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Research Article

Nutritional Interventions for the Prevention and Management of Sarcopenia in Elderly Population: A Comprehensive Review

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Abstract

Background: The age-related decline of muscle bulk and strength, sarcopenia, is a substantial public health concern for an ageing population. It has been suggested that dietary modifications, like protein supplementation, vital vitamins and minerals, and resistance training, can be successful methods of preventing and treating sarcopenia. This review aims to present a summary of the latest research addressing nutritional strategies for both prevention and treatment of sarcopenia in elderly people, with a particular emphasis on consuming protein, essential amino acids, omega-3 fatty acids, vitamin D and antioxidants, as well as the interaction between nutritional interventions and resistance training. **Methods:** A comprehensive literature search was conducted using electronic databases, including PubMed, Scopus, Cochrane Library, and Web of Science, to identify relevant articles published up to March 2023. Randomized controlled trials (RCTs) and observational studies conducted in older adults (≥ 60 years of age) investigating the effects of nutritional interventions on muscle bulk, strength, or function were included. Data extraction, quality assessment, and narrative synthesis of the evidence were conducted. **Results:** A total of 40 studies were included in this review, comprising 27 RCTs and 13 observational studies. Adequate protein intake was consistently associated with improved muscle bulk and strength in older adults, with higher protein intake showing beneficial effects on physical performance and reduced frailty. Leucine, a vital amino acid, has been discovered to increase protein synthesis in muscles and enhance muscle function in elderly individuals. Omega-3 fatty acids, vitamin D, and magnesium supplementation showed mixed results regarding their effects on muscle mass, strength and function. At the same time, antioxidants had limited evidence supporting their benefits for sarcopenia prevention and management. The combination of nutritional interventions

and resistance training was found to have additive or synergistic effects on muscle health in older adults. **Conclusion:** This review provides evidence supporting the role of adequate protein intake and essential amino acids, particularly leucine, in preventing and managing sarcopenia in older adults. The potential benefits of omega-3 fatty acids, vitamin D, magnesium, and antioxidants require further investigation. Combining nutritional interventions with resistance training appears to have additive or synergistic effects on muscle health in this population. Healthcare professionals and researchers should consider these findings when developing strategies to combat sarcopenia in the aging population.

Introduction

The age-related decline of strength and muscle mass, also known as sarcopenia, is a major contributor to weakness, disability, and diminished standard of life in senior individuals [1-2]. It is considered that the number of people suffering from sarcopenia and related healthcare costs will increase as the global population ages, making it an important issue for the public. Since sarcopenia has been linked to an increased risk of falls, fractures and mortality, it is crucial to develop effective interventions to prevent or manage this condition [2]. Nutritional interventions play a significant role in maintaining and improving muscle health in older adults [3]. Previous research has highlighted the importance of adequate protein intake in the elderly to preserve muscle mass and function [4-5]. Inadequate protein intake may exacerbate the age-related decline in muscle mass, leading to the development or worsening of sarcopenia [6]. Moreover, higher protein intake has been associated with reduced frailty and improved physical performance in older individuals [7-8]. However, the optimal amount, type and distribution of protein intake for preventing and managing sarcopenia remain topics of ongoing debate among researchers and healthcare professionals.

Besides protein, other nutrients, such as essential amino acids, vitamins and minerals, have also been suggested to play a role in maintaining muscle health and combating sarcopenia. Leucine, an essential amino acid, has been shown to stimulate muscle protein synthesis and improve muscle function in older adults [9-12]. Furthermore, omega-3 fatty acids, vitamin D, magnesium and antioxidants have all been investigated for their potential benefits in preventing and managing sarcopenia [16-28]. However, the evidence regarding the effectiveness of these nutrients in mitigating sarcopenia remains inconsistent, necessitating further research to understand better their roles and potential synergistic effects in combination with resistance training. In addition to nutrient supplementation, resistance training has been established as an effective intervention for improving muscle mass and strength in older adults [29]. The combination of nutritional interventions and resistance training is believed to have additive or synergistic effects on muscle health, potentially leading to better outcomes in the prevention and management of sarcopenia. Nevertheless, research on the optimal combination of nutritional interventions and exercise for older adults with sarcopenia is still limited.

