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Sarcopenia: what should a pharmacist know?

Sarcopenia: ¿qué tiene que saber un farmacéutico?

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Abstract: Sarcopenia (or muscle insufficiency) is a geriatric syndrome characterized by a progressive and generalized loss of skeletal muscle mass and function which has adverse consequences, particularly physical disability, falls and death. It can develop slowly, as a chronic condition that emerges over many years, or acutely, generally due to immobilization associated with an acute disease.

The physiopathology of sarcopenia is complex, and affects both the muscle and its neurological and hormonal regulation.

The prevalence of sarcopenia increases with age and in certain healthcare settings (nursing homes, hospitals, rehabilitation centres). Its diagnosis is based on the documentation of a low muscle mass associated with low muscle strength and/or low physical performance. Once confirmed, a syndromic approach is needed, based on a comprehensive geriatric assessment in order to determine its causes and prepare a treatment plan which addresses the treatment of symptoms as well as the etiology.

Prevention of sarcopenia starts in the adult age, through the promotion of adequate nutritional habits, an increase in physical activity and, ideally, resistance exercise. Sarcopenia treatment must necessarily include resistance exercises (that can be associated with other types of exercise) and an improvement in diet, increasing protein intake up to 1.2-1.5 g/kg/day and covering caloric requirements. In some cases, this will require the use of nutritional supplements, which can contain leucine, beta-hydroxy beta-methylbutyrate acid (HMB) and vitamin D, in order to optimize its effects on the muscle. There are still no medications available to treat sarcopenia.

KEYWORDS: Frailty, Geriatric nutrition, Mobility, Sarcopenia, Older people, Pharmacist intervention.

Resumen: La sarcopenia (o insuficiencia muscular) es un síndrome geriátrico caracterizado por una pérdida progresiva y generalizada de masa y función del músculo esquelético que tiene consecuencias adversas, especialmente la discapacidad física, las caídas y la muerte. Puede producirse de forma crónica, a lo largo de muchos años, o aguda, generalmente por una inmovilización asociada a una enfermedad aguda.

La fisiopatología de la sarcopenia es compleja y afecta tanto al músculo como a su regulación neurológica y hormonal.

La prevalencia de la sarcopenia aumenta con la edad y en determinados entornos asistenciales (residencias, hospitales, centros de rehabilitación). Su diagnóstico se basa en la documentación de una baja masa muscular asociada a baja fuerza muscular y/o bajo rendimiento físico. Una vez se confirma, es preciso adoptar un enfoque sindrómico y usar una valoración geriátrica integral para determinar sus causas y elaborar un plan de tratamiento que incluya tanto el tratamiento de los síntomas como el etiológico. La prevención de la sarcopenia comienza en la edad adulta, a través de la promoción de hábitos de alimentación correctos, un aumento de la actividad física e, idealmente, ejercicios de resistencia. El tratamiento de la sarcopenia debe incluir necesariamente ejercicios de resistencia (que pueden asociarse a otros tipos de ejercicio) y la mejora de la dieta, aumentando la ingesta proteica hasta 1,2-1,5 g/kg/día y cubriendo los requerimientos calóricos. En algunos casos será preciso para ello el uso de suplementos nutricionales, que pueden contener leucina, ácido β -hidroxi β -metilbutírico (HMB)

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y vitamina D, para optimizar sus efectos en el músculo. Aún no disponemos de medicamentos para tratar la sarcopenia.

PALABRAS CLAVE: Fragilidad, Nutrición geriátrica, Movilidad, Sarcopenia, Personas mayores, Intervención farmacéutica.

In recent years, the term sarcopenia has gone from being hidden in a bunch of research articles for experts to become, together with frailty, one of the trendy terms in Geriatrics, rapidly extending to other specialties. The number of research articles is increasing at exponential rate. It is increasingly frequent for older patients to receive this diagnosis. What is happening? This article offers a brief review of sarcopenia, trying to emphasize some aspects particularly important for the pharmaceutical practice.

