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Joint recommendations on the management of patients with osteoporosis and/or fragility fractures during and after the pandemic due to COVID-19 of SEIOMM, SEFRAOS, SER, SEMI, SEGG, SEMG, SEMERGEN and SEEN

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Introduction

The COVID-19 pandemic has impacted the healthcare of patients with osteoporosis and fragility fractures[1].

Some strategies aimed at protecting against the spread of the virus, such as social distancing, have brought about changes in care models that are been homogeneous in all areas.

The need to limit access to health centers and infections has imposed a system of telemedicine[2] which offers many advantages to professionals and users and has become a key assistance tool to ensure social distancing. Likewise, telematic consultation can have additional applications in routine clinical practice, as it allows medical professionals to attend to patients with displacement problems and efficiently solve doubts and/or problems related to treatment, so it could be especially useful to control therapeutic compliance. However, in order to advance more effectively and secure telematic attention, always seeking the greatest agility in the responses, it should be protocolized.

Based on the joint recommendations of the American Society for Bone and Mineral Research (ASBMR), American Association of Clinical Endocrinologists (AACE), European Calcified Tissue Society (ECTS) and National Osteoporosis Foundation (NOF)[3], a multidisciplinary group of experts from SEIOMM, together with those of other scientific societies (SEFRAOS, SER, SEMI, SEGG, SEMG, SEMERGEN and SEEN), has prepared this docu-

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ment to establish a series of recommendations in the diagnosis, treatment and follow-up of patients with osteoporosis and/or osteoporotic fragility fracture during and after the COVID-19 pandemic in Spain.

Healthcare recommendations

First visit

The first outpatient visit of patients with osteoporosis and/or fragility fractures, both in hospital and in primary care, should preferably be done in person if health circumstances permit. If the face-to-face visit is not possible, it should be carried out electronically (telephone and/or videoconference) without delaying patient care, trying to schedule a face-to-face visit as soon as possible.

In patients with fractures of the femur, vertebra, pelvis and humerus who require hospital admission, it is advisable to carry out the first clinical evaluation in the same admission, as well as to establish the primary care link prior to discharge, to agree on treatment and ensure follow-up and adherence through liaison staff or case manager, when possible.

Follow-up visit

Follow-up can be carried out in person or telematically (telephone/videoconference), depending on the existing health recommendations at the time and the patient's profile.

Telematic follow-up visits should be systematic and protocolized[4], and scheduled in pre-selected patients in advance, after reviewing the clinical history by the assigned physician, whenever possible.

Profile of candidate patient for the telematic consultation:

- Patient previously assessed, in at least one previous face-to-face visit.
- That does not present signs or symptoms that require a directed physical examination.
- That does not present auditory, cognitive or functional problems (unless there is the possibility of another cohabitant interlocutor).
- That does not express refusal to a telecare model.
- That they have access to a fixed or mobile telephone line.
- That present displacement problems.

The steps to follow in the telematic consultation would be:

1. Initial contact with the patient, through administrative staff/case management days before the consultation: locate the patient, inform the patient of the day and time, give a series of recommendations for which visit is more fluid: arrange of the treatment carried out, family member of help in case it is necessary, remember to carry out complementary tests prior to the visit if necessary.
2. Telematic medical consultation using the same system as in the face-to-face visit.
3. Care circuit: request for tests or new consultation if appropriate.
4. Patient flow: through administrative/case management staff.

Recommendations in complementary tests

Lab tests

To reduce the number of trips to a health center, the essential laboratory procedures should be carried out.

It is recommended to perform analytics in the first patient evaluation, whenever possible, prior to the start of treatment, especially if a drug is used parenterally (zoledronic acid, denosumab, teriparatide or romosozumab *).

In the follow-up of the patient, it is recommended to carry out the analytics that, depending on the characteristics of the patient and his pathology, are necessary at the physician's discretion.

Imaging tests

Imaging tests (radiography, computerized axial tomography, magnetic resonance imaging or scintigraphy) should be restricted to cases in which the presence of an osteoporotic fragility fracture or other processes that require a medical history and/or physical examination is suspected differential diagnosis.

In the patient's first visit it is convenient to check if there are chest or spinal radiographs performed previously to investigate the presence of previous vertebral fractures.