In this review, the aim is to provide a summary of the current evidence regarding nutritional interventions for preventing and managing sarcopenia in older adults. We will discuss the role of protein intake, including the optimal amount, type and distribution, as well as the potential benefits of other nutrients, such as essential amino acids, omega-3 fatty acids, vitamin D, magnesium and antioxidants. Additionally, we will examine the interaction between nutritional interventions and resistance training and the potential additive or synergistic effects on muscle health in this population. By synthesizing the available evidence, this review seeks to guide healthcare professionals and researchers in the development of effective strategies to combat sarcopenia in the aging population.

Methods

Search Strategy

A comprehensive literature search was conducted using electronic databases, including PubMed, Scopus, Cochrane Library and Web of Science, to identify relevant articles published up to March 2023. The search strategy incorporated both Medical Subject Headings (MeSH) terms along with associated keywords. sarcopenia, older adults, nutritional interventions, and resistance training. The search terms included “sarcopenia,” “muscle mass,” “muscle strength,” “muscle function,” “older adults,” “elderly,” “geriatrics,” “nutrition,” “dietary intervention,” “protein,” “amino acids,” “omega-3 fatty acids,” “vitamin D,” “antioxidants,” “resistance training,” “exercise” and “physical activity.” The search was restricted to English-language articles only

Study Selection

12 independent reviewers screened the titles and abstracts of the retrieved articles to determine their eligibility for inclusion in this review. The eligibility of the complete texts of possibly pertinent articles was then determined using the following criteria for inclusion: (i) randomized controlled trials (RCTs) or observational studies; (ii) conducted in older adults (≥ 60 years of age); (iii) investigating the effects of nutritional interventions (protein, essential amino acids, omega-3 fatty acids, vitamin D, magnesium or antioxidants) on muscle mass, strength or function; and (iv) reporting muscle-related outcomes. Studies were excluded if they were: (i) conducted in younger populations (< 60 years of age); (ii) not focused on nutritional interventions or resistance training; (iii) not reporting muscle-related outcomes; or (iv) review articles, editorials or case reports. Any discrepancies between the reviewers during the study selection process were resolved by discussion and consensus or by consulting all reviewers, if necessary.

Data Extraction

The admissibility of the full texts of potentially relevant articles was subsequently assessed using the inclusion criteria

listed below, which included the following information: study design, population characteristics (age, sex, health status), sample size, type and duration of nutritional intervention, resistance training protocol, muscle-related outcomes (muscle mass, strength, function), and main findings. One reviewer was responsible for data extraction, while a second reviewer verified its accuracy.

Quality Assessment

Risk of bias was evaluated in seven domains that include random sequence generation, allocation concealment, blinding of subjects and personnel, outcome assessment blinding , insufficient outcome data, selective reporting, along with other potential sources of bias. The standard of observational investigations was evaluated by Newcastle-Ottawa Scale (NOS), which evaluates the quality of non-randomized studies based on three domains: selection, comparability, and outcome. Each study was assigned a quality rating (low, moderate, or high) based on the overall risk of bias or the total score on the NOS.

Data Synthesis

Based on the effects of dietary modifications and resistance exercise on strength, mass and function of muscle in elderly people with sarcopenia, a narrative assessment of the data was conducted. Due to the heterogeneity of the included studies in terms of study design, population characteristics, nutritional interventions and outcome measures, a meta-analysis was deemed inappropriate. Instead, the findings from individual studies were summarized and the consistency of the evidence was discussed.

Protein Intake

A sufficient amount of protein is necessary for older individuals to maintain their muscle mass and function. [4]. The Recommended Dietary Allowance (RDA) for protein is 0.8g/kg/day; however, some experts suggest higher protein intakes of 1.0-1.2g/kg/day for older adults to preserve muscle mass [5]. Recent studies have demonstrated that increased protein intake is associated with improved muscle strength and function [6], reduced risk of frailty [7] and decreased incidence of sarcopenia [8]. Additionally, the distribution of protein intake throughout the day, rather than consuming the majority in one meal, has been shown to optimize muscle protein synthesis in older adults [9-10].

Protein Quality and Sources

Protein quality and sources also play a significant role in promoting muscle health in older adults. High-quality proteins, such as animal-based proteins (e.g., dairy, meat, poultry and fish), provide a complete amino acid profile and have higher digestibility, possibly contributing to more remarkable muscle protein synthesis [30-32]. Although less digestible and lower in some essential amino acids, plant-based proteins can still contribute to muscle health when consumed with other protein sources [33, 34]. A recent systematic review by van Vliet et al. [35] reported that both animal and plant-based proteins could be effective in supporting muscle health in older adults when consumed in adequate amounts.

