FİZİKSEL TIP VE REHABİLİTASYON BİLİMLERİ DERGİSİ
Journal of Physical Medicine and Rehabilitation Sciences

ORIGINAL RESEARCH ORİJİNAL ARAŞTIRMA

DOI: 10.31609/jpmrs.2023-99823

10-year Fracture Risk Assessment with FRAX Türkiye Model in Early Postmenopausal Women

Erken Postmenopozal Kadınlarda FRAX Türkiye Modeli ile 10 Yıllık Kırık Riski Değerlendirmesi

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ABSTRACT Objective: In previous studies, it was found that the sensitivity of major osteoporotic fracture (MOF) threshold of 9.3% or higher calculated by the Fracture Risk Assessment Tool (FRAX) scale to detect disease for osteoporosis (OP) screening in women aged 50-64 was low. The aim of this study was to evaluate whether the FRAX scale is sufficient to detect women under 65 years of age with OP requiring bone mineral density (BMD) screning. **Material and Methods:** The study included 114 postmenopausal women aged 50-64 years who were diagnosed with OP by BMD screning. We calculated the sensitivity, specificity, and area under the receiver operator characteristic (ROC) curve (AUC) of MOF risk ≥9.3% and ≥8.4% (proposed new cut-off) to detect OP as well as the FRAX risk threshold for hip fracture (HF). **Results:** The old and new recommended FRAX threshold were able to identify 0.9% (n=1) and 1.8% (n=2) of all patients for BMD screening. The sensitivity and specificity of a FRAX-calculated MOF risk ≥9.3% and MOF risk ≥8.4% were 0 and 93.4%, 0 and 97.9%, respectively. The AUC was equal to 0.498 [95% confidence interval (CI) 0.367-0.630], demonstrating the quite poor test performance. In our population, the FRAX risk threshold calculated for MOF was ≥4 (with 31.3% sensitivity and 53.6% specificity). The FRAX risk threshold calculated for HF was ≥0.4 [with 75% sensitivity, 39.2% specificity and, 0.549 (95% CI 0.416-0.683) AUC, demonstrating relatively poor test performance]. **Conclusion:** The results of our study show that the recommended FRAX threshold value requiring screening with BMD screning is high for the detection of OP in postmenopausal women under the age of 65. A review of both the FRAX threshold and the risk factors used in the FRAX tool may be considered. Further studies are needed for this.

Keywords: Osteoporosis; FRAX; bone mineral density

ÖZET Amaç: Daha önce yapılan çalışmalarda 50-64 yaş arası kadınlarda osteoporoz (OP) taraması için Kırık Riski Değerlendirme Aracı (FRAX) ölçeği ile hesaplanan %9,3 ve üzeri majör osteoporotik kırık (MOF) eşiğinin hastalık tespitindeki duyarlılığının düşük olduğu tespit edilmiştir. Bu çalışmanın amacı, FRAX ölçeğinin kemik mineral yoğunluğu (KMY) ölçümü gerektiren OP'li 65 yaş altı kadınları saptamada yeterli olup olmadığını değerlendirmektir. **Gereç ve Yöntemler:** Çalışmaya KMY ölçümü ile OP tanısı konulan 50-64 yaş arası 114 postmenopozal kadın dâhil edildi. OP'yi saptamak için önerilen ≥%9,3 (eski cut-off) ve ≥%8,4 (yeni cut-off) MOF riski değerlerinin duyarlılığı, özgüllüğü ve alıcı operatör özelliği [receiver operator characteristic (ROC)] eğrisi altında kalan alanı [area under the curve (AUC)] hesapladık. Ayrıca bu hesaplama kalça kırığı [hip fracture (HF)] riski skoru için de yapıldı. **Bulgular:** Eski ve yeni önerilen FRAX eşiği, BMD taraması için tüm hastaların %0,9'unu (n=1) ve %1,8'ini (n=2) tespit edebildi. FRAX ile hesaplanan ≥%9,3 ve ≥%8,4 MOF riskinin duyarlılığı ve özgüllüğü, sırasıyla %0 ve %93,4, %0 ve %97,9 idi. AUC, MOF riski için 0,498 [%95 güven aralığı (GA) 0,367-0,630] olarak hesaplandı ve oldukça zayıf test performansını gösteriyordu. Bizim popülasyonumuzda MOF riski için hesaplanan FRAX risk eşiği ≥4 idi (%31,3 duyarlılık ve %53,6 özgüllük ile). HF riski için hesaplanan FRAX risk eşiği ≥0,4 [%75 duyarlılık, %39,2 özgüllük ve AUC 0,549 (%95 GA 0,416-0,683) ile] olup, nispeten zayıf test performansı gösteriyordu. **Sonuç:** Çalışmamızın sonuçları, 65 yaş altı postmenopozal kadınlarda OP tespiti için önerilen KMY ölçümü ile tarama gerektiren FRAX eşik değerinin yüksek olduğunu göstermektedir. Hem FRAX eşiğinin hem de FRAX aracında kullanılan risk faktörlerinin gözden geçirilmesi düşünülebilir. Bunun için ileri çalışmalara ihtiyaç vardır.

