



## Secondary prevention of fragility fractures: where do we stand during the COVID-19 pandemic?

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Fragility fractures (FF) represent a public health issue affecting 30% of women and 20% of men aged > 50 years whose incidence is expected to increase by 2050 [1]. After a FF, patients are five times more likely to experience a second fracture within the next 2 years and starting effective treatment and preventive strategies in a timely fashion could be key to the prevention of these secondary fractures. FFs are associated with serious adverse events such as the re-fracture risk, impairing the quality of life, and mortality. Patients undergoing a fragility fracture are at imminent risk of a subsequent fractures, defined as the increased risk of fracture in the next 12–24 months [2]. This has to be considered especially in the light of the coronavirus disease 2019 (COVID-19) pandemic [3]. COVID-19 is still a main worldwide public health threat, causing globally 2.107.554 deaths by January 24th, 2021 (<https://covid19.who.int/>). Bone fragility should be taken into high consideration in COVID-19 patients. Inflammation, immobilization, hospitalization, and home isolation are all factors promoting bone and muscle loss, thereby increasing the risk of falls, fractures and death especially in the elderly [3, 4]. Consequently, patients with

COVID-19 should be considered at imminent risk of fracture and early detection of FFs risk is of paramount importance.

Although FF are considered important warning signs for subsequent fractures at any other skeletal sites, the secondary prevention of FFs is still mostly neglected. The prevention of FF may be considered even more important than treating the first FF that occurs. It is unclear why this gap is still waiting to be culturally and practically filled, especially knowing that the standardized mortality ratio by age is significantly increased after the major types of osteoporotic fractures. It is highly likely that osteoporosis (OP)-related fractures are still undertreated due to misinformation on adequate approaches to patient care and discrepancies existing between treatment guidelines. To overpass such inadequacies, the multitask force of the American Society for Bone and Mineral Research (ASBMR) has recently provided clinical recommendations for optimal prevention of secondary fracture among people aged > 65 years with hip or vertebral fractures [5] (Fig. 1). Clinical questions raised by authors and treatment recommendations are even more important than in the past, given the challenges and restrictions for bone fragility care imposed by the pandemic.

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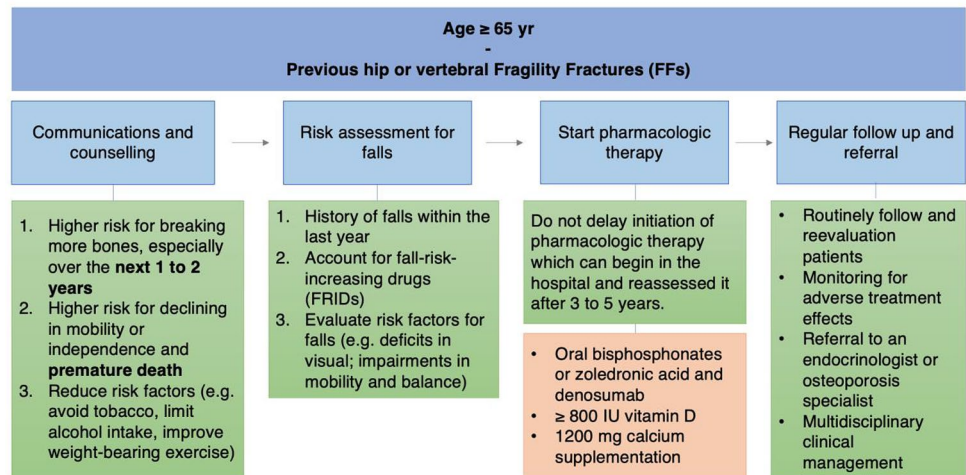
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### Which are the main clinical practice problems impairing an appropriate secondary prevention of fragility fractures?

Low bone mass is almost always the underlying cause for increased bone fragility. In clinical setting, BMD by DXA has a strong predicting value on fracture risk, with a single measurement being able to predict hip fracture risk for up to 25 years [6]. Nevertheless, low bone mass is often ignored or left untreated by primary care and specialist physicians.

Another clinical practice problem is that treatments for OP commonly suffer from a low adherence to anti-fracturing

**Fig. 1** ASBMR recommendations for secondary prevention of fragility fractures [5]



therapies with a low medical possession ratio within the first year of treatment lower than 80% [7]. In particular, in older people, co-morbidity and polytherapy influence the poor compliance.

According to ASBMR task force, it should be recommended that a better knowledge of the fracture risk can improve the adherence to treatment.

It results in crucial importance of communicating with patients on fracture risk, mortality and morbidity associated with FF, and the benefit of fracture risk reduction, either by pharmacological or not pharmacological approach. The GLOW study reported that more than 60% of the investigated women did not know that they were at increased risk of fracture, though they had  $\geq 2$  risk factors, while 10% of women thought of being at increased risk of fracture while they were not [8]. The misinformation on fracture risk together with alarming reports about osteoporosis medications in the news media [9] resulted in an important treatment gap, with only a minority of patients women eligible for treatment, receiving adequate anti-OP medications.

