Original Article
DOI: 10.5152/tftrd.2015.32549
Turk J Phys Med Rehab 2015;61:339-43

Would FRAX Define the High Fracture Risk if the Patients Were Evaluated the Day before Hip Fracture?

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Abstract

Objective: The aim of this study was to evaluate the 10-year major osteoporotic and hip fracture risks in patients with a recent hip fracture.
Material and Methods: The study population comprised 58 patients (32 male and 26 female, mean age 79.1 years) with a recent hip fracture. A bedside questionnaire including fracture risk assessment tool (FRAX®) variables and fall frequency was administered to the patients. The FRAX® 10-year major osteoporotic and hip fracture risks were calculated. Statistical analyses were performed to compare different age groups (60–69 years, 70–79 years, and ≥80 years).
Results: The mean 10-year major osteoporotic and hip fracture risks were 13.9% and 78%, respectively. If the National Osteoporosis Foundation guidelines were taken into account according to major osteoporotic and hip fracture risks using FRAX® the day before the fracture, treatment would not be initiated in 75.8% and 18.9% of patients, respectively. There were significant differences between the age groups according to the 10-year major osteoporotic and hip fracture probability and fall frequency ($p<0.001$, $p<0.001$, and $p=0.005$, respectively).
Conclusion: In our study group, the FRAX® 10-year major osteoporotic fracture probability had an underestimation in younger patients with a history of frequent falling and did not seem to improve the definition of high-risk patients. The 10-year probability of hip fracture by the FRAX® tool can classify populations at risk more effectively.
Keywords: Fracture risk, FRAX®, osteoporosis, FRAX® Turkish thresholds

Introduction

Osteoporosis is the most common metabolic disease of the bone (1). The measurement of bone mineral density with dual energy X-ray absorptiometry (DEXA) is the gold standard for the diagnosis of osteoporosis. The World Health Organization (WHO) defines a T-score (bone mineral density values as compared to young adults) less than -2.5 standard deviation (SD) as measured by DEXA as the cutoff value for osteoporosis (2). Recent studies revealed that most of the osteoporotic fractures occured in individuals with a T-score in the osteopenic range, which highlights the clinical risk factors for fracture (3,4).

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Received: May 2014 Accepted: November 2014

Cite this article as:
Koçyiğit F, Acar M, Baydar M, Kuyucu E, Koçyiğit A. Would FRAX Define the High Fracture Risk if the Patients were Evaluated the Day before Hip Fracture? Turk J Phys Med Rehab 2015;61:339-43.

The fracture risk assessment tool (FRAX®) tool was developed by the WHO collaborating center for metabolic bone diseases to better predict fracture risks based on clinical risk factors. The clinical risk factors include age, sex, height, weight, history of fragility fracture, parental history of hip fracture, current smoking, use of oral glucocorticoids, rheumatoid arhtritis, other causes of secondary osteoporosis, and alcohol intake of three or more units per day. The FRAX® tool calculates the 10-year probability of a major osteoporotic (clinical spine, hip, forearm, proximal humerus) fracture (FRAX® major) and hip fracture (FRAX® hip) (5). The risk of osteoporotic fracture varies remarkably between countries. Therefore, the geographic region should be considered in fracture risk assesment in addition to clinical risk factors. FRAX® models are available for 18 countries, including Turkey, where the incidences of both fracture and mortality are known (6). The FRAX® model for Turkey was based on hip fracture incidence from the Mediterranean Osteoporosis Study (MEDOS), which was reported 20 years ago (7). The application of FRAX® for the selection of an appropriate group for osteoporosis treatment is FRAX® hip >3% or FRAX® major >20% according to 2008 National Osteporosis Foundation recommendations (8,9). In Japan, FRAX® major >15% in postmenopausal women younger than 75 years and in men have been added to the diagnostic criteria and treatment guidelines of osteoporosis as reference for determining treatment initiation (10). We aimed to calculate the FRAX® values in patients with acute recent hip fractures and to investigate the detection rate of patients at a high risk according to the Natioanal Osteoporosis Foundation guidelines in the Turkish population.

