The Assessment of Frailty in Older Adults

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KEYWORDS

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The term frailty is defined as "having a delicate health and not robust," being the concept of frailty broadly used in Geriatric Medicine to identify older adults at an increased risk for future poor clinical outcomes such as development of disabilities, dementia, falls, hospitalizations, institutionalization, or increased mortality. Although there is a universal intuitive recognition of frailty by most physicians caring for older people, there is still a lack of both a consensus definition and a standardized assessment tool to be used in clinical practice and in research.[1–3] The main controversies arise when establishing a frailty model (whether physical, functional, cognitive, social, or any combination in between them) or when considering the previous domains as components of the model or as frailty outcomes. The issue on disability considered by many as a component of the syndrome and by others as an outcome (and therefore distinct from frailty) can be cited as an example of an actual controversy.[1,3–5]

In the presence of a general frailty recognition, the diversity found in the components of frailty models and frailty outcomes must be due to a disagreement on the concept by physicians (with an intuitive but heterogeneous recognition of frailty), and the isolation of research groups, or could also be due to the complexity of the concept so that no easy and simple definition will be available. Therefore it is not surprising that, in the same population of 125 older adults, the prevalence of frailty ranged between 33% and 88% depending on the frailty tool used, and recent

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published articles proposed new definitions and clinical assessment tools based on original definitions and frailty models.[6–10]

Although there is no definition, and it is not possible to know the exact prevalence of frail older adults due to ongoing debate on the exact nature of frailty, there is no disagreement on its catastrophic impact on older individuals and their families.[1,5] The controversy on the exact components of the frailty syndrome is of less importance when all frailty models identify older adults at risk of poor clinical outcomes such as dementia, development of disabilities, institutionalization, hospitalizations, and increased mortality. Even in the presence of many unresolved issues, frailty in older adults should not be neglected, and the explosion of original frailty models is only a reflection of the evolving concept, frailty being an active domain of inquiry.

The aim of the present article was to explore the actual trends of research on the concept of frailty and the different frailty models by performing a comprehensive and updated review of the literature. The current issues on the outcomes and the components of the syndrome (and therefore the older adults identified by a frailty assessment tool) are explored to better understand the complexity of the frailty syndrome and why a definition does not emerge from the literature after more than 30 years of research.

METHODOLOGY

A recent comprehensive review performed by an expert group in frailty was updated for the present article.[1] A new PubMed search, with the MeSH terms Frailty/Frailty-Definition/Frailty-Assessment/frailty, and Elderly-older people-older adults, was performed to retrieve the relevant articles published in the domain in the years 2008 and 2009. The abstracts of these articles were reviewed and for those abstracts that fulfilled the purposes of the current revision, the full articles were retrieved. There has been an explosion of the use of the term frailty by medical specialties (like cardiology or oncology) other than geriatrics, so to limit the heterogeneity of the concept, only studies based on a general (nonspecific) population of older adults were considered for the present update. Finally, the reference lists of the identified articles were also pearled for relevant literature.

RESULTS

The first search with the MeSH term frailty retrieved 498 articles in the years 2008 and 2009; findings that corroborate a recent PubMed search highlighting that the number of publications in the domain of frailty had increased exponentially over the last 20 years.[4] Of these, 78 articles analyzed nonspecific populations of older adults and a final selection of 32 relevant articles for the purpose of the present review were retained, based on the previous exposed search limitations, the revision of abstracts, and the pearling of reference lists.

