BONE HEALTH IN THE AGE OF COVID-19

Osteoporosis management during COVID-19 crisis:
During COVID-19 crisis physicians are receiving calls from patients with osteoporosis who are worried because they heard that those who have chronic diseases are at higher risk of infection and at higher risk of developing severe disease and death if they get infected. It is very important to reassure our patients and explain that:
- Although osteoporosis is a chronic disease, it does not affect their immune system and does not put them at higher risk for COVID-19 or any other infectious disease.
- Emphasize on compliance with medications and healthy lifestyle.
- Give tips on fall prevention at home to reduce the need to visit emergency rooms and hospitals specially during the COVID-19 period.
- Reassure patients that antosteoporotic medications do not increase their risk of infection. For those on IV bisphosphonates it is ok to delay the yearly infusion for a short period, however those who are on Denosumab should take their injections in due time to prevent rebound effect and fractures.
- Stay in touch with their primary care physician and contact him/her if they have any concern.
- Encourage them to follow national recommendations, to stay safe and keep others safe.

ICSD COVID-19 DXA guidance

The International Society for Clinical Densitometry issued the following statement concerning delaying DXA imaging during the COVID-19 crisis. Delaying or deferring DXA for diagnosis or monitoring is appropriate for 3-6 months because:
- For most patients there will be little clinically meaningful change in BMD over the period.
- For those on treatment with established acceptable response, there is a very low likelihood that the response will change.
- For those transitioning from anabolic therapy to anti-resorptive therapy, it is far more important to consolidate gains achieved by switching without DXA results first.
- For those newly on therapy set up for first monitoring DXA, there will also be little meaningful change over the interval.
- DXA services are increasingly performed in facilities, and many of those facilities already are or will be shifted to emergency and/or crisis management, where "elective" radiology will be severely limited if not curtailed. Over this anticipated short duration of 3-6 months, restricting this service does not pose a substantial threat to patients needing BMD testing.

COVID-19 and Vitamin D

The world is in the grip of the COVID-19 pandemic and no treatment or vaccine is available so far. Innumerable ongoing studies worldwide are looking for risk factors associated with morbidity and mortality from this disease. Because maintaining immunity is essential for prevention and management of any viral infection, and because of the plausible role for vitamin D in immune cell function, particularly in modulating the inflammatory response to viral infections, investigators around the world are interested in the association between vitamin D and COVID-19 morbidity and mortality.

Ilie et al studied the association between the reported mean levels of 25 hydroxy-vitamin D (25 OHD), and morbidity and mortality caused by COVID-19 in 20 European countries. They observed that 25 OHD levels were severely low in the aging population, the most vulnerable group in relation to COVID-19. And they found negative correlations between mean 25 OHD levels in each country and the number of COVID-19 cases per million, and mortality per million (Fig 1). Ilie et al, Aging clinical and experimental research, 2020
Laird et al also conducted a literature search on PubMed on vitamin D status in older adults in countries/areas of Europe affected by Covid-19. Covid-19 infection and mortality data was gathered from the WHO. They found that, counter-intuitively, lower latitude countries such as Spain and Italy, had low mean concentrations of 25(OH)D. These countries have also been experiencing the highest infection and death rates in Europe. Conversely, the northern latitude countries (Norway, Finland, Sweden) had higher mean 25(OH)D concentrations, lower infection and death rates (fig 2). The correlation between 25(OH)D concentration and mortality rate reached conventional significance (P=0.046) by Spearman’s Rank. Laird et al, Ir Med J; Vol 113 (5) 2020

In conclusion, there is an emerging epidemiological data supporting a plausible role for vitamin D in Covid-19 infection. Randomized controlled trials are required to fully investigate the effect of vitamin D supplementation on the prevention and on the course of the disease.

