitalization, and death. The prevalence of debility in patients with chronic heart failure is 30%-52% [8], both of which have a poorer prognosis and may be subject to frequent hospitalization and death. Epidemiologic studies have shown that the prevalence of frailty exceeds 70% in chronic heart failure patients ≥80 years of age, and can be as high as 53.3% even in younger patients with chronic heart failure, which is significantly higher than that of the same age group of older adults by 10%-20%, highlighting the close clinical association between the two [9]. In addition, studies have shown a positive association between frailty and chronic heart failure, where patients with chronic heart failure may experience physical dysfunction, cognitive impairment, and decreased quality of life as a result of frailty, and chronic heart failure may lead to a continued decline in the patient's functional status, which may exacerbate frailty. Patients may continue to experience considerable physical dysfunction and a more severe burden of debilitation even after decompensated heart failure subsides. Therefore, identifying risk factors for frailty in patients with chronic heart failure is valuable in guiding clinical care as well as targeted clinical interventions.

4. Pathophysiological mechanisms

The pathophysiological mechanisms of frailty include chronic inflammation and immune activation, and elevated levels of interleukin-6, c-reactive protein, tumor necrosis factor-alpha, and neopterin can lead to increased leukocyte numbers and impaired T cell differentiation [10]. Chronic inflammatory pairs can have an impact on the musculoskeletal and endocrine systems, leading to anemia and nutritional disorders. In particular, skeletal muscle weakness is mainly caused by a combination of factors such as skeletal sarcopenia, muscle atrophy, alpha motor neuron alterations, malnutrition, growth hormone production, decreased levels of sex hormones and insulin-like growth factor 1, and decreased physical activity. [11]. Also impaired skeletal muscle can lead to decreased bone mass and osteoporosis, which can lead to pathologic fractures. Weakness is also an important factor in central nervous system involvement [12], leading to cognitive dysfunction and depression.

Frailty and chronic heart failure often coexist and worsen each other. The following are the core mechanisms by which debility affects cardiac function in patients with chronic heart failure, with complex pathophysiologic mechanisms involving the interaction of multiple systems, including inflammation, metabolism, neuroendocrine, and musculoskeletal.

Patients with chronic heart failure are more prone to falls and cognitive dysfunction due to reduced cerebral perfusion, which accelerates the development of debility [13]. Frailty implies a reduced ability of the organism to cope with biological stresses, a condition associated with inflammatory cytokines and skeletal muscle hypoplasia, features that share a common pathologic basis with chronic heart failure. Both debility and chronic heart failure are associated with pro-inflammatory phenotypes, and debility is highly correlated with cardiovascular dysfunction,[10] which accelerates the progression of end-organ diseases such as chronic heart failure. It has been found that patients with moderate and severe debility are at increased risk of developing chronic heart failure [14]. Chronic skeletal muscle pathologic changes resulting from long-term chronic heart failure promote the development of debility [15]. Chronic heart failure is closely associated with imbalances in cellular homeostasis, suggesting that the disease may accelerate the aging process of the organism [16]. Although patients with chronic heart failure often exhibit molecular biological alterations in the cellular components of skeletal muscle, their pathology is characterized by differences from normal aging and inflammatory processes. Notably, skeletal muscle lesions in patients with chronic heart failure are site-specific, and the mechanism can be seen as a superimposed effect of a chronic maladaptive state and an inflammatory response [17]. Newer studies have pointed out that debilitating syndromes and chronic heart failure may disrupt the internal environment through a synergistic effect, together inducing a low-level chronic inflammatory response [10]. At the pathophysiologic level, chronic inflammatory markers are closely associated with the debilitating syndrome. This sterile inflammation is not only present in acute ischemia-reperfusion injury, but also more prominently in the chronic inflammatory process associated with chronic heart failure. The progressive elevation of circulating pro-inflammatory cytokines (e.g., TNF-α, IL-6) during human aging has been widely demonstrated [18], and the mechanisms may involve structural disruption of adipose tissue, skeletal muscle, and cardiomyocytes, in addition to latent viral infections (e.g., cytomegalovirus), which may exacerbate the chronic inflammatory response. Notably, intestinal stasis and digestive dysfunction due to elevated intravascular pressure in patients with chronic heart failure may further induce cachexia[19], creating a vicious circle. Analyzed from the perspective of molecular mechanisms, cachexia and chronic heart failure have obvious pathological homology, especially at the level of inflammatory markers showing high correlation[20] [17]. Both are characterized by abnormally elevated inflammatory mediators such as TNF-α, IL-6, IFN-γ and CRP [21], suggesting that there may be a common mechanism of inflammatory pathway activation [10]. More in-depth studies have

found that immune cells and cytokines involved in atherosclerosis and vascular aging accelerate the aging process by regulating the body's metabolism, which in turn promotes the onset of debility [20] [17].

