

Nutrition, frailty, and sarcopenia

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Abstract Frailty and sarcopenia are important concepts in the quest to prevent physical dependence, as geriatrics are shifting towards identifications of early stages of disability. Definitions of both sarcopenia and frailty are still developing, and both concepts clearly overlap in their physical aspects. Malnutrition (both undernutrition and obesity) plays a key role in the pathogenesis of frailty and sarcopenia. The quality of the diet along the lifespan has a close relation with the incidence of both entities, and nutritional interventions may be able to reduce the incidence or revert either of them. This brief review explores the role of energy and protein intake and other key nutrients on muscle function. Nutrition may be a key element of multimodal interventions for frailty and sarcopenia. The results of the “Sarcopenia and Physical fRailty IN older people: multi-component Treatment strategies” (SPRINTT) trial will offer key insights on the effect of such interventions in frail, sarcopenic older individuals.

Keywords Frailty · Sarcopenia · Geriatric nutrition · Muscle · Mobility

Introduction

Fighting disability has always been one of the landmarks of geriatric medicine. Some decades ago, the focus was on

identification and treatment of potentially reversible physical or mental disability, with a multidimensional diagnostic approach and multifaceted interventions. In recent years, the focus has shifted towards the identification of early stages of disability—including subclinical disability—to identify and tackle its causes and prevent, or at least retard, its appearance. In this setting, it is not surprising that the concepts of frailty and sarcopenia have come to date. The rate of publications per year in this field has risen exponentially in the last 10 years (Fig. 1).

The concepts of frailty and sarcopenia

Frailty

The first publication with the MeSH term “frailty” is found in Pubmed in 1953 [1]. Initially, it was an intuitive concept, which included both older people with an impending risk of deterioration and those with an already high degree of disability and high risk of further deterioration and death. More recently, the common core of most definitions consider frailty as a clinical state in which there is an increase in an individual’s vulnerability to developing increased dependency and/or mortality when exposed to a stressor [2]. This understanding led to two different operationalizations of the frailty syndrome at the beginning of this century. In 2001, Fried and colleagues [3] focused more on physical components and defined a physical phenotype of frailty that includes evidence of unintentional weight loss, muscle weakness, slow walking speed, low physical activity, and exhaustion. On the other hand, Rockwood and colleagues [4] favoured a multidimensional concept involving psychological and social components, multimorbidity, and disability in addition to the physical impairments (Table 1).

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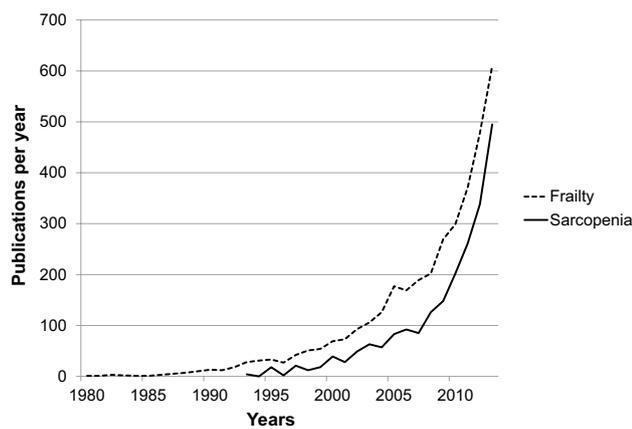


Fig. 1 Publications per year on frailty and sarcopenia

Table 1 Physical and multidimensional phenotype of frailty

Physical phenotype	Multidimensional phenotype
Unintentional weight loss	Physical impairment
Muscle weakness	Sensory limitation
Slow walking speed	Mood
Low physical activity	Cognition
Exhaustion	Social environment
	Comorbidity
	Disability

Many new suggestions on definitions and operationalization of frailty are still being proposed in the most recent literature.

Sarcopenia

The age-associated muscle loss, or sarcopenia, was framed for the first time by Rosenberg in 1997 [5]. Initially, the definitions of sarcopenia were based solely on muscle mass. As muscle strength and physical performance cannot be explained completely by muscle mass, and muscle mass alone does not predict disability or other outcomes [6], the current consensus definitions of sarcopenia include measurements of muscle strength and physical performance [7–10].

Overlap between frailty and sarcopenia

Both the concepts of frailty and sarcopenia are evolving, and there is still no full consensus on where to fit each of them in usual clinical practice, or on how to use either to prevent or retard disability. Frailty seems to be evolving into a framework to detect persons with high risk of disability, where both specific and non-specific interventions

(i.e., nutrition and exercise) may improve outcomes [11], while sarcopenia—considered as an organ failure (muscle failure or muscle insufficiency)—is a frequent cause of physical frailty and may help develop drugs targeted to improve muscle function [12, 13].

