Chapter

Nutritional Approaches for Attenuating Muscle Atrophy

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Abstract

Muscle atrophy occurs under a number of different conditions, including disuse and aging accompanied by the onset of sarcopenia. Although muscle mass is reduced by decreased protein synthesis and/or increased protein degradation, the mechanisms of disuse muscle atrophy and sarcopenia differ. Therefore, nutrition strategies need to be customized for each type of muscle atrophy. Difficulties are associated with assessing the efficacy of nutrients for preventing sarcopenia due to uncontrolled factors in human studies. We herein (a) summarize nutritional epidemiology evidence related to sarcopenia from recent systematic reviews, (b) review nutrient supplementation for attenuating sarcopenia through dietary control, and (c) provide evidence for the efficacy of nutrient supplementation for treating disuse muscle atrophy under dietary control. Epidemiological studies have indicated that diets with a sufficient intake of beneficial foods are useful for preventing sarcopenia. Supplementation with vitamin D and leucine-enriched whey protein have been suggested to help attenuate sarcopenia in geriatric patients, particularly those who are unable to exercise. Further studies are needed to clarify the effects of protein and amino acid supplementation on muscle mass and strength. High-quality studies with controlled diets and physical activities are required to clarify the effects of nutritional interventions on both types of muscle atrophy.

Keywords: diet quality, muscle atrophy, disuse, sarcopenia, epidemiology

1. Introduction

Muscle mass and strength have been linked to overall health and mortality [1, 2], and improvements in skeletal muscle properties and the prevention of muscle wasting with disuse/atrophy are essential for all individuals, particularly inactive older adults [3]. Sarcopenia is characterized by the loss of skeletal muscle mass and physical function (muscle strength or physical performance) with advancing age [4–6]. It is associated with physical disability, poor quality of life, and increased mortality in older adults [5]. Although the loss of muscle mass and physical function is associated with aging, rates of decline vary across the population [7]. Therefore, modifiable behavioral factors, such as diet, may influence the development of sarcopenia. Since a poor diet and nutritional status are common among the elderly [8–10], improvements in these factors may contribute to the prevention and treatment of sarcopenia, thereby promoting better health in later life for this population [11].

The term *diet quality* describes how well an individual's diet conforms to dietary recommendations using a principal component or factor analysis [12, 13]. In older adults, a higher quality diet leads to several positive health outcomes, including a reduced risk of common age-related diseases and greater longevity. For example, a high quality diet is associated with a significantly reduced risk of all-cause mortality, cardiovascular disease, cancer, type 2 diabetes, and neurodegenerative disease, as well as reduced mortality in cancer survivors [14–17].

While there is growing evidence linking healthier diets with greater muscle strength and better physical performance outcomes in older adults, limited information is currently available on how diet quality influences sarcopenia in older adults [11, 18]. A recent systematic review concluded that the number of longitudinal studies was too small to reach concrete conclusions; however, there is growing evidence for the benefits of adhering to a Mediterranean diet [19–21]. The next section summarizes current epidemiological evidence for the relationship between diet quality and sarcopenia in older adults.

2. Nutritional approaches for attenuating muscle atrophy

2.1 Nutritional epidemiology evidence related to sarcopenia

The world's population is getting older [22]. Based on a 2017 report, the number of adults aged 60 years and older will increase worldwide, from 962 million (or one in eight individuals) in 2017 to 2.1 billion (one in five) by the middle of the 21st century [23]. Several environmental and lifestyle factors may modify the aging process [24], including physical activity [25, 26] and diet [27–29].

A large number of observational and intervention studies have used a single-nutrient approach to investigate the relationship between diet and muscle health in aging. However, difficulties are associated with isolating the influence of one dietary component on health outcomes from other components as well as obtaining a clearer understanding of how dietary components interact within a whole diet to affect health outcomes. Previous studies using a whole-diet approach were conducted to clarify the role diet quality plays in muscle health with aging [30–33].

Two main methods of defining diet quality—*a priori* (hypothesis-driven) and *a posteriori* (data driven)—have been used to investigate the relationships between diet quality and muscle health in epidemiological studies on muscle aging. The *a priori* method defines diet quality as adherence to predefined dietary scores or indices based on current knowledge on what constitutes a healthy diet for a particular health condition (e.g., cardiovascular disease or diabetes). In this method, higher scores reflect the greater consumption of beneficial foods (e.g., fruits, vegetables, lean meat, fish, nuts, and low-fat foods) and lower consumption of nutrient-poor foods (e.g., sweets, processed meat, refined grains, and trans-fats) [34–36]. In contrast, the *a posteriori* method is exploratory, using all available dietary data to define diet quality. This method may be used to describe a population's normal diet, which may or may not be related to particular health outcomes. In this method, multivariate statistical tools (e.g., a factor principal component analysis [PCA] and cluster analysis) may be used to assess diet quality. While these two tools follow markedly different procedures, they may be used in tandem to improve the interpretability of the data obtained from each method [37].

