Nutritional Approaches for Sarcopenia

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Abstract

Nutritional approaches to the prevention or treatment of sarcopenia have previously focused on protein. However, several micronutrient vitamins and minerals including the B group of vitamins, vitamins C, E and the carotenoids and minerals such as iron, magnesium, and selenium, may exert effects on sarcopenia or sarcopenic factors (skeletal muscle mass, function or strength). These may be indirect through effects on protein synthesis or direct through effects on mechanisms of aging for skeletal muscle such as inflammaging, counteracting reactive oxygen species, and mitochondrial dysfunction. Other direct mechanisms also exist including the involvement of vitamin C in formation of collagen, a structural component of skeletal muscle, and of carnitine, required for muscle contraction. Better quality dietary intakes, as found with the Mediterranean Dietary pattern and other healthy eating patterns, may also be beneficial to prevention or treatment of sarcopenia though effects on skeletal muscle mass or function during aging. However, current research into the influence of micronutrient vitamins and minerals and optimal dietary patterns for the prevention or treatment of sarcopenia and loss of skeletal muscle mass and function with age is limited, and further research is required.

Keywords: sarcopenia, skeletal muscle mass, skeletal muscle strength, nutrients, dietary patterns, vitamins, minerals trace elements

Introduction

Sarcopenia is associated with the conditions of frailty, falls, osteoporosis and risk of fracture, as well as with malnutrition (1-3). In addition, there are metabolic consequences of loss of skeletal muscle mass during aging which include reduced energy expenditure, which affects obesity as well as glucose dysregulation, effects of glycaemic control, and the onset of type-2 diabetes (1, 4). The loss of, and changes to, skeletal muscle mass with aging also contribute to age-associated reduction in utilisation of dietary protein and fat (1).

In this chapter the terms ‘sarcopenic factors’ refer to the loss of skeletal muscle strength or function or loss or changes in skeletal muscle mass or combinations of these. The term ‘fat free mass’ (FFM) is used, since FFM is often measured and used as a proxy for skeletal muscle mass (SMM). Since FFM increases both with increased body weight and size, measurements of FFM in human studies are scaled for body size either by height (skeletal

muscle mass index – SMI), percentage of total body weight or by BMI ($FFM/_{BMI}$, FFM divided by BMI).

Nutrition is a modifiable lifestyle factor that can interact with the mechanisms of loss of skeletal muscle mass and function, as well as with the mechanisms of aging, and previous research has focused on a number of nutrients that are relevant for skeletal muscle physiology and metabolism. However, the major focus to date has been on protein intake. Lesser focus has been centred on the micronutrient vitamins and minerals, and on intake of fats and fatty acids. There have also been some recent studies examining the relevance of patterns of dietary intake. The relevance of dietary patterns may be due to the individual nutrients such as protein or the micronutrients which are associated with the optimal dietary patterns as well as to the synergistic effects of these nutrients and the foods within these dietary patterns.

This chapter covers the foods, nutrients and dietary patterns that have been linked to either prevention or treatment of sarcopenia and suggests areas for future research in relation to aspects of nutrition and prevention of sarcopenia.

Nitrogen Balance and Exogenous Antioxidants

Maintaining the balance between the continuous anabolism and catabolism of protein occurring in the body and thus ensuring *nitrogen balance* does not become negative is crucial for conserving skeletal muscle during aging (1, 5-8). Thus, factors that interfere with this process such as inflammaging and insulin resistance have an adverse impact on nitrogen balance. There is also an increase in *anabolic resistance*, i.e., lower myofibrillar synthesis of protein, during aging.

A number of micronutrient vitamins or minerals are known to act as exogenous antioxidants or help counteract the increased circulating concentrations of inflammatory cytokines associated with aging, and thus may be beneficial to muscle health and prevention of sarcopenia. These include vitamins C, E, and D, the carotenoids, and the minerals magnesium, selenium, and zinc, but there is also evidence for specific dietary patterns being relevant. Specific relationships between the mechanisms of aging with nutrients and patterns of dietary intake are described in the following sections.

