DEVELOPMENT OF CLINICAL RISK ASSESSMENT TOOL FOR OSTEOPOROSIS (OSTEORISKAPP) USING A SYNDROMIC APPROACH

O. Yilmaz¹, V. Mevsim^{2,*}, E. Kuruoglu³

¹Arpaçay Family Health Center, Kars, “Dokuz Eylül” University Faculty of Medicine, ²Family Medicine, ³Computer Science, Izmir, Turkey

Abstract

Context. DEXA is recommended for osteoporosis screening. However, the rate of screening with DEXA is very low. Therefore, methods that can be used more easily and cost effectively are needed.

Objective. The objective of this study is to develop a clinical risk assessment tool of osteoporosis (OSTEORISKAPP) by using syndromic approach.

Design. A methodological study was performed.

Subjects and Methods. Three hundred and fifty-six participants who are above 50 years old are participants of study and take history and physical examination. Positive likelihood ratio (LR), pre and post test probability, is calculated. A logistic regression analysis and a ROC analysis are made with the model constructed by those criteria.

Results. Eighteen different clinical risk indices are diagnosed. According to LR, 4 of these criteria are minimally effective, 11 of them are weakly effective and 3 of them are medium effective criteria According to results of logistic regression analysis, back pain, waist pain, and usage of cortisone for more than 3 months, vertebra tenderness in physical examination, having dorsal kyphosis and being obese are turned out to be statistically significant in 89.9% confidence interval. AUC is found to be 0.948 and diagnostic test is found to have perfect distinction ability.

Conclusion. Syndromic diagnostic criteria that will be used for osteoporosis screening of population and that is cost effective, no need to refer, practical, reliable and has tried to be developed.

Key words: Osteoporosis, clinical risk factors, logistic regression, syndromic approach.

INTRODUCTION

Osteoporosis (OP) is the most common metabolic bone disease and is characterized by the loss of bone strength and an increase in the risk of bone fracture. It increases bone fragility by decreasing bone strength and results in minimal traumas from daily life

activities causing bone fractures. (1)

As the average life expectancy increases and people increasingly adopt a sedentary lifestyle, the rate of OP increases. Because elderly femur fracture causes mortality, it is more important due to challenges in treatment and rehabilitation. With osteoporotic development, postmenopausal women who are above 50 years of age have the greatest risk. Worldwide, one third of women who are between 60 – 70 years of age and half of women who are 80 years of age and above have osteoporosis (2). The most important clinical results of osteoporosis are complications such as fractures, pain, deformity and loss of function. The mortality rate in the two years after a femur fracture increases by 20% (3).

Osteoporosis is under diagnosed and undertreated despite the availability of effective treatments (4-6). Osteoporosis screening is recommended by many national clinical practice guidelines (7). The gold standard test for diagnosing osteoporosis is dual energy X-ray absorptiometry (DXA), which measures the bone mineral density (BMD). Evidence of osteoporosis treatment efficacy to reduce fracture risk has been shown in clinical trials of individuals with osteoporosis by DXA criteria or prior osteoporotic fracture. For this reason, DXA testing is typically performed to identify individuals who have not previously experienced an osteoporotic fracture and are most likely to benefit from treatment.

Currently, the most common risk assessment tool, which is called FRAX by WHO, is a web-based logarithmic system that is used in calculating the risk of fracture. The FRAX for estimating the individual risk of osteoporotic fracture over 10 years assessed includes the following clinical risk factors: a prior fragility fracture, parental history of hip fracture, current tobacco smoking, long-term use of glucocorticoids, rheumatoid arthritis, other causes of secondary osteoporosis and

*Correspondence to: Vildan Mevsim PhD, “Dokuz Eylül” University Faculty of Medicine, Family Medicine, Izmir, 35340, Turkey, E-mail: vmevsim@gmail.com

daily alcohol consumption.

Prior to the advent of FRAX, other risk assessment tools were available to identify women with a low BMD and/or to estimate the risk of osteoporosis. The ABONE (Age, Body Size, No Estrogen) risk assessment tool and the ORAI (the Osteoporosis Risk Assessment Instrument) use age, weight, and estrogen information (8). The OST (the Osteoporosis Self-assessment Tool equation) uses weight and age information (9). The SCORE (the Simple Calculated Osteoporosis Risk Estimation tool) uses race, rheumatoid arthritis, history of minimal trauma fracture after an age of 45 years, age, estrogen therapy use, and weight information (9, 10).

