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MUSCULOSKELETAL PATHOLOGIES IN PATIENTS WITH COVID-19, ITS INFLUENCE ON OSTEOARTHRITIS: THE ROLE OF VITAMIN D AND HYPOCALCAEMIA

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Abstract

The COVID-19 pandemic of the Severe Acute Respiratory Syndrome Coronavirus-2 has brought healthcare to the forefront, making prevention and treatment strategies a global priority. The relationship between COVID-19 infection and factors such as Vitamin D and calcium levels—particularly in patients with osteoarthritis—remains a topic of active investigation. While coronavirus infections are primarily known for respiratory symptoms, skeletal complications and risks have also been reported.

Although much attention has focused on the respiratory effects of COVID-19, its impact on the musculoskeletal system has also been significant. Patients with COVID-19 have reported a range of musculoskeletal symptoms, which can be both direct (resulting from viral infection) and indirect (related to prolonged inactivity, immune responses, or treatment protocols). Among these, osteoarthritis and conditions related to calcium and vitamin D deficiency have garnered attention in the literature. Epidemiological data from the SARS pandemic also reported myalgias, muscle weakness, osteoporosis, and osteonecrosis as common complications in patients with moderate to severe disease.

We reviewed the literature on investigations of musculoskeletal diseases in COVID-19 patients, as well as the role of vitamin D and calcium. The keywords were used to search for data in international databases. A total of 69 relevant sources were selected. Although long-term follow-up studies have not yet been completed, early research has suggested that certain COVID-19 patients experience significant musculoskeletal impairment. The objective of this article is to summarize known musculoskeletal pathologies in patients with SARS or COVID-19 and to combine this with computational modeling and biochemical signaling studies to predict musculoskeletal cellular targets and long-term consequences of the SARS-CoV-2 infection.

Keywords: *COVID-19, osteoarthritis, vitamin D, calcium*

Introduction

SARS (Severe Acute Respiratory Syndrome) is a type of acute respiratory syndrome. The pandemic of the Coronavirus-2 (SARS CoV- 2) has moved healthcare front and center, making preventive and treatment methods a top global concern. The morbidity and mortality associated with Coronavirus

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disease 2019 (COVID-19) increase with age. COVID-19 is a public health issue that affects people all around the world.

The mortality and morbidity associated with coronavirus infection (COVID-19) increase with age. COVID-19 is a public health issue that affects people all around the world. Because no standard treatment exists yet, numerous minerals and vitamins that act as antioxidants, immunomodulators, and antimicrobials may be sufficient to boost the response of immune system to the condition.

LITERATURE REVIEW AND ANALYSIS

Although coronaviral infections are primarily associated with respiratory symptoms, skeletal complications have also been reported. Osteoarthritis is a painful condition characterized by a progressive degradation of articular cartilage, soft tissue edema surrounding the joints, and bone cysts [*Hunter D, 2011*]. Analgesics are typically prescribed for symptom relief, as no curative treatment currently exists for osteoarthritis [*McHughes M, Lipman A, 2006*]. The role of the inflammatory response and oxidative stress in the onset and progression of osteoarthritis remains one of the unresolved challenges in understanding its pathogenesis [*Torgomyan A, Saroyan M, 2021*]. Elevated levels of inflammatory mediators, including cytokines, growth factors, and prostaglandin E2, have been detected in the joint tissues of patients with osteoarthritis during the disease progression [*Gavriilidis C et al., 2013*]. Inflammatory pathways, along with other risk factors such as mechanical stress and aging, are known to contribute to oxidative stress by producing nitric oxide (NO), reactive oxygen species, hydrogen peroxide, superoxide anion, and peroxynitrite, while simultaneously reducing the activity of antioxidant enzyme [*Marchev A et al., 2017*]. Although osteoarthritis has traditionally been classified as a degenerative rather than an inflammatory joint disease, recent research has found its association with both inflammation and oxidative stress [*Chauffier K et al., 2012*]. High levels of malondialdehyde MDA, a marker of cellular membrane damage, were reported in Sproston's study [*Hamza R, Al-Baqami N, 2019*]. Antioxidant enzymes such as superoxide dismutase and catalase, which regulate oxidative balance, were found to be reduced. Likewise, levels of endogenous antioxidants, including glutathione (GSH) and thiol, were decreased in the induced osteoarthritis group [*Sproston N, Ashworth J, 2018*]. Nnonsteroidal anti-inflammatory drugs (NSAIDs) and joint viscosupplementation (e.g. intra-articular hyaluronic acid injections) remain among the most frequently used treatment options for osteoarthritis. In addition to providing short-term symptom relief, prolonged use of these drugs—particularly NSAIDs—may lead to adverse effects, including toxicity and an increased risk of thromboembolism [*Hamza R, Al-Baqami N, 2019*]. Additionally, oral administration of NSAIDs is associated with a heightened risk of serious gastrointestinal complications [*Cai H et al, 2003*]. These findings support the use of safer anti-inflammatory agents for COVID-19 patients, minimizing the common side effects linked to conventional NSAIDs.