We reviewed nutritional epidemiology studies on the role of diet quality in muscle health and function in older adults (**Table 1**). Only eight studies reported a relationship between diet quality (i.e., the amount of nutrients consumed and/or the uptake of specific nutrients from foods) and sarcopenia components [38–45]. Five of these studies were cross-sectional, while three were longitudinal. Study sample sizes ranged between 156 and 2983 participants. The majority of studies

Reference	Population	Study design	Diet quality (DQ)	Physical function
Robinson et al. (2008) [38]	n = 2983 community-dwelling men (n = 1569) and women (n = 1414), 65.7 ± 2.9 years (men) 66.6 ± 2.7 years (women)	Cross-sectional	Administered FFQ based on EPIC Questionnaire 18, pertaining to the 3-month period preceding the interview.	Men and women with high prudent diet scores had stronger grip strengths.
Martin et al. (2011) [39]	n = 628 community-dwelling men (n = 348) and women (n = 280), 67.8 ± 2.5 years (men) 68.1 ± 2.5 years (women)	Cross-sectional	Administered FFQ pertaining to the 3-month period preceding the interview Data-driven: PCA. A "prudent" dietary pattern was identified.	In women, a higher prudent diet score was associated with a shorter 3-m walk time, shorter chair-rise time, and better balance.
Bollwein et al. (2013) [40]	n = 192 community-dwelling men and women, 83 ± 4 years	Cross-sectional	Administered FFQ of the German part of the EPIC study. Dietary indices: Adherence to a Mediterranean dietary pattern was assessed using the MED score	A relationship was observed between a high MED score and lower risk of a slow walking speed.
Rahi et al. (2014) [41]	n = 156 community-dwelling men (n = 94) and women (n = 62) with type 2 diabetes, 74.3 ± 4.2 years (men) 75.0 ± 4.2 years (women)	Longitudinal	Three non-consecutive 24-h dietary recalls. Dietary indices; DQ was evaluated at recruitment using the Canadian Healthy Eating Index (C-HEI).	Good DQ was combined with stable or increased physical activity, and muscle strength losses were minimal in diabetic older males.
Hashemi et al. (2015) [42]	n = 300 elderly men and women (55 years old and older), 66.8 ± 7.2 years	Cross-sectional	Three major dietary patterns (DP) were identified. a. DP1, Mediterranean b. DP2, Western c. DP3, Mixed	Participants in the highest tertile of DP1 had a lower odds ratio for sarcopenia than those in the lowest tertile.

Reference	Population	Study design	Diet quality (DQ)	Physical function
Granic et al. (2016) [43]	n = 791 men (n = 302) and women (n = 489), living either at home or in a care facility, 68.7 ± 0.3 years	Longitudinal	Three dietary patterns were identified. a. DP1, High Red Meat b. DP2, Low Meat c. DP3, High Butter	Men in DP1 had worse overall hand grip strength and slower timed up and go than those in DP2. Women in DP3 had slower timed up and go than those in DP2. Men in DP3 had a steeper decline in hand grip strength than those in DP1.
Perälä et al. (2016) [44]	n = 1072 participants, elderly men and women, 61.3 ± 0.2 years	Longitudinal	Dietary indices: The *a priori*-defined Nordic diet score (NDS) was calculated as a measure of a healthy Nordic diet.	Women in the highest fourth of the NDS had a 5-point higher Senior Fitness Test score on average than those in the lowest fourth.
Suthutvoravut et al. (2020) [45]	n = 1241 community-dwelling men (n = 646) and women (n = 595), 74.6 ± 5.5 years	Cross-sectional	Three dietary patterns were identified. a. DP1, high factor loading for fish, tofu, vegetables, and fruits b DP2, high factor loading for fish, rice, and miso soup c. DP3, high factor loading for noodles	Men with the lowest tertile of the DP1 score had a higher likelihood of being sarcopenic. Women with the lowest tertile of the DP2 score had a moderate likelihood of being sarcopenic.

Table 1.
Summary of diet quality and physical function in older adults.

were conducted in a community setting (e.g., a nursing home or care facility) and with participants whose mean age ranged between 65 and 75 years.

Robinson et al. examined the relationship between diet quality and grip strength in older men and women [38]. A food frequency questionnaire (FFQ) based on the European Prospective Investigation of Cancer (EPIC) questionnaire was used to assess the subject's diet. They used the FFQ that contained 129 foods and food groups and assessed the average frequency of the consumption of the listed foods over the three months preceding the interview. Nutrient intake for each food item consumed was calculated by multiplying the nutrient content listed in the UK national food composition database or manufacturer composition data. The 129 foods listed in the FFQ were divided into 54 food groups based on similarity and nutrient compositions. The PCA of the reported weekly consumption frequencies of these food groups was used to define diet patterns. The *prudent* diet was characterized by the high consumption of fruit, vegetables, whole grain cereals, and fatty fish and by the low consumption of white bread, chips, sugar, and full-fat dairy products. Participants with higher prudent diet scores had stronger grip strengths. In addition, an increase was observed in grip strength of 0.43 kg in men and 0.48 kg in women for each additional fatty fish portion consumed per week.

