Impact of physical activity on the management of sarcopenia

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INTRODUCTION

The aging process is accompanied by progressive decline in skeletal muscle mass that may lead to decrease strength and physical performance associated with an increased risk of disability. This condition, referred to as sarcopenia, is increasingly recognized as a major risk factor for adverse outcome in frail older people. Several factors seem to play a role in progression of sarcopenia; however, its physiopathology is still unclear. Without any available pharmacological intervention to sarcopenia, physical activity and specific nutritional supplementations represent the only strategies currently available for the management of sarcopenia.

Physical activity is defined as all body movements produced by skeletal muscles that require energy expenditure. The four main types of physical activity are: baseline activity, leisure-time physical activity, moderate-intensity physical activity and exercise. Exercise is a subcategory of physical activity that is planned, structured and repetitive. There are different forms of exercise: aerobic (endurance), resistance (strength), combination of aerobic and resistance exercises, stretching and balance exercises.

Aerobic exercise involves performing continuous movements with large muscle groups for 20 minutes or more. Biking, swimming, walking or jogging are forms of aerobic exercise. Aerobic activity depends primarily on oxygen consumption and improves cardiovascular function. Resistance exercise is a form of exercise that causes muscle contractions against an external resistance with the expectation of increases in strength, tone and mass and requires the use of

Key words: Exercise, Skeletal muscle, Physical performance
weight machines, dumbbells, and barbells as resistance sources for improving muscle strength. In older persons, resistance training has a greater impact on improving mass and strength than aerobic training. Several studies have demonstrated that specific programs of physical activity (combination of aerobic and resistance exercises) can improve muscle mass and muscle strength and reduce the risk of physical disability.

THE EFFECTS OF PHYSICAL ACTIVITY ON MUSCLE: MECHANISM OF ACTION

There are different supposed mechanisms by which physical activity acts against sarcopenia. The recruitment and activation of muscle satellite cells represent a major adaptation to physical exercise. The incorporation of new nuclei from satellite cells into parent cells increases the fiber cross-sectional area. Satellite cell activation is influenced by many factors, including age, nutritional status, type and intensity of physical exercise. In particular, during physical exercise, active muscles release hormones and inflammatory mediators that are satellite cell stimulants.

Among the different types of training, aerobic exercise increases energy production by mitochondria and capillary density. The increased muscle capillary allows matching the enhanced requirements of oxygen flux by muscle mitochondrial. During endurance exercise the muscle mitochondrial compartment (mitochondrial biogenesis and function) can be expanded. Instead, this type of training marginally affects the muscle fiber cross. Resistance exercise program impacts mainly on muscle mass and function (strength and power), by increasing the size and number of fast-twitch fibers (type II A and II X). In response to physical activity/exercise, muscle cells modulate the expression of specific proteins related to mitochondrial biogenesis and function, such as peroxisome proliferator-activated receptor γ co-activator 1α (PGC-1α) and muscle fatty acid binding protein (mFABP). In particular, PGC-1α activates the transcription of mitochondrial genes, while mFABP is involved in the utilization of fatty acid for mitochondrial energy production.

The down regulation of inflammation is another mechanism by which exercise acts against muscle mass and strength loss. Different studies have shown a decrease of levels of C-reactive protein (CRP) and interleukin-6 (IL-6) in older adults engaged in regular physical activity program. Finally, available evidence suggested that regular physical activity impacts positively muscle physiology through local and systemic effects.

THE ROLE OF EXERCISE IN PREVENTING DISABILITY

A sedentary lifestyle is the main modifiable risk factor for sarcopenia and is a well-known risk factor for several chronic diseases and disability in older adults. Conversely, physical activity improves mobility and decreases the risk of disability. In this field, the largest and longest study is the Lifestyle Intervention and Independence for Elders (LIFE), a multicenter randomized controlled trial conducted in the United States designed to compared a moderate-intensity physical activity program with a successful aging health education program on the incidence of major mobility disability (expressed by inability to walk 400 m) in more than 1600 sedentary and functionally limited older persons followed for 3 years. The major inclusion criterion was the presence of functional limitations (Short Physical Performance Battery [SPPB] score ≤ 9). The physical activity program (intervention group) consisted of a combination of walking at moderate intensity, balance, resistance exercise, stretching and behavioral counseling. Preliminary result from the LIFE pilot study (conducted on a sub-group of participants) showed the decrease of the incidence of disability and the increase of SPPB score in the intervention group over 1 year of follow up. The LIFE full study extended the promising results of the pilot study by showing that this specific exercises protocol reduce the risk of disability by 18% compared to the control group especially in participants who were frailer at baseline (SPPB < 8). In conclusion, these results show that a specific physical activity program (combination of endurance and resistance exercises) improves the frail status in older adults at risk of disability and prevent mobility disability.

