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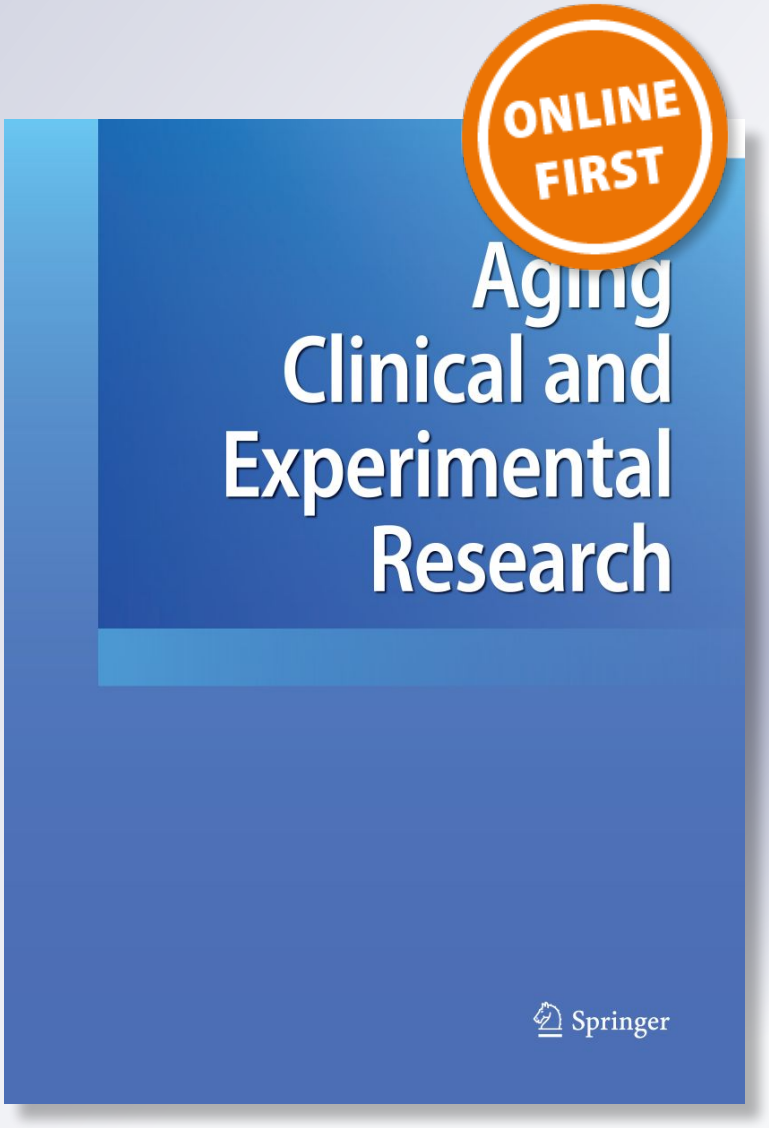

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REVIEW

Nutrition, frailty, and sarcopenia

Alfonso J. Cruz-Jentoft[1] · Eva Kiesswetter[2] · Michael Drey[2] · Cornel C. Sieber[2]

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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: multicomponenT 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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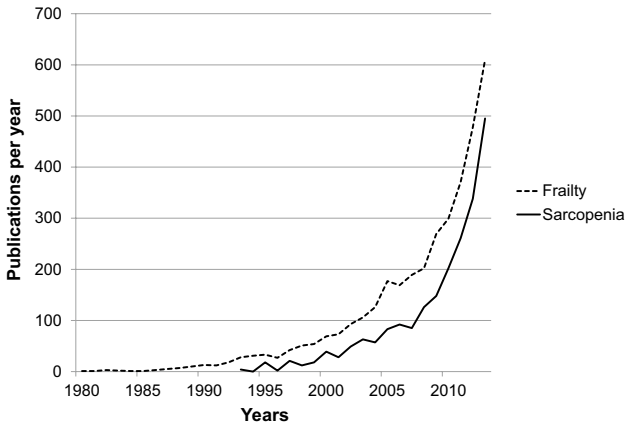

