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# Nutrition, Frailty, Cognitive Frailty and Prevention of Disabilities with Aging

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## Abstract

Older adults can be categorized into three subgroups to better design and develop personalized interventions: the disabled (those needing assistance in the accomplishment of basic activities of daily living), the ‘frail’ (those presenting limitations and impairments in the absence of disability) and the ‘robust’ (those without frailty or disability). However, despite evidence linking frailty with a poor outcome, frailty is not implemented clinically in most countries. Since many people are not identified as frail, their treatment is frequently inappropriate in health care settings. Assessing the frail and prefrail older adults can no longer be delayed, we should rather act preventively before the irreversible disabling cascade is in place. Clinical characteristics of frailty such as weakness, low energy, slow walking speed, low physical activity and weight loss underline the links between nutrition and frailty. Physical frailty is also associated with cognitive frailty. We need to better understand cognitive frailty, a syndrome which must be differentiated from Alzheimer’s disease. At the Gérontopôle frailty clinics, we have found that almost 40% of the patients referred to our center by their primary care physicians to evaluate frailty had significant weight loss in the past 3 months, 83.9% of patients presented slow gait speed, 53.8% a sedentary lifestyle and 57.7% poor muscle strength. Moreover, 43% had a Mini-Nutritional Assessment less than 23.5 and 9% less than 17, which reflects protein-energy undernutrition. More than 60% had some cognitive impairment associated with physical frailty.

## **Introduction**

Disability with aging is a clinical issue representing a priority for public health systems. In fact, besides the increased burden on the patient's quality of life, disability is associated with high health care costs [1]. Assessing the frail and pre-frail older adults can no longer be delayed, we should rather act preventively before the irreversible disabling cascade is in place [2].

## **The Frailty Syndrome: A Common Clinical Situation**

During the last two decades, a growing body of literature has been specifically focused on exploring the 'frailty syndrome'. Frail older adults are at increased risk of negative health-related events, including hospitalization, institutionalization and disability. In particular, frailty is usually considered as a state preceding disability which, in contrast to disability, is still amenable to treatment interventions and reversible [3]. On the basis of this novel concept, the heterogeneous older population was subsequently categorized into three subgroups to be able to design and develop person-tailored interventions. Older persons were then considered 'disabled' if needing assistance in the accomplishment of basic activities of daily living (ADL), 'frail' if presenting limitations and impairments in the absence of disability, and 'robust' if no frailty or disability is present. Frailty has been conceptualized as a physiological syndrome reflecting decreased reserve and resilience, which may lead to a progressive functional decline, vulnerability to stressors and an elevated risk of adverse outcomes, including death. It is a major cause of dependency, yet research suggests that it may be possible to prevent disability and dependency by targeting frail and prefrail older adults with simple screening tools and effective and sustained interventions [2]. A recent consensus conference was convened in Orlando Florida to develop consensus operational approaches along with delegates from IAGG (International Association of Geriatrics and Gerontology), AMDA (American Medical Directors Association), AFAR (American Federation of Aging Research), EUGMS (European Union Geriatric Medicine Society), IANA (International Academy of Nutrition and Aging), SSCWD (Society on Sarcopenia, Cachexia and Wasting Disorders), the EU and GEC (Gateway Geriatric Education Center) [4].

Strong evidence supports the definition of frailty as a syndrome with a distinct etiology consisting of a constellation of signs and symptoms that increase vulnerability to stressors and that, taken together, are better at predicting an adverse outcome than any individual characteristic. Fried et al. [5] have proposed that the signs and symptoms of frailty result from dysregulated energetics

involving multiple molecular and physiological pathways, which lead to sarcopenia, inflammation, decreased heart rate variability, altered clotting processes, altered insulin resistance, anemia, altered hormone levels and micronutrient deficiencies. These physiological impairments result in the five clinical characteristics of frailty: weakness, low energy, slow walking speed, low physical activity and weight loss [5]. The presence of any three of these phenotypes indicates that a person is 'frail'; one or two phenotypes indicate that the person is 'prefrail' and absence of these characteristics indicates the person is 'robust'.

A systematic review incorporating 31 studies of frailty in persons 65 years or older found a prevalence from 4.0 to 17.0% (mean 9.9%) for physical frailty, with a higher prevalence when psychosocial frailty was also included [6]. While the Fried approach quantifies frailty using five measures, Rockwood et al. [7] have developed a Frailty Index based on the Comprehensive Geriatric Assessment which counts up to 70 items. In a study of community-dwelling older adults in Canada, the Frailty Index-Comprehensive Geriatric Assessment estimated a frailty prevalence of 22.7%, with higher scores predicting an increased risk of death.