A syndrome is the group of symptoms and signs that are determined during the examination of the patient (11). Some specific signs and symptoms form a syndrome according to a syndromic approach. Diagnoses and treatments are based on the history, signs and symptoms of the patient examination. This approach has the best chance of curing the patient at the first consultation. The treatment plan is important for inhibiting the disease before it progresses further. The risk instruments/tools that assess the individuals' clinical risk factors for osteoporosis usually use the patient symptoms and history. However, the patient signs can be used as criteria for osteoporosis. From this point of view, the syndromic approach can be used for diagnosing osteoporosis. Since most laboratory tests are highly expensive and require consultation with a doctor during diagnosis and treatment, they reduce the effective use of resources. For these reasons, even in the countries that have highly developed laboratories, syndromic approach guidelines are commonly used for several different diseases (12).

Syndromic criteria are developed using statistical measures in the context of evidence-based medicine. Syndromic criteria are determined by calculating the likelihood ratio and post-test probability. Logistic regression analysis and receiver operating characteristic (ROC) curve analysis are used to construct the diagnosis test model. According to the syndromic criteria, patients who are screened are classified as those with and without osteoporosis as well as those with suspected osteoporosis.

In considering the permanent increase in the rate of life expectancy and the prevalence of osteoporosis, the cost of precautions taken before the development of bone fracture will decrease mortality and morbidity.

The aim of this study is to develop a clinical risk

assessment tool of osteoporosis (OSTEORISKAPP) using the syndromic approach.

METHODS

This research was designed as a methodological study. The Dokuz Eylul University Ethics Committee gave ethical approval for the research. Three hundred fifty-six participants who met the inclusion criteria were evaluated in the study; the sample was drawn from people who applied to Dokuz Eylul University Hospital Radiology Laboratory between April 2015 and May 2015 for a DXA scan with any reason.

Inclusion criteria:

*50 years and over by men and women,
Applicants for DEXA to radiology laboratory,
Volunteers to participate for the study.*

Exclusion criteria:

*Those who have received bisphosphonate or
hormone treatment for OP during the last 5 years,
Those like Marfan's syndrome, Osteogenesis
Imperfecta with genetic disease with a high OP rate,
Participants with implants in the densitometry
drawer area (hip, vertebrae),
Those with severe dementia,
Individuals weighing over 135 kg.*

Initially, the medical histories of the participants are obtained, and physical examinations are performed by researchers; the results are recorded on the data forms. The following details are obtained from the patient histories: demographic information, history of presenting disease, past medical history, risk factors for OP, diet and exercise details, family history and social history. A complete physical examination is performed for the participants, especially evaluation of tenderness of the vertebral spine with pressure and tenderness of tibia shaft; the length, weight and arm span are measured; and the dorsal kyphos is checked. We did not consider the presence of a history of previous fracture as a diagnostic criterion regardless of the T score. The lumbar and femur neck bone intensity of participants are measured with a GE Lunar DPX Bone Densitometer. The T scores and Z scores of all participants are recorded on the data forms after two months via the information system, which is tracked by the patient identification number that is on the data forms.

The T and Z scores reflect the BMD measurements as a degree of standard deviation from the average BMD measurement of same sex young adults. The use of scores depends on age and

menopausal status. For children, premenopausal women, and men under the age of 50, the Z-score is used for diagnosis. If the Z-score is -2.0 or lower, the result is "below the expected range for age." If the Z score is above -2.0, the result is defined as "within the expected range for age." A T score under 1 standard deviation from the adult average (1 SD) is considered normal, while a T score between -1 SD and -2.5 SD is considered osteopenia, and BMD measurements below -2.5 SD (T-Score < -2.5) are considered OP. In the scope of this study, a T-Score > -2.5 is considered normal, and a T-Score < -2.5 is considered OP for men and postmenopausal women also for women who are not in menopause Z-Score > -2.0 is considered normal, and a Z-Score < -2.0 is considered OP.

SPSS 22.0 statistical package program is utilized to evaluate the data. Descriptive analysis, student's t test, and the Chi squared test are used, and a p value less than 0.05 is accepted as the level of significance. In addition, the sensitivity, specificity, likelihood ratio (LR) and positive-negative predictive value (+ and - prediction value) are used. Post-test probability is calculated with the LR and pre-test probability. A constant +LR, which is not affected by the prevalence, in case of a positive utilized test, reflects how much the disease probability will increase. +LR and -LR values are calculated for the variables that are statistically significant in the history and physical examination results. LR values between 1-2 indicate a minimum increase, LR values between 2-5 indicate a low increase, LR values between 5-10 indicate a medium increase, and LR values more than 10 indicate a high increase in the probability of disease (13).

