



Original/*Alimentos funcionales*

Novel insights on intake of meat and prevention of sarcopenia: all reasons for an adequate consumption

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Abstract

Introducción: sarcopenia is defined as a syndrome characterized by progressive and generalized loss of muscle mass and strength. The main cause of sarcopenia is the alteration of protein metabolism, in which the proteolytic processes are not accompanied by an appropriate protein synthesis and muscle cells lose progressively the sensitivity to the anabolic stimulus. The most rational approach to delay the progression of sarcopenia and counteract the anabolic resistance is proper nutrition. Meat contains biologically active compounds, such as creatine, carnitine, Conjugated Linoleic Acid (CLA) which have significant impacts upon human protein metabolism.

Methods: we performed a narrative literature review to evaluate the till-now evidence regarding: 1. adequate intake of meat in elderly as a topic for prevention of sarcopenia; 2. the correct intake of biologically active compounds contain in meat, which have significant impacts upon human protein metabolism and so have beneficial effects on prevention of sarcopenia. This review included 62 eligible studies.

Results: the results demonstrated that in elderly the optimum diet therapy for the sarcopenia prevention and treatment, which must aim at achieving specific metabolic goals, must recommend the consumption of 113 g of meat (220 kcal; 30 g protein) five times a week.

Conclusion: in a varied and balanced diet, for preventing sarcopenia, it is recommended to assume meat 4-5 times a week (white meat 2 times per week, lean red meat less than 2 times per week, processed meat less than 1 time per week), as suggested in the diet pyramid for elderly.

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NUEVOS CONOCIMIENTOS SOBRE EL CONSUMO DE CARNE EN LA PREVENCIÓN DE LA SARCOPENIA: TODOS LOS MOTIVOS DE UN CONSUMO ADECUADO

Resumen

Introducción: la sarcopenia se define como un síndrome caracterizado por la pérdida progresiva y generalizada de la masa muscular y de la fuerza. La principal causa de la sarcopenia es la alteración del metabolismo de las proteínas, en la que los procesos proteolíticos no van acompañados de una síntesis de proteínas y células musculares adecuadas, con lo que se pierde progresivamente la sensibilidad al estímulo anabólico. El enfoque más racional para retrasar la progresión de la sarcopenia y contrarrestar la resistencia anabólica es una nutrición adecuada. La carne contiene compuestos biológicamente activos, tales como creatina, carnitina y ácido linoleico conjugado (CLA) que tienen impactos significativos sobre el metabolismo de la proteína humana.

Métodos: se realizó una revisión de la literatura narrativa para evaluar la evidencia hasta ahora, en relación con: 1. ingesta adecuada de carne en ancianos como prevención de la sarcopenia; 2. la ingesta correcta de compuestos biológicamente activos que contiene la carne, que tienen impactos significativos sobre el metabolismo de la proteína humana y para así obtener efectos beneficiosos en la prevención de la sarcopenia. Esta revisión incluyó 62 estudios elegibles.

Resultados: los resultados demostraron que en personas de edad avanzada la terapia óptima con dieta para la prevención y tratamiento de la sarcopenia, que debe apuntar al logro de los objetivos metabólicos específicos, debe recomendar el consumo de 113 g de carne (220 kcal; 30 g de proteínas) cinco veces a la semana.

Conclusión: en una dieta variada y equilibrada, para prevenir la sarcopenia, se recomienda consumir la carne 4-5 veces a la semana (carne blanca 2 veces por semana, carne roja magra menos de 2 veces por semana, carne procesada menos de 1 vez por semana), como se sugiere en la pirámide de la dieta para personas mayores.

