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Review Article

Effects of Resistance Exercise Training and Protein Supplementation on Muscle Loss in the Elderly

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Aging is an inevitable process for human beings, and it gradually makes physical fitness and organ functions decline. Senescent cells will secrete proinflammatory factors that accelerate organ aging, which result in the deteriorated quality and dysfunction of organs, and increase the risk of death. Mass muscle loss is a major feature in the aging process, as the stem cells in muscle cells will gradually decrease with age, which will reduce the repair rate of muscle cells and cause mass muscle loss. At this time, the body will begin to feel that muscle strength is not as good as before, and activity is greatly reduced, which further accelerates the speed of muscle loss, and even causes muscle atrophy. In addition, during the aging process, the hormone concentration in the body will change due to the decrease in the sensitivity of muscle cells to hormones. Over time, the proportion of body fat increases, which promotes insulin resistance, inhibits protein synthesis signals in muscles, disrupts the balance between synthesis and breakdown rates, and causes mass muscle loss. While resistance exercise training could increase physical activity, elevate cell sensitivity to hormones, and stimulate muscle synthesis, exercise could also cause muscle breakdown during the process of exercise. Therefore, it is necessary to immediately supplement protein during the repair period after exercise for the muscle synthesis rate increase, and promote mass muscular development. Moreover, as aging reduces the body's metabolic rate, the speed of muscle repair is slower after exercise, thus, the quantity of protein needed by the elderly will be more than that of adults. This article reviews the benefits of resistance exercise and recommends protein supplements for improving muscle loss in the elderly.

Key words: aging, muscle loss, exercise training, essential amino acid, branched chain amino acid

Introduction

With the development of society and the advancements of technology and medicine, the social population structure has also changed, as the average life expectancy has been extended, and the proportion of the elderly population has increased significantly (14). In 2018, the proportion of the population over 65 years of age in Taiwan exceeded 14%, and we formally entered an aged society, and the elderly population continues to increase day by day. As Taiwan is one of the countries with the fastest population aging speed in the world, it needs to pay more attention to the issues related to advanced age than some other countries. Aging causes physical degradation, resulting in the so-called geriatric syndrome, which means the occurrence of certain clinical signs in the elderly make it more difficult to diagnose individual diseases. Symptoms include: organ degeneration, poor nutrition, muscle loss, unstable gait, inability to move, incontinence, poor cognitive function, etc. (13), leading to the occurrence of diseases. The diseases related to aging include: cardiovascular diseases, cancer, chronic respiratory diseases, diabetes, and sarcopenia (18). Regarding the payment of health insurance, the government is increasing the payment proportion of elderly people, and the relative expenditures will continue to increase. Therefore, how to alleviate problems in terms of disease prevention and improving physical functions are the popular research topics of preventive medicine today.

Exercise is highly correlated with promoting the health of elderly people; for example, muscle strength and overall body strength can be increased

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through muscle training, while cardiopulmonary functions can be improved by aerobic training. When the level of physical activity increases, the risk of death can be reduced by about 30~40% (1, 21). In addition, protein intake is associated with promoting the health of older people. As older people may suffer from malnutrition due to changes in physical conditions, their bodies will show a negative nitrogen balance state that causes body weight loss, muscle loss, immune dysfunction, and other issues resulting in increased mortality. Supplementing sufficient protein can prevent malnutrition, and supplementing protein after exercise can also prevent muscle protein loss caused by exercise; therefore, exercise and protein are valuable for improving the occurrence of post-senile groups and diseases.

Effects of Aging on the Body

Aging Mechanism

As people age, their internal organs will gradually deteriorate, resulting in changes in physiological functions and increasing the risk of disease. Aging increases the secretion of proinflammatory factors in the body to induce the production of excessive free radicals, which causes oxidative stress on cells and results in cell damage (16). In addition, when the body is affected by proinflammatory factors, it results in impaired DNA gene expression, and the immune system gradually becomes dysfunctional and unable to protect stem cells. As the number of stem cells in the body is reduced, the rate of cell regeneration declines, which accelerates the rate of apoptosis and reduces the repair rate. When cell regeneration capacity decreases, damaged tissues cannot be completely repaired, thus, the remaining cells have to cope with a greater physiological load, organ functions will slowly decline, and complications will start to take place, which lead the body into a vicious circle of the mass loss of organs and increased risk of death (18).

