CURRENT OPINION

Protein supplementation with aging

Juergen M. Bauer and Rebecca Diekmann

Purpose of review

To highlight the recent evicence for optimal protein intake and protein supplementation in older adults. A special focus has been placed on the effects on muscle protein synthesis, strength and overall performance in this population.

Recent findings

Although for older adults, some additional evidence on the benefits of a higher protein intake than 0.8 g/kg body weight per day has been provided, the results of studies focusing on the timing of protein intake over the day have been contradictory. Supplementation with so-called 'fast' proteins, which are also rich in leucine, for example whey protein, proved superior with regard to muscle protein synthesis. First studies in frail older persons showed increased strength after supplementation with milk protein, whereas the combination with physical exercise increased muscle mass without additional benefit for strength or functionality.

Summary

Recent evidence suggests positive effects of protein supplementation on muscle protein synthesis, muscle mass and muscle strength. However, as most studies included only small numbers of participants for short treatment periods, larger studies with longer duration are necessary to support the clinical relevance of these observations.

Keywords

amino acids, elderly, functionality, protein, supplementation

INTRODUCTION

The preservation of functionality and especially mobility has been identified as one of the most important therapeutic goals for all those who care for older individuals, as it lays the ground for continuous social participation in this dramatically growing population. Recent studies provide evidence that protein intake is associated with muscle mass, muscle strength and functionality in older persons [1,2]. In this context, the appropriateness of earlier guidelines for protein intake has been questioned, especially in older individuals at high risk of functional decline [3–5]. It, therefore, seems appropriate to reconsider the evidence on this and to review the studies that explored the effects of supplementation with protein and specific amino acids in older individuals.

RECOMMENDATIONS FOR PROTEIN INTAKE IN OLDER INDIVIDUALS

In the recent past, the WHO, the US Institute of Medicine and the European Food Safety Authority recommended a dietary protein intake of 0.8 g protein/kg body weight per day for all adults without special consideration of the older population [6–9].

These recommendations were mainly based on nitrogen balance studies, which documented a median-estimated nitrogen requirement of 105 mg N/kg body weight per day, corresponding to 0.66 g good-quality protein. Considering the 97.5th percentile, 0.8 g protein/kg body weight was set as the respective recommended daily allowance. However, these studies involved only a small number of older individuals; these older individuals were also considered healthy, and, therefore, did not represent the overall older population in Western countries. In addition, repeated nitrogen balance

Department of Geriatric Medicine, Klinikum Oldenburg gGmbH, Carl von Ossietzky Universität Oldenburg, Oldenburg, Germany

Correspondence to Juergen M. Bauer, MD, PhD, Department of Geriatric Medicine, Klinikum Oldenburg gGmbH, Carl von Ossietzky Universität Oldenburg, Rahel-Straus-Str. 10, 26133 Oldenburg, Germany. Tel: +49 441 403 3351; fax: +49 441 403 3352; e-mail: bauer.juergen@klinikum-oldenburg.de

Curr Opin Clin Nutr Metab Care 2015, 18:24–31

DOI:10.1097/MCO.0000000000000124

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

KEY POINTS

- An intake of 1–1.2 g protein/kg body weight per day is recommended as safe and beneficial for healthy older persons.
- The above recommendation has to be adapted individually in patients with chronic kidney diseases. Here, kidney function and comorbidities have to be taken into account.
- Currently, it cannot be decided whether a more even distribution of protein intake over the day is superior to a more skewed intake toward one main meal.
- Supplementation with so-called 'fast' proteins, which are also rich in leucine, for exampe whey protein, proved superior to other protein sources with regard to muscle protein synthesis.
- Optimization of protein intake and protein supplementation may be considered as a relevant approach for the therapy of sarcopenia and frailty.

protocols may be regarded as impractical in frail older individuals.

The minimally invasive indicator amino acid oxidation technique was introduced recently. Tang *et al.* used this technique to determine the dietary protein requirement of older women aged between 80 and 87 years. In their analysis, the mean protein requirement was 0.85 g/kg body weight per day, which was 29% higher than the current estimated average requirement (EAR) for adults (0.66 g/kg per day) based on the nitrogen balance technique [10▪], as described above. Although the validity of the indicator amino acid oxidation technique continues to be debated among experts, the results it generate may be considered as another sign that the actual protein requirements in older persons may be higher than those reflected in the guidelines cited above.

Numerous studies have documented that muscle loss and a decline in strength are essential features of the aging process. If the loss of muscle mass and strength is pronounced, this condition is called sarcopenia. As a geriatric syndrome, sarcopenia leads to relevant morbidity (e.g., falls, hospital admission, institutionalization) and mortality. Although a general international consensus is still being sought on its definition, the European Working Group on Sarcopenia in Older People approach may be regarded as the most advanced at present [11]. It has become clear that energy and protein intake play a major role in the preservation of muscle mass and strength with aging and that their inadequate supply is a relevant etiologic factor in the pathogenesis of sarcopenia.