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Palabras clave: *Sarcopenia. Carne. Proteínas. Aminoácidos. Creatina.*

Introduction

Sarcopenia is defined by the European Working Group on Sarcopenia in Older People (EWGSOP)¹ as a syndrome characterized by progressive and generalized loss of muscle mass and strength. Sarcopenia is a major contributor to physical frailty in older adults, with a prevalence ranging from 5 to 50% in adults aged 60 y and older, depending upon age and the methodology used to define sarcopenia². In many elderly patients, the onset of sarcopenia is multi-factorial³. As in all body tissue, muscle proteins are subjected to a constant process of synthesis and degradation; in healthy adults (with an adequate protein intake according to their needs) this turnover is balanced, allowing to maintain a positive nitrogen balance and a constant muscle mass^{4,5}. Aging determines the imbalance of this process and the degradation of muscle protein tends to become higher than the synthesis. Several studies have reported as muscle protein synthesis in elderly subjects is reduced by 30% compared to the young and the catabolism is greatly increased, mainly because of the lack of physical activity⁶. In addition, the content of fatty tissue and connective fibrous increases in the muscle. In the etiopathogenesis of primary sarcopenia the main cause is the alteration of protein metabolism at the level of muscle tissue, in which the proteolytic processes are not accompanied by an appropriate protein synthesis within the physiological turnover and muscle cells lose progressively the sensitivity to the anabolic stimulus induced from the essential leucine and IGF-1 (Insulin-like Growth Factor) then the phenomenon known as “anabolic resistance” is manifested⁷.

This phenomenon may be associated with other hormonal, functional, nutritional factors, each of which may contribute to a greater or lesser extent, depending on the sex, age and clinical condition of the patient, in the progression of the disease itself, defining then the secondary sarcopenia⁸. In addition, the economic topic has a significant impact, as a greater adherence to the Mediterranean diet is inversely related to a high BMI, but leads to higher monetary cost, which in 2006 were estimated at 1.2 €/day⁹, due to the higher cost of meat and fish, compared to carbohydrates.

The more rationale approach to delay the progression of sarcopenia is based on the combination of proper nutrition and a regular exercise program¹⁰. An adequate intake of proteins (1,2 g/Kg/day) is essential to prevent sarcopenia¹¹ and improvement of quality of life¹².

After taking a meal containing protein, the degree of protein synthesis remains elevated for more than 5 hours, with a peak 2-3 hours after intake¹³. It has been shown that in adult subject an approximate dose of 15-20 grams of protein (or 7.5 grams of essential amino acids) is sufficient to stimulate the maximization of the degree of muscle protein synthesis¹⁴. Probably to obtain the same maximization of protein synthesis in the elderly compared to the young is required a larger amount of protein, probably 30 grams as shown by

Pennings B. *et al.*¹⁵. The bioavailability of the amino acids plays a decisive role in the regulation of protein metabolism in the elderly subject and it is for this reason that a nutritional therapy must necessarily be stretched to the recovery of muscle and sensitivity to the stimulus induced by the amino acids, going to fight the aforementioned “anabolic resistance”. Over the past few years, the analysis of the different nutritional strategies carried out in this direction has allowed us to define some key concepts, expressed recently by the position paper of the PROT-AGE Study group¹¹, that is: the recommended amount of protein intake for healthy elderly (1.2 g/kg/day); the recommended amount of protein intake for the elderly with acute or chronic pathology; the role of physical activity in association with dietary intake to maintain muscle strength and function in elderly; the practical aspects of administration of food proteins (source and quality of dietary protein, protein intake timing and energy intake).

Given this background, the aim of the present narrative review is to summarize the state of the art according to the extant literature about two topics: 1. adequate intake of meat in elderly as a topic for prevention of sarcopenia; 2. the correct intake of biologically active compounds contain in meat, such as creatine, carnitine, Conjugated Linoleic Acid (CLA), other than the nutrients iron and cobalamin, which have significant impacts upon human protein metabolism and so have beneficial effects on prevention of sarcopenia.

Methods

The present narrative review was performed following the steps by Egger *et al.*¹⁶. Table I showed the summary of methodology used. The flow diagram of narrative review of the literature has been reported in figure 1. At the beginning of each section, the keywords considered and the kind of studies chosen has been reported. Suitable for the narrative review were prospective cohort studies, randomized controlled trials (RCT), reviews, metanalysis, cross sectional studies, position paper which considered elderly with diagnosis of sarcopenia defined by the European Working Group on Sarcopenia in Older People (EWGSOP)¹.

Results

Adequate intake of meat in elderly as a topic for prevention of sarcopenia

For this section 11 articles have been selected and discussed: 5 reviews, 5 Clinical Trial, 1 Cluster RCT.

