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Review Article

Advances in the Treatment of Muscle Mass Loss and Sarcopenia

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Abstract

Sarcopenia and muscle mass loss are problems that affect the population as it ages. Sarcopenia is a condition that is currently defined as the progressive loss of muscle mass and function which leads to deterioration and frailty. The process of aging in human beings results in declines of muscle strength that can vary between 16.6% and 40.9% in people with < 40 years of age to people with >40 years. Sarcopenia represents one of the major causes of disability in elderly people. Recent literature reviews show that there are many potential treatments being developed to prevent and reverse the effects of sarcopenia and muscle mass loss. Currently, nutrition and strength training are two of the most effective interventions. However, further research is needed on drugs, hormones and pharmacological interventions that could provide a more efficient and cost-effective option for people who are diagnosed with sarcopenia. The purpose of this article is to review recent studies that demonstrate advances in the treatments sarcopenia and muscle mass loss.

INTRODUCTION

The human body becomes weaker and increasingly susceptible to injuries as it ages, with many anatomical and physiological changes being responsible for the aging process. According to Walston et al., (2012) changes due to aging are associated to a decrease in motor function, muscle mass and muscular performance [1]. Irwin H. Rosenberg (1994), defined sarcopenia as the involuntary loss of muscle mass and strength associated with age [2]. In 2010 the European Working Group on Sarcopenia in Older People (EWGSOP), defined sarcopenia as "a syndrome characterized by a progressive and general loss of mass, strength and skeletal muscle with the risk of presenting adverse results, physical disabilities, poor quality of life and death" [3] (Figure 1). Recently, it was determined that sarcopenia produces changes in the quantity of skeletal muscle fibers involving a shift from type II to type I fibers [4]. This shift has a negative effect on strength, power and mobility [5]. In addition, many other physiological changes that promote the beginning of sarcopenia have been identified (Figure 1). According to Keller & Engelhardt (2013) the process of aging in human beings results in declines of muscle strength that can vary between 16.6% and 40.9% in people with<40 years of age to people with>40years [6]. Every year, as the cases of sarcopenia increase, there is a risk of developing other conditions and disabilities, such as osteoporosis, diabetes and some types of cancers [7].

During recent years, potential treatments for sarcopenia have been developed. When sarcopenia was first being studied, the only recommended treatments were constant physical exercise and proper nutrition. Even today, strength training is still considered one of the most effective methods to combat sarcopenia, mostly because of the hypertrophy stimulation and strength increase resulting from the training [8]. In addition, a correct nutrition and diet with a proper supplementation, especially in older people, can contribute to the prevention of sarcopenia. The effectiveness of treatment and rehabilitation of patients with sarcopenia would increase significantly if there were more effective treatments for this disease, but evidence for the benefits of drugs is limited. The purpose of this article is to summarize and explain the results of a literature search into recent investigations about possible treatments directed at reducing muscle mass loss and sarcopenia.

OBJECTIVE

The objective of this review is to describe the findings in the scientific literature related to different interventions used to prevent muscle mass loss and sarcopenia in the elderly population.

METHODS

PubMed (http://www.ncbi.nim.nih.gov/pubmed), in both English and Spanish, was used to find research publications before August 2017. The key search words were: sarcopenia, muscle mass loss, sarcopenia treatments, pharmacological treatments for muscle mass loss, potential treatments for muscle mass loss, and strength training.