THE CONCEPT OF FRAILTY

Although frailty is a commonly used term indicating older persons at increased risk for poor clinical outcomes, the concept is unfortunately poorly or variably defined in the literature, and there is still a lack of both consensus definition and a consensual clinical assessment tool.[1]

It is nowadays widely recognized that frailty should be considered as a clinical syndrome resulting from multisystem impairments separated from the normal aging process. As a syndrome, associated impairments such as sarcopenia, functional

decline, neuroendocrine dysregulation, and immune impairments can occur in combination.[11] The cluster of clinical manifestations of frailty is at greater risk for poor clinical outcomes than any single component, and no single manifestation of frailty will explain the whole of symptoms and signs present. Although there is growing evidence on the identification of the components of frailty, defining frailty in clinical practice and clinical research remains paradoxically difficult. The main reason behind this issue is that the concept of frailty differs between working groups and many investigators have treated frailty as synonymous with disability or dependence, whereas others have attempted to describe frailty as a distinct concept.[3–5]

Based on the concept and components used to define frailty, the 2 main phenotypes that nowadays coexist in literature are the phenotype of physical frailty and a much broader phenotype including cognitive, functional, and social circumstances going well beyond just physical aspects, considered as a multidomain phenotype.[2–4,12–14]

Physical Phenotype

This definition was operationalized in 2001 by providing a specific list of 5 measurable items to identify frailty. The phenotype was found to predict consistently various poor clinical outcomes. Clusters of functional impairments shaped the syndrome and no other nonphysical components were included, which were considered by the group as distinct entities.

Multidomain Phenotype

Strong evidence existed to consider additional components as part of the syndrome, which could be affected by the same biologic processes that lead to the manifestations of physical frailty. Cognitive impairment, mood disorders, sensory impairment, poor social conditions and support, chronic diseases, and disability were considered by many investigators as part of the frailty syndrome, and the inclusions of other domains proved to increase the predictive capacity of physical frailty for poor clinical outcomes.

Original Frailty Models

The update also retrieved many articles that continued to propose new tools to assess frailty based on original definitions. These original definitions highlighted that controversy continues to exist on the components of the frailty syndrome, and a wide range of measures from geriatric syndromes to functional impairments, as part of the definition, was found across these studies.

THE PHYSICAL PHENOTYPE OF FRAILTY

Based on their work in the Cardiovascular Health Study (CHS) and the Women's Health and Aging Studies (WHAS), Fried and colleagues[3,15] presented an operational definition of frailty in 2001. The definition conceptualized frailty as a syndrome of decreased resiliency and physiologic reserves, in which a mutually exacerbating cycle of declines across multiple systems results in negative energy balance, sarcopenia, and diminished strength and tolerance for exertion. Accordingly, the working group provided a specific list of 5 measurable items (exhaustion, weight loss, weak grip strength, slow walking speed, and low energy expenditure) as frailty-identifying characteristics. Participants were classified as frail if they met 3 or more of the 5 criteria, as intermediate if they met 1 or 2 of the 5 criteria, and as robust if they met none of the criteria. The study found a prevalence of frailty of 7% in the CHS (4317 community-dwelling

adults aged 65 and older), 30% in the subgroup aged 80 and older, and 28% in the WHAS (1002 community-dwelling women aged 65 and older). The phenotype predicted in these cohorts various poor clinical outcomes, including falls, the development of disability, hospitalization, and mortality.[3,15]

After 2001, numerous secondary analyses using adapted criteria have been performed. The observed differences in the prevalence of frailty were probably linked to the obvious methodological issues when adapting the criteria and to the differences in study populations. Therefore, a prevalence was found of 6.5% in the Invecchiare in Chianti Study (InCHIANTI), 16.3% in the Women's Health Initiative Observational Study (WHI-OS), and 20% in the Hispanic Established Population Epidemiologic Study of the Elderly (EPESE).[16–18] Although the recent analyses, using adapted criteria, predicted similarly poor clinical outcomes like death, hip fracture, disability, and hospitalization, the independent contribution of the 5 frailty items, with the exception of gait speed, to subsequent poor clinical outcomes has not been rigorously evaluated and the added value of each criterion is not known.[1,9,11,19] This issue has marked the trend of current research and recent articles to untangle the initial 5 criteria and to analyze individually each parameter as a single-item assessment tool.