Muscle Loss

Mass muscle loss and functional degradation are the characteristics of aging, and with the increase of age, the number of satellite cells in muscles decrease by 24~35% during the aging process. As satellite cells are responsible for the regeneration of muscle cells in the body, when muscle cells are repaired slowly, muscle fiber cells will gradually shrink and muscle mass will be gradually lost. Decreased muscle mass will reduce muscle strength and cause daily physical activities to gradually become unloadable (22), which in turn leads to reduced activity levels. According to the use and disuse theory, the less frequent use of muscles leads to more serious muscle loss (23). Insufficient physical activity will accelerate the loss of muscle mass and lead to weakness in the limbs, and the decrease in lower limb strength also increases the risk of falls. If the elderly fail to improve the state of their muscle loss before disability, they will face a long-term bedridden future. In addition, aging will cause the nervous system to degenerate and lead to chronic neuropathy, and the loss of motor functions will cause the failure of muscles to effectively contract, thus, reducing the amount of muscle activity (28). During the aging process, hormones in the body are also factors that affect muscle loss. The concentration of hormones that stimulate muscle synthesis in the body is negatively correlated with age, such as Insulin -like Growth Factor 1 (IGF-1) and Growth Hormone (GH), and as muscle cells are less sensitive to hormones, it results in an increase in the proportion of body fat. However, fat cells secrete proinflammatory factors and induce insulin resistance. Insulin is a muscle protein synthesis hormone in the body, and insulin resistance will inhibit the protein synthesis signal in muscle fibers, disrupt the balance between muscle protein synthesis and the breakdown rate, and cause the muscle protein breakdown rate to become greater than muscle protein synthesis, thus, causing mass muscle loss (26). When muscle loss affects the functions of daily life, it is known as sarcopenia, which affects blood sugar regulation and the protein supply in the body, which causes an increased risk of metabolic diseases and the body will exhibit a negative nitrogen balance, resulting in weight loss and decreased immunity, which weakens the body's resistance to disease, leads to wounds that will not heal, and increased risk of death; therefore, a fixed amount of activity must be maintained to prevent muscle degradation and atrophy. In order to initiate muscle protein synthesis signals, which will increase muscle mass, it is necessary to improve the sensitivity of muscle cells to synthetic hormones. As increasing the intensity of muscle training has positive effect on the sensitivity to synthetic hormones, people can reduce the risk of hospitalization and death due to muscle weakness by increasing the intensity of their muscle training to increase muscle strength (24).

Judgment Criteria for Sarcopenia

Sarcopenia is defined as the severity of muscle loss, as determined by the skeletal muscle index, which is calculated by dividing the total muscle mass by the total body weight. There are different judgment standards for different measurement instruments and genders. Using the Dual Energy X-ray

Absorptiometry (DXA) or Bioelectrical Impedance Analysis (BIA), the determination point of tangency is less than 7.0 kg/m^2 for men; while the determination value is less than 5.4 kg/m^2 for women using DXA, or less than 5.7 kg/m^2 using BIA (5). Currently, sarcopenia has been identified as one of the geriatric syndromes; as the name implies, it means muscle loss, which is closely related to the mobility and quality of life of the elderly, and has inherent increased risk of disability and death. Understanding the determination criteria for sarcopenia can provide more precise strategies for exercise and diet planning, and thus, can more effectively prevent the elderly's risk of sarcopenia. In addition, the degree of muscle function degradation is considered in the definition of sarcopenia, and it has been proposed that the diagnosis of sarcopenia requires both loss of muscle mass and the loss of muscle strength and performance (12). Muscle strength is the most commonly used method for assessing muscle function, and is one of the practical clinical definitions and common diagnostic criteria of age-related sarcopenia (7). Due to differences in congenital and acquired physical conditions between Asians and Caucasians, in 2014, the Asian Working Group for Sarcopenia (AWGS) applied Asian data to redefine the judgment criteria for Asians. By taking elderly people over 60 years old as a high-risk group, their muscle strength and physical performance were determined, where low grip strength and slow walking speed were taken as the manifestations of muscle function decline for muscle function assessment, in addition to the skeletal muscle index judgment, and grip strength and walking speed were simultaneously measured. The absolute grip strength judgment standard for men and women is less than 26 kg and 18 kg, respectively; the standard walking speed is 0.8 m per second, and a value below this is considered slow walking (5). Through such judgement criteria, we can detect and prevent sarcopenia in a timely manner, and improving muscle strength with appropriate defensive measures can reduce the incidences of sarcopenia.

