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REVIEW

Exercise and nutritional interventions for improving aging muscle health

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Abstract Skeletal muscle mass declines with age (i.e., sarcopenia) resulting in muscle weakness and functional limitations. Sarcopenia has been associated with physiological changes in muscle morphology, protein and hormonal kinetics, insulin resistance, inflammation, and oxidative stress. The purpose of this review is to highlight how exercise and nutritional intervention strategies may benefit aging muscle. It is well known that resistance exercise training increases muscle strength and size and evidence also suggests that resistance training can increase mitochondrial content and decrease oxidative stress in older adults. Recent findings suggest that fast-velocity resistance exercise may be an effective intervention for older adults to enhance muscle power and functional capacity. Aerobic exercise training may also benefit aging skeletal muscle by enhancing mitochondrial bioenergetics, improving insulin sensitivity, and/or decreasing oxidative stress. In addition to exercise, creatine monohydrate, milk-based proteins, and essential fatty acids all have biological effects which could enhance some of the physiological adaptations from exercise training in older adults. Additional research is needed to determine whether skeletal muscle adaptations to increased activity in older adults are further enhanced with effective nutritional interventions and whether this is due to enhanced muscle protein synthesis, improved mitochondrial function, and/or a reduced inflammatory response.

Keywords Sarcopenia · Creatine · Protein · Amino acids · Fatty acids

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Aging and sarcopenia

Sarcopenia is defined as the age-related loss in muscle mass and strength, which has a negative influence on the ability to perform tasks of daily living leading to a reduced quality of life [1]. Sarcopenia affects approximately 25–50 % of adults between the ages of 70–80 [2–7], resulting in annual health costs of approximately $20 billion in the United States alone [8]. With the projected increase in longevity [9], it is estimated that over 200 million adults in the next 40 years will experience significant muscle and strength loss [1], which may result in a global health care crisis.

While the exact mechanisms explaining sarcopenia remain to be elucidated, the age-related loss in muscle tissue is theorized to be a multi-factorial process influenced by changes in muscle morphology [10–12], protein and hormonal kinetics [13, 14], insulin resistance [15], inflammation and oxidative stress [16, 17], physical activity [7], and nutrition [1]. Exercise promotes numerous adaptations in skeletal muscle, many of which may help to prevent or reverse sarcopenia. Accumulating evidence indicates that the influence of exercise can be modulated by nutritional interventions, particularly in older adults. The purpose of this review is to highlight how exercise and nutritional intervention strategies may benefit aging muscle.

A schematic of how exercise and nutritional interventions may interact to reverse potential causes of sarcopenia is depicted in Fig. 1.

Resistance exercise

It is well established that traditional, slow-velocity resistance exercise (i.e., performing the concentric and eccentric phase of each muscle contraction in 2–3 s) is a safe, feasible, and effective intervention to induce muscle hypertrophy and increase strength in older adults [18–25]. Mechanistically, muscle accretion from resistance exercise may be caused by an increase in muscle protein synthesis [26], satellite cell activation and proliferation [27], anabolic hormone production [28], and a decrease in catabolic cytokine activity [29]. Resistance exercise (10 weeks–2 years) has been shown to increase both type I and II muscle fiber cross-sectional area [30] and whole-body lean tissue mass in older adults [18, 19] leading to an increase in muscle strength [18, 30–32] which could be considered clinically significant. Furthermore, resistance exercise may help to eliminate the age-related deficits in muscle mass and strength. For example, Candow et al. [33] showed that 22 weeks of whole-body resistance exercise training (3 days per week) in healthy older males (60–71 years) was sufficient to overcome the age-related deficits in whole-body lean tissue mass, regional muscle size, and upper and lower body strength such that these parameters became equal to untrained young males. Therefore, resistance exercise is an effective intervention to enhance aging muscle mass and strength and these gains lead to significant improvements in functionality and overall quality of life [21].

