

OSTEOPOROSIS DURING THE COVID-19 ERA

Joint Guidance on COVID-19 Vaccination and Osteoporosis Management from the American Society for Bone and Mineral Research (ASBMR), American Association of Clinical Endocrinology (AACE), Endocrine Society, European Calcified Tissue Society (ECTS), the International Osteoporosis Foundation (IOF), and the National Osteoporosis Foundation (NOF)- 2021

- Oral bisphosphonates

We recommend that oral bisphosphonates should be continued without interruption or delay in patients receiving COVID-19 vaccination.

- Intravenous (IV) bisphosphonates

We recommend a one-week interval between IV bisphosphonate infusion and COVID-19 vaccination to allow for distinguishing between putative acute phase reactions resulting from either IV bisphosphonate administration or COVID-19 vaccination.

- Denosumab

We recommend an interval of 47- days between treatment with denosumab and COVID-19 vaccination to allow for the potential occurrence of injection site reactions with either treatment. Alternatively, denosumab treatment could be administered in the contralateral arm or alternative site (abdomen or upper thigh), if it is necessary to administer concomitantly with COVID-19 vaccine. We also recommend that while denosumab timing may be slightly adjusted to account for vaccine timing, denosumab injections should not be delayed more than 7 months after the previous denosumab dose.

- Teriparatide

We recommend that both teriparatide and abaloparatide should be continued in patients receiving COVID-19 vaccination.

- Romosozumab

We recommend an interval of 47- days between provision of these injections, or consideration for injection in the abdomen (except for a two-inch area around the navel) or thigh if administered concomitantly.

- Raloxifene

We recommend that raloxifene should be continued in patients receiving COVID-19 vaccination.



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How has COVID-19 affected the treatment of osteoporosis? An IOF-NOF-ESCEO global survey. Osteoporosis International 2020

The International Osteoporosis Foundation and National Osteoporosis Foundation conducted a global survey to evaluate the impact of COVID-19 pandemic on the treatment of patients with osteoporosis. A total of 209 healthcare workers from 53 countries responded. The survey demonstrated an increase in telemedicine and video consultations, delays in DXA scanning whereby only 21% of patients were able to obtain a scan as recommended, in addition to interruptions in the supply of medications and reductions in parenteral medication delivery during the COVID-19 crisis.



Radiological Thoracic Vertebral Fractures are Highly Prevalent in COVID-19 and Predict Disease Outcomes-JCEM 2021

This is a retrospective cohort of 114 adults (75% men and mean age 57 years) with PCR confirmed COVID-19 infection. They were all evaluated with lateral chest x-rays and admitted to San Raffaele University Hospital, a tertiary health care hospital in Milan, Italy. Vertebral fractures were detected in 36%; According to Genant classification, 60% were mild, 33.3% moderate, and 7.7% severe. The presence of a vertebral fracture predicted the need for noninvasive mechanical ventilation, and the presence of severe vertebral fracture predicted increased mortality. Given that vertebral fractures are associated with an increased risk of infection and limited pulmonary function, they may represent a marker of poor prognosis.



Influence of anti-osteoporosis treatments on the incidence of COVID-19 in patients with non-inflammatory rheumatic conditions-Aging 2020

This is a cross-sectional study of 2,102 patients treated for osteoporosis, osteoarthritis or fibromyalgia at the Rheumatology Service of Hospital del Mar (Barcelona, Spain). The mean age of the population was 66.4 years (SD, 13.3), 80.5% were women. The distribution of the primary diseases was as follows:

63.7% Osteoarthritis

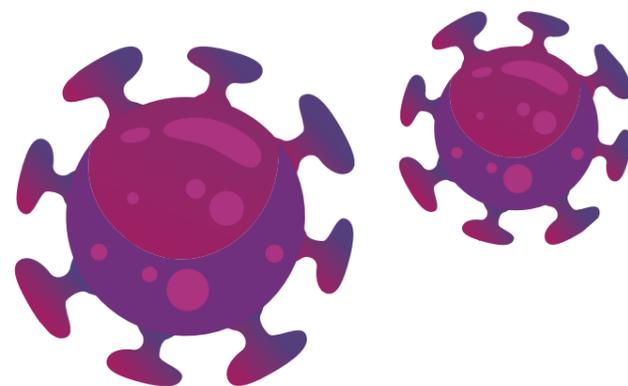
43.5% Osteoporosis

27.2% Fibromyalgia

109 patients (5.2%) has COVID-19 diagnosis

The age-standardized cumulative incidence rate in the included sample was 4.68% (95% CI 3.785.59%-), being slightly higher than that in the general population of Barcelona of 3.69%; (95% CI 3.663.73%-).

There was no association between Denosumab, Zoledronate oral bisphosphonates and COVID-19 infection, after adjusting for age, sex, diabetes, pulmonary disease, cardiovascular disease, kidney disease, cancer and various medications.





