ESPEN endorsed recommendation

Protein intake and exercise for optimal muscle function with aging: Recommendations from the ESPEN Expert Group

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SUMMARY

The aging process is associated with gradual and progressive loss of muscle mass along with lowered strength and physical endurance. This condition, sarcopenia, has been widely observed with aging in sedentary adults. Regular aerobic and resistance exercise programs have been shown to counteract most aspects of sarcopenia. In addition, good nutrition, especially adequate protein and energy intake, can help limit and treat age-related declines in muscle mass, strength, and functional abilities. Protein nutrition in combination with exercise is considered optimal for maintaining muscle function.

With the goal of providing recommendations for health care professionals to help older adults sustain muscle strength and function into older age, the European Society for Clinical Nutrition and Metabolism (ESPEN) hosted a Workshop on Protein Requirements in the Elderly, held in Dubrovnik on November 24 and 25, 2013. Based on the evidence presented and discussed, the following recommendations are made (a) for healthy older people, the diet should provide at least 1.0−1.2 g protein/kg body weight/day, (b) for older people who are malnourished or at risk of malnutrition because they have acute or chronic illness, the diet should provide 1.2−1.5 g protein/kg body weight/day, with even higher intake for individuals with severe illness or injury, and (c) daily physical activity or exercise (resistance training, aerobic exercise) should be undertaken by all older people, for as long as possible.

1. New insights in aging and declining muscle function

The natural aging process is associated with gradual and progressive loss of muscle mass, muscle strength, and endurance, i.e., a condition called sarcopenia [1]. Such changes have been considered

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Table 1
Practical guidance for optimal dietary protein intake and exercise for older adults above 65 years.

Recommendations
For healthy older adults, we recommend a diet that includes at least 1.0–1.2 g protein/kg body weight/day.
For certain older adults who have acute or chronic illnesses, 1.2–1.5 g protein/kg body weight/day may be indicated, with even higher intake for individuals with severe illness or injury.
We recommend daily physical activity for all older adults, as long as activity is possible. We also suggest resistance training, when possible, as part of an overall fitness regimen.

inevitable consequences of aging. This concept has recently been challenged, as new study results suggest that mitochondrial dysfunction, reduced insulin sensitivity, and reduced physical endurance are related, at least in part, to physical inactivity and to increases in adiposity rather than to aging alone [2]. The study results show that regular exercise can help normalize some aspects of age-related mitochondrial dysfunction, in turn improving muscle function [2]. Good nutrition, especially adequate protein intake, also helps limit and treat age-related declines in muscle mass, strength, and functional abilities. Nutrition in combination with exercise is considered optimal for maintaining muscle function [3].

With the goal of discussing recent research findings in order to develop recommendations to help adults sustain muscle strength and function into older age, the European Society for Clinical Nutrition and Metabolism (ESPEN) hosted a Workshop with the ESPEN Expert Group, *Protein Requirements in the Elderly*, held in Dubrovnik, Croatia on November 24 and 25, 2013. This article reflects practical guidance resulting from the presentations and discussions during the workshop. The aim of the workshop was to provide practical guidance for health professionals who care for

older adults, i.e., to recommend optimal protein intake and to advise age- and condition-appropriate exercise.

We offer practical guidance for maintaining muscle health and physical function with aging (Table 1). We provide our rationale and the supporting evidence for these recommendations in the sections following.

2. Changing protein intake and protein needs in older adults

Compared to younger adults, older adults usually eat less, including less protein [4,5]. In Europe, up to 10% of community-dwelling older adults and 35% of those in institutional care fail to eat enough food to meet the estimated average requirement (EAR) for daily protein intake (0.7 g/kg body weight/day), a minimum intake level to maintain muscle integrity in adults of all ages [6]. At the same time, many older adults need more dietary protein than do younger adults [7,8]. An imbalance between protein supply and protein need can result in loss of skeletal muscle mass because of a chronic disruption in the balance between muscle protein synthesis and degradation [9]. As a result, older adults may lose muscle mass and strength and eventually experience physical disability [10,11].