Fig. 1 Publications per year on frailty and sarcopenia

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

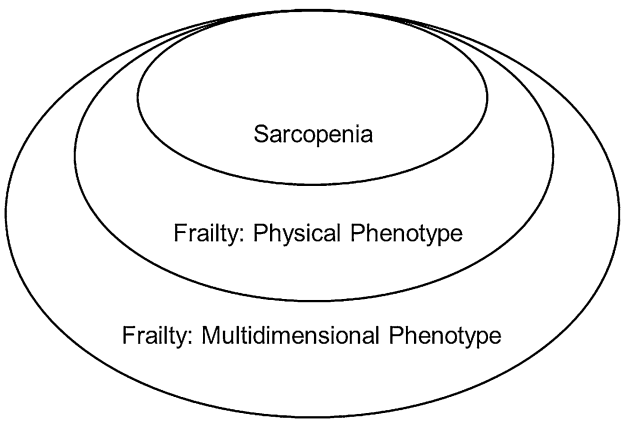

Fig. 2 Overlap between frailty and sarcopenia

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 ± SE: 6648 ± 130, 6966 ± 79, 7280 ± 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 and 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 derivate 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.

References

1. Petit-Dutaillis D, Chavany J, Guiot G (1953) Operative frailty of patients with chromophobe adenoma of abnormal symptomatology; prognostic value of homonymous lateral hemianopsia. Presse Med 61:341–343
2. Clegg A, Young J, Iliffe S, Rikkert MO, Rockwood K (2013) Frailty in elderly people. Lancet 381:752–762. doi:10.1016/S0140-6736(12)62167-9
3. Fried LP, Tangen CM, Walston J et al. (2001) Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 56:M146–M156. doi:10.1093/gerona/56.3.M146
4. Rockwood K, Song X, MacKnight C et al (2005) A global clinical measure of fitness and frailty in elderly people. CMAJ 173:489–495. doi:10.1503/cmaj.050051
5. Rosenberg IH (2011) Sarcopenia: origins and clinical relevance. Clin Geriatr Med 27:337–339. doi:10.1016/j.cger.2011.03.003
6. Goodpaster BH, Park SW, Harris TB et al (2006) The loss of skeletal muscle strength, mass, and quality in older adults: the health, aging and body composition study. J Gerontol A Biol Sci Med Sci 61:1059–1064
7. Fielding RA, Vellas B, Evans WJ et al (2011) Sarcopenia: an undiagnosed condition in older adults. Current consensus definition: prevalence, etiology, and consequences. International working group on sarcopenia. J Am Med Dir Assoc 12:249–256. doi:10.1016/j.jamda.2011.01.003
8. Morley JE, Abbatecola AM, Argiles JM et al (2011) Sarcopenia with limited mobility: an international consensus. J Am Med Dir Assoc 12:403–409. doi:10.1016/j.jamda.2011.04.014
9. Cruz-Jentoft AJ, Baeyens JP, Bauer JM et al (2010) Sarcopenia: European consensus on definition and diagnosis: report of the european working group on sarcopenia in older people. Age Ageing 39:412–423. doi:10.1093/ageing/afq034
10. Cruz-Jentoft AJ, Landi F (2014) Sarcopenia. Clin Med (Lond) 14:183–186. doi:10.7861/clinmedicine.14-2-183