Bone densitometry should be restricted to those cases in which it is necessary for making a therapeutic decision. In all other situations, when sanitary circumstances are not favorable, its performance could be postponed.

Recommendations in non-pharmacological treatment

It is recommended, especially during periods of confinement or restricted mobility, to encourage patients to engage in daily, weighted physical exercise, such as walking around the house or going up and down stairs.

Efforts should be made to avoid falls, controlling polypharmacy, and following the recommendations set out in the consensus document on the prevention of frailty and falls in the elderly of the Ministry of Health[5].

The patient should be insisted on avoiding toxic habits such as smoking or drinking alcohol, maintaining a healthy diet with sufficient protein and calcium intake, without forgetting adequate sun exposure.

Recommendations in pharmacological treatment

General recommendations

Care should be taken to not delay the initiation of fracture prevention pharmacological treatment (antiresorptive or anabolic) in patients at high risk of fracture, especially in those who have suffered a recent fracture (imminent risk of fracture).

There is no evidence osteoporosis treatment increases the risk or severity of COVID-19 infection or alters the course of the disease[6]. However, some thromboembolic complications have been described in infected patients[7,8], so it is prudent to avoid the prescription of estrogens or SERMs (raloxifene, bazedoxifene) in these patients or to temporarily interrupt their administration during COVID-19 infection.

It is recommended, both at the time of the first prescription and at all follow-up visits (in person or online) to remind the patient of the importance of good adherence to treatment.

In patients with low calcium intake in whom it is not possible to increase it through diet, it is recommended to administer supplements, without exceeding 1,200 mg/day.

Patients with osteoporosis and a 25-hydroxyvitamin deficiency or at risk of deficiency should receive treatment with cholecalciferol or calcifediol, with the aim of

not marketed in Spain at the time of writing up this document.

maintaining levels between 30-50 ng/ml[9].

Although there is insufficient evidence to recommend vitamin D treatment for the prevention or treatment of COVID-19, several published studies suggest a better course of the disease in patients who achieve 25-hydroxyvitamin D levels >30 ng/ml[10,11].

Specific recommendations for subcutaneous injectable treatments

Denosumab: Good adherence must be ensured and administration discontinuation or delay should be avoided, as a "rebound" effect may occur after discontinuation, with a marked increase in bone turnover, accelerated loss of bone mineral density[12,13] and in some patients, an increased risk of multiple vertebral fractures[14]. Therefore, it is recommended to confirm the patient's adherence to treatment at each visit.

Teriparatide and romosozumab: Keep in mind the importance of good adherence and correct administration of treatment at each visit.

It is convenient to remember that all subcutaneous treatments for osteoporosis have specific patient support programs for each drug through which they can receive information for its correct administration.

When health and/or patient circumstances make it difficult to administer denosumab or teriparatide, it is recommended to assess the possibility of self-administration assisted by tutorial videos. If this is not possible, and depending on the characteristics of the patient and the possibilities, it is recommended to administer an infusion of zoledronic acid as soon as possible[15] or to prescribe treatment with oral bisphosphonates (alendronate or risedronate).

Specific recommendations for intravenous treatments for osteoporosis (zoledronic acid)

It should be remembered that treatment with zoledronic acid may cause, mainly after the first dose, a flu-like side effect that could be confused with mild COVID-19 symptoms.

In patients at high risk of fracture, especially those with a recent fracture, it is recommended not to delay the initiation of zoledronic acid treatment. In cases where the administration of a first dose of zoledronic acid is not possible due to health circumstances, it is recommended to prescribe denosumab or oral bisphosphonates based on the characteristics of the patient and their risk of fracture (table 1).

Since bisphosphonates have a residual effect that is maintained for months, or even years, on the skeleton after their administration[16-19], the successive administration of zoledronic acid could be delayed for a few months when health circumstances make it difficult for the patient to access the hospital. However, if this situation is prolonged, it is advisable to assess the prescription of oral bisphosphonates or denosumab, depending on the characteristics of the patient and their risk of fracture.

Table 1. Recommendations for the administration of the vaccine against COVID-19 according to the treatment for osteoporosis[3]

Treatment	Recommendations
Oral bisphosphonates	Continue your administration
Intravenous bisphosphonates	Space 7 days between administration and the vaccine
Denosumab	Space 4-7 days between administration and the vaccine. If both are administered in a shorter period of time, use the contralateral arm or an alternative site
Teriparatide	Continue its administration
Romosozumab*	Space 4-7 days between administration and the vaccine
Raloxifene/Bazedoxifene	Continue administration

* not marketed in Spain at the time of writing up this document.