Ingestion of sufficient dietary protein is a fundamental prerequisite for muscle protein synthesis and maintenance of lean muscle mass and function. Elderly are at increased risk of protein-energy malnutrition¹⁷.

Table I
Summary of methodology

Step	General activities	Specific activities
Step 1	configuration of a working group	three operators skilled in clinical nutrition: – one operator acting as a methodological operator – two participating as clinical operators
Step 2	formulation of the revision question	Evaluation of the state of the art on metabolic and nutritional correlates of sarcopenia and their nutritional treatment
Step 3	identification of relevant studies on Pub Med	– a) definition of the key words (sarcopenia, nutrients, dietary supplement), allowing the definition of the interest field of the documents to be searched, grouped in inverted commas (“...”) and used separately or in combination; – b) use of: the Boolean (a data type with only two possible values: true or false) AND operator, that allows the establishments of logical relations among concepts; – c) research modalities: advanced search; – d) limits: time limits: papers published in the last 20 years; humans; languages: English; – e) manual search performed by the senior researchers experienced in clinical nutrition through the revision of reviews and individual articles on sarcopenia in elderly published in journals qualified in the Index Medicus
Step 4	analysis and presentation of the outcomes	the data extrapolated from the revised studies was carried out in the form of a narrative review of the reports and were collocated in tables.

The meat is an excellent source of high quality proteins which are essential for optimal muscle and bone development¹⁸.

Moreover, meat contains a large quantity of essential amino acids: the intake of essential amino acids of meat, for the same weight, is higher than all other foods.

Between essential amino acids, in particular, the content of amino acid leucine is interesting, that stimulates protein synthesis through mTOR signal¹⁹.

It has been shown that a moderate intake of lean meat can increase protein synthesis in both young and elderly patients of both sexes²⁰.

In addition, some studies have shown a synergistic action between meat intake and resistance exercise to increase muscle mass in the elderly^{21,22}.

McLennan²¹ has been demonstrated in a group of elderly subjects, which undertook a lower limb resistance-training program while consuming a diet with 20% energy as protein delivered through 800g/week of red meat intake in combination with other sources of dietary protein, that, after 12 weeks, muscle performance significantly improved: leg muscle strength increased by more than 50% and muscle endurance about 30%.

Moreover, it has been demonstrated²² that a 113 g serving of lean beef (113g; 220 kcal; 30 g protein) increases muscle protein synthesis by approximately 50% in both young and older volunteers. Despite a 3-fold increase in protein and energy content, that has been no further increase in protein synthesis following ingestion of 340 g of lean beef (340 g; 660 kcal; 90 g protein) in either age groups.

Finally, recently it has been demonstrated that protein-enriched diet equivalent to $\sim 1.3 \text{ g} \cdot \text{kg}^{-1} \cdot \text{d}^{-1}$ achieved through lean red meat ($\sim 160 \text{ g}$ cooked to be consumed 6 d/wk) is safe and effective for enhancing the effects of progressive resistance training on lean tissue mass, muscle strength and reducing circulating IL-6 concentrations in elderly women²³.

In conclusion, since it has been demonstrated²² that a 113 g serving of lean beef (220 kcal; 30 g protein) increased muscle protein synthesis by approximately 50% in both young and older volunteers and since the most recent indications recommend an average consumption of meat and dairy products amounted to 142 grams per day²⁴, in elderly subjects lean meat should be consumed 4 or 5 times a week and only one or two of these occasions should resort to the red one.

The correct intake of biologically active compounds contain in meat, such as creatine, carnitine, CLA, other than the nutrients iron and cobalamin, which have significant impacts upon human protein metabolism and so have beneficial effects on prevention of sarcopenia.

Meat contains bioactive peptides capable of stimulating muscle growth²⁵.

Between these compounds, creatine, carnitine and Conjugated Linoleic Acid (CLA) are the most important for prevention of sarcopenia²⁶.

Finally, meat is the food that contains the greatest amount of highly bioavailable iron and vitamin B12 and the assumption of adequate amounts of both of these nutrients is useful in the prevention of sarcopenia²⁷.

