Review Paper

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Exercise as a Treatment for Sarcopenia

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Abstract: Sarcopenia is an age-associated condition classified by a progressive and generalized loss of muscle mass and function and is most common in individuals over the age of 60.[1] Exercise has been shown to have a protective effect on the age-related physiological changes that contribute to the development of sarcopenia.[2] The purpose of this narrative review is to analyze how different exercise modalities stimulate adaptations in the body in order to formulate a comprehensive exercise programme targeted at attenuating the progression of sarcopenia in the geriatric population. Findings indicate that an optimal exercise programme for the treatment of sarcopenia should include resistance, aerobic, power, and balance activities.[3,4,5,6] Resistance training (exercising with resistance at a low velocity) targets the age-associated loss of type II fast-twitch muscle fibres,[7] as well as the age-associated decline in muscle protein synthesis.[8,9] Aerobic exercise promotes mitochondrial function, muscle protein synthesis, and endothelial function, helping to preserve muscle.[10,11,12] Power training (exercising with resistance at a high velocity) acts to increase the area of type II fast-twitch muscle fibres and promotes positive neuromuscular adaptations.[13,14] Finally, balance training serves to treat postural instability, one of the common symptoms of sarcopenia.[15] In accordance with this research, it is recommended that sarcopenic individuals and those at risk integrate the activities presented above into their routines to prevent the decline in muscle strength and function that occurs with age.

Introduction

Sarcopenia, the progressive loss of muscle mass and function,[16] is a common disease that occurs among the geriatric population and presents an immense social and economic burden.[17] The prevalence of sarcopenia among older adults is high and ranges from 8.8%-17.5%.[18] A sarcopenia diagnosis can be confirmed by muscle mass that is less than 2 standard deviations below the mean of healthy young people under 30 years of age.[18,19] The main parameter used to diagnose sarcopenia is low muscle strength, since it is highly correlated with muscle function.[16] Sarcopenia is considered severe when low muscle strength, low muscle quality/quantity, and poor physical performance are detected[16]. In terms of muscle quantity, there is approximately a 50% loss in total fibre number between the ages of 20 and 80 years old, with the reduction accelerating after the age of 60.[20]

In human skeletal muscle, there are three main fibre types: type I oxidative slow twitch fibres, type IIa oxidative and glycolytic fast twitch fibres, and type IIx glycolytic fast twitch fibres.[21] However, there is a greater loss of type II fast twitch fibres relative to type I slow twitch fibres, resulting in a 20-40% decrease in muscle strength at age 70 compared to young adults of age 20.[20] With age, there is also a loss of motor units, which are composed of an alpha motor neuron as well as all the muscle fibres it

Corresponding Author Gabriela Oancea. Faculty of Kinesiology and Physical Education, University of Toronto, 55 Harbord St., Toronto, ON M5S 2W6. (+1)289-387-0202, gabriela.oancea@utoronto.ca. **Keywords:** aging, muscle mass, muscle strength, physical activity, prevention, sarcopenia. Published: **Dec 20, 2022.** ISSN pending.

innervates.[19] Diminished muscle function occurs when an alpha motor neuron is lost and the associated muscle fibres must connect with surviving alpha motor neurons by releasing neural cell adhesion molecules that act to attract axons to the abandoned muscle cells.[19,22] There is also evidence that reactive oxygen species (ROS) that have accumulated in the body over time can act as a trigger for sarcopenia.[23]

Exercise has been found to preserve muscle function and reduce the incidence of sarcopenia.[24] There is evidence that resistance training facilitates hypertrophy in type II muscle fibres and stimulates muscle protein synthesis, helping to mitigate the loss of muscle mass and function that occurs with sarcopenia.[7,8]Additionally, aerobic exercise has been shown to improve oxygen extraction as well as muscular endurance by means of increased mitochondrial energy production and capillary density.[25] Power training has been shown to contribute to increases in the number of type II fast twitch muscle fibres and optimize maximal firing frequency of motor units in the elderly, leading to increases in absolute force and power.[26,27] Balance training may help to prevent postural instability and falls through increases in muscle strength and agility.[28,29] Despite these findings the prevalence of sarcopenia among the aging population remains high as physical inactivity is a risk factor for sarcopenia, and limited physical activity is common in older individuals.[2,24,30,31]

