

Accuracy of a fracture risk assessment tool in Iranian osteopenic and osteoporotic women

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Bone mineral densitometry (BMD) has been well known as a practical method in the detection of osteoporosis. However, it is not accurate in the identification of fracture risk in non-osteoporotic patients because of its low sensitivity. Fracture Risk Assessment Tool (FRAX) is a sensitive WHO recommended risk assessment tool for the prediction of the risk of fracture in order to diagnose patients who would benefit the most from pharmacological treatment. This cross-sectional study included a sample of 361 Iranian women aged 40 to 80 years-old who, for any reason, were referred for humeral BMD. Femoral BMD and FRAX were performed on all of the subjects and the results were compared to one another to figure out the accuracy of FRAX to detect the patients at high risk of fracture. There were 361 participants in the study with a mean age of 56.4 ± 5.5 years, and comprised of 89 (24.7%) osteoporotic (T-score ≤ -2.5), 125 (34.7%) osteopenic (T-Score between -1 and -2.5) and 147 (40.7%) subjects with T-score > -1 . A 10-year probability of hip fracture of more than 3% was detected in only in six women (1.6%) and a major osteoporotic fracture risk (of higher than 20%) was not detected in any subject. Applying FRAX in osteopenic and osteoporotic Iranian women showed no extra benefit in comparison to using BMD alone. It seems that FRAX is not accurate in our population as it underestimates the number of patients that could benefit from osteoporosis treatment.

Keywords: bone mineral densitometry, Fracture Risk Assessment Tool, osteopenia, osteoporosis.

Introduction

Osteoporosis is a systemic skeletal disorder which is nicknamed "silent thief" due to the asymptomatic nature of the disorder until it causes an osteoporotic fracture [1, 2]. Osteoporotic fractures are one of the major causes of death in elderly men and women across the world [3]. Frequent fractures include the hip, pelvic bone, spine and forearm [4].

Approximately nine million osteoporotic fractures were reported in the year 2000 including 1.6 million hip fractures, 1.7 million forearm fractures, and 1.4 million vertebral fractures [5]. It is estimated that more than 50% of women and 20% of men may bear an osteoporotic fracture after the fifth decade of their life [6]. In Europe, years of life lost because of osteoporotic related incidents is greater than many other disabling diseases such as Parkinson's disease, rheumatoid arthritis, migraine or asthma [7].

The increase in the incidences of osteoporotic

fractures in both developed and developing countries could cause the expected burden of osteoporotic fractures to double over the next 50 years [8].

In 1994, the World Health Organization (WHO) published diagnostic criteria for osteoporosis based on bone mineral density (BMD) measurement by dual-energy x-ray absorptions (DXA). The WHO defined osteoporosis with a T-Score ≤ -2.5 at the femoral neck and a T-Score > -2.5 and < -1 was referred to osteopenia [9]. Osteoporotic patients have the highest risk of fracture and most of the fractures occur among osteopenic patients due to the high prevalence of osteopenia [10-13].

Although BMD is the gold standard method of diagnosing osteoporotic patients, it may not be a sensitive method for predicting the risk of a fracture [14, 15]. BMD misses a significant proportion of individuals who have clinical risk factors for osteoporosis and bone fractures. Moreover, its

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availability is limited in many countries [16]. Accordingly, clinical risk factors were added to BMD in order to improve the ability of predicting the risk of a fracture [17]. In 2008, WHO published a novel fracture risk assessment tool (FRAX) by integrating clinical risk factors with and without BMD [18]. The FRAX tool estimates a 10- year risk of hip and other major osteoporotic fractures in 40-90 year old men and women [19]. FRAX, BMD or their combination are the methods applied to diagnose and treat high risk patients in good time in order to prevent fractures occurring and associated complications arising [20].

National Osteoporosis Foundation (NOF) guidelines for the management of osteoporosis, in 2008, recommend pharmacological treatment for individuals with a history of hip or vertebral fractures. T-score ≤ -2.5 at the femoral neck or spine, or $-2.5 < \text{T-Score} > -1$ and 10-year probability of hip fracture $\geq 3\%$ (as estimated by FRAX), or individuals with T-Score between -1 and -2.5 and 10- year probability of major fracture $\geq 20\%$ (as determined by FRAX) [21]. Note from editor: The highlighted section should be modified, perhaps by splitting into smaller sentences, as in its current form it is very difficult to follow.

The prevalence of osteoporosis and osteopenia in Iranian postmenopausal women were reported at 26.7% and 50%, respectively [22]. In Iran and many other countries, FRAX is not routinely used as yet, diagnosis and treatment of high risk patients is therefore based on the BMD criteria. This study is designed to identify the consistency between the BMD and the FRAX criteria for selecting the required treatment for patients according to NOF guidelines of 2008.

