# Frailty: What Is It?

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**Abstract**

Over the past decades, a progressive and exponential aging of the population has been observed. In particular, an absolute e relative increase of old and very old persons is also projected for the next 30 years. This demographic phenomenon is substantially responsible for the growing prevalence of frailty in our societies. Frailty is a clinical condition characterized by an excessive vulnerability of the individual to endogenous and exogenous stressors. This status generates a high risk of developing negative health-related events. Shifting to a construct as frailty to biologically define the perimeter of action for geriatric medicine will probably concur at modernizing the old way of practicing medicine. In this chapter the concept of frailty, its impact on the evolving healthcare systems, the controversies associated with its assessment and, ultimately, the role it plays in the management of older persons are discussed.

**Keywords**

Elderly · Frailty · Ageing · Geriatric assessment

## 1.1 Introduction

Over the past decades, a progressive aging of the population has been observed worldwide. It is noteworthy that the number of old and very old individuals has substantially increased both in absolute and relative terms. Furthermore, demographic projections show that the growth of older age groups is expected to continue for the next 30 years (United Nations 2015).

The aging of our societies contributes at critically challenging the sustainability of the healthcare systems. In fact, older persons are characterized by high clinical complexity (with consequent polypharmacy), disabling conditions, and social issues (National Institute for Health and Care Excellence 2017; Masnoon et al. 2017; Payne 2016). All these factors make the older population quite different from the standards upon which the healthcare systems were originally designed (Tinetti and Fried 2004). In particular, the fragmentation of care services and the rigid disease-centered approach determine a relevant gap between the person's priorities/needs and the provided responses.

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In order to adapt the traditional clinical and research approach to the new (older) older population referring to our services, several theoretical constructs have been proposed in the geriatric literature. Special attention in this context has to be reserved to frailty (Cesari et al. 2017a).

Despite the existence of a largely agreed definition of frailty (i.e., a medical condition characterized by the reduction of homeostatic reserves, exposing the individual to higher vulnerability to stressors and risk of negative health-related outcomes (Morley et al. 2013)), its definition remains controversial (WHO 2015). It is paradigmatic a systematic review of the literature published in 2016 by Buta and colleagues, which listed more than 60 validated instruments for measuring frailty (Buta et al. 2016).

In this chapter, the condition of frailty is presented in its theoretical and operational features. Moreover, its clinical and research relevance as well as the controversies associated with its assessment are discussed.

## 1.2 The Concept of Frailty

In a consensus statement published in 2013, six major international scientific societies (International Association of Gerontology and Geriatrics; Society on Sarcopenia, Cachexia, and Wasting Diseases; International Academy of Nutrition and Aging; European Geriatric Medicine Society; American Medical Directors Association; American Federation for Aging Research) endorsed the definition of frailty as "a medical syndrome with multiple causes and contributors that is characterized by diminished strength, endurance, and reduced physiologic function that increases an individual's vulnerability for developing increased dependency and/or death" (Morley et al. 2013). This definition stands on specific theoretical pillars. In particular, it is established that frailty is different from disability, sarcopenia, and/or multimorbidity. In other words, although a frail subject can be disabled, may present sarcopenia, and/or affected by multiple diseases, none of these three conditions can comprehensively capture the concept of frailty; they may just represent specific aspects of such complex age-related condition (Morley et al. 2013). It was also explained that frailty may find its causal roots in the physical or cognitive domains of the individual (Morley et al. 2013). Frailty was also described as a dynamic entity able to improve or worsen over time.

A growing body of the literature has recently focused on multimorbidity as a parallel concept to frailty. Both are, in fact, designed to capture the clinical complexity of the aging person. Multimorbidity is defined as the coexistence of two or more chronic diseases, not related each other, in the same individual (National Institute for Health and Care Excellence 2017; Mannucci and Nobili 2014). Multimorbidity has attracted a lot of interest in the scientific community, and several societies have provided specific guidance on its management (National Institute for Health and Care Excellence 2017; Muth et al. 2019). Multimorbidity is associated with increased risk for adverse health-related outcomes (Castro et al. 2017; Fraccaro et al. 2016; Barnett et al. 2012). By counting the number of diseases, it is assumed that a more comprehensive assessment and holistic approach to the individual will be possible. Multimorbidity moves from the single-disease approach to a vision characterized by the simultaneous existence of multiple nosological conditions (to be organized and treated) (Cesari et al. 2016a, 2017b).

Frailty and multimorbidity are closely related (Vetrano et al. 2018) and often been alternatively used (as wrongly considered synonymous). Instead, a clear difference exists between them (Cesari et al. 2017b). Whereas multimorbidity relies upon the mono-dimensional construct of disease (i.e., nosologically defined conditions), frailty potentially implies a more exhaustive and comprehensive assessment of the individual (including signs, symptoms, clinical conditions, disabilities). The geriatric background of the former is evident, especially if considering how difficult is to complete a diagnostic *iter* in older persons due to clinical, functional, cost-effectiveness, social, and ethical issues.