Though it is known that general physical activity can promote healthy aging,[32] there is no consensus on recommendations for the treatment of sarcopenia.[33] Evidence-based exercise interventions designed specifically for older adults with sarcopenia are limited.[30] Additionally, regular exercise is an effective strategy found to be consistent in preventing frailty and slowing the progression of sarcopenia in the geriatric population.[34] There are also limited recommendations for frequency or type of balance exercises for older adults.[2] The purpose of this review is to evaluate how different modes of exercise stimulate specific adaptations in the body that are targeted at treating sarcopenia in the geriatric population in order to create an evidence based exercise programme for sarcopenic populations.

Resistance Exercise

Resistance training refers to the contraction of skeletal musculature against a weight or force with the goal of increasing muscle mass and strength.[35] According to Yoo et al., resistance exercise enhances net protein balance by stimulating muscle protein synthesis,[7] which declines in sarcopenic individuals due to an imbalance between muscle protein synthesis and muscle protein breakdown.[9] Resistance exercise is known to increase rates of muscle protein synthesis through the activation of mechanistic target of rapamysin complex (mTORC1).[8,36] The mTOR pathway is activated via signalling molecules PI_3K and Akt, and terminates in the activation of p70s6k.[37] Growth factors such as IGF-1 and MGF are released in response to increased muscle tension and stimulate the mTOR pathway.[37] The activation of p70s6k leads to the phosphorylation of mRNAs which subsequently results in increased rates of translation initiation.[37] However, the mechanisms outlined above cannot lead to a net positive protein balance without the intake of sufficient dietary derived amino acids.[38] With both adequate protein intake and resistance exercise, the elevated protein synthetic response will lead to a net positive protein balance- compounded overtime, this mechanism will eventually result in greater lean body mass.[39]

Aging is also associated with a disproportionate atrophy of type II fast-twitch muscle fibres compared to type I slow-twitch fibres, leading to a notable decrease in the body’s force-generating capacity.[40] Resistance exercise increases the cross-sectional area (CSA) of type II fibres in both young and old adults.[41] The specific process through which resistance training facilitates muscle strength and hypertrophy, especially in type II fibres, may involve satellite cells.[42] Satellite cells proliferate and differentiate into new myonuclei that join with existing muscle fibres and promote hypertrophy.[42] In the early stages, resistance exercise results in myotrauma-this can include tears in the sarcolemma, basal lamina, and supportive connective tissue, as well as contractile and cytoskeleton protein damage.[43] These damages induce the release of growth factors that act on satellite cells, stimulating proliferation and differentiation .[43] If the basal lamina is ruptured as a result of hypertrophic stimuli, satellite cells make their way towards adjacent myofibres to facilitate muscle remodelling.[44] As a result, there is an increase in muscle mass and myonuclear content, helping to counter the age-related decline in muscle CSA that accompanies sarcopenia[42,45]

In terms of resistance exercise recommendations, a study by Taaffe and colleagues compared the effects of high and low intensity resistance training on muscle strength and CSA in elderly women and found that both programs produced notable increases in thigh muscle strength and hypertrophy.[46] Low intensity resistance training may provide the benefits of resistance exercise while being more appropriate for those that are new to resistance training, and reducing the risk of injury in the older population.[47] With respect to exercise frequency, it is recommended by the American College of Sports Medicine that for novice older adults resistance training is performed 2-3 days a week, with alternating days of rest in between.[48] In addition, it is suggested that each resistance exercise session should be comprised of 8-12 repetitions of 1-3 sets, with 1-2 minutes of rest between each set.[48] Beckwée and colleagues' review of exercise interventions for the prevention and treatment of sarcopenia also states that for older individuals, a resistance training program involving 1-4 sets of 8-15 repetitions 2-3 times a week has been shown to produce optimal improvements in muscle strength.[49]

Exercises crossing several joints such as a squat are recommended for older adults as they are relevant to functional activities.[4] Resistance exercise machines may also be more appropriate for the elderly as opposed to free weights due to the safety provided by the movement restrictions of the machines.[4] Additionally, an ideal exercise programme should involve one to two exercises for each major muscle group: chest, back, arms, shoulders, upper legs, and lower legs[50], as well as agonist and antagonistic muscle groups to counter the sarcopenia-related deficient coordination of agonist-antagonist activation.[51] In conclusion, resistance exercise targets the age associated decline in muscle mass and strength by promoting hypertrophy in type II muscle fibres and stimulating muscle protein synthesis.[7,8] Although the decline in muscle strength is closely associated with neuromuscular changes[52], this review is focused on skeletal muscle phenotypic adaptations in response to resistance exercise.

