POINT OF VIEW

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Osteoporosis and fracture risk assessment: improving outcomes in postmenopausal women

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Osteoporosis is a skeletal disease characterized by impaired bone density, bone mineral density (BMD), and bone strength, resulting in bone fragility and an increased risk of fractures[1]. A fracture is the worst outcome for patients with osteoporosis, as it increases morbidity and mortality in addition to increasing the risk of new subsequent fractures. The main cause of osteoporosis in women is estrogen deficiency secondary to menopause[2,3]. Osteoporosis has a high prevalence and a social and financial impact. The prevalence of the diagnosis of osteopenia in postmenopausal women was present in 30–56.5% of the population, and osteoporosis enters the range of 14.7–43.4%[4]. Osteoporosis can lead to a major impact on public health, such as hospitalizations, surgeries with prostheses, temporary or permanent loss of mobility, and death[2,3].

Although BMD is a strong predictor of fracture risk, there are patients who may fracture even without presenting osteoporosis in the bone densitometry exam, making it necessary to evaluate risk factors other than bone density. In this context, the FRAX (Fracture Risk Assessment Tool) tool brings together other risk factors for fracture prediction independent of BMD, such as the presence of previous fragility fracture, hip fragility fracture in the parents, current smoking, use of glucocorticoids, rheumatoid arthritis, secondary osteoporosis, and use of three or more units of alcoholic beverage per day[1-4].

Interestingly, FRAX is an algorithm that analyzes all clinical risk factors together and finally calculates the absolute risk of fracture in 10 years. Patients diagnosed with osteoporosis or those at high risk of fracture by FRAX deserve drug treatment targeting bone mass gain and fracture prevention. Among the drug strategies are anti-resorptive drugs (bisphosphonates and denosumab) and anabolic agents (teriparatide and romosozumab), which must be associated with other measures, such as physical activity, calcium intake, preferably in the diet, and supplementation of vitamin D[2].

The prevalence of osteoporosis increases with age, with a consequent increase in the number of fractures, either due to worsening of the bone structure, with thinning of the cortical bone, reduction of the trabeculae, and alteration of the bone microarchitecture, or due to the increased risk of falls, reduced lean mass, impairment of proprioception, and decreased visual acuity, among other factors. Osteoporotic fractures are those due to fragility, that is, low impact. Fragility fractures may be asymptomatic, mostly when occurred in the vertebral bodies with wedging, leading to height loss and dorsal hyperkyphosis[5].

Annually, almost 9 million fractures occur worldwide due to osteoporosis, which corresponds to an osteoporosis-related fracture every 3 s, and of these fractures, 1.6 million are hip fractures. The world estimate is that there are about 500 million people with osteoporosis, predominantly women, with an estimated fracture resulting from osteoporosis occurring in one in three women over 50 years and one in five men in the same age group[5].

BMD is directly related to fracture risk. The loss of 10% of BMD in the spine is associated with twice the risk of fracture, and the same loss of BMD in the hip leads to an increase in the risk of fracture by two and a half times. A previous fracture increases the risk of a new fracture by 86%, mainly in the subsequent 2 years. Despite the financial cost, morbidity, and mortality associated with osteoporosis, evidence shows that up to 80% of women with fragility fractures are not diagnosed or treated for osteoporosis[5].

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Assessing risk factors is a wise way to optimize resources for the best possible screening scheme. When the issue is fracture and refracture, the concept of the patient at imminent risk of fracture comes into play, a well-established situation whose intervention will be of great importance in the short term. In this concept, we have bone-related factors (mainly osteoporosis) and factors associated with falls, including risks during fracture rehabilitation. Patients at imminent risk of fracture are postmenopausal women who have had a previous fracture in the last 2 years, patients who already have a diagnosis of osteoporosis and start using glucocorticoids, and frail elderly people with a history of frequent falls, including those with neurological diseases or using psychoactive medications[5,6].

In Brazil, the estimated cost of fractures related to osteoporosis in 2018 was 310 million dollars, with 61% of this cost attributed to lost productivity and 19% to hospitalization (Figure 1). In a study involving four countries in Latin America, including Brazil, it was estimated that only 24% of patients with osteoporosis-related fractures received some type of drug treatment[7,8].