Martin et al. investigated the relationship between diet and physical performance (measured using a short physical performance battery) in a group of men and women living in West Hertfordshire who were part of the Hertfordshire Cohort Study [39]. Nutrient intake for each food item consumed was calculated by multiplying the nutrient content listed in the UK national food composition database or manufacturer composition data. Higher prudent diet scores were related to shorter three-meter walk times and shorter chair-rise times in women. Additionally, inverse relationships were observed between physical function and the consumption of vegetables, whitefish, shellfish, and oily fish. These findings indicate that a relationship exists between diet variations in community-dwelling older women and differences in physical performance. However, further studies are needed to clarify the role of diet variations in physical performance, particularly in men.

Bollwein et al. examined whether the risk of frailty was significantly reduced in participants who scored in the highest quartile for Mediterranean diet consumption (MED) [40]. This scoring is an alternative to the MED scoring used by Fung et al. [46], who adapted the original MED score used by Trichopoulou et al. [47] for a non-Mediterranean population. They combined FFQ foods into nine nutritional characteristics, classified as either beneficial (vegetables, legumes, fruits, unrefined cereals, nuts, fish, high monounsaturated fatty acid [MUFA]/saturated fatty acid [SFA] foods, and moderate alcohol consumption) or detrimental (red and processed meats) to health, to calculate the score, and found an inverse correlation between a low walking speed and MED scores. Moreover, a relationship was observed between high diet quality (high MED score) and slow walking speed in older men and women.

Rahi et al. investigated the relationship between diet quality and muscle strength changes over three years in diabetic participants aged 67 to 84 years [41]. Diet quality was evaluated at recruitment using the validated Diet Quality Index-Canada and nine-item Canadian Healthy Eating Index (C-HEI) [48]. Diet quality was calculated using data from the mean of three, non-consecutive, 24-hour dietary recalls collected using the five-step, multiple-pass method [49]. The C-HEI has nine components. The first four components evaluate the extent to which respondents meet age and gender-based recommendations for the number of portions eaten from each of the four groups of Canada's Food Guide (grain products, vegetables and fruits, milk and alternatives, and meat and alternatives). The next four items reflect Canadian nutritional recommendations for moderation: the daily percentage of energy from total fat, the daily percentage of energy from saturated fat, cholesterol intake (mg), and sodium intake (mg). The final component, dietary variety (adapted from the Dietary Diversity Score), was assessed as the daily consumption of at least one food from each food group. The findings obtained indicated that the combination of a high diet quality with stable or increased physical activity minimized muscle strength losses in diabetic older males over the three-year follow-up period.

Hashemi et al. investigated whether adherence to a particular dietary pattern was associated with sarcopenia among elderly adults in a district of Teheran, Iran [42]. A semiquantitative FFQ was used to survey the dietary intake of 300 randomly-selected older men and women. They evaluated the dietary patterns of participants using PCA. Participants in the highest tertile of the Mediterranean dietary pattern had a lower odds ratio for developing sarcopenia than those in the lowest tertile. In contrast, adherence to the Western dietary pattern (characterized by the high consumption of sugar, soy, and fast foods) and mixed dietary pattern (characterized by the high consumption of animal proteins, potatoes, and refined grains) did not affect the odds of developing sarcopenia. These findings suggested that Mediterranean diet adherence was associated with a lower odds ratio for the development of sarcopenia among older Iranian individuals.

Granic et al. examined the relationship between previously established dietary patterns and declines in muscle strength and physical performance among older adults [43]. In total, 791 participants were followed for five years to detect changes in grip strength and timed up and go test (TUG) scores. Trained research nurses kept a detailed record of food intake on the previous day for each participant on two different days of the week, at least one week apart. Each food had a unique food code (>2000), and intakes were entered into a Microsoft Access-based dietary data system, then further grouped into 118 food groups based on McCance and Widdowson's composition of foods [50, 51]. These 118 groups were combined into 33 food groups based on food/nutrient composition similarities and then classified as either absent or present in each participant's food intake. Participants were divided into three groups: dietary pattern 1 (DP1; high red meat); dietary pattern 2 (DP2; low meat); and dietary pattern 3 (DP3; high butter). The findings obtained showed that men in DP1 had worse overall grip strength, whereas those in DP3 had steeper grip strength declines than those in DP2. Additionally, TUG scores were significantly longer for men in DP1 and women in DP3 than those in DP2. Therefore, diets high in red meats, potatoes, gravy, and butter appear to adversely affect muscle strength and physical performance in later life.

