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Sarcopenia and Microbiome

Alvaro Zamudio Tiburcio[1]*, Héctor Bermúdez Ruiz[2], Silverio Alonso López[3], Pedro Antonio Reyes López[4]

[1]*Department of Gastroenterology, Intestinal Microbiota Transplantation Medical Specialties Naples Unit, Mexico.*
[2]*Endoscopy Service, Oncology Hospital, National Medical Center, XXI Century, Mexican Social Security Institute, Hospital Trinidad, Mexico City, Mexico.* [3]*Department of Urologist, Chairman Medical Specialties Naples in Mexico City, Mexico.*
[4]*Immunologist, Rheumatologist, National Institute of Cardiology "I. Chávez", Mexico City, Mexico.*
**Corresponding author: Alvaro Zamudio Tiburcio.*

Abstract

Sarcopenia (muscle dysfunction) is a condition that affects millions of people, hence the importance of influencing it. Likewise, determining the various effects that the microbiome has on this disease is significant, by opening new routes of knowledge or reiterating them, to help patients with this very common pathology. In principle determined as the loss of skeletal muscle mass, with the consequent risk of affecting both function and mobility capabilities.

Currently it has been defined as: low lean mass alone; low lean mass and low muscle strength; low lean mass and low physical function, and low muscle strength and low physical function. The criterion of seeking a single definition being unified. Currently, the treatment is based on physiotherapy, lifestyle modifications and nutrition. There are no specific medications. However, we consider that it is worth exploring the intestinal microbiota in the search for this therapy, which does not exist to date.

The European Working Group on Sarcopenia in the Elderly, points out the following definition (presence of low muscle mass + poor muscle function (strength or performance). And determines phases: "presarcopenia", "sarcopenia" and "severe sarcopenia".

Keywords: sarcopenia; microbiome (M); gut dysbiosis (GD); gut microbiota (GM); fecal microbiota transplantation (FMT)

Introduction

Considered a degenerative condition of skeletal muscle, sarcopenia (Sarc) (a syndrome characterized by progressive and generalized loss of skeletal muscle mass and strength), is an enormous burden on health systems. Along with osteoporosis and obesity, it has become an immense impact on the quality of life. 10 to 16% of the world's elderly population suffers from it and, significantly, those affected by unresectable esophageal malignancies present it in 66% of cases [1]. There is primary Sarc, in relation to age, and secondary, due to a decrease in physical activity, poor nutrition and comorbidities. Its cause is due to different processes, including inflammation, autophagy, apoptosis, calcium metabolism, insulin resistance and mitochondrial dysfunction. Treatment should be personalized, depending on the patient's general status [2].

Sarcopenia

Currently there is evidence that the Gut Microbiota (GM) is present. Demonstrated with 16S rDNA sequencing and metabolomic profiling. There is a lack of understanding between the microbiome (M) and the metabolic processes of patients with Sarc. Zhou J and his group [3]. They detect alterations in 29 genera and 172 metabolites, with alterations in the disease. Being Blautia, unclassified Lachnospiraceae and Subdoligranulum, the most significant. While the metabolism of purines, arginine, proline, alanine, aspartate, glutamate, butanoate and histidine could contribute to the presence of the process.

Do not forget that many of the falls, the loss of independence, and their consequences are the product of the Sarc. On the other hand, mitochondrial dysfunction and the inflammatory process, which is linked to age, are determinants of the development of the disease [4,5]. Nephrological data may appear in Sarc, with increased mortality; hepatobiliary (hepatic encephalopathy); hemato-oncological (chemo toxicity); cardiological (arterial hypertension) and pneumological (respiratory failure). As well as: Increase in hospital infections, cognitive impairment, social dependence and disability [6]. The diagnosis is based on two aspects: modern approaches and measures of physical

performance, as well as evaluation of muscle mass (atomic detection-anatomical measurement). Magnetic resonance imaging and computed tomography are included - although they are expensive studies. Bio-electrical impedance is preferred, as it is easier and cheaper [7].

Oral Microbiome

How much does the oral microbiome influence Sarcopenia? First of all, we must accept that the microbiota of the oral cavity is an autonomous ecosystem, in which more than 700 bacterial species reproduce (Firmicutis, Bacteroidetes, Fusobacteria, Actinobacteria, Proteobacteria, Spirochaetes and Synergistetes), in addition to fungi, little by little they make their appearance [8]. Alterations in the oral microbiota can affect changes in other regions, such as dental cavities. As occurs in a study in 1,442 patients [9].