Materials and Methods

Study population

This cross-sectional study was conducted from January to December 2010 and included a sample of 380 women aged between 40 and 70 years-old who were referred to our teaching hospital (Loghman Hakim) for BMD measurement for any reason. The study was approved by the Pasteur Institute of Iran ethics committee with the code 382/88 (P.I.Ir). The study was explained to all of participants and written informed consent was obtained from them. As all of the participants were referred for BMD measurement by their physicians, there was no extra expense or procedure for them. 19 patients who received treatment for osteoporosis or had major depression as defined by DSM-IV, were excluded from the study.

BMD and FRAX

Hip BMD was measured using the DXA method with a Lunar DPXIQ machine for all of participants. A questionnaire was prepared according to the risk factors accounted for in FRAX, which included age, sex, weight, height, fragility, fractures since age 50, parental history of hip fractures, current smoking history, and alcohol use of more than 2 units per day. A physician filled in all the questionnaires. Past medical history and participants' drug histories were also taken in order to find any reason for a possible secondary osteoporosis. As the population that has the closest reference capabilities with Iranians, a Lebanese population was selected and it was available in Lunar DXA machine setup. Data sheets were collected and the 10-year probability of hip and major osteoporotic fractures were calculated using Lebanon FRAX (www.shefac.uk/FRAX). Femoral neck BMD was also accounted for in all of the fracture risk assessments.

In this study, femoral BMD and FRAX were measured in all of the participants and the results were cross- compared in order to figure out the accuracy of FRAX's detection of patients that are at high risk of bone fracture.

Statistical analysis

Data was presented as a percentage (%) and means \pm standard deviation. Statistical analysis was performed using SPSS 16 for Windows.

Results

The characteristics of the participants are shown in Table 1. 380 women met our inclusion criteria. 19 cases were excluded from the study due to alendronate prescription, after which, 361 remained in the study. The mean age of participants was 56.4 ± 5.5 years with age ranging from 40 to 80 years old. Osteoporosis (T-score ≤ -2.5) and osteopenia (T-Score between -1 and -2.5) were detected in 89 (24.7%) and 125 (34.7%) subjects, respectively. The remaining 147 (40.7%) cases had a T-score > -1 . Only 7 (2%) participants had a BMI of less than 20.

Of the 361 subjects, 7 (2%) had history of fractures since the age of 50 and 14 (3.87%) had parents with a history of fractured hips. 16 (5%) subjects were smokers at the time of the study and none of the sample were alcohol users. Histories of rheumatoid arthritis and glucocorticoid use were reported in 8 (2.2%) cases. 11 (41.27%) cases had secondary causes of osteoporosis, of which 7 (63.7%) had premature

Table 1. Baseline characteristics, BMD and FRAX results among participants

Characteristic	T-score \leq -2.5	BMD		T-score > -1	F RAX [#]
		-2.5 >	T-score < -1		
Age (years)					
40-49	1 (1.1)	13 (10.4)	16 (10.9)	0 (0)	
50-59	54 (60.7)	73 (58.4)	110 (74.8)	1 (0.27)	
60-69	28 (31.5)	38 (30.4)	21 (14.3)	3 (0.83)	
>70	6 (6.7)	1 (0.8)	0 (0)	2 (0.55)	
BMI (kg/m ²)					
< 20	5 (5.6)	1 (1.8)	1 (0.7)	4 (1.1)	
20-25	24 (27)	23 (18.4)	19 (12.9)	1 (0.27)	
25-30	43 (48.3)	66 (52.8)	58 (39.5)	1 (0.27)	
30-35	14 (15.7)	30 (24)	55 (37.4)	0 (0)	
> 35	3 (3.4)	5 (4)	14 (9.5)	0 (0)	
History of a previous fracture	3 (0.83)	4 (1.1)	0 (0)	2 (0.55)	
Parent history of hip fractured	4 (1.1)	5 (1.38)	5 (1.38)	1 (0.27)	
Alcohol use [†]	0 (0)	0 (0)	0 (0)	0 (0)	
Current cigarette smoking	3 (0.83)	7 (1.93)	6 (1.66)	0 (0)	
Glucocorticoid use [‡]	4 (1.1)	1 (0.27)	3 (0.83)	0 (0)	
Rheumatoid arthritis	2 (0.55)	5 (1.38)	1 (0.27)	0 (0)	
Secondary osteoporosis [*]	36 (9.97)	52 (14.4)	52 (14.4)	1 (0.27)	

Data is presented as n (%). BMD, bone mineral density; FRAX, fracture risk assessment tool; BMI, body mass index.

