Physical frailty and sarcopenia: taking advantage of their commonalities

Matteo Cesari

Department of Geriatrics, University Hospital of Toulouse; University of Toulouse III Paul Sabatier, Toulouse, France

Abstract

Physical frailty and sarcopenia are two age-related conditions indicated as key risk factors for incident disability and health-related negative events in the elderly. Nevertheless, to date, their clinical implementation is still limited, largely because of methodological ambiguities and disagreement about their operationalizations. In order to bypass the current stall-position in the field and try to identify an objective, standardized, and clinically relevant target for interventions, it might be hypothesized to redesign the limits of a pre-disability *physical* risk condition around the inner core shared by both physical frailty and sarcopenia. Thus, preliminary research initiatives [like the *sarcopenia and physical frailty in older people: multicomponent treatment strategies* (SPRINTT) project] are proposing to explore whether physical frailty (or poor physical performance) may represent the clinical manifestation of a specific biological substratum (*i.e.*, low muscle mass) on which build up novel interventions against disability in the elderly.

Introduction

An overall agreement exists in the scientific community about the theoretical definitions of frailty, which has recently been described in a consensus article 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.*[1] This syndrome has traditionally been graphically depicted as a vicious cycle,[2] in which multiple age-related risk conditions (including sarcopenia) are directly implied. A frail individual is indeed an older person living on the dangerous border between independency and dependency. Endogenous or exogenous stressors (even those that might be considered as minor illnesses in robust individuals) might precipitate the health status of the frail elder in the vortex of the disabling cascade.[3]

The interest about the frailty syndrome is particularly motivated by: i) its predictive value for negative health-related outcomes in the elderly (including falls, loss of physical function, hospitalizations, institutionalizations, death);[3] ii) the high prevalence this condition presents in our populations;[4] and iii) the dramatic scenario of our healthcare systems burdened by age-related conditions[5] in steadily aging societies.[6]

Materials and Methods

The challenge of the operational definition of frailty

Although the need of tackling frailty is well recognized and the conceptual definition of the syndrome largely agreed, the clinical implementation of it is still lacking. In particular, a controversy exists around which operational definition should be considered as standard for the frailty assessment. The two main operationalizations of frailty are the phenotypic model proposed by Fried and colleagues,[7] and the deficit accumulation model (or frailty index) designed by Rockwood and colleagues.[8,9] The two instruments are completely different in their designs, objectives, clinical relevance, and translational research potentialities.[10] Many other instruments (more or less inspired by the two main models) are also available in the literature. Interestingly, each available frailty instrument is somehow legitimated by its own validity and predictive capacity for negative outcomes. The problem is that all the available instruments present modest (if any) agreement among them in the identification of the at-risk (*i.e.*, frail) population.[11,12] In other words, every available tool is capable of identifying a population at risk of negative outcomes, but the nature of the risk substantially differs from instrument to instrument. Each tool indeed detects a different population as frail and worth to target with proper countermeasures. And this major limitation is at the net of the multiple adaptations and modifications having occurred to some instruments in the literature, determining consequent difficulties at comparing and interpreting available results.[13]

It is noteworthy that the urgency at finding solutions in the implementation of frailty in the clinical practice is not only a request coming from the geriatric and gerontology world. Other medical specialties are today invoking a solution of the problem because challenged by the aging of their patients.[14,15] Too many are today the older patients in our healthcare services for defining the *geriatric* individuals only on the basis of their chronological age. Indeed, we need to shift from a model of care defining the older person according to the number of years lived to an approach founded on the biology of his/her health status. Under this perspective, frailty may represent an important status requiring an in-depth analysis of the risk profile and subsequent adapted/personalized care (coordinated by a geriatrician).

If frailty is the condition of risk to be *screened* or *detected* in order to develop a consequent comprehensive geriatric assessment (with relative follow-up and re-evaluation over time), the instruments to be used might have secondary importance, especially given the diversity of settings and purposes where the assessment is conducted. By stating this, it is not meant that the standardization of procedures is irrelevant in medicine and public health. This is a simple reminder that the action following the identification of frailty is equally (if not more) important in the clinical setting. Such relevance is also related to the fact that, as geriatricians, we know how to deal with frail individuals and we are supported in this by robust evidence.[16-20] The risk is that the long-lasting and never-ending discussion on the specific instruments to be used (again, all presenting their own legitimacy and validity) may left apart the urgent need to act against the consequences of aging in our societies and the availability of a strong methodology to apply.