Both frailty models have an overlap in the physical component [14]. In this regard, muscle plays an important role. Per definitionem, sarcopenia includes low physical performance, which means that sarcopenia is an essential component of physical frailty. In practice, frailty and sarcopenia show a significant overlap [15]. Physical frailty itself is a component of the multidimensional phenotype of frailty (Table 1). These overlaps are illustrated in Fig. 2.

Frailty, sarcopenia and nutrition

Malnutrition plays a key role in the pathogenesis of both frailty and sarcopenia [16, 17]. This fact is quite clear when a syndromic approach is used to address frailty [18] and sarcopenia [19, 20]. Both undernutrition and obesity increase the risk of frailty in community dwelling older individuals [21, 22]. The quality of the diet has a close relation with the incidence of frailty [23]. Many nutritional interventions may be of interest in sarcopenia and frailty [24].

Energy intake

Not only the lack of certain nutrients can be responsible for the onset of sarcopenia and frailty, but also the energy of the consumed food should be considered. Eaten food is metabolized to provide energy for organ function and muscle activity. If intake is not sufficient to meet needs, body fat and muscle are catabolized to provide energy [25]. Therefore, for maintenance of muscle mass and physical performance, the amount of food and energy consumed

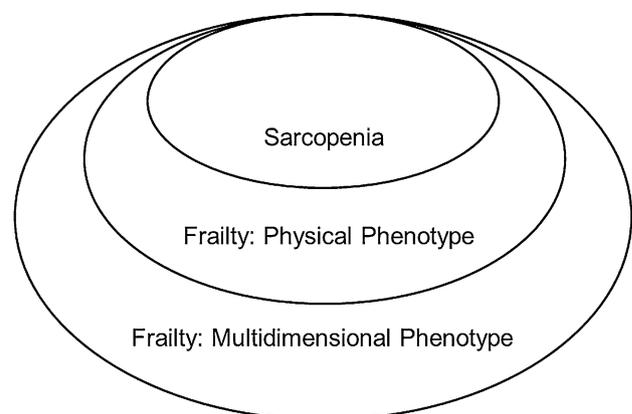


Fig. 2 Overlap between frailty and sarcopenia

is of primary importance. This is also true, in a broader aspect, for the function of any organ or system.

If body weight decreases during periods of starvation, not only fat stores are wasted but always also lean body mass, i.e., muscle mass, is lost. In older adults, reduced energy intake occurs often due to a reduction in appetite or anorexia of aging [26, 27]. Anorexia of aging can be explained by physiologic changes, such as altered taste and smell sensation, slower gastric emptying, and altered hormonal responses, but also as a consequence of physical and mental impairments, chewing or swallowing problems [26, 28]. The presence of multiple diseases in many elderly and the related polypharmacy may also substantially impair dietary intake and lead to malnutrition. The negative consequences of these changes are compounded by the effects of functional and mental impairments that impact on the ability to access and prepare food. Thus, in a vicious cycle, declining muscle strength and physical performance in older adults may increase the risk of poor nutrition, whilst poor nutrition may contribute to further decline and frailty. Data from 802 persons aged 65 years and older participating in the InCHIANTI study have shown that frailty is associated with a daily energy intake of less than 21 kcal/kg (OR: 1.24; 95% CI: 1.02–1.5) [29]. This finding was confirmed in the Third National Health and Nutrition Examination Survey (NHANES III) consisting of 4731 US American participants older than 60 years. Independently of body mass index (BMI), the daily energy intake was lowest in people who were frail, followed by pre-frail, and highest in people who were not frail (mean kJ \pm SE: 6648 \pm 130, 6966 \pm 79, 7280 \pm 84, $p < 0.01$) [30]. The same was shown in the Fourth Korea National Health and Nutrition Examination Survey (KNHANES IV) for sarcopenia. In 940 men and 1324 women aged 65 and older, the energy intake was significantly lower in sarcopenic participants [31].

Protein intake

Older adults usually eat less protein than younger adults [32]. Around 10% of community-dwelling older adults and one-third of those living in care homes do not meet the estimated average requirement (EAR) for daily protein intake (0.7 g/kg body weight/day) [33], a minimum intake level to maintain muscle integrity in adults of all ages that has recently been challenged for older adults [34, 35]. Many, if not all, older adults need more dietary protein than do younger adults. An imbalance between protein supply and protein needs can result in loss of skeletal muscle mass because of a chronic disruption in the balance between muscle protein synthesis and degradation. As a result, older adults may lose muscle mass and strength and eventually experience low muscle and bone mass [36, 37] and frailty [38]. Distribution of protein intake is also related to frailty

[39] and sarcopenia [40], although this is far to be clear [34, 35].