Anahtar Kelimeler: Osteoporoz; FRAX; kemik mineral yoğunluğu

TO CITE THIS ARTICLE:
Yılmaz E, Fırat M, Pasin Ö. 10-year Fracture Risk Assessment with FRAX Türkiye Model in Early Postmenopausal Women.
Turkiye Klinikleri Journal of Physical Medicine and Rehabilitation Sciences. 2024;27(2):121-8.

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Peer review under responsibility of Journal of Physical Medicine and Rehabilitation Science.

Received: 09 Nov 2023 ***Received in revised form:*** 17 Feb 2024 ***Accepted:*** 25 Mar 2024 ***Available online:*** 27 Mar 2024

Osteoporosis (OP) is a progressive systemic skeletal disease characterized by decreased bone mineral density (BMD) and bone strength, increased bone fragility and fracture risk, and deterioration in the microarchitecture of bone tissue. OP is an important public health problem that increases with age and causes morbidity and mortality. The most important cause of morbidity and mortality in OP is osteoporotic hip fractures (HF). HFs are associated with reduced quality of life, limitations in ambulation, chronic pain, disability, and loss of independence. Dual energy X-ray absorptiometry (DEXA), which is used in the diagnosis and follow-up of OP, is a proven, widely used, highly sensitive, and non-invasive method in determining BMD screening.[1,2] OP is defined by the World Health Organization (WHO) as having a BMD screning below -2.5 standard deviations of the T score compared to young adults in the same population. However, osteoporotic fractures can be seen not only in patients who are osteoporotic according to BMD screning and T-score, but also in the osteopenic group.[3] Since BMD screning values are affected by ethnic, genetic, gender, age, environmental, and regional factors, it has been reported that the BMD screning values of the Turkish population are lower than the reference values in various DEXA devices and the prevalence of OP is higher.[1,2] However, the risk of osteoporotic fractures in the Turkish population has also increased significantly.[4] Various factors such as increasing age, previous fracture, history of osteoporotic fracture, and cortisone use are taken into account in the evaluation of osteoporotic fracture risk. Early diagnosis of this important disease is necessary for the prevention and treatment of possible complications. DEXA detects OP and/or osteopenia before fracture occurs. It determines the rate of bone loss with repeated measurements and gives information about the effectiveness or failure of the treatment.[2] DEXA is accepted as the gold standard in determining the risk of fracture, but it is insufficient on its own to predict fractures. Although low BMD screning scores are an important risk factor for osteoporotic fracture, fractures may also occur in some osteopenic patients. In other words, BMD screning can not accurately predict future fractures. For this reason, risk assessment indices have been developed to identify risk factors other than BMD screning. To serve this purpose, an algorithm called Fracture Risk Assessment Tool (FRAX), which can be calculated on a computer-based logarithmic table, has been created by WHO to determine the risk of osteoporotic fracture.[4]