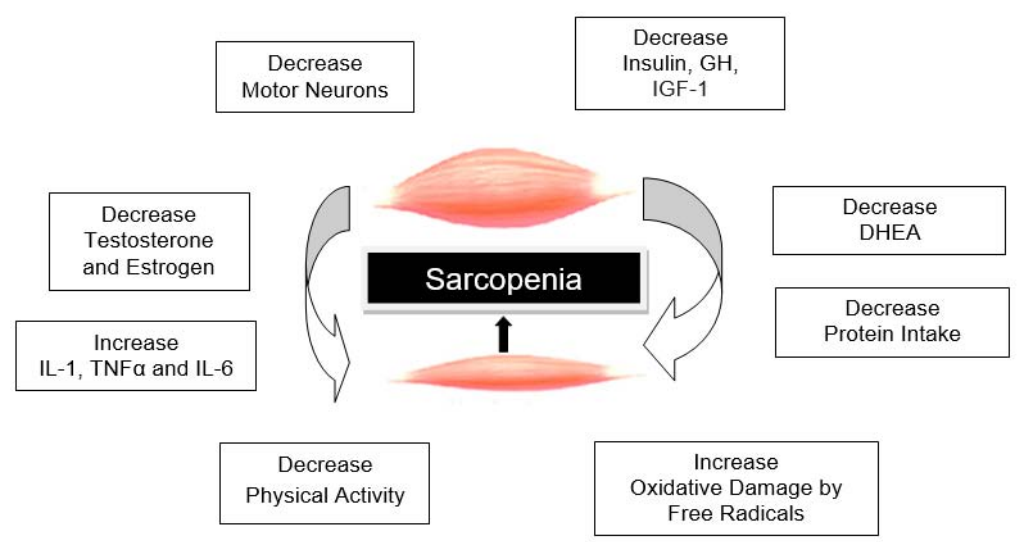

Figure 1 Examples of some mechanisms that promote the beginning and progression of sarcopenia (Growth hormone (GH); (Insulin-Like Growth Factor-1 (*IGF-1);* Dehydroepiandrosterone (DHEA); *Interleukin-1* (*IL-1*); Tumor Necrosis Factor α (TNF-α); *Interleukin 6* (*IL-6).*

CURRENT TREATMENTS FOR MUSCLE MASS LOSS AND SARCOPENIA

Physical exercise and nutrition

Physical exercise: Physical exercise promotes functional development in elderly people. Gadelha et al., (2016) found that physical exercise can improve the symptoms related to sarcopenic obesity in older women [9]. The long-lasting effects of strength training on sarcopenia could be attributed to the protection of mitochondrial disorders (apoptosis, oxidation damages) by increasing the amount of PGC-1ª [10]. Some studies, found that the older population, which is less physically active, has a greater probability of losing skeletal muscle mass and strength, and therefore possesses a greater risk of developing sarcopenia [11,12]. However, strength training is one of the most effective methods to combat sarcopenia and muscle mass loss [13] (Figure 2). Frontera et al., (1988) reported that a group of elderly men (age range 60-72 years) who performed 12 weeks of strength training, demonstrated an 11% increase in muscle mass and an improvement in muscle strength [14]. Strasser et al., (2009) demonstrated that for a group of elderly people, 6 months of strength training, 3 times per week, resulted in the lean corporal mass increasing by 1.0 ± 0.5 kg [15]. This study was a randomized and controlled trial which tested the effects of strength training over 91 subjects of a community with sarcopenia (78 years and older) [15]. Binder et al., (2005) demonstrated, that exercise training resulted in a significant increase in the amount of body composition when compared to a control group. Body composition in this study was defined as maximal voluntary force production for knee extension (p =.05), total body fat free mass (p =.005) and total trunk, intra-abdominal, and subcutaneous fat mass (no significant changes) [16]. Chen et al., (2016) stated that pharmacologic interventions have been unsatisfactory, and that the main treatments available for sarcopenia are physical exercise and effective nutrition [7]. In addition, Denison et al., (2015) concluded that the possible benefits of exercise training, when a proper dietary supplementation is included, indicate that future interventions may be developed [17]. However, more studies are required, particularly in exercise training in combination with dietary supplements.

