

# Bone diseases and the COVID-19 pandemic

Francisco Bandeira<sup>1</sup>  
<https://orcid.org/0000-0003-0290-0742>

John P. Bilezikian<sup>2</sup>  
<https://orcid.org/0000-0002-1570-2617>

<sup>1</sup> Divisão de Endocrinologia e Diabetes, Hospital Agamenon Magalhães, Faculdade de Ciências Médicas, Universidade de Pernambuco, Recife, PE, Brasil  
<sup>2</sup> Department of Medicine, Endocrinology Division, Vagelos College of Physicians and Surgeons, Columbia University, New York, NY, USA

Although much has been learned about the acute consequences of SARS-CoV-2 infection, the chronic impact on human health is still largely unknown (1). In addition to respiratory symptoms, general features such as fatigue, myalgias and joint pain may persist, usually associated with low-grade inflammation (1). Acute SARS-CoV-2 infection in its moderate to severe form can lead to a high mortality rate especially in vulnerable individuals such as the elderly, a subgroup of patients in whom common muscle-skeletal disorders frequently occur. Crosstalk between skeletal muscle and bone is modified by the ageing process with increased myostatin secretion by myocytes, as well as sclerostin by osteocytes, and changes in the RANK/osteoprotegerin ratio (2).

In the acute phase of SARS-CoV-2 infection, the muscle-skeletal consequences vary according to the severity of infection, including the need of hospitalization due to respiratory failure (3). This may cause delays or interruptions in osteoporosis treatment, which may ultimately result in a fracture and other co-morbidities.

SARS-CoV-2 infection causes a systemic inflammatory response often referred to as cytokine storm (4). This occurs due to the virus entering the cells following ACE2 receptor binding with the induction of an inflammatory cascade, mediated by cytokine secretion from T helper 1 cells and neutrophilic extracellular traps (NETs) (4). The cascade of systemic inflammation may have deleterious effects on skeletal muscle mass and may also lead to increased bone turnover with the consequent bone loss and sarcopenia among survivors (2,5,6). In one trial, bone mineral density decreased due to SARS-CoV-2 infection (7). Volumetric bone mineral density (BMD) by computed tomography rapidly was reduced during the 3 months following an acute infection by more than 8% (7).

Prolonged duration of respiratory failure with oxygen therapy by nasal catheter or intubation, followed by mechanical ventilation, may lead to deficient nutrition (8). This may also have a great impact on the muscle-skeletal system (8,9).

The lockdown phase, which caused a substantial decrease in physical activity, also had a profound effect on muscle-skeletal system (9). This may also decrease sun exposure leading to vitamin D deficiency (6,10,11).

During 2020, the first year of SARS-CoV-2, there was a 25% to 30% increase in the rate of depressive and general anxiety disorders globally (12), which usually require the use of specific pharmacotherapy. The antidepressants may have negative effects on bone (13), in particular the selective serotonin reuptake inhibitors (SSRIs), that can lead to reductions in BMD by dual X-ray absorptiometry (DXA), decreases in volumetric cortical BMD by high-resolution peripheral quantitative computed tomography (HR-pQCT) and impairment in hand grip strength (13).

#### Correspondence to:

Francisco Bandeira  
 Av. República do Líbano, 251,  
 Rio Mar Trade Center III,  
 Salas 1.915/1.916, Pina  
 51110-160 – Recife, PE, Brasil  
[francisco.bandeira@upe.br](mailto:francisco.bandeira@upe.br)

Received on July/6/2022  
 Accepted on July/11/2022

DOI: 10.20945/2359-3997000000548

The treatment of osteoporosis and primary hyperparathyroidism were also affected by the pandemic (14,15) leading to an increase in fracture burden (15). Long-term osteoporosis treatment and monitoring is essential (16). Medications such as bisphosphonates, denosumab and teriparatide do not affect the course of SARS-CoV-2 infection (17). The use of telemedicine increased (18), but the number of surgeries for primary hyperparathyroidism (PHPT) decreased and medical treatment with calcimimetics disproportionately increased (14).

Finally, the diagnosis and management of metabolic bone diseases, such as osteoporosis, has been compromised during COVID-19 pandemic. Guidelines to minimize this impact have been proposed with recommendations for clinicians and patients to avoid delay in starting treatment or inadvertent withdrawal (3). This will ultimately reduce the negative consequences on the skeleton.

In this issue of the AE&M you will find a series of articles addressing an update on a variety of conditions related to calcium and bone metabolism, commonly seen in clinical practice, with new data regarding the effects of SARS-CoV-2 infection as well.