Important dietary factors

Protein

Skeletal muscle is the main reserve of protein in the body and protein is required to maintain this reserve of protein in the muscle through protein synthesis. It is thus logical that there has been extensive research into the relevance of protein intake to conservation and prevention of sarcopenia during aging (2, 3, 6, 9, 10). As the relevance of protein to maintenance of sarcopenic factors and prevention of sarcopenia during aging has been studied extensively a summary of the importance of protein as well, as the most recent developments in this area of research are covered in this chapter. Readers may refer to the earlier work in the following publications (2, 3, 6, 9, 10).

A recent review of nutritional interventions to improve sarcopenic factors and sarcopenia found that the evidence was generally not of high quality and was insufficient to establish with any certainty the effects of supplementation with either protein, essential amino acids or creatine, or ß-hydroxy-ß-methylbutyrate (11). The authors determined that the level of evidence supporting most recommendations was low to moderate, but that the best evidence

related to the amino acid leucine which has a significant effect on muscle mass in older people with sarcopenia. However, the review also recommended that increases in protein intake designed to increase muscle mass and strength should be accompanied by resistance exercise programmes (11). By contrast, another systematic review found that protein did not augment the effects of resistance exercise on skeletal muscle mass and function in older people (12). However, most recent research and clinical recommendations have noted that reducing the decline in sarcopenic factors during aging requires that the increase in intake of protein should accompanied by resistance exercise (9, 13-16). This is because an increase in physical activity synergises with increased protein intake to affect regulation of protein synthesis.

Variability in response to interventions with dietary protein

The limited effectiveness of interventions with protein in older people and the variability in response to interventions with dietary protein may be due to a number of reasons including the anabolic resistance that occurs during aging (10, 16). Recent research studied the effect of protein supplementation on muscle disuse in young men and found substantial declines in muscle mass and myofibrillar protein synthesis rates during inactivity (17). The authors also found that the high intake of protein used in their intervention, 1.6g/kg body weight per day, did not attenuate the decreases in quadriceps muscle volume that occurred during inactivity when compared with the control interventions with low, or no, protein intake; the control groups received either 0.5g or 0.15g/kg/d, respectively (9, 17). Therefore, increased protein intake did not counteract the reduced myofibrillar protein synthesis rates that occurred during inactivity, even in young men. Other recent work has also demonstrated that the incorporation of amino acids such as leucine into skeletal muscle, during muscle protein synthesis, occurs only for a period of 2-3 hours in a rested state. This is known as the *muscle full phenomenon* which means that muscle becomes unresponsive to higher doses of protein intake after a short period following protein consumption (14). This phenomenon may also explain the limited effectiveness of increases in protein intake that are designed to overcome the anabolic resistance to protein synthesis in muscle during older age.

Other factors such as sex and race potentially also influence the effectiveness of protein intake in interventions to improve sarcopenic factors during aging. Recent research found that associations between protein intake and sarcopenic factors differed according to sex and race, in a longitudinal study (18).

Some of the variability in response to interventions with protein may also be due to the type of protein used since protein from animal sources such as meat or dairy foods is more biologically available than protein from vegetable sources such as pulses (beans and lentils) and vegetables (19). Animal sources of protein have a profile of amino acids that is higher in indispensable amino acids, including the branch chain amino acids that stimulate the production of mTOR that is required to increase the synthesis of protein (7). However, a recent population study, The NU-AGE Study, found an interaction between plant and animal protein intakes on the risk of sarcopenia (20). Though the risk of sarcopenia decreased with increased intakes of total protein, this decrease was greater when intakes of vegetable protein were also higher (20).

A number of the dietary interventions with protein-containing foods have found variability in sarcopenic outcomes which may be due to not only the protein composition of the foods that were administered, but also to the associated nutrients in the foods. For instance, one intervention in an Australian population that was accompanied by resistance exercise training found positive effects of a red meat intervention on lean muscle mass in women when

compared with a control group (21). However, the increase in protein intake in the group provided with red meat was also accompanied by a significant increase in intake of zinc which may also have increased the effectiveness of the intervention. In a further study of similar design, that also included men, no significant effect of increased intake of meat was found. However, a similar increase in zinc intake occurred during the study that was also associated with the group with increased meat intake (22).

Finally, variation in the interaction between protein intake and the composition of the microbiome in the gut may occur. Thus, it has been hypothesised that the gut microbiome may modulate individual response to dietary protein and thus have effects on sarcopenia and sarcopenic factors (23, 24).