FRAX is based on an individual patient model of osteopenic patients using clinical risk factors with and without a femoral neck BMD measurement or T-score, showing the probability of a 10-year HF and a major osteoporotic fracture (MOF) (proximal femur, vertebrae, humerus, distal radius). Accordingly FRAX, if the risk of HF is 3% and the risk of MOF is 20% or more, the patient should be considered as at risk for osteoporotic fracture and treatment should be given. In this way, patients in the low-risk group do not receive unnecessary treatment, and patients in the high-risk group are more likely to receive treatment independent of DEXA. In the algorithm model defined as FRAX, age, gender, body weight, previous fragility fracture, presence of fracture history in the parents, smoking, glucocorticoid use (more than 5 mg/day for more than 3 months), rheumatoid arthritis, other secondary causes of OP, and excessive alcohol consumption was determined as the factors used to determine the absolute fracture risk of individuals.[4] Some disadvantages of the FRAX value are: a) the absence of some important fracture risk factors such as vitamin D deficiency, diabetes, and thyroid disorders, b) BMD evaluation being limited to the femoral neck T-score value, c) the fracture risk being over- or under-estimated. and d) can not be used in treated patients.[5] It is also recommended to evaluate screening for OP in women younger than 65 years with an estimated 10-year risk of MOF of 9.3% (equal to that of a 65-year-old white woman with no other FRAX clinical risk factors) or greater with the FRAX scale. In previous studies, it was found that the sensitivity of this threshold to detect disease for OP screening in women aged 50-64 was low.[6-9] Therefore, in 2018, the US Preventive Services Task Force (USPSTF) reported a recommendation statement that referenced a cut-off to recommend BMD testing as a MOF risk of 8.4% instead of 9.3% for women under 65.[10] The aim of this study was to evaluate whether the FRAX scale is sufficient to detect

women under 65 years of age with OP requiring DEXA. Another aim of the study is to determine other risk factors that are not included in the FRAX scale.

MATERIAL AND METHODS

This retrospective study was directed at the Department of Physical Medicine and Rehabilitation in Bezmialem Vakıf University and Ankara Etimesgut Şehit Sait Ertürk State Hospital. The trial protocol was confirmed by the Ethics Committee of Bezmialem Vakıf University (date: November 11, 2022, no: 2022/325). The study was conducted in accordance with the principles of the Declaration of Helsinki. Consent form was obtained from all patients participating in the study.

The study included 114 postmenopausal women aged 50-64 years who applied to the Department of Physical Medicine and Rehabilitation of Bezmialem Vakıf University and Ankara Etimesgut Şehit Sait Ertürk State Hospital between May 2021 and 2022 and were diagnosed with OP by DEXA (T-score ≤-2.5 at the lumbar spine or femoral neck). The postmenopausal period for women was considered at least 12 months of amenorrhea. Exclusion criteria are as follows: the patients younger than 50 years of age, previously performed DEXA, previously using medication for the diagnosis of OP, with a history of fracture, previously receiving hormone replacement therapy, and with any disease (such as gastrointestinal disease, endocrine and renal disorder, hemiplegia, malignancy) leading to secondary OP. The data of the patients such as age, height, weight, body mass index (BMI), concomitant chronic diseases [hypertension (HT), hyperlipidemia (HPL), rheumatic disease], menopausal age, menopause duration, smoking and alcohol use, fracture history, family history of fracture, and glucocorticoid use were collected retrospectively from hospital records. Moreover, the level of serum calcium, magnesium, parathormone, alkaline phosphatase, and 25(OH) Vitamin D and lumbar spine (L1-L4) and femoral neck T scores determined by BMD screning were recorded. MOF and HF risk scores obtained without femoral neck T score were calculated with the FRAX Türkiye model.

STATISTICAL ANALYSIS

Descriptive statistics of qualitative variables in the study were given as numbers and percentages, and descriptive statistics of quantitative variables were given as mean±standard deviation. Intra-group comparisons could not be made due to the large difference in average between the groups to be compared. However, we evaluated the sensitivity and specificity of each risk score (MOF and HF). We calculated the areas under the receiver operating characteristic (ROC) curve (AUC) to assess the discriminatory ability of the different risk scores. All the statistical tests were undertaken with a confidence interval (CI) of 95% and with the use of the SPSS statistical package(Version 26.0. Armonk, NY: IBM Corp).