Frailty has been linked to longer hospital stays and increased mortality in hospitalized patients [8]. Moreover, in their study of disability trajectories of community-dwelling older persons during the last year of life, Gill et al. [9] found that frailty was the most common condition leading to death, followed by organ failure, cancer, other causes, advanced dementia and sudden death. Yet, despite evidence linking frailty with a poor outcome, frailty is not implemented clinically in most countries. Since many people are not identified as frail, they frequently are treated inappropriately in health care settings. For example, regardless of age, a frail person may be unable to withstand aggressive medical treatment that could benefit a nonfrail person.

## **Nutrition and Frailty**

Frailty can be influenced by a number of factors, and nutrition has been identified as a factor influencing the development of frailty. The Orlando Task Force [4] felt that evidence supported three treatments which appeared to be effective in decreasing frailty in the majority of individuals:

- Calorie and protein support
- Vitamin D
- Exercise (resistance and aerobic)

In the Women's Health and Aging Studies including 599 women aged 70–79 years and a body mass index greater than 18.5, Blaum et al. [10] showed that

being overweight was significantly associated with prefrailty, and obesity was associated with prefrailty and frailty. In the English Longitudinal Study of Ageing, Hubbard et al. [11] showed in 3,055 patients aged 65 years and older that the association between body mass index and frailty showed a U-shaped curve. Independent of the body mass index, daily energy intake was lowest in people who were frail, followed by prefrail people, and highest in people who were not frail. Energy-adjusted macronutrient intakes were similar in people with and without frailty. Frail [adjusted odds ratio (AOR): 4.7; 95% confidence interval (CI): 1.7–12.7] and prefrail (AOR: 2.1; 95% CI: 0.8–5.8) people were more likely to report being food insufficient than nonfrail people; serum albumin, carotenoids and selenium levels were lower in frail adults than nonfrail adults [12]. Several observational studies have shown an association between inadequate nutritional intake and frailty. In the Invecchiare (aging) in Chianti (InCHIANTI) study, Bartali et al. [13] found that daily energy intake  $\leq 21$  kcal/kg body weight was significantly associated with frailty (OR: 1.24; 95% CI: 1.02–1.5). This study also analyzed the association between frailty and nutrients; after adjusting for energy intake, low intakes of protein (OR: 1.98; 95% CI: 1.18–3.31); vitamin D (OR: 2.35; 95% CI: 1.48–3.73), vitamin E (OR: 2.06; 95% CI: 1.28–3.33), vitamin C (OR: 2.15; 95% CI: 1.34–3.45) and folate (OR: 1.84; 95% CI: 1.14–2.98) were significantly and independently related to frailty [13].

Two studies have shown an association between inadequate protein intake and frailty. In the Women's Health and Aging Studies, 24,417 patients aged 65–79 years were included and followed up during 3 years. After adjustment for confounders, results showed that a 20% increase in uncalibrated protein intake (%kcal) was associated with a 12% (95% CI: 8–16%) lower risk of frailty, and that a 20% increase in calibrated protein intake was associated with a 32% (95% CI: 23–50%) lower risk of frailty [14]. In the second study, protein intake below the estimated average requirement (0.7 g/kg per day) was found in 10% of the community-dwelling and frail elderly and 35% of the institutionalized elderly people [15]. Then, dietary protein intake averaged at  $1.1 \pm 0.3$  g/kg per day in community-dwelling,  $1.0 \pm 0.3$  g/kg per day in frail and  $0.8 \pm 0.3$  g/kg per day in institutionalized elderly men.

Finally, two studies showed an association between Mediterranean diet [based on a Mediterranean diet score (maximum 9 points) evaluated by an interview-based food frequency questionnaire] and frailty. In the InCHIANTI study, 690 patients aged  $\geq 65$  years were included and followed up during 6 years. Results showed that higher adherence (score  $\geq 6$ ) to a Mediterranean-style diet was associated with lower odds of developing frailty (OR: 0.30; 95% CI: 0.14–0.66) compared with those with lower adherence (score  $\leq 3$ ), and that higher adherence to a Mediterranean-style diet at baseline was also associated with a

lower risk of low physical activity (OR: 0.62; 95% CI: 0.40–0.96) and slow walking speed (OR: 0.48; 95% CI: 0.27–0.86) but not with feelings of exhaustion and poor muscle strength [16]. One other recent study showed that the risk of being frail was significantly reduced in the highest quartile of the Mediterranean diet score (OR: 0.26; 95% CI: 0.07–0.98) [17].