Sarcopenia: Background and Concept

The term sarcopenia is formed by two Greek words: sarx, which means flesh, and penia, which indicates the lack of something; summing up: “loss of flesh”. It was first proposed in 1998 in order to define a well-known problem in older persons, but for which there was no adequate descriptive term so far: the loss of muscle mass and function, associated with age, which deteriorates mobility, nutrition status, and physical independence¹. Even though sarcopenia causes major consequences on the life and physical ability of loss persons, it has not been acknowledged as a disease, in the International Classification of Diseases (ICD-10) until 2016.

The best way to understand sarcopenia is as an organ impairment (muscle insufficiency or muscle failure)². It generally appears in a chronic and latent manner, and settles slowly with ageing; but it can also appear rapidly, usually associated with an acute immobility or severe disease (such as during hospitalization). Sarcopenia is closely associated with physical frailty^{3,4}. Sarcopenia is one of the main causes for physical frailty. Both sarcopenia and frailty are factors predicting the development of physical disability; this is why research looking how to stop these conditions before disability appears is so relevant.

How is it diagnosed?

Currently, sarcopenia is defined as a geriatric syndrome characterized by a progressive and generalized loss of skeletal muscle mass and function, which increases the risk to suffer problems such as death, falls, physical disability and impaired quality of life⁵. Up to 30% of impaired people living in the community suffer from sarcopenia, with higher prevalence among those living in nursing homes. It is not yet clear whether its prevalence is higher in women or in men, because there is no agreement between different studies, partly depending on the cut-off points used to determine muscle mass.

In clinical practice, three measurements are needed in order to diagnose sarcopenia: muscle mass, muscle strength, and physical performance (Table 1). It must be considered that the cut-off points for each measurement can vary according to gender and age, and often also to race or country of origin. Densitometry is becoming the standard procedure for measuring muscle mass; this can be conducted with the same equipment used for bone densitometry. Appendicular mass (of the limbs) will often be measured. The usual alternative is bioimpedantometry, which is a portable test. Many pharmacies and obesity clinics have foot bioimpedance meters, which are the least reliable in measuring muscle mass. Usually, the equation calculated by the device is not valid; in many of them it will only provide the lean mass percentage; it is recommended to use a standard equation such as Janssen's⁶. The easiest measurement of muscle strength is a hand grip device. Physical performance (a concept addressing the physical ability of the whole body, and not that of an isolated muscle) it can be measured with simple tests, such as a four-meters gait speed test.

Table 1
Criteria and techniques used to diagnose sarcopenia

Sarcopenia is diagnosed when Criterion 1 is present, as well as at least one of the other two criteria (2 and/or 3).		
1. Low muscle mass 2. Low muscle strength 3. Low physical performance		
Techniques used to diagnose sarcopenia		
Muscle mass	Muscle strength	Physical performance
➤➤ Absorptiometry (DXA) ➤➤ Bioimpedantometry (BIA) • Anthropometry	➤➤ Grip strength • Isokinetic knee extension (quadriceps)	➤➤ Walk speed • Short physical performance battery (SPPB) • Timed Up and Go Test • 6-minute walk test • 400 metre walk test

The most frequently used

It is convenient to remember that sarcopenia is not the only disease which causes a generalized loss of muscle mass. This can be caused by other conditions mostly malnutrition and cachexia, and it is not always easy to differentiate between these three problems⁷, which can be interlinked, and therefore difficult to separate. Malnutrition causes loss of (lean) muscle mass as well as fat mass, and it is caused by an inadequate update of nutrients. In cachexia, the loss of lean and fat mass is caused by a severe disease such as cancer. In sarcopenia, the fat mass is usually normal or increased; the latest is known as sarcopenic obesity⁸.

Once diagnosed, it is convenient to approach sarcopenia in the same way as other geriatric syndromes⁹, conducting a Comprehensive Geriatric Assessment in search of its causes (Table 2). From the point of view of the pharmacist, it is important to review those medications that could be associated with sarcopenia^{10,11,12}. It is best to conduct this task in an interdisciplinary approach which is adapted to the healthcare setting where the intervention is being conducted¹³.