Impact of Resistance Exercise Training

Increasing physical activity can improve the phenomenon of aging; thereby promoting physical fitness, preventing bone mineral loss, maintaining muscle mass, and increasing the number and metabolic functions of the mitochondria. In terms of muscle degeneration in the elderly, muscle strength improvement is very important and people must have basic muscle strength to maintain physical activity and prevent sarcopenia (19). The best exercise for muscle strength training is resistance exercise training, which improves muscle strength and muscle endurance through the number of repetitions and intensity. Moreover, if muscle strength is high enough, it can also increase muscle mass, thus, it is an effective defense measure for the elderly who need to improve their muscle strength. However, as such exercise process will affect the protein balance, the risk of resistance exercise must be considered in the exercise design to effectively achieve the promotion of muscle strength and quality.

Benefits of Resistance Exercise Training

The characteristic of skeletal muscle aging is that the quality and function of skeletal muscles decline with age; therefore, if no timely preventive measures are taken, it will lead to age-related sarcopenia. Muscle decline causes poor muscle quality, resulting in insufficient muscle strength, which reduces the activity of the elderly, and insufficient activity will cause muscle atrophy. In order to prevent muscle degradation and atrophy, improving muscle strength should be a priority for maintaining and increasing muscle mass. Muscle strength is divided into muscle strength and muscle endurance. Muscle strength is defined as the strength of a muscle when it resists a certain resistance, as well as the maximum strength produced when the muscle contracts again. Muscle endurance is defined as the time or the number of repetitions, meaning when a muscle maintains the same strength and can continue to exert force (10). Therefore, muscle strength and endurance training are mainly based on resistance exercise training, where a single repetitive movement of different intensities can improve muscle fitness. Muscle strength will gradually increase as the intensity of each training session becomes higher. In addition, the amount of training is related to the improvement of muscle quality; the theory of use and disuse states that, in order to promote the body to begin the repair of its muscles for muscle regeneration, and then, increase the muscle mass of the aging cells in the muscles, the muscles that are rebuilt by the amount of training must be greater than the original load of the body (9). Increasing muscle mass can promote muscle training for greater strength. When muscle strength is improved and maintained, the activity of the elderly also increases, which can maintain daily physiological activities and reduce the risk of muscle loss due to insufficient activity.

Recommended Prescription for Resistance Exercise Training

Using progressive training to increase the intensity of training will allow the elderly to develop regular exercise habits, meaning people who sit or lie in bed

for a long time in daily life can be encouraged to regularly stand up and walk or engage in physical activities to maintain muscle strength (3). Moreover, progressive resistance exercise training can increase muscle mass and strength. The principle of progressive load is to use the resistance to muscle contraction to strengthen the skeletal muscles, and to break through the maximum load of the body each time, which will facilitate the stable improvement of muscle strength and quality (8). The frequency of exercise will also affect the increase in muscle mass, and studies have shown that exercising should be conducted 2 to 3 days a week and the exercise intensity should reach medium to high intensity. The intensity is often expressed by RM (Repetition Maximum), which means the number of repetitions for the maximum strength, thus, 1 RM is 1 repetition for the maximum strength and a medium-high intensity is about 65~80% 1RM; only by reaching this load weight can people effectively increase muscle quality and function (29). According to literature, the design range of progressive resistance exercise for the elderly is engaging in 2~3 groups of exercises at 30% to 80% of the exercise intensity, where each group repetition is 8~10 times, and there will be significant benefit in improving muscle mass and strength after about 8 weeks of continuous training (4). However, resistance exercise training is riskier for the elderly; as their cardiopulmonary functions decline due to loss of muscle mass, it affects cardiopulmonary fitness during exercise, in addition to insufficient muscle strength caused by muscle decline. If the exercise intensity is too high, it may increase the burden on the body. Thus, considering the appropriate amount and intensity of exercise is the first step in successful resistance exercise training.