Gut Microbiota

It has been shown that the incidence of GM on the host's physiology affects aging, especially when there is little biodiversity, interindividual variation and an increase in pathobionts. A fact corroborated in mice, while in humans, the few studies point to the presence of Faecalibacterium and Bifidobacterium, related to grip strength [10]. On the other hand, disturbed sleep given by changes in GM would suggest a pro-inflammatory state [11].

It has been proposed that by analyzing the GM we can predict Sarc, aided by biochemical indices, having observed that the Provotella/Bacteroides indices increase in the process [12].

In older adults there is usually anabolic resistance, and GM acts through dysbiosis (lower bacterial diversity), decrease in butyrate, increase in pathogenic bacteria and intestinal permeability, resulting in an increase in metabolic endotoxemia [13].

Gut Dysbiosis

It is common in older adults, along with Sarc, and it has been proposed that it exerts its action through the Gut-muscle axis. Without prejudice to the search for inflammatory molecules that appear in aging muscles [14]. Liu C and his team [15] exhaustively search for proposals about the sarcopenia-microbiota binomial and it draws our attention that in seventy-five percent of eight studies, fecal microbiota transplantation (FMT) successfully showed the replication of the muscle phenotype of the donors. Gut Dysbiosis (GD), lifestyle, diet and glucose dysregulation are causes of Sarc. In relation to GM, it does so by modulating the generation of lipopolysaccharides, Short Chain Fatty Acids (SCFA) and metabolites [16]. GD can decrease physiological adaptation, increase inflammatory markers, as well as devastate free radical macromolecules, all of which contribute to skeletal muscle atrophy.

Dysbiosis; Metatranscriptome and Metagenomics

Using what happens in periodontitis as an example, metagenome/metatranscriptome analysis can determine molecular signatures in the progression of the disease. The same occurs in the development of the Sarc. Obtaining community profiles through next generation sequencing (Ilumina). Metabolic modifications are determined, associated with the onset of GD. Suggesting that the community is responsible for the increase in pathology [17].

Gastrointestinal Diseases and Sarcopenia

There are various pathologies related to Sarc, both digestive and extra-digestive. In Parkinson's disease it is present in one in five patients. In unresectable cancer of the esophagus, it occurs in 85%. Pointing out the evidence that there is a link between GM, Sarc and inflammatory status, which comes from the communication of intestinal bacteria with the immune system [18].

The diseases linked to Sarc were gastrointestinal in 99 patients, biliary/pancreatic in 93 and hepatic in 111 [19].

The AMERICAN GERIATRICS SOCIETY reports five thousand nine hundred and ninety-three patients aged 65 years, in whom they determine Sarc, decreased grip strength, activity and slow walking. Concluding that frailty is linked to worse health and risk of mortality [20]. The presence of Sarc has been determined in Inflammatory Bowel Disease, triggered by chronic inflammation, malnutrition, deficiency of vitamins and alterations of the Gut-muscle axis [21].

Although it has not been determined why Sarc appears in gastrointestinal diseases. About 22.6% have been detected [22].

Resilience

Adaptation of a living being against disturbing agents. It is linked to mental health and physical functioning. Its factors are educational level, time spent exercising and high blood pressure.

The population with Sarc is increasing worldwide. Understanding levels of resilience among older adults with probable Sarc is essential to promoting their mental health. Clinicians can use the results of this

study to identify populations at high risk for low resilience and design targeted interventions to promote better health outcomes. Lee SY and her group [23] are among the authors who give enormous importance to the consideration of resilience in Sarc, and in the search for preventive strategies against adverse processes. Stress generates diverse reactions in older adults, generated by different resilience [24]. Resilience has increased its importance, after Covid-19, when trying to develop individual, systemic and community resilience [25].

Gut-Microbiota-Muscle-Brain Axis

This axis that regulates physical frailty and age-related Sarc, abbreviated as the gut-muscle axis, can be affected or improved by diet, intake of proteins and indigestible carbohydrates, exercise, alcohol intake or smoking [26].