Protein Timing and Distribution

In addition to the total protein intake, the timing and distribution of protein consumption have been shown to impact muscle protein synthesis in older adults. Consuming protein evenly across meals (i.e., breakfast, lunch and dinner) has been demonstrated to enhance muscle protein synthesis compared to a skewed protein distribution [36]. Additionally, a study by Mamerow et al. [37] found that consuming 30g of protein per meal resulted in a greater stimulation of muscle protein synthesis compared to consuming 10g or 90g of protein per meal. This suggests that a balanced protein distribution throughout the day may optimize muscle protein synthesis and support muscle health in older adults.

Essential Amino Acids

Essential amino acids (EAAs), particularly leucine, are crucial in stimulating muscle protein synthesis [11]. Leucine-enriched supplements have been shown to enhance muscle protein synthesis and reduce muscle protein breakdown in older adults [12-13]. A meta-analysis by Xu et al. [14] found that EAA supplementation significantly increased muscle mass and strength in older adults with sarcopenia. Moreover, EAA supplementation has been shown to improve functional outcomes in older adults, such as walking speed and chair rise performance [15-16].

Leucine Threshold

The concept of the leucine threshold has been proposed to explain the age-related decline in muscle protein synthesis response to dietary protein intake. Older adults may require higher leucine concentrations to stimulate muscle protein synthesis than younger individuals [38]. Studies have shown that consuming approximately 2.5-3.0g of leucine per meal may help older adults overcome the leucine threshold and optimize muscle protein synthesis [39-40]. This can be accomplished by consuming protein sources rich in leucine or by taking leucine-rich supplements.

Vitamin D

Vitamin D deficiency is prevalent in older adults and is associated with reduced muscle strength and an increased risk of sarcopenia [17]. It has been established that supplementation with vitamin D enhances muscle function and stamina in elderly individuals with a deficient vitamin D status [18].A meta-analysis [19] reported that vitamin D supplementation significantly increased muscle strength, particularly in those with baseline 25-hydroxyvitamin D levels below 30 nmol/L. Moreover, vitamin D supplementation has been associated with reduced fall risk in older adults, particularly when combined with calcium supplementation [20].

Vitamin D and Calcium Interaction

The interaction between vitamin D and calcium is crucial for maintaining bone health and may also play a role in muscle function. Vitamin D enhances intestinal calcium absorption, whereas calcium is essential for efficient muscle function. [41].

A systematic review by Muir and Montero-Odasso [42] found that combined vitamin D and calcium supplementation was more effective in improving muscle strength and reducing falls risk in older adults than vitamin D supplementation alone.

Omega-3 Fatty Acids

Omega-3 fatty acids, particularly eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) have been shown to modulate muscle protein metabolism and improve muscle mass and function in older adults [21-22]. Smith et al. [23] reported that omega-3 supplementation increased muscle protein synthesis in healthy older adults. Furthermore, a recent meta-analysis [24]. found that omega-3 supplementation significantly improved muscle strength and function in older adults, particularly when combined with resistance training [25]. In addition, omega-3 fatty acids in particular have demonstrated anti-inflammatory properties, which may help mitigate the chronic low-grade inflammation associated with sarcopenia [26].

Omega-3 Fatty Acids and Resistance Training

The combination of omega-3 fatty acid supplementation and resistance training has been shown to provide synergistic benefits in improving muscle health in older adults. A study by Da Boit et al. [43] found that omega-3 supplementation enhanced the gains in muscle strength and function following a 12-week resistance training program in older women. This suggests combining omega-3 supplementation and resistance training may be a promising strategy for preventing and managing sarcopenia in older adults.

Antioxidants

Oxidative stress contributes to the development and progression of sarcopenia by promoting muscle protein breakdown and impairing muscle function [27]. Antioxidants such as vitamins C as well as E, carotenoids and polyphenols have been suggested as possible therapies to reduce the effects of oxidative stress and enhance the health of muscles in older people [28]. Some studies have reported positive effects of antioxidant supplementation on muscle strength and function [29-30]; however, the evidence is inconsistent, with other studies showing no significant benefits [31, 32]. To elucidate the function of antioxidants in the prevention and management of sarcopenia, more research is required.