11. Morley JE, Vellas B, Abellan van Kan G et al (2013) Frailty consensus: a call to action. J Am Med Dir Assoc 14:392–397. doi:10.1016/j.jamda.2013.03.022
12. Studenski SA, Peters KW, Alley DE et al (2014) The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. J Gerontol A Biol Sci Med Sci 69:547–558. doi:10.1093/gerona/glu010
13. Morley JE, von Haehling S, Anker SD, Vellas B (2014) From sarcopenia to frailty: a road less traveled. J Cachexia Sarcopenia Muscle 5:5–8. doi:10.1007/s13539-014-0132-3
14. Cruz-jentoft AJ, Michel JP (2013) Sarcopenia: a useful paradigm for physical frailty. Eur Geriatr Med 4:102–105. doi:10.1016/j.eurger.2013.02.009
15. Samper-Ternent R, Reyes-Ortiz C, Ottenbacher KJ, Cano CA (2016) Frailty and sarcopenia in Bogotá: results from the SABE Bogotá study. Aging Clin Exp Res. doi:10.1007/s40520-016-0561-2 (ahead of print)
16. Walston J, Hadley E, Ferrucci L et al (2006) Research agenda for frailty in older adults: toward a better understanding of physiology and etiology: summary from the American Geriatrics Society/National Institute on Aging Research Conference on Frailty in Older Adults. J Am Geriatr Soc 54:991–1001. doi:10.1111/j.1532-5415.2006.00745.x
17. Walston JD (2012) Sarcopenia in older adults. Curr Opin Rheumatol 24:623–627. doi:10.1097/BOR.0b013e328358d59b
18. Ahmed N, Mandel R, Fain MJ (2007) Frailty: an emerging geriatric syndrome. Am J Med 120:748–753. doi:10.1016/j.amjmed.2006.10.018
19. Bauer JM, Sieber CC (2008) Sarcopenia and frailty: a clinician's controversial point of view. Exp Gerontol 43:674–678. doi:10.1016/j.exger.2008.03.007
20. Cruz-Jentoft AJ, Landi F, Topinková E, Michel J (2010) Understanding sarcopenia as a geriatric syndrome. Curr Opin Clin Nutr Metab Care 13:1–7. doi:10.1097/MCO.0b013e328333c1c1
21. Hubbard RE, Lang IA, Llewellyn DJ, Rockwood K (2010) Frailty, body mass index, and abdominal obesity in older people. J Gerontol A Biol Sci Med Sci 65:377–381. doi:10.1093/gerona/glp186
22. Bollwein J, Volkert D, Diekmann R et al (2013) Nutritional status according to the mini nutritional assessment (MNA(R)) and frailty in community dwelling older persons: a close relationship. J Nutr Health Aging 17:351–356. doi:10.1007/s12603-013-0009-8
23. Shikany JM, Barrett-Connor E, Ensrud KE et al (2014) Macronutrients, diet quality, and frailty in older men. J Gerontol A Biol Sci Med Sci 69:695–701. doi:10.1093/gerona/glt196
24. Barillaro C, Liperoti R, Martone AM, Onder G, Landi F (2013) The new metabolic treatments for sarcopenia. Aging Clin Exp Res 25:119–127. doi:10.1007/s40520-013-0030-0
25. Newman AB, Lee JS, Visser M et al (2005) Weight change and the conservation of lean mass in old age: the health, aging and body composition study. Am J Clin Nutr 82:872–878 (quiz 915)
26. Morley JE (2013) Pathophysiology of the anorexia of aging. Curr Opin Clin Nutr Metab Care 16:27–32. doi:10.1097/MCO.0b013e328359efd7
27. Landi F, Laviano A, Cruz-Jentoft AJ (2010) The anorexia of aging: is it a geriatric syndrome? J Am Med Dir Assoc 11:153–156. doi:10.1016/j.jamda.2009.09.003
28. Serra-Prat M, Mans E, Palomera E, Clavé P (2013) Gastrointestinal peptides, gastrointestinal motility, and anorexia of aging in frail elderly persons. Neurogastroenterol Motil 25:291–e245. doi:10.1111/nmo.12055
29. Bartali B, Frongillo EA, Bandinelli S et al (2006) Low nutrient intake is an essential component of frailty in older persons. J Gerontol A Biol Sci Med Sci 61:589–593