Risks of Resistance Exercise Training

Systemic organ functions decline with age. Too high resistance training intensity will increase the risk of cardiovascular and skeletal diseases. Resistance training is a double-sided sword; although it is an effective strategy for the elderly to increase muscle strength, it will also increase the breakdown of protein due to the load of resistance training when improving the muscle protein synthesis rate, which prevents the body from effectively promoting the net protein synthesis rate during the training recovery period (24). Moreover, increased age causes the body repair speed to decrease. If the intensity of resistance training is too high, muscle protein may not be completely repaired, and vigorous exercise will generate free radicals to increase oxidative stress in the body, resulting in increased muscle damage and fatigue (25), thus, resistance training strategies must match with other conditions and strategies, such as protein intake, the use of antioxidants, or both, in order to reduce the adverse effects of resistance training (24).

Resistance Exercise and Protein Supplement

As aging causes slow muscle repair, the elderly will have more proteolysis after resistance exercise training than healthy adults, and they may not be able to significantly increase their muscle mass. As shown in recent literature, a sufficient protein supplement can have a synergistic effect with resistance exercise training, because after the protein is digested into amino acid, and absorbed, the essential amino acid (EAA) can be used as a raw material for muscle protein synthesis. In addition, Branched Chain Amino Acid (BCAA) in EAA can effectively stimulate muscle protein synthesis signals, meaning muscle fibrin tends to be synthesized, and the muscle mass of the elderly can be effectively improved (15).

Essential Amino Acid (EAA)

Without protein supplementation after resistance exercise training, the body's net balance of muscle protein is decomposed; therefore, during the recovery period after exercise, sufficient protein is required to assist the repair of muscle fibers. Protein, which is broken down into amino acids, and then, absorbed by the body after digestion, is the raw material for building and repairing tissue in the body. There are 8 kinds of amino acids in the human body that cannot be synthesized by themselves and must be supplemented by food. They are called essential amino acids (EAA), including tryptophan, lysine, methionine, phenylalanine, threonine, leucine, isoleucine, and valine, which are transported to muscles through the blood as a raw material for building muscle fibrin, and supplementing sufficient EAA can improve muscle mass and promote muscle hypertrophy (15). The BCAAs of EAA, which are leucine, isoleucine, and valine, have high correlation with improving muscle mass, thus, they can be used as a supplement when muscles lack energy, and play an important role in stimulating the rate of protein synthesis during the recovery period.

Branched Chain Amino Acid (BCAA)

In the muscle energy metabolism system, BCAA can be used as a fuel when muscles need energy. When muscle glycogen is depleted during exercise, BCAA can be used as a raw material for the role of glycogen regeneration to promote energy metabolism. However, when the body has insufficient BCAA, muscle protein

will start to break down and release BCAA, in order to achieve the effect of continuous energy supply (27). In addition, BCAA is related to the protein synthesis pathway, where its role is to stimulate the protein synthesis mechanism and use EAA to build muscle fibrin. Leucine has the most significant benefit in BCAA, as it stimulates a series of synthetic signals to promote the protein synthesis rate and accelerate the muscle protein repair rate; thereby reducing damage to myofibrils and cytoskeleton protein, and lowering the risk of mass muscle loss (30). In addition to its role in protein synthesis, BCAA competes with tryptophan, and reduce its entry into the brain, thus, reducing the production of serotonin in the brain, which in turn delays fatigue (6). Therefore, improving BCAA in muscles will help to prevent mass muscle loss and alleviate the fatigue effect after exercise, which in turn enhances the effect of exercise training.