Logistic regression analysis is applied to the model created with the determined criteria. Receiving operating characteristic (ROC) analysis is performed with the significant criteria in the model, and the AUROC is calculated. We used DEXA results as the golden standard of osteoporosis for ROC analysis and logistic regression analysis.

RESULTS

In this study, 62.0% of the participants are between 50 and 64 years of age, and 38.0% are older than 65 years. Participants have an average age of 62.37 ± 8.6 years (min=50 and max=97), while 91.6% are female and 8.4% are male. 96.7% of female participants have had menopause. 3.3% (n = 11) were not menopausal. Housewives accounted for 49.4% of the sample and retired people accounted for 39.9%;

additionally, 69.4% are married, and 46.7% have a high school education or higher.

The bone mineral density results indicate that 39.3% of the participants have osteoporosis, and 60.7% are normal; additionally, 58.1% of the patients declared that they had undergone prior surgery.

Additionally, 35.4% of the participants have a history of non-traumatic or low-trauma broken bones. The percentage of people who took cortisone for more than 3 months is 15.2%. The percentage of participants who stayed in the hospital for more than one month is 9.8%, and the percentage of participants who have a chronic disease is 86.8%.

The personal history, symptoms and family history of the participants are studied and the following relatively high OP diagnosis rates are obtained ($p < 0.05$) (Table 1): an OP diagnosis rate of 55.2% for participants over 65 years of age, 69% for participants who have widespread body pain or bone pain, 68.5% for participants who have back pain, 79.8% for participants who suffered bone fracture after the age of 50, 59.3% for participants who took cortisone for more than 3 months, 74.3% for participants who were hospitalized for more than one month, 41.5% for participants with a chronic disease, 62.5% for participants diagnosed with rheumatoid arthritis, 64.8% for participants with a family history of OP, 61.6% for participants with a family history of fracture with a slight trauma, and 65.5% for participants with a parent with kyphosis.

The gynecological history of the female participants is studied with respect to the presence of OP, and the following high rates are obtained: OP diagnosis rate of 48.5% for participants whose menarche age is above 13 years, 53.7% for participants who started menopause before the age of 47 and 71.4% for participants who have irregularity in menstruation for more than 12 months ($p < 0.05$). Physical examination of the participants showed that 30.3% had tenderness of the vertebral spine, 19.7% had tibia shaft tenderness, 36.2% had increased dorsal kyphosis, 50.6% had height below 155 cm, 53.4% had a height decrease of 5 cm or more, 29.2% had a body-mass index (BMI) of 25 or less, and 29.2% had a 5 cm or more difference between the height and arm span. The straight leg elevation test is positive for 11.5% of the participants.

Physical examination results of the participants are studied with respect to the presence of OP and the following OP diagnosis rates are found: 84.3% for participants with vertebral spine tenderness, 75.7% for participants with tibia shaft tenderness, 80.6% for participants with increased dorsal kyphosis, 50.6%

for participants with a height below 155 cm, 80% for participants with a height decrease of 5 cm or more, 72.1% for participants with a BMI of 25 or less, and 85% for participants with a 5 cm or more difference between the height and arm span ($p<0.001$) (Table 1).

Statistically significant variables of findings from the history and physical examination are studied with respect to likelihood rates, and 18 clinical risk indices are detected. Likelihood rates indicate that 4 of these variables are minimally effective criteria, 11 are

weakly effective criteria and 3 are moderately effective criteria (Table 2).

The following variables are the minimally effective criteria: current age above 65 years, menarche age of 13 or higher, menopause starting at age 47 or less, and current height of 155 cm or less. Widespread body pain, back pain, lower back pain, bone fracture before age of 50, use of cortisone for more than 3 months, diagnosis of rheumatoid arthritis, family history of OP, having a parent with kyphosis or a fracture with slight

Table 1. Descriptive statistics of osteoporosis according to the patient symptoms and signs