Hip fracture \geq 3% or major osteoporotic fracture \geq 20%; [‡] Defined as greater than 2 units per day, unit = one medium glass of wine or a half pint of beer; ^{*} Defined as 5 mg or more for 3 months or more; ^{*} Type 1 diabetes mellitus, osteogenesis imperfecta in adults, longstanding hyperthyroidism, hypogonadism, premature menopause, chronic malabsorption and liver diseases

ovarian failure. The 10-year probability of a major osteoporotic fracture (MOF) risk of more than 20% was not found in any of the participants. However, 6 osteoporotic participants (1.6%) had a 10 year hip fracture risk of more than 3% according to the FRAX tool. Four of which (66.6%) had a BMI of less than 20 and the remaining two in question had secondary causes for osteoporosis. MOF risk in these 6 cases was estimated at less than 10%.

The characteristics of the patients who had 10-year risk of hip fracture \geq 3% or MOF \geq 20% are summarized in Table 2.

Discussion

Although osteoporotic patients have the highest risk of fractures, because of the high prevalence of osteopenia, most of the fractures occur among osteopenic patients

[10-13]. It is not possible, or even beneficial, to treat all of the osteopenic patients. It is therefore necessary to find a way to detect high risk patients who will benefit the most from pharmacological treatment. With this aim, FRAX was suggested as a sensitive assessment tool by WHO.

This study reveals the proportion of osteopenic and osteoporotic patients in whom the 10- year risk of hip and MOF were more than 3% and 20%, respectively. Only 6 patients (of 89 osteoporotic and 125 osteopenic) required pharmacological treatment for osteoporosis according to the FRAX tool. All 6 of these patients had a T-Score \leq -2.5. Our results were consistent with a large prospective study in France [23], in which the mean FRAX value was 3.8 ± 2.4 . The authors also concluded that the FRAX tool had a poor sensitivity for fracture risk prediction.

Table 2. Characteristics of six patients with hip fracture risk \geq 3%

Patients	Age (years)	BMI	History of fracture	Parental history of fracture	Hip fracture	Secondary cause	Femoral BMD	MOF
Patient 1	72	20	Yes	No	Yes [†]	-2.8	3.5	6.2
Patient 2	60	18.5	Yes	Yes	No	-3.3	3.2	5
Patient 3	70	18.6	No	No	No	-4	4.9	8.3
Patient 4	60	25	No	No	Yes [‡]	-3.4	3.4	6.6
Patient 5	65	28.5	No	No	No	-3.2	3	7
Patient 6	54	18.8	No	No	No	-3.6	3.2	5.4

BMI, Body mass index; BMD, Bone mineral density; MOF: Major osteoporotic fracture.

[†] Premature ovarian failure; [‡] End stage renal disease

However, Crabtree et al. [24] showed that there is a high concordance rate between clinician-determined and FRAX-NOGG intervention. They also concluded that the lack of spine BMD in FRAX is the source of the discrepancy. In Framingham's osteoporosis study, applying NOF 2008 guidelines to the participants increased the proportion of individuals who were in need of treatment in comparison with 2003 NOF guidelines (40.1% vs. 47.8%) [21]. Conversely, in our study, using FRAX in accordance with NOF 2008 instead of the clinical risk factors of NOF 2003, significantly reduced the number of patients that were advised for pharmacological treatment (40.72% vs. 20.75%). The mean age of participants in Framingham's study was 67 years old, which was significantly older than ours. This may partially explain the difference between these two studies.

A high prevalence of premature ovarian failure in Iran, as it was shown in our study (26%), would result in bone density loss at a younger age [25]. It therefore seems that considering regional risk factors such as prevalence of premature ovarian failure, age duration after the menopause, sun light exposure, poverty level, vitamin D deficiency, the proportional agricultural land, and adjustment of age according to Iranian race, it is necessary to reduce the discrepancy between BMD and FRAX in Iranian women [22]. Because of the large inconsistency between BMD and FRAX in our population, it is possible that BMD overestimates Iranian osteoporotic patients who require treatment. However, a reduction to the treatment threshold in

FRAX values would increase the sensitivity of FRAX in Iranian women.

This study had some limitations. First, the computed FRAX used in this study was Lebanon FRAX so it was not adjusted for Iranian people or the epidemiology of osteoporosis in Iran. Second, this was a cross-sectional study and cohort designed studies are required to determine sensitivity, specificity, and fracture risk assessment ability of BMD and FRAX in diagnosing patients who would benefit the most from treatment.

In conclusion, applying FRAX in osteopenic and osteoporotic patients showed no extra benefit compared with the use BMD alone. It seems that FRAX, when used on an Iranian population, underestimates the number of patients who require osteoporosis treatment and it should be adjusted for the epidemiology of osteoporosis in our population. Using FRAX as a screening instrument to detect patients who need pharmacological treatment missed all of our osteopenic patients and a significant proportion of osteoporotic patients.

Conflict of interests

Authors have no conflict of interests.

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