In recent years, an ever-increasing body of evidence builds the case for increasing protein intake recommendations for older adults (Table 2).

3. Dietary protein intake

There are many reasons older adults fail to consume enough protein to meet needs—genetic predisposition to low appetite, physiological changes and medical conditions that lead to age- and disease-associated anorexia, physical and mental disabilities that limit shopping and food preparation, and food insecurity due to financial and social limitations (Fig. 1) [5].

Table 2
Recent studies on protein intake and exercise in older adults.

| Study report	Study design and key findings
Gray-Donald et al. 2014 [8]	• Prospective, nested case-control study of healthy, community-dwelling adults older than 70 y • Odds ratio of harmful weight loss in participants with low protein intakes (<0.8 g/kg BW/day) was 2.56 compared with participants with very high protein intakes (≥1.2 g/kg/day) or 2.15 in participants with moderate protein intakes (0.8–1.0 g/kg BW/day).
Tang et al. 2014 [89]	• Assessment of protein requirement in octogenarian women using an indicator amino acid oxidation technique ($n = 6$; tested 3-times per person) • Based on this method, the mean protein requirement (95% CI) was 0.85 g/kg/day, a requirement 29% higher than the current Estimated Average Requirement (EAR) for adults. The corresponding adequate protein allowance of 1.15 g/kg/day is 44% higher than the current Recommended Dietary Allowance (RDA).
Beasley et al. 2013 [11]	• Longitudinal observational study of a subset of subjects in the Women's Health Initiative population ($n = 5346$; women 50–79 years at baseline; followed 6 years) • Higher protein intake is associated with better physical function and performance and with slower rates of decline in postmenopausal women.
Breen et al. 2013 [32]	• Pre-post study experimental design with measures of protein synthesis in healthy older adults ($n = 10$, age 79 ± 1 yrs) before and after 14-day reduction of step count • Step reduction leads to reduced muscle mass that is associated with underlying lowering of the response of muscle protein synthesis to protein ingestion.
Bartali et al. 2012 [90]	• Longitudinal observational study to examine whether protein intake is associated with change in muscle strength in older adults; subjects from the InChianti population ($n = 598$) who were followed for 3 years and had measures of inflammatory markers C-reactive protein, interleukin-6, and tumor necrosis factor-α • Lower protein intake was associated with a decline in muscle strength in older adults with high levels of inflammatory markers.
Kim et al. 2012 [60]	• Randomized controlled trial to evaluate the effectiveness of exercise and amino acid supplementation (high-leucine AAS) in enhancing muscle mass and strength in community-dwelling elderly sarcopenic women ($n = 155$, age ≥ 75 years) • In sarcopenic women, exercise and AAS together enhance muscle strength, as well as combined variables of muscle mass + walking speed and of muscle mass + strength.
Tieland et al. 2012 [91]	• A randomized, controlled trial with 2 arms in parallel among frail elderly subjects ($n = 62$, age 78 ± 1 year); subjects did resistance exercise twice weekly for 24 weeks and consumed placebo or protein supplements (15 g) twice daily • Prolonged resistance-type exercise training improved strength and physical performance in frail elderly people. Dietary protein supplementation is required to allow muscle mass gain during such exercise training.
Yang et al. 2012 [36]	• Dose-response experimental design with measures of protein synthesis in healthy older adults ($n = 10$, age 79 ± 4yrs) who followed a bout of resistance exercise with ingestion of 0, 10, 20, and 40 g of whey protein. • In contrast to younger adults, in whom post-exercise rates of muscle protein synthesis are maximized with 20 g of protein, exercised muscles of older adults respond to higher protein doses of 20 and 40 g protein.
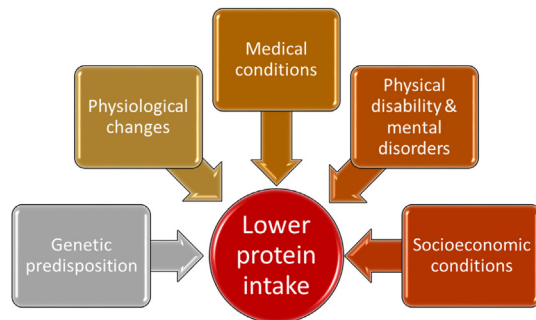
Fig. 1. Protein status: factors leading to lower protein intake in older persons.

