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Review Article

Persistent musculoskeletal symptoms in Acute Post-COVID-19 Syndrome: an integrative review

Sintomas musculoesqueléticos persistentes na Síndrome Pós-COVID-19 Aguda: uma revisão integrativa

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Abstract

Introduction: Studies have demonstrated the progressive involvement of musculoskeletal symptoms in post-COVID-19 sequelae, especially with regard to fatigue and muscle weakness. **Objective:** To identify musculoskeletal symptoms in the literature as sequelae after SARS-Cov-2 infection, as well as to investigate the relationship between these variables. **Methodology:** This is an integrative review of the literature produced in the last four years, indexed in the PubMed, Web of Science, ScienceDirect and Scielo databases. The review was based on PRISMA guidelines. **Results:** Of the 528 records found, 11 were included. The articles concluded that COVID-19 survivors may experience musculoskeletal symptoms after recovery, causing losses over time. The most frequently cited symptoms were: fatigue, myalgia, muscle weakness, frailty, general musculoskeletal pain, low back pain, arthralgia, muscle loss and decreased strength. The persistence of symptoms after infection with the severe acute respiratory syndrome virus – coronavirus 2 (SARS-CoV-2) may be related to a dysregulated immune response, resulting in the excessive production of pro-inflammatory cytokines. **Conclusion:** Publications are still incipient, especially in the Brazilian context, requiring more studies to relate and explain why SARS-CoV-2 leaves long-term consequences on the musculoskeletal system. A holistic view from the multidisciplinary team is necessary when caring for patients with long COVID.

Keywords: Musculoskeletal System, Coronavirus, SARS-CoV, Review.

Resumo

Introdução: Estudos têm demonstrado o envolvimento progressivo de sintomas musculoesquelético nas sequelas pós-COVID-19, principalmente no que se refere

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à fadiga e à fraqueza muscular. **Objetivo:** identificar na literatura os sintomas musculoesqueléticos como sequelas pós-infecção por SARS-Cov-2, bem como investigar a relação dessas variáveis. **Metodologia:** Trata-se de uma revisão integrativa da literatura produzida nos últimos quatro anos, indexadas nas bases de dados PubMed, Web of Science, ScienceDirect e Scielo. A revisão foi baseada nas diretrizes do PRISMA. **Resultados:** Dos 528 registros encontrados, 11 foram incluídos. Os artigos concluíram que os sobreviventes da COVID-19 podem apresentar sintomas musculoesqueléticos após a recuperação, acarretando prejuízos ao longo do tempo. Os sintomas mais citados foram: fadiga, mialgia, fraqueza muscular, fragilidade, dor musculoesquelética geral, lombalgia, artralgia, perda muscular e diminuição da força. A persistência dos sintomas após a infecção pelo vírus da síndrome respiratória aguda grave – coronavírus 2 (SARS-CoV-2) pode estar relacionada a uma resposta imunológica desregulada, resultando na produção excessiva de citocinas pró-inflamatórias. **Conclusão:** As publicações ainda são incipientes, principalmente no contexto brasileiro, necessitando de mais estudos para relacionar e explicar o motivo do SARS-CoV-2 deixar sequelas a longo prazo no sistema musculoesquelético. É necessário um olhar holístico da equipe multiprofissional ao atender pacientes com COVID longa.

Palavras-chave: Sistema Musculoesquelético, Coronavirus, SARS-CoV, Revisão.

Introduction

In recent years, COVID-19 has represented a significant global threat, receiving important attention from public health researchers worldwide. This is critical as the pandemic involved a new pathogen (SARS-CoV-2), about which there is limited knowledge regarding long-term outcomes (Park et al., 2020).

Four years after the first case of COVID-19 in Brazil, its repercussions are still present. From the first symptoms to the most serious phase of the infection, musculoskeletal complaints have been reported, such as myalgia, arthralgia, low back pain and fatigue, almost always frequently (Cipollaro et al., 2020). It is still uncertain how COVID-19 sequences are mediated in the musculoskeletal system.

It is known that, in some individuals, the symptoms of COVID-19 persist for a long period after the acute phase of the disease, leading to the creation of the term “long COVID”, which encompasses a variety of symptoms, whether new, recurrent or persistent (Maccarone et al., 2024). Long COVID impacts an individual's neurological, cardiovascular, pulmonary, musculoskeletal and psychological health, affecting the ability to work and perform daily activities (Spatz et al., 2023).