EXERCISE AND SARCOPENIA

Sarcopenia is a major component of the frailty syndrome and is also a strong predictor of disability, morbidity, and mortality in older persons. The term sarcopenia identifies a condition characterized by loss of lean body mass and decreased strength and functionality. Several studies have explored the benefits of exercise in improving muscle mass and function and in preventing disability. Fielding and colleagues compared two different exercise programs (high-velocity and low-velocity resistance training) in frail, community-dwelling older women with self-reported physical disability. This study revealed that high-velocity resistance training has a greater effect on lower extremity muscle power than low-velocity training, despite the high-intensity arm is equally as efficacious as low-intensity arm for improving muscle strength.
Muscle composition and function are regulated by exercise and nutritional interventions. This is crucial for muscle health because it provides the anabolic response required for muscle turnover rate.

Table I. Physical activity: guidelines.

<table>
<thead>
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<th>General recommendations</th>
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<td>• Start slowly</td>
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<td>• Warm-up and cool down</td>
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<td>• Exercise sessions should last a minimum of 10 minutes for intermittent aerobic activity</td>
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<td>• At least a total energy expenditure of 150/250 kcal for each session</td>
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Recommendations for endurance training

- 30-60 minutes of moderate-intensity physical activity/day or at least 20-30 minutes of vigorous intensity/day
- Exercise sessions should last a minimum of 10 minutes for intermittent aerobic activity
- At least a total energy expenditure of 150/250 kcal for each session

Recommendations for flexibility training

- Set of 8-10 exercise on two or more non consecutive days/week using the major muscular groups
- 8-12 repetitions of each exercise resulting in volitional fatigue
- Flexibility exercise at least two days/week and 10 minutes/day involving areas of neck, shoulder, wrist, hip, knee and ankle

Goodpaster and colleagues evaluated the effects of a specific physical activity program (aerobic, strength, flexibility and balance training) on strength and skeletal muscle fat infiltration in sedentary, community-dwelling older persons over a follow-up of 12 months. This trial demonstrated a clear effect of exercises program to prevent progressive loss of muscle strength in older adults. Furthermore, the significant age-associated increase in muscle fat infiltration was prevented with increased physical activity.

Marques and colleagues evaluated the effects of a multicomponent training with weight-bearing exercises on muscle strength, balance, agility, and bone mineral density in older women and demonstrated that this training is effective at increasing bone mineral density, muscle strength, and distinct functional fitness skills, which are associated with aging and increased risk of falling and fracture.

Based on this evidence, recommendations for frail older people should include a specific activity program with endurance training and resistance training at least 3 days a week.

**EXERCISE AND NUTRITIONAL INTERVENTIONS ON MUSCLE HEALTH**

Muscle composition and function are regulated by muscle protein turnover rate. Protein intake and physical activity are the main anabolic stimuli for muscle protein synthesis. An adequate dietary protein intake is necessary for muscle health because it provides the essential amino acids needed to replace those lost from catabolism and stimulates muscle protein synthesis and growth. Low protein intake is associated with increased muscle loss in older adults. Leucine is the essential amino acid that can directly activate the mechanistic target of rapamycin (mTOR) signaling pathway in skeletal muscle stimulating protein synthesis. It is recommended that older persons consume food with higher proportion of essential amino acid (high quality protein), such as lean meat and leucine-rich foods (soybeans, peanuts, cowpea and lentils). Because of metabolic changes, older persons may produce less muscle protein than younger person from the same protein intake. Therefore, the current recommended dietary allowance for protein (RDA:0.8 g/kg/day), although sufficient for young people, fails to prevent muscle and strength loss with aging. The minimal amount required to maintain muscle function is 1.0 g/kg/day. It is recommended that older persons consume between 1.0 and 1.5 g of protein/kg/day. In addition, a balance caloric supplement should be considered to prevent sarcopenia. Foods are used to provide energy for organ function and muscle activity. If caloric intake is not enough to meet needs, muscle protein deposition in older men more efficiently than casein.

The absorption kinetics and the amino acid composition of dietary proteins are also relevant factors that must be considered to prevent muscle and strength loss. The speed of absorption of dietary amino acids by the gut influences postprandial protein synthesis, breakdown, and deposition and has contributed to the development of the fast versus slow protein concept which may have significant involvements on the management of sarcopenia. In young individuals, slowly digested proteins (e.g., casein) produce greater protein retention than those that are rapidly digested (e.g., whey). An opposite pattern has been observed in elderly individuals. Pennings et al. have demonstrated that the ingestion of whey proteins stimulates postprandial muscle protein deposition in older men more efficiently than casein.

Muscle protein synthesis is influenced by several factors including timing of protein intake and functional and training status. In this context, an optimal time window for protein ingestion in relation to physical activity is still a matter to be solved. Generally, it is assumed...
that muscle is responsive to amino acids ingestion for up three hours after physical activity. Older persons practicing physical activity may also be recommended to ingest fast proteins (e.g., whey) or amino acids (e.g., leucine-enriched balanced EAA mix) immediately before or 2-3 hours after the training session to enhance exercise-induced muscle hypertrophy. However, inconsistent results in timing of protein ingestion have been reported in older persons involved in physical activity programs. In this respect, larger clinical trials are needed to identify the optimal timing of protein intake during the day and in relation to physical activity.