Recommended Amount and Source of Protein Supplement

As the concentration of amino acids are digested and decomposed in the body after ingestion, muscle growth depends on protein consumption. When the concentration of amino acids in the blood rises, it will stimulate muscle protein synthesis (MPS) and inhibit muscle protein breakdown (MPB). However, the recommended protein intake for the elderly is higher than the average adult; during the aging process, the ability to activate MPS is reduced, resulting in imbalanced protein balance and lower skeletal muscle quality. Many studies have shown that the recommended protein intake of 0.8-1 g per kg of body weight for general adults may not be sufficient to promote muscle health in the elderly, thus, it is recommended that the protein intake for the elderly is 1.2~2 g per kg of body weight, which is about 1.5~2 times the intake of adults. Protein supplementation and resistance exercise have a synergistic effect. In a cross design for comparing the intake of 20 g and 40 g of whey protein after resistance exercise for young people of about 20 years old, the intake of 40 g significantly increased the MPS rate by 20%, as compared with the intake of 20 g, while the protein digestion and absorption rate reached the peak at 20 g and the MPS response was greatest after exercise. Thus, in the young population, supplementing 20 g is enough to increase the MPS rate and increase muscle mass (17). However, in one retrospective study comparing the effect of protein intake between 70-year-old men and 20-year-old men, the elderly required a higher maximum effective protein dose when recovering after exercise, as compared with young people (20), as their MPS rate reached the peak when 35~40 g was supplemented after resistance exercise. In addition, after resistance exercise, supplementing with BCAA can help increase MPS, and the recommended amount of BCAA is 2~2.5 g per kg of body weight (2). As BCAA is a stimulating factor, it is recommended that the amount of supplementation is not significantly different between young and old people. Protein sources are divided into animal and plant-based, animal protein is mostly intact protein, that is, proteins that contain all EAAs, in which casein and whey protein are rich in BCAA and can greatly help muscle repair. However, research shows that long-term excessive intake of red meat will increase the risk of cardiovascular, kidney, and metabolic diseases, and thus, may increase the physical burden of the elderly. Therefore, it is recommended that vegetable protein can be interspersed in the weekly diet. The vegetable protein that has recently attracted attention is soy protein. In addition to being a complete protein, soy protein has BCAA contents second only to casein and whey protein, and it also has the effects of anti-oxidation and lowering blood lipids, thus, it may be a good source of protein for the elderly. As the elderly need longer time to repair muscles (11), the protein source chosen after exercise may need to be absorbed for a longer time. It is currently confirmed that, while whey protein is the most effective among adults, from the perspective of absorption speed, it may not be the most effective for the elderly due to its rapid absorption rate. Therefore, this issue requires more research.

Conclusion

As aging is a natural progression for organisms, in the geriatric syndrome, sarcopenia is a topic of concern. As muscle performance gradually declines, it will increase hospitalization and mortality rates, thus, we must understand the definition of sarcopenia, and its consequences, before we can effectively apply defensive measures against sarcopenia. Regular exercise training helps to delay muscle degeneration; via muscle breakdown, muscle training promotes the synthesis of muscle protein signals, promotes the body to rebuild and repair muscles, increases muscle mass, and uses the progressive training mode to gradually increase muscle strength. During muscle reconstruction, the body requires sufficient protein as the raw material, and these synthetic raw materials are EAA, where BCAA is a protein that stimulates synthetic signals, and has a synergistic effect with resistance exercise training. As the body repairing ability in elderly people is slow due to aging, in order to improve their muscle strength and athletic performance, the elderly need to intake

35~40 g of protein after exercise to effectively promote their muscle protein synthesis rate and increase their muscle mass. In addition to higher protein needs, elderly people require protein that can cope with slow absorption in the body, thus, they require protein other than whey protein, which has the fastest absorption rate and is most effective for adults. Therefore, the best protein source still needs to be confirmed, and it is hoped that future studies can determine the most effective defense measures against sarcopenia.

Conflicts of Interest

The authors declare no conflict of interest.