Studies have demonstrated the progressive involvement of musculoskeletal symptoms in post-COVID-19 sequelae (Aschman et al., 2023; Azadvari et al., 2022), especially with regard to fatigue and muscle weakness (Maccarone et al., 2024). Long COVID can be confused with other pathologies, such as chronic fatigue or fibromyalgia. Therefore, investigations are necessary, including for the creation of diagnostic criteria and treatment protocols (Maccarone et al., 2024).

Few national and international studies have investigated muscle and bone symptoms in post-COVID-19 sequelae, even fewer with follow-up of survivors and the cause-and-

effect relationship. Investigating these symptoms is crucial for better early treatment management, given the need for rehabilitation of patients with long COVID. Therefore, the objective of this review is to identify musculoskeletal symptoms in the literature as sequelae after SARS-Cov-2 infection, as well as to investigate the relationship between these variables.

Methodology

This is an integrative literature review, a method that synthesizes data and analyzes information from studies published on a specific topic, enabling a broad and comprehensive knowledge of the subject. This type of study is widely used in the health sector, as it supports practical actions in everyday clinical practice, reiterating evidence-based medicine (Souza et al., 2010).

This review followed the six phases proposed by Souza et al. (2010), which are as follows: 1st Phase: elaboration of the guiding question; 2nd Phase: search or sampling in the literature; 3rd Phase: data collection; 4th Phase: critical analysis of included studies; 5th Phase: discussion of results; 6th Phase: presentation of the integrative review.

Furthermore, the level of evidence of the studies selected for the final review was verified, according to the evidence classification systems, as characterized in an orderly manner by Fineout-Overholt & Stillwell (2011). These levels of evidence correspond to: Level 1: evidence based on meta-analysis results of randomized clinical studies; Level 2: studies with an experimental design (randomized clinical trial); Level 3: quasi-experimental studies (non-randomized clinical trial); Level 4: evidence from descriptive, cross-sectional or qualitative studies; Level 5: case study or experience report; Level 6: evidence resulting from expert opinions (Fineout-Overholt & Stillwell, 2011).

Aiming to guide the study, the following research question was formulated: "What are the scientific contributions on the relationship between SARS-CoV-2 and musculoskeletal symptoms in adults and elderly people who survived COVID-19?". To answer the research question, searches were conducted in the Web of Science, ScienceDirect and PubMed databases, as well as in the Scientific Electronic Library Online (SciELO). The terms from DeCS (Health Sciences Descriptors) and MesH (Medical Subject Headings) were used to assist in the search. The sets of descriptors, as well as the Boolean operators, are described in Table 1.

Table 1. Data on the strategies used in searches

Database / Electronic library	Strategies used	Number of articles found
Web of science	Musculoskeletal System AND Post-Acute COVID-19 Syndrome	79
	Musculoskeletal System AND Post-Acute COVID-19 Syndrome AND Survivors	10
Pubmed	Musculoskeletal System AND Post-Acute COVID-19 Syndrome	63
	Musculoskeletal System AND Post-Acute COVID-19 Syndrome AND Survivors	0
ScienceDirect	Musculoskeletal System AND Post-Acute COVID-19 Syndrome	294
	Musculoskeletal System AND Post-Acute COVID-19 Syndrome AND Survivors	73
Scielo	Musculoskeletal System AND Post-Acute COVID-19 Syndrome	0
	Musculoskeletal System AND COVID-19	9
	Musculoskeletal System AND Post-Acute COVID-19 Syndrome AND Survivors	0
	Dor Musculoesquelética AND Síndrome Pós-COVID-19 Aguda	0

The inclusion criteria during the searches were the following: original research articles, carried out from 2020 until February 10, 2024, with the participation of human beings, adults and elderly people, whose main objective was to verify the relationship between COVID-19 and the muscular and/or skeletal system. After that, the following types were excluded: reviews, expert comments, books, editorials and articles that included somatic/mental symptoms, reactions to medications and/or vaccines, studies carried out with athletes, and mandibular bone problems related to intubation.