In 2008, Houston *et al.* [2] demonstrated that changes in both total lean mass and appendicular lean mass were associated with energy-adjusted protein intake over a 3-year follow-up period. Study participants in the highest quintile of protein intake lost approximately 40% less lean mass and appendicular lean mass than those in the lowest quintile. In 2013, Beasley *et al.* [12▪▪] published a study based on data from the Women's Health Initiative Clinical Trials and Observational Study. This study explored the association between calibrated protein intake and physical function in postmenopausal women. Calibrated protein intake was derived from regression equations using baseline food frequency questionnaire data collected for the entire cohort and doubly labeled water and 24-h urinary nitrogen collected from a representative sample as reference measures. Higher calibrated protein intake at baseline was associated with higher self-reported physical function on the basis of the short-form RAND-36 and a slower rate of functional decline. Higher calibrated protein intake was also associated with higher grip strength and more chair stands at baseline as well as with a slower decline in grip strength during the follow-up.

However, the relevance of protein intake in older age goes clearly beyond muscle mass and muscle strength, as higher protein intake is also associated with bone structure and immune competence [5,13]. In a very recent study, Beasley *et al.* [14▪] were able to show that a higher biomarker-calibrated protein intake was firstly, inversely associated with forearm fracture and secondly, associated with a better maintenance of total and hip bone mineral densities in postmenopausal women. However, the authors were unable to show any association with the total fracture or hip fracture rate.

In 2013 and 2014, several international working groups reviewed the scientific literature focusing on protein intake in older individuals. Although a number of questions in this field have not yet been answered adequately, the participating experts considered it necessary to propose a higher protein intake of 1.0–1.2 g/kg body weight per day for optimal protein intake in older individuals, as this would obviously generate positive effects on relevant aspects of functionality in this population without causing them harm [3–5]. This recommendation for protein intake still remains well within the generally advocated 10–35% of the overall macronutrient intake for adults. Nevertheless, it has to be individualized according to the overall morbidity of the older person. The above-cited studies also illustrate the mechanisms that generate the need for a higher protein intake in older individuals

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

compared to younger ones. The interested reader is referred to these overviews.

It must also be borne in mind, however, that a relevant percentage of the older population does not consume adequate amounts of protein, even if a low threshold of 0.8 g/kg body weight per day is applied. The National Health and Nutrition Examination Study demonstrated that 5 to 6% of the population above the age of 70 years consume less than the EAR for protein [15]. In the German National Consumption Survey II, 14% of older men and 15% of older women failed to meet the recommended intake of 0.8 g/kg body weight per day [16]. A secondary data analysis based on four previously conducted studies among community-dwelling, frail and institutionalized elderly people in the Netherlands showed that 10% of the community-dwelling, frail elderly and 35% of the institutionalized elderly exhibited a protein intake below the EAR (0.7 g/kg body weight per day) [17]. Among Finnish service house residents, 47% consumed less than 60 g per day protein and 11% less than 40 g per day protein. Among all residents, very old women exhibited the lowest consumption level for protein [18].

Volpi *et al.* recently listed the risk factors for low protein intake in older adults. The most relevant risk factors were reduced energy intake in higher age, physical dependence, anorexia, change in food preference and food insecurity [19].

If protein needs for optimal intake cannot be met under the above-characterized circumstances, protein supplementation should be considered as an important option.

SUPPLEMENTATION IN HEALTHY OLDER INDIVIDUALS

Recent studies focused on the amount as well as on timing of protein intake. In addition, protein quality has been a major point of interest. Here, especially the effects of supplementation with proteins that are rich in branched-chain amino acids were investigated.

Amount and timing of supplementations

Studies by Walrand *et al.* and Symons *et al.* point toward a ceiling effect of higher protein intake with regard to muscle protein synthesis in older persons. According to their observations, the proportion of protein used as fuel increases beyond a certain threshold. Their results led to the conclusion that the maximum stimulation of muscle protein synthesis occurs with an intake of 20–30 g protein per meal [20,21].

In addition to defining the optimal amount of protein intake per meal, the distribution of protein intake over the day was also investigated. Examining the 24-h mixed muscle protein fractional synthesis rate with evenly distributed protein intake at breakfast, lunch and dinner against a skewed distribution toward the evening meal, Mamerow *et al.* [22] found a 25% higher rate for the first approach compared to the second. In order to ensure these results are interpreted correctly, it must be considered that the protein was consumed without carbohydrates.

