



## Review Article

### Impact of Exercise on Fall and Its Consequences among Elderly People

Mehdi Kushkestandi<sup>1</sup>, Mohsen Parvani<sup>\*2</sup> , Raheleh Baradaran<sup>3</sup>, Alireza Rezaei<sup>4</sup>, Hamed Pourhamzeh<sup>5</sup>

<sup>1</sup>. Wellness and Lifestyle Science Initiative Group, School of Art and Science, Rutgers University New Brunswick, New Jersey, United States

<sup>2</sup>. Department of Physical Activity and Health, Faculty of Sport Sciences and Physical Education, University of Coimbra, Coimbra, Portugal

<sup>3</sup>. Allameh Bohlool Gonabadi Hospital, Gonabad University of Medical Sciences, Gonabad, Iran

<sup>4</sup>. Department of Exercise Physiology, Faculty of Physical Education and Sport Sciences University of Tehran, Alborz Campus, Tehran, Iran

<sup>5</sup>. Department of sport pathology, Faculty of Physical Education and Sports Sciences, Islamic Azad University, South Tehran Branch, Tehran, Iran

\* **Corresponding Author:** Department of Physical Activity and Health, Faculty of Sport Sciences and Physical Education, University of Coimbra, Coimbra, Portugal. **Tel:** +351239247741, **Email address:** mparva2020@gmail.com

## ABSTRACT

### Article history

Received 22 Aug 2022

Accepted 25 Jun 2023

**Citation:** Kushkestandi M, Parvani M, Baradaran R, Rezaei A, Pourhamzeh H. Impact of exercise on fall and its consequences among elderly people. *Elderly Health Journal*. 2023; 9(1): 44-54.

Falls are a threat to the health of older adults and can reduce their ability to remain independent. Furthermore, fall is known as one of the geriatric syndromes and is more common in older people and about 20 to 40 percent of older people have reported a history of falling per year. It should be noted that fall or fear of falling causes immobility in the elderly and immobility is linked with various non-communicable diseases, geriatric syndromes development, and mortality in the long term. As a result, finding a cost-effective, safe, and proper approach to prevent, control, and even treat of falls is absolutely crucial. Regarding the exercise benefits in all ages especially in the elderly, we supposed that various types of exercise such as aerobic, balance, and resistance training with different intensities have variant advantages in these subjects. Therefore, in this review study, we investigated the charter of different types of exercise in preventing and controlling fall based on recent evidence, providing involved mechanisms, as well as the effects of exercises on fall-related risk factors.

**Keywords:** Aerobic Exercise, Exercise Therapy, Sarcopenia, Elderly, Health

### Definition of fall and prevalence

Falling is defined as a location change from an upper surface to a lower surface like the floor or the ground. Despite that many definitions are considered for falls, there is a key point in most opinions that a falling is involuntary (1), and it is not affected by medical reasons such as blood pressure or a stroke and/or a strong extrinsic force (2). It is important to attend to the definition of falls in studies because it leads to collecting of wrong data and can affect occurrence and prevalence rates. Falls are known as one of the geriatric syndromes and are more common in older people according to the reasons will discuss in the next

sections. Falls are liable for immobility, morbidity, and mortality, therefore in aged people are highlighted as a one of the main problems of social health (1).

The prevalence determination of falls in this high-risk population is considered essential for identifying risk factors and prevention programs. About 20 to 40 percent of older people ( $\geq 65$  years) have reported a history of fall per year, while older adults over 70, reported more than that (3). According to a systematic review and meta-analysis in 2019, the lowest prevalence of falls has been reported in the United States 22% and in England 28% while the highest

prevalence of falls was in Egypt 60.3% (1). These variations in the prevalence of falls may be related to the ethnicity, culture, study designs, sample size, sampling methods, age, the definition of fall, and the presence of various risk factors (1).

Of five hospital events, two cases related to falls and their frequency daily varies from 1.4 to 13.0 per 1000 patients (4). For a person who has experienced a fall once, the chance of falling would increase two-thirds in the following year (5). Among those who experienced a fall, about 65% of females and 44% of males fell inside their homes and about 25% of males and 11% of females had a fall in their gardens. Falling indoors occurs in the rooms that are most commonly used including bedrooms, kitchens and dining rooms (6). People under 75 years have more likely to fall outdoors than people over 75 years (6). In the community, 80% of falls occur during the day and only 20% during the night. Some studies have been proven that the rate of falls are superior in women than men (7). The reason could be that females have hormonal changes during elderly or after menopause that could be followed with loss in bone mass and sarcopenia faster than males (1). The results of previous studies showed a low level of education was associated with falls in the elderly which means a lack of awareness would impress people for accepting healthcare advice about their health (8). In a study in 2011, presented fall prevalence are different in various races that reflect differences in culture, socioeconomic status, and geographic distribution. In addition, the rate of falls increase on cold and wintry days (9). Plus, older patients in psychiatric problems are more expected to experience fall than normal older adults, regarding the psychiatric signs, cognitive disorders and psychotropic drugs' side effects.

### Fall and complications

Falls are more prevalent in older adults and mostly leads to injury (10), suffering from various diseases, delay in improvement, decreasing social relationships, increasing psychosocial complications, depression, low quality of life and also it imposes a great burden on the people and their families or relatives (11).

#### Physical complications

##### Fractures

Fractures and injuries are considered part of fall complications which lead to disability and even death. Sixty four percent of whole fall-induced injuries are related to fractures. The most common fractures include the proximal femur, limbs, spine, and hip. It should be noted that females aged 50 years and older regarding osteoporosis are mostly at risk of a fracture (12). A quarter of the female and a third of the male with a femoral fracture usually passed over within a next year of fracture; and among survived subjects, half were disabled constantly and the other half needed long-term treatment or specific care (13). Also, there is potent evidence to reveal that after hospital discharge, osteoporotic fracture patients have higher morbidity,

subsequent fractures, and mortality (5). They cause a decrease in height, an increase in thoracic kyphosis and consequently cardiorespiratory failure, reduction in quality of life and life expectancy. Fall-induced hip fractures are known as a serious worry among the elderly and are the most common. Annually, hip fractures are reported more than 258,000. In addition, the prevalence of this complication among females is estimated twofold as high as males (5).

Fall syndrome in older adults (> 75 years) forms 70% of whole emergency unit visits and 40% of hospital receptions; also, the average recovery time in the mentioned subjects is estimated around 30 days (14). Even after discharge from the hospital, half of the elderly require special nursing care (5).