The searches were conducted on February 10, 2024 by a trained researcher, who adopted more than one search strategy in the different databases, with the aim of covering the largest possible collection on the topic in question. After the searches, article screening was conducted using the Rayyan web application. This application organizes the findings within the platform, streamlining the process of preliminary screening of titles and abstracts, using a semi-automatic method, while maintaining a high standard of usability (Ouzzani et al., 2016).

All stages of screening, selection and inclusion in the study went through different phases: inclusion of findings in Rayyan (n=528); duplicate detection (n=127); resolution and exclusion of duplicates (n=73); title and abstract reading (n=455); inclusion of articles for full analysis (n=14); exclusion after analysis of the full text (n=3); records included in the qualitative analysis (n=11) (Figure 1).

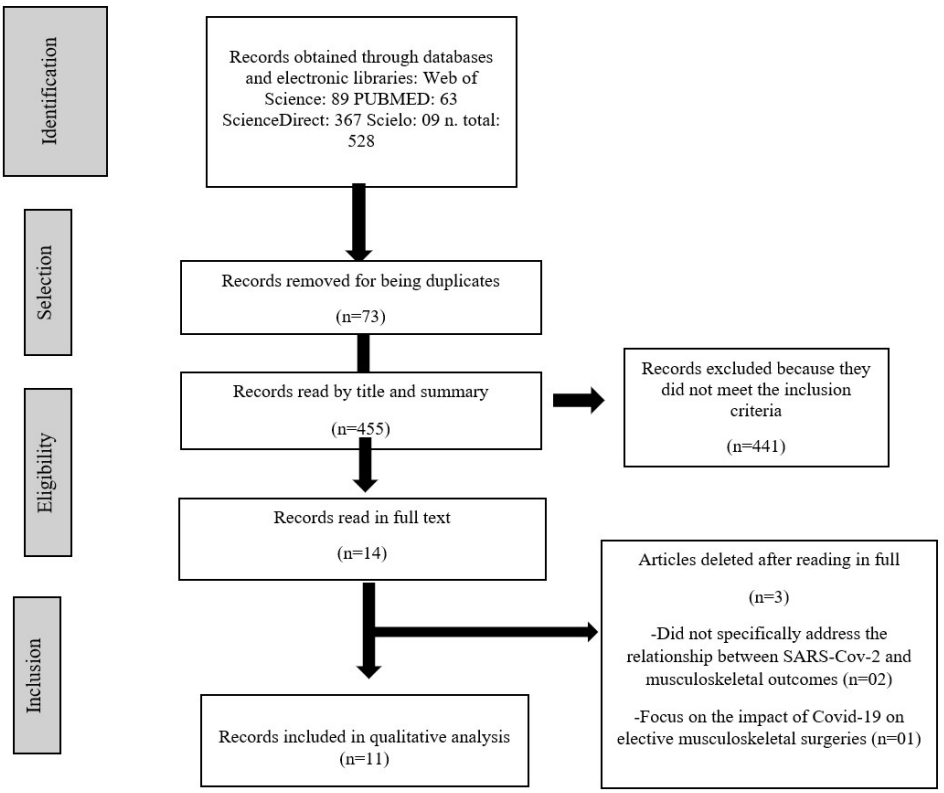

Figure 1. Flowchart of the selection of studies based on the PRISMA guidelines (Galvão et al., 2015).

The critical analysis of the remaining 11 articles was conducted by two specialists in diseases of the musculoskeletal system, with the aim of improving the analysis and discussion of the findings. All steps were iteratively handled to ensure a robust analysis. After all the selection, data from the articles included for analysis were synthesized following a standard format: title, methodology, country in which the research was carried out, year of publication of the article, objective, main results and conclusions.

Results

Of the 528 articles found, 11 were included for complete reading and data analysis and discussion. Of these, only two are national (Azevedo Vieira et al., 2023; Gil et al., 2023), the others encompass Iran (Azadvari et al., 2022), the Netherlands (Stoffels et al., 2022), Turkey (Erden et al., 2023; Pasin et al., 2023), India (Jeyaraman et al., 2022), Italy (Greco et al., 2021), and Germany (Aschman et al., 2023). Furthermore, two studies were multicenter; one tracked the Nordic countries (Iceland, Sweden, Denmark, and Norway) (Shen et al., 2023), and another encompassed the United Kingdom countries (England, Scotland, Wales, and Northern Ireland) (McAuley et al., 2023). All articles were available in English only.