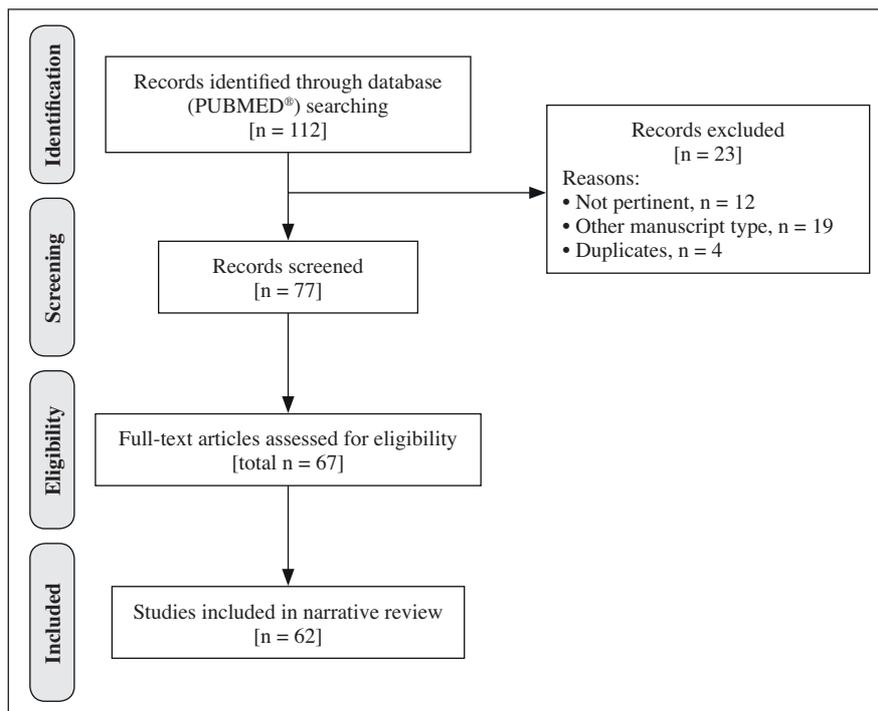


Fig. 1.—Flow diagram of narrative review of literature.

Creatine

For this section 33 articles have been selected and discussed: 5 reviews, 3 Clinical Trial, 1 Controlled Clinical Trial, 1 RCT, 1 Single Blind RCT, 13 Double Blind RCT, 2 Double Blind Cross-Over, 7 Observational Study.

Creatine is a guanidine-derived compound naturally produced in the body (i.e., 1-2grams/day)²⁸ from reactions involving the amino acids glycine, arginine and methionine²⁹ and consumed in the diet from red meat (i.e., 1-2grams/day)³⁰. Very little creatine is retained at the site of production. The majority of creatine is transported from areas of synthesis (i.e., liver, kidney) to areas of storage and utilization (i.e., skeletal muscle)³¹. Skeletal muscle contains approximately 95% of the entire creatine stored in the body^{32,33}.

Age-associated reductions in skeletal muscle creatine/phosphocreatine have been reported in some³⁴⁻³⁹, but not all studies⁴⁰⁻⁴².

It is unknown if this is an unavoidable consequence of aging (i.e. denervation, Type II fiber atrophy), related to physical activity (reduced physical activity or reduced intense physical activities that recruit type II fibers), decreased dietary creatine intake or if there are synergistic effects between these three factors.

Various studies have been published that included pre- and post-supplementation measures of muscle creatine in older adults^{38,43-45}.

Recent evidence suggests that creatine ingestion, in close proximity to resistance training, may be more beneficial than a creatine assumption held at any other time of day.

It has been demonstrated that consuming creatine immediately before (0.05 g kg⁻¹) and immediately after (0.05 g kg⁻¹) resistance training sessions (3 days/week, 10 weeks) resulted in greater whole-body muscle hypertrophy (2.0 ± 0.3 cm) compared to placebo (0.8 ± 0.3 cm) and resistance training in healthy older males⁴⁶. These results support previous findings of a significant increase in lean tissue mass (6%), type II muscle fiber area (29%) and insulin growth-factor I (78%) in adults (19-55 years) who ingested creatine before (0.03 g kg⁻¹) and after (0.03 g kg⁻¹) resistance training (6 days/week, 8 weeks)^{47,48}.

