

SARCOPENIA IN EVIDENCE IN PATIENTS WITH COVID-19: A SYSTEMATIC LITERATURE REVIEW

Marina Batista Gondim

Universidade Federal do Cariri, Barbalha-CE
<http://lattes.cnpq.br/9858439304975585>

Hugo Mendes Alencar Furtado

Universidade Federal do Cariri, Barbalha-CE
<http://lattes.cnpq.br/697259943534875527>

Ana Beatriz Vitorino e Silva

Universidade Federal do Cariri, Barbalha-CE
<http://lattes.cnpq.br/7795300796627598>

Matthews Correia do Nascimento

Universidade Federal do Cariri, Barbalha-CE
<http://lattes.cnpq.br/6203259371147419>

Marina Catunda Pinheiro Jucá

Universidade Federal do Cariri- Barbalha, CE

Luíza Alencar Moura

Universidade Federal do Cariri, Barbalha-CE
<http://lattes.cnpq.br/7930110400194252>

Álvaro Maciel Oliveira

Universidade Federal do Cariri, Barbalha-CE
<http://lattes.cnpq.br/3446069065327278>

Lucas Mori de Lima

Universidade Federal do Cariri, Barbalha- CE
<http://lattes.cnpq.br/2365550697282312>

Pedro Henrique Matos Granjeiro Cruz

Universidade Federal do Cariri, Barbalha CE
<http://lattes.cnpq.br/4191974662260296>

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Dara Almeida Maurício de Alencar

Universidade Federal do Cariri, Barbalha-CE
<http://lattes.cnpq.br/8282335046440847>

Brunno Alexander Oliveira

Universidade federal do Ceará, campus Sobral
<http://lattes.cnpq.br/5723350936631861>

Cristovão Jackson Lins da Costa

Universidade Federal do Cariri, Barbalha - CE

Abstract: There has been much debate about the relationship between Covid-19 infection and sarcopenia. This is a systematic literature review where data collection was performed in PubMed (NCBI), Virtual Health Library (BVS) and Google Scholar databases, during the month of October/2021. During the search carried out in the databases, 16 articles were selected that met the eligibility prerequisites, 8 of which had the full text available online and were included in this work. Sarcopenia in the context of Covid-19 is a condition of severe muscle insufficiency in which factors such as inflammation, obesity, vitamin D deficiency, immobilization and nutritional conditions are associated. More research is needed to help characterize this condition and understand its long-term consequences, as well as the development of effective therapies to reduce its morbidity and mortality. Meanwhile, physicians must be aware of this condition in their own practice and seek early involvement of the multidisciplinary team in the support offered to the affected patient.

Keywords: Sarcopenia, Covid-19, pandemic.

INTRODUCTION

The pandemic caused by SARS-CoV-2 of the coronavirus family has persisted in Brazil since March 2020, with the virus originating in China with first report in 2019 (BULUT *et. al.* 2021). Currently, more than 21 million cases of Covid-19 have been confirmed throughout Brazil, leading to around 600,000 deaths by the first week of October 2021 (BRASIL, 2021).

Sarcopenia is a term used to define the loss of muscle mass and strength that plays an important role in the pathogenesis of frailty and functional impairment (MORLEY *et al.* 2001). Screening for sarcopenia, especially in elderly patients, can be done using the SARC-F score, which is highly specific in identifying people with sarcopenia (MORLEY, 2021).

There has been much debate about the relationship between Covid-19 infection and sarcopenia. The present study aims to carry out a systematic review of the literature on the subject.

METHODOLOGY

Data collection was carried out in the PubMed (NCBI), Virtual Health Library (BVS) and Google Scholar databases, during the month of October/2021, through the combination of Boolean descriptors in English, Portuguese and Spanish:

1 “Covid-19” OR “SARS-CoV-2” (Medical Subject Headers - (MeSH)) AND

2 “Sarcopenia” (MeSH) AND

The following were selected: (1) articles that had at least a combination of two of the terms described in the search strategy and (2) articles with the full text available online. Additionally, textbooks, protocols from internationally recognized institutions such as the World Health Organization (W.H.O.) were also consulted.

RESULTS AND DISCUSSION

During the search carried out in the databases, 16 articles that met the eligibility prerequisites were selected, of which 8 of them had the full text available online. Thus, 8 articles were included in this study and fully evaluated. Of the selected articles, 1 was a quantitative article (ANKER *et al.* 2021), 2 were articles with comments (WELCH, *et al.* 2020; CASEY, 2021), 2 articles were qualitative (WANG, 2021; EKIZ *et al.* 2020) and 3 were letters to the editor (LIM, 2021; RIBEIRO, 2021; KUMAR, 2021).

The restrictions implemented due to the Covid-19 pandemic in early 2020 led individuals to adopt a sedentary behavior, characterized by physical inactivity, inadequate eating habits and irregular sleep patterns, which promote the deterioration

of muscle mass and function, loss of bone mineral density and increasing body fat (LIM, 2021; RIBEIRO, 2021).

Sarcopenia is defined as the depletion of skeletal muscle mass and muscle strength (WANG, 2021; WELCH *et al.* 2020) associated with limitations in physical function and quality of life, as well as an increased risk of falls and increased mortality being considered as a precursor of greater vulnerability (WELCH *et al.* 2020).