#### Diseases

Fall or fear of falling causes immobility in the elderly. Given the literature, elderly immobility is linked with a risk of various diseases such as type 2 diabetes, cardiovascular disease and mortality in the long-term (15-17). It has been reported that physical inactivity reduced lipoprotein lipase (LPL) level as a regulating lipoprotein. Low LPL leads to increased triglyceride, reduced plasma HDL levels, as well as affect blood pressure and metabolic situations (18). Falls may cause trauma brain injury (TBI). It was reported that fall in elderly induced TBI, and was associated with dementia. Pathologic studies have proven that  $\beta$ -amyloid protein increases in the brain immediately after a TBI (19). Also, the Apolipoprotein E overexpresses amongst those who have an experience of fall. Apolipoprotein E disturbs the lipid transportations to regenerating neurons; and this way would reduce growth and branching of neuritis and causes dementia (18).

#### Social complications

Fall restricts mobility to the extent that may decrease the ability to do routine activities including dressing, bathing, shopping, or housekeeping. Also, a decrease in mobility in older adults could cause avoiding heading public events, meeting, and ceremony and consequently leads to social isolation within the family or the community (20). It is even possible to increase dependence on family and friends. In other words, excessive and permanent inactivity may lead to a decrease in muscle strength and postural control, which could cause limitations in physical and social activities; subsequently, muscle atrophy, lower mobility, and imbalance as well as increasing the risk of falling would happen (21).

#### Psychosocial complications

After fall, most physicians pay attention to urgent injuries and fractures and often ignore its psychological consequences. Falls can cause serious psychological trauma to the elderly, which make rehabilitation period more difficult (22). Psychological consequences that appear immediately including fear, self-efficacy, decreased confidence, body image impairment, insecurity, embarrassment, depression, and anxiety

(22). The sum of these psychological consequences that is linked with a motor part is called post-fall syndrome (23). Fear of falling and post-fall syndrome are psychosocial problems that cause decrease in aged people's mobility (23).

Despite these descriptions, the main reason for the social isolation and psychological consequences could be considered inactivity or sedentary lifestyle regarding falling or fear of falling. Falls can disrupt older people's lives, even if the damage is not severe enough to require hospitalization; therefore, any kind of falls in these people should be considered and followed.

#### *Financial complications*

According to a systematic review, it has shown that fall-related costs were estimated between 0.85% and 1.5% of the whole healthcare costs (24). Of course, these costs depended on fall severity, injury type, and recovery time. Treatment fees for fall-induced fractures are extremely expensive including hospitalization costs, emergency department costs, outpatient treatment costs, and indoor care. Estimates of these costs have been reported to be different between different countries, which can be related to differences in the quality of health care, insurance coverage, or variations in complications. Annually, a substantial amount of approximately \$50 billion is allocated to cover medical expenses associated with non-fatal fall injuries, while an additional \$754 million is dedicated to addressing fatal falls. This financial burden is distributed across different sources, with Medicare shouldering approximately \$29 billion, private or out-of-pocket payers contributing \$12 billion, and Medicaid covering \$9 billion of the total costs (25, 26). The direct medical expenditures encompass a wide range of healthcare services, including hospitalization, nursing home care, and professional fees for medical practitioners, rehabilitation programs, community-based services, utilization of medical equipment, expenses related to prescription drugs, and administrative costs associated with insurance processing. However, it is important to note that these direct costs do not fully account for the comprehensive impact of fall injuries, such as long-term consequences including disability, reliance on others for daily activities, productivity loss due to absence from work and household responsibilities, as well as diminished overall quality of life (25, 26).

#### **Etiology of fall / risk factors**

There are potentially many risk factors for falling, which are categorized into intrinsic, extrinsic and combined causes (17, 27-29). Intrinsic risk factors known individual characteristics that linked with risk of falling in elderly. Extrinsic risk factors are social and physical factors that related to the environment. Fall external factors are more common in people under 75 years of age. If both intrinsic and extrinsic factors are present, falls are classified as combined risk factors

(27). In this review, we examine the most common risk factors for falls in the elderly.

#### *Osteoporosis*

Osteoporosis and sarcopenia are two musculoskeletal aging's symptoms that increase risk of fall in the elderly. There are many reasons for musculoskeletal aging such as alterations in body composition, inflammation and hormonal imbalance. Inflammatory molecules directly and indirectly affect musculoskeletal metabolism and endocrine system (30). Inflammaging is defined as age-related chronic inflammation and it is caused by the lifetime exposure to antigenic agents including clinical and subclinical infections (31). Inflammaging leads to a decrease in muscle mass and strength, bone loss, sex steroids and growth hormone decline (32).

Furthermore, with age subcutaneous fat reduces, and visceral fat and fat infiltration to muscle fibers increase. These events lead to insulin resistance and inflammation which show musculoskeletal metabolism alterations and disruption in mesenchymal stem cell differentiation and cause sarcopenia and osteoporosis (32). In other terms, an increase in abdominal fat and fatty acids in the muscle fibers disrupt natural cellular signaling and lead to inflammation and hormonal imbalance that affect muscle and bone tissues (33). Sex steroids hormones are crucial for bone and muscle metabolism and functions, reduces with age. This leads to osteoporosis, sarcopenia, and the increase of the inflammatory markers; it ultimately increases the risks of fall in the elderly (33).

#### *Sarcopenia*

Sarcopenia is known as loss of strength and muscle mass as well as diminished physical performance (29, 34, 35). The agents that lead to the progress of sarcopenia in the elderly include chronic inflammation and hormonal imbalance (with the same previous section mechanisms), atrophy of motoneurons, reduced protein intake and immobility (36). Sarcopenia has been linked with poor toleration, physical inactivity, slow gait speed and decreased mobility that all of the mentioned factors increase the risk of fall. Also, it was reported that weakness of lower body muscles that caused by loss of muscle mass and strength, leads to increased 2-3-fold of fall risk (34). Sarcopenia-induced fall happens because the physical performance in the elderly (36).

#### *Impaired sensory system*

Visual, vestibular, and somatosensory information are basic parts of maintaining balance during standing and walking (37). It has been shown that impaired eyesight especially decreased contrast sensitivity, disrupted visual field and depth conception have a direct relationship with fall risk (38). Allen et al., published a review article concerning age-related changes in the vestibular system, and how this may lead to imbalance and falling. They concluded somatosensory information from the hip and ankle is important to maintain balance during standing (38).

Plus, Quigley et al., reported that bilateral polyneuropathy in lower limbs decrease somatosensory input from feet and ankles; disrupts balance during standing and noticeably increases risk of falls (37).

#### *Diseases*

Certain conditions such as arthritis, diabetes, hypertension, visual impairment, and chronic obstructive pulmonary disease enhance fall risks in the elderly (39). Chronic diseases are on the rise in the elderhood concerning physiological and psychological alterations. Approximately 92% of elderly are involved in at least one chronic disease and 65-85% are involved in two or more chronic diseases (40).