4. Dietary protein needs

There are also many reasons older adults have higher protein needs (Fig. 2). Physiologically, older adults may develop resistance to the positive effects of dietary protein on synthesis of protein, a phenomenon that limits muscle maintenance and accretion; this condition is termed *anabolic resistance* [12,13]. Mechanisms underlying anabolic resistance and the resultant need for higher protein intake are: increased splanchnic sequestration of amino acids, decreased postprandial availability of amino acids, lower postprandial perfusion of muscle, decreased muscle uptake of dietary amino acids, reduced anabolic signaling for protein synthesis, and reduced digestive capacity [7,12,14]. Older adults likewise have higher protein needs to offset the elevated metabolism of inflammatory conditions such as heart failure, chronic obstructive pulmonary disease (COPD), or chronic kidney disease (CKD) undergoing dialysis. In healthy older adults and in a variety of disease, protein anabolism is related to net protein intake [15]. Most older adults will therefore benefit from higher protein intake.

Further, prolonged disuse of muscle, as with bed rest for illness or injury, leads to changes in protein synthesis and breakdown, which cause disuse atrophy of muscle. For example, bed rest for more than 10 days leads to a decline in basal and postprandial rates of muscle protein synthesis, especially in older adults [16]. Decreased muscle protein synthesis is the main mechanism for muscle loss, but there is also indirect evidence that an early and transient (1–5 days) increase in basal muscle protein breakdown may contribute to disuse atrophy [16]. While disuse due to acute illness or injury causes muscle atrophy, so too does physical inactivity due to sedentary lifestyle [17].

In spite of many differences in general health status and physiology of old versus young adults, the recommended dietary allowance (RDA) has traditionally been set the same for healthy adults of all ages—0.8 g protein/kg body weight/day [18]. However,
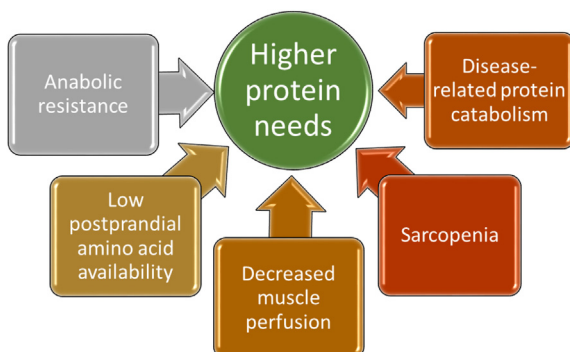
evidence continues to build in favor of increasing this recommendation for optimal protein intake to 1.0–1.2 g/kg body weight/day for adults older than 65 years [5,7,19,20].

Taken together, evidence shows that when usual dietary protein intake does not meet increased protein needs of older adults, negative nitrogen balance results and protein levels decline, especially skeletal muscle proteins.

5. Consequences of malnutrition and negative nitrogen balance

In older adults, age- or disease-related malnutrition leads to negative nitrogen balance and ultimately to frailty and primary or secondary sarcopenia [1,21]. These conditions can result in disability, and eventually to loss of independence, falls and fractures, and death [7]. Primary (age-related) and secondary (disease-related) sarcopenia are difficult to distinguish in older adults because of the high prevalence of chronic disease in this population—92% after age 65 years, and 95% after age 80 years [22]. Frailty is defined as a biological syndrome with low reserve and low resistance to biomedical stressors; frailty results from cumulative declines across multiple biological systems, and worsening frailty is associated with disability [23]. Physical frailty and sarcopenia are closely linked [24]. While limited protein intake predicts incident frailty, it also predicts low bone mass [25,26]. In fact, the presence of osteoporosis doubles risk for frailty [27]. Notably, frailty can be prevented or reversed by intervention, particularly by greater protein intake and exercise [28,29].