The majority of studies were published in 2023 (63.6%), followed by 2022 (27.2%), and only one in 2021. Regarding the type of study, it was observed that all were quantitative in nature, with approaches cross-sectional, observational, prospective, descriptive, longitudinal and case control. The level of evidence of all articles was classified as IV.

The objectives ranged from: evaluating the prevalence of musculoskeletal physical symptoms, weakness, pain, loss of skeletal muscle mass, muscle function, general fatigue and post-exertional malaise in COVID-19 survivors, post-infection. It is interesting to note that the number of participants varied considerably, from 11 individuals to 64,880. This variation was due to several factors, such as the population of interest, the availability of resources and the ability to recruit participants.

All 11 articles concluded that COVID-19 survivors may experience musculoskeletal symptoms after recovery, causing harm over time. The most cited symptom was fatigue (Aschman et al., 2023; Azadvari et al., 2022; Azevedo Vieira et al., 2023; Gil et al., 2023; Shen et al., 2023; Stoffels et al., 2022), followed by myalgia (Azadvari et al., 2022; Stoffels et al., 2022; Gil et al., 2023; Aschman et al., 2023), muscle weakness and frailty (Stoffels et al., 2022; McAuley et al., 2023; Greco et al., 2021), general musculoskeletal pain (Jeyaraman et al., 2022; Pasin et al., 2023), and/or low back pain (Azadvari et al., 2022; Shen et al., 2023), arthralgia (Erden et al., 2023), muscle loss (Gil et al., 2023), decreased strength (Greco et al., 2021) and gait speed (Greco et al., 2021) (Table 2) .

Table 2. Information about the articles analyzed (n=11).

Title	Type of study/	Country	Year of publication	Main objective	N. participants	Main results	Conclusion	Level of evidence
Musculoskeletal symptoms in patients with long COVID: A cross-sectional study on Iranian patients	Cross-sectional study	Iran	2022	To evaluate the prevalence of musculoskeletal symptoms after the acute phase of COVID-19 and its associated factors.	239	98.74% of patients presented at least one musculoskeletal symptom after recovering from COVID-19, and the most common symptom was fatigue, as 91.2% of participants presented this symptom, followed by myalgia, headache and low back pain.	This study indicated a high prevalence of persistent musculoskeletal symptoms among patients who recovered from COVID-19	IV
Longitudinal Analysis of Quadriceps Muscle Strength in Patients with Previous COVID-19 Hospitalization and in Patients with Post-Acute Sequelae following Mild COVID-19	Observational study	Netherlands	2022	To explore the prevalence, determinants, and 1.5-year change of objectively assessed quadriceps muscle weakness in two post-COVID-19 cohorts: (1) patients after discharge from COVID-19 hospitalization and (2) patients with post-COVID-19 sequelae. - acute cases of COVID-19 (PASC) after mild pathology without hospitalization.	148	Muscle weakness was found in 59% of post-hospitalized patients and in 65% of those with PASC after mild COVID-19, approximately 14 weeks after acute COVID-19. While during approximately 1.5 years of follow-up MVC improved modestly, the prevalence of muscle weakness remained unchanged.	Clinically relevant muscle weakness is common after COVID-19 and its long-term improvement is poor.	IV
Musculoskeletal system symptoms in patients with COVID-19 and the impact of these symptoms on quality of life	Prospective and descriptive study	Turkey	2023	To investigate musculoskeletal symptoms, type of pain and effect on quality of life in patients presenting with pain after COVID-19.	97	Myalgia started after COVID-19 infection in 47 of the 96 patients who presented with this complaint, while arthralgia started after COVID-19 infection in 37 of the 77 patients who reported it among those who registered at the post-COVID-19 clinic. 19 due to musculoskeletal pain following COVID-19 infection. Pain intensity increased after infection in 49 patients who already had myalgia and/or arthralgia before COVID-19 infection.	Arthralgia, myalgia and neuropathic pain, which negatively affect quality of life, are frequently observed in patients infected with COVID-19.	IV
Acute Muscle Mass Loss Predicts Long-Term Fatigue, Myalgia, and Health Care Costs in COVID-19 Survivors	Prospective and observational study	Brazil	2023	To examine the impact of skeletal muscle mass loss on post-acute sequelae of SARS-CoV-2 infection.	80	The group with high muscle loss had a higher prevalence of fatigue (76% vs 46%, P = 0.0337) and myalgia (66% vs 36%, P = 0.0388) and lower muscle mass (-8% vs 3%, P < 0.0001) than the group with low muscle loss at 6 months after discharge.	COVID-19 survivors who experience a high loss of muscle mass during hospital stay are unable to fully recover muscle health.	IV