Rossini et al., have demonstrated that rheumatic diseases and inability to get up from the floor are the strongest risk factors for fall in elder women living at home. They confirmed that corticosteroid therapy that is used for treating of rheumatic diseases could induce osteoporosis and consequently fall risk (41).

Several studies introduced diabetes mellitus as a fall risk factor among elderly. Possible mechanisms for that consist of peripheral neuropathy, autonomic neuropathy, retinopathy, diabetic foot ulcers, hypoglycemia, and diabetes medications (42, 43).

#### *Vitamin D deficiency*

Previous studies have shown that vitamin D, in addition to bone density and bone resorption, affects muscle strength (44). The main source of vitamin D is the skin and exposure to sunlight. In the elderly, the concentration of vitamin D3 precursor decreases in the skin, so they are involved in vitamin D deficiency and reduced muscle strength and bone health, and alternatively, experience falls (45). Especially if the condition is empowered with malnutrition in the elderly, the risk of falls would enhance multifold.

#### *Medications*

Drugs groups linked with increased fall risk are known "Fall risk increasing drugs". The most common group are sedatives, hypnotics, antipsychotics, antidepressants, antihypertensive and cardiovascular drug. They may cause sedation, disrupt balance and coordination that lead to increase of fall risk (46). Also, Physiological alterations created by age in blood pressure-regulating systems leads to disruption cardiovascular function and cause a change in blood pressure (47). On the other hand, vascular diseases such as coronary or carotid stenosis are common in aged people, so blood pressure is needed to provide adequate blood supply to tissues (46). In addition, Antihypertensive drugs, diuretics or antiarrhythmic drugs that interfere with the cardiovascular system may empower some falls-related risk factors (47).

#### *Insomnia*

Insomnia is prevalent among the elderly and may have considerable adverse consequences including falls. It has been reported that insomnia is notably linked with falls in adults  $\geq 60$  years aged. Insomnia symptoms are poor postural control, poor

consciousness, attention, slow reflex time, distress, and mood changes (48), which can raise the risk of falls. Furthermore, it has been shown that a decreasing of sleep duration, extreme daily sleepiness, or sleep disorders that are common in the elderly would enhance fall risk (48).

Although, elderly used psychotropic medications for insomnia treatment, including antipsychotics, antidepressants, and antianxiety, it has been proven that the association between insomnia and falls is independent of medication usage (49). Some evidence have indicated that non-pharmacological interventions, including meditation, yoga, Tai Chi, acupuncture, or acupressure are useful to treat insomnia and can diminish the risk of falls (50).

#### *Environmental factors*

In general, the most important factor that increases the risk of falling in the elderly is related to environmental factors. It has been shown that 81.7% of people who are exposed to environmental factors have experienced falls. Some of these environmental hazards include the entrance door, poor staircase design or its damage, irregularity and clutter in the environment, slippery passages or bathroom floors, unsafe mattresses, insufficient lighting (51, 52). According to previous researches, improving the conditions of the living environment such as optimizing sidewalks, streets, parks and public places, improving the construction of infrastructure facilities can be effective in preventing the elderly falling (52).

#### *Exercise role*

The role of exercise types in the falls as noted previously, falls are the main cause of injury in the elderly (53). Falls mostly threaten the older adults' physical and mental health. In the introduction, the types of injuries related to falls were described briefly. With the increased healthcare costs associated with falls, sports and clinical professionals have put a stronger emphasis on prevention and controlling of this trouble than in the past. In a recent study, researchers documented the role of exercise and physical activity as a healthy and cost-effective method for preventing non-communicable diseases and their side effects (53-61). In this section, we intend to describe the roles of various types of exercises (balance, aerobic, and resistance exercise) and their mechanisms with a focus on fall prevention.

#### *Balance training*

The ability to stand on one foot is known as balance (62-63). As a result, balance training should be included in the training program for the elderly as one of the key components of fall prevention (64). Leiros-Rodriguez R, Garcia-Soidan et al., found that 6 weeks balance training (two 50-minute sessions a week) substantially improved the balance in 14 elderly women (Berg Balance Scale) (65). In addition, Zhao et al., used two different training protocols; one of them included Tai chi training and the other one included



specific balance training. They reported that the risk of falls reduced significantly in both groups (15.2 and 18.8 percent, respectively). The balance marker was evaluated in this study by chair stand test, which is one of the fall risk tests (66). One of the most important compatibilities of balance training is the improvement in neuromuscular coordination, vestibular sense, and proprioception (64). This can lead to a better understanding of the person's stance in space and controlling his/her movements and would play an effective role in fall prevention. Importantly, it was proven that increased sensorimotor control of the brain by balance training could increase activities of the supplementary motor area in the brain (67). In fact, one of the most important compatibilities in the brain is the increasing of the brain's sensorimotor control after balance training, which is closely related to improved balance. At the same time, it has been shown that balance training can improve the spinal cord reflection by playing a positive role in neuromuscular activities such as improving the information processing in the spinal cord through the afferent and efferent nerves and in turn improve the balance by better controlling of autonomous system and voluntary motions (68). Furthermore, the Central Nervous System seems to be able to set the responses to the spinal cord reflection more effectively after one course of balance training. It also seems to be able to prevent fluctuations of the joints involved in movements and falls (68). As mentioned in the introduction, fear of falling is also an important factor in reducing the quality of life among the elderly, which can sometimes lead to fall directly (69). Moreover, balance training can psychologically diminish the fear of falling apart from the aforementioned neurophysiologic and physical adaptations (68) and reduce the rate of falls in the elderly. In the meantime, it is noteworthy that balance training should increase gradually from easy to difficult levels, such that apart from the mentioned physiological adaptations, the moves are learned more effectively and the risks of injuries will be reduced (70). According to the American College of Sports Medicine, performing balance training 2 or 3 times a week can lead to the best outcomes in reducing the risks of falling among the elderly (71).

#### *Aerobic training*

Aerobic training mainly includes walking, running, swimming, cycling, etc. which provides various advantages such as cardiovascular, muscular, and metabolic adaptations (72, 61). At the same time, previous studies have been indicated the direct effect of the reduction in cardiovascular fitness and its complications on risk of fall. Furthermore, regarding etiology of aging, getting older is accompanied by various systematic physiological and cellular dysfunctions that pave the way for the reduction of cardiovascular functions (73). Moreover, the positive effects of aerobic training on the reduction of falling among the elderly have been proven in several Meta analyses and review studies (74). Sousa et al., reported in a study, that three sessions of aerobic training for 32

weeks could reduce the risk of fall in old men significantly (75). It should be noted that the research in this field has been carried out with the focus on the effect of aerobic training on the fall risk indicators and the probable mechanisms induced by the aerobic training for fall prevention have received less attentions. Aerobic training like running is mainly performed in the form of rhythmic movements (that call for neuromuscular coordination). The most important factors of these training includes neuromuscular coordination, balance, and the mobility enhancement (76). At the same time, with doing aerobic exercise, the brain (the central and peripheral nervous system) provides better adaptations to motion demands, however, the mechanisms of this response have not been well clarified so far. Studies have indicated the significant increase in walking speed, balance test, and the reduced time of chair squat as a results of endurance training for the elderly (76). Therefore, it can be stated that aerobic training can improve neuromuscular coordination, mobility, and reduce the risks of falls significantly.