RESULTS

The mean age of the patients was 56.86±4.61 years. Of all patients, 83 (72.8%) and 46 (40.4%) had OP of the lumbar spine and femoral neck, respectively. The mean BMI of patients was 27.43±4.25. Of the patients, 69.3% (n=79) were non-smokers, 30.7% (n=35) were smokers. None of the patients had alcohol use. Of the patients, 29.8% (n=34) had a family history of fracture and 70.2% (n=80) had no family history of OP. The mean age of menopause was 45.04±6.03 years. The mean duration of menopause was 12.13±6.99 years. The percentages of chronic diseases were 33.4% for HT (n=38), and 8.9% for HPL (n=10). The mean of MOF and HF risk score were 4.7% and 0.7%, respectively. The old and new recommended FRAX threshold were able to identify 0.9% and 1.8% of all patients for BMD screening. Since one patient had a MOF risk score ≥9.3% and two patients had a MOF risk score ≥8.4, intergroup comparisons could not be made statistically due to small sample size in our population. The demographic, characteristic and laboratory findings of the patients are presented in Table 1.

The sensitivity and specificity of a FRAX-calculated MOF risk ≥9.3% for detecting OP of the femoral neck and/or lumbar spine were 0 and 93.4%, respectively. The sensitivity and specificity of a FRAX-calculated MOF risk ≥8.4% for detecting OP of the femoral neck and/or lumbar spine were 0 and 97.9%, respectively. The AUC was equal to 0.498

TABLE 1: The demographic, characteristics and laboratory findings of the patients.

Variables	MOF risk score ≥9.3% (n=1)	MOF risk score <9.3% (n=113)	MOF risk score ≥8.4 (n=2)	MOF risk score <8.4 (n=112)
Age (year)	57	56.88±4.63	56.5±0.71	56.87±4.65
Body mass index	28.4	27.4±4.22	28.4±3.61	27.4±4.21
Smoking				
Yes	0 (0%)	35 (30.7%)	0 (0%)	35 (30.7%)
No	1 (0.9%)	78 (68.4%)	2 (1.8%)	77 (67.5%)
Family history of fracture				
Yes	0 (0%)	34 (29.8%)	0 (0%)	35 (30.7%)
No	1 (0.9%)	79 (69.3%)	2 (1.8%)	77 (67.5%)
Age of menopause (year)	53	44.96±6.01	49±5.66	44.95±6.04
Duration of menopause (year)	22	12.04±6.96	16.5±7.78	12.05±6.99
The level of vitamin D (ng/mL)	10.80	14.71±7.77	11.18±0.54	15.06±7.78
The level of parathormone (ng/L) (range 15-68)	63.7	70.64±25.0	88.60±35.21	70.26±24.78
The level of alkaline phosphatase (U/L) (range 43-115)	83	83.30±23.69	85±2.83	83.26±23.79
The level of calcium (mg/dL) (range 8.6-10.6)	9.9	9.5±0.35	10.05±0.21	9.48±0.34
The level of magnesium (mg/dL) (range 1.6-2.6)	2.11	2.03±0.16	2.05±0.09	2.03±0.16
Chronic diseases				
None	0 (0%)	57 (50%)	1 (0.9%)	56 (49.1%)
Hypertension	1 (0.9%)	37 (32.5%)	1 (0.9%)	37 (32.5%)
Hyperlipidemia	0 (0%)	10 (8.8%)	0 (0%)	10 (8.8%)

All values are expressed as mean±standard deviation, number and percentage; MOF: Major osteoporotic fracture.

