Published in final edited form as:
Endocr Pract. 2013 ; 19(5): 780–784. doi:10.4158/EP12416.OR.

FRAX Prediction Without BMD for Assessment of Osteoporotic Fracture Risk

Ramesh Keerthi Gadam, MD[1], **Karen Schlauch, PhD**[2], and **Kenneth E. Izuora, MD, MBA**[1]

[1]Department of Internal Medicine, University of Nevada School of Medicine, Las Vegas, Nevada

[2]Department of Biochemistry and Molecular Biology, University of Nevada, Reno, Nevada

Abstract

Objective—To compare Fracture Risk Assessment Tool (FRAX) calculations with and without bone mineral density (BMD) in predicting the 10-year probability of hip and major osteoporotic fractures (MOF).

Methods—A cross-sectional review of patients requiring screening for osteoporosis as part of their routine medical care was conducted. Postmenopausal women and men over 50 years of age who were never diagnosed with osteoporosis or treated with U.S. Food and Drug Administration-approved agents for osteoporosis were included. Height, weight, FRAX questionnaire, femoral neck BMD, and T-score data were obtained. FRAX scores with BMD (*FRAX/BMD*) and without BMD (*FRAX*) were calculated. Subjects were separated on the basis of identical and different treatment recommendations. Fracture risk factors were compared between groups using simple Student's *t* test analysis of numerical variables and Fisher's exact test analysis of binary variables.

Results—Of 151 total subjects, 127 (84%) had identical fracture risk predictions with or without BMD included in the FRAX calculation. Thirty subjects met treatment criteria and 97 did not, but the FRAX prediction was the same with risk factors alone or with risk factors plus BMD. Age was the only risk factor that was significantly different between those with identical and different predictions (median age, 64.42 and 76.25 years, respectively; $P<.001$).

Conclusion—In most cases, FRAX alone provides the same prediction as FRAX with BMD. Younger age is more indicative of an identical prediction.

Introduction

Osteoporosis is a skeletal disorder characterized by compromised bone strength, which predisposes individuals to an increased risk of fracture (1). The World Health Organization (WHO) defines osteoporosis as bone mineral density (BMD) that is ≥2.5 SDs below the

Address correspondence to Dr. Kenneth Izuora, Department of Endocrinology, University of Nevada School of Medicine, 2040 W. Charleston Blvd., Suite 300, Las Vegas, NV 89102. kizuora@medicine.nevada.edu.

Disclosure: The authors have no multiplicity of interest to disclose. This manuscript's contents are solely the responsibility of the authors and do not necessarily represent the official views of the National Institutes of Health (NIH).

The results of this research were presented at the annual meeting of the American Association of Clinical Endocrinologists in Philadelphia, Pennsylvania, May 23-27, 2012.

young-adult mean value (T-score, −2.5 or lower) in postmenopausal women and in men over 50 years of age. BMD with a T-score of −1 to −2.5 is classified as osteopenia (2). According to the National Health and Nutrition Examination Survey (NHANES), approximately 10% of women and 2% of men aged 50 years and above in the U.S. have osteoporosis. In the same age group, about 49% of women and 30% of men have osteopenia (3). Due to this higher prevalence, the total number of fractures is greater in patients with osteopenia than in those with osteoporosis (4).

Relying on BMD alone, a number of patients with osteopenia who are at increased risk for fracture will be missed. The WHO introduced the Fracture Risk Assessment Tool (FRAX) in 2008 for use in estimating the 10-year probability of hip fracture as well as other major osteoporotic fractures (spine, forearm, or humerus) in untreated patients with osteopenia. The tool evaluates risk based on easily obtainable clinical risk factors, such as age, history of previous fractures, long-term glucocorticoid therapy, low body mass index (BMI), family history of hip fracture, cigarette smoking, and excess alcohol intake, with or without information on BMD (5,6). Therapeutic interventions are recommended if the 10-year risk of fractures is more than 20% for major osteoporotic fractures (MOF) and more than 3% for hip fractures.

The aim of our study was to determine if FRAX calculations without BMD (*FRAX*) and with BMD (*FRAX/ BMD*) would produce identical predictions for the 10-year probability of hip fracture and other MOFs. We also assessed whether the predictive value of the FRAX calculation alone is better in subgroups of subjects with certain clinical risk factors.