**Combination and cyclic treatment versus standard treatment for osteoporosis**


In the Denosumab and Teriparatide Administration (DATA) study, it was shown that combination of denosumab and teriparatide resulted in larger increases in hip and spine bone mineral density (BMD) than with either drug alone. DATA-HD, an open-label, randomised, controlled phase 4 trial done at Massachusetts General Hospital assessed whether administration of denosumab with high dose teriparatide would stimulate larger increases in bone mass than those observed in the DATA study. 76 participants were randomly assigned to 20 μg teriparatide (n=39) or 40 μg teriparatide (n=37). At 15 months areal BMD increased to a greater extent in the 40 μg group than the 20 μg group at the spine (difference 8.1%), total hip (difference 2.2%) and femoral neck (difference 2.5%). The difference was significant at all skeletal sites. Similarly, volumetric bone density and estimated bone strength assessed by QCT increased to a significantly greater extent in the 40 group compared to the 20 group at all skeletal sites.


In a 3 year randomized study, Cosman et al assessed the effect of 18 months of teriparatide followed by 18 months of denosumab (standard) or three separate 12 month cycles of 6 months of teriparatide followed by 6 months of denosumab (cyclic) in 70 postmenopausal women (mean age 65 years). There was no difference in BMD between cyclic and standard group at 36 months. At 18 months, the cyclic regimen obviated the declines at the radius and total body found with the standard regimen. The investigators concluded that although the cyclic regimen did not improve BMD compared with standard at 36 months, there appeared to be a benefit at 18 months, especially in the highly cortical skeletal sites. This could be clinically relevant in patients at high imminent risk of fracture, particularly at non-vertebral sites.

**ONGOING TRIALS: ClinicalTrials.gov Identifier: NCT03994172: Novel Combination therapy for Osteoporosis in Men (Osteo-Men)**

An ongoing trial is testing a novel combination therapy for osteoporosis in men. The study aims at determining the effects of 11 months treatment with Teriparatide + cinacalcet vs Teriparatide+placebo on spine BMD (primary endpoint), femoral neck BMD, and biochemical markers.

**Study Type:** Interventional (Clinical Trial)

**Estimated Enrollment:** 48 participants

**Allocation:** Randomized

**Intervention Model:** Parallel Assignment

**Intervention Model Description:** The study design is that of a randomized double-blind, placebo (PBO)-controlled trial of the combination of teriparatide (TPTD) + the calcimimetic cinacalcet compared to monotherapy with TPTD alone in men with low BMD

**Masking:** Triple (Participant, Care Provider, Investigator)

**Study Start Date:** July 1, 2019

**Estimated Primary:** June 30, 2023

**Completion Date:**
Bone disease following solid organ transplantation


Although organ transplantation improves quality of life of the recipient, fracture risk remains high especially during the first years following transplant. Bone density is affected differently according to each organ, however the use of immunosuppressants, drugs including glucocorticoids is a common aggravating factor for all organs. The European Calcified Tissue Society (ECTS) working group provided guidance for the prevention and treatment of post transplanted osteoporosis. Below is a summary of these recommendations:

Pretransplantation measures
- All transplant candidates should be assessed for osteoporosis & fractures and, if indicated, treated before transplantation. The evaluation should include:
  - Fracture history.
  - DXA testing of the spine and hip and Spine radiographs or VFA.
  - Estimation of BTM.
  - Biochemical testing to identify secondary causes of osteoporosis.
  - Address lifestyle factors such as immobilization, smoking and alcohol abuse.
  - Assess current medications to minimize use of those negatively affecting bone health.
- The FRAX tool needs further evaluation in organ transplant recipients.
- TBS has been used to improve fracture risk prediction in the setting of renal transplant, it has not yet been validated for other organs.
- HR-pQCT has yielded important information about effects of organ transplantation at individual bone compartments; however, lack of large-scale availability prevent its wide implementation at this time.
- For kidney transplant, a bone biopsy pretransplant may help treatment decisions post-transplant by identifying the specific type of the underlying bone disease, and thus the rate of bone turnover.

Posttransplantation measures
- Use lowest possible doses of glucocorticoids and taper and withdraw as early as possible.
- Supplementation with calcium and vitamin D to maintain serum levels above 50 nmol/l seems reasonable.
- In kidney transplant recipients where 1α-hydroxylation may be impaired, alfacalcidol or calcitriol may be indicated.
- Limited data on bisphosphonates and scarce data on denosumab have revealed some efficacy in terms of BMD improvement. Thus, these agents could be considered as treatment options.
- There is not enough data to support the use of osteoanabolic agents, hormone replacement therapy or SERMs to date.
- Lacking solid evidence, it is even more important to apply the principal of individualized treatment.