**PHYSICAL ACTIVITY FOR OLDER ADULTS: GENERAL RECOMMENDATIONS**

Sedentary behavior enhances with aging and has been shown to increase risk of chronic diseases, particularly diabetes and cardiovascular disease. Participation in a regular exercise program is an effective intervention to reduce a number of functional declines associated with aging. Recommendations for physical activity in older adults comprises a specific exercise program including combination of endurance and strength exercises at least three times a week. Endurance training can help maintain and improve various aspects of cardiovascular function and contribute to an increase in life expectancy. Strength training helps offset the loss in muscle mass and strength typically associated with normal aging. Additional benefits from regular exercise include improved bone health with reduction in risk for osteoporosis; improved postural stability reducing the risk of falling and increased flexibility. The regular physical activity can also produce a number of psychological benefits related to preserved cognitive function and alleviation of depression symptoms.

The activity should be initiated with low intensity to gradually increase in order to minimize the risk of injury. Each session is preceded by a brief warm-up and followed by a brief cool-down. These exercises allow to gradually modifying the individual’s heart rate and/or breathing. The aerobic physical activity should be performed for 30-60 minute of moderate-intensity per day or at least 20-30 minutes per day of vigorous intensity and the resistance training should be performed two or more non consecutive day with gradual increase (from moderate to vigorous).

**EXERCISE PROTOCOL IN THE SPRINTT CLINICAL TRIAL**

The “Sarcopenia and Physical frailty IN older people: multicomponent Treatment strategies” (SPRINTT) is a multi-center randomized clinical trial designed to evaluate the efficacy of a multicomponent intervention (MCI) program compared with a healthy aging lifestyle education (HALE) program on mobility disability, in community-dwelling older people with physical frailty and sarcopenia. The MCI consists of a combination of structured physical activity, nutritional counseling/dietary intervention and information and communication technology intervention (ICT) and is designed to help older persons improve their physical function to prevent disability. In the ICT, actimetry data are collected through a dedicated device to monitor adherence to physical activity. The HALE program consists of a series of workshops aimed at increasing awareness of important health issues relevant to older persons.

The physical activity intervention has been designed based on the exercise protocol adopted in the “Lifestyle Interventions and Independence for Elders” (LIFE) study which has been shown to be safe and effective at preventing mobility disability and improving physical frailty status. Physical activity includes aerobic, strength, flexibility, and balance training. Walking is the primary mode of aerobic physical activity and should be performed for 150 min per week at moderate intensity. The physical activity intensity will be gradually regulated on the basis of perceived exertion, according to the Borg's scale. Each session is preceded by a brief warm-up (5 minutes) consisting of low intensity walking and followed by a brief cool-down period (3 minutes) in which the walking speed is gradually reduced. Strength exercises based on five lower extremities exercise using adjustable ankle weights. This is followed by a brief lower extremity stretching routine. Balance training is introduced during the initial phase of the program as a complement to the aerobic and strength components. Upper body exercises are included at the end of the session.

This exercise program is designed to be performed both at the center and at home. During the intervention, participants train at the center twice a week. In order to optimize participant compliance to the intervention, the total amount of physical activity is monitored by actimetry devices which allows to provide personalized feedback to the participant.

Finally, the nutritional component of the MCI has been designed to maximize the benefits of physical activity. Indeed, the combination of nutritional interventions and physical activity appears to be the most effective strategy presently available for improving sarcopenia and preventing disability.
CONCLUSIONS

Physical inactivity is a major risk factor for muscle loss and weakness, which results in increased fatigability. The regular exercise is effective at improving aerobic capacity, muscle mass, strength and endurance in adult and older persons. Engagement in regular physical activity brings many health benefits in young and old person. Indeed, the World Health Organization recommends people of all ages being as physically active as possible and including a minimum of 30 minutes of moderate-intensity physical activity on most, if not all, days of the week. In older persons, regular exercise provides the same beneficial effects as in younger individuals. The combination of regular physical activity with appropriate nutritional support seems to be the most effective strategy to improve physical function and prevent disability. High-quality clinical trials are needed to identify the type and duration of multicomponent intervention (exercise and nutrition) that maximizes the health benefits in older persons.

The SPRINTT trial will provide evidence of combining long-term moderate-intensity physical activity and nutritional supplementations in preventing several adverse outcomes in older adults and its finding are expected to promote significant advancements in the management of sarcopenia.

CONFLICT OF INTEREST

The authors declare no conflict of interest.

References

24 Andrews RD, MacLean DA, Riechman SE. Protein intake