Table 2
Causes and types of sarcopenia

Primary Sarcopenia	Examples
Age-related sarcopenia	No other evident cause except for ageing.
Secondary Sarcopenia	
Activity-related	Can be due to rest in bed, sedentary lifestyle, deconditioning, or zero gravity situations.
Disease-related	Due to advanced organ disease (heart, lung, liver, kidney, brain), inflammatory diseases, neoplasias, endocrinological conditions (overlapping with cachexia).
Nutrition-related	Consequence of an insufficient intake of energy and/or proteins, malabsorption, GI diseases, or use of medications with anorexigenic effects.

Physiopathology

The physiopathology of sarcopenia is quite complex, including muscle processes as well as endocrinological and neurological regulatory processes^{14,15}. With normal ageing, the quality of muscle fibers deteriorates, with a reduction in their maximum potency, shortening speed and elasticity. This deterioration in muscle cell function can be due to different changes associated with age, including the loss of anabolic stimulus secondary to a reduction in testosterone and other anabolic hormones, age-related sub-clinical inflammation (inflammaging) and molecular changes in cell contraction mechanisms. Some of these changes can be partially reversed through continuous physical exercise.

Anatomic changes also occur, such as a reduction in the number and activation of muscle satellite cells, a reduction in the number of muscular fibers (particularly those of type IIA) and fat infiltration of muscle, both at macro and microscopic level. The circulating levels of myostatin (a growth factor that limits muscle mass growth) also increase with age; and there is a modification in the regulation of different genes that regulate the muscle protein metabolism.

The neurological control of movement is also affected in sarcopenia, with a relevant role control by the loss of motor plates, which has not been fully understood yet. Many other neurological, endocrinological, and even microvascular mechanisms seem to be involved in the genesis of this disease.

How to detect patients with sarcopenia

The prevalence of sarcopenia increases with age; thus, older people present a higher risk of sarcopenia. Its frequency is so high at very advanced ages that it would be probably worth using screening tests to detect it in this population; however, there is still no agreement about the age at which this screening should start, and it has not been proved that population screening improves relevant clinical outcomes. Screening can be conducted using tools such as the SARC-F¹⁶ questionnaire, currently under validation in several European languages. The measure of walk speed could also be used, and all those people who walk less than 1 metre per second should be considered at risk.

An alternative approach is to search for sarcopenia in certain healthcare settings or risk populations. The groups at special risk are older people admitted in hospitals, nursing homes or rehabilitation centres, and those who attend Geriatric outpatient clinics. Acute sarcopenia will frequently appear during hospitalization, as a consequence of long stays in bed and the presence of acute diseases. Another alternative is to search for sarcopenia in risk populations, such as patients with repeated falls, those who seem to walk slower, show prolonged limitation in their physical activity, use a cane, or have problems getting up from their seat¹⁷.

Prevention and Treatment

Sarcopenia prevention should start in adult age, because the loss of muscle mass and function starts at around age 30-year-old, and becomes more evident when patients are over 50-year-old. Prevention is based on maintaining a high level of physical activity in daily life, conducting specific resistance exercises (muscle strength), an adequate diet (adherence to Mediterranean Diet, with a special emphasis on a high protein intake and avoiding risk behaviours (smoking, drinking alcohol). Implementing these habits can delay the development of sarcopenia possibly in over a decade, depending on the age at which changes start.

Once established, it will be important to detect sarcopenia at the earliest stage possible. There are data suggesting that severe sarcopenia is more difficult to reverse than mild sarcopenia. The first step is to identify and treat its causes, generally through a Comprehensive Geriatric Assessment and a sequential therapeutic approach (Figure 1). Nutritional intervention and exercise will be the basis of treatment¹⁸. There are no medications approved for sarcopenia, though some are already in clinical research¹⁹.