6. Physical activity and exercise can maintain or enhance muscle mass

Loss of muscle mass with aging is primarily due to decreased muscle protein synthesis rather than to increased muscle protein breakdown. While the basal level of post-absorptive myofibrillar protein synthesis may decline with age, this decline is minimal [30]. Inactivity with consequent anabolic resistance are major contributors to the development of sarcopenia [30]. This concept is supported by the observation that immobilization induces resistance of muscle to anabolic stimulation [31]. Similarly, reduction of step count for two weeks induces anabolic resistance in older adults, as shown by decreased response of muscle protein synthesis to protein ingestion, decreased insulin sensitivity, and lowered leg muscle mass [32].

Aging muscle does respond to exercise, especially resistance exercise. In a classic study of nursing home residents older than 90 years, those who underwent 8 weeks of high-intensity resistance training experienced significant gains in muscle mass, strength, and walking speed [33]. A meta-analysis of studies on progressive resistance training in older adults showed clear benefits for improved physical function [34]. Resistance exercise may support these benefits by way of increased insulin sensitivity for [1] improved glucose utilization [35] and [2] enhanced myofibrillar protein synthesis [36]. Study results showed that resistance exercise was as effective in older adults as it was in young adults to reverse muscle loss and low muscle protein synthesis [37]. It was recently suggested that exercise-induced improvement in protein synthesis may be due to nutrient-stimulated vasodilation and nutrient delivery to muscle rather than to improved insulin signaling [38].

In addition, the timing of protein ingestion relative to the exercise may be important for muscle mass accretion. In a study of younger adult men, the benefits of resistance exercise on protein synthesis persisted up to 24 h post-exercise [39]. More research is needed to delineate mechanisms that link physical activity/nutrition to recovery of lost muscle protein in older adults.

Fig. 2. Protein status: factors leading to higher protein needs in older persons.

7. Protein requirements without and with chronic diseases or conditions

Older adults are expected to benefit from increased dietary protein intake, especially those with anorexia and low protein intake along with higher needs due to inflammatory conditions such as heart failure, COPD, or CKD undergoing dialysis [40]. Further research is needed to identify and develop tools that can precisely define protein needs in older individuals with chronic conditions. Research is likewise needed to determine whether increased protein intake can measurably improve functional outcomes. The goal for future studies is to identify specific protein and amino acid needs for older adults, including those who are healthy and those with diseases common to aging.

8. Optimal protein or amino acid type and amount

A wide range of factors can affect the amount of dietary protein needed by an older person -digestibility and absorbability of protein in foods consumed, whether chewing capacity is normal or impaired, protein quality and amino acid content, sedentary lifestyle (including immobilization or inactivity due to medical condition), and presence of stress factors (inflammation and oxidative stress).

8.1. Amount of protein

Debate continues about whether a per-meal threshold amount of protein intake is needed to stimulate protein synthesis in older adults [41] or whether protein synthesis is linearly related to protein intake [15]. Either way, evidence suggests that older adults who consume more protein are able to maintain muscle mass and strength [8,10,42,43]. Older adults who consumed 1.1 g protein/kg body weight/day lost less lean body mass (muscle) than did those who consumed only 0.7–0.9 g protein/kg body weight/day [10]. Among hospitalized older patients, at least 1.1 g protein/kg body weight/day was needed to achieve nitrogen balance, and safe intake was up to 1.6 g protein/kg body weight/day [43].

Recent dietary recommendations for older adults are now including higher protein intake than for younger adults [7,44]. The international PROT-AGE study group recommended 1.0–1.5 g protein/kg body weight/day for individuals older than 65 years [7] with or without disease, and the new Nordic Nutrition Recommendations suggest targeting 1.2–1.4 g protein/kg body weight/day with protein as 15–20% of total energy intake for healthy older adults [44,45].