Gait Speed

There is growing evidence that the development of functional limitations is an initial manifestation of frailty, and recent published articles consider the use of slow gait speed as a criterion for frailty.[1,9,20–24] The assessment of gait speed and the identification of a specific threshold of slow gait speed could identify a vulnerable older population at risk of poor clinical outcomes (such as development of disabilities, dementia, mortality, institutionalization, and falls) on which preventive strategies could be implemented. The possibility of prevention is supported by the fact that improvements as small as 0.1 m per second (m/s) in gait speed resulted in a substantial reduction in mortality, and that physical activity with improvement in physical function prevented or delayed the onset of frailty.[25–29]

A recent systematic review proposed a threshold of 0.8 m/s, and a population moving slower than this velocity is at risk of the mentioned poor clinical outcomes.[20] Although the proposed threshold was based on the evidence coming from the review, the issue is not resolved as other investigators prefer an "easy to remember" threshold of 1 m/s. This alternative threshold is also supported by evidence (mainly by data on mortality), and is probably a more sensible but less specific threshold, and therefore more suitable for screening purposes. Before a generalization of the use of these thresholds, they need to be validated across a variety of populations and clinical settings. Gait speed, also influenced by age and the presence of disabilities and comorbidities, could represent the most suitable single-item assessment tool of frailty to be implemented in usual clinical practice. The assessment of gait speed at usual pace over 4 m is a quick, safe, easy, inexpensive, and highly reliable measure, with the capacity to identify older adults at risk of poor clinical outcomes over time.[20]

Hand Grip Strength (Weakness)

Hand grip strength has repeatedly been reported as a single-item assessment tool for frailty. Patients with diminished grip strength were 6 times as likely to be frail, and recent surveys also concluded that grip strength was a powerful predictor of self-perceived fatigue, disability, morbidity, and mortality. Even though the WHAS-I could not find a statistically significant association between low grip strength and development of disabilities,[30–33] weakness (identified by low grip strength) has been explored as an initial manifestation of frailty being present even before the onset of other

functional impairments like diminished gait speed.[34] One of the main limitations of grip strength is the availability of standardized dynamometers for use across different settings and populations.[35]

Fatigue

Fatigue has been recently explored as a single assessment tool for frailty, with contradictory results. Self-reported tiredness in daily activities was found to be an independent and strong predictor for disability and mortality in 705 nondisabled seniors after 15 years of follow-up.[36] Exhaustion was not associated with poor clinical outcomes in a recent study of 754 older adults after 8 years of follow-up.[9] Finally, exhaustion was not a risk factor for new-onset disabilities in 749 participants of the WHAS.[33] Probably one of the main limitations is the subjectivity of this criterion without an exact notion of what is being explored.

Weight Loss and Low Energy Expenditure

No article was found when limiting the initial PubMed search to frailty. The assessment of weight loss and physical activity as predictors of poor clinical outcomes over time probably was performed without taking into account the notion of frailty. In the light of the present research, it is probable that these criteria were currently not seen as single-item frailty criteria. Worthy of mention is that a statistically significant U-shaped curve association was found between frailty (assessed by physical and multidomain phenotypes) and body mass index (BMI; weight in kilograms divided by height in meters squared) in the English Longitudinal Study of Ageing (ELSA), so that the lowest and highest BMI presented the strongest association. Weight loss over time was not specifically assessed in the survey.[37]

EXPANDED MODELS OF THE PHYSICAL PHENOTYPE

A broader phenotype including cognitive, functional, and social circumstances, going well beyond just physical aspects, was also reported in the literature. The inclusion of other domains to the 5 items proved to increase the predictive capacity of the physical phenotype of frailty for poor outcomes. With the nonphysical components being considered as distinct entities by the working groups on physical frailty, current research is focused on the predictive capacity of the added value of these domains to the physical phenotype. The models resulting from the addition of different domains to the physical phenotype have been called expanded models of physical frailty.

