

# Frailty in patients with heart failure

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## KEYWORDS

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The importance of frailty in heart failure (HF) patients has been increasingly recognized because of its high prevalence and its significantly adverse impact on prognosis and quality of life. Due to the impact of frailty on both prognosis and treatment of HF patients, all patients with HF, regardless of their chronological age, should be evaluated for the presence of, or the risk for developing frailty. However, although several instruments are available, there is still no consensus as to which is the best method to assess frailty in patients with HF. Therefore, a validated and easy to apply instrument to assess frailty in HF patients in daily practice is warranted.

## Introduction

Heart failure (HF) is one of the most important and rapidly growing diseases due to its high prevalence worldwide and the significant impact on morbidity and mortality.<sup>1-4</sup> The phenotype of patients with HF is often complex because of their improved survival from other chronic conditions and the progressive aging of developed societies,<sup>5</sup> leading to an increased prevalence in particular if heart failure with preserved ejection fraction (HFpEF) in the elderly.<sup>6,7</sup> The typical patient with HF presents with an involvement and impairment of multiple organs and body systems that require complex and intricate poly-therapeutic schemes.<sup>8</sup> Common clinical impairments and comorbidities in HF patients include kidney injury, diabetes, arrhythmias, anaemia, depression, while common non-clinical comorbidities are isolation, living alone, dependency, institutionalization, sub-optimal self-care (Table 1).<sup>9-11</sup>

Comorbidities present with different patterns in patients with HF and can cause an accumulation of defects that makes patients more vulnerable to stressors with consequential negative outcomes and prognosis. This increased patient's vulnerability is commonly described with the term frailty, that originates from the French 'frêle' and means little resistance.<sup>12,13</sup>

According to a recent HFA position paper on frailty in HF patients, frailty is defined as a *multidimensional dynamic state, independent of age, that makes the individual with HF more vulnerable to the effect of stressors*.<sup>14</sup> When exposed to clinical and non-clinical stressors, acute or chronic, HF patients are at higher risk for the occurrence of decompensation and negative outcomes, such as adverse clinical events, prolonged recovery times, functional decline, disability, and mortality compared to those patients without frailty. Therefore, all patients with HF, due to their state of vulnerability, are at higher risk to be frail. Several studies have shown that frailty is common in HF patients with an estimated prevalence of around 45%.<sup>1,15,16</sup> The overlap between frailty and HF is complex: patients with HF were up to six times more likely to be frail and frail people had a significantly increased risk of developing new-onset HF. Although both frailty and HF are more common in older than younger adults, their occurrence is independent of age, and frailty should be not considered as an inevitable part of aging or as a state exclusive of the elderly.<sup>17</sup> All patients with HF, irrespective of their chronological age, should be evaluated for the presence or the risk of frailty.

Although the precise pathogenesis of frailty has yet to be elucidated, the concomitant presence of frailty and HF worsen each another via multiple complex pathogenic mechanisms, such as disorders and dysregulation in neuro-hormonal, muscular,<sup>18-20</sup> immune, metabolic,<sup>21</sup> and endocrine systems and up-regulation of inflammatory

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**Table 1** Main clinical and non-clinical comorbidities in patients with heart failure

Clinical comorbidities	Non-clinical comorbidities
<b>Cardiovascular:</b> coronary artery disease, arrhythmias, valvular heart disease, arterial hypertension	Isolation & living alone
<b>Psycho-cognitive:</b> cognitive impairment, depression & anxiety	Lack of support
<b>Metabolic:</b> Iron deficiency & anaemia, Cachexia & sarcopenia, malnutrition, diabetes mellitus & metabolic impairment	Dependency
<b>Organic:</b> kidney injury, chronic obstructive pulmonary disease, cancer, erectile dysfunction	
<b>Functional:</b> falls, lack of mobility	

**Table 2** Activities of Daily Living (ADLs) and Instrumental Activities of Daily Living (IADLs)

Activities of Daily Living (ADLs)	Instrumental Activities of Daily Living (IADLs)
are activities in which people engage on a day-to-day basis. These are every day personal care activities that are fundamental to caring for oneself and maintaining independence.	are activities related to independent living and are valuable for evaluating persons with early-stage disease, both to assess the level of disease and to determine the person's ability to care for himself or herself.
Bathing	Shopping
Dressing	Cooking
Grooming	Managing medications
Mouth care	Using the phone and looking up numbers
Toileting	Driving or using public transportation
Transferring bed/chair	Doing housework
Walking	Doing laundry
Climbing stairs	Managing finances
Eating	

cytokines.<sup>22-25</sup> This leads to an imbalance between the anabolic and catabolic state in HF patients that may exacerbate the decline in muscle mass and strength,<sup>26,27</sup> thus favouring the occurrence of reduced lean muscle mass (sarcopaenia) and cachexia (defined as a generalized wasting process affecting all body compartments).<sup>28-31</sup> Both

sarcopaenia and cachexia are common in patients with HF, particularly in those at an advanced stage of the disease. The higher risk of disability and dependency in performing simple daily activities (activities of daily living and instrumental activities of daily living; *Table 2*) impairs quality of life of HF patients and it is associated with a higher

occurrence of depression and isolation, in particular, in those HF patients that do not have a familiar and social support.<sup>32-36</sup>