The gut-muscle axis, through which GM can mediate the effects of nutrition on muscle, including inflammation, nutrient absorption, oxidative stress, immune function and anabolic balance, and, therefore, in the Sarc, although it must be reiterated that the causal link remains uncertain. An association has been demonstrated between the composition of the GM and muscle function (strength, gait speed and physical frailty). More studies are required that consider that it is the gut-muscle axis that regulates the progression of Sarc. Although existing studies suggest that GM is associated with physical performance in aging, through two pathways [27]. Zhao J and his team [28] point out that GM affects muscle mass and muscle function, through immunity and inflammation, as well as endocrine sensitivity, insulin, energy and substance metabolism, with direct communication between Sarc and gut-muscle axis.

The ideal composition of GM can affect muscle protein synthesis, biogenesis and mitochondrial function, as well as muscle glycogen storage [29].

Neurotransmitters

Intestinal microorganisms are capable of generating γ-aminobutyric acid (GABA), which is the most important inhibitory neurotransmitter of the CNS. The Akermansia muciniphila bacteria contributing to its production [30]. Casati M and her team [31] point out that a single marker is not enough to determine a condition, and that these can lead to dysfunction of the neuromuscular junctions; Which by the way, they reiterate is not related to age, but is an independent process.

It is confirmed that efficient rehabilitation decreases inflammation and the result could be determined by modulation of the neuro-immune axis, generated by an increase in norepinephrine [32].

Short Chain Fatty Acids

Der-Sheng H and collaborators [33] point out that in patients with normal muscles, fecal butyrate decreased significantly in the group with low muscle mass, correlating with the skeletal muscle mass index. Highlighting, with this, the changes in the GM, ingesting SCFA can prevent loss of muscle strength in older adults. Associated with the conservation of skeletal muscle mass [34]. Chen F and her team are trying to test whether fecal SCFA affect skeletal muscle mass and strength in healthy Chinese children, ages 6 to 9; Children with higher levels of fecal butyric acid, acetic acid and total SCFA exhibited higher scores. And the links between GM and SCFA with skeletal muscle quality may depend on total body fat.

Wan-Qiang LV and her team [35] search through a causal-mechanistic relationship for new interventions for the loss of musculoskeletal mass and find it through Magnetic Resonance. The presence of butyrate is interesting, due to greater microbial synthesis of Faecalibacterium prausnitzii and Butyricimonas virosa.

Another corroboration that fecal SCFA do act in the loss of musculoskeletal mass is made by Wan-Quiang LV et al. [36]. Even though the matter has not been fully resolved.

Bile Acids

"The composition of bile acids and metabolites differs between cirrhotic patients without and with Sarc and contributes to the pathogenesis." Bacteroides fragilis, Blautia marsella, Sutterella spp. And Veillonella parvula, were associated with cirrhotic patients with Sarc. The study by Aliwa et al. [37], point out possible functional interaction between GM and the host that links Sarc with altered intestinal microbiomes, bile acid profiles and amino acids that point towards possible mechanistic interaction in understanding the pathogenesis of Sarc.

Abrigo J and his team [38] describe a murine model of Sarc caused by chronic liver disease, through the ingestion of hepato-toxin 3,5-diethoxycarbonyl-1,4-dihydrocholidine, with an increase in plasma bile acids. And they generate skeletal muscle atrophy.

Differences have been determined in the plasma metabolic profile, associated with various degrees of

Sarc, identifying very long chain fatty acids, with variables associated with the severity of the process. The amino acid citrulline was the only metabolite with a significant group difference and "Positive propensity was observed between severe Sarc score and very long chain fatty acids as well as dicarboxylic acid carnitines. These findings point to a potential link between Sarc and mitochondrial dysfunction and describe a number of possible biochemical pathways that could be involved in the pathogenesis of the disease [39]."

Biotics

Modulation of GM with probiotics, prebiotics, dietary fiber, and FMT are recognized therapies to improve health and prevent disease. The M formulation is useful as a biomarker. Lactobacillus and Bifidobacterium strains restored age-related muscle loss. For all of the above, we delve into FMT, as well as other biotics, used for the benefit of Sarc [40].

