The impact of resistance training and protein interventions on age-related sarcopenia

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Abstract

Sarcopenia is an involuntary loss of muscle mass, which may be an intrinsic part of the ageing process rather than the effect of age associated disease. The degradation of muscle mass leads to loss of strength, and eventually to decreased functional status such as poor balance, gait speed, increased risk of falls, fractures, and ultimately an increased risk of mortality. Present guidelines state that physically inactivity or a decreased physical activity level is an important part of the mechanisms of sarcopenia, and therefore physical activity can be seen as an important factor in reversing or modifying the development of sarcopenia. Most research on sarcopenia tends to focus on（1）Preventing muscle protein breakdown and（2）Adequate muscular stimulation in order to increase muscle protein synthesis by resistance training in combination with nutritional intervention（adequate protein and energy intake）. The researches show that exercises and the adequate amounts of dietary protein from high-quality sources are two important ways to increase muscle protein synthesis（MPS）and slow the progression of sarcopenia. Some scholars suggested that intake of 1.5 g protein/kg/day, or about 15-20% of total caloric intake is a target for elderly populations in terms of health and physiology function. Resistance training combined with protein（or amino acid）supplements is utilized frequently to prevent age-related sarcopenia. Therefore, the beneficial interaction between dietary protein or amino acid and resistance exercise has to be considering an effective tool to improve physiology functionality and life quality in older age.

Key word: Sarcopenia, muscle protein synthesis（MPS）, aging, resistance exercise.

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1. Introduction

Aging is associated with a progressive loss of neuromuscular function and performance that often leads to loss of muscle mass (Vandervoort, 2002; Kallio et al., 2010; Aoki & Demura, 2011). This includes declines in muscle strength and function, which is a condition known as sarcopenia (Doherty, 2003). From the National Health and Nutrition Examination Survey (NHANES) data, these investigators found that 35% of the older adults was in moderate sarcopenia, whereas 10% had severe sarcopenia (Booth & Zwetsloot, 2010). Age-related sarcopenia results in the decreases in muscle fiber area, especially in type II fiber area.

The nutrients that have been most consistently linked to sarcopenia in older adults are vitamin D, protein, long-chain polyunsaturated fatty acid, and a number of antioxidant nutrients, which include carotenoids, selenium, and vitamins E and C (Kallio et al., 2010). Optimizing diet and nutrition throughout life may be key to preventing sarcopenia and promoting physical capability in older age. However, dietary protein is considered a key nutrient to muscle protein synthesis (MPS) in older age (Vandervoort, 2002). Physical activity is an important factor that has the ability to reverse or modify the sarcopenia, especially with resistance modalities of exercise. Resistance training is probably the most effective measure available to prevent and treat sarcopenia (Sundell, 2011). Some researchers demonstrated the fact that the combination of resistance training and nutritional interventions may be a promising candidate for combating sarcopenia. Therefore, the purpose of this review was to focus on the possible factors and mechanisms which lead to the development of the age-related sarcopenia. Furthermore, the effects of resistance training or/and dietary protein intervention on muscle synthesis was also be discussed in this article.

2. Changes in muscle mass with age-related sarcopenia

It is well known that aging is associated with a decrease in skeletal muscle mass, as well as a greater decline in lower body skeletal muscle mass when compared to upper body skeletal mass (Bemben,Massey,Bemben,Misner & Boileau, 1991). Lower limb weakness has significant implications for the performance of functional tasks and the maintenance of balance (Doherty, 2003; Sanchis-Gomar,Gomez-Cabrera & Vina, 2011). After about age 50, muscle mass decreases at an annual rate of 1–2% (Doherty, 2003; Abellan van Kan, 2009). The decline in muscle strength is even higher, amounting to 1.5% per year between ages 50 and 60 and 3% per year thereafter (Von Haehling,Morley & Anker, 2010). Therefore, the average reported age-related decreases in strength are on the order of 20-40% (Young,Stokes & Crowe, 1985). Sarcopenia is an involuntary loss of muscle mass, which may be an intrinsic part of the aging process rather than the effect of age associated disease (Roubenoff, 2000). More specifically, sarcopenia was defined as a height-adjusted muscle mass (muscle mass/height^2) of two standard deviations (2 SDs) or more below the mean of a young reference population. New definitions by the Evans and the European