If, for a moment, we forget about the multiple operationalizations of frailty *per se* and try to look at the problem of risk assessment in

Correspondence: Matteo Cesari, Department of Geriatrics, University of Toulouse III Paul Sabatier, 37 Allées Jules Guesde, 31000 Toulouse, France.
Tel.: +33.5.61145628; Fax: +33.5.61145640.
E-mail: macesari@gmail.com

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older persons with a more flexible and broader approach, we cannot ignore the huge body of evidence supporting the use of physical performance measures in clinical practice.[21] Instruments like the short physical performance battery,[22,23] the timed up-and-go test,[24] the usual gait speed,[25] *etc*., have a long history in the literature and have shown to be robust tools for capturing the inner biological aging of the older person.[26] It has been shown that the accuracy at predicting negative outcomes of physical performance-based instruments is comparable to a full clinical evaluation conducted by a physician.[27] Moreover, the use of these instruments is not only increasing in geriatric settings, but also among other medical specialties (*e.g*., respiratory medicine,[28] cardio-surgery,[29,30] oncology[31], *etc*.).

Sarcopenia and physical frailty

The history of the sarcopenia condition presents many overlapping with that of frailty. Even in this case, sarcopenia has a well-established and agreed theoretical definition, but finds hard time at being implemented in the clinical setting.

In 1988, Rosenberg proposed the use of the term *sarcopenia* (or sarcomalacia) to indicate the most dramatic and significant decline occurring to our organisms with aging, that of lean body mass.[32] In particular, sarcopenia was described as an important change in both body composition and function. Although the sarcopenia concept was bi-dimensional since the very beginning (*i.e*., low muscle mass and poor muscle function), the first operationalizations proposed in literature were more focused on the quantitative component (*i.e*., lean mass).[33,34] Only later, the second qualitative dimension of sarcopenia (*i.e*., muscle function) was more consistently included in the operational definitions.

As occurred for frailty, the operationalization of sarcopenia is also burdened by multiple issues, doubts, and controversies. A wide spectrum of instruments is available for measuring the two components of sarcopenia,[35] and different algorithms have been proposed by several panels of experts.[36] Interestingly, even if each proposal is today addressing the bi-dimensionality of sarcopenia, the algorithms are built on the use of different instruments and parameters. The unavoidable consequence is the lack of agreement in the identification of a single specific population of sarcopenic individuals if different models are applied. Moreover, it cannot be ignored the fact that the two components of sarcopenia present different clinical relevance. In fact, muscle function can surely be considered as more relevant in the clinical setting (and, thus, more important to assess and target with specific interventions) compared to the muscle mass quantity.[37] This issue is not irrelevant because questioning the clinical implementation of sarcopenia as a whole. In this context, it is not possible to ignore that pharmacological and non-pharmacological interventions are available for targeting the muscle decline.[38] If the concept of sarcopenia is not operationalized in a sufficiently robust, valid, and clinically relevant way, a significant component of the frailty syndrome (*i.e*., sarcopenia) might be left apart and never taken into consideration although detrimental for the individual's health status.

In 2014, the Foundation of National Institutes of Health-Sarcopenia Project released results from analyses conducted in a large sample.[39] The initiative was aimed at providing data-derived algorithms and cut-points for defining the muscle mass loss and, separately, the muscle weakness of the older person. The provision of these new thresholds of risk based on objective evaluations has opened new scenarios in the field. By standardizing the assessment of the two sarcopenia dimensions around clear gender-specific cut-points of (body mass index-adjusted) appendicular lean mass and handgrip strength, Authors have completed an important step forward in the standardization of the approach. These data indeed facilitate the focus on the shared biological commonalities existing between frailty (intended as physical performance loss) and sarcopenia (*i.e*., muscle mass loss). In fact, it will now be easier and less controversial to build up algorithms combining physical performance measures and muscle mass quantifications into a single condition measuring the muscle quality.[40] Preliminary research initiatives in this direction are already ongoing, such as the *sarcopenia and physical frailty in older people: multi-component treatment strategies* (SPRINTT) project.[41] SPRINTT is a 48-million euros project funded by the Innovative Medicines Initiative designed with the specific aims of: i) providing a clear operationalization of frailty; ii) identifying a target population with unmet medical needs; iii) validating a new methodology for implementing strategies against disability in Europe; and iv) defining the background for regulatory and pharmaceutical investigations purposes.

Conclusions

In conclusion, frailty and, even more, sarcopenia are not yet sufficiently implemented in the clinical setting. Although frailty is a wide risk condition potentially (but not necessarily) including sarcopenia as key contributor, the reduction of the frailty syndrome to its only physical domain might be important in some contexts. For example, physical frailty (or poor physical performance) may represent the clinical manifestation of a specific biological substratum (*i.e*., low muscle mass) on which build up novel interventions against disability in the elderly.

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