Material and Methods

Approval of the local ethical committee was obtained prior to the study. All of the participants gave written informed consent. Patients who were hospitalized for osteoporotic hip fracture between September 2011 and March 2012 were evaluted for the study. A questionnaire including FRAX® variables, demographic parameters, and fall frequency were recorded. In total, 80 patients were evaluated during the study period. Patients with a pathological femur fracture (n=2), patients older than 90 years of age (n=5), patients who were not able to complete the questionnaire (n=8), and patients with previous osteoporosis treatment (n=7) were excluded from the study cohort. Finally, the study included 58 patients. Fall frequency was classified into four groups and indicated as follows: more frequent than once a week, 1; more frequent than once a month, 2; more frequent than once a year, 3; and less frequent than once a year, 4. Fall frequency was assessed by two questions. First, patients were asked "Did you fall during the last one year?" If the answer was "No", the patient was scored 4. If the answer was "Yes", the patient was further asked "Which defines your fall frequency best?" Options and scorings were explained as above.

Statistical Analysis

Statistical analysis of the data was performed by the Statistical Package for Social Sciences (SPSS Inc.; Chicago, IL, USA) 17.0 for Windows. Descriptive analyses were performed for studied parameters. Continuous variables such as FRAX® values were expressed as mean±SD of the mean. The Kruskal–Wallis test was used to analyse the difference according to age groups which were defined as follows: group 1 (n=5), 60–69 years; group 2 (n=24), 70–79 years; and group 3 (n=29), ≥80 years. Furthermore, the Mann–Whitney U test was used to analyze post-hoc comparisons of each group with Bonferroni correction to evaluate the significance found by the Kruskal–Wallis test. Statistical significance was defined as a p value of less than 0.05.

Results

The study included 26 female (44.8%) and 32 male (55.2%) patients. The mean age of the study patients was 79.1±6.7 years (range, 62–90 years). The mean body mass index (BMI) was 23.7±3.88 kg/m^2 (ranged between 16.6 and 34.2 kg/m^2). Descriptive parameters of group 1 (n=5, 60–69 years), group 2 (n=24, 70–79 years), and group 3 (n=26, ≥80 years) are demonstrated in Table 1.

The most common risk factor was having a previous fracture, which was present in 17 (29.3%) patients. Alcohol consumption was absent for all of the patients. Table 2 shows the characteristics of the risk factors of the FRAX® tool in the study group. Twenty-one patients (36.2%) had only one FRAX® clinical risk factor, 2 patients (3.4%) had more than one clinical risk factor, and 35 patients (60.4%) had none of the clinical risk factors. The mean FRAX® major and FRAX® hip were 13.9% and 7.8%, respectively. If FRAX® major is considered, 44 patients (75.8%) were not at a high risk the day before the fracture. Furthermore, if FRAX® hip is considered, 11 patients (19%) were not at a high risk the day before the fracture. Table 3 represents the distribution of patients according to FRAX® major <20% and FRAX® hip <3%.

When we compared the age groups with Kruskal–Wallis test according to different parameters, there was a significant difference for FRAX® hip, FRAX® major, and fall frequency ($p<0.001$, $p<0.001$, and $p=0.005$, respectively). Because of the significant difference in FRAX® hip, FRAX® major, and fall frequency parameters, the Mann–Whitney U test was used to analyze the post-hoc comparisons of each group with Bonferroni correction to evaluate the significance found by the Kruskal–Wallis test. There was a significant difference between groups 1 and 2 according to FRAX® hip, FRAX® major, and fall frequency ($p<0.001$, $p=0.016$, and $p=0.004$, respectively) and between groups 1 and 3 ($p<0.001$, $p<0.001$, and $p=0.005$, respectively). On the other hand, there was a significant difference between groups 2 and 3 according to FRAX® hip and FRAX® major ($p<0.001$ and $p<0.001$, respectively), but there was no significant difference according to fall frequency ($p=0.881$).

Discussion

Osteoporosis is a highly prevalent metabolic bone disease. The development of new evidence-based treatments for osteoporosis and the increased importance of the cost effectiveness of treatment thresholds have brought about the need for new risk prediction models. FRAX® was released in 2008 by WHO to provide an assesment tool with use of clinical risk factors (11).