Effect of a Single High Dose of Vitamin D3 on Hospital Length of Stay in Patients With Moderate to Severe COVID-19: A Randomized Clinical Trial-JAMA 2021

This was a multicenter, double-blind, randomized, placebo-controlled trial conducted in 2 sites in Sao Paulo, Brazil, comparing a single high dose of vitamin D3 200,000 IU (N=120) to Placebo (n=120). The trial enrolled moderately to severely ill hospitalized COVID-19 patients. The primary outcome was the length of hospital stay, and several secondary outcomes were considered, including mortality, admission to intensive care unit (ICU) and others (NCT04449718). Baseline 25-Hydroxyvitamin D level was 20.9 (9.2) ng/ml and reached 44.4 ng/mL and 19.8 ng/mL, in the intervention and the placebo group respectively. Comparing the two arms, there was no significant difference in the length of hospital stay, mortality, need for mechanical ventilation, or ICU admission.

UPCOMING EVENTS

LSEDL _____ June 11 - 13, 2021

WCO-IOF-ESCEO _____ August 26 - 29, 2021

ASBMR _____ October 1 - 4, 2021

Metabolic bone changes after bariatric surgery: 2020 update, American Society for Metabolic and Bariatric Surgery Clinical Issues Committee position statement. *Surgery for Obesity and Related Diseases* (2020)

Recently, evidence has been accumulating on the deleterious effect of bariatric surgery on bone health, including deterioration in BMD and increased fracture risk. The American Society for Metabolic and Bariatric Surgery has issued the 2020 update position statement on metabolic bone changes after bariatric surgery. It supported the AACE/ACE/TOS 2019 guidelines for calcium (1,200,500- mg/d for malabsorptive and restrictive procedures and 1,800,400- mg/d for bilio-pancreatic diversion) and vitamin D supplementation (3,000 IU/d). The statement suggested bone mineral density measurement by DXA at baseline and at 2 years post-surgery, and highlighted the importance of exercise to mitigate adverse bone changes.



Bone Mineral Density and Turnover After Sleeve Gastrectomy and Gastric Bypass: A Randomized Controlled Trial (Oseberg). *JCEM* 2021

A randomized triple blind trial from Norway compared the changes in areal BMD and bone markers in Roux-en-Y Gastric Bypass (RYGB) and Sleeve Gastrectomy (SG). A total of 92 participants with diabetes mellitus were included, mean age 48.50 years, majority women with a mean baseline BMI 41 kg/m². At 12 months post-operatively, the drop in areal BMD at the femoral neck, total hip, and lumbar spine was significantly higher after RYGB compared to SG; Between group differences were -2.8% [-4.7 to -0.8], -3.0% [-5.0 to -0.9], -4.2% [-6.4 to -2.1], respectively. Similarly, bone turnover markers, type 1 N-terminal propeptide (PINP) and C-telopeptide of type I collagen (CTX-1), were higher following RYGB compared to SG. Interestingly, these changes were correlated with the surgical procedure and were independent of the weight change.

The Effect of an Exercise Intervention Program on Bone Health After Bariatric Surgery: A Randomized Controlled Trial. *JBMR* 2021

This is 11-month trial randomizing patients following bariatric surgery, RYGB or SG, to a supervised multicomponent exercise program or control, starting at 1 month after surgery. The program consisted of 3 weekly nonconsecutive days lasting 75 minutes each, and was organized as follows: (i) warmup (5 minutes); (ii) high impact (10 minutes); (iii) balance (10 minutes); (iv) high impact (10 minutes); (v) resistance (35 minutes); and (vi) cooldown (5 minutes). At study completion, the exercise group had higher BMD at lumbar spine (+0.024 g/cm² [95% confidence interval (CI) 0.004, 0.044]; p = .015) and 13/ radius (+0.013 g/cm² [95% CI 0.003, 0.023]; p = .020), compared to the control group. There was no difference at the total hip and femoral neck.



Fracture Risk and Management of Discontinuation of Denosumab Therapy: A Systematic Review and Position Statement by European Calcified Tissue Society (ECTS)- JCEM 2021

Denosumab discontinuation may lead to a rapid bone turnover which may translate into increased vertebral fractures. The European Calcified Tissue Society (ECTS) conducted a systematic review on the topic and issued a position statement.

If Denosumab treatment is for a short duration (≤ 2.5 years) in a patient with low fracture risk

Switch to oral or IV bisphosphonates for 12- years, depending on the re-evaluation of bone turnover markers and BMD

If Denosumab treatment is for a long duration (> 2.5 years) in a patient with high fracture risk

Switch to Zoledronate. Begin zoledronate 6 months after the last Denosumab injection and consider repeated infusion of

Zoledronate in case of persistently elevated bone markers

In case bone markers are not available, administer Zoledronate at 6 and 12 months after the last Denosumab injection
If Zoledronate is not an option, treat with oral bisphosphonates for 12-24 months depending on bone markers and BMD

In case of vertebral fractures within 12- years after Denosumab cessation

Avoid vertebroplasty and/or monotherapy with Teriparatide

Consider one of the following:

- Prompt re-initiation of Denosumab
- Treat with intravenous or oral Bisphosphonates
- Consider combination of Denosumab and Teriparatide for 2 years followed by Zoledronate