Aerobic Exercise

Aerobic exercise is defined as activity involving rhythmic and repetitive movements of gross musculature, while primarily using the aerobic pathway to satisfy energy demands.[53] According to the free radical theory of aging, the mitochondria contain high amounts of ROS, which are highly reactive molecules that have been found to play a role in the age-associated skeletal muscle function decline.[54] These reactive elements can induce oxidative stress, damaging cellular components including DNA, proteins, and lipids.[23] Aerobic training has been shown to counter this phenomenon by stimulating cell activity involved in regulating the production of ROS.[5] Spina et al. demonstrate that aerobic exercise results in the increase in activity of several important mito-

-chondrial enzymes such as citrate synthase, beta-hydroxyacyl-Co-A dehydrogenase, and succinate dehydrogenase.[55] These enzymes show a decrease in activity with age and may account for muscle fatiguability, reduced endurance capacity, and loss of strength.[56] The mechanism of action through which aerobic exercise treats declining muscle mass/ function involves several intracellular signalling pathways, including calcium/calmodulin-dependent protein kinase (CaMK) and AMP-activated protein kinase (AMPK).[57] These pathways activate the transcription of mitochondrial genes leading to the production of new mitochondrial proteins,[15] which have been reported to decline in older adults.[58] This decline in muscle mitochondrial function is a potential contributor to age-related muscle dysfunction in humans.[58]

Aerobic exercise has also been shown to activate PGC-1 alpha, a transcriptional co-activator that is heavily involved in the regulation of mitochondrial biogenesis.[59] An increase in the amount of mitochondria in the cell has been found to enhance metabolic control by reducing oxidative stress and enhancing exercise capacity, thus creating a higher resistance to muscle atrophy.[60,61] Menshikova et al. found that mitochondrial function, reflected by electron transport chain activity and mitochondrial content, increased following an aerobic exercise program in older adults.[62] Short and colleagues found that in old adults, 4 months of moderate-intensity aerobic exercise increased muscle mitochondrial enzyme activity of citrate synthase (45%) and cytochrome c (76%) which are connected to increases in oxidative capacity and the capability to sustain muscular activity.[63] In a similar study, the activity of PGC-1 alpha increased by 46%, reflecting an increase in mitochondrial biogenesis.[64]

Aerobic exercise also plays a role in reducing the age-associated impairment of muscle protein synthesis,[63] which leads to increased ATP synthesis and improved muscle function.[65] Mitochondrial dysfunction is associated with reactive oxygen species that have the potential to damage mitochondrial DNA, impede calcium regulation, and compromise myofilament structure and function which all contribute to a decrease in skeletal muscle force production.[66] Short et al. showed that a 4 month bicycle program increased mixed muscle protein synthesis rates by 20% in older adults, helping to counter the decline in mitochondrial proteins, mixed myofibrillar proteins, and contractile proteins that occurs with aging.[63]

There is also an age-related decline in muscle blood flow, associated with abnormal vasodilator responses due to endothelial dysfunction.[5] Aerobic exercise was shown to reduce this decline in endothelium-dependent vasodilation in old rats.[12] The mechanism through which aerobic exercise improves endothelial function involves an increase in nitric oxide signalling which plays a key role in the vasodilation process.[12] Finally, the capillary density of skeletal muscle tissue is reduced with aging.[67] Coggan et al. found that after aerobic training, older individuals showed an increased capillary density as a result of increased capillary to fibre ratio and increases in the number of capillaries in contact with each fibre.[68] Ample muscle perfusion is critical for the maintenance of skeletal muscle, as muscle protein synthesis requires the delivery of amino acids, nutrients, and growth factors to the muscle.[67]

deJong and Franklin recommend that older individuals should perform moderate-intensity aerobic exercise every day with a minimum of 30 minutes per session in order to prevent age-associated diseases, improve muscle strength, and maintain independence.[69] The intensity of exercise can be measured using the rating of perceived exertion (RPE) which measures the perceived effort of exercise on a scale from 0 (nothing at all) to 10 (extremely strong), with moderate being 5-6.[70] Fol-