Disability

Dementia and disability are the 2 main domains of controversy. Whereas many investigators include dementia and disability as components of frailty, others look at them as outcomes depending very much on how frailty is defined. No recent research article has evaluated the added value of the activities of daily living (ADL) and instrumental activities of daily living (IADL) disability to the physical phenotype of frailty in order to assess prediction of poor clinical outcomes. Although frailty frequently exists concurrently with disease and disability, and is generally accepted to be independent and distinct from these characteristics, more research needs to be performed to untangle disability from frailty.[3] Data on the predictive value for poor clinical outcomes of frailty, ADL dependency, or both, in the presence or not of the former condition could shed light on the actual controversies. Although no article has assessed the added value of dependency to the frailty syndrome, many recent original frailty models include ADL dependency as a component (discussed later in the multidomain section).

A cross-sectional analysis of the Montreal Unmet Needs Study (MUNS) supported previous studies and provided further evidence on the fact that although frailty is a distinct geriatric concept, it overlaps with other concepts like disability and comorbidity. Of the participants identified as frail, 29.1% presented ADL disability, 92.7% IADL disability, and 81.8% comorbidity.[38]

Dementia

As for disability, dementia was considered as a component or as an outcome depending on the frailty definition. Recent research explored the added value of dementia to the predictive value of the physical phenotype criteria, establishing an expanded model of frailty. Adding the diagnosis of lower cognitive function to slower gait, weaker grip, and lower physical activity increased slightly the prediction of developing disability in the MacArthur Study of Successful Aging (MSSA) (from an odds ratio [OR] of 1.7 and 95% confidence interval [CI] 1.3–2.2 to an OR of 1.8 and 95% CI 1.3–2.4), with no effect on mortality.[39] The added value of cognitive impairment was also assessed in the Three-City Study. Comparing frail older adults with frail and cognitively impaired older adults, the 4-year adjusted predictive value increased considerably for ADL disability (from an OR of 3.28 [95% CI 1.61–6.67] to an OR of 5.6 [95% CI 2.13–14.7]), IADL disability (from an OR of 2.2 [95% CI 1.47–3.24] to an OR of 3.17 [95% CI 1.47–6.83]), and mortality (from an OR of 1.3 [95% CI 0.83–2.04] to an OR of 1.91 [95% CI 1.00–3.68]). Of note, cognitive impairment was unable to predict development of ADL disability or mortality when analyzed separately in the nonfrail participants.[40] Two recent publications from the Rush Memory and Aging Project established causal links between the frailty syndrome and Alzheimer disease (AD), suggesting that frailty and AD may share similar etiologies. The first study found an increase in incident AD in the presence of baseline frailty, with a hazard ratio (HR) of 2.24 [95% CI 1.49–3.37] during a 3 years of follow-up.[41] In the same cohort, brain autopsies from 165 deceased participants proved that the level of AD pathology was associated with frailty proximate to death. This statistically significant association did not differ with the presence of dementia diagnosis.[42]

Quality of Life and Socioeconomics

Although the added value to the physical phenotype has not been searched, recent cross-sectional analyses showed a statistically significant association between the presence of frailty and lower health-related quality of life scores in the Hispanic EPESE, and highlighted a statistically significant association between the presence of frailty and lower socioeconomic status in the WHAS. These domains need further enquiry and, like dementia, poor clinical outcomes of frailty need to be explored in the presence of poor self perception of health and in subgroups of lower socioeconomic status.[43,44] Prevention of frailty by leisure activities has been supported by analyses performed in the MSSA and Hispanic EPESE. Mainly volunteer work, but also providing care for children and paid work proved to decrease the risk of becoming frail after 3 years of follow-up (OR 0.73 [95% CI 0.55–0.98]).[45]

NEW MODELS OF PHYSICAL PHENOTYPE

Original clusters of physical impairments other than the initial 5 items from the CHS have been explored recently, probably due to the nonavailability of particular study cohorts of the latter.