Methods

This was a cross-sectional study involving patients requiring screening for osteoporosis as a part of routine medical care according to current National Osteoporosis Foundation (NOF) recommendations. Those included in the study were postmenopausal women and men over 50 years of age. Patients diagnosed with osteoporosis or who had received prior treatment for osteoporosis with U.S. Food and Drug Administration (FDA)-approved agents were excluded. After providing informed consent, patients were assessed by the investigator using the FRAX questionnaire for age, race, sex, history of previous fractures, family history of hip fracture in a parent, glucocorticoid use (equivalent to ≥5 mg of prednisolone for ≥3 months), current smoking, rheumatoid arthritis, risk for secondary osteoporosis (history of type 1 diabetes mellitus, osteogenesis imperfecta, long-standing untreated hyperthyroidism, menopause at <45 years of age, chronic liver disease, long-standing malnutrition), and alcohol intake (≥3 units/ day). Height and weight were measured by the investigator using professional medical scales. Femoral neck BMD and T-score data were collected following dual-energy X-ray absorptiometry (DXA) examination. The DXA examinations were carried out at one location using the same instrument (Hologic Upgrade Discovery™ QDR® Series, Bedford, MA).

FRAX/BMD and *FRAX* prediction values were calculated based on a patient's risk at the time of the DXA examination (Fig. 1). Subjects were separated into one group if they received identical treatment recommendations from FRAX calculations with and without BMD and

another group if they received a different treatment recommendation when BMD was included in the FRAX calculation. Numerical variables for each group were compared using a simple Student's *t* test; binary variables were compared using Fisher's exact test. All analyses were performed using the statistical programming language R (cran.r-project.org/), version 2.15.0.

Results

Of a total of 950 subjects screened, 151 met our inclusion criteria and were recruited for the study. Of these, 145 (96%) were women, 86 (57%) were Caucasian, 32 (21%) were African American, 19 (12.6%) were Hispanic, and 14 (9%) were of Asian origin (Fig. 2). The subjects ranged in age from 44 to 89 years. Twelve subjects were between 44 and 50 years of age, 32 were between 51 and 60 years of age, 54 subjects were between 61 and 70 years of age, and 53 subjects were over age 70.

We found that *FRAX* and *FRAX/BMD* produced identical fracture risk predictions for 127 of 151 subjects (84%) (Fig. 3). Of these 127 subjects, 30 met the NOF treatment threshold criteria while 97 did not when using the FRAX tool to calculate their 10-year fracture risk. The inclusion of BMD in the FRAX calculation did not result in a different prediction for these 127 subjects. Of the 24 subjects (16%) for whom BMD inclusion resulted in a different FRAX treatment recommendation, treatment was recommended for only 2 subjects (1.32%) who were not identified as requiring treatment by the *FRAX* calculation. The *FRAX* calculation recommended treatment for 22 subjects (14.6%) who were not identified as requiring treatment by the *FRAX/BMD* calculation.

The only risk factor that differed significantly between subjects with identical and different treatment predictions was age ($P<.001$) (Fig. 4). The median age of the 24 subjects who received different predictions was 76.25 years (SD, 6.46 years), whereas the median age of the 127 subjects who received identical predictions was 64.42 years (SD, 10.18 years).

No significant differences between groups were found for BMI, T-score, and femoral neck BMD as determined by Student's *t* test ($P = .36$, .8, and .74, respectively). None of the binary variables showed statistically significantly differences: gender ($P = 0.59$), history of previous fracture ($P = .484$), parent fracture ($P = 1$), smoking ($P = .53$), steroid use ($P = .214$), rheumatoid arthritis ($P = .58$), osteoarthritis and secondary risk factors ($P = .81$), and alcohol use ($P = .59$) (Table 1).

Discussion

The FRAX tool is recommended for use in patients with osteopenia to identify those at high risk for osteoporotic fracture so they can be treated with FDA-approved agents (7). Current guidelines recommend screening of postmenopausal women over 65 years of age and younger postmenopausal women with risk factors for osteoporosis with a DXA scan (8). With FRAX, treatment is recommended if the 10-year risk is ≥20% for MOF and/or ≥3% for hip fractures in patients with osteopenia (9). Because BMD data may not always be available, it was important to determine if *FRAX* alone is an accurate fracture prediction tool. There has been recent emphasis on increasing the interval between the first and follow-

up DXA scans in postmenopausal women. This is based on the finding that in most women with normal BMD or mild osteopenia (T-score greater than −1.5), it takes at least 15 years for osteoporosis to develop (10). Also, the cost of screening using a DXA scan in every woman after the age of 65 would impose a significant healthcare financial burden. For patients with limited access to DXA, such as those living in rural areas and uninsured patients, *FRAX* alone would serve as an inexpensive alternative and would be an efficient predictive tool to determine a patient's risk for fracture if it provides results comparable to *FRAX/BMD*. Our results suggest that *FRAX* provides predictions that are identical to those of *FRAX/BMD*.