Refat et al. studied the production of N,N′-bis (1,5-dimethyl-2-phenyl-1,2-dihydro-3-oxopyrazol-4-yl) sebacamide (DPDO) to alleviate osteoarthritis symptoms and improve bone marrow matrix structure and cartilage alterations caused by monoiodoacetate (MA) in a rat model of osteoarthritis [*Refat M et al, 2021*]. They proposed that DPDO might be used as a potential ameliorative drug in an animal model of osteoarthritis and could also function as an anti-inflammatory compound in case of a severe COVID-19 infection. Histological and transmission electron microscopy clearly demonstrated that the novel compound improved the bone cortex and bone marrow structure in the treated group, which is a very important finding in the context of severe infections that have significant effects on blood indices and the decline of blood corpuscles, such as COVID-19, which are known to impact hematological parameters and cause a decline in blood corpuscles. In addition, DPDO reduced the genotoxicity and inflammation induced by monoiodoacetate in male rats. All measured parameters showed significant improvement following treatment with this newly developed compound All of the above-mentioned metrics were significantly improved by the newly created chemical [*Refat M et al, 2021*].

SARS (Severe Acute Respiratory Syndrome) is a type of acute respiratory syndrome. The pandemic of the Coronavirus-2 (SARSCoV- 2) has brought healthcare front and center, making pre-

ventative and treatment methods a top global concern. The morbidity and mortality associated with COVID-19 increase with age. COVID-19 is a public health issue that affects people all around the world. Because there is no standard treatment for it yet, numerous minerals and vitamins that act as antioxidants, immunomodulators, and antimicrobials may be sufficient to enhance the response of the immune system to the condition.

The role of Vitamin D

Serum 25-hydroxyvitamin D [25(OH)D] is the most accurate indicator of vitamin D status [*Sempos C et al, 2018*]. Due to decreased skin capacity for synthesis, reduced sunlight exposure, and malabsorption, hypovitaminosis D is highly prevalent among the elderly population [*Holick M, 2007*].

Vitamin D's potential beneficial effect in COVID-19 patients is supported by both in vitro and in vivo evidence demonstrating its role as a musculoskeletal and immunological modulator, as well as its efficacy in managing co-morbidities commonly observed in these patients – particularly pulmonary complications. COVID-19 patients often have prolonged hospital stays, as increased likelihood of requiring intensive care unit admission, and some degree of immobilization. Following discharge, complete recovery and return to daily functioning may take several weeks. Muscle function in the elderly usually deteriorates with age, and immobilization accelerates this process by reducing protein synthesis by 30%, decreasing lower extremity lean mass by 6.3%, and diminishing muscle strength by 15.6% [*Ebeling P et al, 2018*]. Muscle loss causes difficulties in daily tasks following discharge, and significantly increases the risk of falls, fractures, and mortality [*Kortebein P et al, 2007*].

Acute and chronic immobility promote bone resorption [*Chen D et al, 2006*], and older adults, who constitute the majority of COVID-19 patients, are likely to experience even more pronounced bone loss due to hypersecretion of inflammatory cytokines [*Nakashima T, Takayanagi H, 2009*] and treatment with high doses of glucocorticoids. The resulting decrease in bone mass can lead to bone loss, skeletal fragility, and an increased risk of fractures [*Napoli N et al, 2014*]. Supplementation with Vitamin D in combination with calcium has been demonstrated to reduce fracture risk. Compared to placebo or control, the most consistent protective effect is a 16–33% reduction in the hip fracture risk and a 5–19% reduction in overall fracture risk [*Chakhtoura M et al, 2020*]. When combining trials in community dwelling and institutionalized individuals, this impact is demonstrated, although it is most likely driven by data from institutionalized individuals, as three meta-analyses have consistently indicated [*Chakhtoura M et al, 2020*]. Hip fractures have substantial death rates of 15–30% after 1–3 years, and half of the patients lose functional independence [*Tajeu G et al, 2014*].