Frailty exacerbates the pathophysiologic progression of chronic heart failure through multisystem interactions, and clinical emphasis needs to be placed on early recognition and multidimensional intervention to improve patient prognosis.

5. Assessment tools for frailty

Since the term debility was introduced in the 1960s, there are still no internationally recognized definitions or diagnostic criteria, and there is no standardized methodology for the assessment of debility [22]. Currently, more than 30 tools for assessing frailty have been used in different populations around the world, but there is confusion in the use of assessment tools and differences in clinically relevant data due to differences in study sites and subjects, among other reasons. Tools for measuring frailty include a variety of scales and questionnaires, such as the Fried Frailty Phenotype (FFP), the Tilburg Frailty Indicator (TFI), the Edmonton Frailty Scale (EFS), the Deficit Cumulation Scale (DCS), and the Cumulative Deficiency Index (CDI). EFS), Deficit AccumulationFrailty Index (FI-CD), Clinical Frailty Level Scale (CFS), and self-report questionnaires. A related study stated [23] that there are seven methods of assessing frailty mainly for heart failure patients. The commonly used methods include the Fried frailty phenotype score (FFP), the comprehensive geriatric assessment (CGA), the Tilburg Frailty Indicator (TFI), Frailty Index of accumulative deficits (FI-CD), Frailty Staging System (FSS), Self-assessed Clinical Frailty Scale (Chinese-Canadian study of health and aging clinical frailty). Chinese-Canadian study clinical frailty scale (CSHA-CFS) and Survey of Health, Ageing and Retirement in Europe Frailty Index I (SHARE-FI I).). Among them, the Fried Frailty Scale is the most commonly used assessment method.The Fried Frailty Scale is a scale developed by Fried et al. The scale consists of five indicators, which are unexplained weight loss, loss of grip strength, reduction in physical activity, slowing of gait speed, and feeling of fatigue, which is one of the most widely used scales for the measurement of frailty [24].

6. Conclusion

The impact of weakness on cardiac function in patients with heart failure is characterized by a complex interaction of multiple aspects and levels, involving multiple dimensions of cardiac structural changes, functional decline, symptom exacerbation, and prognostic deterioration. This effect is not only reflected in traditional echocardiographic parameters, but also in patients' exercise tolerance, quality of life, and response to therapy. An in-depth analysis of the specific impact of frailty on cardiac function is important for the clinical assessment and management of this special population.

In conclusion, physical debility, social dysfunction, and cognitive dysfunction are prevalent in hospitalized elderly patients with heart failure and overlap considerably with each other. This overlap becomes more pronounced with advancing age, and a comprehensive assessment of frailty status through a holistic approach is important, especially in older heart failure patients, not only for prognostic prediction but also for individualized decision making regarding therapeutic interventions.

References

[1] Vitale C, Spoletini I, Rosano GM (2018) Frailty in heart failure: implications for management. Card Fail Rev4(2):104–106.

[2] van den Bussche, H., Schön, G., Kolonko, T., Hansen, H., Wegscheider, K., Glaeske, G., et al. (2011). Patterns of ambulatory medical care utilization in elderly patients with special reference to chronic diseases and multimorbidity — results from a claims data based observational study in Germany. BMC Geriatr. 11:54. doi: 10.1186/1471-2318-11-54.

[3] Wang Xiaoming. Emphasizing the clinical diagnosis and treatment characteristics of chronic heart failure in the elderly [J]. Chinese Journal of Geriatric Cardiovascular and Cerebrovascular Disease, 2021, 23(10): 1009-1011.

[4] Savarese G, Becher PM, Lund LH, Seferovic P, Rosano GMC, Coats AJS. Global burden of heart failure: a comprehensive and updated review of epidemiology. Cardiovasc Res. 2022;118:3272–87.

[5] Virani SS, Alonso A, Benjamin EJ, et al. Heart disease and stroke statistics-2020 update: a report from the American Heart Association. Circulation. 2020;141:E139–596.

[6] Seferovic PM, Vardas P, Jankowska EA, et al. The heart failure association atlas: heart failure epidemiology and management statistics 2019. Eur J Heart Fail. 2021;23:906–14.

[7] Wang H, Chai K, Du M, et al. Prevalence and incidence of heart failure among urban patients in China a national population-based analysis. Circ Heart Fail. 2021;14:1127–35.