Nutrition: There is limited information related to the nutritional aspects and diets of different elderly individuals. However, there is a direct correlation between a poor physical function and poor nutrition, insufficient protein ingestion, vitamin D deficiencies, lack of consumption of antioxidant nutrients and long chain polyunsaturated fatty acids [17,18]. Limited nutrition and monotonous diets are common in individuals of an advanced age, which increases the probability of insufficient nutrient ingestion [18]. Interventions aimed at improving nutritional consumption by frail adults have the potential of delaying the loss of muscle mass and physical function [18]. Presently high protein diets and oral protein supplementation are the most effective nutritional treatments for sarcopenia and loss of skeletal muscle mass. In an article by Landi et al., (2016) it was stated that the current recommendation for the quantities of protein consumption (0.8 g/kg/day) may not be enough to sustain healthy muscles in the elderly population, mainly because of the possibility of "anabolic resistance" [19]. Anabolic resistance is defined as the reduction of the stimulation of muscle protein synthesis when a dose of protein/amino acids is administered [20]. Anabolic resistance greatly contributes to decreases in skeletal muscle mass. As a result, elderly individuals require greater amounts of proteins to maintain proper muscle functioning [19]. The metabolism of muscle proteins depends on the proper ingestion of proteins and amino acids [19]. The rates of muscle protein synthesis are regulated mostly by different responses to anabolic stimuli (physical activity and food consumption) [19]. Dietary proteins and specific amino acid ingestion can greatly increase muscle protein synthesis rates and can also inhibit protein breakdown. Thus, aiming to stimulate a response that results in muscle protein synthesis can be a potential way to prevent and treat sarcopenia. For this reason,

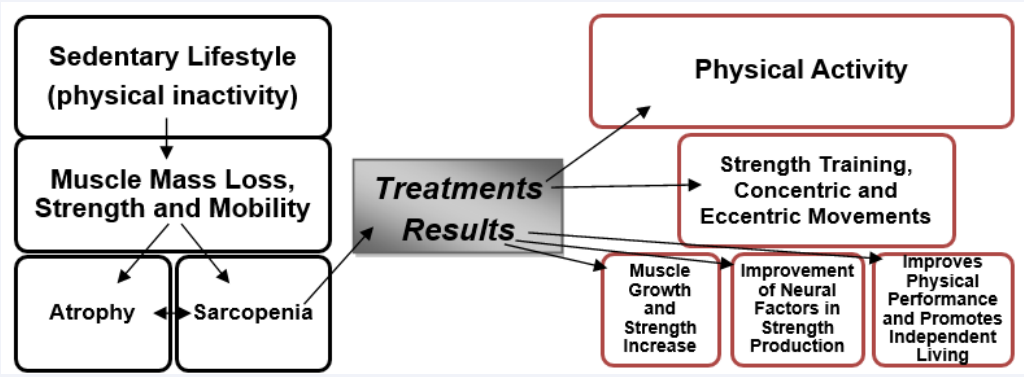

Figure 2 The consequences of physical inactivity are muscle atrophy and sarcopenia. Among the most effective treatments for sarcopenia and muscle mass loss are physical activity and strength training..

it is recommended that older patients have a protein intake of 1.0–1.2 g/kg/day in order to preserve healthy muscles. In addition, 1.2–1.5 g/kg/day of protein intake may be better suited for older patients that struggle with acute or chronic diseases [19]. In the case of elderly people with severe illness or excessive malnutrition, 2.0 g/kg/day of protein consumption may be more appropriate [19].

POTENTIAL TREATMENTS FOR MUSCLE MASS LOSS AND SARCOPENIA

Allopurinol

Allopurinol, an inhibitor of xanthine oxido-reductase (XOR), an intracellular enzyme involved in purine catabolismis widely used in clinical practice [21]. XOR catalyzes the reduction of hypoxanthine and xanthine to uric acid. XOR is found in the xanthine dehydrogenase (XDH) and xanthine oxidase (XO) forms. Derbre et al., (2012) concluded that allopurinol can have clinical benefits to treat skeletal muscle atrophy in sarcopenic patients [21]. Oxidative stress may contribute to muscle weakness in older people via mitochondrial dysfunction [22]. Most of the factors associated with muscle weakness due to oxidative stress include: protein degradation, inflammation, and hormonal dysfunction [22]. XO causes the generation of free radicals during skeletal muscle contraction [22], and allopurinol provides a protection against free radicals generated due to prolonged exercise. Thus, inhibiting XO with allopurinol may improve muscle function by reducing oxidative stress. According to Ferrando, et al., (2014) administrations of allopurinol have shown promising results in maintaining muscle mass and strength [23].