Fast-velocity resistance exercise (i.e., performing the concentric phase as quickly as possible and taking 2 s to perform the eccentric phase of each muscle contraction) appears to be a novel intervention for older adults to enhance muscle power [33, 34]. Muscle power, defined as a function of both strength and speed of contraction [35], is a significant predictor of performing activities of daily living (i.e., gardening, carrying groceries, climbing stairs) and is reduced with age at both slow and fast velocities. With the subsequent atrophy of type II fibers with aging, power decreases faster and at a much greater rate (3–4 % per year after 60 years of age) than strength [36]; suggesting that fast-velocity movements are important for preserving aging muscle health [35]. A number of studies have shown a significant increase in power from fast-velocity resistance exercise in older adults, possibly because of greater motor unit recruitment of type II fibers [35]. Therefore, fast-velocity contractions may be considered when designing resistance exercise training programs for older adults.

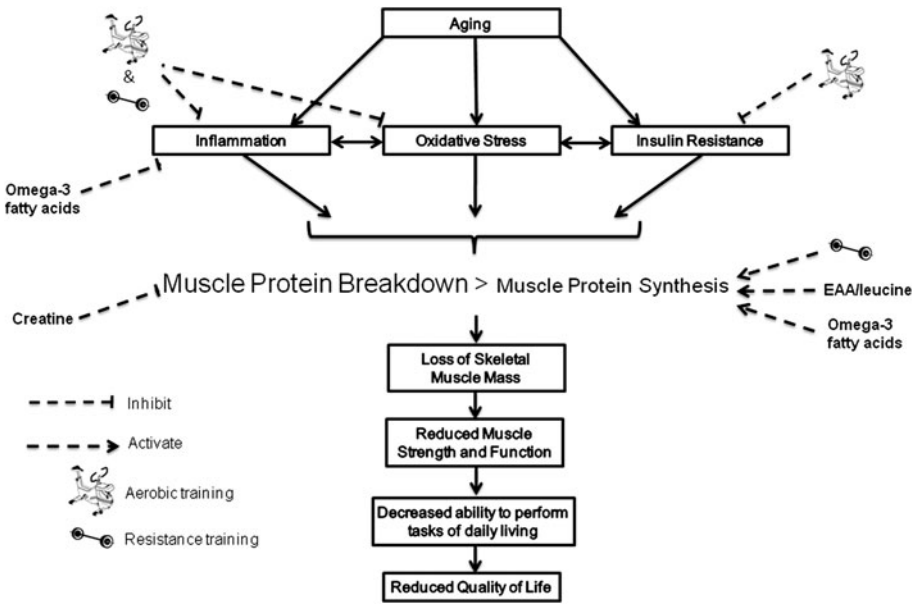

Fig. 1 Summary of the potential underlying causes of sarcopenia and the beneficial effects of exercise and nutrition to counteract age-related muscle loss. Aging is accompanied by chronic low-grade inflammation, increased oxidative stress, and insulin resistance. Collectively, these physiological processes result in an increase in muscle protein breakdown and/or a decrease in muscle protein synthesis such that net muscle protein balance is negative, resulting in loss of muscle mass. Aging-related muscle loss contributes to reduced function and independence. The influence of aerobic and resistance exercise training as well as selected nutritional interventions on several of the key underlying processes of sarcopenia are summarized