On the basis of food frequency questionnaires in 195 community-dwelling elderly, Bollwein *et al.* explored the association between the amount and distribution of protein intake and frailty according to Fried. The median daily protein intake was 77.5 and 1.07 g/kg body weight with respective ranges from 38.5 to 131.5 g and from 0.58 to 2.27 g/kg body weight per day. No significant differences between robust, prefrail and frail individuals were yielded. However, frail individuals exhibited a more skewed distribution of their protein intake over the day, with lower intake at breakfast and higher intake at lunch [23]. The above results provided by Mamerow *et al.* and Bollwein *et al.* would support the recommendation to evenly distribute individual protein intake over the three main meals.

In a recent study, Deutz and Wolfe [24▪▪] challenged this perspective, drawing attention to net protein synthesis, calculated as the difference between the rate of synthesis and the rate of breakdown. Net protein synthesis after a meal is influenced by the presence of insulin, which inhibits protein breakdown. Increasing protein intake during a meal leads to higher protein synthesis, for which a ceiling effect will be observed. However, it also causes a decrease in protein breakdown, thereby leading to a higher net protein synthesis. The authors concluded that there is no practical upper limit to the anabolic response generated by higher intakes of protein or amino acids during a meal. As a consequence, the effect of protein intake on muscle protein synthesis could either be improved by ensuring a more even distribution over the day, with higher protein intake at breakfast and lunch, or by increasing the intake of protein at dinner to a maximum. The above conclusions are supported by a recent study involving 66 geriatric rehabilitation patients who were malnourished or at risk of malnutrition. Protein pulse feeding with a consumption of 72% of the total daily protein intake at lunch led to a significantly higher improvement of lean muscle index and appendicular muscle index than spreading protein intake over the three main meals [25].

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

However, the amount of protein consumed in one meal by older individuals may be limited by its satiating effects. Certain individuals may thereby be at risk of a decreased energy intake when attempting to optimize their protein consumption. The practical relevance of pulse feeding in older individuals may, therefore, be limited, and discussions in this field will most probably remain controversial [26].

For certain individuals, it may be feasible to consider temporary feeding via a nasogastric tube or a percutaneous endoscopic gastrostomy. For this group, it may make sense to consider alternatives to daytime feeding. Groen *et al.* [27] investigated protein application during sleep. A single bolus of intrinsically L-[1-13C]phenylalanine-labeled casein during sleep stimulated protein synthesis in older persons, resulting in a more positive overnight whole-body protein balance compared to placebo. No gastrointestinal disturbance, no nausea and no interruption of sleep were observed. Night-time or late evening protein feeding may cause little or no interference with overall energy intake, which may be of relevance during the day as outlined above. This approach may therefore prove useful for stabilizing muscle mass in certain patient groups, especially in the context of immobilization.

Protein quality

The anabolic effects of dietary proteins are influenced to a relevant extent by their composition. Branched-chain amino acids are considered the most relevant group, of which leucine is the most potent single one. This is because it is not only a substrate for protein synthesis, but it also activates translation. In an observational study by Lustgarten *et al.* [28], seven branched-chain amino acid-related metabolites were associated with both muscle cross-sectional area and the fat-free mass index in 73 functionally limited older adults.

It has been demonstrated that 'fast' proteins, which exhibit a superior digestion rate compared to 'slow' proteins, have a positive impact on the protein balance because the digestion rate of protein is regarded as an independent regulating factor of postprandial protein retention. This effect appears to be especially relevant in older individuals.

In a 10-day trial, Gryson *et al.* [29▪] demonstrated that the leucine balance was better with a high-protein diet (1.2 g/kg body weight) than with an adequate protein diet (1.0 g/kg body weight) in older persons. They also showed that soluble milk proteins characterized as 'fast' proteins provide better leucine retention than casein, a representative of so-called 'slow' proteins. The authors concluded that improving the quality of protein by combining the digestion rate and the leucine content may be more effective for improving protein retention in older adults than simply increasing the quantity of protein consumed.

Casein protein (20 g) with or without a crystalline leucine supplement (2.5 g) was recently tested in 24 elderly men (mean age 74). The authors were able to show that leucine supplementation resulted in higher plasma leucine concentrations. The percentage of muscle protein-bound amino acids and the muscle protein synthetic rate were both greater in the supplemented group [30].

Pennings *et al.* [31] tested the effect on plasma peak values of marker amino acids, whole-body protein net balance and postprandial muscle protein accretion of three different doses of whey protein (10, 20 and 35 g) in healthy older men. Thirty-five grams of whey protein yielded the highest peak values as well as the best effect on the whole-body protein net balance and postprandial muscle protein accretion. According to these results, higher doses of whey protein further increase protein synthesis in older persons, and may be considered as a relevant option for overcoming the anabolic resistance, especially in the context of sarcopenia.

Beta-alanine

In a recent trial [32], a nutritional supplement with two different doses of beta-alanine, 800 and 1200 mg, was tested regarding the effect on body composition, muscle function and physical capacity in older adults. Whereas there was no difference with regard to body composition and handgrip, significant increases were yielded for physical working capacity, which was tested by discontinuous, submaximal cycle ergometry.