Problems in self-care and difficulties in leaving home may reduce also patient's access to healthcare, which also contributes to insufficient treatment surveillance, delayed responses, and untimely treatment modifications, thus increasing the risk of negative outcomes.<sup>37</sup>

Frailty has an important prognostic role in patients with HF, as can exacerbate the progression of HF as well as the occurrence of negative outcomes such as mortality, lower probability of surviving more than 10 years, and increased health care use (higher risk of hospitalization, prolonged recovery, institutionalization, etc.).<sup>38-43</sup>

Therefore, the identification of frailty is of utmost importance in patients with HF. Recognizing those HF patients who are not only frail but also at risk of frailty ('pre-frail'), may allow an early and immediate multidisciplinary therapeutic intervention with the aim to improve their prognosis, outcomes, and management. To this aim, possible treatments for frailty in HF are, besides those indicated as GDMT by the scientific guidelines,<sup>44</sup> exercise (resistance and aerobic), caloric and protein support, vitamin D supplementation, and a reduction in polypharmacy. The therapeutic approach should also take into consideration the non-clinical components of frailty and should include occupational therapy, psychological and social support as well as education of patients and their families.

The disease-centred approach (organ system-based model) is no longer acceptable in the management of frail multi-morbid HF patients and has to be abandoned in favour of a holistic and multidimensional approach. This approach will allow us to recognize all the impairments, clinical and non-clinical, present in HF patients and to identify those patients with or at risk of frailty. Only using an holistic approach, is it possible to identify those impairments that have to be addressed with priority thus building a personalized and tailored healthcare program.

However, although several instruments are available to assess frailty, there is still no agreement on which is the best method to assess frailty in patients with HF. In brief, two main models are used to identify frailty: the physical frail phenotype<sup>45</sup> and the cumulative deficit model.<sup>46,47</sup>

The Physical Frailty Phenotype is defined by the presence of three or more of the following physical components: unintentional weight loss; self-reported exhaustion; weakness (reduced hand grip strength); slow walking speed, low self-reported physical activity. A pre-frail status is described when one or two criteria are present and this identifies an individual at high risk of progressing to frailty. The cumulative deficit model, describes frailty as an accumulation of individual impairments and conditions, such as cognition, activities of daily living, comorbid diseases, deficits of social relations, and social support present or abnormal laboratory results, thus creating a Frailty Index. The greater the number of deficits the higher the degree of frailty.

Both the Fried phenotype and the cumulative index definitions have been widely used and have demonstrated their predictive value; however, their applicability in HF patients is limited by major weaknesses. Although, the

Fried phenotype is easier to apply compared to the cumulative model, it is burdened by the fact that it does not take into consideration all the main domains: clinical, physical-functional, cognitive-psychological, and social, which combine to be responsible for frailty, as it is focused mainly on the physical component of frailty.

In addition, the overlap between the presence of symptoms shared between HF and frailty, such as the limited physical activity in performing basic activities of daily living, weakness, fatigue and shortness of breath, or the difficulty in correctly identifying weight loss in HF patients taking diuretics can be responsible for frequently missing the diagnosis of frailty in HF patients.

Conversely, the cumulative model is more reliable to evaluate all the clinical and non-clinical aspects of frailty, but its assessment is time consuming. Therefore, the routine use of the Frailty index in the busy cardiac clinic in which HF patients are followed is difficult.

These major limitations as well as the availability of a plethora of assessment instruments have limited the routine assessment of frailty in daily practice. This has facilitated the use of the clinical subjective judgments (eyeball test or foot-of-the-bed assessment) to define frailty in HF patients.<sup>48</sup>

However, due to the prognostic and therapeutic implications of frailty in HF patients, the use of a subjective assessment in routine daily practice is no longer acceptable. To this end, the aim to find validated and prognostic instruments to evaluate frailty in an objective, easy and reliable way is essential.

## Conclusion

The presence of a complex overlap between frailty and HF, the emerging and increasing data on the prognostic role of frailty, as well as the interference of frailty with the possible treatments for HF patients are only some of the reasons why frailty should be routinely identified in HF patients. An accurate assessment of frailty in HF patients is the first and mandatory step to build a tailored and individualized healthcare program in order to reduce dependency, increase quality of life, and improve prognosis.

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