Vitamin D also improves muscle strength and function, which is beneficial to muscle health [*Napoli N et al, 2010*]. The muscle-building properties of vitamin D are expected to reduce the risk of falls. Although meta-analyses on the impact of vitamin D on fall prevention report varying results, these differences can be attributed to variation in interventions, populations studied, and trial durations. Notably, a 2018 Cochrane meta-analysis of strategies for fall prevention found that vitamin D supplementation reduced the incidence of falls by 28% among individuals in care facilities [*Cameron I et al, 2018*]. The anticipated benefits of vitamin D for muscle and bone health in COVID-19 patients may contribute to a lower incidence of falls and fractures during hospitalization and rehabilitation. The extra-skeletal effects of Vitamin D should not be overlooked [*Giustina A et al, 2019*]. COVID-19 infection leads to increase of pro-inflammatory cytokines, which may trigger the severe "cytokines storm" that causes both pulmonary and systemic inflammation. Systemic inflammation in COVID-19 is characterized by elevated blood levels of interleukin-6 and other pro-inflammatory cytokines, and is associated with greater disease severity and worse clinical outcomes [*Ruan Q et al, 2020*]. As a result, regulation of the inflammatory response has been proposed as a potential therapeutic strategy. The role of vitamin D in modulating both innate and adaptive immunity may support the control of inflammation [*Mehta P et al, 2020*]. Calcitriol, the active metabolite of vitamin D, interacts with macrophages and activated B and T cells, and promotes immunoglobulin and cytokine production via vitamin D receptors. It is also involved in the Toll-like receptor 2/1 (TLR2/1) signaling pathway [*Greiller C, Martineau A, 2015*]. Although the pathophysi-

ology underlying Coronavirus virulence is still being unraveled, TLR2 is known to identify viral proteins and may therefore play a role in the cellular pathways leading to pulmonary complications in COVID-19.

Low levels of 25(OH)D in the blood are associated with poor respiratory health and increased susceptibility to acute respiratory infections [*Martineau A et al, 2017*]. Acute respiratory distress syndrome affects approximately 67 to 85% of COVID-19 patients, and represents one of the leading causes of mortality. Previous studies have shown that vitamin D deficiency is common among acute respiratory distress syndrome patients, with serum levels 1,25(OH)2D found to be higher in survivors compared to non-survivors [*Dancer R et al, 2015*]. Collectively, these findings suggest that vitamin D may have broader clinical potential [*Giustina A et al 2020*]; while benefits related to musculoskeletal outcomes are well established, possible effects on the immune system require further investigation.

In the respiratory mucosa, vitamin D has been demonstrated to stimulate the production of β -defensins and cathelicidin [*Fabbri A et al, 2020*]. Human β -defensins and cathelicidin (which contains the antimicrobial domain called LL-37) represent the first line of defense against bacterial and viral infection. These peptides, generated by neutrophils and mucosal epithelial cells - particularly those in the respiratory tract – possess antimicrobial properties and enhance innate and adaptive immunity [*Tecle T et al, 2010*]. Tight junctions and adherens junctions maintain epithelial and endothelial barrier integrity. The expression levels of different tight junctions and adherent junction proteins, including claudins, -catenin, and VE-cadherin, are markedly decreased in the lungs of VDR-deficient mice (VDR -/-), according to a recent study, and this phenomenon is expected to induce increased alveolar permeability [*Chen D et al, 2018*]. These findings indicate that vitamin D/VDR signaling plays a key role in epithelial permeability and defensive mechanisms. In another study using a lipopolysaccharide (LPS)-induced lung injury model**,** vitamin D was found to promote proliferation of alveolar epithelial type II (AT-II) cells, while preventing their apoptosis and transdifferentiation into mesenchymal cells [*Zheng SX et al, 2020*].