Perälä et al. researched whether the consumption of a healthy Nordic diet for 10 years was associated with improved physical performance measures [44]. After the diets of 1072 participants (mean age 67 years) had been examined using a validated 128-item FFQ, the *a priori* Nordic diet score was calculated. The diet items checked included Nordic fruits and berries, vegetables, cereals, low-fat milk, fish, red and processed meat, alcohol, polyunsaturated omega-3 fatty acids (PUFA)/SFA and trans-fatty acids ratios, and total fat. Since participants had a mean age of 71 years, their physical performance was measured using the Senior Fitness Test (SFT), and an overall SFT score was calculated. The findings obtained revealed that women with the highest diet scores had 17% better in that of walk, 16% better in that of arm curl, and 20% better in that of chair-stand than women with the lowest diet scores. These findings indicated that women who consumed a healthy Nordic diet had better physical performance (i.e., better aerobic endurance and upper and lower body strength) 10 years later.

Suthutvoravut et al. investigated the relationship between dietary patterns and sarcopenia in a sample of older community-dwelling Japanese adults [45]. The sample included 1241 older adults aged 65 years and older who were not eligible for long-term care. Dietary intake by participants was assessed using the brief self-administered diet history questionnaire. Dietary patterns were identified using both PCA and Japanese diet scores (soybeans and soybean products, fish, vegetables, pickles, mushrooms, seaweeds, and fruits). Participants were classified into three groups: dietary pattern 1 (DP1; high factor loading for the consumption of fish, tofu, vegetables, and fruits found in typical Japanese side dishes); dietary pattern 2 (DP2; high factor loading for fish, rice, and miso soup found in typical Japanese main dishes); and dietary pattern 3 (DP3; high factor loading for noodles). The findings obtained showed that men with the lowest tertile DP1 score had a higher likelihood of being sarcopenic, while women with the lowest tertile DP2 score had a moderate likelihood of being sarcopenic. Additionally, low adherence to Japanese dietary patterns increased with the prevalence of sarcopenia in both genders.

Many traditional regional diets may have similar benefits to those described here. We then focused on diets with demonstrated effects on muscle mass, reported by randomized controlled trials that investigated diet quality using precise parameters. For example, the traditional diets of Korea and China may be beneficial for preventing sarcopenia in the populations of these countries. Healthier diets are higher in plant-based food and lower in animal-based foods than Western diets. Further epidemiological studies are needed to investigate the relationship between healthy diets and development of sarcopenia throughout the world, particularly in developing countries.

2.2 Nutrient supplementation for attenuating sarcopenia

Skeletal muscle is a dynamic, plastic tissue with a mass that is regulated by the balance between the rates of muscle protein synthesis and breakdown. Adopting an appropriate dietary strategy is crucial for facilitating an anabolic response that may prevent muscle wasting with atrophy by suppressing the breakdown of muscle protein. An adequate nutrient intake is essential for maintaining and improving muscle properties. Many supplements have been proposed to enhance muscle mass and strength. More than 50% of adults in the United States take some form of dietary supplement to improve their health or well-being [52]. However, there is no scientific evidence for the effectiveness of many of these supplements. In some cases, their use has been linked to serious adverse side effects. This section summarizes the effects of several popular nutritional supplements when administered under strict dietary controls, either alone or in combination with other supplements.

In a randomized study, Tieland et al. examined the effects of 24 weeks of dietary protein supplementation on muscle mass, strength, and physical performance in a sample of frail older adults [53]. This study included 65 frail participants who were allocated to either the daily protein supplementation group (15 g protein consumed at breakfast and lunch) or placebo group (0 g protein at breakfast and lunch). Participants recorded their food intake for three days with the help of trained dieticians. Dietary intake data were coded (the type of food, time of intake, and amount), and energy and macronutrient intakes were calculated using a food-calculation system from the 2006 Dutch food composition database. The findings obtained indicated that skeletal muscle mass did not change in either the protein or placebo group following the 24-week intervention. However, leg extension strength increased more in the protein group than in the placebo group. Furthermore, physical performance significantly improved (from 8.9 to 10.0 points) in the protein group, but not in the placebo group. Therefore, while dietary protein supplementation appeared to improve physical performance in frail older adults, it did not increase their skeletal muscle mass.