Gait speed along with a repeated chair-stand test categorized older adults as severe, moderate, or nonfrail in The Treviso Longeva (TRELONG) Study. Severe frail

participants (gait speed < 0.6 m/s and unable to perform repeated chair-stands) were at an increased risk of developing disability and decreased survival after 20 months of follow-up.[46] With an aim of providing a frailty assessment tool easy to be used in clinical practice, extensive work in the Study of Osteoporotic Fractures (SOF) and the Osteoporotic Fractures in Men (MrOS) Study was performed on the SOF Index.[7,47,48] This index (presence of 2 or more of following components: weight loss, inability to perform repeated chair-stands, and poor energy) was constructed based on the predictive validity of the individual components, and has been compared with the 5 frailty items of physical phenotype. The conclusions drawn from these analyses is that the SOF Index performed as well as the 5 frailty items in predicting risk of poor clinical outcomes such as falls, development of IADL disability, fractures, and death after 9 years and 3 years of follow-up in the SOF and MrOs studies, respectively.[7,47,48]

THE MULTIDOMAIN PHENOTYPE OF FRAILTY

Even if the physical phenotype has been validated and modified for use in numerous published reports and could currently be considered as a gold standard when assessing frailty, limitations remain that challenge its generalizability and usefulness in the clinical setting. Furthermore, controversies still exist when defining (or limiting) the frailty components, as many investigators defend a broader phenotype of frailty including cognitive, functional, and social circumstances. These limitations could be the main reason behind the current validation of an increasing number of original frailty models beyond the physical aspects. However, most multidomain models are based on the results of regression models (as a sum of positive independent associated risk factors for different poor clinical outcomes), and do not propose a pathophysiological line of causation between the attributes that are assessed at baseline and the outcomes experienced by the patients.[49] Moreover, when 3 different frailty models in the Health and Retirement Study were compared, almost one-third (30.2%) of the participants were frail according to at least 1 model, but only 3.1% were frail according to all 3 models, so it is highly probable that different models of frailty, based on different components, capture different groups of older adults with different frailty pathways or trajectories to poor clinical outcomes.[50]

Comprehensive Geriatric Assessment

Most of the work performed on the multidomain phenotype is based on comprehensive geriatric assessment (CGA), with frailty measures that reflect the accumulation of identified deficits. The procedure of constructing a frailty measure has been standardized by Searle and colleagues[51] by creating a Frailty Index. The resulting Frailty Indexes predicted poor clinical outcomes such as survival, progression of disability, or institutionalization in different populations.[52–55] As an example, Rockwood and colleagues[52] compiled a Frailty Index based on identified deficits in the domains of cognition, mood, motivation, communication, mobility, balance, bowel and bladder function, ADL, nutrition, and social resources, as well as several comorbidities. The index, with 4 levels from fitness to frail, was found to be highly predictive of death (from a Relative Risk [RR] of 1.2 [95% CI 1.0–1.4] to an RR of 3.1 [95% CI 2.7–3.6]) or institutionalization (from an RR of 1.7 [95% CI 1.3–2.1] to an RR of 9.4 [95% CI 7.7–11.5]).

Rather than applying and validate a proposed Frailty Index, current research explored original Frailty Indexes, based on data availability and study characteristics. The different accumulations of deficits, identified by CGA, constructed original Frailty

Indexes that predicted similarly poor clinical outcomes (fractures, hospitalization, development and progression of disability, or mortality) in different populations and clinical settings.[6,10,50,56,57] Disability and dementia were components of the Frailty Index at the same time were assessed as poor clinical outcomes.