Disclosure: no potential conflict of interest relevant to this article was reported.

## REFERENCES

- Jarrott B, Head R, Pringle KG, Lumbers ER, Martin JH. "LONG COVID"-A hypothesis for understanding the biological basis and pharmacological treatment strategy. *Pharmacol Res Perspect*. 2022;10(1):e00911.
- He C, He W, Hou J, Chen K, Huang M, Yang M, et al. Bone and Muscle Crosstalk in Aging. *Front Cell Dev Biol*. 2020;8:585644.
- Hampson G, Stone M, Lindsay JR, Crowley RK, Ralston SH. Diagnosis and Management of Osteoporosis During COVID-19: Systematic Review and Practical Guidance. *Calcif Tissue Int*. 2021;109(4):351-62.
- Hu B, Huang S, Yin L. The cytokine storm and COVID-19. *J Med Virol*. 2021;93(1):250-6.
- Bilezikian JP, Bikle D, Hewison M, Lazaretti-Castro M, Formenti AM, Gupta A, et al. MECHANISMS IN ENDOCRINOLOGY: Vitamin D and COVID-19. *Eur J Endocrinol*. 2020;183(5):R133-r147.
- Bandeira L, Lazaretti-Castro M, Binkley N. Clinical aspects of SARS-CoV-2 infection and vitamin D: COVID-19 and the endocrine system: special issue for reviews in endocrine and metabolic disorders. *Rev Endocr Metab Disord*. 2022;23(2):287-91.
- Berktaş BM, Gökçek A, Hoca NT, Koyuncu A. COVID-19 illness and treatment decrease bone mineral density of surviving hospitalized patients. *Eur Rev Med Pharmacol Sci*. 2022;26(8):3046-56.
- Barrea L, Grant WB, Frias-Toral E, Vetrani C, Verde L, de Alteriis G, et al. Dietary Recommendations for Post-COVID-19 Syndrome. *Nutrients*. 2022;14(6):1305.
- Kirwan R, McCullough D, Butler T, Perez de Heredia F, Davies IG, Stewart C. Sarcopenia during COVID-19 lockdown restrictions: long-term health effects of short-term muscle loss. *Geroscience*. 2020;42(6):1547-78.
- Azevedo M, Bandeira L, Luza C, Lemos A, Bandeira F. Vitamin D Deficiency, Skin Phototype, Sun Index, and Metabolic Risk Among Patients with High Rates of Sun Exposure Living in the Tropics. *J Clin Aesthet Dermatol*. 2018;11(8):15-8.
- Bandeira F, Griz L, Freese E, Lima DC, Thé AC, Diniz ET, et al. Vitamin D deficiency and its relationship with bone mineral density among postmenopausal women living in the tropics. *Arq Bras Endocrinol Metabol*. 2010;54(2):227-32.
- Daly M, Robinson E. Depression and anxiety during COVID-19. *Lancet*. 2022;399(10324):518.
- Agarwal S, Germosen C, Kil N, Bucovsky M, Colon I, Williams J, et al. Current anti-depressant use is associated with cortical bone deficits and reduced physical function in elderly women. *Bone*. 2020;140:115552.
- Radulova-Mauersberger O, Keßler J, Keßler U, Stange K, Korn S, Weitz J, et al. The Effect of the Frequently Used Cinacalcet for pHPT during the COVID-19 Pandemic on Perioperative Decrease in Parathyroid Hormone. *J Clin Med*. 2022;11(7):2015.
- De Vincentis S, Domenici D, Ansaloni A, Boselli G, D'Angelo G, Russo A, et al. COVID-19 lockdown negatively impacted on adherence to denosumab therapy: incidence of non-traumatic fractures and role of telemedicine. *J Endocrinol Invest*. 2022;45(10):1887-97.
- Bandeira F, Dantas W, Bilezikian JP. Controversies in the treatment of postmenopausal osteoporosis: How long to treat with bisphosphonates? *Arch Endocrinol Metab*. 2020;64(4):331-6.
- Atmaca A, Demirci I, Haymana C, Tasci I, Sahin I, Cakal E, et al. No association of anti-osteoporosis drugs with COVID-19-related outcomes in women: a nationwide cohort study. *Osteoporos Int*. 2022;33(1):273-82.
- Salvio G, Gianfelice C, Firmani F, Lunetti S, Ferroni R, Balercia G, et al. Remote management of osteoporosis in the first wave of the COVID-19 pandemic. *Arch Osteoporos*. 2022;17(1):37.