Kim et al. investigated whether protein-energy supplementation prevented functional declines in frail older adults with a low socioeconomic status [54]. In that study, 84 frail elderly participants were assigned to either an intervention or control group. The intervention group received two 200-ml cans of commercial liquid formula (an additional 400 kcal of energy, 25 g of protein, 9.4 g of essential amino acids, and 400 ml of water) each day for 12 weeks, while the control group did not. Dietary intake was assessed in three, non-consecutive 24-hour recall sessions (one face-to-face and two by telephone; weekday and weekend ratio of 2:1) to show the nutritional status. The same research dietitian coded dietary data, and a nutrient analysis was performed using CAN-Pro 3.0. No significant changes were observed in grip strength in either group; however, physical functioning, usual gait speed, and TUG scores were significantly better in the protein group than in the control group. Therefore, protein-energy supplementation administered to frail older adults with a low socioeconomic status appeared to reduce the progression of functional decline.

Veronese et al. investigated whether 12 weeks of oral magnesium supplementation improved physical performance in healthy older women [55]. In that study, 124 participants were grouped into either a treatment group (300 mg of magnesium/day) or control group (no treatment). A dietary assessment was examined by a modified method including an estimated three-day record and a questionnaire about the frequency that participants generally ate certain foods. They used the data from the previous month as a reference and calculated the macronutrients and micronutrients of usual food intake by a national food composition table. After 12 weeks of supplementation with magnesium, the treatment group had significantly higher total short physical performance battery scores, chair-stand times, and four-minute walking speeds than the control group. These findings indicated that magnesium supplementation prevented or delayed age-related physical performance declines.

Roma et al. examined the effects of PUFA supplementation on the parameters of body composition, muscle strength, and physical performance in the elderly [56]. Fifty participants were randomly assigned to a PUFA-treated group (receiving 1.3 g of PUFA and 10 mg of vitamin E) or control group (receiving 11 mg of vitamin E). Participants were assessed using the mini nutritional assessment (composed of six questions related to decreased food intake in the three months before the test) and a 12-question survey on diet (number of meals consumed and consumption of protein, fruits, vegetables, and liquids) and the ability to feed themselves. No significant between-group differences were observed in muscle mass, grip strength, or TUG scores. Therefore, the 12-week PUFA supplementation did not appear to affect the parameters evaluated in elderly individuals with a decreased muscle mass.

Bauer et al. sought to test the hypothesis that a specific oral nutritional supplement may improve selected sarcopenia measures [57]. The active group (n = 184) consumed a vitamin D and leucine-enriched whey protein nutritional supplement twice daily for 13 weeks. The control group (n = 196) consumed an iso-caloric control product twice daily for 13 weeks. A dietary assessment was completed at baseline and week 13 using three-day prospective diet records for two weekdays and one weekend day. Additional energy and protein intakes from both supplements were added to habitual three-day intakes to assess total intake. The active group gained more appendicular muscle mass and performed better in the chair-stand test than the control group. These findings demonstrated that specific nutritional supplementation alone may benefit geriatric patients, particularly those unable to exercise.

Porter et al. investigated whether participants following an enhanced protein regimen have greater functional status improvements and better lean muscle mass preservation than control group participants [58]. In that study, 67 obese older adults were randomly assigned to either a traditional weight loss regimen (control group) or one with a higher protein intake at each meal (protein group). Control group participants were prescribed a 500-kcal deficit diet (15% protein, 30% fat, and 55% carbohydrate), which met the recommended dietary allowance (RDA) for protein intake (0.8 g/kg of body weight). Protein group participants were also prescribed a 500-kcal deficit, but with a macronutrient distribution of 30% protein, 30% fat, and 40% carbohydrate, for a total prescribed protein intake of 1.2 g/kg. Both groups exhibited significant weight loss at the six-month endpoint. However, while both groups had improved muscle function, the Short Physical Performance Battery response was greater in the protein group than in the control group. These findings indicated that functionally limited obese adults undergoing a six-month weight loss intervention that included a meal-based protein enhancement lost similar amounts of weight, but had better functional improvements than the control group.

Only one of the studies used an iso-caloric control supplement to investigate the efficacy of a vitamin D and leucine-enriched whey protein nutritional supplement (not combined with exercise) for attenuating sarcopenia. To produce the most useful data, future studies that investigate whether a simple nutrient supplement contributes to the prevention of sarcopenia will need to use dietary control in a sample of more than 100 elderly participants. Evidence from two *in vivo* studies showed that calorie restriction or fasting may help to prevent reductions in muscle mass or strength [59, 60]. Future human studies need to focus on the effects of the removal of some nutrients from the diet, instead of solely assessing the effects of their addition, in order to obtain more useful data (**Table 2**).

2.3 Nutrient supplementation effects on muscle mass and strength during muscle disuse

A number of conditions, such as recovery from injury or illness or space flight, require prolonged periods of muscle disuse (i.e., unloading) in otherwise healthy individuals, resulting in the progressive loss of skeletal muscle mass that impairs functional strength, reduces the basal metabolic rate, and increases body fat mass. Therefore, prolonged muscle disuse is a significant health concern, particularly in aging populations. While nutrition is an important factor regulating muscle mass, the development of effective nutritional strategies that attenuate muscle loss during periods of muscle disuse warrants further efforts. **Table 3** shows an overview of studies that have assessed the efficacy of nutritional interventions for attenuating muscle disuse atrophy under controlled diet quality.

