A significant interval decline in bone mineral density in osteopenic patients is not part of the FRAX report

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ABSTRACT

Background: Bone mineral density (BMD), considered to be a gold standard for the diagnosis of osteoporosis, is most commonly measured by dual-energy x-ray absorptiometry (DXA). For patients with osteopenia, the Fracture Risk Assessment Tool (FRAX) incorporates acknowledged other risk factors to assess overall fracture risk and aids in patient management. If the FRAX score in an osteopenic patient predicts a 10-year fracture risk of >20% for a major osteoporotic fracture or >3% for a hip fracture, pharmacologic therapy is indicated. However, FRAX does not include an assessment of a significant decline in BMD over time.

Methodology: Our goal was to determine the frequency with which BMD declines in patients with osteopenia by DXA, but whose FRAX score continues to be below treatment thresholds.

Results: Over a 2-year interval, 1112 (15.6%) of 7133 patients with osteopenia by DXA experienced a significant decrease in BMD but had their FRAX score remain in the range where therapy would by convention not be recommended.

Conclusion: Since a decline in BMD is, by itself, a clinical risk factor for an osteoporotic fracture, FRAX assessment may therefore potentially underestimate true fracture risk if a significant interval decline in BMD is measured.

Keywords: *Osteopenia, DXA, FRAX*

INTRODUCTION

To assess fracture risk assessment and to establish recommendations for pharmacologic intervention, the World Health Organization (WHO) Collaborating Center for Metabolic Bone Diseases developed in 2008 the FRAX algorithm [1]. FRAX is a computer-based tool that calculates fracture probability from acknowledged and quantifiable clinical risk factors to predict the 10-year likelihood for a major osteoporotic fracture and/or a hip fracture. Although FRAX can be used alone, without BMD, it is a more powerful predictor of fracture risk with BMD. In the United States, FRAX tends to be reserved for those with osteopenia, because those whose T-scores are < -2.5 are recommended for treatment because of the major fracture risk conferred by those low T-scores. Also in the United States, among these osteopenic individuals, "intervention thresholds" are set at >20% for major os-

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DOI:10.54235/27382737-2022.v2.1-44. Published online: 5 September 2022

teoporotic fracture and >3% for hip fracture over a ten-year period [2,3]. The FRAX score, thus, aids the clinician in the decision to begin therapy in the setting of an osteopenic patient.

A major limitation of FRAX is that it does not include provision for interval declines in BMD when in fact an interval decline in BMD is by itself a clinical risk factor for fracture [4]. If the decline in BMD, although significant, does not place these individuals in the osteoporotic range, namely < -2.5, current standards of care would not necessarily target them for pharmacological intervention.

The aim of our study was to determine how often a patient who is being monitored by BMD experiences a significant decline in BMD, but by FRAX continues to be in a range where therapy would not customarily be recommended.

MATERIALS AND METHODS

DXA measurements were obtained on a Hologic Discovery C, Apex software version 3.3 (Hologic, Waltham, MA) which was calibrated daily. The calculated precision error (CV) was 1.4% for the lumbar spine (L1 through L4), 2.16% for the total hip, and 2.70% for the femoral neck. The scans were reported according to the World Health Organization classification i.e. normal (T score ≥-1.0), osteoporosis (T-score ≤-2.5) and osteopenia (-1.0 > T-score >-2.5).

Patient databases were used to recognize patients identified as osteopenic from Jan 1, 2018 through Dec 31, 2019 who had the following: 1. prior DXA scan; 2. significant reduction in BMD of one or more of the lumbar spine, total hip, or femoral neck regions; 3. FRAX score that consistently was below the threshold for therapy, < 20% for a major osteoporotic fracture and < 3% for a hip fracture. IRB approval was not required for this study.

RESULTS

In 2018 and 2019, a total of 7,133 patients at our center were identified with osteopenia by DXA. Of these, 1,112 patients demonstrated both a significant decline of BMD in comparison to an earlier DXA at the lumbar spine, total hip, or femoral neck, and a corresponding FRAX score that continued to be below the therapeutic 10-year fracture risk threshold of < 3% for a hip fracture and < 20% for a major osteoporotic fracture. Thus, over this 2-year period 15.6% of osteopenic patients experienced both a significant decline in BMD but still did not meet therapeutic guidelines by FRAX.

DISCUSSION

The FRAX algorithm is a well-validated fracture risk assessment tool that utilizes a set of verified and quantifiable clinical risk factors to calculate the 10-year probability of a major osteoporotic fracture (spine, proximal humerus, hip, forearm), or hip alone, with or without incorporation of the femoral neck BMD. The FRAX tool is most helpful in those whose BMD is not in the frankly osteoporotic range, a level that by itself is sufficient for a recommendation for therapy. For these osteopenic individuals, the National Osteoporosis Foundation in the USA selected a 10-year hip fracture probability of >3% and/or a > 20% major osteoporotic fracture probability as sufficient intervention thresholds [3,5]. The FRAX tool and the recommendations for intervention have been very helpful in the decision-making challenge for the clinician caring for these patients.

The great clinical utility of FRAX, however, is limited because it does not include several other clinical risk factors such as falls [6,7]. This has become a common criticism of the FRAX tool. A low, lean body mass is also associated with a higher fracture risk [8], and again is not incorporated into the FRAX model.

Another major limitation of FRAX is that it does not consider a significant interval decline in BMD which by itself is associated with increased fracture risk [4]. In subjects who experience a significant interval decline in BMD and in whom the FRAX treatment threshold is reached, this is not an issue. But, in subjects who experience a significant interval decline in BMD but in whom FRAX continues to be below the treatment threshold, such interval declines may not be considered with regard to clinical decision-making. In our study, 16% of a large cohort fell into this category. We are not advocating that those patients should be treated, because that decision has to be individualized. However, we do recommend that in such a situation, the DXA report should alert the clinician that because of the significant interval decline in BMD, fracture risk has increased, despite the BMD still being osteopenic and the FRAX score still being in the subtherapeutic range. This approach would provide better direction to the clinician whose further evaluation and judgement would be determining factors as to the next steps.

CONCLUSION

While FRAX is a very useful tool for fracture risk assessment in patients with osteopenia, it fails to

Ներկայացվեց/Получено/Received **13.05.22**: Գրախոսվեց/Рецензировано/Accepted **20.06.22**: Տպագրվեց/Опубликовано/Published **15.09.2022**:

recognize other risk factors such as falls, low lean body mass, and interval losses in BMD. We have shown that significant interval losses in BMD occur in a substantial number of patients whose FRAX scores continue to be below treatment thresholds. However, such interval declines in BMD should be considered in the overall follow up evaluation of the patient. To make this point clearer for the clinician caring for the patient, we recommend providing this information in the formal DXA report that is prepared and disseminated.

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