30. Smit E, Winters-Stone KM, Loprinzi PD, Tang AM, Crespo CJ (2013) Lower nutritional status and higher food insufficiency in frail older US adults. Br J Nutr 110:172–178. doi:10.1017/S000711451200459X
31. Kim JE, Lee YH, Huh JH, Kang DR, Rhee Y, Lim SK (2014) Early-stage chronic kidney disease, insulin resistance, and osteoporosis as risk factors of sarcopenia in aged population: the fourth Korea National Health and Nutrition Examination Survey (KNHANES IV), 2008–2009. Osteoporos Int 25:2189–2198. doi:10.1007/s00198-014-2745-y
32. Volpi E, Campbell WW, Dwyer JT et al (2013) Is the optimal level of protein intake for older adults greater than the recommended dietary allowance. J Gerontol A Biol Sci Med Sci 68:677–681. doi:10.1093/gerona/gls229
33. Tieland M, Borgonjen-Van Den Berg K, van Loon LJ, de Groot LC (2012) Dietary protein intake in community-dwelling, frail, and institutionalized elderly people: scope for improvement. Eur J Nutr 51:173–179. doi:10.1007/s00394-011-0203-6
34. Bauer J, Biolo G, Cederholm T et al (2013) Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE study group. J Am Med Dir Assoc 14:542–559. doi:10.1016/j.jamda.2013.05.021
35. Deutz NE, Bauer JM, Barazzoni R et al (2014) Protein intake and exercise for optimal muscle function with aging: recommendations from the ESPEN Expert Group. Clin Nutr 33:929–936. doi:10.1016/j.clnu.2014.04.007
36. Houston DK, Ding J, Nicklas BJ et al (2009) Overweight and obesity over the adult life course and incident mobility limitation in older adults: the health, aging and body composition study. Am J Epidemiol 169:927–936. doi:10.1093/aje/kwp007
37. Meng X, Zhu K, Devine A, Kerr DA, Binns CW, Prince RL (2009) A 5-year cohort study of the effects of high protein intake on lean mass and BMC in elderly postmenopausal women. J Bone Miner Res 24:1827–1834. doi:10.1359/jbmr.090513
38. Beasley JM, LaCroix AZ, Neuhouser ML et al (2010) Protein intake and incident frailty in the women's health initiative observational study. J Am Geriatr Soc 58:1063–1071. doi:10.1111/j.1532-5415.2010.02866.x
39. Bollwein J, Diekmann R, Kaiser MJ et al (2013) Distribution but not amount of protein intake is associated with frailty: a cross-sectional investigation in the region of Nürnberg. Nutr J 12:109. doi:10.1186/1475-2891-12-109
40. Valenzuela RE, Ponce JA, Morales-Figueroa GG, Muro KA, Carreón VR, Alemán-Mateo H (2013) Insufficient amounts and inadequate distribution of dietary protein intake in apparently healthy older adults in a developing country: implications for dietary strategies to prevent sarcopenia. Clin Interv Aging 8:1143–1148. doi:10.2147/CIA.S49810
41. Wyss M, Kaddurah-Daouk R (2000) Creatine and creatinine metabolism. Physiol Rev 80:1107–1213
42. Harris RC, Söderlund K, Hultman E (1992) Elevation of creatine in resting and exercised muscle of normal subjects by creatine supplementation. Clin Sci (Lond) 83:367–374. doi:10.1042/cs0830367
43. Gualano B, Roschel H, Lancha-Jr AH, Brightbill CE, Rawson ES (2012) In sickness and in health: the widespread application of creatine supplementation. Amino Acids 43:519–529. doi:10.1007/s00726-011-1132-7
44. Kley RA, Tarnopolsky MA, Vorgerd M (2011) Creatine for treating muscle disorders. Cochrane Database Syst Rev. doi:10.1002/14651858.CD004760.pub3
45. Santos RV, Bassit RA, Caperuto EC, Costa Rosa LF (2004) The effect of creatine supplementation upon inflammatory and muscle soreness markers after a 30 km race. Life Sci 75:1917–1924. doi:10.1016/j.lfs.2003.11.036