Paddon-Jones et al. examined whether supplementation with essential amino acids and carbohydrates offset the catabolic response to 28 days of bed rest [61]. Thirteen healthy male participants were randomly assigned to either the experimental or control groups. The control group consumed nutritionally mixed meals three times a day. The experimental group consumed the same meals plus 30 g of carbohydrate and 16.5 g of essential amino acids three times a day. The Harris-Benedict equation was used to estimate daily caloric requirements, according to the following formula: daily energy requirement (kcal) = $[66 + (13.7 \times \text{kg}) + (5 \times \text{cm}) - (6.8 \times \text{yr})] \times 1.3$ (activity factor for bed rest). Participants were placed on a three-day rotating diet with daily nutrient intake evenly distributed between the three meals. The findings obtained revealed that the experimental group maintained lean leg mass throughout bed rest (+0.2 kg), whereas the control group lost mass (−0.4 kg). In addition, strength loss was more pronounced in the control group (exp group, −8.8 kg; cont group, −17.8 kg). Therefore, supplementation with essential amino acids and carbohydrates during bed rest appeared to provide an anabolic stimulus that ameliorated lean muscle mass loss in an otherwise catabolic environment. However, it currently remains unclear whether additional energy intake contributed to these findings.

Reference	Population	Diets	Nutritional intervention	Changes in muscle mass and strength	Physical function
Tieland et al. (2012) [53]	n = 65 frail elderly subjects	1935 kcal/day, 49% CHO, 35% fat, 16% protein (1.0 g protein/kg/day)	15 g protein × twice/day for 24 wks vs. non protein × twice/day for 24 wks	No change in muscle mass in both groups Significant increase in muscle strength in both groups.	Significantly improved physical performance in the protein group, but not in the control group
Kim et al. (2013) [54]	n = 84 frail elderly subjects, 78.7 ± 5.8 years	896 kcal/day (0.7 g protein/kg/day)	400 kcal (25 g protein, 9.4 g amino acids, 56 g carbohydrate, 9 g lipids, micronutrients)/day for 12 wks vs. non-supplemental control	No change in hand grip strength in both groups	Significantly improved physical functioning, usual gait speed, and timed up-and-go in the protein group, but not in the control group
Veronese et al. (2014) [55]	n = 124 elderly women, 71.5 ± 5.2 years	1490 kcal/day (383 mg magnesium/day)	300 mg magnesium/day for 12 wks vs. non-supplemental control	No change in hand grip strength in both groups	Significantly improved Short Physical Performance Battery score, chair-stand times, and 4-m walking speeds in the magnesium group, but not in the control group
Roma et al. (2015) [56]	n = 50 elderly subjects, 74.9 ± 7.9 years	Mini Nutritional Assessment score 24.1 ± 3.1 points	1.3 g omega-3 fatty acids/day for 12 wks vs. non-supplemental control	No differences in muscle mass or hand grip in both groups	No differences in timed up-and-go in both groups
Bauer et al. (2015) [57]	n = 380 sarcopenic primarily independent-living older adults, 77.7 ± 6.9 years	1612 kcal/day (1.0 g protein/kg/day)	800 IU vitamin D + 20 g whey protein +3 g leucine twice/day for 13 wks (active) vs. iso-caloric control	Significantly higher appendicular muscle mass in the active group than in the control	Significantly improved chair-stand test in the active group from those in the control group
Porter et al. (2016) [58]	n = 67 obese older adults with a Short Physical Performance Battery (SPPB) score of 4–10, 68.2 ± 5.6 years	1458 kcal/day, 55% CHO, 30% fat, 15% protein (0.8 g protein/kg/day)	30 g protein × 3 times/day for 6 mo vs. non-supplemental control	No differences in lean body mass or hand grip in both groups	Significantly improved total and chair-stand scores in the protein group from those in the control group

Table 2.
Summary of effects of nutrient supplementation for attenuating sarcopenia.