In another study involving 18 older persons (aged 60–80 years), supplementation with 3.2 g beta-alanine per day for 12 weeks versus placebo resulted in an improved time-to-exhaustion for constant-load submaximal and incremental testing [33]. The clinical relevance of these observations will have to be confirmed in future trials.

Hydroxymethylbutyrate

Hydroxymethylbutyrate (HMB) is a leucine metabolite to which significant effects on muscle preservation and muscle growth have been attributed. However, few trials have investigated the effectiveness of this substance in older persons.

Although Dirks *et al.* [34] found no positive effect of protein supplementation (20.3 g twice daily) on muscle loss over an immobilization period

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

of 5 days, in contrast, Deutz *et al.* [35■] were able to demonstrate a positive effect of supplementation with HMB in a bed rest study over 10 days. Neither study revealed significant differences between supplemented and control groups for functional parameters.

A recent study by Fukagawa systematically reviewed trials involving the investigation of the effects of specific amino acids and amino acid mixtures on older peoples' health and independence. The authors reported major difficulties when trying to draw conclusions, which was a consequence of significant variability among the tested supplements and among the study outcomes [36].

PROTEIN SUPPLEMENTATION IN COMBINATION WITH EXERCISE

Several studies have been published in recent years that investigated the effect of protein and amino acid supplementation on muscle mass and muscle function when combined with exercise. Physical exercise increases muscle protein synthesis and decreases muscle protein degradation in both younger and older adults. It may thereby be one way of overcoming the so-called anabolic resistance of aging [37]. A meta-analysis of 22 studies in young and older adults documented that protein supplementation in combination with resistance exercise increased fat-free mass and leg press strength. Various kinds of protein, such as whey, casein, milk protein, essential amino acids and egg protein, were supplemented in the included studies [38].

Protein

Daly *et al.* evaluated a protein-enriched diet with the use of lean meat (total intake 1.3 g/kg body weight daily) in combination with progressive resistance training in healthy older people. They were able to show a significant increase in total-body lean tissue mass and in muscle strength when comparing the supplemented group to the control group that underwent resistance training only [39■]. In contrast, Leenders *et al.* [40] were unable to demonstrate a positive effect on muscle mass and strength of functional capacity when 15 g protein was supplemented over 24 weeks of a resistance-type training program in healthy older persons. In this study, a milk protein concentrate consisting of 80% casein and 20% whey protein was used. When comparing the results of these two studies, it has to be acknowledged that not only the supplementation but also the study populations differed. In the study by Daly *et al.*, the study participants were females living in retirement villages; in the study by Leenders *et al.*, slightly younger, healthy women and men were included. In addition, the total protein intake was lower in the second study (1.2 g/kg body weight per day in women and 1.1 g/kg body weight per day in men compared to 1.3 g/kg body weight per day consumed in the study by Daly *et al.*).

Okazaki *et al.* [41] showed that macronutrient supplementation (7.6 g protein, 32.5 g carbohydrate and 4.4 g fat) during a 5-month home-based interval walking training program increased the exercise-induced gains in thigh muscle mass and knee strength in healthy middle-aged and older women compared to controls who underwent interval walking training only. The macronutrient supplement was consumed at least four times a week within 30 min after each training session. The protein supplement was mainly whey protein mixed with several percent skimmed milk powder.

Whey and leucine

In rested and exercised muscle of trained young men, a 20 g dose of whey protein appears to be sufficient for maximal stimulation of postabsorptive rates of myofibrillar protein synthesis (MPS). Doses exceeding 20 g stimulate amino acid oxidation and ureagenesis in this young population [42]. Reitelseder *et al.* [43] investigated the effect of whey and casein supplementation on MPS after resistance exercise in young study participants. Despite temporal differences in amino acid concentrations, they were unable to demonstrate a significant difference in MPS for this young test population. However, the situation in older individuals seems to differ significantly.

Yang *et al.* [44] tested the effect of different doses of whey protein isolate (0, 10, 20 or 40 g) on MPS in healthy older persons. The supplements were consumed after a bout of resistance exercise. The authors were able to show that the maximum effect of supplementation on MPS after exercise was achieved with 40 g; the optimal dose at rest was identified as 20 g.

Combining supplementation with whey protein and resistance exercise training was investigated in mobility-limited older persons by Chalé *et al.* [45]. In a randomized controlled trial, the supplemented intake of 40 g whey protein was tested over a 6-month period. Resistance training was provided for both groups. Lean mass, muscle cross-sectional area, muscle strength and stair-climbing performance failed to improve to a considerable extent in the whey supplemented group compared to the control group.