Aerobic training leads to better social life and reduces the fear of falls (one of the most important factors of falls) among the elderly by preventing psychological and behavioral problems, improving mood and the feeling of usefulness (77). The main mechanisms include the increased synthesis of hormones such as dopamine (effective in improving learning and focusing), serotonin (effective in improving the mood and the feeling of happiness), oxytocin (effective in improving and controlling anxiety), norepinephrine (effective in improving the focus and motivation), and increased expression of brain-derived neurotrophic factor. These can lead to the survival, growth, differentiation of nerve cells, and inducing synaptic plasticity in the long run and improving the function of impaired neural pathways (77). It should also be noted that the aforementioned points are the long-term aerobic training adaptations.

Apart from the reduction of fall risks, another advantage of aerobic training is preventing musculoskeletal disorders such as Sarcopenia, arthritis, and osteoporosis (36). It has been well proven that aerobic training is effective on most of the signaling pathways involved in Sarcopenia (78). Results of various studies show that aerobic training improves the mitochondria and muscular functions by improving maximal oxygen consumption ( $VO_{2max}$ ), mitochondrial density and numbers, insulin sensitivity, and energy expenditure (79), reducing the fat accumulation in skeletal muscle (79), improving the function of the mitochondrial enzymes such as citrate synthase and cytochrome c oxidase in muscular fibers and increasing the gene expressions involved in mitochondrial biogenesis (80). Furthermore, it has been well proven that chronic aerobic activities are accompanied by the expression of mitochondrial fusion factors such as mitofusin 1 and 2 and fission protein 1, dynamin-related protein 1, and IGF1 and increase the PGC1alpha levels significantly (81). These mechanisms mainly increase muscular protein

synthesis, improve muscular functions, and play an important role in preventing Sarcopenia in the elderly. As Sarcopenia is one of the most serious causes of falls and its consequences, it can be stated that aerobic activities probably improve the musculoskeletal functions, balance, and fall prevention indirectly by suppressing muscle loss indices.

Moreover, aerobic training plays an important role in bone health and preventing osteoporosis (82). The major mechanisms in this field consist an increase in Bone Mineral Density caused by the increasing osteoblast activities, enhancing the levels of bone formation biomarkers such as bone-specific alkaline phosphatase, Osteocalcin, calcium serum, and reducing the levels of bone resorption biomarkers such as deoxypyridinoline (83). Consequently, it can be stated that aerobic training can reduce the risk of falls and reduce their complications such as pelvic fractures in the elderly by improving bone health (preventing osteoporosis) through the aforementioned mechanisms.

Notably, moderate-intensity aerobic training improves sleep quality (increasing the sleep time, reducing the falling asleep time, reducing hypnotics by playing a positive role in the circadian melatonin rhythm, rectal temperature, sleep stages (reducing the time of light sleep, increasing the time of REM (Rapid Eye Movement)) and increasing the parasympathetic nervous system activity (48, 83). Consequently, since the reduction of the quality of sleep is one of the risk factors of falls among the elderly, the mentioned mechanisms would be considered as indirect effects of aerobic training that reduces the risk of falls in the elderly.

#### *Resistance training*

Resistance training is considered as body fitness program mainly performed by a variety of training modalities such as body weight, elastic bands, free weights, machines, and medicine balls with different goals (84). Weakness and muscle mass reduction are the most known problems in the elderly that are mainly accompanied by poor balance and poor gait ability, reduction of body activities and body weight, and finally leads to the increased risk of falls, hospitalization and even death (85). Among the recommended physical interventions, resistance training has a crucial strategy to prevent weaknesses and falls (70). Results of several studies have shown a significant improvement in the balance, gait speed, and SPPB and TUG test scores that all indicate a reduction in the fall risks regarding adaptability to resistance training (70). Nonetheless, few studies have focused on the other mechanisms involved.

It has been well proven that getting older is one of the reasons for the degeneration of the neuromuscular system, which is accompanied by a decrease in muscle abilities to power generation, impaired control in body movements, and daily activities (84). It is noteworthy that the neuromuscular system in the elderhood maintains its adaptability to training stimuli (86). The muscle activation pattern in movements that call for neuromuscular coordination decline by aging. The

heightened levels of agonist-antagonist co-activation in the elderly leads to a reduction in joint stability and maintaining balance (87). The aforementioned change in the movement pattern in the elderly can be accompanied by an improvement in mobility and fall prevention. Moreover, this activation pattern can reduce the perception of individuals from their environmental position while moving. Resistance training is considered as one of the most effective strategies in improving neuromuscular coordination and movement patterns in the elderly (88). These mechanisms mainly include decreased agonist-antagonist co-activation, improved coordination between agonist/synergist muscles in movements, increased neural drive to the primary agonist resulting in greater motor unit recruitment and higher motor unit firing rates, and improved Golgi tendon function and the vestibular sense (87), which could lead to better neuromuscular system feedback to the movements. Ultimately, improved mobility and neuromuscular coordination through these mechanisms can directly reduce the risks of falling and its consequences in the elderly.

Tensile and/or compressive stress, which is induced by resistance exercises, plays a significant role in increasing muscle protein synthesis (MPS) and its contractility (89). The other major mechanisms involved in this field consist of increased protein synthesis through the insulin-like growth factor 1 /Akt/ mammalian Target of Rapamycin (80), increased expression of transcription factors involved in muscle growth such as FOXO1, FOXO2, and FOXO3 (90), decreased myostatin expression (the factor involved in protein breakdown) and increased follistatin expression (the factor involved in protein synthesis) (80), increased intrinsically sensitive mechanical molecules expression (91), decreased expression of some other genes involved in the muscular atrophy such as Atrogin-1 and MuRF-1 (92), modulated protein expressions involved in mitophagy and autophagy. In a stark contrast, by improving of mitochondria quality, cellular homeostasis, and reducing cellular apoptosis could prevent mass reduction and muscle strength (93). On the other hand, an increase in anabolic process of muscles through the explained mechanisms can be considered as the most important effect of resistance exercises for Sarcopenia prevention and reduction of fall risks.