Reference	Population	Diets	Nutritional intervention	Changes in muscle mass	Loss of strength
Paddon-Jones et al. (2004) [61]	n=13 young males, Bed rest (28 days)	2487 kcal/day, 59% CHO, 27% fat, 14% protein (1.0 g protein/kg/day)	30 g carbohydrate +16.5 g EAA vs. non-supplemental control	Leg lean mass maintained in EAA, but lost in the control	Significantly lower decrease of 11% in EAA than in the control (23% down)
Trappe et al. (2007) [62]	n = 24 young women, Bed rest (60 days)	1557 kcal/day, 56% CHO, 30% fat, 14% protein (1.0 g protein/kg/day)	1.0 (low), 1.6 (high) g/kg body mass/day dietary protein	Greater loss of quadriceps femoris muscle volume in high protein (24%) vs. low protein (21%)	19 ~ 33% decreased for the supine square in both groups
Ferrando et al. (2010) [63]	n = 21 elderly, Bed rest (10 days)	(0.8 g protein/kg/day)	15 g × 3 times/day EAA vs. the non-supplemental control	~6% decrease in leg lean mass in both groups	Better functional capacity in EAA than in control
Deutz et al. (2013) [64]	n=19 older adults, Bed rest (10 days)	1900 kcal/day (0.8 g protein/kg/day)	3 g/day HMB vs. non-supplemental control, 5 days prior to bed rest	Leg lean mass maintained in HMB, but lost in control	No difference in the knee extensor in both groups
Dirks et al. (2014) [65]	n = 23 elderly men, One-legged immobilization (5 days)	2150 kcal/day, 51% CHO, 33% fat, 16% protein (1.1 g protein/kg/day)	9.3 g carbohydrate +20.7 g protein +3.0 g fat twice/day vs. the non-supplemental control	1.5 ~ 2.0% decrease in quadriceps CSA in both groups	8.3 ~ 9.3% decrease in maximal muscle strength in both groups
English et al. (2016) [66]	n=19 middle-aged adults, Bed rest (10 days)	2111 kcal/day, 55% CHO, 30% fat, 15% protein (1.1 g protein/kg/day)	4.5 g × 3 times/day leucine vs. 4.5 g × 3 times/day alanine	5.3 ~ 6.9% reduction in leg lean mass in both groups	Significantly smaller decrease of 7% in leucine than in alanine (15% down) with knee extensor peak torque
Holloway et al. (2019) [67]	n = 20 young men, One-legged immobilization (8 days)	2521 kcal/day (1.0 g protein/kg/day)	23.7 g × 3 times/day amino acids vs. 23.7 g × 3 times/day maltodextrin (iso-caloric control)	Significantly lower decrease of 3.1% in amino acids than in control (2.4% down) in quadriceps muscle volume	No difference in both groups in peak leg isometric torque

Table 3.
Summary of effects of nutritional interventions on muscle mass and strength during a period of muscle disuse.

Trappe et al. investigated whether nutritional countermeasures, consisting of additional protein and free leucine, reduced volume and strength losses in lower-limb skeletal muscle during 60 days of simulated weightlessness [62]. Young women were assigned to either the bed rest group (control) or the bedrest plus a nutrition countermeasure group (intervention). Dietary staff prepared all meals for both groups. These meals contained controlled amounts of total energy and macronutrients. The findings obtained demonstrated that thigh muscle (quadriceps femoris) volume decreased in both the control (−21%) and intervention groups (−24%). Moreover, both groups exhibited similar large decreases in isometric and dynamic (centric force, eccentric force, power, and work) muscle strength for the supine squat (−19% to −33%). Therefore, the nutrition countermeasure did not appear to be effective at offsetting volume or strength losses in lower-limb muscles. Furthermore, exercise countermeasures may need to be modified to protect the calf muscles of participants.

Ferrando et al. examined the effects of an increasing protein intake (through essential amino acid supplementation) in older individuals subjected to 10 days of bed rest on their lean body mass and muscle function [63]. Participants received either a placebo or 15 g of essential amino acids, three times a day throughout 10 days of bed rest. The placebo was a non-caloric diet soda. During diet stabilization and bed rest, subjects consumed a lacto-ovo vegetarian diet providing the RDA for protein (0.8 g/kg of protein per day). The diet consisted of a three-day rotation based on the Harris-Benedict equation designed to maintain body weight throughout the study. An activity factor of 1.3 was used to estimate daily energy requirements during bed rest. The findings obtained indicated that essential amino acids did not affect the maintenance of total or leg lean muscle mass. However, stair ascent power and standing plantar flexion appeared to be maintained with essential amino acid supplementation. Therefore, increasing protein intake above the RDA may preserve muscle function in elderly individuals during compulsory inactivity. However, this protocol may need to be operated under iso-caloric nutritional interventions.

Deutz et al. attempted to clarify whether beta-hydroxy-beta-methylbutyrate (HMB), a leucine metabolite, was capable of attenuating muscle decline in healthy older adults during 10 days of bed rest [64]. Healthy older adults were randomly assigned to a control group or HMB group (Ca-HMB, 1.5 g twice daily, total 3 g/day). Participants were fed a metabolically controlled diet for diet stabilization, providing the RDA for protein intake (0.8 g protein/kg of body weight per day). Total calorie needs were estimated using the Harris–Benedict equation for resting energy expenditure. An activity factor of 1.35 was used to estimate daily energy requirements during bedrest. The study protocol significantly decreased total lean body mass in the control group. In contrast, the treatment with HMB prevented these declines in all but one participant in the HMB group. However, differences in functional parameters were not observed between the two groups. These findings indicated that HMB supplementation contributed to the preservation of muscle mass during 10 days of bed rest. Further studies using larger samples and iso-calorie conditions for nutritional interventions are needed to clarify the preventative effects of HMB on the acute decline in muscle mass.