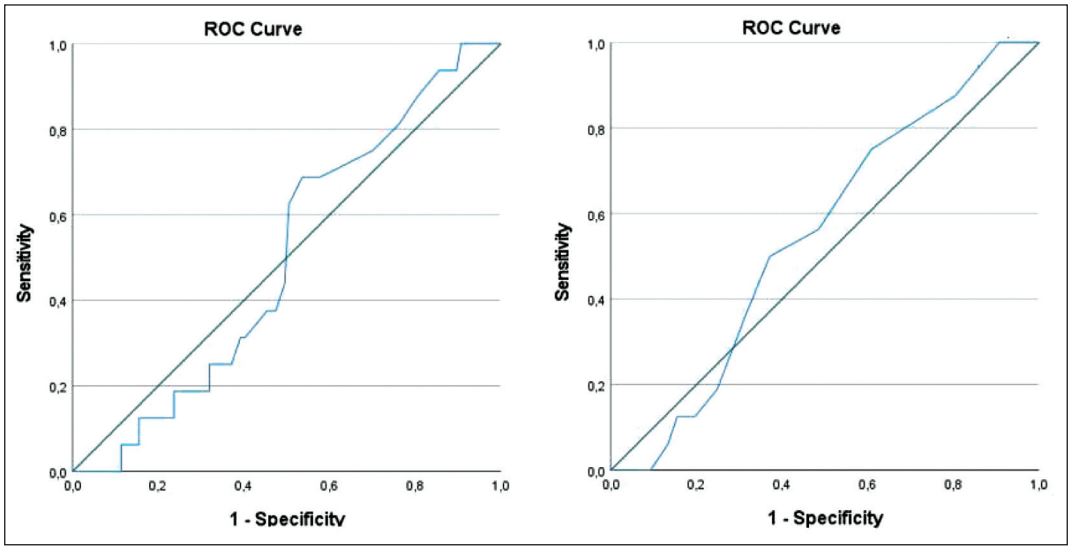

FIGURE 1: ROC curve for an estimated Fracture Risk Assessment Tool major osteoporotic fracture risk ≥9.3% (left picture) and hip fracture risk ≥0.4% detected in our population (right picture) for discriminating between persons with bone mineral density T-score ≤-2.5.
ROC: Receiver operating characteristic.

(95% CI 0.367-0.630) (Figure 1). This demonstrated the quite poor test performance of the recommended 9.3% MOF risk threshold for OP detection with DEXA. In our population, the FRAX risk threshold calculated for MOF was 4 and greater. The sensitivity and specifivity of this threshold for the detection of OP by DEXA were 31.3 and 53.6%, respectively. We also calculated the FRAX risk threshold for HF. It was 0.4 and higher. The sensitivity and specifivity of this threshold for the detection of OP by DEXA

were 75 and 39.2%, respectively. However, the AUC was equal to 0.549 (95% CI 0.416-0.683), demonstrating relatively poor test performance (Figure 1).

DISCUSSION

Risk factors for OP include age, ethnicity, family history, female gender, decreased physical activity, low body weight, low calcium intake, vitamin D deficiency, excessive tobacco or alcohol use, glucocorticoid use, early menopause, and secondary causes. Apart from low BMD screning values, risk factors for fracture development are age, previous fragility fracture history, and steroid use. Therefore, current guidelines have emphasized the usefulness of combining BMD screening and clinical risk factors to determine an absolute risk of fracture and to decide which patient should be treated and monitored. The National Osteoporosis Foundation (NOF), the International Society for Clinical Densitometry (ISCD), and the USPSTF suggest BMD screning for postmenopausal women over 65 age, regardless of risk factors. Women with previous fragility fractures do not need BMD screening as they have OP by definition of fragility fracture. For postmenopausal women younger than 65, NOF and the ISCD recommend BMD testing for women with additional risk factors. Although there are many tools used to estimate fracture risk, FRAX is among the most widely used tools to estimate fracture risk. In previous studies, the performance of the FRAX tool was generally evaluated in older women over 65 years of age and focused mainly on HFs. There is some uncertainty as to whether this screening tool will have the same performance in early postmenopausal women.[6,9] Therefore, we evaluated whether the FRAX scale is sufficient to detect women under 65 years of age with OP requiring DEXA. In our study, the sensitivity and specificity of a FRAX-calculated MOF risk ≥9.3% and MOF risk ≥8.4% for detecting OP were 0 and 93.4%, 0 and 97.9%, respectively. According to our study, the old and new FRAX-calculated MOF risk thresholds was able to detect only 1 and 2 patients with OP. This indicates that the recommended FRAX-calculated MOF thresholds are insufficient to determine the vast majority of women with a T-score ≤-2.5. Moreover, the FRAX risk threshold calculated for MOF was ≥4% in our population. This threshold was lower than the results obtained in studies by Crandall et al. (5.04%) and Bansal et al. (5.5%). However, the sensitivity and specifivity of this threshold for the detection of OP by DEXA were 31.3 and 53.6%, respectively. This could be interpreted as that the factors used to determine the absolute fracture risk of individuals in the FRAX algorithm model may be revised.[7,8]