Table 2. Continued…

Title	Type of study/	Country	Year of publication	Main objective	N. participants	Main results	Conclusion	Level of evidence
Assessment of short- and long-term functionality and quality of life in patients with post-acute COVID-19 syndrome	Observational and longitudinal study	Brazil	2023	To evaluate muscle function and quality of life at 3, 6, 9 and 12 months in patients with post-acute COVID-19 syndrome and evaluate their associations with general fatigue and lung function.	350	In the sixth month after COVID-19, 111 participants returned due to persistent symptoms, 29 (26.1%) with general tiredness, 26 (23.4%) with dyspnea. In the ninth month, 46 participants returned due to continued symptoms, with 9 (19.6%) experiencing general fatigue. On the 12th, 32 participants returned due to continued symptoms, 6 (18.8%) with general fatigue.	In patients with post-acute COVID-19 syndrome, there was a progressive improvement in quality of life, general fatigue and lung function during the 12 months of follow-up, with this improvement being more pronounced in the first 6 months. There was a relationship between functionality and quality of life in these patients.	IV
COVID-19 illness severity and 2-year prevalence of physical symptoms: an observational study in Iceland, Sweden, Norway and Denmark	Observational study	Iceland, Sweden, Denmark and Norway	2023	Assess the prevalence of physical symptoms in relation to the severity of the acute illness up to more than 2 years after the diagnosis of COVID-19.	64.880	Individuals who were diagnosed with COVID-19, compared to those undiagnosed, had a 37% higher overall prevalence of severe physical symptom burden. Prevalence was statistically significantly elevated among individuals diagnosed with COVID-19 for eight of the fifteen symptoms measured: shortness of breath, chest pain, dizziness, fast heartbeat, headaches, low energy/fatigue, difficulty sleeping, and back pain.	These data suggest an elevated prevalence of some, but not all, physical symptoms for more than 2 years after COVID-19 diagnosis, particularly among individuals suffering from a severe acute illness, highlighting the importance of continued monitoring and alleviation of these symptoms.	IV
Pain, Anxiety, and Quality of Life of COVID-19 Survivors with Myofascial Pain Syndrome: A cross sectional study	Cross-sectional observational study	Turkey	2023	To investigate the difference in the level of pain, anxiety, functional status and quality of life in COVID-19 survivors with Myofascial Pain Syndrome (MPS) in the trapezius muscle compared to MPS patients without COVID-19.	80	A significant difference was observed between the groups in terms of pain, anxiety and disability ($p < 0.001$). The MPS + COVID-19 group had significantly higher pain intensity.	After recovering from COVID-19, patients with MPS experienced increased pain, anxiety, disability, and decreased quality of life.	IV
Post-COVID exercise intolerance is associated with capillary alterations and immune dysregulations in skeletal muscles	Case-control study	Germany	2023	To analyze, in depth, skeletal muscle biopsies obtained from patients suffering from long-lasting fatigue and post-exertional malaise following a SARS-CoV-2 infection.	11	Seven patients (78%; n = 7/9) presented abnormal values of maximum and average strength, fatigue index and recovery rate in the handgrip strength test. Seven patients (70%; n =7/10) walked a shorter distance in six minutes than expected for their age and sex. Most patients reported post-exertional malaise lasting at least 14 hours. Routine histopathological examination revealed selective atrophy of type 2b muscle fibers of different extents in 72% (n = 8/11). The ratio of capillaries per fiber was significantly lower in the group with Post-COVID-19 Syndrome.	The initial viral infection may have caused immune-mediated structural changes of the microvasculature, potentially explaining the exercise-dependent fatigue and muscle pain.	IV