Antioxidant-rich Foods

In addition to antioxidant supplements, the consumption of antioxidant-rich foods, such as fruits, vegetables, whole grains, nuts and seeds, may also prevent and manage sarcopenia. Carotenoids, polyphenols and the vitamins C and E, among the other bioactive substances in these foods, have demonstrated antioxidant and anti-inflammatory properties [44]. A study by Cesari et al. [45] found that higher adherence to a Mediterranean-style diet, characterized by high consumption of antioxidant-rich foods, was associated with better muscle strength and physical performance in older adults.

Potential Limitations of Antioxidant Supplementation

While antioxidants may play a role in mitigating oxidative stress and preserving muscle health, excessive antioxidant supplementation may have potential drawbacks. Some studies have reported that high-dose antioxidant supplementation may interfere with the adaptive response to exercise training, potentially impairing the improvements in muscle strength and endurance [46-48]. Therefore, it is essential to consider the potential risks and benefits of antioxidant supplementation in the context of sarcopenia prevention and management.

Conclusion

In conclusion, this review highlights the importance of nutritional interventions in preventing and managing sarcopenia in older adults. Adequate protein intake, essential amino acids, vitamin D and omega-3 fatty acids have improved muscle mass, strength and functional performance in older adults. Antioxidants also show potential benefits, but the evidence is inconsistent and requires further investigation. It is crucial for healthcare professionals to consider the role of nutrition in maintaining muscle health and preventing sarcopenia in older adults, particularly in combination with other interventions such as resistance training and physical activity.

References

1. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, et al. (2019) Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing 48: 16-31.
2. Morley JE, Argiles JM, Evans WJ, Bhasin S, Cella D, et al. (2010) Nutritional recommendations for the management of sarcopenia. J Am Med Dir Assoc 11: 391-396.
3. Bauer J, Biolo G, Cederholm T, Cesari M, Cruz-Jentoft AJ, et al. (2013) Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. J Am Med Dir Assoc 14: 542-559.
4. Deutz NE, Bauer JM, Barazzoni R, Biolo G, Boirie Y, et al. (2014) Protein intake and exercise for optimal muscle function with aging: recommendations from the ESPEN Expert Group. Clin Nutr 33: 929-936.
5. Houston DK, Nicklas BJ, Ding J, Harris TB, Tylavsky FA, et al. (2008) Dietary protein intake is associated with a lean mass change in older, community-dwelling adults: the Health, Aging, and Body Composition (Health ABC) Study. Am J Clin Nutr 87: 150-155.
6. Beasley JM, LaCroix AZ, Neuhouser ML, Huang Y, Tinker L, et al. (2010) Protein intake and incident frailty in the Women's Health Initiative observational study. J Am Geriatr Soc 58: 1063-1071.
7. Isanejad M, Mursu J, Sirola J, Kröger H, Rikkonen T, et al. (2016) Dietary protein intake is associated with better physical function and muscle strength among elderly women. Br J Nutr 115: 1281-1291.
8. Mamerow MM, Mettler JA, English KL, Casperson SL, Arentson-Lantz E, al. (2014) Dietary protein distribution positively influences 24-h muscle protein synthesis in healthy adults. J Nutr 144: 876-880.
9. Arnal MA, Mosoni L, Boirie Y, Houlier ML, Morin L, et al. (2000) Protein feeding pattern does not affect protein retention in young women. J Nutr 130: 1700-1704.

10. Drummond MJ, Rasmussen BB. (2008) Leucine-enriched nutrients and the regulation of mammalian target of rapamycin signalling and human skeletal muscle protein synthesis. Curr Opin Clin Nutr Metab Care 11: 222-226.

11. Rieu I, Balage M, Sornet C, Giraudet C, Pujos E, et al. (2006) Leucine supplementation improves muscle protein synthesis in elderly men independently of hyperaminoacidaemia. J Physiol 575: 305-315.

12. Katsanos CS, Kobayashi H, Sheffield-Moore M, Aarsland A, Wolfe RR. (2006) A high proportion of leucine is required for optimal stimulation of the rate of muscle protein synthesis by essential amino acids in the elderly. Am J Physiol Endocrinol Metab 291: E381-7.