Trémollieres et al. evaluated whether a risk score identifying clinical risk factors for an MOF and combining these factors with the BMD screning or FRAX score improved the ability to identify women at high risk of fractures in early postmenopausal women. They found that the mean FRAX value (average probability of having a major OP fracture over the next 10 years) was 3.8%±2.4. They also found that the sensitivity, specificty, and AUC of FRAX and hip BMD screning was 49%, 70%, and 0.63, respectively and the sensitivity, specificity and AUC of hip BMD screning was 55%, 70%, and 0.66, respectively. This value indicated that the FRAX tool had a poor sensitivity for fracture prediction. They also identified the clinical risk factors such as a spine BMD screning, personal history of fracture, number of pregnancies (3 or more), and current postmenopausal hormone therapy use as important predictors of an MOF. Therefore, they also examined whether adding parity to the predictive model that included FRAX significantly improved the ability to identify women at high risk of fractures and found that the new FRAX+parity score with an AUC of 0.65 was not superior to the FRAX or hip BMD screning score alone. Moreover, they examined the discriminant value of a simple risk score containing the four factors (age, hip BMD screning, fracture history, and parity) that best predicted fracture. They found that this model-based risk score with an AUC of 0.69 was significantly better than FRAX alone, but not better than hip BMD screning alone. After excluding women who started postmenopausal hormone therapy during follow-up, due to the overestimation of fracture risk, they reanalyzed and found the same result for FRAX (AUC=0.64), hip BMD screning (AUC=0.69), FRAX+parity score (AUC=0.63), and the model-based risk score (AUC=0.63). They also found that the use of postmenopausal hormone therapy and having 3 or more

children resulted in a significant protection against fractures.[6] Although adding new clinical risk factors to FRAX did not significantly improve fracture prediction based on the results of this study, we think these risk factors might be revised because our study had low specificity, sensitivity, and AUC values due to the absence of some risk factors (such as alcohol consumption, previous history of fracture, family history of fracture, glucocorticoid use, and rheumatoid arthritis) in the FRAX tool in our study population. Ultimately, the task of a screening tool should be to detect occult disease before fracture occurs and serve for early initiation of treatment. Therefore, further studies are needed to identify additional clinical risk factors.

Crandall et al. compared the FRAX tool with the Simple Calculated Osteoporosis Risk Estimate (SCORE) tool and the Osteoporosis Self-assessment (OST) tool in postmenopausal women 50 to 64 years old. They found 34.1% sensitivity, 85.8% specificity, and 0.60 AUC for the ability of FRAX to detect a femoral neck T-score <-2.5% in the study populations, whereas the sensitivity, specificity, and AUC rate was 74.0%, 70.8%, and 0.72 for the SCORE and 79.8%, 66.3%, and 0.73 for the OST. This indicated that the ability of FRAX to discriminate between women with and without densitometric OP was significantly lower than SCORE and OST. They noted that in their study population, a FRAX threshold of 5.04% would increase the sensitivity of FRAX to 80.2% while reducing the specificity to 40.9% for detecting OP of the femoral neck in this age group. They emphasized that the FRAX threshold of ≥9.3% for screening women aged 50-64 would not identify the vast majority of women with T-score ≤-2.5. They suggested that current OP screening guidelines are mostly based on studies in women 65 years of age and older, and there is limited data on optimal OP screening strategies for young postmenopausal women. They also found that the 10-year FRAX-predicted MOF risk ≥4.1% captured 90.7% of participants with a femoral neck T-score ≤-2.5.[7] This threshold is equivalent to the FRAX risk threshold calculated for MOF (≥4%) in our study.

