

Review Article

Effects of oxidative stress, physical exercise and caloric restriction on muscle atrophy: a systematic review

Abstract

Purpose: The decline of muscle function, aging-related diseases, and consequent onset of sarcopenia are directly triggered by oxidative stress. In addition to reducing muscle function, the ability to defend against oxidative stress by the antioxidant system is also deficient in this situation. Thus, the fight against oxidative stress is reduced, which leads to progressive decline of the skeletal muscle system. **Materials and Methods:** Systematic review with a sample of six scientific papers published in academic journals. **Results and Conclusion:** Studies show that exercise then induces a prevention response to free radical damage. Furthermore, physical exercise induces effects on the concentration of SOD, catalase, AMP, SIRT-1 and PGC-1a, which are important for better skeletal muscle condition. Understanding how the elderly muscle responds to exercise is important, and it is necessary to understand the mechanisms of Reactive oxygen species (ROS) and reactive nitrogen species (NOS) generation and the modulation of the proinflammatory cytokines and the antioxidant system in response to the exercise.

Key-words: Sarcopenia; Cachexia; Exercise; Atrophy.

Introduction

Reactive oxygen species (ROS) and reactive nitrogen species (NOS) are produced in several ways. Physical exercise contributes, in an acute way, to the increase of free radicals [1]. Physical exercise stimulates the production of free radicals, and as a response to this system, an increase of antioxidant enzymes occurs [2].

Aging is also associated with increased generation of ROS and NOS, which cause changes in proteins, lipids and DNA. Moreover, the elderly muscle presents in a state of chronic inflammation, due to the increase of inflammatory cytokines. The inflammatory response to injury may subject the elderly muscle to increased oxidative stress [3]. In this scene, the muscle has a greater risk of injuries and capacity of regeneration reduced.

Aging is a natural process directly related to genetic and environmental factors that can slow down or accelerate an individual's development. Changes in muscle conformation, oxidative stress, inflammation, physical activity and nutrition are all independently balanced, interacting and maintaining factors affecting the body's ability to perform physical activity.

Exercise and caloric restriction effects on antioxidant actions, muscle content and oxidative stress are important for understand in aging [4]. Different effects how increased antioxidant, anti-inflammatory action, mitochondria increase and muscle content after exercise and caloric restriction should observed. The effects of aging on muscle atrophy were attenuated with exercise and caloric restriction. [4,5].

Sarcopenia is a disease associated with aging that causes an exponential reduction in skeletal muscle [6] The reduction of muscle directly affects the muscular function, reduction of the functional capacity and consequently of the physical fitness of the bearer. Thus, sarcopenia causes reduced quality of life, increased falls and consequently mortality [7].

In skeletal muscle, the action of SIRT 1, a protein that increases the amount of PGC-1 α occurs. PGC-1 α acts on the biogenesis and proliferation of mitochondria. There was a reduction for SIRT-1 and PGC-1 α in elderly rats compared to young rats [8].

Skeletal muscle cells produce transient ROS flux in response to a variety of stimuli, such as intense contractile activity, thermal stress, disuse atrophy, acute hypoxia, and physical stress [1]

As shown, the decline in muscle function, age-related diseases, and consequent onset of sarcopenia are directly triggered by oxidative stress. In addition to reducing muscle function, the ability to defend against oxidative stress by the antioxidant system is also deficient in this situation. Thus, the fight against oxidative stress is reduced, which leads to progressive decline of the skeletal muscle system.

Oxidative stress increases the levels of free radicals that destroy structural proteins and lipids, deoxyribonucleic acid (DNA) and also mitochondria [1,3,9].

In this way, as the muscle becomes more vulnerable by the antioxidant, structuring and gene changes, sarcopenia is favored to appear. Thus, muscle mass reduction is signaled by factors such as myostatin action and increased effects of the ubiquitin proteasome system [8]. The relationship between free radicals, oxidative stress, atrophy, sarcopenia, exercise and antioxidants can be observed in figure 1.