8.2. Protein source, digestion, and absorption

Properties of the protein itself have the potential to affect digestion and absorption, e.g., whey, a milk protein, is considered a "fast" protein due to its quick release of amino acids, while casein, another milk protein, is a "slow" protein [46,47]. In a study by Tang et al., ingestion of whey protein increased muscle protein synthesis more than casein [48]. However, it was shown that whey and casein resulted in equally increased protein synthesis when ingested after resistance exercise [49]. The difference between these studies is likely due to the form of casein used. Micellular casein, a form that leads to slower digestion, was used by [48], while calcium caseinate was used by [49].

From other perspectives, a person's poor dentition can limit chewing capacity and protein availability [50], as can under- or over-cooking of protein foods [51].

8.3. Protein intake pattern

While terminology used to describe patterns of protein intake varies, intake patterns in research studies were to "spread" protein evenly over 4 meals or to deliver protein mostly as a large "pulse" in a single meal. Results of several studies suggest that the pulse protein feeding pattern may be useful to improve feeding-induced stimulation of protein synthesis in older adults [52–54]. These results are seemingly contradictory to those suggesting that 4 doses of 20 g of protein across 12 h is the optimal pattern [55]. It is not clear whether the discrepancy between these studies is due to age differences, in inclusion of exercise, or most likely, the fact that 20 g protein is not enough to maximally stimulate muscle protein synthesis in older adults. Further studies are needed to clarify optimal patterns of protein intake for older adults, and such studies must include protein synthesis as well as improvements in muscle strength and performance as outcome measures.

8.4. Specific amino acids and metabolites

Branched chain amino acids (BCAA), especially leucine, positively regulate signaling pathways for synthesis of muscle proteins [56]. A higher proportion of leucine was required for optimal stimulation of the rate of muscle protein synthesis in older adults, as compared to younger adults [57]. In adults who were critically ill, mixed BCAA likewise increased muscle protein synthesis [58,59]. In a randomized, controlled study of exercise and nutrition in older sarcopenic adult women in the Japanese community, those who exercised and consumed supplemental amino acids rich in leucine showed increased leg muscle mass and strength, and faster walking speed [60]. Moreover, Borsheim et al. demonstrated that older adult who were given supplemental essential amino acids (EAA) for 16 weeks developed increased muscle mass and improved function, even in the absence of exercise interventions [61]. However, other study results showed that long-term leucine supplementation alone did not increase muscle mass or strength [62,63].

In addition, beta-hydroxy beta-methyl butyrate (β-HMB), an active metabolite of leucine, has been used by athletes to improve performance [64]. HMB ingestion increased muscle protein synthesis and reduced muscle protein breakdown in young adults in insulin-independent manner [65]. Further evidence shows that β-HMB may also help increase muscle mass and strength in older adults and in specific clinical populations (AIDS, cancer), and can help attenuate muscle loss in patients who are critically ill and require prolonged ICU care (ICU-acquired weakness) [66–68].

9. Sarcopenic obesity and protein intake

Sarcopenic obesity is a deficiency of skeletal muscle tissue mass relative to fat tissue (Table 3). Obesity and inactivity contribute to decreased muscle mass and to lower muscle quality, especially with aging [69]. Lower muscle quality is attributed in part to infiltration of fat into the muscle, which affects both muscle strength and muscle function [70]. Intramyocellular lipid accumulation also reduces synthesis of muscle proteins [71].

Working definitions of sarcopenic obesity have been used in research studies, but there is not yet a universal definition for clinical practice [72,73]. Sarcopenic obesity is under-diagnosed due to a lack of agreement on which body composition indices and cutoff points to use. A suitable definition should be based on a measure of fat mass along with a measure of skeletal muscle mass normalized for height (fat-free mass index, FFMI, or appendicular skeletal muscle mass index, SMI) [74]. Age-specific reference values are more advantageous because FFMI or SMI may be misleading in adults of advanced age, in those with severe obesity, or in weight-reduced obese patients who have more connective tissue relative to lean mass. A simplified diagnosis of sarcopenic obesity can be based on a single image of muscle and adipose tissue of the thigh (magnetic resonance image or dual X-ray absorptiometry) [74]. This

Table 3
Profile of sarcopenic obesity.