References

1. Arem, H., Moore, S. C., Patel, A., Hartge, P., De Gonzalez, A. B., Visvanathan, K., Campbell, P. T., Freedman, M., Weiderpass, E., Adami, H. O., Linet, M. S., Lee, I. M. and Matthews, C. E. Leisure time physical activity and mortality: a detailed pooled analysis of the dose-response relationship. *JAMA internal medicine 175*: 959-967, 2015.
2. Baum, J. I., Kim, I. Y. and Wolfe, R. R. Protein consumption and the elderly: what is the optimal level of Intake? *Nutrient 8*: 359, 2016.
3. Best-Martini, E., and Jone-DiGenova, K. A. (2014). *Exercise for Frail Elders. (2nd ed.)* Campaign: Human Kinetics.
4. Cadore, E. L., Pinto, R. S., Bottaro, M. and Izquierdo, M. Strength and endurance training prescription in healthy and frail elderly. *Aging Dis. 5*: 183-195, 2014.
5. Chen, L. K., Woo, J., Assantachai, P., Auyeung, T. W., Chou, M. Y., Iijima, K., Jang, H. C., Kang, L., Kim, M., Kim, S., Kojima, T., Kuzuya, M., Lee, J. S. W., Lee, S. Y., Lee, W. J., Lee, Y., Liang, C. K., Lim, J. Y., Lim, W. S., Peng, L. N., Sugimoto, K., Tanaka, T., Won, C. W., Yamada, M., Zhang, T., Akishita, M. and Kojima, T. Asian Working Group for Sarcopenia: 2019 consensus update on sarcopenia diagnosis and treatment. *JAMDA. 21*: 300-307, 2020.
6. Choi, S., Disilvio, B., Fernstrom, M. H. and Fernstrom, J. D. Oral branched-chain amino acid supplements that reduce brain serotonin during exercise in rats also lower brain catecholamines. *Amino Acids 45*: 1133-1142, 2013.
7. Cruz-Jentoft, A. J., Bahat, G., Bauer, J., Boirie, Y., Bruyère, O., Cederholm, T., Cooper, C., Landi, F., Rolland, Y., Sayer, A. A., Schneider, S. M., Sieber C. C., Topinkova, E., Vandewoude, M., Visser, M. and Schneider, S. M. Sarcopenia: revised European consensus on definition and diagnosis. *Age Ageing 48*: 16-31, 2019.
8. De Oliveira Silva, A., Dutra, M., De Moraes, W. M., Funghetto, S., Lopes de Farias, D., Fernandes dos Santos, P. H. and Schoenfeld, B. J. Resistance training-induced gains in muscle strength, body composition, and functional capacity are attenuated in elderly women with sarcopenic obesity. *Clin. Interv. Aging*. *13*: 411-417, 2018.
9. Fisher, J. P., Steele, J., Gentil, P., Giessing, J. and Westcott, W. L. A minimal dose approach to resistance training for the older adult; the prophylactic for aging. *Exp. Gerontol.* 99: 80-86, 2017.
10. Goulet, E. D., Mélançon, M. O., Lafrenière, D., Paquin, J., Maltais, M. and Morais, J. A. Impact of mild hypohydration on muscle endurance, power, and strength in healthy, active older men. *J. Strength Cond. Res. 32*: 3405-3415, 2018.
11. Hackney, K. J., Trautman, K., Johnson, N., Mcgrath, R. and Stastny, S. Protein and muscle health during aging: benefits and concerns related to animal-based protein. *Anima. Front. 9*: 12-17, 2019.
12. Janssen, I., Heymsfield, S. B. and Ross, R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. *J. Am. Geriatr. Soc. 50*: 889-896, 2002.
13. Larsson, L., Degens, H., Li, M., Salviati, L., Lee, Y. I., Thompson, W., Kirkland, J.L. and Sandri, M. Sarcopenia: aging-related loss of muscle mass and function. *Phys. Rev.* 99: 427-511, 2018.
14. Lee, R. D. and Mason, A. Generational economics in a changing world. *Popul. Devel. Rev. 37*: 115-142, 2011.