Fecal Microbiota Transplantation (FMT)

The procedure often stimulates us, reading: seventy-five percent of the mice successfully replicated the muscle phenotype of the donors [41]. Not forgetting that older adults do not anabolic muscle in response to protein supplementation as well as younger people ("anabolic resistance").

FMT has a probiotic function, its effectiveness in patients with Sarc and advanced age being unknown. M based on metabolomic studies, integrity of the intestinal wall and muscle transcriptome, they detected that the destruction of the intestinal barrier was prevented by increasing the density of goblet cells. Concluding that FMT could remodel the GD of GM and its metabolites, maintain the integrity of the intestinal barrier and improve muscle mitochondrial dysfunction [42].

Probiotics

Substance produced by a microorganism, capable of stimulating the growth of another microorganism; live, non-pathogenic microbes that, when consumed, positively influence host physiology and health; WHO: "Live microorganisms, which when administered in adequate quantities confer a health benefit to the host." Lactobacillus and Bifidobacterium strains restored age-related muscle loss. Shokri-Mashhadi N and her team point out that [43]. Probiotics did not produce improvement in anthropometric indices, even though they would generate improvement in muscle mass and function, in adults over 55 years of age, 12 weeks after their administration.

Prebiotics

Components that are selectively fermented and allow specific changes in the composition or activity of the microorganisms that inhabit the gastrointestinal tract of the human body. Neither Lochlainn et al. [44] study the prebiotic effect, accompanied by proteins in GM. Considering that this determination can reduce anabolic resistance and therefore, reduce Sarc and fragility. Another report states that it is not clear whether prebiotics modify the composition of the GM and generate recovery from muscle atrophy in elderly patients with Sarc [45].

Symbiotics

Product containing probiotics and prebiotics. These have been used to try to remedy Sarc and Lactobacillus pluralis (spp.) and possibly Bifidobacterium appear. Which have been reported to improve muscle atrophy and intestinal permeability in mouse models. Action, they exert through lactate, butyrate and reduction of inflammation mediated by the gut-muscle axis. Symbiotics linked to vitamin D can modulate M, improving Sarc (strength, muscle function and body composition in overweight and obese middle-aged women) [46].

Paraprobiotics

Non-viable microorganisms, which could produce health benefits, similar to those generated by live probiotics.

Because paraprobiotics have the ability to regulate the immune systems, both adaptive and innate, and are safe, without the complications that another biotics can produce, I consider that they can be tested in Sarc [47].

Psychobiotics

Living organism that, when ingested in adequate quantities, produces health benefits in patients suffering from psychiatric diseases.

Treatment directed at GM is a current approach to health and anti-aging.

This new class of probiotics translates light of hope for the effective treatment of neurodegenerative diseases and various psychiatric disorders, especially with the increase in life expectancy [48]. These gerobiotics can be used as biomarkers of aging [49].

Postbiotics

Preparation of inanimate microorganisms and/or their components that confer a health benefit to the

host. They have also been called "paraprobiotics," "heat-killed probiotics," "ghost probiotics," "nonviable probiotics," and "bacterial lysates." They are referred to as better than probiotics, given their acid-base and thermal stability; ease of storage and use and high security [50]. They are made from lactic acid bacteria and can improve Sarc, through metabolic reprogramming of GD. WDK, which is produced from polyphenol-rich melon peel extract and Lentilactobacillus kefiri whey, significantly improved palmitate-induced atrophy of C2 C12 cells, restoring the length and diameter of myotubes. Also, it enhanced the expression of myogenic genes, including Atrogin-1, Igf-1, and MyoD [50].

Conclusion

- There is a lack of method to measure muscle mass in large cohort studies.
- Cases of unresectable esophageal malignancies with Sarc must be further analyzed.
- Having a diverse GM is essential to maintain our proper body functioning.
- The intake of SCFA can prevent loss of muscle strength in older adults.
- FMT could remodel the GD of GM and its metabolites, maintain the integrity of the intestinal barrier, and improve muscle mitochondrial dysfunction.
- The development of Sarc is closely associated with the GD of the GM.
- Postbiotics are referred to as better than probiotics.

Declarations

Conflicts of Interest

The authors declare that do not have affiliation or participation in organizations with financial interests.

Ethical Approval

This report does not contain any study with human or animal subjects carried out by the authors.

Informed Consent

The authors obtained informed written consent from the patients, in order to develop this article.

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