The concept of frailty is very close to the resilience one. Resilience is described as the

human ability to adapt when a traumatic life stressor suddenly occurs (Morley et al. 2013). On a purely theoretical basis, the same stressor will generate heterogeneous consequences in different individuals. Therefore, a resilient person will be able to completely restore his/her health status after a negative stressor in a relatively short time, whereas a poorly resilient individual will struggle to restore the *quo ante* condition and will also take more time to recover.

Interestingly, the World Health Organization (WHO) published in 2015 the 'World Report on Ageing and Health'. In this document, the novel concept of intrinsic capacity was theoretically framed and presented (WHO 2015). Intrinsic capacity is here defined as the composite of all the physical and mental capacities of an individual. By interacting with the environment, intrinsic capacity determines the functional ability of the individual, that is the health-related attributes that enable people to be and to do what they have reason to value (WHO 2015). Intrinsic capacity and functional capacity tend to diverge with advancing age. The environment becomes more and more burdening on the capacity of the person to function at his/her best. The document thus insists on the importance of reducing the environmental barriers and/or increasing the intrinsic capacity by levering on the individual's reserves in order to promote the optimal functional ability. It is noteworthy that this novel framework is largely based on the background literature of frailty. In fact, although differences between frailty and intrinsic capacity are quite evident, the two concepts are both (1) designed to promote a novel and comprehensive approach to the aging individual, and (2) based on the necessary integration of care services.

## 1.3 The Assessment of Frailty

Several tools exist to measure frailty and the number of validated tools has steadily increased over the years (Cesari et al. 2017a). Table 1.1 presents the most commonly known tools, although the list is far to be exhaustive (Buta et al. 2016).

Among the different models of frailty, two major school of thoughts might be identified in the literature. Probably, the most commonly known is the model of the frailty phenotype proposed by Fried and colleagues (Fried et al. 2001), based on five signs/symptoms (i.e. weight loss, fatigue, weakness, slowness, reduced or absent physical activity).

Differently, Rockwood and Mitnitski proposed in 2001 the so-called "age-related accumulation of deficits" model of frailty (Mitnitski et al. 2001). It is based on the concept that aging is a continuous process characterized by the accumulation of deficits. Its operationalization gives life to the Frailty Index (FI).

The frailty phenotype and the FI are clearly different. The frailty underlying them is not the same. The frailty phenotype presents a clinical manifestation based on five predefined signs/symptoms. It is not necessary to adequately know the individual for observing this physical evidence. Differently, the FI consider frailty as a heterogeneous state captured during the aging process. It requires a comprehensive assessment of the person for computing the FI, which may consequently resemble a surrogate of biological age.

Independently of the instrument used to measure frailty, it is always important to contextualize the assessment with the subsequent actions. If the detection of frailty is not able to modify the clinician's decisional algorithm, then the assessment is useless (Cesari et al. 2017a).

## 1.4 Frailty and Disability

As discussed, a controversy exists around the concept of frailty. One of the major issues in this field can be found in the positioning of frailty in relation to disability (i.e., the functional limitation of the individual in the accomplishment of activities of daily living (Cesari et al. 2017b)). Although Fried and colleagues did not exclude the possibility that frailty and disability might co-exist, the condition captured by the frailty phenotype has often been considered as a sort of "pre-disability" disability (Fried et al. 2011). This is probably due to the fact that most studies

**Table 1.1** Examples of validated instruments for the screening and assessment of frailty (Cesari et al. 2016a; Morley et al. 2013)

| Author | Model |
|---|---|
| Fried (2001) | Frailty Phenotype |
| Mitnitski (2001) | Frailty index |
| Schuurmans (2004) | Groningen frailty index |
| Rockwood (2005) | Clinical frailty scale |
| Ensrud (2008) | Study of osteoporotic fractures index |
| Romero-Ortuno (2010) | SHARE frailty instrument |
| Gobbens (2010) | Tilburg frailty index |
| Morley (2012) | FRAIL |
| Pilotto (2012) | Multi-prognostic index |
| Mossello (2016) | INTER-FRAIL |

have used the phenotype to capture a risk condition for incident disability. On the other hand, disabilities can be part of the frailty status captured by the deficit accumulation model.

This issue is not trivial, especially if it is taken into account the relevance that disability has for geriatric medicine. If disability is left outside of frailty, then frailty may become the key target for preventive interventions against disability. It means anticipating the geriatric practice to the community, where frail non-disabled individuals live. On the other hand, by accepting that disability is included under the frailty umbrella does not necessarily anticipate, but surely redefine the perimeter of action for geriatric medicine (having biological age as criterion to set the target).

As discussed elsewhere, the interactions of frailty, multimorbidity, and disability may give life to three main scenarios:

- Phenotype model. In this model, the three entities are considered at the same level and independent each other. They can coexist and overlap. A person can thus be at the same time multimorbid, disable, and frail (as suggested by Fried and colleagues in (Fried et al. 2011));
- Pre-disability model. Frailty and multimorbidity act as risk factors for disability. This latter represents the endpoint of interest, and a methodological choice is driving the decision of considering frailty (with/without multimorbidity) as a pre-disability condition;
- Model for adapted care. Frailty is here considered in a broader sense, that is as a condition of public health interest. Frailty is here a biological condition of accentuated vulnerability, where multimorbidity and disability may serve as contributors. In other words, multimorbidity and disability are "contained" within the concept of frailty, as suggested by the FI (Cesari et al. 2017b; Fried et al. 2011).