Aerobic exercise training

In addition to resistance exercise, aerobic activities also have the potential to benefit aging muscle. Aging is characterized by a progressive deterioration in aerobic exercise capacity (i.e., maximal oxygen consumption) and this attenuation in cardiovascular efficiency may be linked to reduced quantity or quality of skeletal muscle mitochondria [37, 38]. It is well known that aerobic exercise induces an increase in skeletal muscle mitochondria [39, 40] and these benefits are evident in aging muscle [41, 42]. Muscle mitochondrial adaptations to aerobic training appear to be the result of exercise-induced increases in the transcription of mitochondrial genes. Various signals, including Ca2+ and adenosine monophosphate (AMP), produced within working skeletal muscle during acute exercise activate intracellular signaling pathways [e.g., calcium/calmodulin-dependent protein kinase (CaMK), AMP-activated protein kinase (AMPK)] that culminate in increased transcription of target mitochondrial genes [43, 44]. Over the course of training, the cumulative effect of these acute pulses in gene transcription results in the synthesis and incorporation of new mitochondrial proteins. The transcriptional co-activator peroxisome proliferator-activated receptor gamma co-activator 1-α (PGC-1α) is regarded as a crucial regulator of this process by virtue of its ability to co-activate several transcription factors to orchestrate a program of mitochondrial biogenesis [45]. Acute exercise increases the expression and activation of PGC-1α in human skeletal muscle [46, 47]. Exercise induces transient transcriptional activation of the PGC-1α gene in human skeletal muscle [47]. Interestingly, PGC-1α has been shown to decline with aging in rodent skeletal muscle [48]; however, there is no decline in skeletal muscle oxidative capacity with aging in long-term calorically restricted rats, effects are independent of mitochondrial DNA integrity [48]. Therefore, aerobic exercise may help to preserve muscle quality and aerobic capacity in aging through activation of PGC-1α.

Increased muscle mitochondrial content and/or improved mitochondrial function following aerobic exercise leads to improved metabolic control [40], enhanced exercise capacity [49] and reduced oxidative stress [50, 51]. Mitochondrial energy production also supports anabolic processes and a reduction in markers of mitochondrial function is an early sign of muscle atrophy [52]. Furthermore, muscle-specific PGC-1α knockout mice, which display impaired mitochondrial biogenesis, experience accelerated sarcopenia with aging [53]. Conversely, muscle-specific PGC-1α overexpressing mice, which have increased muscle mitochondrial volume analogous to a state of aerobic exercise training, are resistant to muscle atrophy induced by denervation and fasting [54], conditions which are of possible clinical relevance to aging. As such, aerobic exercise-induced mitochondrial biogenesis may be involved in maintenance of muscle mass with aging.

Aerobic exercise training also increases skeletal muscle insulin sensitivity [55]. The exact mechanisms by which exercise improves muscle insulin sensitivity are not fully known, but are related to improved insulin signaling, reduced inflammation, increased muscle glucose transporters, and possibly mitochondrial function [55, 56]. Insulin resistance is a common feature of aging [57] and may precipitate loss of skeletal muscle mass by reducing the normal physiological effects of insulin or insulin-like growth factors. It appears that the primarily role of insulin in the regulation of muscle mass is to inhibit muscle protein breakdown, as increasing insulin within the physiological range results in a dose-dependent reduction on markers of muscle protein breakdown with no effects of increasing insulin concentrations on the stimulation of muscle protein synthesis [58]. Improving insulin sensitivity in skeletal muscle may therefore aid in the preservation of muscle mass with aging mainly by inhibiting muscle protein breakdown but also through enhanced stimulation of muscle protein synthesis [59, 60].

In addition to aerobic-based exercise training, a growing body of evidence indicates that high-intensity interval training (HIT) may also have substantial effects on muscle mitochondrial biogenesis [61–63]. HIT involves repeated short bursts of vigorous exercise (lasting a few seconds up to several minutes) interspersed by periods of rest or recovery. The influence of HIT on sarcopenia in older adults has not been addressed, but due to the potent effects on PGC-1α [62, 64], mitochondrial biogenesis [61, 65], and insulin sensitivity [66, 67]; HIT may be an alternative exercise strategy with therapeutic potential. In addition, higher motor unit recruitment during HIT may be able to target higher threshold type II muscle fibers to a greater extent than low- to moderate-intensity aerobic training, which may have potential importance in aging given the preferential atrophy of type II fibers.

Future research should investigate which exercise training strategies (i.e., resistance, aerobic, HIT, or concurrent training) are most effective for preventing or delaying sarcopenia and to improve older adults' ability to participate in habitual physical activity. In addition, further investigations are required to examine potential alternatives to traditional exercise programs for individuals who have marked physical limitations. And finally, how can nutrition and exercise regimens be combined for prevention or treatment of sarcopenia.