Working Group on Sarcopenia in older People（EWGSOP）defines that the gradual decline in muscle mass and muscle strength is also significantly related to low physical performance and function, and furthermore to loss autonomous ability in older persons（Cruz-Jentoft et al., 2010）. Numbers studies have demonstrated that sarcopenia is multi-causal with mechanisms including age-sedentary lifestyle, malnutrition（reduction in dietary protein）, inactivity, declines in neuron function, hormone concentration, and proinflammatory state（figure 1）（Leiter,Peeler & Anderson, 2011; Walsh et al., 2011）. The consequences of sarcopenia include decreases in certain body functions, such as metabolic rate, muscular strength, and maximal oxygen consumption（VO_2max）（Roubenoff, 2000; Doherty, 2003）. Therefore, sarcopenia may also form disability linked to poor balance, gait speed, falls, fractures, and probably contributes in daily living function（Roubenoff, 2000）.

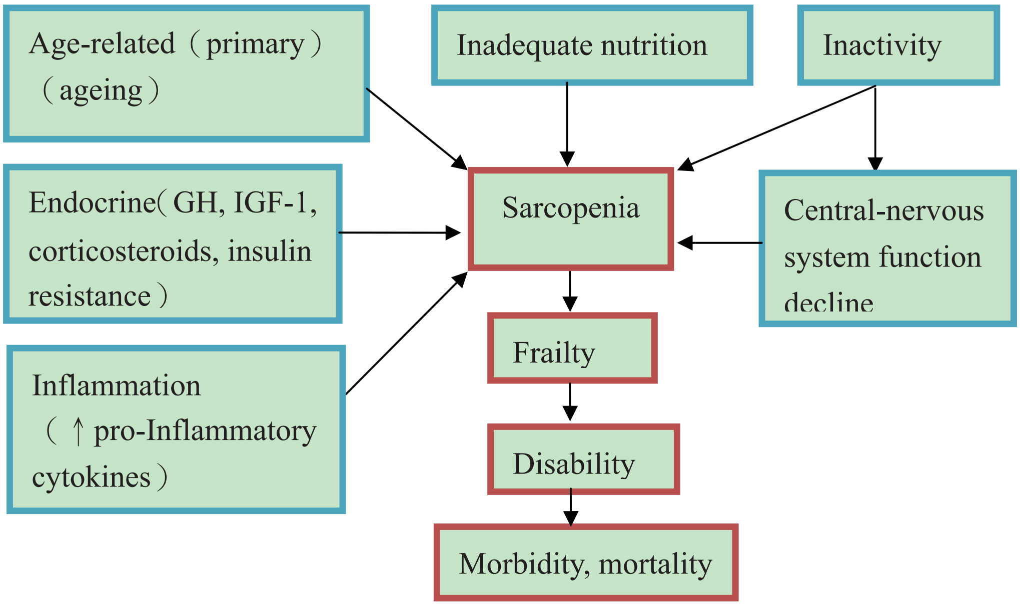

Figure 1. The Mechanism and Effect of Sarcopenia in Elderly. Adapted from Roubenoff（Roubenoff, 2000）and Hickson（Hickson, 2006）. GH: growth hormone, IGH-1: insulin-like growth factor 1.

3. Resistance exercise and muscular adaption for sarcopenia

In clinical trials, the best non-hormonal tool to prevent and treat method on sarcopenia is physical activity or exercise. Multitudes studies show that exercise, especially resistance exercise, has positive effects on sarcopenia(Binder et al., 2005; Kosek,Kim,Petrella,Cross & Bamman, 2006;

Sanchis-Gomar,Gomez-Cabrera & Vina, 2011）. Because increase exercise or physical activity in elderly population may delays the decline in physical function（VO2max or muscle strength）with aging. Resistance exercise which provides a means of preserving skeletal muscle tissue with age has been reported to have improved muscular mass and strength. Furthermore, repeated bouts of resistance exercise are well known to bring protein synthesis by causing microscopic damage to the muscle cells(catabolism), which in turn are quickly repaired(anabolism)(Yarasheski et al., 1999). Binder et al.(2005)investigated the effects of resistance training in frail elderly adults(78 years and older）. Their results showed that muscle strength was significantly increased after 6 weeks of resistance training（2-3 session per week）, and muscular strength and whole body fat-free mass in elderly men and women was also improved after finishing three months of progressive training（Binder et al., 2005）. Kosek et al.（2006）observed that muscular fitness improve both in young and older adults after 4 months of resistance exercise training for 3 times per week, whilst skeletal muscle hypertrophy in young was significantly greater than in older men and women individuals（Kosek,Kim,Petrella,Cross & Bamman, 2006）. Strasser et al.（2009）demonstrated that maximum strength was significantly increased by an average 15% for leg press（$P<0.05$）, 25% for bench press（$P<0.05$）, 30% for bench pull（$P<0.05$）, and lean body mass increased by 1.0 ± 0.5□kg after 6 months of resistance training for 3 times per week in elderly adults.