Vitamin D has important effects on various components of innate immunity, as evidenced in both cell-based studies and animal models. Thus, the active form of vitamin D inhibits TLR2 and TLR4 expression, as well as and the lipopolysaccharide -induced production of α-TNF and CD142 (pro-coagulatory tissue factor) in human monocytes via VDR signaling [*Sadeghi K et al, 2020*]. Vitamin D supplementation, which activates RIG-I signaling pathways, has been shown to reduce elevated levels of IL-2, IL-6, and α-TNF in the serum of pigs challenged with porcine rotavirus [*Zhao Y et al, 2014*]. Another study found that when human monocytes were exposed to lipopolysaccharide, both 1,25-dihydroxyvitamin D3 and 25-hydroxyvitamin D3 may decrease the production of IL-6 and α-TNF and upregulated the expression of mitogen-activated protein kinase phosphatase-1 (MKP-1) [*Zhang Y et al, 2012*]. These finding demonstrate that vitamin D significantly influences CD4+ T-helper cells (Th1 and Th2) and regulatory T cells (Treg). It inhibits the synthesis of inflammatory cytokines IL-2 and interferon-gamma (INF-γ), thereby suppressing the immune response mediated by T helper cells (Th1) [*Wei R et al, 2015*]. Furthermore, 1,25-dihydroxyvitamin D3 increases cytokine synthesis by Th2 helper T cells, which suppresses Th1 cell functions [*Jeffrey LE et al, 2009*]. Overall, our in vitro and in vivo mice investigations suggest that vitamin D plays a complex role in the differentiation and proliferation of many T cell subsets engaged in adaptive immunity. The active form of Vitamin D, 1,25-dihydroxyvitamin D3, can suppress the cytokine storm triggered by virally infected epithelial cells of the respiratory tract and lungs, as well as infiltrating leucocytes. It also promotes an antiviral state in the infected epithelial cells. In addition, vitamin D may help prevent dysfunction of the renin- angiotensin-aldosterone system caused by SARS-CoV-2 infection [*D'Avolio A et al, 2020*].

Multiple studies have identified a relationship between low vitamin D levels in the blood and COVID-19. For example, a Swiss cohort study found that serum vitamin D concentrations were significantly lower in SARS-CoV-2 positive individuals, compared to negative cases [*Baktash V et al, 2020*]. Similarly, hypovitaminosis D has been clearly associated with COVID-19 in people over 65, leading to worse clinical morbidity. A major

number of COVID-19 patients with acute respiratory failure had hypovitaminosis D, and severe vitamin D deficiency was linked to a significantly higher fatality rate [*Carpagnano G et al, 2020*]. In another study of 149 individuals, more than 93% of those with severe COVID-19 had lower serum vitamin D levels, and vitamin D status was identified as an independent predictor of mortality [*Karahan S et al, 2020*]. Likewise, in a study of 154 asymptomatic and severe COVID-19 cases, markedly low levels of vitamin D were found in severe cases, along with increased blood levels of pro-inflammatory cytokines, and vitamin D-deficient participants had a higher mortality rate [*Jain A et al, 2020*]. Vitamin D deficiency was linked to an elevated incidence of COVID-19 in a retrospective cohort research; patients were tested for vitamin D status a year before COVID-19 testing [*Meltzer et al, 2020*]. Across several European countries, a study found an inverse relationship between mean blood vitamin D and COVID-19 positive cases per million and illness mortality per million [*Ilie P et al, 2020*]. Overall, vitamin D appears to be a major disease- modifying factor in COVID-19, based on both epidemiological data and biochemical and immunological evidence. While its effects on innate immunity and the renin–angiotensin–aldosterone system are likely beneficial, its general suppression of adaptive immunity may potentially limit the body's ability to fight off the virus.

The role of Calcium

In addition to Vitamin D, the role of calcium has also been investigated. Hypocalcemia and low vitamin D levels in severe covid-19 have been frequently observed in studies, indicating that more research is needed. Osmana *et al* examined the relationship between the severity of disease and progression and calcium levels at presentation as a primary endpoint and pre-existing calcium levels as a secondary objective. They concluded that, regardless of underlying comorbidities, hypocalcemia is a substantial and reliable measure of disease severity and progression. Notably, vitamin D levels do not appear to be associated with the severity of COVID-19 infections [*Osmana O et al, 2021*]. According to Sun et al, serum calcium can be used as a biomarker of clinical severity and prognosis in patients with coronavirus [*Sun J et al 2020*]. On admission, serum calcium levels, hormone levels, and clinical laboratory indicators were all documented in their retrospective analysis. Variables relating to clinical outcomes were also recorded. The study revealed that hypocalcemia and Vitamin D deficiency were particularly common in COVID-19 patients. An imbalance between vitamin D and parathyroid hormone levels may contribute to hypocalcemia. Lower serum calcium levels were associated with worse clinical outcomes, including higher incidences of multiple organ dysfunction syndrome, septic shock, and higher 28-day mortality. The overall mortality of COVID-19 was 4.1%, while the mortality of critically ill patients reached 40.0%. Thus, serum calcium was associated with the clinical severity and prognosis of patients with COVID-19. Hypocalcemia may be associated with imbalanced Vitamin D and Parathyroid hormone levels [*Sun J et al 2020*]. In addition to its systemic influence, parathyroid hormone also influences articular cartilage regeneration and subchondral bone tissue, previously demostrated [*Torgomyan A, 2019*].