Bansal et al. evaluated whether the DEXA indication seems appropriate based on the FRAX tool and other risk factors and the performance of the 9.3% MOF risk threshold to detect OP. MOF risk calculation without BMD screning with FRAX in 82 of the patients (27.9%) was found to be 9.3% or more. They found that the overall sensitivity and specificity of 9.3% for the MOF risk calculated with FRAX was 37% and 74%, respectively, for the detection of OP. They suggested that 9.3% of the USPSTF-recommended MOF risk threshold for OP screening in women aged 50-64 years had a low sensitivity to detect OP.[8] The results of our study were compatible with this study. Moreover, Bansal et al. found that lowering the FRAX risk threshold to 5.5% would increase the sensitivity of detecting OP from 37% to 80%, but decrease the specificity from 74% to 27%. They suggested that in a disease such as OP with clinically significant morbidity and mortality, a screening test should have greater sensitivity than specificity and a lower risk threshold may increase the sensitivity of detecting densitometrically defined OP in premenopausal women.[8] According to the results of our study, we also agree with them on this issue.

Azagra et al. evaluated the FRAX tool to measure its discriminative capacity as a model for the prediction of osteoporotic fracture compared to the BMD screning model, as well as to measure predictive capacity and goodness of fit among the Spanish female population. They also provided information on the frequency of risk factors for osteoporotic fractures. They found that the AUC for MOF and HF using FRAX without DEXA was 0.686 (95% CI 0.630-0.742) and 0.883 (95% CI 0.827-0.938), respectively. They demonstrated that clinical risk factors are age, previous fragility fracture, low BMI, rheumatoid arthritis or glucocorticoid intake, as in other previous studies. They also found that the FRAX tool showed a good discrimination capacity to detect women at high risk of fragility fractures, but it is better for HF than major fracture. They suggested that the estimation capacity of the FRAX tool without BMD screning is better for HF prediction in women under 65 years of age, but needs some adjustment.[9] Considering HF with higher AUC compared to MOF, the results of our study is consistent with this study. Based on these results, it can be thought that not only the MOF risk score but also the HF risk score should be taken into account when using the FRAX tool.

Ghannam et al. determined whether FRAX identifies women under the age of 65 with OP needing BMD screning. They also tried to characterize women under the age of 65 with OP that FRAX fails to identify and provide descriptive data on their study population. MOF risk calculation without BMD screning with FRAX in 51 of the patients (45.1%) was found to be 9.3% or more (high risk group). They demonstrated that the sensitivity of FRAX for identifying women with a T-score <-2.5 and a history of fracture was 40% and 32%, respectively. They also found that the sensitivity of FRAX for identifying women with a T-score <-2.5 or identifying women with a history of fracture was 32%. When they lowered the MOF from 9.3% to 8.4%, they found the sensitivity for this threshold value to be 43% and they identified 3% more women under 65 (later diagnosed with OP) who needed BMD screning. They proposed that the FRAX tool alone fails to define many women under the age of 65 with OP in requirement of BMD screening.[10] In our study, the sensitivity and specificity of a FRAX-calculated MOF risk ≥9.3% and MOF risk ≥8.4% for detecting OP were 0 and 93.4%, 0 and 97.9%, respectively. Our findings regarding the poor sensitivity of the FRAX tool are consistent with previous studies. Moreover, Ghannam et al. showed that older age, long postmenopausal period, excess number of FRAX risk indicators, and a MOF risk of 9.3% or higher are important risk factors for determining women under 65 with OP. They demonstrated a significant relationship between the detection of OP and age, ethnicity, postmenopausal period, number of FRAX risk factors, fracture history, family history, smoking, and glucocorticoid use. They also suggested that adding the number of postmenopausal years to the screening tool could help identify more women who would benefit from BMD screning. They also proposed that more studies are needed to explore the effective and additional risk factors to improve existing screening tools used in clinical practice.[10] We also agree with them on this issue.