Table 1. Descriptive parameters of the study population according to age groups

Parameter		n	Mean±SD	95% CI	Min–max
FRAX® Hip	60–69 years	5	0.9±0.5	0.243–1.716	0.4–1.8
	70–79 years	24	4.7±2.8	3.577–6.014	1.2–11.0
	≥80 years	29	11.6±5.4	9.531–13.669	3.5–24.0
	Total	58	7.8±5.7	6.355–9.382	0.4–24.0
FRAX® Major	60–69 years	5	4.3±1.9	1.924–6.795	2.3–7.2
	70–79 years	24	9.7±5.2	7.541–11.974	3.6–22.0
	≥80 years	29	19.1±8.9	15.747–22.590	6.4–36.0
	Total	58	13.9±8.9	11.639–16.356	2.3–36.0
Fall frequency	60–69 years	5	2.2±0.4	1.644–2.755	2.0–3.0
	70–79 years	24	3.5±0.8	3.126–3.873	1.0–4.0
	≥80 years	29	3.4±0.8	3.167–3.798	1.0–4.0
	Total	58	3.3±0.8	3.144–3.614	1.0–4.0
BMI	60–69 years	5	272±5.5	20.396–34.063	21.9–34.2
	70–79 years	24	24.2±3.4	22.837–25.734	16.6–33.3
	≥80 years	29	22.6±3.3	21.399–23.963	17.5–31.1
	Total	58	23.7±3.7	22.745–24.729	16.6–34.2

BMI: body mass index; Min: minimum; Max: maximum; N: number of patients; SD: standard deviation; FRAX®: fracture risk assessment tool

Table 2. Baseline characteristics of the risk factors of the FRAX® tool in the study group

FRAX® Risk factor (n)	Mean or percentage
Age, years (58)	79.1 (range, 60–90)
Body mass index, kg/m² (58)	23.7 (range, 16.6–34.2)
Previous fracture (17)	29.3%
Parent hip fracture (2)	3.4%
Current smoking (5)	8.6%
Current glucocorticoid use (2)	3.4%
Alcohol consumption (0)	0%
Rheumatoid arthritis (1)	1.7%
Secondary osteoporosis (4)	6.9%

n: number of patients; FRAX®: fracture risk assessment tool

Table 3. Patient distribution according to FRAX® major <20% and FRAX® hip <3%

Age (n)	FRAX® major <20%	FRAX® hip <3%
60–69 years (5)	5 (100%)	5 (100%)
70–79 years (24)	23 (95.8%)	6 (25%)
≥80 years (29)	16 (55.1%)	0
Total (58)	44 (75.8%)	11 (18.9%)

n: number of patients; FRAX®: fracture risk assessment tool

In addition to clinical risk factors, the geographic area should be considered in fracture risk assessment because fracture probability varies remarkably among different countries. The FRAX® models were based on the epidemiological studies of hip fracture incidence. The FRAX® model for Turkey is based on MEDOS. MEDOS is a prospective study, which assessed hip fracture rates in 14 centers and 5 countries (7). In 2009, another prospective study was conducted to estimate hip fracture risks in Turkey. The FRACTURK study reported that despite still being one of the countries with a low fracture risk, the hip fracture incidence markedly increased in Turkey. The study proposed the recalibration of the FRAX® Turkey model on the basis of new fracture incidences (12).

In France, the Os des Femmes de Lyon (OFELY) cohort compared the observed fracture incidence with predicted probability from FRAX®. Among women aged at least 65 years with low bone mineral density, the 10-year predicted probabilty of major osteoporotic fracture with FRAX® was 48% lower than the observed incidence of fracture (13). Therefore, the OFELY cohort reported a substantially higher incidence of major osteoporotic fractures than the FRAX® predicted probabilty. A similar cohort from Spain aimed to compare estimated and observed hip and major osteoporotic fracture incidences in women aged at least 65 years without bone mineral density measurement. The estimated risk for hip fractures was similar to the observed fractures; however, the Spanish FRAX® underestimated major osteoporotic fractures (14). Kanis et al. (15) proposed the cautious interpretation of the results of these external validation studies.

Fraser et al. (16) conducted a study to validate Canadian FRAX® in a large Canadian population-based study (CAMOS). They concluded that the Canadian FRAX® tool provides predictions consistent with observed fracture rates in the Canadian population. Despite Spanish and French external validation studies, the CAMOS study reported that the Canadian FRAX® tool showed good calibration and discrimination for both major osteoporotic and hip fractures.

