Research Article
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Effects of creatine supplementation in the prevention of sarcopenia

Abstract

Much is discussed about the importance of healthy aging, which involves by a combination of several factors. Allied to population aging, there is the emergence of non-communicable chronic diseases and some limiting conditions that compromise the functional capacity of the elderly, such as sarcopenia. This natural condition of the aging process has emerged as one of the most common problems in the elderly population, thus becoming a public health problem. The objective of the present work is to analyze in the literature the effect of creatine supplementation for the prevention of sarcopenia in the elderly. This article is an integrative review based on research on the effects of creatine in the prevention of sarcopenia in elderly individuals. Four randomized controlled trials (N = 330) were included in the review. Overall, creatine brought beneficial effects for the prevention of sarcopenia in elderly individuals.

Keywords: healthy aging, muscle strength, food supplementation

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Introduction

Aging is a reality in the world, stimulated by the reduction in the rate of fertility, related to increased survival due to technological advances of medicine and improvement of living conditions.[1] According to the European Consensus on Sarcopenia, it is defined as a syndrome characterized by a gradual and generalized loss of muscle mass and strength, with a risk of adverse effects such as physical disability, worsening of quality of life and mortality. In this process, muscle fibers are replaced by adipose and fibrotic tissue, with a decrease in protein synthesis, resulting in reduced muscle strength and efficiency.[2]

This natural condition of the aging process has emerged as one of the most common problems in the elderly population, thus becoming a public health problem. Sarcopenia is associated with several health hazards such as; increased risk of fractures and falls, increased insulin resistance and the risk of pre-diabetes, cardiovascular disease, cognitive impairment, depression, among others.[3]

According to the Brazilian Society of Parenteral and Enteral Nutrition (BRASPEN) guideline on nutritional therapy in aging, nutrition is an important component to maintain the health and well-being of the elderly. Inadequate nutrition contributes to the progression of several diseases and is also considered to be an important contributing factor to the complex etiology of sarcopenia and the frailty syndrome. Recommendations must be individualized in order to ensure adequate nutritional intake, mainly of proteins and micronutrients. The objective is to maintain or adjust nutritional status, in addition to improving clinical conditions and quality of life.[4]

The search for alternatives that circumvent the changes caused by aging is increasing. In this scenario, several pharmacological and non-pharmacological strategies are studied in order to prevent or contain negative changes in muscle tissue.[5] For this purpose, guided nutritional therapy, through food supplementation, is an effective alternative, whether in recovery or in maintaining the nutritional status of the elderly. This is because, through conventional food alone, there is a difficulty in meeting the metabolic demand, as well as ensuring adequate intake of energy and nutrients.[6]

Creatine is a natural compound in protein foods of animal origin, which plays an important role in mitochondrial energy metabolism. Possessing anti-inflammatory properties and having evidence of a safe use, even in the elderly with chronic diseases, suggesting that it is beneficial in various human neurological diseases or not. The benefit of creatine supplementation has been shown in several pathologies such as sarcopenia due to age.[7] Given the above, the present study aims to analyze in the literature the effect of creatine supplementation for the prevention of sarcopenia in the elderly.

Methods

The work is an integrative review based on research on the effects of creatine in preventing sarcopenia in elderly individuals, answering the following question: What are the possible effects of creatine in preventing sarcopenia? The achievement of the review followed the following steps: identification of the theme and elaboration of the guiding question; search for studies using eligibility criteria; identification of previously selected studies; data extraction; analysis and interpretation of the results and, finally, elaboration of the review.

For data collection, the acronym PICOT (Population of interest, Intervention, Comparator, Outcomes, Type of Study) was used, in which elderly individuals were defined as population, creatine supplementation intervention, comparison group with the one that was not exposed to creatine supplementation and outcomes such as increased fat-free mass and strength as a prevention of sarcopenia. Given the above, the present study aims to analyze in the literature the effect of creatine supplementation for the prevention of sarcopenia in the elderly.

The research was carried out between April and May 2022 in the following Pubmed and Medline databases, using the following descriptors: "creatine" and "sarcopenia" according to Decs/Mesh and their combination using the Boolean operator AND OR NOT. In the second stage, a search for articles in the databases was carried

out, considering eligibility, following the inclusion criteria: original articles published in the last 10 years with availability in full, which were randomized clinical trials in individuals aged from of 60 years. Articles that were performed in animals or "*in vitro*", bedridden patients, use of anabolic drugs or hormonal therapies, neoplasms, neuromuscular disorders and review studies were excluded.