Feature	
Definition	• Deficiency of skeletal muscle relative to fat tissue; evolving definitions should include measure of muscle performance too
Prevalence	• 4%—12% in individuals aged >60 years, depending on the defining cutoffs used [72]
Health consequences	• Mobility limitations [70] • Reduced quality of life [75] • Risk of mortality [76]
Clinical management	• Weight loss with focus on losing fat but not muscle • Increased dietary protein intake • Resistance training for building muscle and endurance exercise [75]

method does have limitations; the ratio of skeletal muscle to fat tissue varies by sex and by body region in individuals with very high adiposity [74].

In older adult men and women, low muscle mass and high fat infiltration into the muscle were associated with decreased strength and increased risk of losing mobility [70]. Similarly, low muscle mass correlated with low functionality [70]. The consequences of sarcopenic obesity are serious, including mobility limitations, lower quality of life, and risk of early death [70,75—77]. Therefore, management of sarcopenic obesity aims primarily to sustain muscle strength and function and secondarily on weight loss with focus on losing fat but not muscle. Physical exercise is important in weight loss, as restriction of energy intake is otherwise likely to induce loss of skeletal muscle [78]. Taken together, the recommended strategy for management of sarcopenic obesity is a combination of moderate calorie restriction, increased protein intake, and exercise (endurance and resistance training).

10. Concerns about negative effects of higher protein intake in older adults

While the benefits of increased dietary protein are acknowledged for maintenance of muscle health in older adults, health professionals often express concern that high-protein diets will stress and worsen declining kidney function in this population. However, evidence shows that many healthy older adults have preserved kidney function [79—81]. On the other hand, those older adults who are unhealthy are more likely to develop mild kidney insufficiency or CKD. For such individuals with a short life expectancy, nutritional recommendations (such as restriction of dietary protein intake) should support quality of life in the short-term. Specifically, when making recommendations for protein intake, consider the balance between risk of disability/death and risk of developing end-stage renal disease.

Serum creatinine and creatinine clearance are poor markers of glomerular filtration rate (GFR) in older adults since these values are strongly determined by muscle mass, which is reduced in this population. For recommendation of dietary intake, it is helpful to use serum creatinine-derived formulas to estimate GFR. The Modification of Diet in Renal Disease (MDRD) Study equation, which incorporates information about age, sex, race, and serum creatinine concentration is most commonly used in clinical practice and in research studies [82]. However, it systematically underestimates GFR in individuals with normal or near-normal GFR ($>$60 ml/min/1.73 m^2). The Chronic Kidney Disease Epidemiology Collaboration (CKD-EPI) is a new and improved equation to estimate GFR, particularly in individuals with normal GFR ($>$60 ml/min/1.73 m^2) [83]. Although these equations improve the estimation of GFR compared to serum creatinine in older adults, the MDRD equation still underestimates mean measured GFR by 25%, and the CKD-EPI equation by 16%, respectively, in this population. This bias may lead to misclassifying healthy older persons as having CKD [84]. Based on GFR estimates, kidney function is categorized as *normal or mild* dysfunction (GFR $>$ 60 ml/min/1.73 m^2), *moderate* dysfunction (30 $<$ GFR $<$ 60 ml/min/1.73 m^2), or *severe* dysfunction (GFR $<$ 30 ml/min/1.73 m^2). It is notable that CKD can also result from defects in kidney structure or kidney function that are evident as proteinuria or other problems but not as altered GFR [85].