Creatine monohydrate

Creatine is a nitrogen-containing compound produced endogenously (1–2 g day^{-1}) and is also consumed ($\sim$1–3 g day^{-1})

primarily from seafood and red meat [68]. Creatine is a component of phosphocreatine (PCr), which is a high-energy phosphate compound found in high abundance in skeletal muscle that is involved in the rapid resynthesis of adenosine diphosphate (ADP) to adenosine triphosphate (ATP) during intense muscle contraction (i.e., PCr + ADP $\leftrightarrow$ATP + Cr). In aging adults, creatine supplementation and resistance exercise have been shown to have a beneficial effect on muscle mass and strength [33]. The potential mechanisms by which creatine supplementation is hypothesized to benefit muscle are many, and include influencing high-energy phosphate metabolism [69], satellite cell differentiation [70], activity [71], and content [72], transcription factor activity [73], hormonal secretion (i.e., IGF-I) [74], muscle protein kinetics [18, 75], and inflammatory pathways [76, 77].

The majority of PCr is found in skeletal muscle [78] and with progressive muscle atrophy with aging, high-energy phosphate metabolism may be subsequently jeopardized [79]. From a theoretical perspective, increasing intramuscular creatine (i.e., PCr and free creatine) from creatine supplementation should enhance PCr resynthesis and high-energy phosphate metabolism which may enhance exercise training capacity leading toward greater muscle accretion and strength. For example, creatine supplementation (0.1 g kg^{-1}) during 10 weeks of structured resistance exercise training (3 sets of 10 repetitions, 3 days $week^{-1}$; 9 exercises) increased whole-body muscle thickness compared to placebo and resistance exercise training in healthy older males [18]. Furthermore, Chrusch et al. [80] observed significant increases in whole-body lean tissue mass and muscle strength from creatine (0.3 g kg^{-1} × 5 days; 0.07 g kg^{-1} for 79 days) during 12 weeks of supervised resistance training in older men compared to placebo. Supplementing with creatine enhanced resistance exercise training capacity (load × sets × repetitions) by 31 %; possibly indicating that high-energy phosphate metabolism was enhanced from creatine.

In addition to high-energy phosphate metabolism, creatine may also stimulate myogenic transcription factors (i.e., myogenin and MRF-4), which initiate transcription and regulate gene expression of muscle-specific genes such as myosin heavy chain [73], which may lead to muscle hypertrophy. For example, creatine supplementation (6 g day^{-1}) during 12 weeks of resistance exercise training significantly increased mRNA and protein expression of myogenin and MRF-4 in young male subjects [73]. The increase in MRF-4 expression correlated to an increase in muscle cross-sectional area [81].

Satellite cells are mononucleated cells, which reside between the basal lamina and sarcolemma [82] and once activated (i.e., resistance exercise), produce muscle precursor cells, which undergo activation, proliferation and differentiation to form new muscle fibers [83]. Aging has a negative effect of satellite cell function and quality [84], which may be a contributing factor of sarcopenia. Creatine has been shown to have a positive effect on satellite cell differentiation [70], activity [71], and content in young males performing structured resistance exercise training [72]. However, the effects of creatine on aging satellite cells are unknown.

Regarding hormonal and protein kinetics, creatine supplementation (0.25 g kg^{-1} lean tissue mass for 7 days; 0.06 g kg^{-1} lean tissue mass for 49 days) during 8 weeks of resistance exercise training significantly increased intramuscular insulin-like growth factor–I (IGF-I) content by 78 % in males and females [74]. A decrease in IGF-I may play a role in the pathogenesis of sarcopenia [85]. Creatine also appears to exhibit anti-catabolic properties. For example, older men supplementing with creatine during a resistance exercise training program experience a significant reduction in urinary excretion of 3-methylhistidine, an indicator of muscle protein catabolism, by 40 % compared to an increase of 29 % for placebo [18]. Short-term creatine supplementation has also been shown to decrease whole-body protein breakdown (e.g., plasma leucine rate of appearance) in young men [75].