Oxandrolone

Oxandrolone is an androgenic steroid with a potent anabolic effect that is suitable for oral administration [24]. In one study, twenty-nine sedentary women were randomly assigned to two groups, one receiving twelve weeks of progressive resistance training (PRT) and oxandrolone, and the other receiving PRT and a placebo. After twelve weeks of intensive PRT a significant increase in lean tissue for the whole body, ($P = 0.003$), arms ($P = 0.001$), legs ($P = 0.018$), and trunk ($P = 0.004$) was observed in the group of women that received oxandrolone in combination with PRT. In addition, the results of this group demonstrated significant changes in fat tissue loss of the whole body ($P = 0.002$), arms ($P = 0.032$), legs ($P = 0.009$), and tended to reduce trunk fat ($P = 0.07$). However, even though improvements in body composition were significant between the PRT + oxandrolone group and the PRT + placebo group, there was no significant change between the observed strength, power, or functional outcomes ($P>0.05$) between these two groups [24]. The results of this study indicate that oxandrolone can be a potential treat for muscle mass loss, but not sarcopenia. Further studies will be needed to determine how oxandrolone can improve muscle function.

Ursolic acid

Ursolic acid is a pentaciclyc triterpenoid found in apples. Ebert et al., (2015) demonstrated that ursolic acid has the potential to reduce muscle weakness and atrophy associated to aging [25]. Ursolic acid may stimulate an increase in muscle mass by repressing atrophy-associated skeletal muscle gene expression [25]. To test the hypothesis that ursolic acid might reduce age-related skeletal muscle weakness and atrophy, 22-month-old mice were fed with diets that contained either 0.27% ursolic acid for 2 months. The results demonstrated that ursolic acid significantly increased skeletal muscle weight by 9 ± 2%. In addition, ursolic acid significantly increased the size of type IIb muscle fibers in the quadriceps of the mice that consumed ursolic acid, without increasing the size of type IIx. Ursolic acid also significantly increased grip strength 12 ± 3% and specific force by 30 ± 8% in mice. The molecular mechanisms of ursolic acid remain elusive [25]. Kunkel et al. (2011), demonstrated that ursolic acid treatment decreased the levels of Atrogin-1 and MuRF1 mRNA, which are associated to muscle atrophy, in mice [10].

Omega 3 polyunsaturated fatty acids (n3-PUFA)

The administration of omega-3 fatty acids, eicosapentaenoic fatty (EPA) acids and capsules or supplements with EPA may play a role in stabilizing weight and in promoting an increase of lean corporal mass and quality of life, especially in patients with advanced pancreatic cancer [26]. Smith et al., (2011) found that omega-3 supplementation had no effect on the muscle basal rate of protein synthesis [27]. Lalia et al., (2017) compared the influences of omega-3 fatty acids on skeletal muscle protein metabolism and mitochondrial bioenergetics on twelve young