Among the studies that assessed muscle mass, the majority showed a greater increase in lean tissue accretion following creatine ingestion plus resistance training than resistance training alone^{44,49-51}.

The most typical finding is enhanced fatigue resistance, which has been demonstrated in many different studies using a variety of exercise tests^{38,42,52-55}. Some investigators have reported increased strength⁵⁴⁻⁵⁵, but this is not always found^{42,52}. Importantly, in later publications, investigators began to test for performance of activities of daily living (ADL) and demonstrated that creatine ingestion could improve the performance of daily tasks^{54,56,57}. The improvement in performance of ADLs is an important finding, due to the link between performance of ADLs, fall risk and mortality. Although only one study has reported changes in muscle creatine and muscle function in the same study³⁸ (in middle-aged), it does appear that creatine supplementation improves muscle function in older adults independently of exercise training.

A final benefit of combining creatine supplementation with resistance exercise is increased bone mineral content. Chilibeck *et al.*⁵⁸ showed a greater increase (3.2 vs. 1%) in bone mineral content in older men (71 year) following 12 weeks of creatine supplementation (0.3 g/kg for 5 days, 0.07 g/kg for 11 weeks) plus resistance training versus resistance training alone. Dalbo *et al.*⁵⁹ have stated that creatine supplementation is an effective intervention for combating sarcopenia.

In conclusion, an adequate creatine intake could represent an intriguing intervention to counteract sarcopenia, in particular fatigue related to sarcopenia.

Carnitine

For this section 10 articles have been selected and discussed: 6 reviews, 1 Clinical Trial, 1 Single Blind RCT, 2 RCT.

Carnitine, a trimethylated amino acid roughly similar in structure to choline, facilitates the transfer of activated long-chain fatty acids from the cytoplasm to the mitochondria, where they are processed by oxidation to produce ATP⁶⁰.

It is involved in the transfer of the products of peroxisomal beta-oxidation to the mitochondria and in the removal of short-chain and medium-chain fatty acids from these organelles, in which it is responsible for maintaining coenzyme A levels. Carnitine thus plays a central role in the metabolism of fatty acids and energy by regulating the mitochondrial ratio of free coenzyme A to acyl-coenzyme A.

The muscle is the most prominent carnitine depository as it stores about 95% of the total carnitine contained in the adult human body, showing a concentration 70-fold greater than that of the plasma. Carnitine is critical for normal skeletal muscle bioenergetics⁶¹ and indeed skeletal muscle is greatly affected in states of carnitine deficiency.

Approximately 75% of carnitine in the organism is derived from dietary source⁶² and red meat and dairy products are particularly rich in the amine, while 25% is synthesized in the liver and kidneys from lysine and methionine⁶³.

Animal by-products contain the highest amount of L-carnitine and these are, e.g. beef (139 mg per 100 g of dry weight), kangaroo meat (637 mg) and horse meat (423mg)⁶⁴.

Serum carnitine level is lower in vegetarians⁶⁵ and in patients on parenteral diet⁶⁶ than in omnivores, suggesting that serum carnitine is a potential marker of meat intake.

Carnitine has been tested as immunomodulating and antioxidant agents: in particular, carnitine supplementation has been shown to reduce chronic inflammation and oxidative stress⁶⁷.

Moreover, other chronic conditions like diabetes mellitus, heart failure, Alzheimer disease may cause carnitine deficiency, also observed in conditions with

increased catabolism as in critical illness, such as sarcopenia and cancer cachexia^{68,69}.

Conjugated Linoleic Acid

For this section 8 articles have been selected and discussed: 2 reviews, 4 RCT, 1 Double Blind RCT, 1 Cohort Study

Conjugated linoleic acid (CLA) is a naturally occurring fatty acid that is found in beef and dairy products; it has been reported that the mean CLA content in beef ranges between 1 and 19 mg/g lipid⁷⁰.

In some animal models, dietary CLA reduces carcinogenesis, decreases body fat, increases lean body mass, enhances feed efficiency, protects against oxidative stress, modulates circulating lipids and prevents impaired glucose tolerance in diabetes⁷¹.

One property that has been suggested to be responsible for CLA's bioactivity is its ability to act as an antioxidant. CLA has been shown to control oxidative status⁷².