To improve people's health by reducing economic and social costs, multidisciplinary management, prevention of osteoporosis, as well as its active search, population screening with various diagnostic tools and its secondary prevention are urgent in global public health[5].

The first tool to assess fracture risk due to bone fragility is the clinical history. A good anamnesis makes it possible to identify classic risk factors as well as to suspect secondary causes that may contribute to a future fracture. BMD, usually performed by dual-energy X-ray absorptiometry (DXA), known as bone densitometry, is just one of several tools to stratify fracture risk[9]. It is not uncommon to observe in clinical practice patients with fractures outside the osteoporosis range. An important epidemiological study[10] demonstrated that most fractures occur in individuals whose T-score does not meet the conventional definition of osteoporosis (≤-2.5 SD) and therefore has low sensitivity when used alone for screening[10]. Glucocorticoid users, rheumatoid arthritis patients, diabetics, and long-term smokers are examples of patients whose risk of fracture is underestimated by DXA, since they present impairment of bone microarchitecture in addition to reduction of bone density[11].

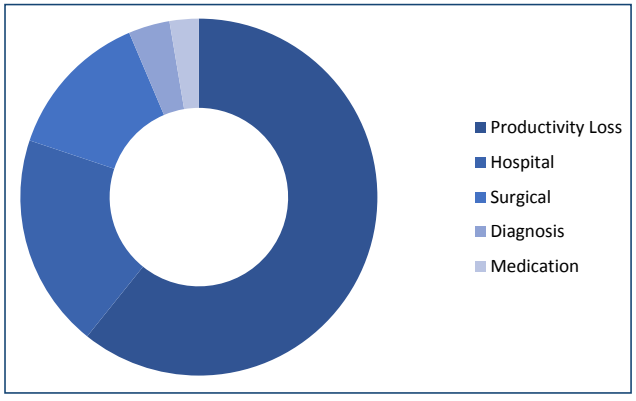

Figure 1. Osteoporosis in Brazil, financial cost. Adapted from Aziziyeh et al.[6].

Considering that not all patients will have easy access to DXA, the FRAX was implemented as a mathematical algorithm that brings together risk factors such as gender, age, use of glucocorticoids, presence of rheumatoid arthritis, current smoking, and history of parents with hip fracture, alone or in association with DXA of the femoral neck region. The FRAX is validated for women and men, 40–90 years old, and estimates in 10 years the absolute risk of hip fracture and major fractures (hip, proximal humerus, forearm, and spine)[9].

FRAX has some limitations; among them, it does not include the presence of diabetes mellitus and it does not distinguish between smoking history or glucocorticoid dose. Thus, in Brazil, it is recommended to adjust the FRAX with the NOGG/UK (National Osteoporosis Guidelines Group) strategy, accessed through the ABRASSO (Brazilian Association of Bone Evaluation and Osteometabolism) website (http://abrasso.org.br/calculadora/calculadora)[9].

In more than 10 years of use, it was observed that the current FRAX also has important limitations because it does not reliably contemplate some patient profiles[12]. In fact, FRAX does not consider diabetic patients, fracture time, or glucocorticoid dose. A patient who has had a recent fracture does not have the same risk as another who fractured more than 5 years ago[13]. A patient who uses glucocorticoids at a dose equivalent to prednisone 5 mg/day does not have the same risk as another who uses doses greater than 15 mg/day[12].

There are also other factors known to increase the risk of fractures, such as chronic falls, chronic kidney disease, or the use of drugs with a negative impact on bone metabolism[14,15]. Interestingly, it is possible to adjust FRAX for certain populations and even for patients who underwent TBS (Trabecular Bone Score), an image method that evaluates the bone microarchitecture of lumbar spine region. Some studies have already shown that the association of DXA and FRAX adjusted by TBS increases the number of individuals at high risk for osteoporotic fractures by up to 30% when compared to DXA alone[11,16].

Therefore, it is essential to consider tools to carry out fracture risk stratification more reliably, as well as evaluating the patient as a whole, considering genetic background, clinical,

and laboratory profiles. Attention should also be given to other environmental factors such as risk of falls, ability to perform physical activity, and nutritional support, as well as socioeconomic context and access to osteoporosis drugs. Figure 2 shows the fracture risk stratification criteria (low, moderate, high, and very high risk) and the main drug strategies for each group[17].