(18-35) and twelve older (65-85) men and women [28]. Radiolabeled phenylalanine was administrated intravenously to determine the rates of skeletal muscle protein synthesis and mass spectrometry was used to determine the rates of incorporation of the radioactive amino acid into muscle proteins. The results indicated that the baseline post-absorptive fractional synthesis rates (FSR) had minor differences in the mixed muscle pools, mitochondrial fractions, sarcoplasmic fractions, and myofibrillar fractions of young and older adults. After a resistance exercise was performed in both groups, protein synthesis was measured again after 15-18 hours to determine if gene expression changes due to age are related to anabolic resistance. The results indicated that the baseline and post-exercise measurements of mixed muscle FSR and subcellular fractions did not demonstrate impairments due to age in post-absorptive muscle protein synthesis or anabolic responsiveness [28]. Post-absorptive and post-exercise muscle protein synthesis measurements were retaken in the older adults group. These measurements were taken after 16 weeks of dailyn3-PUFA supplementation (3.9g/day). The results demonstrated a significant increase in post-absorptive mitochondrial and sarcoplasmic protein synthesis in older adults after receiving n3-PUFA supplementation. However, non-significant increases were obtained in mixed muscle and myofibrillar fractions in the basal measurements. The exercise-induced increase in FSR for each fraction was compared before and after the n3-PUFA intervention in older adults. There were diverse responses where some individuals demonstrated high increases in exercise stimulated protein synthesis and others demonstrated little improvement. The exercise stimulated increases in mitochondrial FSR which were significantly greater in older adults following n3-PUFA supplementation compared to the young adults [28].

Myostatin inhibition

Myostatin is part of the muscle-specific transforming growth factor-β (TGF-β) family and negatively regulates skeletal muscle growth. Considerable evidence shows that myostatin regulates energy metabolism and its inhibition attenuates the progression of obesity and diabetes [29]. Tinkleberg et al., (2016) administered intravenously10 mg/kg of mRK35 once a week in two groups of mice, one with nemaline myopathy and the other a wild type (Tg$ACTA1^{D286G}$ and WTC57), until they were 6 months of age, to determine the effects of myostatin inhibition [30]. mRK35 is an antibody against myostatin that prevents myostatin from binding to ActRIIB receptors, thereby interrupting the downstream signal pathway [29]. According to the results, the Tg$ACTA1^{D286G}$ mice treated with mRK35 demonstrated an increase in bodyweight, skeletal muscle mass, myofiber size and forelimb grip strength when compared to the wild type group. In addition, the treatment with mRK35 significantly increased the weights of triceps, quadriceps, and gastrocnemii in both wild type and Tg$ACTA1^{D286G}$ mice ($p<0.05$ for each). These findings suggest that myostatin inhibition with mRK35 can become a potential treatment to promote muscle growth in patients with nemaline myopathy, which results in muscle mass loss and weakness. However, this treatment is only applicable in the context of Acta1 mutations (which are associated with the development of nemaline myopathy), like the one present in the Tg$ACTA1^{D286G}$ group of mice, which means that further research is needed in human patients with nemaline myopathy [30].

Creatine Supplementation

Creatine oral supplementation can improve muscle mass levels and function and can help reverse the effects of muscle mass loss [31]. Several studies on creatine supplementation in healthy elderly individuals have shown that it may improve muscle strength and resistance, which could assist in the rehabilitation of sarcopenic individuals. A study in which 28 men (mean age 67.8 ± 4.0 years) and women (69.3 mean age ± 6.3 5 years) ingested 5g of creatine per day, demonstrated that creatine consumption results in greater muscle fat free mass and strength [31]. In another study, thirty healthy men (average age 70) took creatine (a 0.3g/kg dose for five days followed by a dose of 0.07g/kg for 4 weeks or a placebo) while undergoing a regime of strength training exercises three times per week [32]. Subjects who took creatine had a 3.3 kg increase of lean muscle mass compared with a 1.3 kg increase in the placebo group [32]. However, the potential effects of creatine to help treat muscle mass loss and sarcopenia is still controversial due to contradicting results in different studies. For example, are search study by Forbes et al., (2017) sought to determine the effects of four weeks of high intensity interval training, where three sessions were performed weekly, and the combination with creatine supplementation in a group of females (n=17) [33]. The females in the study were either assigned to a group that would receive 0.3 g·kg-1·d-1 of creatine for 5 days followed by 0.1 g·kg-1·d-1for 23 days or a placebo. The results demonstrated that there were no changes over time for fat mass, whole-body lean mass, or insulin resistance. The authors concluded that the use of creatine supplementation, in this case combined with high-intensity interval training, did not promote improvements in cardio-respiratory fitness, performance or body composition [33].