Rahman⁷³ have already demonstrated that CLA can preserve age associated muscle loss in mice.

Another succeeding study by the same group⁷⁴ observed a slight rise of mitochondrial Reactive Oxygen Species (ROS) (expressed as H₂O₂) production in CLA isomers fed mice, compared to that of corn oil fed mice. However, mitochondrial ATP production and ROS neutralizing antioxidant enzymes production was also higher in CLA isomers supplemented groups than that of corn oil fed group. Elevated oxidative stress is closely linked to age associated sarcopenia. Oxidative damage occurs due to imbalance between oxidants and antioxidants systems, in favor of the former.

Finally, CLA has been reported to preserve the gastrocnemius muscle mass, by reducing TNF receptors in muscle⁷⁵.

It was suggested that CLA may preserve muscle mass, by reducing the catabolic effects of TNF- α on skeletal muscle. Resistance exercise therapy also improves muscle mass and strength by reducing the inflammatory state. Inflammation and oxidative stress promote catabolic stimuli, such as IL-6, IL-1, and TNF- α . Elevated levels of IL-6 carry a poor prognosis in older persons and cellular IL-6 is a significant predictor of sarcopenia in women⁷⁶. There are indications that cytokines, especially IL-1 β , TNF- α and IL-6, play a role in the pathogenesis of sarcopenia.

An interesting study was published in 2007 by Tarnopolsky *et al.*⁵⁰ in which creatine supplementation has been associated with CLA.

In this study, lasted six months, volunteers (subjects with a mean age of approximately 70 years) were subjected to a program of exercise against resistance (isotonic) twice a week. The results show that, compared with placebo, supplementation with creatine + CLA in the elderly has fostered a significant improvement in lean body mass and a reduction in fat mass, a result

that provides additional perspectives as regards the modulation antiaging body composition.

Discussion

The traditional view of the role of meat has been greatly expanded in recent years beyond the horizon of nutritional subsistence of elderly: it is now recognized to be more than a source of nutrients for nourishment of elderly population. Meat contains biologically active compounds, such as carnitine, creatine, Conjugated Linoleic Acid, which have important physiological and biochemical functions and significant impacts upon human metabolism, nutrition and health.

Moreover, concerning the topic about meat intake and CVD, it is important to note the results of a meta-analysis by Micha *et al.*^{77,78} that examined more than a million subjects to identify the relationship between consumption of red meat and processed meat and the development of cardiovascular diseases and diabetes. Results of this meta-analysis reported that there is no association between consumption of red meat (one serving of 100 g/day) and the development of coronary heart disease or diabetes mellitus, while the relative risk (RR) increases considerably if the consumption of processed meat (a portion of 50 g/day) and the development of coronary heart disease or diabetes mellitus are related (RR 1:42 and 1:27 respectively).

Meat has the peculiarity to contain all the eight essential amino acids, without limitations and its proteins have high biological value. Therefore meat is an excellent source of proteins and contains a large quantity of amino acid leucine that stimulates protein synthesis through mTOR signal¹⁹.

Primary sarcopenia is mainly caused by an alteration of protein metabolism in the muscle tissue and due to the gradually loss of muscle cells to their sensitivity to the anabolic stimulus induced by leucine. In this case occurs the phenomenon defined as “anabolic resistance”⁷⁷.

It has been shown that a moderate intake of lean meat can increase protein synthesis in young and elderly patients of both sexes²⁰.

In addition, some studies have demonstrated that a synergistic action between meat intake and resistance exercises increases muscle mass in the^{21,22}.

It has been proved²² that a 113 g serving of lean beef (220 kcal; 30 g protein) increases muscle protein synthesis by approximately 50% in both young and old volunteers. Despite a 3-fold increase in protein and energy content, there has been no further increase in protein synthesis following ingestion of 340 g of lean beef (340 g; 660 kcal; 90 g protein) in either age groups.

In conclusion, in a varied and balanced diet, for preventing sarcopenia, it is recommended to assume meat 4-5 times a week (white meat 2 times per week, lean red meat less than 2 times per week, processed

meat less than 1 time per week) as suggested in the diet pyramid for elderly^{79,80}.

Author disclosure statement

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