Table 2. Continued…

Title	Type of study/	Country	Year of publication	Main objective	N. participants	Main results	Conclusion	Level of evidence
Prevalence of physical frailty, including risk factors, up to 1 year after hospitalisation for COVID-19 in the UK: a multicentre, longitudinal cohort study	Prospective cohort study	England, Scotland, Wales and Northern Ireland	2023	Describe the Prevalence of physical frailty, including risk factors, up to 1 year after hospitalization for COVID-19.	1.785	240 (13.4%), 1,138 (63.8%), and 407 (22.8%) were frail, pre-frail, and robust, respectively, at 5 months, compared with 123 (6.9%), 1,046 (58.6%) and 616 (34.5%) in 1 year. Factors associated with pre-frailty or frailty were invasive mechanical ventilation, advanced age, female sex and greater social deprivation. Frail participants had a greater reduction in quality of life compared to pre-COVID-19, and were less likely to describe themselves as recovered.	Physical frailty and pre-frailty are common after hospitalization with COVID-19. Improvement in frailty was observed between 5 and 12 months, although two-thirds of the population remained pre-frail or frail.	IV
Assessment of risk factors in post- COVID-19 patients and its associated musculoskeletal manifestations: A cross-sectional study in India	Retrospective multicenter cross-sectional study	Índia	2022	Analyze the musculoskeletal manifestations of COVID-19 infection and the factors that determine its severity.	2.334	Musculoskeletal manifestations (MSK) were significantly higher among unvaccinated individuals. The total mean MSK scores calculated were about 15.94 ± 54.86. MSK scores were significantly higher among men, those with no education, those with comorbidities, and unvaccinated individuals.	Factors such as male gender, non-vaccination and associated comorbidities increased the risk of developing severe manifestations of MSK after COVID-19 infection and require monitoring.	IV
Increase in Frailty in Nursing Home Survivors of Coronavirus Disease 2019: Comparison With Noninfected Residents	Nested case-control study	Italy	2021	We investigated the impact of COVID-19 on the level of frailty, physical and cognitive performance in nursing home residents.	152	Between pre- and post-COVID-19 assessments, we found a 19% greater deterioration in handgrip, a 22% greater decrease in walking speed, and a 21% greater increase in frailty scores in COVID-19 survivors relative to those who did not have the disease.	COVID-19 can accelerate the aging process of institutionalized elderly people in terms of physical performance and frailty by around 20%.	IV

Discussion

Based on the results of this review, it is observed that the effects of COVID-19 can persist for weeks to months after infection, with musculoskeletal symptoms standing out. Although few studies have focused specifically on muscle and bone symptoms, there is a predominance of specific symptoms, such as fatigue, muscle weakness, frailty, low back pain, arthralgia, loss of muscle mass and decreased strength.

Among the two studies carried out in Brazil, the first was conducted between March 2020 and August 2021, in São Paulo. The researchers assessed handgrip strength and muscle cross-sectional area at three different times: two days after hospitalization for severe to moderate COVID-19, at discharge and six months after discharge. Persistent symptoms, including frequency of fatigue and myalgia, were assessed six months after discharge. The cross-sectional area of the vastus lateralis muscle and handgrip strength were checked to assess muscle mass loss, dividing participants into two groups: low muscle loss group and high muscle loss group. Those who experienced greater loss of muscle mass during hospitalization did not fully recover after six months and showed decreased strength. The group with high muscle loss had a higher prevalence of fatigue and myalgia. Fifteen percent of patients in the high muscle loss group were readmitted to the hospital within two months of discharge, which is also the group that had the highest health care expenditure (Gil et al., 2023).

The second Brazilian study was carried out between October 2020 and July 2022, in Rio de Janeiro. Participants were followed for 12 weeks after hospital discharge for COVID-19 to check for persistent symptoms. Those who remained symptomatic were evaluated for an additional 9 months. Six months after hospital discharge, 111 participants still had symptoms, with 26.1% of them reporting general tiredness. In the ninth and tenth months, the complaint of general fatigue persisted. It was also observed that muscle recovery in COVID-19 survivors is slow over time, which directly affects the quality of life of these individuals (Azevedo Vieira et al., 2023).