In addition, the influential role of resistance exercises in bone health is well proven (94). According to the Mechanostat theory, the bones have an intrinsically biological system that reinforces the bones in response to high mechanical strain (94). The mechanical load induced by resistance exercises is accompanied by an increase in Sclerostin expression and activity that acts as a Wnt antagonist. Wnt-signaling pathway increases the osteoprogenitor cell populations, decreases apoptosis (immature osteoblasts), and forms osteoblastic bones and reduces bone decomposition by the inhibition of osteoclast activity (95). Furthermore, resistance exercises play a significant role in preventing and reducing bone fractures by positive effects on the geometric markers

of bone strength (86). It has been proven that mechanical loads should 1- be applied dynamically, 2- induced high-frequency strains, and 3- applied rapidly. Moreover, if the high-impact mechanical loading is observed in the exercises, few repetitions suffice the best bone adaptations (94). In addition, since the osteocytes desensitize repetitive loadings (high numbers in one set), performing the exercises in short repetitions and rests between the sets will be more effective than the fixed number of movements in fewer sets (94). Moreover, it has been shown that the bones are adapted better with the normal movement patterns such as one-directional movements therefore, performing various movements like multi-directional training will be more useful for the skeletal response (88). In addition to the mentioned benefits, the prevention of osteoporosis and osteosarcopenia can be considered the most important advantages of resistance exercises to reduce fall risks in the elderly. Resistance exercise is recommended as an appropriate strategy to improve the quality of sleep (97). It is noteworthy that if the resistance exercises are performed 3 sessions a week, they will be clinically vital in improving the sleep quality and daily functions of the individuals (97). According to the proposed mechanism, resistance exercises increase body temperature before falling asleep and improve the Slow Wave Sleep (SWS) (98). Consequently, these exercises are more effective near sleep time. In a review study, Kovacevic et al. reported that higher intensity and frequency of resistance exercises are more advantageous in improving the quality of sleep (97). Consequently, resistance exercises can be used as a non-pharmacological and cost-effective intervention that improves the quality of sleep and indirectly reduces the risk of falls in the elderly.

## Conclusion

Exercising can be used as a safe and cost-effective strategy to prevent falls and their complications and the subsequent high medical costs in the elderly. Balance, aerobic, and resistance exercises decrease the risks of falls through the various mechanisms explained in this paper. The mechanisms mainly include improved body structure, increased balance, improved musculoskeletal condition, less drug use, lower risk of various aging-related diseases, improved sleep quality, improved muscle mobility, and decreased fear of fall.

## Suggestions for further studies

Considering the above-mentioned reports in this study, it can be stated that multi-component training including balance, aerobic, and resistance training or combination of mentioned training can be the most effective approach to prevent falls among the elderly. Moreover, it should be noted that further studies are required for a better understanding of the mechanisms involved in falls and the role of various exercises in them.

## Conflict of interest

The authors declare no conflict of interest, financial or otherwise.

## Acknowledgment

There was no financial support for this study.

## Authors' contribution

Conceptualization: Mehdi Kushkestanti, Mohsen Parvani

Methodology: Mehdi Kushkestanti

Investigation: Mohsen Parvani,

Writing – Original Draft: Mohsen Parvani, Raheleh Baradaran, Alireza Rezaei

Writing – Review & Editing: Mehdi Kushkestanti,

Resources: Mohsen Parvani,

Supervision: Mehdi Kushkestanti,

Supervision: Mehdi Kushkestanti,

All authors read and approved the final version of the manuscript.

## References

1. Alqahtani BA, Alshehri MM, Hoover JC, Alenazi AM. Prevalence of falls among older adults in the Gulf Cooperation Council countries: a systematic review and meta-analysis. *Archives of Gerontology and Geriatrics*. 2019; 83: 169–74.
2. Sharif SI, Al-Harbi AB, Al-Shihabi AM, Al-Daour DS, Sharif RS. Falls in the elderly: assessment of prevalence and risk factors. *Pharmacy Practice (Granada)*. 2018; 16(3): 1-7.
3. Stanaway FF, Cumming RG, Naganathan V, Blyth FM, Handelsman DJ, Le Couteur DG, et al. Ethnicity and falls in older men: low rate of falls in Italian-born men in Australia. *Age and Ageing*. 2011; 40(5): 595–601.
4. Severo IM, Almeida M de A, Kuchenbecker R, Vieira DFVB, Weschenfelder ME, Pinto LRC, et al. Risk factors for falls in hospitalized adult patients: an integrative review. *Revista da Escola de Enfermagem da USP*. 2014; 48(3):540–54.
5. Nazrun AS, Tzar MN, Mokhtar SA, Mohamed IN. A systematic review of the outcomes of osteoporotic fracture patients after hospital discharge: morbidity, subsequent fractures, and mortality. *Therapeutics and Clinical Risk Management*. 2014; 10: 937-48.
6. Kelsey JL, Berry SD, Procter-Gray E, Quach L, Nguyen USD, Li W, et al. Indoor and outdoor falls in older adults are different: the maintenance of balance, independent living, intellect, and Zest in the Elderly of Boston Study. *Journal of the American Geriatrics Society*. 2010; 58(11): 2135–41.
7. Bergen G, Stevens MR, Burns ER. Falls and fall injuries among adults aged ≥ 65 years—United States, 2014. *Morbidity and Mortality Weekly Report*. 2016; 65(37): 993–8.
8. Abreu DR de OM, Azevedo RC de S, Silva AMC da, Reiners AAO, Abreu HCA. Factors associated with