[8] Han Jiaqi. A study on the correlation between debilitation and self-care behavior in elderly heart failure patients [D]. Jilin University,2019.

[9] Deek H, Itani L, Davidson PM. Literacy critical to heart failure management: a scoping review. Heart Fail Rev.

2021;26:1413–9.
[10] McDonagh J, Martin L, Ferguson C,et al.Frailty assessment instruments in heart failure: A systematic review[J]. Eur J Cardiovasc Nurs,2018,17(1):23-35.
[11] Narici, M. V., and Maffulli, N. (2010). Sarcopenia: characteristics, mechanisms and functional significance. Br. Med. Bull. 95, 139–159. doi: 10.1093/bmb/ldq008.
[12] Hogrel, J.-Y., Barnouin, Y., Azzabou, N., Butler-Browne, G., Voit, T., Moraux, A., et al. (2015). NMR imaging estimates of muscle volume and intramuscular fat infiltration in the thigh: variations with muscle, gender, and age. Age 37, 60–71. doi: 10.1007/s11357-015-9798-5.
[13] Singh, M., Stewart, R., and White, H. (2014). Importance of frailty in patients with cardiovascular disease. Eur. Heart J. 35, 1726–1731. doi: 10.1093/eurheartj/ehu197.
[14] Khan, H., Kalogeropoulos, A. P., Georgiopoulou, V. V., Newman, A. B., Harris, T. B., Rodondi, N., et al. (2013). Frailty and risk for heart failure in older adults: the health, aging, and body composition study. Am. Heart J. 166, 887–894. doi: 10.1016/j.ahj.2013.07.032.
[15] Kitzman, D. W., Nicklas, B., Kraus, W. E., Lyles, M. F., Eggebeen, J., Morgan, T. M., et al. (2014). Skeletal muscle abnormalities and exercise intolerance in older patients with heart failure and preserved ejection fraction. Am. J. Physiol. Heart Circ. Physiol. 306, H1364–H1370. doi: 10.1152/ajpheart.00004.2014.
[16] Wohlgemuth, S. E., Calvani, R., and Marzetti, E. (2014). The interplay between autophagy and mitochondrial dysfunction in oxidative stress-induced cardiac aging and pathology. J. Mol. Cell. Cardiol. 71, 62–70. doi: 10.1016/j.yjmcc.2014.03.007.
[17] Goldwater, D. S., and Pinney, S. P. (2015). Frailty in advanced heart failure: a consequence of aging or a separate entity? Clin. Med. Insights. Cardiol. 9, 39–46. doi: 10.4137/CMC.S19698.
[18] De Martinis, M., Franceschi, C., Monti, D., and Ginaldi, L. (2006). Inflammation markers predicting frailty and mortality in the elderly. Exp. Mol. Pathol. 80, 219–227. doi: 10.1016/j.yexmp.2005.11.004.
[19] Valentova, M., von Haehling, S., Bauditz, J., Doehner, W., Ebner, N., Bekfani, T., et al. (2016). Intestinal congestion and right ventricular dysfunction: a link with appetite loss, inflammation, and cachexia in chronic heart failure. Eur. Heart J. 37, 1684–1691. doi: 10.1093/eurheartj/ehw008.
[20] Uchmanowicz, I., Łoboz-Rudnicka, M., Szeląg, P., Jankowska-Polańska, B., and Łoboz-Grudzień, K. (2014). Frailty in heart failure. Curr. Heart Fail. Rep. 11, 266–273. doi: 10.1007/s11897-014-0198-4.
[21] Kalogeropoulos, A., Georgiopoulou, V., Psaty, B. M., Rodondi, N., Smith, A. L., Harrison, D. G., et al. (2010). Inflammatory markers and incident heart failure risk in older adults: the health, aging, and body composition study. J. Am. Coll. Cardiol. 55, 2129–2137. doi: 10.1016/j.jacc.2009.12.045.
[22] Benetos A,Petrovic M,Strandberg T.Hypertension Management in Older and Frail Older Patients. Circ Res,2019,124(7):1045-1060.
[23] McDonagh J, Martin L, Ferguson C,et al.Frailty assessment instruments in heart failure: A systematic review[J]. Eur J Cardiovasc Nurs,2018,17(1):23-35.
[24] Denfeld QE, Winters-Stone K, Mudd JO, Gelow JM, Kurdi S, Lee CS. The prevalence of frailty in heart failure: a systematic review and meta-analysis. Int J Cardiol. 2017;236:283–9.