Inflammation decreases the rate of muscle protein synthesis [37] by blunting the stimulation of the mammalian target of rapamycin (mTOR) signaling pathway [86]. The age-related increase in interleukin (IL)-6 and tumor necrosis factor (TNF)-α have been shown to result in muscle atrophy, strength loss [87, 88] and muscle protein catabolism [9]. Research in young adults suggests that creatine may have anti-inflammatory properties and accelerate muscle recovery following exercise. Triathletes, who have been supplemented with creatine (20 g day^{-1}) for 5 days before competition experienced a significant decrease in exercise-induced inflammation (IL-1: −50 to 80 %, TNF-α: −42 to 64 %, Prostaglandin E(2): −86 to 91 %) compared to athletes who consumed placebo [76]. Furthermore, well-trained marathon runners who ingested creatine (20 g day^{-1}) for 5 days before running 30 km experienced a reduction in post-exercise inflammation (Prostaglandin E(2): −61 %, TNF-α: −34 %) compared to placebo [77].

A decrease in oxidative homeostasis is considered a main contributing factor to muscle deterioration with aging [37]. Over time, there is an accumulation of cellular damage caused by reactive oxygen species (ROS) to cellular components resulting in impaired function and cellular degeneration [89]. There is a growing appreciation for the role of ROS as key signaling molecules involved in muscle adaptation to acute exercise [90]. Exercise activation of muscle PGC-1α signaling is redox sensitive [90], and in aging the physical stress from an acute bout of

intense resistance exercise may increase ROS to an extent that compromises muscle health. Creatine supplementation has been shown to decrease radical and reactive species ions in vitro [91, 92] and protect against DNA and RNA damage [93]. In a group of young, resistance-trained males ($n = 15$), creatine ingestion (20 g day^{-1}) for 7 days attenuated the rise in urinary 8-hydroxy-2-deoxyguanosine excretion, an indicator of oxidative DNA damage, and plasma malondialdehyde, an indicator of lipid peroxidation following an acute bout of resistance exercise (7 sets of 3–6 repetitions at 80–90 % 1-repetition maximum, exercises: bench press, leg press, lat pull down, seated row) compared to placebo [89]. While the mechanistic actions explaining how creatine decreases oxidative stress in response to exercise is not fully known, it is possible that the antioxidant properties of arginine, required for creatine synthesis, is involved [89]. Arginine has a direct antioxidant effect in endothelial cells [94].

In addition to sarcopenia, osteoarthritis is an age-related progressive degenerative joint disease resulting in chronic pain, functional limitations and the inability to perform activities of daily living [95]. Osteoarthritis is systematically determined by varying joint symptoms (e.g., inflammation) and structural pathology abnormalities (e.g., damage and loss of cartilage, muscle atrophy) [96]. In examining the potential beneficial effects of creatine supplementation in patients with rheumatoid arthritis ($N = 8$), Willer et al. [97] showed that 3 weeks of creatine (20 g day^{-1} for 5 days, 2 g day^{-1} for 16 days) had small beneficial effects on isometric elbow and knee muscle strength. Recently, Neves Jr. et al. [98] discovered that creatine supplementation (20 g day^{-1} for 7 days, 5 g day^{-1} for 77 days) during supervised lower-limb resistance exercise (3 days week^{-1}, 4 sets of 8–12 repetitions, exercise: leg press, leg extension, half squat), in postmenopausal women ($N = 7$) with knee osteoarthritis resulted in significant improvements in lean tissue mass and physical function (pain, stiffness, quality of life) compared to placebo.