Scientists have proposed that hydrolysated protein is more effective regarding MPS stimulation

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

than intact nonhydrolyzed proteins [46]. The effect of pure whey isolate on MPS was compared to the effect of pure isolated micellar casein at rest and after unilateral leg resistance exercise in 14 elderly men in a study by Burd *et al.* Twenty grams isonitrogenous quantities of casein or whey were consumed before and after exercise. MPS after whey consumption was significantly higher in the rested leg as well as after resistance exercise. According to these results, whey supplementation after exercising stimulates MPS in older men to a greater extent than casein [47].

Soy

So far, little evidence has been provided on the specific benefits of soy protein for aging muscles. The effect of isolate soy protein on muscle strength was investigated by Shenoy *et al.* in osteporotic postmenopausal women in combination with and without progressive resistance exercise. Supplementation resulted in an increase in muscle strength compared to placebo; the best results were obtained by combining supplementation with exercise [48].

PROTEIN SUPPLEMENTATION IN CLINICAL SITUATIONS

Certain diseases in older age require special consideration with regard to protein intake. First studies have addressed protein supplementation in frail older persons. Additional evidence has been provided that protein supplementation in patients with hip fracture or knee arthroplasty may be beneficial.

Frailty and sarcopenia

Frailty in older persons has been characterized by a reduced reserve capacity, an increased vulnerability to external and internal stressors and a propensity toward negative health events and higher mortality [49]. In a cohort of more than 2000 older Japanese women aged above 65 years, a higher intake of protein was associated with a less likelihood of being frail based on the Fried criteria [50,51]. In a study by Shikany *et al.* [52] that included 5925 men aged above 65 years, protein intake, assessed by a food frequency questionnaire, exhibited no significant association with frailty. However, the overall Diet Quality Index did so for frailty at baseline as well as for incident frailty (4.6 years). The Diet Quality Index is a tool that considers not only the amount but also the source of protein.

In another trial, frail older people (gait speed <0.6 m/s, Mini Nutritional Assessment <24) received energy-protein supplementation containing 25 g protein or placebo over 12 weeks [53]. On the basis of the Short Physical Performance Battery as the primary outcome parameter, supplementation reduced functional decline in this population.

It has to be appreciated that, in the highly vulnerable frail population, small gains, and even the stabilization of functional status, should be regarded as relevant therapeutic achievements [54] that imply major effects from an individual and a public health perspective.

In 2012, Tieland *et al.* published two studies focusing on frail older persons. In the first study [55▪], 65 frail older persons received either a protein supplement twice daily (15 g milk protein concentrate at breakfast and lunch) or placebo. At the end of the 24-week supplementation period, it was found that muscle mass had not improved. However, muscle strength had increased in both groups, with no significant difference between the two groups. Physical performance based on the Short Physical Performance Battery had also improved significantly in the supplemented group. In the second study, Tieland *et al.* [56] combined protein supplementation as described above with resistance-type exercise over 24 weeks. Lean body mass increased in the supplemented group, but not in the placebo cohort. Strength and physical performance improved in both groups, with no significant difference between the groups.

HIP FRACTURE AND KNEE ARTHROPLASTY

Hospital patients with hip fractures frequently suffer from protein–energy malnutrition. Prevalence rates range between 30 and more than 50% [57,58]. Protein–energy malnutrition negatively affects the outcome of rehabilitation [59]. Evidence supports the assumption that higher protein intake and protein supplementation are effective under these circumstances. In a randomized controlled trial in older hip fracture patients, supplementation with 18–24 g protein and 500 kcal per day was tested. In the supplemented group, the BMI decreased less, the length of stay in the rehabilitation ward was shortened and the number of infections was reduced [60].

Dreyer *et al.* [61] tested in a small double-blind, randomized, placebo-controlled trial the effect of 20 g essential amino acids twice daily 1 week before until 2 weeks after knee arthroplasty. The supplementation group showed significantly lower quadriceps muscle atrophy than the placebo group. Essential amino acid intake attenuated atrophy also in the nonoperated quadriceps and resulted in better mobility.

CONCLUSION

In recent years, evidence has accumulated that supports the relevance of optimal protein intake for

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

successful aging. A modest increase up to 1.2 g/kg body weight per day can be safely recommended in healthy individuals, although higher doses may be indicated for certain disease states. However, chronic kidney disease has to be appreciated individually and the satiating effects of high protein intake have to be balanced, especially if a person is at risk for malnutrition. When educating those that are involved in the care of older inidividuals – professionals and nonprofessionals – the role of protein should be highlighted. Especially in the context of rehabilitation when the acute or chronic loss of strength and functionality is obvious, the optimization of protein intake and, if indicated, protein supplementation may become cornerstones of individually adapted programes. Although the timing of protein intake is stil very much debated, high-quality proteins with the best stimulation of muscle protein synthesis should be the preferred choice.

Future studies should provide evidence whether different health conditions may warrant different approaches toward supplementation. For example, the individual approach may differ, if a supplement should be selected and timed for an immobilized older person, or if it has to be selected for a patient in rehabilitation, when the combination with physical exercise may be standard.