Several studies showed that lower levels of 25-hydroxyvitamin D were associated with a higher prevalence of frailty [18–21].

Observational studies have found an association between serum antioxidants (vitamin E, vitamin C and carotenoids) [22–25], vitamin B<sub>6</sub> and folate [24, 25] and frailty.

In the G erontop ole frailty screening, approximately 40% of the patients had weight loss and a poor nutritional status [26].

## **Physical Activity and Frailty**

Many studies have shown that physical activity and exercise are beneficial in older adults along the full spectrum of the health status. The demonstrated benefits of exercise in older adults include increased mobility, enhanced performance of ADL, improved gait, decreased falls, improved bone mineral density and increased general well-being. Decreased muscle strength occurs normally with age but is even more pronounced in the frail older adult and more likely to impact adverse outcomes such as disability. Studies suggest that even the frailest oldest adults are likely to benefit from physical activity at almost any level that can be safely tolerated [27]. Regular physical activity has been shown to protect against diverse components of frailty such as sarcopenia, functional impairment and depression [28].

Exercise is believed to be the most effective of all interventions proposed to improve functionality in older adults. In a systematic review, Theou et al. [29] found that 45–60 min of exercise three times a week had positive effects on frailty. Exercise in the frail increases functional performance, walking speed, chair stand, stair climbing and balance, and decreased depression and fear of falling.

A more recent systematic review has been published on the effect of exercise on frail older adults [30]. The authors concluded that the exercise intervention only slightly affected physical function, mainly by increasing gait speed and the Berg Balance Scale score, and improved performance in ADL. Nevertheless, they underlined that participants included in these trials may be not representative of the total frail older adult population because of those who would have benefited from exercise but were excluded from the trial because of age or other comorbidities that prevented them from exercising.

## **Multidomain Approach**

Multidomain interventions are currently tested in large programs [31]. This multidomain approach will aim to treat physical and cognitive frailty with a combination of nutrition supplementation and physical and cognitive exercise.

## **Implementing Frailty into Clinical Practice**

In order for frailty to be incorporated into the routine practice of primary care physicians, a simple screening test is needed. Several different methods of screening for frailty have been developed and validated. The Fried criteria were operationalized into a screening algorithm for use in the Cardiovascular Healthy Study. Other frailty measures have also been proposed, including the Study of the Osteoporotic Fractures Index [32]. All of these measures count deficits and all of them quantify the degree of frailty and thus the degree of vulnerability to adverse outcomes. Moreover, all of them reflect an aging-associated failure of physiological systems.

Another frailty screening tool that relies on the clinical opinion of the general practitioner has been developed in France. In response to the French government's policy for preventing disability in older persons, a day hospital was established in 2011, the G erontop ole of Toulouse (i.e. the geriatric center of Toulouse), for the evaluation of frailty and prevention of disability [26]. Geriatric patients are referred to the center by general practitioners who detect signs or symptoms of frailty, and patients are screened using a simple, quick frailty questionnaire as well as an assessment of gait speed. The frailty screening tool asks six questions regarding living alone, weight loss, fatigue, mobility, memory and slow gait speed. If the physician identifies one of these areas as an area of concern, he/she is asked: 'In your own clinical opinion, do you feel that your patient is frail and at an increased risk for further disabilities?' It is this last question that is used to identify patients who are frail (table 1).

The aims of the G erontop ole frailty clinics are to identify frailty in the early stages through a multidisciplinary evaluation and its cause(s), i.e. underlying diseases or risk factors, and to implement multidisciplinary interventions adapted to each patient's individual needs. These interventions may include nutrition, physical exercise and/or physical therapy, social support and education. Patients are followed up principally by their general practitioner as well as through phone contact and a structured interview with a nurse from the center to assess the efficacy of the interventional plan.

**Table 1.** The Gérontopôle frailty screening tool (from Vellas et al. [36], with permission): a questionnaire for the detection of frail older patients by general practitioners

	Yes	No	Don't know
Does your patient live alone?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Has your patient involuntarily lost weight in the last 3 months?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Has your patient been more fatigued in the last 3 months?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Has your patient experienced increased mobility difficulties in the last 3 months?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Has your patient complained of memory problems	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Does your patient present slow gait speed (i.e. >4 s to walk 4 m)?	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
If you have answered yes to one or more of these questions:			
Do you think your patient is frail?	<input type="checkbox"/>	<input type="checkbox"/>	
If yes, is your patient willing to be assessed for his/her frailty status at the Frailty Clinic?	<input type="checkbox"/>	<input type="checkbox"/>	
Patients aged 65 years and older without both functional disability (ADL score 5/6) and current acute disease.			