Bimagrumab

Bimagrumab is a monoclonal antibody that binds to type II activin receptors and blocks the attachment of its ligands (e.g., myostatin, activin A). These ligands usually prevent muscle growth and protein anabolism. Bimagrumab prevents the effects caused by these ligands and have shown to increase muscle mass in young and older adults. In a study by Rooks et al., (2017) 40 subjects with sarcopenia were treated with 30 mg/kg of intravenous bimagrumab. This resulted in a "measured change from baseline levels in thigh muscle volume (TMV), subcutaneous and intermuscular fat, appendicular and total lean body mass, grip strength, gait speed and 6-minute walk distance (6MWD)" [34]. Thus, TMV, in the subjects treated with bimagrumab, increased by week 2 and maintained the same levels above the baseline measures through the duration of the treatment. The placebo group did not demonstrate changes in TMV levels. In addition, the subjects who performed a slow walking speed test at baseline, during the weeks of treatment with bimagrumab had a statistically significant improvement (p-value= 0.022) in their gait speed and 6MWD measures. The placebo did not present a statistically significant change from the

baseline values. The authors concluded that a 16-week period of bimagrumab treatment improved muscle mass strength and slow walking speed in sarcopenic older adults [34].

Tirasemtiv

Tirasemtiv is an investigational drug that is a highly selective activator of the fast-skeletal muscle (type II) troponin complex [35]. It was developed to increase muscle strength by amplifying the response of muscle when neuromuscular input is diminished secondary to a neuromuscular disease [35]. In a recent study by Hansen et al. (2014), healthy men received tirasemtiv or placebo in a randomized, double-blind, 4-period, and crossover design to determine if tirasemtiv could amplify the response of muscle to neuromuscular input in humans [35]. The results demonstrated that "tirasemtiv increased the force produced by the tibialis anterior in a dose, concentration, and frequency-dependent manner with the largest increases (up to 24.5% (SE 3.1), $P < 0.0001$) produced at sub-tetanic nerve stimulation frequencies (10 HZ)" [35]. The authors concluded that the results indicate that future studies should be performed to test the efficacy of tirasemtiv as a "potential therapy in conditions marked by diminished neuromuscular input." [35].

CONCLUSION

Diverse investigations show that sarcopenia is caused by multiple factors, such as physical inactivity, bad nutrition, cellular changes related to the age; nevertheless, more research is needed to understand these influences. It has been demonstrated that progressive strength training is an excellent intervention for delaying the onset of muscle mass loss and sarcopenia. In addition, good nutrition can have a positive effect in sarcopenic patients and stimulate the increase of muscle mass, especially for older people. Further clinical studies are critical to develop new treatments that prevent the development of, or reverse sarcopenia and muscle mass loss. Allopurinol, oxandrolone, ursolic acid, omega-3 fatty acids, myostatin inhibition, bimagrumab and tirasemtiv are each currently being investigated as potential treatments that may improve the efficiency, cost-effectiveness and quality of life of the elderly populations around the world. It is important to understand that these potential treatments have limitations. For example, the effects of ursolic acid and inhibitors of myostatin have been mostly studied on mice. Thus, further research is needed to determine how these treatments can be developed for humans. In addition, creatine supplementation is still under investigation because of the heterogeneity of the results in many research studies.