Social Vulnerability

Social isolation is considered as a frailty marker, and social circumstances of older adults may affect health conditions such as development of dementia or disability.[58,59] Self-reported social deficits were identified in the Canadian Study of Health and Aging (CSHA) and the National Population Health Survey (NPHS). A social vulnerability index was constructed based on social support, living situation, socially oriented activities, leisure activities, and socioeconomics, among others. After 5 years of follow-up in the CSHA and 8 years in the NPHS, the odds of mortality increased for each additional social deficit in the index, and a meaningful gradient across quartiles of social vulnerability was found even after the equations were controlled for age, gender, and a Frailty Index.[60] The ELSA was assessed for a Frailty Index, neighborhood deprivation (based on the Index of Multiple Deprivation 2004), and individual socioeconomics. The presence of frailty increased with decreasing individual and neighborhood socioeconomic factors, so that the poorest older adults living in the most deprived neighborhoods also presented a higher score in the Frailty Index based on CGA deficits.[61,62]

DISCUSSION

This new update of a recent task force on frailty addresses the current research on the concept and domains of frailty. The actual lines of research in the domain did not solve previous controversies on the topic, and no clear consensus regarding frailty emerges from recent studies. Once more a large array of models, definitions, and criteria has been proposed to define frailty.

Although there seems to be a growing consensus to differentiate frailty from disability when using the physical phenotype and no current study has proposed disability as a component of the phenotype, the distinction of the 2 entities is less clear in the multidomain phenotype. When a Frailty Index is based on CGA and on an accumulation of deficits, disability will obviously be included as a component. Hence, the choice of components to be included in the frailty definition continues to be an issue, and the relationship between frailty and disability depends very much on how frailty is defined. While the contradictory presence of disability as a component coexists with the presence of disability as outcome, no consensus will emerge from the literature and more original frailty models will be validated in the near future. The promotion of integration of concepts bringing together researchers from different fields could bridge the actual controversies, and a future hypothetical model of frailty should probably be not as restrictive as the physical phenotype but neither as broad as the multidomain phenotype. This idea is supported by the fact that the expanded physical frailty models (where dementia was added to the phenotype) were much stronger predictors of poor clinical outcomes than the physical phenotype by itself.[40]

Diminished physical performance and sarcopenia are key elements in the cycle of physical frailty, but no recent research has been performed on muscle-wasting effects.[3] Similar to frailty, sarcopenia is nowadays ambiguously defined, with many working groups proposing original definitions. A recent Task Force in the domain has proposed a new operational definition on sarcopenia by combining a physical performance measure (gait speed) with a muscle mass measure (appendicular muscle

mass by appendicular fat mass). It needs to be proven that this new definition can capture the expected poor clinical outcomes of sarcopenia.[63] Once sarcopenia is clearly defined, the exact relationship with the other components of the frailty cycle should be determined, along with the role of sarcopenia in the frailty syndrome.

Recent research has been focused on physical performance measures and mainly on gait speed. Diminished gait speed has been proven to be a strong predictor of poor clinical outcomes in different populations.[20] Even if consistent data come from research, this assessment tool is not widely implemented and CGA does not include a systematic evaluation of physical performances in usual clinical practice. To enhance and generalize its use, clinicians should be aware of the use of simple, quick, and safe assessment tools that could increase the sensitivity of detecting impairments when performing CGA, but at the same time easy-to-remember thresholds, such as 1 m/s, should be assessed by researchers to obtain predictive values for poor clinical outcomes useful in clinical practice.

A major limitation for frailty models could be the current cluster approach of the syndrome. Clustering components increases the predictive capacity of individual components, but no pathophysiological line of causation, between the attributes that are assessed at baseline and the outcomes experienced by the patients, is proposed. Furthermore, the patient might be excluded from intervention as he or she does not satisfy the minimum of items needed from a chosen cluster, knowing that all the individual items of the cluster also increase the risk of poor clinical outcomes. As patients who meet only some of the criteria will suffer from a lack of attention, it is important to stress that although clustering might unify clinical characteristics, all individual components when present need to be treated.

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