Finally, fracture risk assessment remains another neglected issue in clinical practice.

Since decrease in height could be the first sign of asymptomatic vertebral fractures in the elderly regular height measurement should be a part of the physical examination of every patient assessed for fracture risk or OP. Importantly, before starting a pharmacological treatment of OP or switching to a different drug category, appropriate clinical and biochemical evaluation should be recommended to rule out any secondary causes of OP.

## Clinical recommendations of the ASBMR task force

There is a need for increased communication with the patients, especially regarding their own fracture risk, fracture-associated mortality and morbidity, and fracture risk reduction. Patients should be also strongly encouraged to participate in regular physical loading exercises and fall prevention strategies, also avoiding tobacco and consuming alcohol in moderation. Lack of communication with the patient's primary care provider regarding the occurrence of fracture has been regularly identified as one of the key barriers to secondary prevention of fractures.

An accurate fall risk assessment, with particular attention to fall history, should be repeated at regular intervals, not by limiting it to the only basal visit. Improvement of mobility, gait or balance disorders should be considered and the use of medications that increase the fall risk should be minimized in this group of patients. Because of the prolonged immobilization of COVID-19 patients, home isolation imposed by the lockdown, the high risk of muscle loss, falls assessment is particularly important during the pandemic. Alternative ways rather than in person assessment should be implemented.

Pharmacological therapy for OP should be offered to all patients  $> 65$  years after hip or vertebral FFs. Treatment does not need to be delayed to obtain a BMD since the risk of subsequent fracture is significantly elevated for the patients at all BMD levels. Oral pharmacological treatment

for hip or vertebral fracture are generally safe and can be initiated while the patient is hospitalized. As suggested by Conley et al. [5] intravenous and subcutaneous injections can be started after 2 weeks of the postoperative period due to concerns of hypocalcemia and flu-like symptoms after zoledronic acid infusion.

Vitamin D is a key element in bone health maintenance, and it is necessary for patients with hip and vertebral FFs. Potential benefits on the immune system, support the recommendations of achieving optimal vitamin D status in COVID-19 subjects [10–12], with the goal of preventing also falls, frailty and fractures either during and after hospitalization [4]. Importantly, COVID-19 severity is increased in subjects with visceral obesity which are often characterized by low vitamin D [13].

First-line pharmacologic treatments include oral bisphosphonates (BPs) such as alendronate and risedronate which are usually well tolerated and have a low cost. If oral BPs are not well tolerated, intravenous zoledronic acid or subcutaneous denosumab could be considered. Anabolic medications could be also considered for patients at high risk for fractures especially vertebral fractures. The optimal duration of pharmacotherapy is not well defined in the literature. It has been suggested that the treatment with BPs need to be reassessed after 3–5 years [14]. The interruption of denosumab without starting another antiresorptive medication should be avoided since it could lead to a rapid bone loss while an antiresorptive treatment is recommended after anabolic medications use. OP is a lifelong condition and after hip or vertebral fractures patients should be regularly followed for identifying barriers to adherence to the treatment plan. During the pandemic, anti-osteoporotic treatment should not be neglected and ASBMR guidelines should be followed for single treatments [15]. Tele-health solutions should be in place to ensure timely follow-up on reassessing fall risk and monitoring the adverse effects and efficacy of treatment.

Referral to an endocrinologist or OP specialist should be considered also through an online consultation in patients who experience bone loss or fractures while on OP treatment or in patients who have other comorbidities that complicate the management.

Optimal management of patients with FFs would occur in a multidisciplinary clinical setting. *Fracture Liaison Service* (FLS) as a multidisciplinary case management approach has been reported by many as one of the most effective organizational approaches for secondary fracture prevention. It has been reported as cost effective and even cost saving in several clinical settings. FLS typically consists of a small group of healthcare providers that identify, evaluate, provide treatment recommendations, and routinely follow-up patients with FFs. In the last year, many of the FLS have been closed to give space and resources to COVID-19 patients. Given the simple and costless organization of FLS, health care

providers should prioritize this model and guarantee access to patients also by innovative virtual approaches.

## Conclusions

Clinical management of patients with osteoporosis or FF is still complex and neglected. The importance of obtaining an appropriate treatment right after FF diagnosis, a clinical follow-up and adherence to treatments is strongly recommended. This becomes particularly important in the COVID-19 era, facing a lack of osteoporosis clinics, rehabilitation centers, difficult access to hospitals and the practical gap in preventing FFs [3]. Patients should regularly receive their anti-osteoporotic treatments and having follow-up also by a tele-health approach. In this scenario, maintaining optimal vitamin D levels will support bone and muscle health especially in elderly patients [4].

The continuity of care for patients with FF should be guaranteed as pre-requisite for treatment success, but also to obtain a positive outcome on fracture treatment, survival rate and recovery.

## Compliance with ethical standards

**Conflict of interest** The authors declared no conflict of interest.

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