After the commencement of symptoms, Zhou and colleagues looked at the changes in different electrolytes. Although serum potassium and calcium levels in COVID-19 patients have been demonstrated to fall [*Zhou X et al, 2020*], only serum calcium varied with the number of days from symptom start in individuals with severe COVID-19, which was statistically significant. Serum calcium levels were measured based on days from symptom onset and COVID-19 severity. Multiorgan injuries and blood levels of immune cytokines were also studied. In the early stages of viral infection, all cases, regardless of the severity of their condition, had low calcium levels, with severe/critical cases having significantly lower calcium levels than mild/moderate cases. It was also discovered that in the later stages of COVID-19, the age-related calcium imbalances affected the mild/moderate population's ability to recover. This is because as people age, their liver and kidney functions decline, leading to a decrease in serum levels of 25-hydroxyvitamin D in the human body, resulting in an intestinal calcium absorption disorder and thus affecting blood calcium recovery [*Vandenbroucke A et al, 2017*]. Furthermore, calcium was associated with

multiorgan injuries, especially in severe/critical cases, so keeping calcium balance was important for preserving normal organ functions.

In both mild/moderate and severe/critical instances, the pro-inflammatory cytokine IL-6 was associated with changes in calcium levels. One of the most important aspects of COVID-19 prevention and treatment is preventing mild/moderate cases from progressing to severe/critical illness. Identifying individuals who are predisposed to severe/critical illness can help to act early and minimize the rate at which mild/moderate sickness becomes severe/critical [*Chen D et al, 2020*]. According to the New Coronavirus virus Pneumonia Diagnosis and Treatment Program published by the National Health Commission of China, there are four severe/critical warning indicators: progressive decline in peripheral blood lymphocytes, gradual increase in peripheral blood inflammatory cytokines (such as IL-6 and C-reactive protein), rising lactic acid levels, and rapid evolution of pulmonary lesions over a short period of time This study suggested that, even at the early stages of viral infection, calcium levels could serve as a biomarker to evaluate the severity of COVID-19.

Elham and colleagues also examined vitamin D, calcium, and zinc levels in the serum of COVID-19 patients. There was a substantial difference in vitamin D levels between the case and control groups. Statistically significant differences were also observed in serum calcium and serum zinc levels between the two groups. They came to the conclusion that COVID-19 patients had lower serum zinc, calcium, and vitamin D levels than the control group. Supplementing with these nutrients was identified as a low-cost and safe approach to deal with the increased demand in individuals at risk of contracting the COVID-19 virus [*Elham A et al, 2021*].

Liu et al. were the first to examine the frequency of hypocalcemia in patients with severe COVID-19. They found that 62.6 % of COVID-19 patients had hypocalcemia, including three severe cases. Hypocalcemia was also associated with a poorer prognosis in patients with severe COVID-19. Additionally, 63.6% of the patients were over 65 years old, with a median age of 68, suggesting that older adults are more susceptible to severe COVID-19 [*Liu J et al., 2020*].