It is noted that fatigue was mentioned in several studies that evaluated the post-infection sequelae of Acute SARS-CoV-2 (Aschman et al., 2023; Azadvari et al., 2022; Azevedo Vieira et al., 2023; Gil et al., 2023; Shen et al., 2023; Stoffels et al., 2022). Fatigue is defined as physical and/or mental exhaustion that can range from mild to severe and impair routine activities (Mota et al., 2005). Physical fatigue is a common symptom of COVID-19, but it's unclear why it persists for months after recovery. It is considered that this may be due to dysregulation in the autonomic nervous, immune and metabolic systems post-infection, manifesting mainly after exercise (Castro et al., 2021).

In parallel to this, it is worth highlighting that one of the drug classes used in the treatment of acute COVID-19 are corticosteroids. Abrupt discontinuation of corticosteroid therapy may predispose to adrenal insufficiency, which has fatigue and myalgia as one of its symptoms (Alves et al., 2008). That said, more investigations are needed into the relationship between corticosteroids and persistent post-COVID-19 symptoms.

An important point to highlight is that most of the studies found in this review, as well as other findings, revealed that women are the most affected by fatigue and other musculoskeletal symptoms in long COVID. A possible explanation is hormonal factors and the greater production of interleukin-6 (IL-6) in women. It is known that increased

IL-6 worsens the prognosis of COVID-19. This suggests a persistent dysregulation in the immune system, predominantly in women affected by post-COVID-19 syndrome. A study showed that the majority of COVID-19 survivors had elevated levels of the pro-inflammatory cytokine IL-6 at least 3 months after infection, being more significant in women (69% vs. 39% in men; P = 0 .05) (Ganesh et al., 2022).

On the other hand, the study by Jeyaraman et al. (2022) revealed that male sex is one of the risk factors for the development of severe musculoskeletal manifestations after COVID-19 infection. Another survey demonstrated that women have lower rates of COVID-19 infection, and a lower likelihood of hospitalization compared to men. The study suggests that estrogen is a protective factor in COVID-19 infections, due to its contribution to the recruitment of the body's defense cells (Raza et al., 2021). In this sense, it seems plausible to say that this protective factor is only valid during acute infection. In general, the evidence on the factors involved in the difference by sex in persistent complaints of musculoskeletal symptoms requires further study.

The present review also highlighted that myalgia was one of the main complaints post-COVID-19. It is still unclear why the virus continues to affect the musculoskeletal system, mainly causing myalgia. Understanding the pathophysiology behind Post-COVID-19 Syndrome is still developing. Some theories suggest that the persistence of symptoms after infection with the severe acute respiratory syndrome virus – coronavirus 2 (SARS-CoV-2) may be related to a dysregulated immune response, resulting in the excessive production of pro-inflammatory cytokines. This can trigger a chronic state of low-grade inflammation, which can make it difficult to completely eliminate the virus or its molecular components. This hypothesis has been discussed and explored in the scientific literature as a possible explanation for Post-COVID-19 Syndrome (Buonsenso et al., 2022).

Based on these findings, it is believed that there may be a genetic basis for the fact that some individuals have lower immunological resistance to the elimination of the coronavirus (Buonsenso et al., 2022). The innate hyper-inflammatory reaction of cytokine dysregulation syndrome in coronavirus infection is an important finding that explains adverse outcomes (Ganesh et al., 2022). It is known that SARS-CoV-2 exploits ACE2 (Angiotensin-converting enzyme 2) to enter the host cell, which acts as a receptor for the SARS-CoV-2 Spike protein (Hoffmann et al., 2020). It is unclear whether the virus infects skeletal muscle cells by binding to ACE2. It is hypothesized that a large load of pro-inflammatory cytokines in serum may trigger skeletal muscle damage (Mao et al., 2020; Muus et al., 2021).

Another challenge posed by the virus concerns frailty, especially in the elderly. This issue was highlighted in the case-control study carried out by Greco et al. (2021). In the study, the authors used a validated scale to assess frailty, which included factors such as fatigue, resistance, mobility, nutritional status, incontinence, among others. To evaluate physical performance, handgrip strength and traditional walking tests were conducted. A 21% increase in frailty scores was observed among elderly people who contracted COVID-19, in addition to a reduction in handgrip strength and walking speed (Greco et al., 2021).