15. Liao, C. D., Tsauo, J. Y., Wu, Y. T., Cheng, C. P., Chen, H. C., Huang, Y. C., Chen, H. C. and Liou, T. H. Effects of protein supplementation combined with resistance exercise on body composition and physical function in older adults: a systematic review and meta-analysis. *Am. J. Clin. Nutr*. *106*: 1078-1091, 2017.
16. López-Otín, C., Blasco, M. A., Partridge, L., Serrano, M. and Kroemer, G. The hallmarks of aging. *Cell. 153*: 1194-1217, 2013.
17. Macnaughton, L. S., Wardle, S. L., Witard, O. C., McGlory, C., Hamilton, D. L., Jeromson, S., Lawrence, C. E., Wallis, G. A. and Tipton, K. D. The response of muscle protein synthesis following whole-body resistance exercise is greater following 40 g than 20 g of ingested whey protein. *Phy. Rep. 4*: e12893, 2016.
18. MacNee, W., Rabinovich, R. A. and Choudhury, G. Ageing and the border between health and disease. *Eur. Respir. J.* 44: 1332-1352, 2014.
19. McPhee, J. S., French, D. P., Jackson, D., Nazroo, J., Pendleton, N. and Degens, H. Physical activity in older age: perspectives for healthy ageing and frailty. *Biogerontology 17*: 567-580, 2016.
20. Moore, D. R., Churchward-Venne, T. A., Witard, O., Breen, L., Burd, N. A., Tipton, K. D., and Phillips, S. M. Protein ingestion to stimulate myofibrillar protein synthesis requires greater relative protein intakes in healthy older versus younger men. *J. Gerontol. A Biol. Sci. Med. Sci. 70*: 57-62, 2015.
21. Moore, S. C., Lee, I. M., Weiderpass, E., Campbell, P. T., Sampson, J. N., Kitahara, C. M. and Adami, H. O. Association of leisure-time physical activity with risk of 26 types of cancer in 1.44 million adults. *JAMA internal medicine. 176*: 816-825, 2016.
22. Patel, K., Simbi, B., Ritvos, O., Vaiyapuri, S. and Dhoot, G. K. Dysregulated cell signalling and reduced satellite cell potential in ageing muscle. *Exp. Cell Res*. *385*: 111-685, 2019.
23. Petroni, M. L., Caletti, M. T., Dalle, Grave, R., Bazzocchi, A., Aparisi, Gomez, M. P. and Marchesini, G. Prevention and treatment of sarcopenic obesity in women. *Nutrient 11*:1302, 2019.
24. Ren, G., Yi, S., Zhang, H. and Wang, J. Ingestion of soy-whey blended protein augments sports performance and ameliorates exercise-induced fatigue in a rat exercise model. *Food Funct. 8*: 670-679, 2017.
25. Ribeiro, A. S., Deminice, R., Schoenfeld, B. J., Tomeleri, C. M., Padilha, C. S., Venturini, D. and Cyrino, E. S. Effect of resistance training systems on oxidative stress in older women. *Int. J. Sport Nutr. Exerc. Metab. 27*: 439-447, 2017.
26. Sachs, S., Zarini, S., Kahn, D. E., Harrison, K. A., Perreault, L., Phang, T. and Schoen, J. A. Intermuscular adipose tissue directly modulates skeletal muscle insulin sensitivity in humans. *Am. J. Physiol. Endocrinol. Metab. 316*: E866-E879, 2019.
27. Sanz, J. M. M., Navarro, A. N., García, E. S. and López, I. S. An overview on essential amino acids and branched chain amino acids. *Nutr. Enhan. Sports Perform.* 509-519, 2019.
28. Tang, J. E. and Phillips, S. M. Maximizing muscle protein anabolism: the role of protein quality. *Curr. Opin. Clin. Nutr. Metab. Care. 12*: 66-71, 2009.
29. Walker, S., Serrano, J. and Van, Roie E. Maximum dynamic lower-limb strength was maintained during 24-week reduced training frequency in previously sedentary older women. *J. Strength Cond. Res. 32*: 1063-1071, 2018.
30. Wolfe, R. R. Branched-chain amino acids and muscle protein synthesis in humans: myth or reality? *J. Int. Soc. Sports Nutr. 14*: 30, 2017.