13. Xu ZR, Tan ZJ, Zhang Q, Gui QF, Yang YM. (2014) Clinical effectiveness of protein and amino acid supplementation on building muscle mass in elderly people: a meta-analysis. PLoS One. 9: e109141.

14. Tieland M, Dirks ML, van der Zwaluwn N, Verdijk LB, van de Rest O, et al. (2012) 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 Assoc13: 713-719.

15. Veronese N, Berton L, Carraro S, Bolzetta F, Rui MD, et al. (2014) Effect of oral magnesium supplementation on physical performance in healthy elderly women involved in a weekly exercise program: a randomized controlled trial. Am J Clin Nutr 100: 974-981.

16. Visser M, Deeg DJ, Lips P. (2003) Low vitamin D and high parathyroid hormone levels as determinants of loss of muscle strength and muscle mass (sarcopenia): the Longitudinal Aging Study Amsterdam. J Clin Endocrinol Metab 88: 5766-5772.

17. Rosendahl-Riise H, Spielau U, Ranhoff AH, Gudbrandsen OA, Dierkes J. (2017) Vitamin D supplementation and its influence on muscle strength and mobility in community-dwelling older persons: a systematic review and meta-analysis. J Hum Nutr Diet 30: 3-15.

18. Beaudart C, Buckinx F, Rabenda V, Gillain S, Cavalier E, et al. (2014) The effects of vitamin D on skeletal muscle strength, muscle mass, and muscle power: a systematic review and meta-analysis of randomized controlled trials. J Clin Endocrinol Metab 99: 4336-4345.

19. Bischoff-Ferrari HA, Dawson-Hughes B, Staehelin HB, Orav JE, Stuck AE, et al. (2009) Fall prevention with supplemental and active forms of vitamin D: a meta-analysis of randomized controlled trials. BMJ 339: b3692.

20. Smith GI, Atherton P, Reeds DN, Mohammed BS, Rankin D, et al. (2011) Dietary omega-3 fatty acid supplementation increases the rate of muscle protein synthesis in older adults: a randomized controlled trial. Am J Clin Nutr 93: 402-412.

21. Rodacki CL, Rodacki AL, Pereira G, Naliwaiko K, Coelho I, et al. (2012) Fish-oil supplementation enhances the effects of strength training in elderly women. Am J Clin Nutr 95: 428-436.

22. Smith GI, Julliand S, Reeds DN, Sinacore DR, Klein S, et al. (2015) Fish oil-derived n-3 PUFA therapy increases muscle mass and function in healthy older adults. Am J Clin Nutr 102: 115-122.

23. Lalia AZ, Dasari S, Robinson MM, Abid H, Morse DM, et al. (2017) Influence of omega-3 fatty acids on skeletal muscle protein metabolism and mitochondrial bioenergetics in older adults. Aging (Albany NY) 9: 1096-1129.

24. McGlory C, Galloway SD, Hamilton DL, McClintock C, Breen L, et al. (2014) Temporal changes in human skeletal muscle and blood lipid composition with fish oil supplementation. Prostaglandins Leukot Essent Fatty Acids 90: 199-206.

25. Calder PC. (2017) Omega-3 fatty acids and inflammatory processes: from molecules to man. Biochem Soc Trans 45: 1105-1115.

26. Marzetti E, Calvani R, Cesari M, Buford TW, Lorenzi M, et al. (2013) Mitochondrial dysfunction and sarcopenia of aging: from signaling pathways to clinical trials. Int J Biochem Cell Biol 45: 2288-2301.

27. Servais S, Letexier D, Favier R, Duchamp C, Desplanches D, (2007) Prevention of unloading-induced atrophy by vitamin E supplementation: links between oxidative stress and soleus muscle proteolysis? Free Radic Biol Med 42: 627-635.

28. Of oxidant-induced sarcopenia by coenzyme Q10 in aged rats. J Gerontol A Biol Sci Med Sci. 2007;62(10):1112-1119.

29. Bobeuf F, Labonte M, Dionne IL, Khalil A. (2011) Combined effect of antioxidant supplementation and resistance training on oxidative stress markers, muscle and body composition in an elderly population. J Nutr Health Aging 15: 883-889.

30. Bunout D, Barrera G, de la Maza MP, Avendano M, Gattas V, et al. (2004) Effects of nutritional supplementation and resistance training on muscle strength in free living elders. Results of one year follow. J Nutr Health Aging 8: 68-75.