Hypocalcemia is a common laboratory finding in viral infection and pneumonia [*Sankaran R et al, 1997*]. The origin of hypocalcemia in COVID-19 patients with severe status is unknown; however, several explanations have been proposed. The majority of patients in our study were elderly and undernourished. Chronic malnutrition leads to vitamin D deficiency, which impairs calcium absorption and contributes to hypocalcemia [*Holick M, 2007*]. It can interfere with calcium absorption in the intestine, resulting in insufficient intake and a negative calcium balance [*Bhraonain S, Lawton L, 2013*]. Moreover, as plasma calcium is largely bound to albumin, a decrease in serum albumin levels contributes to lower total serum calcium. Hypoxia-induced tissue and organs cell membrane damage can disrupt cell membranes, causing intracellular calcium influx. Finally, elevated levels of pro-inflammatory cytokines in COVID-19 may suppress parathyroid hormone secretion, resulting in impaired parathyroid hormone response and calcium imbalance [*Fong J, Khan A, 2012*]. COVID-19 continues to spread globally. In their research and Liu et al. were the first to focus on hypocalcemia in COVID-19 individuals with severe disease. On admission, nearly two-thirds of severe COVID-19 patients had hypocalcemia. Patients who presented with hypocalcemia were more severely ill on admission, and had poorer outcomes [*Liu P et al, 2017*].

DISCUSSION

In individuals with COVID-19, bone and joint pathologies are less well understood than skeletal muscle disorders. Arthralgias have been reported in various anatomical regions, including the humeral head, talus, and calcaneus, with varying severity [*Griffith J, 2011*]. Patients receiving larger or longer dosages of corticosteroids are at increased risk of developing osteonecrosis, similar to osteoporosis. Patients with COVID-19 and SARS have both been found to have hypercoagulability, which may lead to large-vessel stroke in some cases [*Panigada M et al, 2020*]. Additionally, SARS-CoV-1 infection has been shown to cause the E3 ubiquitin ligase gene TRIM55 to be expressed in vascular smooth muscle cells, which is associated with leukocyte aggregation and blood vessel inflammation [*Chen et al Y, 2021*].

Hypercoagulability, leukocyte aggregation, and vessel inflammation may contribute to osteonecrosis by impairing bone microvascular blood flow to bone tissue. In patients with COVID-19, systemic inflammation may also play a role in bone and joint tissue physiology. Cytokines elevated in COVID-19- such as CXCL10, IL-17, and α-TNF – are known to enhance osteoclastogenesis while inhibiting osteoblast proliferation and differentiation, leading to an overall reduction in bone mineral density. Chondrolysis can be caused by IL-1b, IL-6, and α-TNF, which might result in arthralgias or the advancement of osteoarthritis in some patients [*Latourte A et al, 2017*].

Similarly, IL-1b, IL-17, and α-TNF are believed to induce inflammation in tendinopathy and may impair normal biological activity of tenocytes, resulting in reduced matrix remodeling and potential progression of degenerative tendon diseases [*Millar N et al, 2016*]. Preliminary data suggest that COVID-19 is associated with various musculoskeletal sequelae. Based on these reports, epidemiological data from SARS patients during the 2002–2004 pandemic, genetic and pathological similarities between SARS-CoV-1 and SARSCoV-2, and the frequent reports of sarcopenia and osteoporosis in other critical illnesses [*Gumucio J, Mendias C, 2013*], it is reasonable to conclude that SARS-CoV-1 and SARS-CoV-2 cause sarcopenia and osteoporosis as short-term and long-term musculoskeletal complications in patients with moderate and severe COVID-19. Conservative rehabilitation programs have been shown to improve functional recovery in patients with SARS and are similarly beneficial in other critical illnesses [*Kou K et al, 2019; Sanders J et al, 2020*].

Conclusion

Coronavirus disease 2019 is a new pandemic disease caused by severe acute respiratory syndrome coronavirus 2. Although the majority of individuals infected with SARS-CoV-2 are asymptomatic or experience only moderate symptoms, some develop severe complications that may have long-term impacts on quality of life. SARS-CoV-2 is closely related to SARS-CoV-1, the virus that causes severe acute respiratory syndrome. Both viruses primarily affect the respiratory system, but the infection also has direct and indirect effects on multiple organ systems, including the musculoskeletal system. Myalgias, muscle weakness, osteoporosis, and osteonecrosis were typical sequelae in individuals with moderate and severe disease, according to epidemiological data from the SARS pandemic. Although long-term follow-up studies on COVID-19 are still ongoing, early research suggests that certain COVID-19 patients experience significant musculoskeletal impairment [*Ceribelli A et al, 2020*].

The objective of this study was to compile existing data on musculoskeletal involvement in SARS or COVID-19 patients and integrate it with computational modeling and molecular signaling analyses to predict musculoskeletal cellular targets and the potential long-term consequences of SARS-CoV-2 infection.

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