AUTHORS' CONTRIBUTIONS

MOP: Conceptualization, Writing – original draft, Writing – review & editing. **PPAP:** Conceptualization, Writing – original draft, Writing – review & editing. **AML:** Conceptualization, Writing – original draft, Writing – review & editing. **FMFG:** Conceptualization, Writing – original draft, Writing – review & editing. **MAARL:** Writing – review & editing.

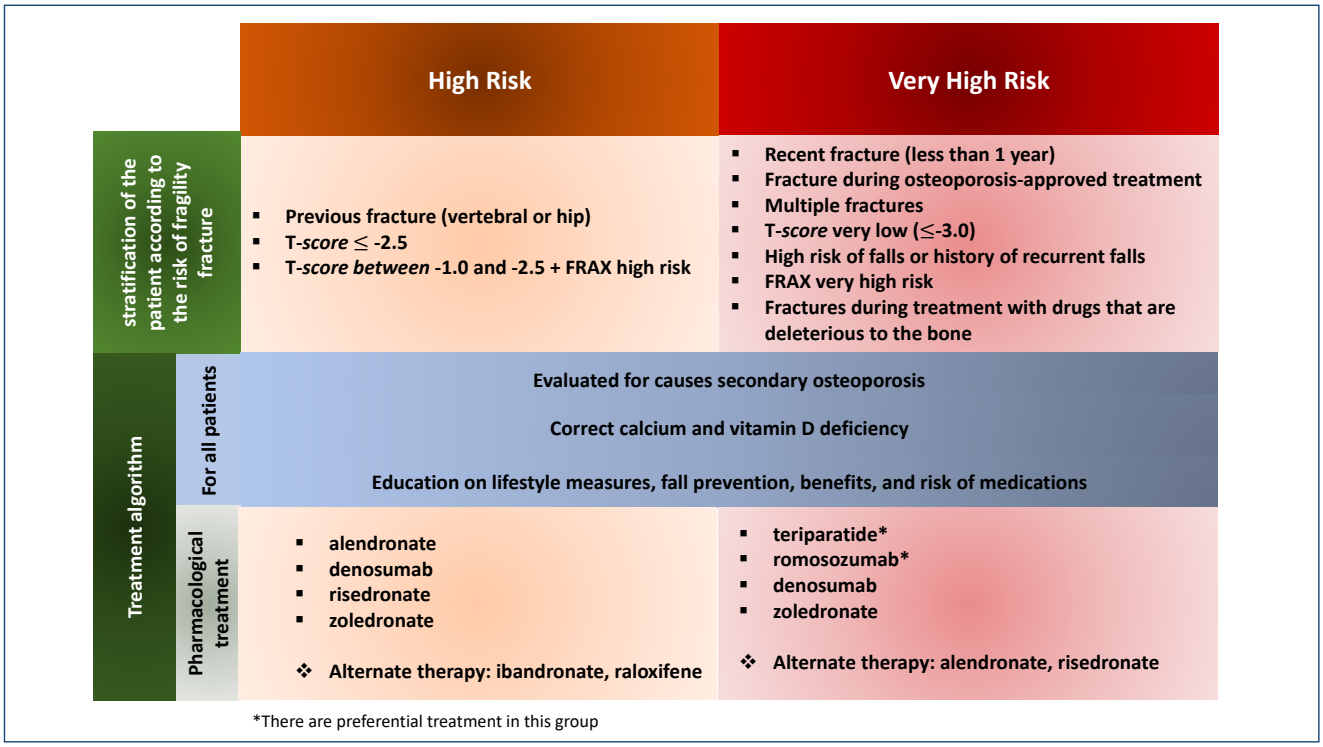

Figure 2. Stratification of the patient according to the risk of fragility fracture and their treatment algorithm in postmenopausal osteoporosis[17].