- recurrent falls in a cohort of older adults. *Ciencia & Saude Coletiva*. 2016; 21: 3439–46.
9. Unguryanu TN, Grijbovski AM, Trovik TA, Ytterstad B, Kudryavtsev AV. Weather conditions and outdoor fall injuries in Northwestern Russia. *International Journal of Environmental Research and Public Health*. 2020; 17(17): 1–16.
  10. Luk JK, Chan TY, Chan DK. Falls prevention in the elderly: translating evidence into practice. *Hong Kong Medical Journal*. 2015; 21(2): 165–71.
  11. Demanze Laurence B, Michel L. The fall in older adults: physical and cognitive problems. *Current Aging Science*. 2017; 10(3): 185–200.
  12. Liu W, Yang LH, Kong XC, An LK, Wang R. Meta-analysis of osteoporosis: fracture risks, medication and treatment. *Minerva Medica*. 2015; 106(4): 203–14.
  13. Ehlinger M, Favreau H, Eichler D, Adam P, Bonnomet F. Early mechanical complications following fixation of proximal femur fractures: From prevention to treatment. *Orthopaedics & Traumatology: Surgery & Research*. 2020; 106(1): 79–87.
  14. Pi HY, Hu MM, Zhang J, Peng PP, Nie D. Circumstances of falls and fall-related injuries among frail elderly under home care in China. *International Journal of Nursing Sciences*. 2015; 2(3): 237–42.
  15. Kushkestani M, Nosrani SE, Parvani M, Rezaei S. The relationship between the level of physical activity and dementia in elderly residents of nursing homes in Tehran. *Biomedical Journal of Scientific & Technical Research*. 2020; 29(3):22437–43.
  16. Kushkestani M, Parvani M, Bathaezadeh SY, Pour Nosrani SE. The evaluation of differences on geriatric syndromes between active and sedentary elderly. *Journal of Sports Science*. 2020; 8: 56–66.
  17. Kushkestani M, Parvani M, Nosrani SE, Rezaei S. The physical activity and fall risk among Iranian older male adults. *The Open Nursing Journal*. 2020; 14(1): 159–67.
  18. Kersten S. Physiological regulation of lipoprotein lipase. *Biochimica et Biophysica Acta (BBA)-Molecular and Cell Biology of Lipids*. 2014; 1841(7): 919–33.
  19. Johnson VE, Stewart W, Smith DH. Traumatic brain injury and amyloid- $\beta$  pathology: a link to Alzheimer's disease?. *Nature Reviews Neuroscience*. 2010; 11(5): 361–70.
  20. Boltz M, Resnick B, Capezuti E, Shuluk J. Activity restriction vs. self-direction: hospitalised older adults' response to fear of falling. *International Journal of Older People Nursing*. 2014; 9(1): 44–53.
  21. Hadjistavropoulos T, Delbaere K, Fitzgerald TD. Reconceptualizing the role of fear of falling and balance confidence in fall risk. *Journal of Aging and Health*. 2011; 23(1): 3–23.
  22. Hull SL, Kneebone II, Farquharson L. Anxiety, depression, and fall-related psychological concerns in community-dwelling older people. *The American Journal of Geriatric Psychiatry*. 2013; 21(12): 1287–91.
  23. Meyer M, Constancias F, Vogel T, Kaltenbach G, Schmitt E. Gait disorder among elderly people, psychomotor disadaptation syndrome: post-fall syndrome, risk factors and follow-up—a cohort study of 70 patients. *Gerontology*. 2021; 67(1): 17–24.
  24. Heinrich S, Rapp K, Rissmann U, Becker C, König HH. Cost of falls in old age: a systematic review. *Osteoporosis International*. 2010; 21: 891–902.
  25. Florence CS, Bergen G, Atherly A, Burns E, Stevens J, Drake C. Medical costs of fatal and nonfatal falls in older adults. *Journal of the American Geriatrics Society*. 2018; 66(4): 693–8.
  26. Haddad YK, Bergen G, Florence C. Estimating the economic burden related to older adult falls by state. *Journal of Public Health Management and Practice: JPHMP*. 2019; 25(2): 17–24.
  27. de Almeida ST, Soldera CLC, de Carli GA, Gomes I, de Lima Resende T. Analysis of extrinsic and intrinsic factors that predispose elderly individuals to fall. *Revista da Associação Médica Brasileira (English Edition)*. 2012; 58(4): 427–33.
  28. Kushkestani M, Moghadassi M, Parvani M, Nosrani SE, Rezaei S. Physical activity as a preventive factor to aging-related physical dysfunction in Iranian community-dwelling elderly. *Journal of Aging Science*. 2020; 8(4): 1–7.
  29. Kushkestani M, Nosrani SE, Parvani M, Moghadassi M, Rezaei S, Tartibian B, et al. Active lifestyle prevent sarcopenia in older men. *Lifestyle Medicine Research & Reviews*. 2023; 1(1): 35–40.
  30. Collins KH, Herzog W, MacDonald GZ, Reimer RA, Rios JL, Smith IC, et al. Obesity, metabolic syndrome, and musculoskeletal disease: common inflammatory pathways suggest a central role for loss of muscle integrity. *Frontiers in Physiology*. 2018; 9: 1–25.
  31. Baylis D, Bartlett DB, Patel HP, Roberts HC. Understanding how we age: insights into inflammaging. *Longevity & Health Span*. 2013; 2(1): 1–8.
  32. Kob R, Bollheimer LC, Bertsch T, Fellner C, Djukic M, Sieber CC, et al. Sarcopenic obesity: molecular clues to a better understanding of its pathogenesis? *Biogerontology*. 2015; 16(1): 15–29.
  33. Migliaccio S, Greco EA, Wannenes F, Donini LM, Lenzi A. Adipose, bone and muscle tissues as new endocrine organs: role of reciprocal regulation for osteoporosis and obesity development. *Hormone Molecular Biology and Clinical Investigation*. 2014; 17(1): 39–51.
  34. Landi F, Liperoti R, Russo A, Giovannini S, Tosato M, Capoluongo E, et al. Sarcopenia as a risk factor for falls in elderly individuals: results from the iLSIRENTE study. *Clinical Nutrition*. 2012; 31(5): 652–8.
  35. Kushkestani M, Parvani M, Ghafari M, Avazpoor Z. The role of exercise and physical activity on aging-related diseases and geriatric syndromes. *SPORT TK-Revista EuroAmericana de Ciencias del Deporte*. 2022; 11:1–32.
  36. Malafarina V, Úriz-Otano F, Iniesta R, Gil-Guerrero L. Sarcopenia in the elderly: diagnosis, physiopathology and treatment. *Maturitas*. 2012; 71(2): 109–14.
  37. Quigley PA, Bulat T, Schulz B, Friedman Y, Hart-Hughes S, Richardson JK, et al. Exercise interventions,