Intake of dietary amino acids

To date there is little data on intakes of amino acids in general populations of middle and older age who are at risk of sarcopenia. In recent unpublished research, we investigated the full range of amino acids in the diet and contributors to sarcopenia, skeletal muscle mass, and function, and found a number of differences in the associations between individual amino acids and sarcopenic factors in both younger and older women in the UK-Twin cohort.

Current clinical recommendations for protein intake

Current recommendations regarding protein intake during aging include increasing total protein intakes, to between 1.0g and 1.5g protein per kg body weight per day, for individuals older than 65 years (10). However, other reviews and dietary recommendations do not recommend intakes higher than 1.0g protein/kg/day in older age groups (25). It has also been suggested that ensuring protein intake is balanced across meal occasions is important in older people, to ensure maximal utilisation of protein and muscle protein synthesis (10, 15) .

In summary, adequate protein is undoubtably important for the maintenance of skeletal muscle function and structure during aging, but to date the evidence is mixed for the effectiveness of dietary interventions with protein to rectify or prevent sarcopenia. Accompanying increases in protein intake with sufficient micronutrient vitamins and minerals or as part of improvements in overall dietary intakes may be important in the prevention and treatment of sarcopenia, as described in the following sections.

The B group vitamins

The B vitamins are a diverse group of vitamins with important biological functions. Several of the B vitamins are highly relevant to muscle, acting as cofactors in processes involved in muscle synthesis and as neurotrophic agents that maintain neural integrity and function (26, 27). In addition, deficiencies of a number of B vitamins result in neuromuscular problems (e.g. beri beri) and neurological symptoms (e.g. pellagra). So, maintenance of vitamin B status may be important for prevention of sarcopenia. However, very few studies have investigated relationships between dietary intake of B vitamins or circulating blood concentrations (26). One study in the Netherlands found associations between dietary folate, vitamin B_6, and B_{12} intakes and physical function in older adults in the Netherlands (28). Another, in adults older than 65 years, found lower intakes of vitamin B_6 and folic acid in adults with sarcopenia compared with those without (29). Two further studies found that lower intakes and concentrations of circulating vitamin B_{12} were associated with low SMI, sarcopenia or dynapenia (30, 31). Lastly, in unpublished work from our group, using the Twins UK Study of adult women aged 18-79 years, significant positive associations were

evident in multivariable models between dietary B vitamin intakes (niacin, folate, pantothenate, riboflavin, thiamine, and B_6) and measures of fat free mass. Similarly, positive trends were observed across niacin, folate, pantothenate, riboflavin, and thiamine dietary intakes and leg explosive power (measured using a Nottingham Power Rig). Therefore, although more research is required, the current evidence suggests that dietary intake of B vitamins is important for both skeletal muscle mass and function.

Vitamin C

Vitamin C has several mechanistic functions relevant to skeletal muscle metabolism and physiology, which could prevent age-related loss of skeletal muscle. Vitamin C in muscle is involved in synthesis of carnitine, an important factor involved in energy production, and collagen, an essential structural component of muscle. (32, 33). It also has a strong capability to act as an electron donor. Reactive oxygen species (ROS) are produced during normal oxidative metabolism in muscle, but capable of cellular damage if uncontrolled (34). Under normal physiological conditions, the presence of ROS is controlled by antioxidant and enzymatic defence systems including superoxide dismutase and glutathione peroxidase as well as antioxidants from the diet (34, 35). Age-related increases in ROS due to mitochondrial dysfunction, modification to enzymatic defences, and changes to muscle fibres, may lead to cellular damage in muscle, as does the age-related increase in circulating concentrations of inflammatory cytokines (34, 36). If in sufficient supply, the antioxidant capacity of vitamin C may therefore help to reduce oxidative damage to muscle, as well as reducing potentially damaging concentrations of inflammatory cytokines in the circulation (36). In previous observational studies positive associations between dietary vitamin C and measures of skeletal muscle function were found in the Italian InCHIANTI Study, and for women only in the UK (37-40). One study examined both FFM and muscle function with intake as well as circulating vitamin C, finding positive associations between measures of physical function but not FFM (39). A further study found intake of vitamin C was associated with FFM after 2.6 years of follow up (37). More recent observational evidence in women of all ages found that higher intakes of vitamin C were associated with significantly higher indices of FFM and leg explosive power (41). The differences between the highest intakes in quintile 5 versus those in quintile 1 ranged between 2.0% and 12.8% ($P < 0.01$-0.02) (41). Further observational study evidence shows positive associations of both dietary and circulating vitamin C with measures of skeletal muscle mass in middle- and older-aged men and women (42). Overall, the evidence thus points towards potential protective effects of vitamin C on measures of skeletal muscle mass and function.