COVID-19 can have a significant impact on worsening frailty and physical condition among survivors. However, it is still unclear to what extent the elderly, who are already more susceptible to frailty, may suffer musculoskeletal damage caused by SARS-Cov-2. This is due to the fact that other factors, such as the pandemic situation, the interruption

of leisure programs and social isolation, may be associated with the fragility of these elderly people (Greco et al., 2021).

The results of this review also highlight the significant prevalence of muscle weakness among COVID-19 survivors. One possible explanation is the increase in pro-inflammatory cytokines associated with COVID-19, particularly high levels of IL-6, which may favor muscle atrophy, resulting in muscle weakening (Moresi et al., 2019). Furthermore, an increase in creatine kinase is a strong indicator of skeletal muscle damage in patients with COVID-19 (Silverthorn, 2017).

Therefore, it is important to carry out routine tests to measure the levels of this enzyme in the body, in addition to other complementary tests. Severe respiratory complications, length of stay, among other factors, are also related to muscle weakness (Paliwal et al., 2020). Multidisciplinary care and monitoring are necessary to establish relationships and long-term effects, as well as to promote the best care, based on scientific evidence.

In line with the findings already mentioned, musculoskeletal pain is one of the main symptoms observed. Evidence indicates that this pain is common in patients with Post-Infection Sequelae from SARS-CoV-2, with studies reporting a variable prevalence of 0.3% to 65.2% (Khoja et al., 2022). It is pain arising from musculoskeletal structures, such as bones, muscles, joints and tendons. The concept of musculoskeletal pain is presented in the current International Code of Diseases (ICD-11), classifying it as primary and secondary. Primary chronic musculoskeletal pain is an isolated condition, unrelated to a specific pathology. Secondary disease is caused by an underlying disease, inflammation, changes in structure or trauma to the central nervous system (Perrot et al., 2019).

One of the challenges related to pain is the increase in the use of anti-inflammatory medications, especially in the elderly. These medications, when used indiscriminately, can cause negative effects and degeneration in the renal system, as well as changes in the gastrointestinal system. This occurs because anti-inflammatory drugs inhibit the production of prostaglandins, which are important for renal perfusion (Lucas et al., 2018). Therefore, caution should be exercised in chronic use, and medical professionals should always evaluate the specific risk-benefit for each patient (Lucas et al., 2018). Furthermore, individuals with musculoskeletal complaints in long COVID are more likely to receive high doses of corticosteroids and immunosuppressants (Molto et al., 2022). The latter, if used for long periods and at a high dose, presents a risk of reducing bone density (Bressan et al., 2010).

The evidence from this review contributes to healthcare professionals being able to identify the symptoms and mechanisms underlying musculoskeletal pain in long COVID, essentially to find possible biomarkers targeting specific occupational therapeutic interventions (Khoja et al., 2022).

The limitations of this study include the low production of original research on persistent musculoskeletal symptoms post-COVID-19, especially in the national context. Furthermore, the scientific evidence found was only level IV (observational and cross-sectional studies). It was also found that there were only formulations of hypotheses in an attempt to explain the underlying mechanisms and reasons for these persistent symptoms. This is mainly because it is a relatively new pathology, a variation of the coronavirus family.

Based on the data presented, the importance of long-term monitoring of COVID-19 survivors is highlighted to better understand the potential of the virus to continue affecting the musculoskeletal system. This is mainly due to the impact on the population's quality

of life, costs for the health sectors and the increase in occupational evasion. Continued monitoring will allow us not only to better understand the long-term effects of COVID-19, but also to develop more effective intervention and treatment strategies for affected patients. Furthermore, implementing multidisciplinary rehabilitation and support programs can be critical in helping survivors regain functionality and improve their quality of life after COVID-19 infection.

Conclusion

The results of this review indicate that COVID-19 survivors may experience musculoskeletal symptoms after recovery, causing losses over time. The most frequently cited symptoms were fatigue, myalgia, muscle weakness, general musculoskeletal pain, frailty, muscle loss, low back pain and decreased strength.

Publications are still incipient, especially in the Brazilian context, requiring more studies to relate and explain why SARS-CoV-2 leaves long-term consequences on the musculoskeletal system. A holistic view from the multidisciplinary team is necessary when caring for patients with long COVID.

Finally, it is worth highlighting that new studies consider monitoring COVID-19 survivors, focusing on the musculoskeletal system, as well as investigating alternatives for the non-pharmacological treatment of these symptoms.

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