In the mediation between frailty and disability, an important role is also played by sarcopenia, intended as the loss of muscle lean mass and muscle strength (Cruz-Jentoft et al. 2019). Similar to frailty, there is large discussion about definition and measurement of sarcopenia (Cesari et al. 2016b). Nevertheless, there is a growing consensus in the literature about the importance of introducing the evaluation of the skeletal muscle in the clinical routine in order to identify (and eventually manage) individual exposed to an increased risk of mobility and physical disability.

Irrespective of the debate around defining and measuring it, that is outside the aims of this chapter, sarcopenia may represent the organ-specific pathophysiological background of the progressive reduction of the physical domain of intrinsic capacity, thus potentially influencing the ability to reach and maintain the full functional ability of the individual (Cesari et al. 2016b).

Sarcopenia may represent a novel clinical condition (a specific ICD10 is today available for

it), legitimately entering in the computation of the multimorbidity construct, and have the role of biological substratum for the fragilization of the aging individual (Cesari et al. 2016b).

## 1.5 Frailty Epidemiology

Given the heterogeneous way of measuring frailty, it is clear that every estimate of its prevalence in the population might become easily arguable or (at best) provide a very partial vision of the phenomenon. Nevertheless, several studies have tried to estimate how frail some populations are across settings, countries, and regions.

In a systematic review and meta-analysis based on 21 studies (Collard et al. 2012), the prevalence of frailty ranges between 4.0% and 59.1%. The estimates were significantly lower when the analysis was restricted only to those studies adopting the frailty phenotype. When different subgroups were examined, women showed a substantially higher prevalence of frailty compared to men. As expected, prevalence increased with age, being the highest in subjects $\geq 85$ years (Collard et al. 2012). These data are consistent with those coming from the Survey of Health, Aging and Retirement in Europe (SHARE) project and also further verified in other cohorts coming from the Asian countries (Cesari et al. 2016c).

Socio-economic factors are also closely related to frailty prevalence (Poli et al. 2017; Bandeen-Roche et al. 2015). Several studies have demonstrated that socially and/or economically disadvantaged persons present particularly high prevalence of frailty.

Last but not least, it is important to consider the weight of clinical conditions in the prevalence of frailty. It is obvious that a sicker person is more likely to appear frailty, independently of the adopted instrument to assess it. What is here meant is that frailty prevalence may be very different across clinical settings (Bandeen-Roche et al. 2015; Searle et al. 2018).

## 1.6 The Geriatric Approach to Frailty

In a recent document published by the British Geriatrics Society (British Geriatrics Society 2017), frailty is described as the condition defining individuals in the need of an adapted/integrated care approach based on the comprehensive geriatric assessment. The recommendations do not indicate a single tool to screen frailty (thus implicitly allowing a non-standardization of the results). The intervention offered to the individuals screening positive to frailty is prioritized over the eventual heterogeneity of the screening results. The document explains that, once the frail status of the individual is detected, the possible causes should be explored via a comprehensive geriatric assessment conducted by a multidisciplinary team, pursuing the final aim of designing a person-tailored intervention.

A change of paradigms for moving from the traditional disease-based approach towards a person-tailored model based on the comprehensive assessment of the aging individual is necessary. Today, the reshaping of our healthcare and clinical models is even solicited by the WHO, which recognize the inadequacy of available systems and evokes cornerstone messages of geriatric medicine (e.g., comprehensive assessment, focus on functions, evaluation of the environment, integration of care) (WHO 2015, 2017). In this context, shifting the focus from the disease to frailty may imply more attention to those deficits that concur at the fragilization of the individual but are not (yet) nosologically recognized. It implies paying attention to those abnormalities that are often complained by the older person but find no solution in a system concentrated in the prescription of drugs.

This type of approach has been classically a prerogative of geriatric medicine (Cesari et al. 2016a, c). It is today necessary to train other health professionals at the key principles of geriatrics for two main reasons: (1) age-related

conditions requiring pills of geriatric expertise are today burdening every clinical setting and specialty; (2) geriatricians are too few for taking charge of every individual older than 65 (or 70? or 75?…) years.

## 1.7 Conclusions

Frailty is a clinical condition characterized by an excessive vulnerability of the individual to endogenous and exogenous stressors. This status generates a high risk of developing negative health-related events. Although sharing some characteristics with conditions such as multimorbidity and disability, frailty should not be confused with them. Several tools exist to evaluate frailty, and the choice of the proper one should be driven by the decisional algorithm and intervention it is going to feed.

Our aging societies require a substantial revision of our models of care. Frailty may represent a condition able to lever these changes and introduce neglected aspects of old age (e.g., function, social issues, Ethics) in the traditional medicine (largely based on the obsolete concept of disease). Shifting to a construct as frailty to biologically define the perimeter of action for geriatric medicine will probably concur at modernizing the old way of practicing medicine.

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