Vitamin D

Vitamin D may be protective for development of sarcopenia through a number of direct or indirect mechanisms (7). Receptors for vitamin D are found in skeletal muscle, but discussion is still ongoing as to the importance of this and the relevance to aging, such as whether levels or expression of these receptors decline during aging and whether they are important for the morphological changes that affect both skeletal muscle mass and function during aging (43). Known roles of vitamin D are participation in myogenesis, cell proliferation, differentiation and regulation of cell signalling cascades, as well as signalling for potential genomic targets (44). The functional effects of vitamin D in muscle may be through calcium and phosphate handling and signalling, particularly in relation to muscle strength and contraction (43). Deficiency of vitamin D leads to muscle weakness which is one of the symptoms found in rickets, in children, as well as in adults where it is accompanied by muscle pain, in the condition of osteomalacia (43).

A recent systematic review summarised the evidence for supplementation of vitamin D in community dwelling older adults aged 65 years and older in relation effects on muscle strength and function (45). Studies included were those testing supplementation with vitamin D alone, or alongside calcium supplementation. Of the 15 studies included in the review, the majority found no improvement in muscle strength and mobility after administration of vitamin D with or without calcium supplements. In the meta-analyses performed, non-significant changes in hand grip strength were found in the seven studies analysed and a small, but significant, increase in the timed-up and-go test of 0.3 s (95% CI = 0.1 to 0.5 s) in five studies. However, there was a high degree of heterogeneity between the studies. The overall conclusion was supplementation with vitamin D or with calcium did not result in improvements in skeletal muscle function (45). A more recent intervention study with vitamin D in men aged 60 years and over, with low concentrations of circulating vitamin D, found no effect on lower-extremity power, strength or lean mass over a period of 12 months of supplementation (46). Further recent intervention studies, over shorter periods of 3-6 months, found either effects on appendicular skeletal muscle mass, but not grip strength (47), or improvements in skeletal muscle mass, but not strength.

There is also limited evidence that co-administration of vitamin D alongside the amino acid leucine is more likely to improve the efficacy of leucine supplementation on skeletal muscle mass (48). It is clear from the existing evidence that vitamin D plays a role in maintenance of skeletal muscle mass strength or function, but in older populations the effects of supplementation on sarcopenic outcomes is mixed. Differences in the findings of intervention trials with vitamin D may be due to initial concentrations of circulating vitamin D, as well as to dosages used in the interventions, the age of the intervention groups, and duration of the studies.

Vitamin E

Vitamin E, like vitamin C, has the potential to act as an antioxidant, preventing build-up of free radicals in cell membranes and in plasma lipoproteins. Vitamin E consists of two classes of molecules, tocopherols and tocotrienols, which are categorised according to the saturation of their phytyl tail groups. Observational data of individuals 65 years or over has shown a positive association between plasma alpha-tocopherol concentration and knee extension strength and physical performance, and between gamma-tocopherol and physical performance (49, 50). In addition, low circulating vitamin E concentrations have been identified in frail individuals, compared to non-frail individuals, suggesting a lack of vitamin E may be linked to the transition from non-frail to frail (51). Other cross-sectional analyses, of data from women aged 18-79 years in the Twins UK cohort, found that higher intake of vitamin E was associated with higher indices of skeletal muscle mass, but not function (41). Further work in the EPIC-Norfolk Study has found potentially protective associations in fat free mass with higher intakes of dietary vitamin E or circulating concentrations of α-tocopherol (52).

The observational data are supported by mechanistic evidence from a number of animal studies, which demonstrate the role of vitamin E as an antioxidant and anti-inflammatory agent. This includes evidence that: in a rat model vitamin E prevents increased nuclear translocation of NF-kB, increased expression of chemokines, and the resultant leukocyte infiltration associated with H_2O_2-induced oxidative stress (53); and in a mouse model vitamin E reduces lipopolysaccharide (LPS)-induced inflammation by modulating the LPS-induced, and NF-kB mediated, upregulation of IL-6 gene and protein expression (54).