Numerous studies examined the cellular mechanisms responsible for the effects of resistance exercise on human skeletal muscle protein synthesis（Dreyer et al., 2006; Fujita et al., 2007）. Scholars prove that resistance exercises can augment the type Ⅱ fibers size and slow down the rate of sarcopenia, due to the training reversing the age-related decline in skeletal muscle satellite cell content（Snijders,Verdijk & van Loon, 2009）. Muscle satellite cells（SCs）are also the main contributor to muscle maintenance, growth, and repair（Thornell, 2011）. Another concept is that resistance exercise leads to activation of mammalian target of the rapamycin（mTOR）and various up and downstream kinases during the immediate postexercise recovery period（Parkington,LeBrasseur,Siebert & Fielding, 2004; Dreyer et al., 2006）. Those studies appear that resistance training can active in promoting synthesis of proteins in skeletal muscle. The important of the key intracellular pathway signals in the regulation of protein synthesis is the phosphatidylinositol 3-kinase（PI3K）-mTOR pathway（Moore,Atherton,Rennie,Tarnopolsky & Phillips, 2011）. That plays a key role in integrating the stimulating effects of amino acids, insulin, and muscle contraction on muscle protein synthesis. Therefore, mTOR pathways increases protein synthesis through hyperphosphorylating eukaryotic initiation factor binding protein 1(eIF4E-BP1), thereby freeing up eIF-4E to initiate translation, and by phosphorylating ribosomal protein S6（rpS6）kinase（p70S6K）（Kim,Wilson & Lee, 2010）, and it is important pathway to prevent muscle loss in sarcopenia individuals or aging process.

The researchers identified that progressive resistance training is an effective and safe tool against muscle loss, and loading intensity to promote hypertrophy with resistance training should approach 60–80% of one repetition maximum（1RM）and exercise volume ranging from 3 to 6 sets per muscle group per week（Strasser,Keinrad,Haber & Schobersberger, 2009）. The high intensity exercise may have the positive effects for muscle build and hypertrophy. However, many elderly are contraindicated or trouble to high load resistance training and are limited to low-load, low-intensity exercise. Therefore, the American College of Sports Medicine recommends progressive weight training program or weight bearing calisthenics（8–10 exercises involving the major muscle groups of 8–12 repetitions each）, stair climbing, and other strengthening activities that use the major muscle groups（Chodzko-Zajko et al., 2009）. The American Heart Association（AHA）also recommends that the initial weight used for moderate resistance training in the elderly be approximately 30-40% 1RM which may be inadequate to promote gains in muscle mass, due to the importance of exercise volume, particularly with the MPS response（Williams et al., 2007）. Furthermore, recommendations for the prescription of resistance training should allow for and be limited to 8–12 repetitions per set for healthy sedentary adults or 10–15 repetitions at a low level of resistance, for example, < 40% of 1RM, for older（>50–60 y of age）, more frail persons, or cardiac patients. The involving the major muscle groups should contain the upper and lower extremities, eg, chest press, shoulder press, triceps extension, biceps curl, pull-down（upper back）, lower-back extension, abdominal crunch/curl-up, quadriceps extension or leg press, leg curls（hamstrings）, and calf raise（Williams et al., 2007）. In Summary of the prevention viewpoint, all elderly subjects should be advised to start such an exercise program and continue it as long as possible.

In recent, a novel mode of low-load, low-intensity bout of exercise in combination with blood flow restriction（BFR）for elderly or older people has recently received attention in the scientific literature（Loenneke & Pujol, 2011）. For example, Karabulut et al. compared the training effects on high-intensity（80% 1RM）resistance training, low-intensity（20% 1RM）resistance training with vascular restriction, and a control group that performed no exercise in older males（50-64 years）. These investigators demonstrated that the high intensity and the low intensity group with occlusion had significantly greater strength in every exercise, when compared with control group. Although they did note that the percentage increase in the high intensity group's leg extension strength was significantly greater than low intensity exercise, the researchers concluded that low intensity occlusion training was almost as effective as high intensity training in older males（Karabulut,Abe,Sato & Bemben, 2010）. Their findings suggested that leg muscle strength improves with the low-load vascular restriction training may provide a resistance training mode to the elderly. However, the cellular mechanisms responsible for the BFR which induced increase in muscle growth are still unclear.