Rehabilitation treatment

The home confinement imposed during the pandemic in most countries has led to a change in routines and a decrease in physical activity of our elderly, which translates into a loss of strength and muscle mass and, consequently, in a greater risk of falls and fractures[20].

Thus, it is essential to recommend the patient carry out regular physical activity adapted to each situation. It will be important to provide information to be able to perform this activity at home, in the event that the authorities indicate periods of confinement.

Recommendations of physical activity for frail older people and those at risk of falls

The most beneficial type of physical exercise in the frail elderly is the so-called multicomponent training, which combines strength, endurance, balance and gait training and is the one that has been shown to be the most effective in the recovery/improvement of functional capacity. The Vivifrail Multicomponent Physical Exercise Program (www.vivifrail.com) tries to provide the necessary knowledge for the prescription of physical exercise in the prevention of frailty and the risk of falls in the elderly[21].

This program makes it possible to assess the degree of frailty and the risk of falls, and provides recommendations for physical exercise adapted to the condition of the person evaluated. It also has graphic and visual material on directed physical activity to carry out at home.

Recommendations for the control in the evolution of the fracture consolidation

For the clinical and radiological evolutionary control of the fracture consolidation, we must follow the specific recommendations of the traumatologist. In general, follow-up visits may be carried out in person or online depending on the patient's profile, the type of fracture, the type of treatment carried out, the need or not to carry out a radiological control and the existing health recommendations in the moment. We recommend that follow-up visits are always in person in those cases in which problems with wound healing or infection, joint stiffness or other complications related to the fracture are suspected[22].

Recommendations for the functional recovery of the patient who has suffered a fracture

In fragile patients who have suffered a fracture, mainly the hip, it is essential to continue with a rehabilitation program with the aim of improving functionality, and if possible, reaching the situation prior to the time of the fracture.

Among the tele-rehabilitation platforms there is the ACTIVEHIP+[23] educational program. This program offers advice and training to patients and caregivers to improve functional recovery, favoring the independence of the patient to carry out their daily activities and helping to improve their quality of life in general after having suffered a hip fracture. It is based on the implementation of a multicomponent exercise program and occupational therapy through the online platform and an app.

Conflict of interests: The authors declare no conflict of interest.

Decalogue of recommendations for the management of patients with osteoporosis and/or frailty fractures during and after the COVID-19 pandemic

1. **It is recommended that the first outpatient visit, both in hospital and in Primary Care, be preferably in person, if health circumstances allow it.**
2. **It is recommended that follow-up telematic visits be scheduled in pre-selected patients, after reviewing the medical history by the responsible physician, whenever possible.**
3. **It is recommended to carry out the minimum laboratory and imaging tests necessary for a correct diagnosis, in order to reduce the number of trips to a health center.**
4. **It is recommended, especially during periods of confinement or restricted mobility, to encourage patients to carry out daily physical exercise with load, avoid toxic habits and take appropriate measures to reduce falls at home.**
5. **It is recommended to prescribe cholecalciferol or calcifediol, if the patient has a 25-hydroxyvitamin D deficiency, due to the beneficial effects on his bone pathology and the possible effect on the evolution of the COVID-19 infection.**
6. **It is recommended not to delay the start of antiresorptive or anabolic treatment, especially in patients with high or very high risk of fracture.**
7. **It is recommended to insist on adherence to treatment, particularly with teriparatide and denosumab, due to the adverse effects of their discontinuation, especially denosumab.**
8. **It is recommended not to delay the first administration of zoledronic acid, either due to discontinuation of denosumab or for any other reason.**
9. **A time interval is recommended between the administration of denosumab, zoledronic acid, or romosozumab and the COVID-19 vaccine. In the case of zoledronic acid, it should also be taken into account that its administration can produce a flu-like syndrome that could be confused with the symptoms of COVID-19 infection.**
10. **It is recommended that patients who have suffered a hip fracture follow a rehabilitation program, with the aim of improving functionality, with access to tele-rehabilitation platforms.**

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