Acknowledgements

None.

Conflicts of interest

R.D. has no conflicts of interest.

J.M.B.: Research grants from Nestlé and Nutricia Danone, consultant for Nestlé, Nutricia Danone and Novartis, speaker honoraria from Nestlé, Nutricia Danone, Novartis, Glaxo.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:

■ of special interest

■■ of outstanding interest

1. Beasley JM, LaCroix AZ, Neuhouser ML, *et al.* Protein intake and incident frailty in the Women's Health Initiative observational study. J Am Geriatr Soc 2010; 58:1063–1071.
2. Houston DK, Nicklas BJ, Ding J, *et al.* Dietary protein intake is associated with lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study. Am J Clin Nutr 2008; 87:150–155.
3. Bauer J, Biolo G, Cederholm T, *et al.* 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 2013; 14:542–559.
4. Deutz NE, Bauer JM, Barazzoni R, *et al.* Protein intake and exercise for optimal muscle function with aging: recommendations from the ESPEN Expert Group. Clin Nutr 2014. [Epub ahead of print]
5. Rizzoli R, Stevenson JC, Bauer JM, *et al.* The role of dietary protein and vitamin D in maintaining musculoskeletal health in postmenopausal women: a consensus statement from the European Society for Clinical and Economic Aspects of Osteoporosis and Osteoarthritis (ESCEO). Maturitas 2014; 79:122–132.
6. World Health Organization. Protein and amino acid requirements in human nutrition: report of a Joint WHO/FAO/UNU expert consultation. WHO Press; 2007 ; http://whqlibdoc.who.int/trs/who_trs_935_eng.pdf. [Accessed 15 October 2014]
7. Dietary reference intakes for energy, carbohydrate, fiber, fat, fatty acids, cholesterol, protein, and amino acids (macronutrients). http://www.nap.edu/openbook.php?record_id=10490. [Accessed 4 August 2014]
8. Deutsche Gesellschaft für Ernährung. D-A-CH Referenzwerte. Referenzwerte für die Nährstoffzufuhr. 1. Auflage, 5., korrigierter Nachdruck 2013. [German Society for Nutrition. D-A-C-H reference values]
9. European Food Safety Authority. Scientific opinion on dietary reference values for protein. EFSA Journal 2012; 10:2557. http://www.efsa.europa.eu/de/efsajournal/doc/2557.pdf.
10. ■ Tang M, McCabe GP, Elango R, *et al.* Assessment of protein requirement in octogenarian women with use of the indicator amino acid oxidation technique. Am J Clin Nutr 2014; 99:891–898.

Although controversial from a methodological point of view, Tang *et al.* showed with this new technique that the recommended daily allowance for protein might be significantly higher than 0.8 g/kg body weight per day.

11. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, *et al.* Sarcopenia: European consensus on definition and diagnosis: report of the European Working Group on Sarcopenia in Older People. Age Ageing 2010; 39:412–423.
12. ■■ Beasley JM, Wertheim BC, LaCroix AZ, *et al.* Biomarker-calibrated protein intake and physical function in the Women's Health Initiative. J Am Geriatr Soc 2013; 61:1863–1871.

Beasley *et al.* showed in a large data set that in older persons low protein intake was associated with a steeper decline of functionality.

13. Kanis JA, McCloskey EV, Johansson H, *et al.* European guidance for the diagnosis and management of osteoporosis in postmenopausal women. Osteoporos Int 2013; 24:23–57.
14. ■ Beasley JM, LaCroix AZ, Larson JC, *et al.* Biomarker-calibrated protein intake and bone health in the Women's Health Initiative clinical trials and observational study. Am J Clin Nutr 2014; 99:934–940.

This analysis provides relevant information on the relationship of protein intake with bone mineral density and fracture risk.