- gait, and balance in older subjects with distal symmetric polyneuropathy: a three-group randomized clinical trial. *American Journal of Physical Medicine & Rehabilitation*. 2014; 93(1): 1–16.
38. Yip JL, Khawaja AP, Broadway D, Luben R, Hayat S, Dalzell N, et al. Visual acuity, self-reported vision and falls in the EPIC-Norfolk Eye study. *British Journal of Ophthalmology*. 2014; 98(3): 377–82.
39. Sibley KM, Voth J, Munce SE, Straus SE, Jaglal SB. Chronic disease and falls in community-dwelling Canadians over 65 years old: a population-based study exploring associations with number and pattern of chronic conditions. *BMC Geriatrics*. 2014; 14(1):1–11.
40. Hung WW, Ross JS, Boockvar KS, Siu AL. Recent trends in chronic disease, impairment and disability among older adults in the United States. *BMC Geriatrics*. 2011; 11(1): 1–12.
41. Rossini M, Viapiana O, Vitiello M, Malavolta N, La Montagna G, Bonghi SM, et al. Prevalence and incidence of osteoporotic fractures in patients on long-term glucocorticoid treatment for rheumatic diseases: the Glucocorticoid Induced Osteoporosis Tool (GIOTTO) study. *Reumatismo*. 2017; 69(1): 30–9.
42. Berlie HD, Garwood CL. Diabetes medications related to an increased risk of falls and fall-related morbidity in the elderly. *The Annals of Pharmacotherapy*. 2010; 44(4): 712–7.
43. Hewston P, Deshpande N. Falls and balance impairments in older adults with type 2 diabetes: thinking beyond diabetic peripheral neuropathy. *Canadian Journal of Diabetes*. 2016; 40(1): 6–9.
44. Rothenbacher D, Klenk J, Denking MD, Herbolzheimer F, Nikolaus T, Peter R, et al. Prospective evaluation of renal function, serum vitamin D level, and risk of fall and fracture in community-dwelling elderly subjects. *Osteoporosis International*. 2014; 25(3): 923–32.
45. Sanders KM, Scott D, Ebeling PR. Vitamin D deficiency and its role in muscle-bone interactions in the elderly. *Current Osteoporosis Reports*. 2014; 12(1): 74–81.
46. Milos V, Bondesson A, Magnusson M, Jakobsson U, Westerlund T, Midlöv P. Fall risk-increasing drugs and falls: a cross-sectional study among elderly patients in primary care. *BMC Geriatrics*. 2014; 14(1): 1–7.
47. Campanelli CM. American Geriatrics Society updated beers criteria for potentially inappropriate medication use in older adults. *Journal of the American Geriatrics Society*. 2012; 60(4): 616–31.
48. Stone KL, Blackwell TL, Ancoli-Israel S, Cauley JA, Redline S, Marshall LM, et al. Sleep disturbances and risk of falls in older community-dwelling men: the outcomes of Sleep Disorders in Older Men (MrOS Sleep) Study. *Journal of the American Geriatrics Society*. 2014; 62(2): 299–305.
49. Zhang Y, Cifuentes M, Gao X, Amaral G, Tucker KL. Age-and gender-specific associations between insomnia and falls in Boston Puerto Rican adults. *Quality of Life Research*. 2017; 26(1): 25–34.
50. Simoncini M, Gatti A, Quirico PE, Balla S, Capellero B, Obialero R, et al. Acupressure in insomnia and other sleep disorders in elderly institutionalized patients suffering from Alzheimer's disease. *Aging Clinical and Experimental Research*. 2015; 27(1): 37–42.
51. Ang GC, Low SL, How CH. Approach to falls among the elderly in the community. *Singapore Medical Journal*. 2020; 61(3): 116–21.
52. Zhang L, Ding Z, Qiu L, Li A. Falls and risk factors of falls for urban and rural community-dwelling older adults in China. *BMC Geriatrics*. 2019; 19(1): 1–17.
53. Jin J. Prevention of falls in older adults. *JAMA Patient Page*. 2018; 319(16): 1734.
54. Kushkestani M, Parvani M, Ebrahimpour Nosrani SEP, Bathaezadeh SY. The relationship between body composition with blood pressure and sleep quality in male dormitory student at Allameh Tabataba'i University. *New Approaches in Exercise Physiology*. 2022; 4(7): 91–106.
55. Kushkestani M, Parvani M, Nosrani SE, Bathaezadeh SY. The relationship between drug use, sleep quality and quality of life in dormitory students at Allameh Tabataba'i University, Iran. *Population Medicine*. 2020; 2: 1–7.
56. Kushkestani M, Parvani M, Maria Teixeira A. physical activity is a preventive factor against sars-cov-2 in healthy subjects (Possible Cellular and Molecular Mechanisms). *Biomedical Journal of Scientific & Technical Research*. 2020; 29(3): 22429–36.
57. Kushkestani M, Parvani M, Kazemzadeh Y. SARS-COV-2 in type 2 diabetic patients: Possible roles of exercise training as a medicine. *Current Diabetes Reviews*. 2022; 18(7): 1–7.
58. Kushkestani M, Parvani M, Nosrani SE, Rezaei S. The relationship between Anthropometric indices and lipid profiles in-officeemployees. *Journal of Sports Science*. 2020; 8: 76–82.
59. Kushkestani M, Parvani M, Moghadassi M, Kazemzadeh Y, Moradi K. Impact of hypertension and physical fitness on SARS-COV-2 and related consequences.(Possible mechanisms with focusing on ACE2). *Caspian Journal of Internal Medicine*. 2022; 13(3): 148–54.
60. Kushkestani M, Parvani M, Moghadassi M, Baradaran R. The effect of six-week high-intensity interval training on muscle expression of FTO and PPAR- $\gamma$  in obese diabetic rats. *Iranian Journal of Health Sciences*. 2022; 10(2): 29–39.
61. Tartibian B, Kushkestani M, Ebrahimpour Nosrani SE. The effect of 12-week endurance training on lipid profiles and fat percentage of overweight girls. *New Approaches in Exercise Physiology*. 2019; 1(1): 189–200.
62. Osoba MY, Rao AK, Agrawal SK, Lalwani AK. Balance and gait in the elderly: A contemporary review. *Laryngoscope Investigative Otolaryngology*. 2019; 4(1): 143–53.
63. Ghasemi P, Nazem F, Etemadifar M, Parvani M. Comparing the effects of selected TRX and Pilates training on balance parameters, fatigue index, and quality of life in female patients of multiple sclerosis. *New Approaches in Exercise Physiology*. 2022; 4(8).

