

## EDITORIAL COMMENT

# Can Frailty Assessment Help in the Primary Prevention of Heart Failure?



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**F**railty is clinically defined as an age-related decline in the functionality of several physiological systems in the body, resulting in a reduced reserve capacity for tolerating internal and external stress. However, even within the same age group, functional reserves significantly vary, and in fact, frailty is not necessarily age related<sup>1</sup> but can be influenced by various physical factors, mental illness, cognitive function, socioeconomic status, and other factors that affect the human body.

Heart failure (HF) is a condition of reduced functional capacity characterized by chronic shortness of breath, peripheral edema, and fatigue. The association between HF and frailty has been documented in several studies. Although there is no standardized way to diagnose and assess frailty, patients with HF are generally more frail than the general population, and the severity of frailty increases with that of HF symptoms.<sup>2,3</sup> The presence and severity of frailty in patients with HF also affect the clinical course of HF, with more severe frailty being associated with more frequent health care use and an increased risk for readmission and death.<sup>4,5</sup>

HF and frailty have clinically similar symptoms, making it difficult to distinguish between the two. HF is not only a chronic inflammatory condition per se but can also be caused and exacerbated by chronic inflammation, and it is thought to play a role in the pathogenesis of frailty.<sup>6</sup> Therefore, HF and frailty share a common pathophysiology of chronic inflammation, and each may influence the development of the other, making it very difficult to describe a causal relationship between the two. Although the clinical importance of frailty in HF has been recognized in guidelines and standardized measures of frailty in

patients with HF are being developed, there is a lack of evidence as to whether frailty per se is a factor in the development of HF.

In a study reported in this issue of *JACC: Asia* to assess the role of physical frailty in the development of HF, Shi et al<sup>7</sup> used UK Biobank data to examine the longitudinal association between frailty and the development of HF in a large general population. They found that physical frailty was positively associated with the risk for developing HF, suggesting that frailty may be a predisposing factor for incident HF. Interestingly, the relationship between physical frailty and incident HF was not affected by genetic susceptibility to HF, suggesting that frailty may be an independent risk factor for the development of HF. However, it is important to note that the polygenic risk score (PRS) did not have an absolute influence on the development of HF. Although it is clear that some monogenic causes contribute to the development of HF, the heritability of HF is estimated to be up to 26%,<sup>8</sup> and HF is a very complex clinical syndrome that can be caused by the interaction of various comorbidities and environmental factors. In this study, 11 of the 12 single-nucleotide variants considered in the PRS calculation were known to be associated with conditions that can cause HF and strongly associated with left ventricular function.<sup>8</sup> The association between PRS and HF was significant, although not strong, and it is noteworthy that the risk for incident HF increased with increasing genetic risk in nonfrail patients. However, if genetic risk and frailty were completely independent, an increased risk for incident HF with increased genetic risk should be evident in the prefrail and frail groups, which was not the case. Whether this is simply a matter of statistical power due to insufficient sample size or a complex interaction of multiple comorbidities or differences in risk factor traits due to genetic variants requires further study.

Among the various components of physical frailty, Shi et al<sup>7</sup> found that exhaustion, slow walking speed, and low handgrip strength were significantly

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associated with the risk for HF. These components are associated with decreased muscular fitness and aerobic exercise capacity, which are also present in HF. In addition, frail patients with HF have a more reduced aerobic exercise capacity than nonfrail patients with HF.<sup>9</sup> The study by Shi et al suggests that some of the symptoms thought to be common to HF and frailty can precede the development of HF. Decreased muscle strength and aerobic fitness in patients with HF may also increase the risk for rehospitalization for HF,<sup>10</sup> and in patients with HF preceded by frailty, the decline in physical performance may be more severe and can be expected to have an adverse prognostic impact. Therefore, efforts to prevent or reverse physical frailty, such as aggressive nutritional support and cardiac rehabilitation, are being emphasized in patients with HF,<sup>11,12</sup> and they evidently have health benefits in patients with pre-HF as well.

Although frailty has traditionally been considered a geriatric syndrome and therefore has been assessed mainly in older adults, the importance of frailty in younger individuals has recently been recognized. The prevalence of frailty in younger patients with HF is high,<sup>13</sup> and guidelines for HF recommend frailty assessment at any age in patients with HF.<sup>14,15</sup> However, few studies have longitudinally analyzed the occurrence of HF in younger patients with frailty. This study showed that the association between frailty and the risk for incident HF was stronger in

younger patients, suggesting that the development of HF in younger patients with frailty should be carefully monitored and surveilled.

Shi et al<sup>7</sup> comprehensively analyzed the association between physical frailty and incident HF risk, considering age and genetic susceptibility to developing HF. Although this study was limited in that it included only an assessment of baseline frailty, did not determine the effect of temporal changes in frailty on HF, and did not examine subclinical measures of cardiovascular function according to the degree of frailty, it demonstrated that prior frailty may be a risk factor for incident HF. If future studies establish the role of assessing frailty and interventions to correct it, it can be cautiously anticipated that frailty assessment will become increasingly crucial in the primary prevention of HF.

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