For protein intake in patients with possible alteration of kidney function, the following guidance is offered:

- In older adults with healthy kidneys or with only mild dysfunction, standard protein intake is safe.
- In older patients with moderately impaired GFR or another form of CKD, physicians customarily assess the balance between risks and benefits, and use clinical judgment to make recommendations.
- In patients with severe CKD, it is usual to recommend a lower protein intake of 0.6—0.8 g/kg/day with sufficient energy intake (about 30 kcal/kg/day). However, multi-morbid patients on palliative care are an exception to this rule. These individuals may benefit from unrestricted intake of dietary protein because
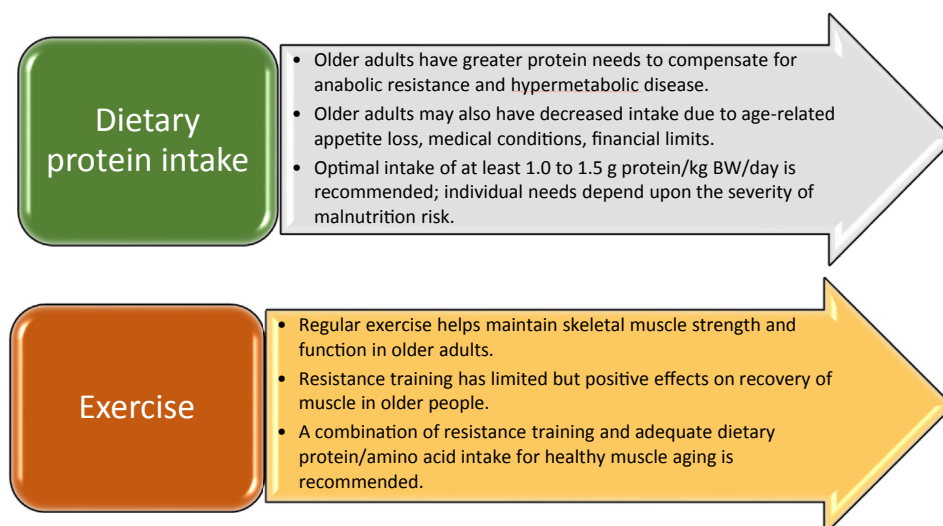

Dietary protein intake
- Older adults have greater protein needs to compensate for anabolic resistance and hypermetabolic disease.
- Older adults may also have decreased intake due to age-related appetite loss, medical conditions, financial limits.
- Optimal intake of at least 1.0 to 1.5 g protein/kg BW/day is recommended; individual needs depend upon the severity of malnutrition risk.

Exercise
- Regular exercise helps maintain skeletal muscle strength and function in older adults.
- Resistance training has limited but positive effects on recovery of muscle in older people.
- A combination of resistance training and adequate dietary protein/amino acid intake for healthy muscle aging is recommended.

Fig. 3. Recommendations for maintaining healthy muscle with aging.

the short-term risks associated with protein energy wasting are greater than the long-term risks of worsening renal function due to diet with standard protein content.

11. Conclusions

If the increasing life expectancy over the past two centuries continues at the same rate through the 21st century, many babies born since 2000 will celebrate their 100th birthdays [86]. In fact, average lifespan has increased 7–10 years in just 3 decades [86].

What distinguishes a generally healthy, long-lived person today? A study of Japanese centenarians (100 years or older) found that those who remained autonomous, i.e., performed activities of daily living, had good cognition, and had good social networks, had more frequent intake of protein and regular exercise as distinguishing features compared to their non-autonomous peers [87].

Adequate dietary protein intake and continuing exercise are important to healthy aging. Trajectories of greater muscle protein breakdown are more likely when older age is confounded by acute or chronic disease, e.g., cancer, heart failure, COPD, or CKD undergoing dialysis. If protein catabolism not offset by increasing protein intake, along with maintaining physical activity, older adults are at higher risk for sarcopenia, frailty, disability. Results of a recent study showed that low dietary protein intake can help prevent cancer and other diseases in young adults, while older adults need high protein intake to sustain healthy aging and longevity [88].

In order to help prevent or delay adverse consequences, we encourage increased intake of dietary protein for older adults ($\geq$65 years) compared to younger adults, and continued participation in routine exercise or physical activities (Fig. 3). At the same time, it is important for older people to balance total energy intake with total body energy demands—a rationale for consuming protein as a higher proportion of daily energy intake.

Conflict of interest

None.

Acknowledgments

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