DISCLAIMER

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REFERENCES

1. Walston JD. Sarcopenia in older adults. CurrOpinRheumatol. 2012; 24: 623-627.
2. Rosenberg IH. Sarcopenia: origins and clinical relevance. J Nutr. 1997; 127: 990S-991S.
3. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, Boirie Y, Cederholm T, Landi F, et al. Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. Age Ageing. 2010; 39: 412-423.
4. Marzetti E, Leeuwenburgh C. Skeletal muscle apoptosis, sarcopenia and frailty at old age. ExpGerontol. 2006; 41: 1234-1238.
5. Bean JF, Leveille SG, Kiely DK, Bandinelli S, Guralnik JM, Ferrucci L. A comparison of leg power and leg strength within the In CHIANTI study: which influences mobility more? J GerontolABiol Sci Med Sci. 2003; 58: 728-733.
6. Keller K, Engelhardt M. Strength and muscle mass loss with aging process. Age and strength loss. Muscles Ligaments Tendons J. 2013; 3: 346-350.
7. Chen LK, Lee WJ, Peng LN, Liu LK, Arai H, Akishita M. Recent Advances in Sarcopenia Research in Asia: 2016 Update From the Asian Working Group for Sarcopenia. J Am Med Dir Assoc. 2016; 17: 767.e1-7.
8. Johnston AP, De lisio M, Parise G. Resistance training, sarcopenia, and the mitochondrial theory of aging. ApplPhysiolNutrMetab. 2008; 33: 191-199.
9. Gadelha AB, Paiva FM, Gauche R, De oliveira RJ, Lima RM. Effects of resistance training on sarcopenic obesity index in older women: A randomized controlled trial. Arch GerontolGeriatr. 2016; 65: 168-1673.
10. Kunkel SD, Suneja M, Ebert SM, Bongers KS, Fox DK, Malmberg SE, et al. "mRNA expression signatures of human skeletal muscle atrophy identify a natural compound that increases muscle mass." Cell Metab. 2011; 13: 627-638.
11. Arany Z, Foo SY, Ma Y, Ruas JL, Bommi-Reddy A, Girnun G, et al. HIF-independent regulation of VEGF and angiogenesis by the transcriptional coactivator PGC-1alpha. Nature. 2008; 451: 1008-1012.
12. Lee JS, Auyeung TW, Kwok T, Lau EM, Leung PC, Woo J. Associated factors and health impact of sarcopenia in older chinese men and women: a cross-sectional study. Gerontology. 2007; 53: 404-410.
13. Rolland Y, Czerwinski S, Abellan Van Kan G, Morley JE, Cesari M, Onder G, et al. Sarcopenia: its assessment, etiology, pathogenesis, consequences and future perspectives. J Nutr Health Aging. 2008; 12: 433-450.
14. Frontera WR, Meredith CN, O'reilly KP, Knuttgen HG, Evans WJ. Strength conditioning in older men: skeletal muscle hypertrophy and improved function. J Appl Physiol. 1988; 64: 1038-1044.
15. Strasser B, Keinrad M, Haber P, Schobersberger W. Efficacy of systematic endurance and resistance training on muscle strength and endurance performance in elderly adults--a randomized controlled trial. Wien KlinWochenschr. 2009; 121: 757-764.
16. Binder EF, Yarasheski KE, Steger-May K, Sinacore DR, Brown M, Schechtman KB, et al. Effects of progressive resistance training on body composition in frail older adults: results of a randomized, controlled trial. J GerontolABiol Sci Med Sci. 2005; 60: 1425-1431.
17. Denison HJ, Cooper C, Sayer AA, Robinson SM. Prevention and optimal management of sarcopenia: a review of combined exercise and nutrition interventions to improve muscle outcomes in older people. ClinInterv Aging. 2015; 10: 859-869.
18. Lambert CP, Wright NR, Finck BN, Villareal DT. Exercise but not diet-induced weight loss decreases skeletal muscle inflammatory gene expression in frail obese elderly persons. J Appl Physiol. 2008; 105: 473-478.

19. Landi F, Calvani R, Tosato M, Martone AM, Ortolani E5, Savera G, et al. Protein Intake and Muscle Health in Old Age: From Biological Plausibility to Clinical Evidence. Nutrients. 2016; 8.

20. Morton RW, Traylor DA, Weijs PJM, Phillips SM. Defining anabolic resistance: implications for delivery of clinical care nutrition. CurrOpinCrit Care. 2018; 24: 124-130.