When data for the group with common predictions were compared with those for the group with different predictions using Fischer's exact test, age was found to be the most significant risk factor ($P<.001$). Other risk factors in the prediction model, including BMI, current smoking, history of parental hip fracture, corticosteroid use, alcohol use, history of previous fracture, and secondary risk factors of osteoporosis, did not differ significantly between the two groups. The median age of patients with common predictions was 65 years, and the median age of the patients with different predictions was 76 years. These findings are supported by previous findings regarding age as a predictor of fractures (11).

Our findings suggest that in younger postmenopausal women who are evaluated for fracture risk, allocation of subjects to treatment versus observation is seldom altered by inclusion of BMD in the FRAX calculations. Among the group with different predictions, *FRAX* recommended treatment for 22 out of the 24 subjects (98.68%). *FRAX* identified all of the subjects meeting treatment criteria except for 2 of the 151 subjects. Therefore, use of the FRAX tool without BMD will identify most subjects for treatment and may be a more predictive tool than DXA alone. We advocate use of DXA for monitoring treatment after diagnosis is made with the FRAX tool.

In a retrospective study of a large clinical cohort of 36,730 women and 2,873 men 50 years and older from Manitoba, Canada, Leslie et al (12) concluded that a FRAX designation of high risk of fracture is usually associated with a densitometric diagnosis of osteoporosis. The subjects included in the Manitoba study were both men and women age 50 years and older with valid DXA measurements, irrespective of menopausal status. Unlike the Manitoba study, information for FRAX assessment was gathered by direct assessment and interviews of the subjects by the investigator. In addition, we recruited postmenopausal women irrespective of their age, thereby including a wider range of women at risk for osteoporotic fractures and making our findings more applicable to real-world clinical practice.

In a recent study involving 4,957 postmenopausal women with normal BMD or mild osteopenia, Gourlay et al (10) advocated increasing the screening interval of BMD testing in postmenopausal women according to their BMD values. The *FRAX* score can be used as a screening tool in postmenopausal women, and if the score is indicative of risk for osteoporotic fracture, then a DXA scan can be obtained to get baseline BMD data prior to treatment. Our study findings support this approach.

The distribution of our population is representative of the population of Las Vegas, Nevada, but as the FRAX scores are comparable to the standard curves in the WHO database (which are not absolute calculations), we believe our results can be applied to the general population of the United States.

One limitation of our study is its small sample size. However, based on our power calculation, our sample size was adequate to evaluate our primary aim. There is also possible recall bias associated with subjects answering the FRAX questionnaire, as the investigator did not have access to the subjects' previous health records while conducting the study. We believe a larger study would negate any effects of this bias. Also, in an earlier study we reported poor compliance of physicians with FRAX recommendations, and this is a potential limitation to the application of our study findings (13). Some recent studies have shown that FRAX performs well in older men and that addition of BMD to the calculations would enhance the performance of the tool (14). Our study had only six male subjects, therefore limiting our ability to conduct a separate analysis of the utility of the FRAX tool with and without BMD in men.

Conclusion

In our study, *FRAX* produced predictions that were identical to those of *FRAX/BMD* in most cases. Younger age is more indicative of an identical prediction. Thus, *FRAX* alone is an effective screening tool for predicting the risk of osteoporotic fracture. This is especially relevant given the potential impact it will have on healthcare costs. In rural settings where DXA scanning is unavailable, FRAX could play an important role, as the tool is easily accessible. In cases of limited finances, FRAX is a good alternative for predicting osteoporosis risk.

Acknowledgments

We thank Desert Radiologists, Las Vegas, Nevada, for general support of the research. This publication was made possible by grants from the National Center for Research Resources (5P20RR016464-11) and the National Institute of General Medical Sciences (8 P20 GM103440-11) of the NIH.