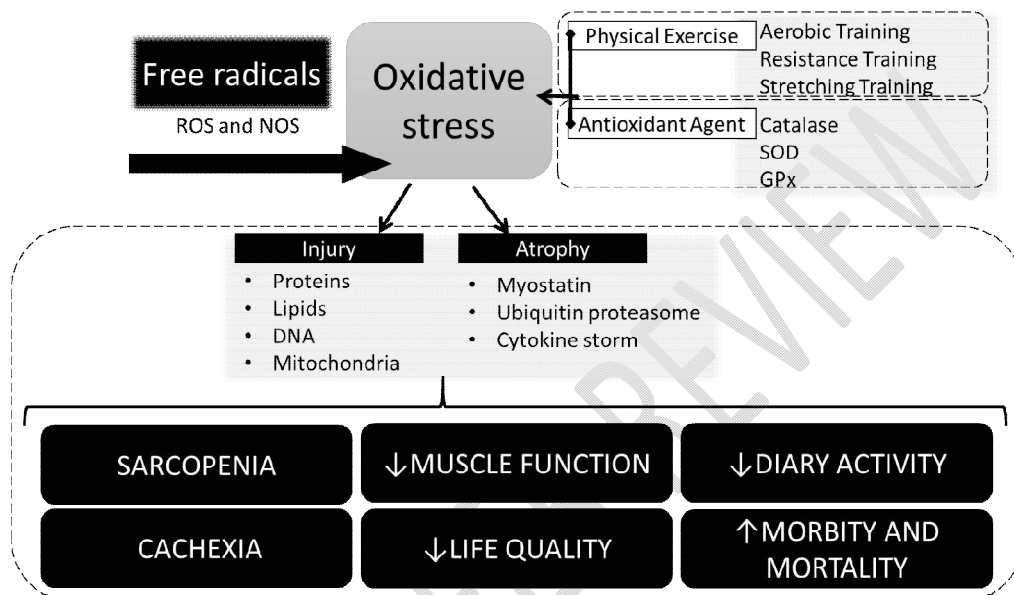


Figure 1. The relationship between free radicals, oxidative stress, atrophy, sarcopenia, exercise and antioxidants.

Thus, the elderly muscle presents conditions that contribute to the muscular atrophy development and consequent sarcopenia. The increase of proinflammatory cytokines and oxidative stress have significant roles. Exercise, even temporarily raising free radicals, these are counteracted by the system antioxidants, balancing the whole system. The exercise then induces a prevention response to the damages caused by free radicals. Thus, understanding how the elderly muscle responds to exercise is important, and it is necessary to understand the mechanisms of ROS and NOS generation and the modulation of antioxidant system in response to exercise.

Material and methods

A literature search through PubMed, ResearchGate and HOLLIS Harvard Library Online Catalog was performed from the date of inception until 10/06/2021. A combination of the following keywords was used: Sarcopenia; Oxidative stress; free radicals; physical exercise; atrophy; and antioxidants. Furthermore, studies that were cited in the selected articles were verified.

Studies on association of sarcopenia, oxidative stress and physical exercise were included. Those excluded were: a) association between exercise and other pathologies

only; b) association between exercise and young people's only; c) association between atrophy and neurodegeneration only; d) studies that utilized other isolated or concomitant supplementation.

Results

From the researches made in the mentioned databases, there were 654 articles related to the key-words, from which, based on the titles scanning, 88 studies were separated in order to read the respective abstracts. After reading, 39 articles were selected to a complete reading and from these, 12 studies matched with the inclusion criteria and then were selected to this review.

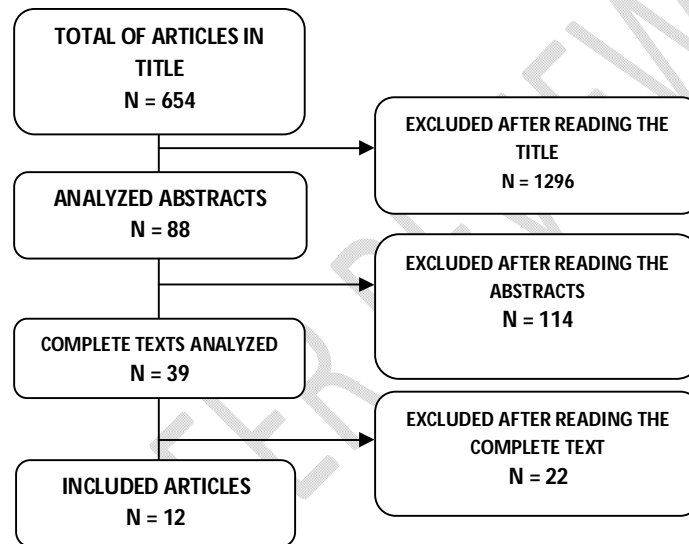


Figure 2. Organogram of the stages to sample delimitation

In table 1 there are six articles in which oxidative stress and exercise analysis in situation of metabolic and muscular assessment, with pre-clinical models (animals) and clinical ones (humans).

Table 1: Baseline characteristics of articles, which reported effects of oxidative stress and exercise analysis in situation of metabolic and muscular assessment.