Acute sarcopenia is characterized by a reduction in muscle mass and strength that occurs within a short period of six months, usually after a stressful event and is commonly associated with hospitalized patients. (WELCH *et al.* 2020) due to an imbalance in muscle homeostasis with increased degradation and reduced synthesis.

Recent studies show that the low amount of muscle has been associated with an increased risk of postoperative infections, higher mortality (WELCH *et al.* 2020) and a higher relative risk of fracture among individuals with sarcopenia (LIM, 2021).

Weight loss in Covid-19 patients is well documented and is caused by many different factors. (ANKER *et al.* 2021). Virus entry into the cell occurs through the angiotensin 2 converting enzyme receptor (CASEY, 2021) present in muscle tissue (CASEY, 2021; KUMAR, 2021) causing a direct impact on it. (CASEY, 2021).

The renin-angiotensin system (RAS) correlates not only with blood pressure, but also with muscle blood flow and skeletal muscle metabolism. The increased activity of this system is associated with muscle atrophy, decline in strength and endurance/ muscle performance, due to increased protein degradation, decreased muscle regeneration and increased apoptosis in muscle tissue (EKIZ *et al.* 2020; KUMAR, 2021).

Thus, it was initially proposed that hypertensive patients using medications that act on the RAS, such as angiotensin-converting enzyme inhibitors (ACEI) or angiotensin receptor blockers (ARB) could have an increased risk of mortality from Covid-19, however studies and discussions on the subject are still inconclusive (EKIZ *et al.* 2020). On the other hand, data show that patients using ACE inhibitors/ARB affected by SARS-CoV-2 infection had a lower risk of mortality when compared to non-users of these medications (EKIZ *et al.* 2020).

Sarcopenia is associated with a reduction in the thickness of the diaphragm muscle, which can lead to respiratory failure and the need for prolonged mechanical ventilation in critically ill patients (WELCH *et al.* 2020), factors that were evidenced during the Covid-19 pandemic.

Skeletal muscle mass loss influences both motor activity, respiratory function and the swallowing profile, as well as the immune response and metabolic stress against acute infections. Therefore, sarcopenic patients present multisystemic impairment and the main mechanism involved in immunity is the abnormal myokines, such as interleukin IL-15, IL-17 and IL-6, which modulate the proliferation and function of innate and adaptive immune cells (WANG, 2021; CASEY, 2021).

In the studies of Wierdsma *et al.* (2021), it was showed that although most of the patients analyzed were overweight or obese, more than a third of them had suffered substantial weight loss before hospital admission, indicating a profound negative impact on the nutritional status caused by the virus even before admission.

The acute inflammatory process triggered by Covid-19 infection results in a storm of cytokines, among them is the tumor necrosis factor alpha (TNF- α) which promotes a state of

anabolic resistance (WELCH *et al.* 2020) and high metabolic stress and muscle catabolism (WANG, 2021; ANKER, *et al.* 2021) through the increase in protein degradation together with depression of protein synthesis (KUMAR, 2021). Furthermore, the release of pro-inflammatory cytokines is associated with the induction of leptin and anorexia (WELCH *et al.* 2020).

Kumar (2021) states that a recent report of results from a preclinical study showed that suppression of the host's inflammatory response in early stages of the disease can reverse cachexia and increase survival.

In addition to systemic inflammation, vitamin D deficiency has been implicated in sarcopenia, as it promotes type II muscle fiber atrophy and affects the immune response to respiratory infections (WELCH *et al.* 2020). Another factor that can influence the cause of sarcopenia is obesity. Obesity itself is associated with increased systemic inflammation exacerbating the acute effects of the disease on muscle metabolism (WELCH *et al.* 2020).

The increase in nutritional demand is on the rise in these patients, on the other hand, loss of taste and/or smell are symptoms recognized and associated with Covid-19 and directly impact the nutrition of these patients (ANKER, *et al.* 2021; CASEY, 2021; WIERDSMA *et al.* 2021; WELCH *et al.* 2020).

In critically ill patients, confined to bed, there is a reduction in muscle protein synthesis through the altered expression of *ubiquitin ligase* (WELCH *et al.* 2020) what contributes to muscle wasting and sarcopenia (ANKER, *et al.* 2021).

There is still no specific consensus definition for patients with Covid-19, however cachexia in these patients can be diagnosed when there is weight loss greater than or equal to 5%, the functional status is impaired and the metabolic disorder can be documented (ANKER, *et al.*

2021). The use of the SARC-F questionnaire can be useful to detect sarcopenia and allow dynamic surveillance (WANG, 2021).

The multiprofessional follow-up of this patient can help to avoid lasting morbidity, as well as the promotion of protein intake accompanied by physical exercise as a benefit to the treatment of both sarcopenia and Covid-19 (WANG, 2021). For patients with sarcopenia and Covid-19 infection, nutritional support must adjust to increased inflammatory reaction and metabolic stress.

FINAL CONSIDERATIONS

Sarcopenia combined with the context of Covid-19 is a condition of severe muscle insufficiency in which factors such as inflammation, obesity, vitamin D deficiency, immobilization and nutritional conditions are associated. More research is needed to help characterize this condition and understand its long-term consequences, as well as the development of effective therapies to reduce its morbidity and mortality. Meanwhile, physicians must be aware of this condition in their own practice and seek early involvement of the multidisciplinary team in the support offered to the affected patient.

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