Carotenoids

The carotenoid family of phytochemical vitamins are found in yellow, orange and green leafy fruits and vegetables and include β-carotene, β-cryptoxanthin, lycopene, and lutein and zeaxthanin. These carotenoids function as exogenous antioxidants and anti-inflammatory agents thus interacting with the mechanisms of muscle aging.

Relatively few studies have investigated the relevance of total carotene, carotenoid intakes, or circulating concentrations, in relation to sarcopenia and sarcopenic factors. Two studies from a UK cohort found positive associations between higher intakes of carotene on grip strength or physical activity, with the latter finding of associations only in women (38, 40). Several studies also found protective associations with higher circulating concentrations of β-carotene and indices of knee strength or function, or rate of decline in walking speed (50, 52-58).

Few studies have investigated associations with more detailed dietary inakes of the individual carotenoids and sarcopenic factors. In the UK Twin cohort we found that higher intakes of total and individual carotenoids were significantly associated with indices of FFM and Leg Explosive Power with differences across quintiles of between 1.0–7.5% (42). The strongest associations for indices of FFM were found with α-carotene intake (Q5-Q1 0.24 kg/m2 ± 0.1 P-trend = 0.03), a 1.6% difference across quintiles. Significant associations were also found with FFM% for ß-cryptoxthanin and with FFM% and FFM_{BMI} for lutein and zeaxthanin, with interquintle differences ranging from 1.1 to 7.2% (41). LEP was associated significantly with carotenoid intakes, with the exception of α-carotene, with differences in LEP ranging from 6.3 to 7.5% when comparing extreme quintiles of carotenoid intakes (41). A previous study found that dietary carotenoid intake as total carotene, ß-cryptoxthanin, and combined lutein and zeaxanthin was positively associated with FFM, expressed as percentage body weight, in both men and women, with lycopene associated only in women (59). The greatest association was found for combined lutein and zeaxanthin in women with an interquintile difference of 2.5%. A more recent longitudinal analysis from the Framingham Cohort Study also found protective effects with higher intakes of total carotenoids, lycopene and combined lutein and zeathanin with annualised change in grip strenth or faster gait speed, over a period of follow up which ranged from 4.5 to 15.4 years (60). However, replication of the analyses in the Cardiovascular Heart Study found no associations between total carotenoid intake and either grip strength or gait speed (60). The research findings, though limited, indicate that future intervention studies with carotenoid containing foods are warranted.

Minerals: magnesium

Skeletal muscle acts as a major store of magnesium where it is important for energy metabolism, protein synthesis and turnover, transmembrane transport, and muscle contraction and relaxation (61, 62). Magnesium is also integral to function of the mitochondria thus influencing muscle performance through energy metabolism (ATP generation).

A number of observational studies have shown dietary magnesium intake, serum magnesium or muscle magnesium concentrations, are positively associated with measures of skeletal muscle mass (63, 64) and function (65). Magnesium supplementation has also been shown to increase the muscle strength young adults gained through exercise (66) and improve physical performance in older individuals (67). Lower magnesium intake has also been associated with sarcopenia (29, 30). However, the mechanisms by which magnesium may be acting in muscle are not fully understood. Cell-culture and animal studies have demonstrated that magnesium depletion can cause structural damage to muscle cells due to oxidative stress and disrupted calcium homeostasis (68). It has also been suggested that magnesium protects against inflammaging, a known risk factor for sarcopenia (7). Indeed, circulating concentrations of inflammatory cytokines, including C-reactive protein (CRP), IL-6, and TNF-α, have been

negatively associated with skeletal muscle measures of both mass and function in a number of studies (65, 69-71). Systematic review evidence also indicates that dietary magnesium intake is inversely associated with serum CRP concentration (72). Furthermore, it is relevant that age-related physiological decline in function of the gastrointestinal and renal systems may lead to an increased susceptibility of older individuals to develop low magnesium status (73).