Teriparatide did not increase adult osteosarcoma incidence in a 15-Year US Post marketing Surveillance Study JBMR 2020

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Using the cancer registries in the United States, the aim of this study was to identify incident cases of osteosarcoma (January 1, 2003, and December 31, 2016) among men and women aged ≥ 40 years, and to determine if any relationship to teriparatide exposure can be demonstrated. The exposure history was reported by patient or by proxy and verified from data abstracted from charts for a sample of patients. 24% (1173) of patients identified completed the study interview, and three cases used Teriparatide before their diagnosis. Based on the background incidence rate, the expected number of osteosarcoma cases among patients treated with teriparatide was 4.17. Therefore, the standardized incidence ratio comparing the observed and expected numbers of osteosarcoma patients with a prior history of teriparatide treatment was 0.72 (90% confidence interval [CI], 0.20 to 1.86). These findings demonstrate that the use of Teriparatide does not increase the rate of osteosarcoma.



PUBLICATIONS

- Chakhtoura M, El Hajj Fuleihan G. Letter to the Editor: Reply to Vitamin D deficiency in COVID-19: mixing up cause and consequence. *Metabolism*. 2021 Feb;115:154462
- Ahmadi H, Kreidieh O, Akl EA, El-Hajj Fuleihan G. Minimally invasive parathyroidectomy guided by intraoperative parathyroid hormone monitoring (IOPTH) and preoperative imaging versus bilateral neck exploration for primary hyperparathyroidism in adults. *Cochrane Database Syst Rev*. 2020 Oct 21;10:CD010787. doi: 10.1002/14651858/CD010787.pub2.PMID: 33085088
- El Sabeh M, Ghanem P, Al-Shaar L, Rahme M, Baddoura R, Halaby G, Singh RJ, Vanderschueren D, Bouillon R, El-Hajj Fuleihan G. Total, Bioavailable, and Free 25(OH)D Relationship with Indices of Bone Health in Elderly: A Randomized Controlled Trial. *J Clin Endocrinol Metab*. 2021 Jan 23;106(2):e990-e1001. doi: 10.1210/clinem/dgaa780.PMID: 33280041
- Randa Saad , Maya Beydoun , Ghada El-Hajj Fuleihan. Management of Hip Fractures at an Academic Center: Challenges and Opportunities. *J Clin Densitom*. 2020 Oct-Dec;23(4):524533-. doi: 10.1016/j.jocd.2019.01.002. Epub 2019 Jan 6. PMID: 30691870.
- Bassatne A*, Basbous M*, Chakhtoura M, El Zein O, Rahme M, El-Hajj Fuleihan G. The Link between coronaVlruses and Vitamin D (VIVID): A Systematic Review and Meta-Analysis, *Metabolism* In Press
- Barake M, El Eid R, Chakhtoura M, Osteoporotic Fractures in the Arab Region: A Systematic Review, *Osteoporosis International* In Press
- Robert A.Adler, Mariam A.Assaad, Ghada A.El-Hajj Fuleihan. Chapter 79 - Long-term bisphosphonate treatment: continuation and interruption. Volume 2, 2021, Pages 18051825-.

FUND RAISING

CaMOP Director and Faculty have launched a major fundraising initiative, in collaboration with the Development Office at AUB and with support from Mrs. Shirine Daouk, to sustain and ensure the continued growth and expansion of the Calcium Metabolism and Osteoporosis Program. This Center is to be designated as Center of Excellence in Metabolic Diseases for the region and worldwide. Donations of any amount to the CaMOP Fund are welcome – and will make a profound difference. Here are just some of the many initiatives you will be benefiting through your support for this critically important program:

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| Support
CaMOP |



1. Osteoporosis evaluation for high-risk patients

Support needy patients by providing free bone mineral density (BMD) and lab tests that are critical to bone health. Target population are patients seeking care at AUB's Outpatient Department (OPD), children with cancer, patients with breast cancer, and patients with prostate cancer.

2. The Fracture Liaison Service

Ensure the delivery of the highest standards of care to patients with hip fractures, the most devastating of all osteoporotic fractures. Hip fractures are associated with pain, loss of functional independence, and a 2540%- mortality rate within three years of the fracture.

3. Outreach efforts

Develop educational materials on osteoporosis, vitamin D, and densitometry, for patients and the public, organizing workshops for health professionals, and participating in World Osteoporosis Day activities on October 20 each year.

4. Fellowship training program in osteoporosis and metabolic bone disorders

Train recent medical graduates, who will become future healthcare leaders for osteoporosis and bone diseases for our country and the region.

IT'S NEVER TOO EARLY OR TOO LATE TO PREVENT OR TREAT OSTEOPOROSIS



Calcium Metabolism & Osteoporosis Program

Department of Internal Medicine American University of
Beirut Medical Center Office 5th floor, Room W542
Tel: 961374374- ext.5362

camop@aub.edu.lb

Editor-in-Chief

Ghada El-Hajj Fuleihan, MD, MPH, FRCP

Issue Editor

Marlene Chakhtoura MD, MSc

Narrator

Abir Bou Khalil, MD