Milk-based proteins and essential amino acids

It is generally accepted that adequate dietary protein intake is required for the maintenance of muscle mass in older adults [99]. Increasing attention has focused on dietary protein quality and source, with evidence that essential amino acids (EAA) play the predominant role in promoting positive muscle protein balance [100, 101]. EAA are primarily responsible for the amino acid stimulation of muscle protein anabolism in healthy elderly adults [101]. In particular, leucine appears to be of primary importance in initiating molecular events associated with muscle hypertrophy [102].

Both in vitro [103] and in vivo [102, 104] studies indicate that leucine can activate mTOR and p70S6K in human skeletal muscle. These signaling kinases are regarded as central nodes in the molecular sequence of events leading to muscle hypertrophy. Older adults typically experience a blunted response to dietary protein ingestion [105]. However, supplemental leucine ingestion has been shown to overcome resistance to the anabolic effects of amino acid consumption [106], providing evidence that increasing dietary leucine consumption (i.e., 3–6 g), via supplementation, may play a pivotal role in preserving muscle mass with aging [102, 104, 106]. Further research is needed to determine if leucine alone, or in combination with whole-proteins and/or resistance exercise, has the potential to alleviate symptoms of sarcopenia [107].

A simply strategy for older adults to support muscle hypertrophy in response to resistance exercise is the consumption of essential amino acids (i.e., leucine) from food products. In this regard, research indicates that milk-based proteins are an effective protein source for stimulating muscle protein synthesis and promoting gains in muscle mass over time. Bovine milk contains a relatively high proportion of leucine and a compliment of whey and casein proteins, which are absorbed at different rates upon digestion [108–110]. This mixture of proteins has been hypothesized to promote both rapid (whey) and sustained (casein) muscle protein synthesis coupled with reductions in muscle protein breakdown [108]. Resistance exercise training studies in young adults indicate that post-exercise milk-based protein supplementation ($\sim$17.5 g protein, equivalent to that found in 500 mL fat-free milk, consumed immediately and 1 h following each training session over 12 weeks) may promote greater muscle hypertrophy when compared to other protein sources such as soy [111]. However, a recent randomized-controlled trial in middle-aged and older adults failed to find added benefits of milk consumption over that provided by resistance exercise training alone [112]. These latter findings may not be surprising given that milk supplementation was not provided in close proximity to the resistance exercise training sessions, and therefore would not take advantage of exercise-induced blood flow [113] or the potential synergy between resistance exercise- and amino acid-induced increases in muscle protein synthesis [107, 114]. In addition, due to the impaired muscle protein synthetic response to dietary protein or amino acid feeding, perhaps older adults require greater post-exercise protein consumption. For example, Candow et al. [19] failed to find an increase in muscle mass from whey protein ingestion ($\sim$25 g) immediately before or after resistance exercise training sessions for 10 weeks in older men compared to placebo while Yang et al. [115] recently demonstrated that older

adults may require more protein to maximally stimulate muscle protein synthesis compared to young adults [116].

Fatty acids

In addition to amino acids, dietary fatty acids may also influence aging muscle biology. The source of dietary fat seems to be important in modulating inflammatory responses, in turn affecting muscle anabolism and catabolism. It is generally accepted that saturated fatty acids, such as palmitic acid and stearic acid, promote pro-inflammatory responses in various cell types, including circulating monocytes [117], macrophages [118], and skeletal muscle [119]. Activation of pro-inflammatory signaling by saturated fatty acids increases levels of pro-inflammatory cytokines, such as TNF-α, which are implicated in muscle wasting [120]. Recent molecular signaling evidence also indicates that saturated fatty acids can impair muscle hypertrophy. Deldicque et al. [121] demonstrated in C2C12 myoblasts that incubation with high levels of palmitate initiated endoplasmic reticulum (ER) stress and activated the unfolded protein response (UPR). A key aspect of the UPR is the inactivation of translation initiation and therefore, a reduction in global protein synthesis is observed. Since initiation of translation is the primary regulator of muscle protein synthesis [114], induction of ER stress by palmitate provides molecular clues as to how increased saturated fatty acids might impair muscle hypertrophy [122]. Work in rodents suggests that high saturated fat diets can impair anabolic signaling and skeletal muscle hypertrophy in response to mechanical overload using the synergistic ablation model [122]. It is important to note that human studies on the influence of saturated fatty acid diets on muscle mass, specifically in older adults, are lacking.