References

1. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. JAMA. 2001; 285:785–795. [PubMed: 11176917]
2. Kanis JA, Melton LJ 3rd, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. J Bone Miner Res. 1994; 9:1137–1141. [PubMed: 7976495]
3. Looker AC, Melton LJ 3rd, Harris TB, Borrud LG, Shepherd JA. Prevalence and trends in low femur bone density among older US adults: NHANES 2005-2006 compared with NHANES III. J Bone Miner Res. 2010; 25:64–71. [PubMed: 19580459]
4. Pasco JA, Seeman E, Henry MJ, Merriman EN, Nicholson GC, Kotowicz MA. The population burden of fractures originates in women with osteopenia, not osteoporosis. Osteoporos Int. 2006; 17:1404–1409. [PubMed: 16699736]
5. Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis. Am J Med. 1993; 94:646–650. [PubMed: 8506892]
6. Wasnich R. Bone mass measurement: prediction of risk. Am J Med. 1993; 95:6S–10S. [PubMed: 8256798]

7. Siris E, Delmas PD. Assessment of 10-year absolute fracture risk: a new paradigm with worldwide application. Osteoporos Int. 2008; 19:383–384. [PubMed: 18297369]
8. U.S. Preventive Services Task Force. Screening for osteoporosis: U.S. preventive services task force recommendation statement. Ann Intern Med. 2011; 154:356–364. [PubMed: 21242341]
9. Dawson-Hughes B, Tosteson AN, Melton LJ 3rd, et al. Implications of absolute fracture risk assessment for osteoporosis practice guidelines in the USA. Osteoporos Int. 2008; 19:449–458. [PubMed: 18292975]
10. Gourlay ML, Fine JP, Preisser JS, et al. Bone-density testing interval and transition to osteoporosis in older women. N Engl J Med. 2012; 366:225–233. [PubMed: 22256806]
11. Clark EM, Gould VC, Morrison L, Masud T, Tobias J. Determinants of fracture risk in a UK-population-based cohort of older women: a cross-sectional analysis of the Cohort for Skeletal Health in Bristol and Avon (COSHIBA). Age Ageing. 2012; 41:46–52. [PubMed: 22107913]
12. Leslie WD, Majumdar SR, Lix LM, et al. High fracture probability with FRAX usually indicates densitometric osteoporosis: implications for clinical practice. Osteoporos Int. 2012; 23:391–397. [PubMed: 21365460]
13. Izuora KE, Alazraki N, Byrd-Sellers J, Tangpricha V, Nanes MS. Fracture assessment tool risk scores in bone density reports do not change physician prescribing behavior for osteoporosis. Am J Med Sci. 2011; 342:5–8. [PubMed: 21412137]
14. Ettinger B, Liu H, Blackwell T, et al. Validation of FRC, a fracture risk assessment tool, in a cohort of older men: the Osteoporotic Fractures in Men (MrOS) Study. J Clin Densitom. 2012; 15:334–342. [PubMed: 22445858]

Abbreviations

BMD	bone mineral density
DXA	dual-energy X-ray absorptiometry
FRAX	fracture risk assessment tool
MOF	major osteoporotic fractures
WHO	World Health Organization

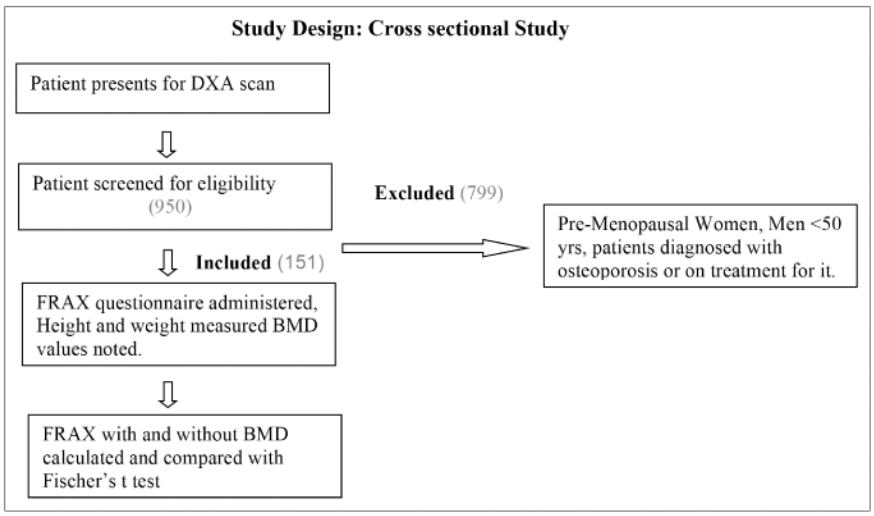

Fig. 1.

Cross-sectional study design. *BMD* = bone mineral density; *DXA* = dual-energy X-ray absorptiometry; *FRAX* = fracture risk assessment.