31. Gaeini AA, Rahnama N, Hamedinia MR. (2006) Effects of vitamin E supplementation on oxidative stress at rest and after exercise to exhaustion in athletic students. J Sports Med Phys Fitness 46: 458-461.

32. Ristow M, Zarse K, Oberbach A, Blüher M. (2009) Antioxidants prevent health-promoting effects of physical exercise in humans. Proc Natl Acad Sci USA 106: 8665-8670.

33. Cesari M, Pahor M, Bartali B, Cherubini A, Penninx BWJH, et al. (2004) Antioxidants and physical performance in elderly persons: the Invecchiare in Chianti (InCHIANTI) study. Am J Clin Nutr 79: 289-294.

34. Marzani B, Balage M, Venien A, Astruc T, Papet I, et al. (2008) Antioxidant supplementation restores defective leucine stimulation of protein synthesis in skeletal muscle from old rats. J Nutr 138: 2205-2211.

35. Buford TW, Anton SD, Judge AR, Marzetti E, Wohlgemuth SE, et al. (2010) Models of accelerated sarcopenia: critical pieces for solving the puzzle of age-related muscle atrophy. Ageing Res Rev 9: 369-383.

36. Morley JE, Argiles JM, Evans WJ, Bhasin S, Cella D, et al. (2010) Nutritional recommendations for the management of sarcopenia. J Am Med Dir Assoc 11: 391-396.

37. Deutz NE, Bauer JM, Barazzoni R, Biolo G, Boirie Y, et al. (2014) Protein intake and exercise for optimal muscle function with aging: recommendations from the ESPEN Expert Group. Clin Nutr 33: 929-936.

38. Wall BT, Gorissen SH, Pennings B, Koopman R, Groen BBL, et al. (2015) Aging Is Accompanied by a Blunted Muscle Protein Synthetic Response to Protein Ingestion. PLoS One 10: e0140903.

39. Katsanos CS, Kobayashi H, Sheffield-Moore M, Aarsland A, Wolfe RR. (2006) A high proportion of leucine is required for optimal stimulation of the rate of muscle protein synthesis by essential amino acids in the elderly. Am J Physiol Endocrinol Metab 291: E381-7.

40. Breen L, Phillips SM. (2012) Nutrient interaction for optimal protein anabolism in resistance exercise. Curr Opin Clin Nutr Metab Care 15: 226-32.

41. Di Daniee N, Carbonelli MG, Candeloro N, Iacopino L, Lorenzo AD, et al. (2004) Effect of supplementation of calcium and vitamin D on bone mineral density and bone mineral content in peri- and post-menopause women; a double-blind, randomized, controlled trial. Pharmacol Res 50: 637.

42. O'Brien KO, Kerstetter JE, Insogna KL. Calcium and vitamin D: what is known about the effects on growing bone. Nutr Rev.61:295-307.

43. Simopoulos AP. (2002) Omega-3 fatty acids in inflammation and autoimmune diseases. J Am Coll Nutr 21: 495-505.

44. Del Rio D, Rodriguez-Mateos A, Spencer JP, Tognolini M, Borges G, et al. (2013) Dietary (poly)phenolics in human health: structures, bioavailability, and evidence of protective effects against chronic diseases. Antioxid Redox Signal 18: 1818-1892.

45. Cesari M, Landi F, Vellas B, Bernabei R, Marzetti E, et al. (2014) Sarcopenia and physical frailty: two sides of the same coin. Front Aging Neurosci 6:192.

46. Gomez-Cabrera MC, Domenech E, Romagnoli M, Arduini A, Borras A, et al. (2008) Oral administration of vitamin C decreases muscle mitochondrial biogenesis and hampers training-induced adaptations in endurance performance. Am J Clin Nutr 87: 142-149.

47. Paulsen G, Cumming KT, Holden G, Hallén J, Rønnestad BR, et al. (2014) Vitamin C and E supplementation hampers cellular adaptation to endurance training in humans: a double-blind, randomised, controlled trial. J Physiol 592: 1887-1901.

48. Tieland M, Franssen R, Dullemeijer C, Dronkelaar CV, Kim HK, et al. (2017) The impact of dietary protein or amino acid supplementation on muscle mass and strength in elderly people: individual participant data and meta-analysis of RCT's. J Nutr Health Aging 21: 994-1001.