4. Effect of dietary Protein and Exercise intervention

Previous studies confirmed the relationship between several nutritional factors and muscle mass, strength, function and physical performance（Kim,Wilson & Lee, 2010; Kim et al., 2011）. In the following, the present knowledge about the role of nutrition, such as protein, vitamin D, polyunsaturated fatty acid, and antioxidant nutrients, will be reviewed and practical nutritional recommendations derived in the prevention of sarcopenia（Hickson, 2006; Kallio et al., 2010; Volkert, 2011）. However, researches indicate that protein is considered a key nutrient in older age among those nutrients. Since skeletal muscles mainly consist of protein, and muscle protein synthesis can be stimulated by dietary protein. Dietary protein provides amino acids that are needed for the synthesis of muscle protein, and importantly, absorbed amino acids have a stimulatory effect on muscle protein synthesis（Evans, 2004; Campbell & Leidy, 2007）. Research evidence that the RDA for elderly should be greater than 0.8 g/kg/day, because the RDA for protein amount may not be adequate to completely meet the metabolic and physiological needs of virtually all older people（Campbell,Trappe,Wolfe & Evans, 2001）. In addition, many elderly people may reduce appetite and fail to eat enough protein, while they suffer from chronic diseases（e.g., diabetes, low-grade inflammation）, so that further should increase their dietary protein requirements. Therefore, ensuring adequate dietary protein intake, especially essential amino acids（EAA）, using high quality proteins is essential for this special population（Aoki & Demura, 2011）. Because the essential amino acids stimulate human muscle protein synthesis primarily by activating the mammalian target of rapamycin signaling pathway in human skeletal muscles（Little & Phillips, 2009）. Therefore, optimal health status, reduced risk of chronic diseases, and improved outcomes may be achieved by increasing protein intake to approximately 1.5 g protein/kg/day（or about 15-20% of total caloric intake）（Campbell,Trappe,Wolfe & Evans, 2001; Wolfe,Miller & Miller, 2008）. It is generally accepted that 25-30 g of high quality protein, is the amount needed per meal to maximally stimulate MPS in the elderly. However, there has a big problem about eating behavior in elderly and older populations. Research showed that most people regardless of age inadequately distribute their protein throughout the day and they may consume over 65% of their daily protein after 1830 hour（De Castro, 1987）. Scholars figure that the elderly should focus on consuming at least 25g of protein three times a day, separated by approximately 4-5 hours. Eating at 800 h, 1300 h, and 1800 h would maximally stimulate protein synthesis three times a day promoting skeletal muscle hypertrophy and/or maintenance of muscle mass（Loenneke & Pujol, 2011）.

It also has the extent to combine protein or amino acid supplementation and resistance exercise interventions that may be more effective than changing nutrient intake alone. For example, Drummond et al.（2008）investigated the muscle protein synthesis responses after ingesting essential amino acids（EAA: 20 g）one hour following a leg resistance exercise. The results showed that the acute MPS response after resistance exercise and EAA ingestion is similar between young and old men. The authors concluded the combination of resistance exercise and EAA ingestion should be a useful strategy to combat sarcopenia（Drummond et al., 2008）. Drummond et al.（2008）also noted that the rapid and very large increases detected in mTOR and S6 kinase-1 phosphorylation（S6K1）following the EAA intake（Drummond et al., 2008）. In Fujita et al. study showed that after leucine-enriched EAA supplementation intervention, the phosphorylation status of Akt, mTOR, 4E-BP1, and S6K1 increased whereas the phosphorylation status of eukaryotic elongation factor 2（eEF2）was decreased. However, amino acid supplementation studies showed to increase MPS, lean mass, and improve physical function in short-term experimental evidence, further work with longer term trails is needed to define optimal protein intakes in older age.

5. Conclusion

In summary, habitual, lifelong physical activity is very important to delay the loss of skeletal muscle mass with aging, especially with progression resistance exercise. Prolonged participation in resistance exercise has clear benefits for slowing the loss of muscle and bone mass and strength. High-quality dietary protein consumption are considered contributors to an adult person's skeletal muscle size and strength, whole body fat-free mass, and health through the lifespan. Studies also prove that the interactive effects of diet and exercise on physical function have been studied most extensively in relation to protein/amino acid supplementation. Therefore, adequate dietary protein and resistance training may be key to preventing sarcopenia and promoting physical capacity function in older age.

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