15. Fulgoni VL 3rd. Current protein intake in America: analysis of the National Health and Nutrition Examination Survey, 2003–2004. Am J Clin Nutr 2008; 87:1554S–1557S.
16. EisingerM. Microsoft Word – NVSII_Ergebnisbericht_Teil2_Sep08.doc.http://www.was-esse-ich.de/uploads/media/NVSII_Abschlussbericht_Teil_2.pdf.
17. Tieland M, Borgonjen-Van den Berg KJ, van Loon LJ, de Groot LC. Dietary protein intake in community-dwelling, frail, and institutionalized elderly people: scope for improvement. Eur J Nutr 2012; 51:173–179.
18. Vikstedt T, Suominen MH, Joki A, *et al.* Nutritional status, energy, protein, and micronutrient intake of older service house residents. J Am Med Dir Assoc 2011; 12:302–307.
19. Volpi E, Campbell WW, Dwyer JT, *et al.* Is the optimal level of protein intake for older adults greater than the recommended dietary allowance? J Gerontol A Biol Sci Med Sci 2013; 68:677–681.
20. Walrand S, Short KR, Bigelow ML, *et al.* Functional impact of high protein intake on healthy elderly people. Am J Physiol Endocrinol Metab 2008; 295:E921–E928.
21. Symons TB, Sheffield-Moore M, Wolfe RR, *et al.* A moderate serving of high-quality protein maximally stimulates skeletal muscle protein synthesis in young and elderly subjects. J Am Diet Assoc 2009; 109:1582–1586.
22. Mamerow MM, Mettler JA, English KL, *et al.* Dietary protein distribution positively influences 24-h muscle protein synthesis in healthy adults. J Nutr 2014; 144:876–880.
23. Bollwein J, Diekmann R, Kaiser MJ, *et al.* Distribution but not amount of protein intake is associated with frailty: a cross-sectional investigation in the region of Nurnberg. Nutr J 2013; 12:109.
24. ■■ Deutz NE, Wolfe RR. Is there a maximal anabolic response to protein intake with a meal? Clin Nutr 2013; 32:309–313.

Stimulating study that provides a controversial point of view with regard to the suspected ceiling effect for the amount of protein intake.

25. Bouillanne O, Curis E, Hamon-Vilcot B, *et al.* Impact of protein pulse feeding on lean mass in malnourished and at-risk hospitalized elderly patients: a randomized controlled trial. Clin Nutr 2013; 32:186–192.
26. Paddon-Jones D, Leidy H. Dietary protein and muscle in older persons. Curr Opin Clin Nutr Metab Care 2014; 17:5–11.
27. Groen BB, Res PT, Pennings B, *et al.* Intragastric protein administration stimulates overnight muscle protein synthesis in elderly men. Am J Physiol Endocrinol Metab 2012; 302:E52–60.
28. Lustgarten MS, Price LL, Chale A, *et al.* Branched chain amino acids are associated with muscle mass in functionally limited older adults. J Gerontol A Biol Sci Med Sci 2013; 69:717–724.
29. ■ Gryson C, Walrand S, Giraudet C, *et al.* Fast proteins' with a unique essential amino acid content as an optimal nutrition in the elderly: growing evidence. Clin Nutr 2014; 33:642–648.

Well conceived study that supports the concept of fast proteins being advantageous for postprandial protein retention in older persons.

30. Wall BT, Hamer HM, Lange Ade, *et al.* Leucine co-ingestion improves postprandial muscle protein accretion in elderly men. Clin Nutr 2013; 32:412–419.

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.

31. Pennings B, Groen B, Lange A de, *et al.* Amino acid absorption and subsequent muscle protein accretion following graded intakes of whey protein in elderly men. Am J Physiol Endocrinol Metab 2012; 302:E992–E999.
32. McCormack WP, Stout JR, Emerson NS, *et al.* Oral nutritional supplement fortified with beta-alanine improves physical working capacity in older adults: a randomized, placebo-controlled study. Exp Gerontol 2013; 48:933–939.
33. del Favero S, Roschel H, Solis MY, *et al.* Beta-alanine (Carnosyn) supplementation in elderly subjects (60-80 years): effects on muscle carnosine content and physical capacity. Amino Acids 2012; 43:49–56.
34. Dirks ML, Wall BT, Nilwik R, *et al.* Skeletal muscle disuse atrophy is not attenuated by dietary protein supplementation in healthy older men. J Nutr 2014; 144:1196–1203.
35. ▪ Deutz NE, Pereira SL, Hays NP, *et al.* Effect of beta-hydroxy-beta-methylbutyrate (HMB) on lean body mass during 10 days of bed rest in older adults. Clin Nutr 2013; 32:704–712.

Study that provides evidence on potential beneficial effects of HMB with regard to the preservation of muscle mass in immobilized older persons.

36. Fukagawa NK. Protein and amino acid supplementation in older humans. Amino Acids 2013; 44:1493–1509.
37. Burd NA, Gorissen SH, van Loon LJ. Anabolic resistance of muscle protein synthesis with aging. Exerc Sport Sci Rev 2013; 41:169–173.
38. Cermak NM, Res PT, de Groot LC, *et al.* Protein supplementation augments the adaptive response of skeletal muscle to resistance-type exercise training: a meta-analysis. Am J Clin Nutr 2012; 96:1454–1464.
39. ▪ Daly RM, O'Connell SL, Mundell NL, *et al.* Protein-enriched diet, with the use of lean red meat, combined with progressive resistance training enhances lean tissue mass and muscle strength and reduces circulating IL-6 concentrations in elderly women: a cluster randomized controlled trial. Am J Clin Nutr 2014; 99:899–910.

Important study that shows for the first time the combined effects of meat protein and resistance exercise on lean tissues mass and muscle mass in older study participants.