Minerals and trace elements: calcium, iron, potassium, phosphorus, selenium and zinc

Although a number of minerals and trace elements such as selenium, zinc, potassium, iron, and phosphorus, play roles in muscle metabolism and function, comparatively little research has focused on this area (7, 74). The minerals calcium, potassium, and sodium are necessary for healthy muscle and nerve activity. Calcium is the main regulatory signalling molecule for skeletal muscle fibres. Also, low iron blood serum concentrations may be associated with poor physical performance. Phosphorus can lead to muscle weakness, and selenium deficiency is associated with several muscular diseases that also include symptoms of weakness. Both selenium and zinc potentially play a role in protecting skeletal muscle from oxidative damage, and zinc is also integral to protein synthesis and in animal studies zinc deficiency has been shown to impaired protein synthesis in skeletal muscle (75).

One observational study in older people found that higher iron, phosphorus and zinc intakes were associated with conservation of lean mass over a period of 2.6 years, indicating a potential role for minerals in sarcopenic factors or prevention of sarcopenia (37). A more recent systematic review identified only 6 studies investigating the role of minerals on prevention or treatment of sarcopenia in individuals, aged 65 years or over (74). Evidence was provided mainly from observational studies, finding that serum selenium and calcium intake were significantly associated with muscle mass, and selenium, iron, and zinc intakes were significantly and positively associated with physical performance in older adults (74). Also, selenium, calcium, and phosphorus intakes were associated with the prevalence of sarcopenia (75). Although the majority of studies in this review reported on dietary intakes only, a study of community dwelling older individuals that measured selenium in the serum of participants found that those in in the lowest tertile of circulating selenium concentrations were at an increased risk of low skeletal muscle mass (76). Also, an earlier study in men and women, that was not included in the review, found those individuals in the lowest quartile of circulating selenium concentration had lower measures of grip, knee and hip strength (77).

As comparatively little research has involved the relevance of minerals and trace elements to skeletal muscle health and sarcopenia, further research is needed to improve our knowledge and understanding in this area.

Fatty acids

Dietary sources of fat exist as a combination of different classes of fatty acid. Thus, dietary fat intake may vary significantly between individuals with regard to both total consumption and the ratios of different fatty acids including saturated (SFA), monounsaturated (MUFA), polyunsaturated (PUFA), and trans (TFA) fatty acids (78, 79).

There are several aspects to the rationale for dietary fat being important to muscle health. During aerobic exercise fatty acids provide energy by acting as a critical substrate for production of ATP (80). Phospholipid fatty acids also act as key structural components of muscle cell membranes (sarcolemma) and incorporation of different types of fatty acids may influence cellular signalling and function (81). Fatty acids may also affect inflammatory pathways, which could have consequences on muscle. Indeed, in general terms it is though

that higher SFA and total fat intakes are associated with higher risk of inflammation, while other fatty acids, including n-3 PUFA are associated with anti-inflammatory properties and protein synthesis (82).

A number of observational studies have suggested a role for fatty acids and their dietary profiles and measures of skeletal muscle mass or sarcopenia. In an analysis of Twins UK data, positive associations were evident between the PUFA to SFA ratio and indices of FFM, and negative associations were evident with the proportion of energy from fat in the diet, and SFA, MUFA, and TFA, individually as a percentage of total dietary energy (83). There is also some suggestion that a higher omega-3: omega-6 ratio is desirable as omega-3 fatty acids may provide protective effects for muscle, while omega-6 has pro-inflammatory effects which result in adverse effects. However, a recent systematic review showed no significant effects of total PUFA or specific omega-3 or omega-6 fatty acids on indices of skeletal muscle mass (84). In conclusion therefore, there is rationale for the importance of different profiles of fatty acid in the diet, with ratios of different fatty acids relevant to measures of muscle health and sarcopenic risk factors. However, further investigation is required before definitive conclusions can be made, and recommendations given to optimise fatty acid intakes for muscle health.

Dietary patterns

Most previous research has studied associations between individual components of the diet and musculoskeletal health, but it is likely that the balance of dietary components is also important. Indeed, we consume nutrients in combinations in food, and thus there may be synergistic and cumulative effects of different dietary components including protein and micronutrients on health and disease which might not be seen by examining the effects of nutrients or foods individually.