In contrast to the potential negative effects of saturated fatty acids on skeletal muscle mass, there is growing evidence that omega-3 fatty acids, which are thought to possess anti-inflammatory properties [123], have positive effects. Aging reduces mTOR signaling efficiency which impairs muscle protein synthesis [123]. However, omega 3-fatty acid ingestion stimulates mTOR in the presence of amino acids and carbohydrates [124]. For example, eight weeks of omega-3 fatty acid supplementation (1.86 g eicosapentaenoic acid + 1.50 g docosahexanoic acid per day) increased activation of mTOR and p70S6K and an augmented muscle protein synthesis during a hyperinsulinaemic/hyperaminoacidaemic clamp when compared to corn oil supplementation in healthy older adults [124]. These findings suggest that increased intake of omega-3 fatty acids may help preserve muscle mass in older adults by relieving the anabolic resistance that contributes to sarcopenia in older adults. Interestingly, omega-3 fatty acid supplementation had no effect on selected circulating markers of inflammation in this study [124], suggesting that omega-3 fatty acids may be working through pathways other than reducing inflammation. It must be noted that the older adults in this study were healthy with relatively low levels of inflammation and inflammatory markers in skeletal muscle were not assessed.

In addition to the potential benefits of omega-3 fatty acids, a recent study in aged rats provides evidence that the monounsaturated fatty acid oleate may also benefit muscle anabolism. Tardif et al. [125] compared old rats on a control diet with diets enriched in olive or palm oil to achieve conditions of high monounsaturated fatty acid or high saturated fatty acid consumption. Muscle protein synthesis and mTOR activation in response to amino acids and insulin was increased in the group of aged rats on the high monounsaturated fatty acid diet only. These results appeared to be related to reduced inflammation and/or improved mitochondrial fatty acid oxidation in the group of aged rats fed the diet enriched in oleate. Collectively, these findings suggest that dietary fatty acid composition may play a significant role in muscle health during aging. Specifically, high intake of saturated fatty acids may have negative effects on maintenance of muscle mass [115, 121], whereas higher intakes of omega-3 fatty acids [124] or oleic acid [125] may be beneficial. In order to determine the clinical significance of these findings, it will be important to determine if the results of these studies, which are primarily based on acute molecular signaling and muscle protein synthetic responses, translate to markers of whole body or appendicular muscle mass in older adults. Nonetheless, the influence of dietary fat source, along with the ratio and composition of dietary fatty acids, on the regulation of muscle mass in older adults is an area that is ripe for investigation.

Conclusion

Sarcopenia, the age-related decline in muscle quantity and quality, is a major health concern and has a negative influence on the ability to perform tasks of daily living leading to a reduced quality of life. Resistance exercise training can increase muscle mass and strength and may lead to improved mitochondrial content and reduced oxidative stress in older adults. Recent evidence suggests that muscle power is an important determinant of functional capacity. A novel and effective approach to enhance power in older adults is fast-velocity resistance exercise. Aerobic exercise may also benefit aging skeletal muscle through enhanced mitochondrial bioenergetics, improved insulin sensitivity, and/or reduced oxidative stress. HIT is an emerging exercise strategy with demonstrated benefits on

muscle health in young adults and patients with metabolic disease. HIT may have important therapeutic value for older adults because it can potently stimulates PGC-1α and mitochondrial biogenesis and may effectively target type II muscle fibers. Beyond exercise alone, creatine monohydrate, milk-based proteins, and essential fatty acids all have biological effects that may potentiate the beneficial effects of exercise in older adults. Future research is warranted and is required to determine the most appropriate nutritional intervention(s) to augment skeletal muscle adaptations to exercise training in older adults.

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