For the achievement of the third stage, initially, the studies were selected by reading the title, later, the abstracts were analyzed in order to identify the articles that addressed creatine supplementation in elderly individuals. It is important to point out that there were duplicate articles in the researched databases that were excluded, and those that remained were selected by reading titles and abstracts until they were read in full in order to identify whether the research, in fact, addressed the effects of creatine. in the prevention of sarcopenia in elderly individuals.

After completing the reading of the previously selected articles, in the fourth step, a standardized table was prepared to assist in the extraction of data referring to the studies, with information about the database, journal, year of publication, title, authors, objective, methodology, main results and authors' conclusions.

Results

The initial search on the search platforms was carried out with the descriptors and their combinations and the selection criteria of publication time were applied in the last 10 years, since it is a recent topic, and articles in full, identifying 67 publications. Among them, 11 duplicate articles were first removed. Subsequently, 31 review articles and 3 articles with studies in rodents or "in vitro" trials were removed. Thus, 22 articles were selected for analysis by reading the abstract. At this stage of selection, 4 publications were excluded because they did not meet the age criteria and 14 because they were studies that did not match the object of the research. Thus, 4 articles met the eligibility parameters, and the publications were read in full and the 4 articles were included in the review (Figure 1), where the findings are represented in Table 1.

Table 1 Characteristics of the analyzed studies

Authors/ Year/ Type of study	Sample characterization and duration of study	Creatine dose	Associated supplementation	Type of exercise	Study objective	Main outcomes
Nilsson MI, et al.,[8] Randomized, placebo-controlled, double-blind study	32 participating men Age: > 65 years Intervention time: 12 weeks	3g/day	Whey (24g/d), micellar casein (16g/d), Vitamin D (1,000 IU/d), Omega 3 (EPA – 1.51g/d and DHA – 0.95g/d)	Unsupervised home resistance training (UHRE) 3x/ week	To verify the effects of UHRE/ MIS on muscle mass, strength and function in free-living elderly men.	Supplementation is safe, well tolerated and effective, associated with UHRE, improving: lean mass, strength and muscle quality in old age.
Negro M, et al.,[13] Randomized, placebo-controlled, double-blind study	38 participants, including: 8 men and 30 women. Age: 65 to 80 years Intervention time: 12 weeks	3g/day	AAS (10,000mg/d), Vitamin D (2,000 IU/d), Alpha Lipoic Acid (ALA) (600mg/d), Coenzyme Q10 (CoQ10) (100mg/d), Resveratrol (100mg/d)	No physical activity	To evaluate the effectiveness of a multi-ingredient nutritional supplementation based on AAS, regardless of exercise, for the combating the loss of muscle mass, strength and power during aging.	It has shown that in healthy older adults multi-ingredient nutritional supplementation can positively affect muscle mass, strength and power.
Roschel H, et al.,[11] Multifactorial, randomized, placebo-controlled, double-blind study	200 participants, including: 154 women and 46 men. Age: > 65 years Intervention time: 16 weeks	6g/day	Whey protein (30g/ day)	Resistance training (2x/ week)	To investigate the effectiveness of different dietary strategies to enhance adaptations to resistance training in the elderly.	Supplementation with Whey protein and creatine did not potentiate the adaptations to resistance training in relation to strength and muscle mass.
Gualano B, et al.,[9] Randomized, placebo-controlled, double-blind clinical trial	60 participating women Age: 60 years Intervention time: 24 weeks	20g/day for 5 days, after 5g/ day	no associations	Resistance training (2x/ week)	To examine the effectiveness of creatine supplementation, associated or not with resistance training in elderly women.	Creatine supplementation combined with resistance training improved appendicular lean mass and muscle function in elderly women.

UHRE, unsupervised home resistance exercise; AAS, androgenic anabolic steroids; MIS, multi-ingredient supplementation

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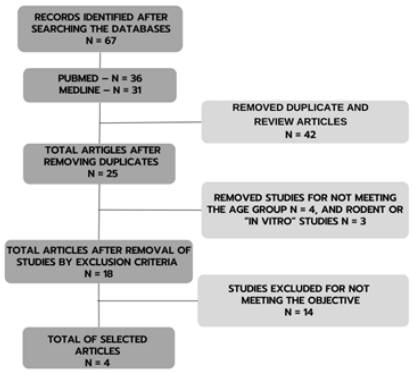

Figure 1 Flowchart of article selection.

Discussion

Although biological aging is inevitable and the etiology of sarcopenia is complex and multifactorial[8], malnutrition and physical inactivity are well-known factors that can worsen muscle function impairment in the elderly[9]. In this sense, the beneficial effects related to creatine supplementation for the prevention of sarcopenia in elderly individuals observed in the studies were related to increases in lean mass and maximal strength, thus improving general muscle quality.