46. Palus S, von Haehling S, Springer J (2014) Muscle wasting: an overview of recent developments in basic research. J Cachexia Sarcopenia Muscle 5:193–198. doi:10.1007/s13539-014-0157-7
47. Rieu I, Balage M, Sornet C et al (2007) Increased availability of leucine with leucine-rich whey proteins improves postprandial muscle protein synthesis in aging rats. Nutrition 23:323–331. doi:10.1016/j.nut.2006.12.013
48. Leenders M, van Loon LJ (2011) Leucine as a pharmaconutrient to prevent and treat sarcopenia and type 2 diabetes. Nutr Rev 69:675–689. doi:10.1111/j.1753-4887.2011.00443.x
49. Szcześniak KA, Ostaszewski P, Fuller JC, Ciecierska A, Sadkowski T (2015) Dietary supplementation of β-hydroxy-β-methylbutyrate in animals—a review. J Anim Physiol Anim Nutr (Berl) 99:405–417. doi:10.1111/jpn.12234
50. Fitschen PJ, Wilson GJ, Wilson JM, Wilund KR (2013) Efficacy of β-hydroxy-β-methylbutyrate supplementation in elderly and clinical populations. Nutrition 29:29–36. doi:10.1016/j.nut.2012.05.005
51. Wilson JM, Fitschen PJ, Campbell B et al (2013) International Society of Sports Nutrition Position Stand: beta-hydroxy-beta-methylbutyrate (HMB). J Int Soc Sports Nutr 10:6. doi:10.1186/1550-2783-10-6
52. Dupuy C, Lauwers-Cances V, Van Kan GA et al (2013) Dietary vitamin D intake and muscle mass in older women. Results from a cross-sectional analysis of the EPIDOS study. J Nutr Health Aging 17:119–124. doi:10.1007/s12603-012-0089-x
53. Kim JS, Wilson JM, Lee SR (2010) Dietary implications on mechanisms of sarcopenia: roles of protein, amino acids and antioxidants. J Nutr Biochem 21:1–13. doi:10.1016/j.jnutbio.2009.06.014
54. Kim J, Lee Y, Kye S, Chung YS, Kim KM (2015) Association of vegetables and fruits consumption with sarcopenia in older adults: the Fourth Korea National Health and Nutrition Examination Survey. Age Ageing 44:96–102. doi:10.1093/ageing/afu028
55. Mulero J, Zafrilla P, Martinez-Cacha A (2011) Oxidative stress, frailty and cognitive decline. J Nutr Health Aging 15:756–760
56. Hutchins-Wiese HL, Kleppinger A, Annis K et al (2013) The impact of supplemental *n*-3 long chain polyunsaturated fatty acids and dietary antioxidants on physical performance in postmenopausal women. J Nutr Health Aging 17:76–80. doi:10.1007/s12603-012-0415-3
57. Gill TM, Gahbauer EA, Allore HG, Han L (2006) Transitions between frailty states among community-living older persons. Arch Intern Med 166:418–423. doi:10.1001/archinte.166.4.418
58. Cruz-Jentoft AJ, Landi F, Schneider SM et al (2014) Prevalence of and interventions for sarcopenia in ageing adults: a systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). Age Ageing 43:748–759. doi:10.1093/ageing/afu115
59. Talegawkar SA, Bandinelli S, Bandeen-Roche K et al (2012) A higher adherence to a Mediterranean-style diet is inversely associated with the development of frailty in community-dwelling elderly men and women. J Nutr 142:2161–2166. doi:10.3945/jn.112.165498
60. Kobayashi S, Asakura K, Suga H, Sasaki S, Three-generation SOWODAHSG (2013) High protein intake is associated with low prevalence of frailty among old Japanese women: a multicenter cross-sectional study. Nutr J 12:164. doi:10.1186/1475-2891-12-164
61. Kim CO, Lee KR (2013) Preventive effect of protein-energy supplementation on the functional decline of frail older adults with low socioeconomic status: a community-based randomized controlled study. J Gerontol A Biol Sci Med Sci 68:309–316. doi:10.1093/gerona/gls167
62. Brown JC, Harhay MO, Harhay MN (2016) Physical activity, diet quality, and mortality among sarcopenic older adults. Aging Clin Exp Res. doi:10.1007/s40520-016-0559-9 (ahead of print)
63. Cesari M, Demougeot L, Boccalon H, Guyonnet S, Vellas B, Andrieu S (2014) The multidomain intervention to preveNt disability in ElDers (MINDED) project: rationale and study design of a pilot study. Contemp Clin Trials 38:145–154. doi:10.1016/j.cct.2014.04.006
64. Tikkanen P, Lonnroos E, Sipila S, Nykanen I, Sulkava R, Hartikainen S (2014) Effects of comprehensive geriatric assessment-based individually targeted interventions on mobility of pre-frail and frail community-dwelling older people. Geriatr Gerontol Int 15:80–88. doi:10.1111/ggi.12231