Author/ Year	Design	Analyses	Results
Gianni et al., [10]	Humans 12 young people's 12 aged people's	8-OHdG Carbonyls Proteins mitDNA suppression SOD Catalase	Aged group ↑ Oxidative stress ↑Antioxidant action ↓ mitDNA
Morales-Alamo et al, [11]	Humans 9 young (Antioxidant and Control groups)	Carbonyls Proteins ACCB AMPK α AMPK α_{1e2} AKT total	Antioxidant Group ↓ Proteolysis ↑Proteogenesis
Kujoth et al., [12]	Animals (Wild mouse) 3 at 30 months of age	Caspase-3 Quadriiceps and gastrocnemius weight	Aged group (D257A) ↑Proteolysis ↓Peso muscular
Siu et al., [13]	Animals (Fischer 344 rats) 6 at 30 months of age	Gastrocnemius weight Protein content T-bars H ₂ O ₂ Nitrotyrosine SOD Catalase	Old Group and Suspension ↓Muscular weight ↑Oxidative stress ↑Antioxidant action ↓Antioxidant enzymes
Kim et al., [14]	Animals (Fischer-344 rats) 6 at 24 months of age	Plantar muscle weight Cross-sectional area (CSA) % Connective tissue Citrate Sintase H ₂ O ₂ SOD IGF-1	Exercise group + Caloric Restriction (8%) ↑ Muscle Fibers ↑ IGF-1 ↑ Antioxidant ↓ Oxidative stress
Jackson et al., [15]	Animals (C57BL/6 mouse) 3, 18 and 28 months of age	SIRT-1 SOD H ₂ O ₂ T-bars Carbonyls Proteins	Resveratrol Aged Group ↑ Sirt 1 ↑ Antioxidant action ↓ Oxidative stress

Discussion

The effects of exercise and caloric restriction on antioxidant actions, muscle content and oxidative stress were evaluated by the studies. Different effects were observed, but with increased antioxidant, anti-inflammatory action, mitochondria increase and muscle content after exercise and caloric restriction. The effects of aging on muscle atrophy were attenuated with exercise and caloric restriction.

Gianni et al [10] demonstrated the effect of mitochondrial aging theory, where there is an increase in EROS and reduction of antioxidants in the elderly. The study showed increased carbonylated proteins, DNA degradation, 37% reduction of mitochondrial DNA, and reduced activation of SOD and catalase.

In the study by Morales-Alamo et al [11], the effects of free radicals on the activation of AMPK and CaMKII after physical exercise were evaluated in youngsters who were supplemented with antioxidants. During exercise there was no difference in protein oxidation. However, the higher activation for AMPK and lower for CaMKII during exercise for the antioxidant group. This effect shows an action of free radical control during exercise by the muscle, avoiding oxidative stress.

Kujoth et al [12] showed that genetically aged D257A mice show signs of sarcopenia at 9 and 30 months of age. They analyzed the content of Caspase-3 and the amount of skeletal muscle in the animals. It was shown a greater action of protein degradation by the increase of Caspase-3 related to age. Furthermore, progressive reduction with age for the amount of skeletal muscle was shown.

In the study by Siu et al [13], aged and suspended rats were evaluated. The concentration of EROS and ENOS was higher in these animals compared to the young animals and controls. Still, the amount of antioxidant enzymes was exaggeratedly higher. Skeletal muscle weight was lower for aged and suspended animals.

Kim et al [14] demonstrated that caloric restriction and physical exercise attenuated aging effects on skeletal muscle as a function of aging. The association of calorie restriction and exercise increased the amount of muscle fibers, increased IGF-1, increased antioxidant enzymes and reduced oxidative stress.

Jackson et al [15] have shown that resveratrol supplementation reduces the effects of oxidative stress but does not attenuate sarcopenia. They found that in elderly rats the supplementation of resveratrol increased the biogenesis and proliferation of mitochondria, reduction of inflammatory cytokines and also of free radicals.

The integrity of the antioxidant system is particularly important in aging. It is well established that aging is associated with increased free radical generation, resulting in accumulated oxidative damage, leading to the development of numerous diseases [3,16].

The evaluation of physical exercise and antioxidant actions are interesting for the attenuation of aging actions on skeletal muscle. These effects may favor the reduction of the effects of sarcopenia on the individual and, consequently, increase in physical fitness, functional capacity and quality of life in the elderly.

Conclusions

Old skeletal muscle presents conditions that contribute to the development of muscular atrophy and consequent sarcopenia. The increase of proinflammatory cytokines and oxidative stress have significant roles. Physical exercise, even temporarily raising free radicals, are counteracted by the antioxidant system, balancing the entire system.

The exercise then induces a prevention response to the damages caused by free radicals. Furthermore, physical exercise induces effects on the concentration of SOD, catalase, AMP, SIRT-1 and PGC-1 α , which are important for better skeletal muscle condition. Understanding how the elderly muscle responds to exercise is important, and it is necessary to understand the mechanisms of EROS and ENOS generation and the modulation of the proinflammatory cytokines and the antioxidant system in response to the exercise.

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