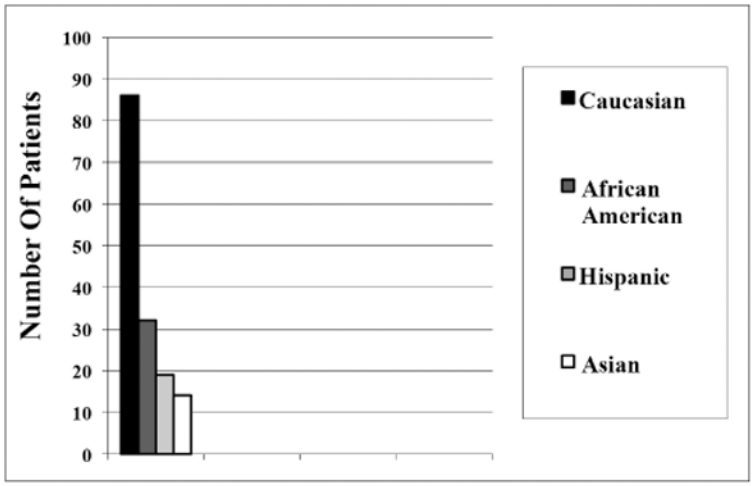

Fig. 2.
Demographic distribution of subjects.

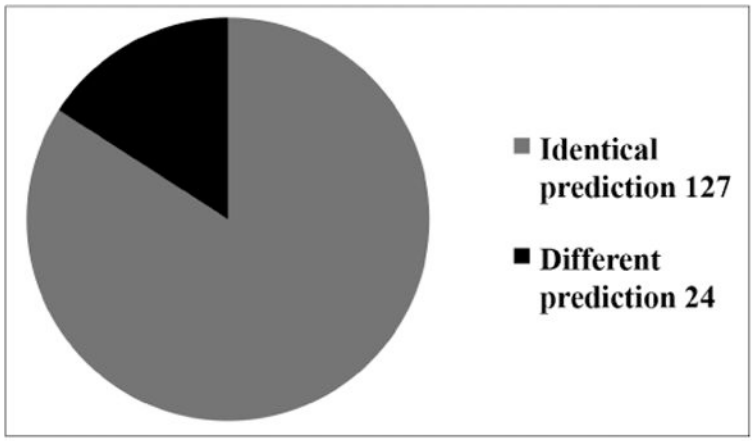

Fig. 3.
Number of identical and different fracture risk assessment prediction results.

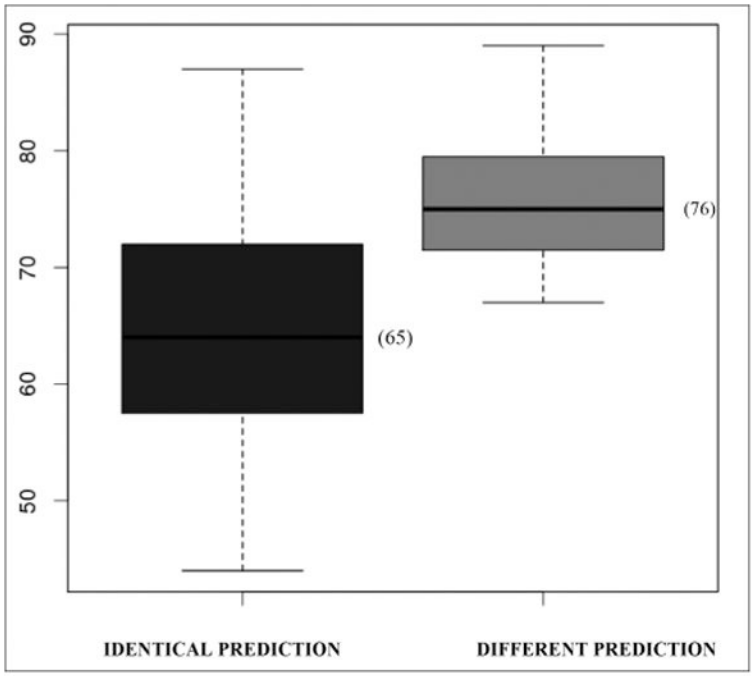

Fig. 4.

Box plot graph showing the median age of subjects with identical and different fracture risk assessment prediction results.

Table 1

Comparison of Variables Between the Groups With Identical and Different Treatment Predictions

Numerical Variables (Student's *t* tests)	**Variable**	***P* value**
	BMI	.36
	T-score	.8
	Femoral neck BMD	.74
Binary Variables (Fischer's Exact tests)		
	Gender	.59
	Previous fracture	.484
	Parent fracture	1
	Smoking	.53
	Steroid use	.214
	Rheumatoid Arthritis	.58
	Osteoarthritis, secondary risk factors	.81
	Alcohol use	.59

Abbreviations: BMD = bone mineral density; BMI = body mass index.