A study, evaluated the intervention of 20g of creatine during the first 5 days and 5g in the following 23 weeks, combined or not with resistance training twice a week in vulnerable elderly women. They resulted in increased muscle strength in the upper and lower body as well as lean mass. The combination of creatine supplementation and resistance training may be of therapeutic relevance in the management of vulnerable elderly, where this study expanded knowledge about the application of creatine in senescence, as it provided evidence of the beneficial effect of this nutrient associated with physical activity.[9]

In the same sense, researches[10] in their recent meta-analysis found that there are no significant effects in studies lasting 14 weeks or less, with results being significant in studies of 24 weeks or more. Whereas, creatine supplementation elevates intramuscular creatine stores and increases exercise capacity which, over time, will translate into greater gains in muscle strength. Their subanalyses revealed unique findings in these studies, where creatine supplementation increased upper and lower body strength and further demonstrated that creatine plus resistance training attenuated the rate of muscle loss, however there was no effect on muscle mass.

Another research,[11] suggests that certain proteins, such as whey, which are higher in leucine, or leucine itself, may be able to overcome the anabolic resistance of aging muscle and stimulate an increase in lean body mass. Although it is a non-protein supplement, creatine can also be additive to resistance exercise in the elderly to stimulate gains not only in muscle mass, but also in strength and function. However, in their study with 200 participants, supplemented for 16 weeks with 30g/day of whey associated with 6g/day of creatine and resistance exercise twice a week, they observed that the supplementation used did not improve muscle adaptations to training. Thus suggesting that the ability to co-supplement with creatine and whey to counteract muscle wasting and weakness in elderly individuals may have limited clinical relevance. However, the authors do not rule out the possibility that suboptimal adherence to the intervention may have impacted the results. They further hypothesize that a higher protein intake than that adopted in this study (ie ~1.2g/kg/day) may be necessary to overcome anabolic resistance and outweigh the benefits of exercise.

In another research[8] with 32 individuals with the intervention of a multi-ingredient supplementation (MIS), composed of 3g of creatine, 24g of whey, 16g of micellar casein, 1,000IU of vitamin D and Omega 3, being 1.51g of EPA and 0.95g of DHA, associated with unsupervised home resistance exercise, over a period of 12 weeks, resulted in improvements in total lean mass, muscle fiber size, muscle/fat ratio, strength and performance. and general muscle quality in elderly men. The compound proved to be safe to use, well tolerated and an effective adjunct to strength training for maintenance of skeletal muscle in old age, being beneficial in mitigating sarcopenia as the magnitude of the improvements appeared to be greater in sarcopenic versus healthy subjects.

The idea of using MIS supplementation is primarily based on the simultaneous targeting of multiple metabolic and signaling pathways to potentiate gains in the skeletal muscle system, including protein synthesis, energy production, contractile and recovery function. As MIS stimulates multiple processes simultaneously, it theoretically circumvents the main limitation of using traditional single nutrient strategies to maintain the skeletal muscle system in old age which is anabolic resistance.[8]

The effectiveness of using MIS in the elderly was demonstrated,[12] who found that whey protein, creatine, EPA, DHA, and vitamin D increased lean mass, strength, cognition, n-3 index, and decreased markers of inflammation in older adults. Importantly, there were no reported side effects associated with the use of MIS, such as kidney or gastrointestinal problems, after use of relatively high doses of total daily protein (60g) and creatine (5g).

Corroborating these outcomes, Negro et al.,[13] in their study used a mixture containing 1.5g of creatine, 5,000mg of essential amino acids (EAA), 1,000IU of vitamin D, 300mg of alpha lipoic acid (ALA), 50mg of coenzyme Q10 (CoQ10) and 50mg of resveratrol, twice a day, before lunch and dinner, for 12 weeks in 38 sedentary subjects. For each participant, an adequate food plan was designed to ensure an average protein intake of 1.2g/kg of body weight/day. They demonstrated that the multi-ingredient supplement used can improve the results related to muscle aging, such as muscle mass, muscle strength and muscle power in a medium-short period and without physical effort. The authors hypothesized that the creatine in the mixture could be highly effective in increasing functional tests and may have contributed to the observed effect.

Conclusion

Studies indicate that the use of creatine promotes beneficial effects related to the prevention and treatment of sarcopenia in elderly individuals. In addition, the benefits were related to increases in lean mass and maximal strength, thereby improving overall muscle quality. Thus, the present study indicates the use of creatine as an aid in the prevention and treatment of sarcopenia. More in-depth future studies on the subject are suggested in order to clarify dosage, duration of use and possible associations to achieve effective results and increase general knowledge.

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Conflict of interest

The authors declare that they have no conflicts of interest.

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