64. Phu S, Vogrin S, Al Saedi A, Duque G. Balance training using virtual reality improves balance and physical performance in older adults at high risk of falls. *Clinical Interventions in Aging*. 2019; 14: 1567-77.
65. Leiros-Rodríguez R, García-Soidan JL. Balance training in elderly women using public parks. *Journal of Women & Aging*. 2014; 26(3): 207-18.
66. Zhao Y, Chung PK, Tong TK. Effectiveness of a balance-focused exercise program for enhancing functional fitness of older adults at risk of falling: a randomised controlled trial. *Geriatric Nursing*. 2017; 38(6): 491-7.
67. Ogaya S, Ikezoe T, Soda N, Ichihashi N. Effects of balance training using wobble boards in the elderly. *The Journal of Strength & Conditioning Research*. 2011; 25(9): 2616-22.
68. Taube W. Neurophysiological adaptations in response to balance training. *German Journal of Sports Medicine/Deutsche Zeitschrift für Sportmedizin*. 2012; 63(9): 273-7.
69. Vitorino LM, Teixeira CAB, Boas ELV, Pereira RL, Santos NO dos, Rozendo CA. Fear of falling in older adults living at home: associated factors. *Revista da Escola de Enfermagem da USP*. 2017; 51: 1-11.
70. Cadore EL, Rodríguez-Mañas L, Sinclair A, Izquierdo M. Effects of different exercise interventions on risk of falls, gait ability, and balance in physically frail older adults: a systematic review. *Rejuvenation Research*. 2013; 16(2): 105-14.
71. Liguori G, Medicine AC of S. ACSM's guidelines for exercise testing and prescription. 11th ed. Lippincott Williams & Wilkins; 2020.
72. Bouaziz W, Vogel T, Schmitt E, Kaltenbach G, Geny B, Lang PO. Health benefits of aerobic training programs in adults aged 70 and over: a systematic review. *Archives of Gerontology and Geriatrics*. 2017; 69: 110-27.
73. Lakatta EG. So! What's aging? Is cardiovascular aging a disease? *Journal of Molecular and Cellular Cardiology*. 2015; 83: 1-13.
74. Lee PG, Jackson EA, Richardson CR. Exercise prescriptions in older adults. *American Family Physician*. 2017; 95(7): 425-32.
75. Sousa N, Mendes R, Silva A, Oliveira J. Combined exercise is more effective than aerobic exercise in the improvement of fall risk factors: a randomized controlled trial in community-dwelling older men. *Clinical Rehabilitation*. 2017; 31(4): 478-86.
76. Levin O, Netz Y, Ziv G. The beneficial effects of different types of exercise interventions on motor and cognitive functions in older age: a systematic review. *European Review of Aging and Physical Activity*. 2017; 14(1): 1-23.
77. Pedersen BK, Saltin B. Exercise as medicine—evidence for prescribing exercise as therapy in 26 different chronic diseases. *Scandinavian Journal of Medicine & Science in Sports*. 2015; 25: 1-72.
78. Ruas JL, White JP, Rao RR, Kleiner S, Brannan KT, Harrison BC, et al. A PGC-1 $\alpha$  isoform induced by resistance training regulates skeletal muscle hypertrophy. *Cell*. 2012; 151(6): 1319-31.
79. Johnson ML, Robinson MM, Nair KS. Skeletal muscle aging and the mitochondrion. *Trends in Endocrinology & Metabolism*. 2013; 24(5): 247-56.
80. Ziaaldini MM, Marzetti E, Picca A, Murlasits Z. Biochemical pathways of sarcopenia and their modulation by physical exercise: a narrative review. *Frontiers in Medicine*. 2017; 4: 1-8.
81. Broskey NT, Greggio C, Boss A, Boutant M, Dwyer A, Schlueter L, et al. Skeletal muscle mitochondria in the elderly: effects of physical fitness and exercise training. *The Journal of Clinical Endocrinology & Metabolism*. 2014; 99(5): 1852-61.
82. Alghadir AH, Aly FA, Gabr SA. Effect of moderate aerobic training on bone metabolism indices among adult humans. *Pakistan Journal of Medical Sciences*. 2014; 30(4): 840-4.
83. Armamento-Villareal R, Aguirre L, Waters DL, Napoli N, Qualls C, Villareal DT. Effect of aerobic or resistance exercise, or both, on bone mineral density and bone metabolism in obese older adults while dieting: a randomized controlled trial. *Journal of Bone and Mineral Research*. 2020; 35(3): 430-9.
84. Fragala MS, Cadore EL, Dorgo S, Izquierdo M, Kraemer WJ, Peterson MD, et al. Resistance training for older adults: position statement from the national strength and conditioning association. *The Journal of Strength & Conditioning Research*. 2019; 33(8): 2019-52.
85. Lopez P, Pinto RS, Radaelli R, Rech A, Grazioli R, Izquierdo M, et al. Benefits of resistance training in physically frail elderly: a systematic review. *Aging Clinical and Experimental Research*. 2018; 30(8): 889-99.
86. Papa EV, Dong X, Hassan M. Resistance training for activity limitations in older adults with skeletal muscle function deficits: a systematic review. *Clinical Interventions in Aging*. 2017; 12: 955-61.
87. Conlon JA, Newton RU, Tufano JJ, Peñailillo LE, Banyard HG, Hopper AJ, et al. The efficacy of periodised resistance training on neuromuscular adaptation in older adults. *European Journal of Applied Physiology*. 2017; 117(6): 1181-94.
88. Beck BR, Daly RM, Singh MAF, Taaffe DR. Exercise and Sports Science Australia (ESSA) position statement on exercise prescription for the prevention and management of osteoporosis. *Journal of Science and Medicine in Sport*. 2017; 20(5): 438-45.
89. Atherton PJ, Smith K. Muscle protein synthesis in response to nutrition and exercise. *The Journal of Physiology*. 2012; 590(5): 1049-57.
90. Schiaffino S, Dyar KA, Ciciliot S, Blaauw B, Sandri M. Mechanisms regulating skeletal muscle growth and atrophy. *The FEBS Journal*. 2013; 280(17): 4294-314.
91. Jacobs BL, You JS, Frey JW, Goodman CA, Gundermann DM, Hornberger TA. Eccentric contractions increase the phosphorylation of tuberous sclerosis complex-2 (TSC2) and alter the targeting of TSC2 and the mechanistic target of rapamycin to the lysosome. *The Journal of Physiology*. 2013; 591(18): 4611-20.
92. Gumucio JP, Mendias CL. Atrogin-1, MuRF-1, and sarcopenia. *Endocrine*. 2013; 43(1): 12-21.

93. Luo L, Lu AM, Wang Y, Hong A, Chen Y, Hu J, et al. Chronic resistance training activates autophagy and reduces apoptosis of muscle cells by modulating IGF-1 and its receptors, Akt/mTOR and Akt/FOXO3a signaling in aged rats. *Experimental Gerontology*. 2013; 48(4): 427–36.
94. Hong AR, Kim SW. Effects of resistance exercise on bone health. *Endocrinology and Metabolism*. 2018; 33(4): 435–44.
95. Galea GL, Lanyon LE, Price JS. Sclerostin's role in bone's adaptive response to mechanical loading. *Bone*. 2017; 96: 38–44.
96. Kukuljan S, Nowson CA, Sanders KM, Nicholson GC, Seibel MJ, Salmon J, et al. Independent and combined effects of calcium-vitamin D3 and exercise on bone structure and strength in older men: an 18-month factorial design randomized controlled trial. *The Journal of Clinical Endocrinology & Metabolism*. 2011; 96(4): 955–63.
97. Kovacevic A, Mavros Y, Heisz JJ, Singh MAF. The effect of resistance exercise on sleep: a systematic review of randomized controlled trials. *Sleep Medicine Reviews*. 2018; 39: 52–68.
98. Miller DJ, Sargent C, Roach GD, Scanlan AT, Vincent GE, Lastella M. Moderate-intensity exercise performed in the evening does not impair sleep in healthy males. *European Journal of Sport Science*. 2020; 20(1): 80–9.