-lowing these aerobic exercise regimens may counter the age-associated decrease in mitochondrial enzyme activity, muscle protein synthesis, and muscle blood flow that play a role in the decline in muscle mass and function associated with sarcopenia.[55,58,71]

Power Training

Power training is characterized by exercise in which the concentric phase of the movement is completed as fast as possible.[72] Although resistance training has been shown to increase muscle strength, it has a small to moderate effect on the ability to independently perform activities of daily living (ADLs).[73] Additionally, since power training involves a light resistance moved at a fast velocity whereas resistance training involves a heavy resistance moved at a slow to moderate velocity, power training may improve motor-unit firing rate, synchronization of discharge, and levels of muscle activation to a further extent than strength training.[72,74] Power decreases at a faster rate with age than muscle strength due to the selective loss of type II fast twitch muscle fibres, which are associated with power production as they have a greater speed of muscle contraction.[20,75] Power training is known to contribute to increases in the number of type II fast twitch muscle fibres in the elderly.[14] The increase in CSA of type II muscle fibres leads to increases in absolute force and in turn, absolute power.[26] Since sarcopenia results in a reduction of force per unit of muscle CSA and a decline in peak power per unit volume, power training may aid in treating sarcopenic individuals.[76,77]

Van Cutsem et al. found that a 12 week period of power training led to earlier onset of EMG muscle activity and an optimized maximal firing frequency of motor units in human muscle, which accounts for the increased strength and speed of contraction observed after training.[27] Additionally, after the training program, brief 2-5 ms motor unit inter-spike intervals (doublets) were observed during muscle contraction.[27] The presence of doublets after training reflects an adaptation that allows the muscle to exhibit properties of faster muscles, leading to greater power.[27] Increases in strength with power training can be attributed to an increase in the number of active motor units as well as increased excitatory input and/or decreased inhibitory input.[13] Fielding et al. sought to determine whether these neuromuscular adaptations also occur in older adults.[78] Elderly women completed 16 weeks of a high-velocity resistance training program and found an increase in skeletal muscle peak power, which they speculate is attributed to enhanced firing rates or adaptations in the recruitment or activation of motor units.[78] Hakkinen et al. have also reported notable increases in maximal voluntary neural activation of agonist muscles in older adults following an intervention that included both resistance and power training.[13]

The ACSM recommends that a power training program includes 1-3 sets of 6-10 repetitions for 2 days per week, using a light-to-moderate load, meaning 30-60% 1RM for upper body and 0-60% 1RM for lower body.[48] Although resistance training using heavy loads may be optimal in terms of improving muscle strength, power, and endurance in older adults, peak muscle power increases similarly using light, moderate, or heavy resistances.[79] An important finding from Claflin et al.'s study is that using lighter weights and moving them more rapidly promotes similar adaptations at the fibre level than lower velocity power training, which may allow for a wider acceptance and executability of resistance training among the geriatric population.[26] According to Rice et al., older adults should be able to safely perform 1-2 days of power training per week if the exercise program is based on appropriate guidelines and progression is gradual.[80] Studies by Seynnes et al. and Henwood and Taffe reported no injuries or detrimental outcomes in both healthy and frail old adults during a power training program.[81,82] Due to the effects of power training on type II fast twitch fibres and motor unit adaptations, this type of exercise should be incorporated into an intervention targeted at mitigating the loss of muscle function and power that is prevalent in sarcopenic individuals.