REFERENCES

1. Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Report of a WHO Study Group. World Health Organ Tech Rep Ser. 1994;843:1-129. PMID: 7941614.
2. LeBoff MS, Greenspan SL, Insogna KL, Lewiecki EM, Saag KG, Singer AJ, et al. The clinician's guide to prevention and treatment of osteoporosis. Osteoporos Int. 2022;33(10):2049-102. https://doi.org/10.1007/s00198-021-05900-y
3. Zerbini CA, Szejnfeld VL, Abergaria BH, McCloskey EV, Johansson H, Kanis JA. Incidence of hip fracture in Brazil and the development of a FRAX model. Arch Osteoporos. 2015;10:224. https://doi.org/10.1007/s11657-015-0224-5
4. Pinheiro MM, Ciconelli RM, Martini LA, Ferraz MB. Clinical risk factors for osteoporotic fractures in Brazilian women and men: the Brazilian Osteoporosis Study (BRAZOS). Osteoporos Int. 2009;20(3):399-408. https://doi.org/10.1007/s00198-008-0680-5
5. International Osteoporosis Foundation. Epidemiology of osteoporosis and fragility fractures. [Internet]. [cited on 2023 Feb 15]. Available from: https://www.osteoporosis.foundation/facts-statistics/epidemiology-of-osteoporosis-and-fragility-fractures.
6. Aziziyeh R, Amin M, Habib M, Garcia Perlaza J, Szafranski K, McTavish RK, et al. The burden of osteoporosis in four Latin American countries: Brazil, Mexico, Colombia, and Argentina. J Med Econ. 2019;22(7):638-44. https://doi.org/10.1080/13696998.2019.1590843
7. Roux C, Briot K. Imminent fracture risk. Osteoporos Int. 2017;28(6):1765-9. https://doi.org/10.1007/s00198-017-3976-5
8. Johansson H, Siggeirsdóttir K, Harvey NC, Odén A, Gudnason V, McCloskey E, et al. Imminent risk of fracture after fracture. Osteoporos Int. 2017;28(3):775-80. https://doi.org/10.1007/s00198-016-3868-0
9. Ribeiro P, Peixoto F, Reis Neto E, Sato E. Manual de reumatologia. 2nd ed. Rio de Janeiro: Guanabara Koogan; 2020. p. 327-39.
10. Barrett-Connor E, Weiss TW, McHorney CA, Miller PD, Siris ES. Predictors of falls among postmenopausal women: results from the National Osteoporosis Risk Assessment (NORA). Osteoporos Int. 2009;20(5):715-22. https://doi.org/10.1007/s00198-008-0748-2
11. Martineau P, Leslie WD, Johansson H, Harvey NC, McCloskey EV, Hans D, et al. In which patients does lumbar spine trabecular

bone score (TBS) have the largest effect? Bone. 2018;113:161-8. https://doi.org/10.1016/j.bone.2018.05.026

12. Kanis JA, Johansson H, Harvey NC, McCloskey EV. A brief history of FRAX. Arch Osteoporos. 2018;13(1):118. https://doi.org/10.1007/s11657-018-0510-0
13. Geel TA, Helden S, Geusens PP, Winkens B, Dinant GJ. Clinical subsequent fractures cluster in time after first fractures. Ann Rheum Dis. 2009;68(1):99-102. https://doi.org/10.1136/ard.2008.092775
14. Kanis JA, Johansson H, Oden A, McCloskey EV. Guidance for the adjustment of FRAX according to the dose of glucocorticoids. Osteoporos Int. 2011;22(3):809-16. https://doi.org/10.1007/s00198-010-1524-7
15. Ahmed LA, Center JR, Bjørnerem A, Bluic D, Joakimsen RM, Jørgensen L, et al. Progressively increasing fracture risk with advancing age after initial incident fragility fracture: the Tromsø study. J Bone Miner Res. 2013;28(10):2214-21. https://doi.org/10.1002/jbmr.1952
16. Silva BC, Broy SB, Boutroy S, Schousboe JT, Shepherd JA, Leslie WD. Fracture risk prediction by non-BMD DXA measures: the 2015 ISCD official positions. Part 2: trabecular bone score. J Clin Densitom. 2015;18(3):309-30. https://doi.org/10.1016/j.jocd.2015.06.008
17. Camacho PM, Petak SM, Binkley N, Diab DL, Eldeiry LS, Farooki A, et al. American Association of Clinical Endocrinologists/American College of Endocrinology Clinical Practice Guidelines for the diagnosis and treatment of postmenopausal osteoporosis – 2020 update. Endocr Pract. 2020;26(Suppl 1):1-46. https://doi.org/10.4158/GL-2020-0524SUPPL