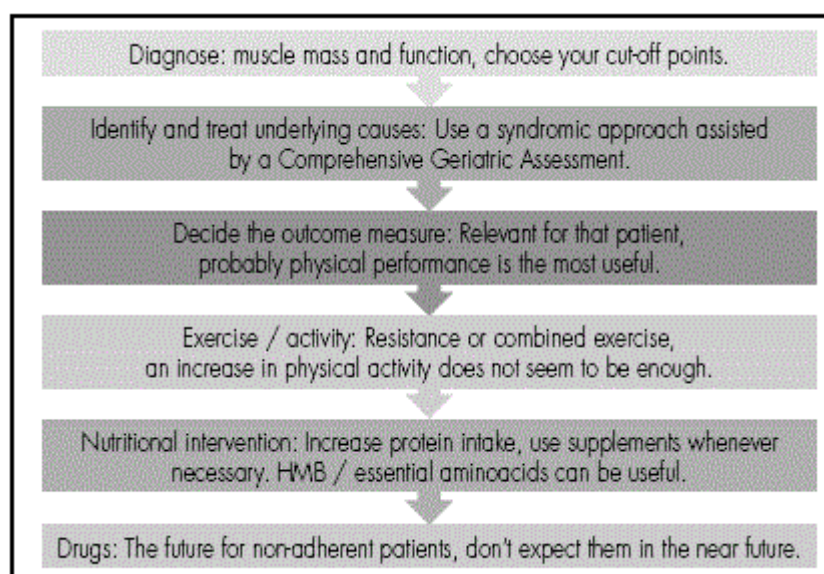


Figure 1.
Outline of sarcopenia management.

Recommendations about exercise and physical activity

First of all, it must be understood that exercise and physical activity are different concepts. The American Institute of Medicine defines physical activity as any movement caused by the contraction of skeletal muscles that increases the use of energy, and exercise as planned, structured and repetitive movements that seek to improve or maintain one or more components of physical fitness. Physical activity includes any daily activity (housework, going for a walk, moving around the house, hobbies); physical exercise needs dedication and planning. There are very comprehensive recommendations by the American College of Sports Medicine on physical activity and exercise in older people²⁰, and recent recommendations about how to promote them in persons living in nursing homes²¹.

Sarcopenia management requires both an increase in physical activity and conducting a specific program of exercises, which must include resistance exercises with weights or elastic bands, to improve muscle function of lower limbs; therefore, it is usually beneficial to start them under the supervision of an expert in exercise. It seems advisable to associate resistance exercise with other types of exercise (aerobic, balance and flexibility) in order to obtain the maximum benefit of said exercise. There are increasingly more resources available on-line (videos and written material) on exercise for older persons.

Dietary recommendations

Currently it seems clear that a low protein intake in the adult age will predict to a high extent the risk of suffering physical disability in the future²². Therefore, it is reasonable to start by advising older patients with sarcopenia about their diet, correcting any nutritional deficiency found. Protein intake recommendations have experienced a great variation in recent years, going from 0.8 grams per kg of body weight to a minimum 1.0 grams in healthy older people, and 1.2-1.5 grams in patients with sarcopenia²³. Caution is only required in those patients who suffer advanced renal disease (glomerular filtration rate <30 ml/min).

Caloric intake must be sufficient (and cover also the increased needs from exercise and physical activity), because otherwise proteins won't be used to build muscle, but due to their caloric value. It is also recommended to distribute proteins regularly throughout the day, insisting on protein intake immediately after exercise, because the muscle appears to have the priority at that time in terms of receiving the proteins ingested.

The role of nutritional supplements

Many older people won't reach their nutritional requirements only through diet interventions. For this reason, several interventions have been studied in order to improve the quality and quantity of diet in patients with sarcopenia, even though there are still limited data available²⁴. The intake of essential aminoacids (especially those rich in leucine) represents a powerful stimulus for protein formation in the muscle, even though isolated protein supplements have not yet demonstrated benefits in clinical practice. The same applies to

creatine supplements. Beta-hydroxy beta-methylbutyrate acid (HMB), a metabolic derivate of leucine, seems to have an important effect in mass improvement, and particularly in muscle function; however, in most clinical trials, it has been studied as part of a complete nutritional supplement. It is also appropriate to attain normal Vitamin D levels, because it's deficiency will worsen muscle function.

Even though many of the previously mentioned supplements are used in Sports Medicine, the most robust studies in older people have been made with complete nutritional supplements, covering the needs in terms of calories as well as proteins; therefore, high-protein preparations are usually recommended. While expecting further data, it makes sense to choose supplements which will also contain Vitamin D and leucine / HMB.

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