The Mediterranean diet (MD) pattern is characterised by high intakes of fruits and vegetables, legumes, nuts, cereals, and olive oil with low intakes of saturated fat, moderately high intakes of fish, low to moderate intakes of dairy products, low intake of meat, and regular but moderate intake of alcohol (85). This micronutrient rich diet is associated with a number of favourable health outcomes, including overall mortality and protective effects on cardiovascular disease, hypertension, and cancer (86, 87). Comparatively few studies have explored the relationship between the MD and sarcopenia or sarcopenic factors (88). In terms of muscle health and relevance to sarcopenia, observational studies, including data from the Twins UK study of adult women have demonstrated that higher adherence to the MD is associated with higher measures of fat free mass, and leg explosive power (89). Likewise in the EPIC-Norfolk cohort, higher adherence to a Mediterranean diet was associated with significantly higher indices of FFM (90).

Potential Renal Acid Load (PRAL) is a means to quantify acid-base load of the diet as well as the effect of diet on systemic acid-base balance. A more alkalinogenic load, low PRAL, is considered protective. Fruits and vegetables have a low PRAL and tend to promote systemic alkalinity due to the bicarbonate present, while hepatic oxidation of the sulphur-containing amino acids, cysteine and methionine found in meats, grains, and cheeses, generates hydrogen ions and thus has the opposite effect (91).

Metabolic acidosis may be detrimental to skeletal muscle by decreasing protein synthesis and increasing proteolysis and oxidation of amino acids, through actions of the ubiquitin proteasome pathway and insulin-like growth factor-1 signalling (92). It has been associated with muscle wasting in patients with chronic renal failure (93), and in acidotic obese

individuals undergoing very low calorie diets for weight-loss (94, 95). Whilst this process is a useful adaptive response to acidosis resulting in release of amino acids in the blood as a substrate for synthesis of glutamine and in turn ammonia, which helps mop up excess hydrogen ions for excretion as ammonium ions and thus reduce the acidosis (96), it does nevertheless occur to the detriment of muscle. A number of population studies have therefore investigated PRAL in relation to muscle health in young and old individuals (97-98). For example, evidence from the Twins UK study in women (98) aged 18-79 years showed a positive association between a more alkaline diet and muscle mass indexes, and this association was also evident in the middle- to older-aged men and women in the EPIC-Norfolk cohort (99).

Summary, recommendations, guidelines.

To date, published observational studies, both cross-sectional and longitudinal in design, have demonstrated significant relationships between specific dietary factors and dietary patterns with muscle measures of mass and function, and thus sarcopenic risk factors. They have also highlighted a number of differences in these relationships according to sex. The major evidence for micronutrients that may be relevant during muscle aging involves vitamin C and the mineral magnesium, with much less evidence available for the carotenoids, vitamin E, and other minerals and trace elements including iron, selenium, calcium, phosphorus. Many of these findings have not been translated into intervention study designs, but evidence from observational studies is nevertheless somewhat convincing. There is also a small but growing body of evidence to suggest that adherence to specific dietary patterns, including the Mediterranean diet, and diets with a more alkalinogenic, low PRAL, also have improved muscle measures and thus reduced sarcopenic risk factors. Within the observational studies for both micronutrients and dietary patterns there are differences between extremes of population intakes of a magnitude that could be clinically relevant. These suggest that more optimal dietary intakes may have beneficial effects on sarcopenic factors during aging.

Until recently, the impact of nutrition on muscle health and sarcopenia has been largely underestimated. Indeed, efforts to promote or retain muscle mass and strength and thus reduce the risk of sarcopenia have mainly been focused on a combination of increased protein intake alongside resistance exercise. However, as summarised here, increasing evidence is emerging to show that overall diet quality and intake of a range of nutrients including vitamins and minerals, not only protein, may play an important role in muscle health in older people.

Dietary recommendations for older adults in relation to skeletal muscle health are limited. The current recommendations are summarised in Table 1. In making recommendations for intakes of specific nutrients for muscle health it is important to consider that current dietary recommendations and clinical deficiency or sufficiency criteria have not been generated using muscle health outcomes. The current published recommended nutrient intakes or body the status criteria utilised to derive dietary recommendations thus may not be directly relevant to maintaining or improving muscle health. Indeed, it may be necessary to achieve higher intakes for optimal muscle health than might be predicted using other health outcomes, and further investigation will be required to determine this in the future. With this caveat, it is nevertheless reasonable to deduce from the current evidence that individuals should, in conjunction with an active lifestyle, aim to consume sufficient fruits and vegetables, and protein, and to limit their saturated fat intake, for muscle health in later life.

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