21. Derbre F, Ferrando B, Gomez-Cabrera MC, Sanchis-Gomar F, Martinez-Bello VE, Olaso-Gonzalez G, et al. Inhibition of xanthine oxidase by allopurinol prevents skeletal muscle atrophy: role of p38 MAPKinase and E3 ubiquitin ligases. PLoS ONE. 2012; 7:e46668.

22. Eyigör S, Kutsal YG. Reason of progressive loss of function and frailty in elderly: sarkopenia. Turkısh Journal of Geriatrics. 2013; 16: 45463.

23. Ferrando B, Olaso-gonzalez G, Sebastia V, Viosca E, Gomez-cabrera MC, Viña J. [Allopurinol and its role in the treatment of sarcopenia]. Rev EspGeriatrGerontol. 2014; 49: 292-298.

24. Mavros Y, O'Neill E, Connerty M, Bean JF, Broe K, Kiel DP, et al. Oxandrolone Augmentation of Resistance Training in Older Women: A Randomized Trial. Med Sci Sports Exerc. 2015; 47: 2257-2267.

25. Ebert SM, Dyle MC, Bullard SA, Dierdorff JM, Murry DJ, Fox DK, et al. Identification and Small Molecule Inhibition of an Activating Transcription Factor 4 (ATF4)-dependent Pathway to Age-related Skeletal Muscle Weakness and Atrophy. J Biol Chem. 2015; 290: 25497-25511.

26. Arterburn LM, Hall EB, Oken H. Distribution, interconversion, and dose response of n-3 fatty acids in humans. Am J ClinNutr. 2006; 83: 1467S-1476S.

27. Smith GI, Atherton P, Reeds DN, Mohammed BS, Rankin D, Rennie MJ, et al. "Dietary omega- 3 fatty acid supplementation increases the rate of muscle journal of aging research protein synthesis in older adults: a randomized controlled trial. Am J Clin Nut. 2011; 93: 402-412.

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

29. White TA, Lebrasseur NK. Myostatin and sarcopenia: opportunities and challenges - a mini-review. Gerontology. 2014; 60: 289-293.

30. Tinklenberg JA, Siebers EM, Beatka MJ, Meng H, Yang L, Zhang Z, et al. Myostatin inhibition using mRK35 produces skeletal muscle growth and tubular aggregate formation in wild type and TgACTA1D286G nemaline myopathy mice. Hum Mol Genet. 2018; 27: 638-648.

31. Hespel P, Op't Eijnde B, Van Leemputte M, Ursø B, Greenhaff PL, Labarque V, et al. Oral creatine supplementation facilitates the rehabilitation of disuse atrophy and alters the expression of muscle myogenic factors in humans. J Physiol (Lond). 2001; 536: 625-633.

32. Brose A, Parise G, Tarnopolsky MA. Creatine supplementation enhances isometric strength and body composition improvements following strength exercise training in older adults. J GerontolABiol Sci Med Sci. 2003; 58: 11-19.

33. Forbes SC, Sletten N, Durrer C, Myette-côté É, Candow D, Little JP. Creatine Monohydrate Supplementation Does Not Augment Fitness, Performance, or Body Composition Adaptations in Response to Four Weeks of High-Intensity Interval Training in Young Females. Int J Sport NutrExercMetab. 2017; 27: 285-292.

34. Rooks D, Praestgaard J, Hariry S, Laurent D, Petricoul O, Perry RG, et al. Treatment of Sarcopenia with Bimagrumab: Results from a Phase II, Randomized, Controlled, Proof-of-Concept Study. J Am Geriatr Soc. 2017; 65: 1988-1995.

35. Hansen R, Saikali KG, Chou W, Russell AJ, Chen MM, Vijayakumar V, et al. Tirasemtiv amplifies skeletal muscle response to nerve activation in humans. Muscle Nerve. 2014; 50: 925-931.

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