Dirks et al. investigated whether protein supplementation preserved muscle mass during a short period of limb immobilization [65]. Healthy older men were subjected to five days of one-legged knee immobilization using a full-leg cast with or without the twice-daily administration of a dietary protein supplement (20.7 g of protein, 9.3 g of carbohydrate, and 3.0 g of fat). Weighted dietary intake records were completed by participants for the five-day immobilization period and on a separate consecutive five-day occasion, either before or after the immobilization period. Immobilization decreased the quadricep cross-sectional area by 1.5 and 2.0%, and muscle strength by 8.3 and 9.3% in the control and protein groups, respectively. These findings indicated that dietary protein supplementation (~20 g twice daily) did not attenuate muscle loss during short-term muscle disuse in healthy older men.

English et al. investigated whether leucine protects skeletal muscle health during bed rest [66]. In that study, a group of middle-aged adults were randomly assigned to a leucine group (4.5 g leucine × 3 times/day) or alanine group (4.5 g alanine × 3 times/day). Participants were fed controlled isoenergetic diets with protein intake evenly distributed across three daily meals for diet stabilization. Daily energy requirements were estimated using the Harris-Benedict equation. An activity factor of 1.3 was used during the bedrest period. The findings obtained indicated that while leg lean mass significantly decreased in both groups, leucine supplementation protected knee extensor peak torque more than in the alanine group. Therefore, leucine supplementation appeared to protect muscle health during relatively brief periods of physical inactivity. The parameters of this study allowed for the strict control of diets and nutritional supplementation under energy-matched conditions; therefore, leucine supplementation may help protect muscle function in muscle disuse atrophy.

Holloway et al. examined the safety, tolerability, and atrophy-mitigating effects of a novel amino acid composition (containing essential amino acids and arginine, glutamine, and N-acetylcysteine) during single-limb immobilization [67]. Twenty young men were randomly assigned to receive either the amino acid mixture or an energy-matched, non-amino acid-containing placebo three times a day (two hours after breakfast, lunch, and dinner) for consecutive days. Diets were designed to achieve an energy balance, and meal plans included protein derived from dairy sources held constant at 1.0 g/kg/day. The reduction in the cross-sectional area of the quadriceps muscle was significantly lower in the amino acid group than in the placebo group. However, immobilization resulted in similar relative declines in peak torque in both groups. These findings indicated that the daily consumption of an amino acid mixture (three times a day for 28 days) attenuated muscle atrophy, and are bolstered by the use of well-controlled diets and nutritional supplementation with energy-matched conditions.

A number of human studies examined the effects of nutritional interventions on muscle mass and strength during a period of muscle disuse [68, 69]. Due to insufficient dietary control, these studies were not sufficient to clarify the nutritional value of such supplements. Despite these deficits, many studies have reported the efficacy of nutritional supplementation for preventing the loss of muscle mass and strength during a period of muscle disuse *in vivo* [70–72]. Future studies are needed to clarify whether these candidates for nutritional supplementation preserve muscle mass during disuse. These studies must control diet quality and modify the nutritional intervention period (e.g., expand the duration of nutritional administration before muscle disuse) to provide sufficient evidence.

3. Conclusions

In this chapter, we (a) summarized nutritional epidemiology evidence related to sarcopenia from recent systematic reviews; (b) reviewed the role nutrient supplementation plays in attenuating sarcopenia through dietary control; (c) provided evidence for the efficacy of nutrient supplementation for treating disuse muscle atrophy under controlled diet quality conditions.

a. Dietary patterns of adequate quality for older adults (i.e., ensuring a sufficient intake of beneficial foods, such as fruits, vegetables, whole grain products, fish, nuts, and low-fat foods) are useful for preventing sarcopenia. While the Mediterranean diet has been touted as a healthy diet, other diets (healthy Nordic or traditional Asian diets) also help prevent sarcopenia in older adults.

b. Vitamin D and leucine-enriched whey protein supplement may be useful for attenuating sarcopenia in geriatric patients, particularly in those unable to exercise.

c. Further studies are needed to clarify the effects of protein and amino acid supplementation on muscle mass and strength.

Based on the strong evidence linking nutrition to muscle mass and function, nutrition plays a crucial role in both the prevention and management of sarcopenia. Further high quality studies, particularly those using large sample sizes, controlled diet quality, and iso-caloric placebo supplementation, are needed to provide a clear understanding of the dose and duration effects of nutrients on muscle atrophy.

Conflict of interest

The authors declare no conflict of interest.

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