In Turkey, there are no external validation or calibration studies regarding FRAX® yet. In this study, we obtained the FRAX® 10-year fracture probability in a population who recently had osteoporotic hip fractures. We aimed to document whether osteoporosis treatment would be initiated according to the FRAX® probabilities and National Osteoporosis Foundation guidelines the day before the fracture. If the 10-year probability of osteoporotic fracture is considered, 75.8% of patients were not at a high risk and osteoporosis treatment would not be initiated. However, if the 10-year probability of osteoporotic hip fracture is considered, 19% of patients were not at a high risk and would be followed without treatment. In our study group, the FRAX® 10-year major osteoporotic fracture probability does not seem to improve the definition of high-risk patients. The increase of hip fracture incidence in Turkey in the last 20 years, as documented by the FRACTURK study, may explain this underestimation. The FRAX® Turkey model may be recalibrated in the light of recent prospective studies regarding fracture incidence. If a calibration is not performed, the 10-year probabilty of hip fracture seems to define populations at risk more effectively.

We performed further analysis of FRAX® major and FRAX® hip according to age groups and determined statistically significant differences between group 1, group 2, and group 3. FRAX® major and FRAX® hip were lower between individuals aged 60 and 69 years than older ages. However, fall frequency was significantly higher in group 1 than in group 2 and group 3. According to our results, it can be assumed that younger patients, although having lower FRAX® major and FRAX® hip, experience hip fractures if they fall frequently. In group 1, none of the patients were at a high risk, according to the National Osteoporosis Foundation guidelines. FRAX® could not evaluate fall frequency, and our results show a possible underestimation of fracture risk between 60 and 69 years of age if there is a history of frequent falls. Fall frequency was not evaluated in previous similar studies with FRAX® and external validation studies of FRAX® (13,16,17).

FRAX® aims to improve risk assesment by evaluating clinical risk factors. In our study group, 60.4% of patients had no clinical risk factors. This may also contribute to the possible underestimation of the FRAX® Turkey model. The mean age of our study population (79.1 years) was relatively high compared with a similar study (17). Independent of clinical risk factors, increasing age may be simply used for treatment initiation. A similar study was conducted in Switzerland in patients who recently had osteoporotic fracture. The treatment thresholds for the FRAX® 10-year fracture probabilities were proposed according to age groups in this study. It was reported that the proposed thresholds were not able to classify patients at a high risk in 50%–70% of the studied population (17). Our study had several limitations. The study population was small, thereby limiting our results. There is a need for further studies in large Turkish patient populations. The study comprised patients with osteoporotic hip fractures. However, patients who had osteoporosis without a hip fracture or patients with different fracture sites were not considered as a control group, thereby limiting our results in the border of hip fracture. Further studies that include the other sites of fractures in the Turkish population are needed.

The aim of this study was not to perform external validation. Debates on the methodology of external validation studies regarding the FRAX® tool are ongoing (15,18). We assesed whether FRAX® could detect patients at a high risk the day before the fracture. FRAX® hip could detect vast majority of patients at a high risk. FRAX® major should be used with caution if the treatment goal is the prevention of hip fracture more than fractures at other sites. There is a possible underestimation with the use of FRAX® major, particularly in younger patients with a history of frequent falling. The study group consisted of patients with hip fractures. This may explain the better definition of high risk with the 10-year probability of hip fracture obtained with FRAX®.

Conclusion

We documented that the FRAX® 10-year major osteoporotic fracture probability had an underestimation in younger patients with a history of frequent falling and did not seem to improve the definition of high-risk patients. The 10-year probability of hip fracture of the current FRAX® tool can classify populations at risk more effectively.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of Pamukkale University.

Informed Consent: Written informed consent was obtained from the patients who participated in this study.

Peer-review: Externally peer-reviewed.

Author Contributions: Concept - F.K., E.K., A.K.; Design - F.K., E.K., M.A.; Supervision - F.K., A.K., M.B.; Resources - F.K., E.K., M.A.; Materials - F.K., E.K., M.A.; Data Collection and/or Processing - F.K., E.K., M.A.; Analysis and/or Interpretation - F.K., E.K., A.K.; Literature Search - F.K., M.B.; Writing Manuscript - F.K.; Critical Review - A.K., M.B.

Conflict of Interest: No conflict of interest was declared by the authors.

Financial Disclosure: The authors declared that this study has received no financial support.

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