40. Leenders M, Verdijk LB, Van der HoevenF L, *et al.* Protein supplementation during resistance-type exercise training in the elderly. Med Sci Sports Exerc 2013; 45:542–552.
41. Okazaki K, Yazawa D, Goto M, *et al.* Effects of macronutrient intake on thigh muscle mass during home-based walking training in middle-aged and older women. Scand J Med Sci Sports 2013; 23:e286–e292.
42. Witard OC, Jackman SR, Breen L, *et al.* Myofibrillar muscle protein synthesis rates subsequent to a meal in response to increasing doses of whey protein at rest and after resistance exercise. Am J Clin Nutr 2014; 99:86–95.
43. Reitelseder S, Agergaard J, Doessing S*, et al.* Whey and casein labeled with L-[1-13C]leucine and muscle protein synthesis: effect of resistance exercise and protein ingestion. AJP: Endocrinology and Metabolism 2010; 300:E231-E242. http://ajpendo.physiology.org/content/ajpendo/300/1/E231.full.pdf#zoom=75.
44. Yang Y, Breen L, Burd NA, *et al.* Resistance exercise enhances myofibrillar protein synthesis with graded intakes of whey protein in older men. Br J Nutr 2012; 108:1780–1788.
45. Chalé A, Cloutier GJ, Hau C, *et al.* Efficacy of whey protein supplementation on resistance exercise-induced changes in lean mass, muscle strength, and physical function in mobility-limited older adults. J Gerontol A Biol Sci Med Sci 2013; 68:682–690.
46. Manninen AH. Protein hydrolysates in sports nutrition. Nutr Metab (Lond) 2009; 6:38.
47. Burd NA, Yang Y, Moore DR, *et al.* Greater stimulation of myofibrillar protein synthesis with ingestion of whey protein isolate v. micellar casein at rest and after resistance exercise in elderly men. Br J Nutr 2012; 108:958–962.
48. Shenoy S, Bedi R, Sandhu JS. Effect of soy isolate protein and resistance exercises on muscle performance and bone health of osteopenic/osteoporotic postmenopausal women. J Women Aging 2013; 25:183–198.
49. Clegg A, Young J, Iliffe S, *et al.* Frailty in elderly people. Lancet 2013; 381:752–762.
50. Fried LP, Tangen CM, Walston J, *et al.* Frailty in older adults: evidence for a phenotype. J Gerontol A Biol Sci Med Sci 2001; 56:M146–M156.
51. Kobayashi S, Asakura K, Suga H, *et al.* High protein intake is associated with low prevalence of frailty among old Japanese women: a multicenter cross-sectional study. Nutr J 2013; 12:164.
52. Shikany JM, Barrett-Connor E, Ensrud KE, *et al.* Macronutrients, diet quality, and frailty in older men. J Gerontol A Biol Sci Med Sci 2014; 69:695–701.
53. Kim C, Lee K. 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 2013; 68:309–316.
54. Cesari M. Perspective: protein supplementation against sarcopenia and frailty: future perspectives from novel data. J Am Med Dir Assoc 2013; 14:62–63.
55. ▪ Tieland M, van de Rest O, Dirks ML, *et al.* Protein supplementation improves physical performance in frail elderly people: a randomized, double-blind, placebo-controlled trial. J Am Med Dir Assoc 2012; 13:720–726.

One of the first studies that investigated the effect of protein supplementaion on muscle mass and muscle strength in a well described population of frail older persons.

56. Tieland M, Dirks ML, van der Zwaluw N, *et al.* Protein supplementation increases muscle mass gain during prolonged resistance-type exercise training in frail elderly people: a randomized, double-blind, placebo-controlled trial. J Am Med Dir Assoc 2012; 13:713–719.
57. Drevet S, Bioteau C, Maziere S, *et al.* Prevalence of protein-energy malnutrition in hospital patients over 75years of age admitted for hip fracture. Orthop Traumatol Surg Res 2014; 100:669–674.
58. Bell J, Bauer J, Capra S, *et al.* Barriers to nutritional intake in patients with acute hip fracture: time to treat malnutrition as a disease and food as a medicine? Can J Physiol Pharmacol 2013; 91:489–495.
59. Li H, Cheng H, Liang J, *et al.* Functional recovery of older people with hip fracture: does malnutrition make a difference? J Adv Nurs 2013; 69:1691–1703.
60. Myint MW, Wu J, Wong E, *et al.* Clinical benefits of oral nutritional supplementation for elderly hip fracture patients: a single blind randomised controlled trial. Age Ageing 2013; 42:39–45.
61. Dreyer HC, Strycker LA, Senesac HA, *et al.* Essential amino acid supplementation in patients following total knee arthroplasty. J Clin Invest 2013; 123:4654–4666.

Copyright © Lippincott Williams & Wilkins. Unauthorized reproduction of this article is prohibited.