As noted in previous studies, the results of our study also indicate that current USPSTF recommendations for OP screening are inadequate and miss many women with OP who would benefit from BMD screning and treatment. The purpose of BMD screening is to identify postmenopausal women with a T-score ≤-2.5 and to initiate pharmacological therapy to prevent fractures in this group. The role of the screening test is to define silent disease where early intervention can prevent a bad outcome. Therefore, the ability of the FRAX tool to detect individuals with a BMD screning T-score of -2.5 or less is of great clinical importance. As hip BMD screning increases exponentially with advancing age, osteoporotic fractures affect the lumbar spine more than the hip in early menopause. Moreover, vertebral fractures are asymptomatic in the majority of cases (about two-thirds). The FRAX tool also has a number of limitations such as dose exposure to glucocorticoids, concurrent data on lumbar spine BMD, trabecular bone score (TBS), hip axis length (HAL), fall history, Type 2 diabetes, migration status, and novelty of previous fracture.[11,12] Most of the clinical risk factors included in the FRAX tool (notably, family history of fractures, current use of systemic glucocorticoids, high alcohol intake, and rheumatoid arthritis) were not significantly associated with fracture risk in our population. In addition, our results highlight the need to revise the screening guidelines for OP detection. A review of selected clinical risk factors may be helpful in improving the performance of the FRAX tool.

The limitations of our study are small sample size, retrospective nature, limited study population (therefore it cannot be generalized), not including patients with a history of fracture and using hormone replacement therapy and inability to make a comparison in terms of clinical risk factors due to small sample size. However, our results are similar to those of previous studies.

CONCLUSION

In summary, FRAX can be a valuable tool for assessing fracture risk in women under 65, but it should not be the sole determinant for recommending DEXA scans. Clinical judgment, additional risk factors, local guidelines, and patient preferences should all be considered when making decisions about OP screening and DEXA scans in this population The results of our study show that the recommended FRAX threshold value requiring screening with DEXA is high for the detection of OP in postmenopausal women under the

age of 65, consistent with previous studies. Considering that the task of a screening tool is to detect occult disease, a review of both the FRAX threshold and the risk factors used in the FRAX tool may be regarded. In the position paper of the International Osteoporosis Foundation and the European Society for Clinical and Economic Aspects of Osteoporosis, Osteoarthritis and Musculoskeletal Diseases, it has been suggested that the need for diagnostic criteria be questioned as the field moves toward risk-based assessment and intervention, including adjustments to FRAX and guidance thresholds to distinguish high risk from very high risk to optimize the use of anabolic agents.[13] Moreover, the next generation of FRAX, including novel and updated existing risk factors, is being developed. FRAX Plus, an enhanced version of the tool, incorporates additional parameters and refinements to further enhance risk assessment accuracy and clinical utility. The adjustments in FRAX plus are recency of osteoporotic fracture, high exposure to oral glucocorticoids, the information on TBS, falls history, HAL, and concurrent data on lumbar spine BMD screning. FRAX plus offers clinicians the ability to further refine risk prediction, optimize detection of those at highest risk of fracture and initiate appropriate treatment.[14,15] Further studies are needed to develop FRAX plus.

Authorship Contributions

Surgical and Medical Practices: *Ebru Yılmaz;* ***Concept:*** *Ebru Yılmaz;* ***Design:*** *Ebru Yılmaz;* ***Data Collection or Processing:*** *Ebru Yılmaz, Mehpare Fırat;* ***Statistical analysis:*** *Özge Pasin;* ***Analysis or Interpretation:*** *Ebru Yılmaz;* ***Literature Search:*** *Ebru Yılmaz;* ***Writing:*** *Ebru Yılmaz.*

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