Balance Exercise

Balance exercises are directed at improving body stability, particularly through the strengthening of lower body and core muscles.[83] Examples of balance exercises include walking or standing on unstable surfaces such as foam, standing on the heels or toes, or single leg stances.[53] According to Liang et al., a mixed exercise program including balance and resistance training improved ADLs, strength, and physical performance in older adults to a further extent compared to resistance exercise alone.[84] Exercises targeting balance can also be beneficial in treating postural instability, a condition that is common in sarcopenic patients.[15] Avelar et al. evaluated the effects of a balance exercise circuit program specifically designed to target sensory inputs from mechanoreceptors and the visual and vestibular systems in older women.[28] The authors found that the intervention significantly improved muscle strength and agility.[28] Hamed et al. demonstrated that in older adults, dynamic stability exercises performed under unstable conditions considerably improved muscle strength and stability performance, which are risk factors for future falls.[29] It is recommended that balance exercise sessions take place twice a week with 1.5 hours per session and focus on strengthening lower extremity and trunk muscles.[29] These exercises have been shown to produce optimal improvements in muscle strength and sensory information processing in order to counter sarcopenia-related postural instability.[85]

Summary

There is considerable evidence that exercise can induce positive adaptations in muscle and aid in treating sarcopenia.[15] Benefits including improved muscle strength, hypertrophy, aerobic capacity, peak power, and stability performance are observed when an exercise programme incorporates resistance training, aerobic exercise, power training, and balance exercises.[5,7,29,43,86] Resistance exercise promotes type II muscle fibre hypertrophy and increases rates of muscle protein synthesis, improving muscle mass and strength.[8,40] Aerobic exercise plays a role in increasing the activity of important mitochondrial enzymes involved in muscle contraction, muscle protein synthesis rates, and muscle vasculature .[57,63,65,71] Power training is involved with increasing the CSAof type II fast twitch muscle fibres and inducing positive neuromuscular adaptations.[27] Finally, balance exercises are targeted at treating postural instability by increasing strength and agility in lower body and core muscles.[15,28] Therefore, an exercise intervention directed at sarcopenic individuals should include 1-4 sets of 8-15 repetitions of resistance training 2-3 times per week, 30 minutes of moderate intensity aerobic exercise 5 times per week or 20 minutes of vigorous aerobic exercise 3 times per week, 1-3 sets of 6-10 repetitions of power training 2 times per week, and balance exercises 2 times per week with 1.5 hours per session.[4,28,48,49,57] Combined, these activities preserve muscle mass and function which is essential for healthy aging. However, for safety concerns it is recommended that exercise-naïve individuals consult their doctors prior to beginning an exercise regime. An exercise programme containing the type, amount, intensity, and frequency of exercise as well as examples of specific exercises can be found in Appendix A.

Conclusion

This review contributes to the current body of literature by providing a detailed evidence-based exercise programme that is specific for sarcopenic individuals, and demonstrates how different modes of exercise provide distinct benefits. This review also contributes to the limited body of evidence surrounding exercise interventions specifically targeted at older adults with sarcopenia. Furthermore, the studies used in this review were done on elderly individuals, making the exercise recommendations applicable to the geriatric population. The general consensus is that older adults should perform a minimum of 150 minutes of moderate intensity aerobic activity as well as muscle-strengthening activities for at least two days every week.[87] Although health benefits increase as the amount of physical activity increases, any physical activity is better than being sedentary.[87] Therefore, individuals should attempt to complete this programme to their own ability. Finally, since sarcopenia is now known to develop earlier in life than previously thought[16], the exercise programme produced from this review may also be appropriate for adults looking to delay the loss of muscle mass and function associated with sarcopenia and aging.

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Appendix A

Mode	Amount Per Session	Intensity	Frequency Per Week	Examples
Resistance	1-4 sets of 8-15 repetitions	Low	2-3 times	Leg press machine, standing calf raises, chest press machine, bicep curls with dumbbell
Aerobic	30 minutes	Low to moderate	Every day	Brisk walking, stationary cycling, swimming, community exercise programs (e.g. YMCA, Zumba, water aerobics)
Power	1-3 sets of 6-10 repetitions	High velocity low load	2 times	Leg press machine, chest press machine, lat pull down machine with short concentric phase followed by a longer eccentric phase
Balance	1.5 hours	N/A	2 times	Single leg stances, walking backwards, standing on unstable surfaces

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Appendix B

Monday	Tuesday	Wednesday	Thursday	Friday	Saturday	Sunday
Aerobic Resistance	Aerobic Balance	Aerobic Power	Aerobic Re-sistance	Aerobic Balance	Aerobic Power	Aerobic