Comparison of the clinical effectiveness and safety between the use of denosumab vs bisphosphonates in renal transplant patients, H. McKeen et al, Osteoporos Int (2020) 31:973–980

In a retrospective chart review of 85 renal transplant patients aged 19–88 years, treated with denosumab (DMAb) or bisphosphonate (BP) for an average duration of 3.4 years, McKeen et al compared BMD measures between treatment groups. At final follow-up, DMAb resulted in significantly greater increases in LS and hip BMD compared to BP, thus providing evidence for the efficacy of DMAb treatment in renal transplant patients.
Exercise and bone health

The Associations Between Seven Different Types of Physical Activity and the Incidence of Fracture at Seven Sites in Healthy Postmenopausal UK Women, Armstrong et al, J Bone Miner Res 35(2), 277-290

In a population based prospective study of 371,279 postmenopausal women (mean age 59.8 years), Armstrong et al examined risk of fracture at seven different sites associated with seven different types of physical activity including walking, cycling, gardening, doing housework, yoga, dance, and sports club activities. During an average follow up of 12 years, gardening more than 1 hour/week associated with a lower risk of upper limb fractures (RR = 0.91; 99% CI, 0.86 to 0.96), whereas for fractures of the lower limb (hip included) there was no significant heterogeneity by type of activity, with significant approximately 5% to 15% reductions in risk associated with most activities, except cycling. For hip fractures, there was a significant 15% to 20% reductions in risk associated with walking for 1 hour/day and participating in yoga and sporting activities. Physical activity is a modifiable risk factor for fracture, but the effects differ between different types of activities and different fracture sites.

Effect of Aerobic or Resistance Exercise, or Both, on Bone Mineral Density and Bone Metabolism in Obese Older Adults While Dieting: A Randomized Controlled Trial. Armento-Villareal et al, J Bone Miner Res, 35 (3), 430-439

Weight loss therapy of older adults with obesity is limited by weight loss–induced decrease in BMD. In a randomized controlled trial, Armento-Villareal et al performed a head to head comparison of aerobic or resistance exercise, or both, during matched ~10% weight loss in 160 older adults with obesity. After 6 months of intensive lifestyle interventions, BMD of the hip decreased less in the resistance group (~0.7%) and combination group (~1.1%) than in the aerobic group (~2.6%), (p = 0.001 for between-group comparisons). The decline in whole body mass and serum leptin were the independent predictors of the decline in hip BMD (multiple R = 0.45 [p<.001]). This concludes that both resistance and combined aerobic and resistance exercise can prevent better bone loss during weight loss therapy of older adults.
You can now book your online video visit with an expert faculty from the Calcium Metabolism and Osteoporosis Program through MyChart.

For more information, please call 01-350 000 or 1545 ext. 7470 or visit www.myaubhealth.aubmc.org

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WE’VE GOT YOUR BACK!
PREVENT AND TREAT OSTEOPOROSIS BY BOOKING YOUR ONLINE VIDEO VISIT TODAY.

STAY HOME; STAY SAFE

The Calcium Metabolism and Osteoporosis Program (CaMOP) launched its faculty TeleMedicine visits early April. This is in alignment with the AUBMC initiative to facilitate remote care, as best applicable, for patients who elect to do so to minimize hazard exposures caused by COVID-19. Online visits can be booked with all CaMOP faculty, namely Dr Asma Arabi on Mondays, and Dr Marlene Chakhtoura on Tuesdays, and Dr Ghada El-Hajj Fuleihan on Wednesdays, by contacting our clinic staff on 01-350000 ext 7470, or through MyChart. On-site visits are also available for those who elect to do so, with Drs Arabi and Chakhtoura.

https://www.aub.edu.lb/fm/CaMOP/Pages/default.aspx