There are many reasons older adults fail to consume enough protein to meet needs, but most of them are similar to those described for energy intake: physiological changes and medical conditions that lead to age- and disease-associated anorexia, physical and mental disabilities, and food insecurity due to financial and social limitations [32].

Creatine

Creatine is an organic acid that is synthesized endogenously or can be taken up by foods, such as meat and fish. In the body, creatine is mainly stored as free creatine or phosphocreatine in skeletal muscles [41]. Phosphocreatine reconverts adenosine triphosphate (ATP) during muscle contraction and works as temporal energy buffer in times of high-energy demand [41]. The supplementation of creatine monohydrate was shown to increase total creatine and phosphocreatine levels in the skeletal muscle, especially in persons with low creatine stores [42]. In athletes, taking creatine is common to enhance strength and fatigue resistance during high-intensity exercise [43]. Moreover, treatment with creatine was proven to increase muscle strength in muscular dystrophies [44] and to reduce cell damage and inflammation after intensive running [45].

Creatine may have a role as a nutritional aid against sarcopenia [46], but there are no solid studies linking creatine intake or deficiency in the genesis of muscle wasting or frailty.

Leucine

Leucine is an essential amino acid that plays an important role in muscle mass and function [47]. Amino acids function as precursors for de novo protein synthesis, and play a role as nutritional signals that regulate multiple cellular processes. Leucine up-regulates mRNA translation, thereby increasing muscle protein synthesis, and is a strong insulin secretagogue. Experimental data show that leucine ingestion can reverse the blunted response of muscle protein synthesis to amino acid/protein intake in the elderly [48]. There are no studies on the role of leucine on frailty separate from its role in muscles.

β -hydroxy- β -methylbutyrate (HMB)

HMB occurs naturally in human muscle cells as a derivative of leucine and may positively affect protein balance by increasing protein synthesis and decreasing protein degradation [49, 50]. Recently, the International Society of Sports has stated that HMB can promote muscle recovery and, additionally, can enhance muscle hypertrophy, strength

and power in trained and untrained persons if appropriate exercise prescription is utilized [51]. HMB may have a role, as a nutrient or a drug, in promoting muscle function.

Other nutrients

Other nutrients have also been linked with the development of sarcopenia and frailty. Vitamin D is the most relevant. However, the link between sarcopenia and dietary intake of vitamin D is still unclear [52], and in most intervention trials, vitamin D has been used in pharmacological doses, so it will not be further considered in this review.

Antioxidant intake may also have a role in sarcopenia and frailty. High intake of antioxidants may prevent sarcopenia [53, 54]. Oxidative stress has also been linked to frailty, although evidence is still sparse [55]. Fish oil supplementation may improve physical performance [56].

Nutrition intervention in frailty and sarcopenia

Frailty has proven to be a dynamic and reversible process: frail individuals can experience either improvement or worsening in their frailty status along time [57]. The same is true for sarcopenia. Being nutrition a key element in the pathophysiology of both conditions, it may have a strong role in their prevention and treatment.

However, strong evidence to base recommendations is still lacking. A very recent systematic review looked at intervention studies in sarcopenia that used muscle mass and function (as opposed to muscle mass alone) as outcome measures found moderate quality evidence suggesting that exercise interventions improve muscle strength and physical performance [58]. However, results of nutrition interventions were equivocal due to the low number of studies and heterogeneous study design. Essential amino acid (EAA) supplements, including around 2.5 g of leucine, and HMB supplements showed some effects in improving muscle mass and function parameters. Protein supplements did not show consistent benefits on muscle mass and function.

With this in mind, there are still some recommendations that may be sound for the prevention and treatment of sarcopenia and frailty. A balanced diet can be proposed: adhering to a Mediterranean-style diet is associated with a significantly lower risk of incident frailty, mostly due to improved physical activity and walking speed [59]. High total protein intake in usual diet may also preserve from frailty, regardless of the source of protein and the amino acid composing the protein [60]. Importantly, in those individuals who are already frail, protein-energy supplementation may reduce the progression of functional decline [61].

Being sarcopenia and frailty complex geriatric syndromes, multimodal interventions that include physical

exercise, nutrition intervention, and other approaches seem to be the most sensible approach if these conditions are to be prevented and reversed [62], and recent clinical trials are using such approaches [63, 64]. The “Sarcopenia and Physical Frailty IN older people: multi-component Treatment strategies” (SPRINTT) trial is an ambitious multicenter European trial trying to prove the effect of multimodal interventions in frail, sarcopenic patients.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

Ethical approval This article does not contain any studies with human participants or animals performed by any of the authors.

Informed consent For this type of study informed consent is not required.

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