We recently published the description of the 160 first patients referred for frailty by general physicians to the Gérontopôle frailty clinics, a new clinical facility developed in Toulouse to implement frailty into clinical practice. The mean age of our population was 82.7 years, with a large majority aged 75 years and older. Most patients were women (61.9%). Approximately two thirds of the patients received any kind of regular help. Regarding the level of frailty, 65 patients (41.4%) were prefrail and 83 (52.9%) frail [26].

Near 40% had significant weight loss (more than 4.5 kg in the past 3 months). With respect to the functional status, 83.9% of the patients presented slow gait speed, 53.8% had a sedentary lifestyle and 57.7% had poor muscle strength. Only 27.2% of the patients had a Short Physical Performance Battery score equal to or higher than 10. Autonomy in ADL was quite well preserved (mean ADL score:  $5.6 \pm 0.8$ ) as expected, suggesting that the study patients had not yet developed disability. Consistently, Instrumental ADL showed a marginal loss of autonomy reporting a mean score of  $6.0 \pm 2.3$ . Numerous patients presented vision problems. Finally, it is noteworthy that 9% of the study population presented an objective state of protein-energy malnutrition, i.e. Mini-Nutritional Assessment (MNA) less than 17, and 34% an early alteration of nutritional status with the MNA between 17 and 23.5, while almost everyone (94.9%) had vitamin D deficiency. These results are confirmed in a larger sample with now more than 1,000 patients from the Gérontopôle frailty clinics with similar characteristics.

To have a real impact, the intervention must be strong. To do this, a complete geriatric assessment of the prefrail and frail patients is necessary to be able to diagnose an age-related disease at a prodromal stage, where it is still possible to cure the patient. The evaluation must use specific tools to enable the most accurate diagnosis of potential age-related diseases. The assessment must include also social, health, economic and psychosocial assessments, as well as the evaluation of deficit accumulation. We also need to adapt some of our tools to frailty, e.g. many studies have found that individuals with MNA scores between 17 and 23.5 are more likely to be frail [33, 34].

Due to the aging population, we need long-term and sustained interventions. Physical exercise, cognitive exercise, nutritional interventions and social services will be needed for the detection and treatment of age-related diseases. More standardization of these multidomain interventions is an important area for further research. We have to balance very strong interventions (which will be accepted by few frail older adults) against very weak interventions (which will usually not be strong enough to have a real impact).

### *Cognitive Frailty*

To date, most research efforts on frailty have focused on its 'physical' aspects, and little work has been done, however, to clarify how the process of frailty itself affects the brain. A brain deemed 'frail' and not robust for age may still possess a plastic reserve that could respond to rehabilitative and eventually to preventive strategies to significantly attenuate its functional decline. Considering the current increased interest in the frailty syndrome and aging brain, as well as in the development of strategies to attenuate disability in the elderly, a workshop on cognitive frailty was conducted by an International Consensus Group from the IANA (International Academy on Nutrition and Aging) and IAGG (International Association of Gerontology and Geriatrics) on April 16, 2013, in Toulouse (France) [35]. This report presents current issues related to the relationship between frailty and cognition and results from the Consensus Group. Cognitive frailty, when clearly defined, may represent a novel and more actionable condition to consider in the complex and heterogeneous scenario of cognitive and emotional impairment in older persons. The consensus panel proposed the identification of the so-called 'cognitive frailty' as a heterogeneous clinical manifestation characterized by the simultaneous presence of both physical frailty and cognitive impairment. In particular, the key factors defining such a condition include: (1) the presence of physical frailty and cognitive impairment (Clinical Dementia Rating = 0.5) and (2) exclusion of concurrent Alzheimer's disease or other dementias. Under different circumstances, cognitive frailty may represent a precursor of neurodegenerative processes. A potential for reversibility

may also characterize this entity. A psychological component of the condition is evident and concurs with increasing vulnerability of the individual to stressors.

To identify frail older adults is the future of geriatric medicine and must also be addressed by primary care physicians as well as specialists facing an aging population. Moreover, it is a unique opportunity to prevent further disabilities. All health care professionals play an important role, including dietitians and physical therapists.

## Disclosure Statement

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