Descriptive variables	n	Osteoporosis %	No Osteoporosis %	p
Age				
50-64 years	222	29.7	70.3	<0.001
65 years and above	124	55.2	44.8	
Widespread body pain/ bone pain				
Yes	120	69.1	30.8	<0.001
No	236	24.2	75.8	
Back pain				
Yes	149	68.5	31.5	<0.001
No	207	18.4	81.6	
Lower back pain				
Yes	187	60.5	39.5	<0.001
No	169	16.0	84.0	
Bone fracture before the age of 50				
Yes	51	66.6	33.3	<0.001
No	305	34.8	65.2	
Bone fracture after the age of 50				
Yes	94	79.8	20.2	<0.001
No	262	24.8	75.2	
Cortisone for more than 3 months				
Yes	54	59.3	40.7	0.001
No	302	35.8	64.2	
Hospitalization for more than 1 month				
Yes	35	74.3	25.7	<0.001
No	319	35.8	64.2	
Chronic Disease				
Yes	309	41.5	58.5	0.038
No	47	25.5	74.5	
Rheumatoid Arthritis				
Yes	32	62.5	37.5	0.005
No	324	36.2	63.8	
OP in the family history				
Yes	105	64.8	35.2	<0.001
No	251	28.7	71.3	
Maternal/paternal fracture with slight trauma				
Yes	71	61.6	32.4	<0.001
No	285	32.3	67.7	
Maternal/paternal kyphosis				
Yes	110	65.5	34.5	<0.001
No	246	27.7	72.3	
Vertebral tenderness spine				
Yes	108	84.3	15.7	<0.001
No	248	19.8	80.2	
Tibia shaft tenderness				
Yes	70	75.7	24.3	<0.001
No	286	30.4	69.6	
Increased dorsal kyphosis				
Yes	129	80.6	14.0	<0.001
No	227	12.8	87.2	
Current height				
155 cm and below	180	50.6	49.4	<0.001
Above 155 cm	176	27.8	72.2	
Height decrease				
5 cm or more	150	80.0	20.0	<0.001
Less than 5 cm	172	7.6	92.4	
BMI				
25 and below	104	72.1	27.9	<0.001
Above 25	252	25.8	74.2	
Difference between height and arm span				
5 cm and more	100	85.0	15.0	<0.001
Less than 5 cm	241	19.1	80.9	

Table 2. Sensitivity, specificity, +LR, -LR, pre-test probability, post-test probability and statistical significance of clinical risk indices for osteoporosis

	Sensitivity %	Specificity %	+LR	-LR	Pre-test probability %	Post-test probability %	p
Minimally Effective Criteria							
Age > 65	53	72	1.90	0.65	39	55	<0.001
Age of menarche < 13	52	65	1.48	0.74	39	48	0.003
Age of menopause < 47	63	63	1.73	0.58	40	54	<0.001
Height < 155 cm	65	59	1.58	0.60	39	51	<0.001
Weakly Effective Criteria							
Widespread body pain / bone pain	59	82	3.46	0.49	39	69	<0.001
Back pain	72	78	3.34	0.34	39	68	<0.001
Lower back pain	80	65	2.35	0.29	39	60	<0.001
Bone fracture before age 50	24	92	3.08	0.82	39	66	<0.001
Cortisone use > 3 months	22	89	2.24	0.85	39	59	0.001
Rheumatoid arthritis	14	94	2.57	0.90	39	62	0.005
OP family history	48	82	2.84	0.62	39	65	<0.001
Parental history of low traumatic fracture	34	89	3.21	0.73	39	67	<0.001
Parental gibbus deformity	51	82	2.92	0.58	39	65	<0.001
Tibial shaft fragility	37	92	4.81	0.67	39	75	<0.001
BMI < 25	53	86	3.99	0.54	39	72	<0.001
Moderately Effective Criteria							
Fracture at age < 50	53	91	6.09	0.51	39	79	<0.001
Vertebral spinous fragility	65	92	8.25	0.37	39	84	<0.001
Increase in dorsal kyphosis	79	91	9.51	0.23	39	86	<0.001

Table 3. Area under the curve for OSTEORISKAPP clinical risk indices in the model

Clinical risk index	Area	Std. Error ^a	Asymptotic Sig. ^b	Asymptotic 95% Confidence Interval	
				Lower Bound	Upper Bound
Back pain	0.245	0.027	0.000	0.191	0.298
Low back pain	0.268	0.027	0.000	0.214	0.321
Steroid therapy >3 months	0.437	0.032	0.043	0.375	0.499
Vertebral spine fragility	0.214	0.027	0.000	0.161	0.267
BMI 25 or less	0.701	0.030	0.000	0.643	0.759
Increase in dorsal kyphosis	0.145	0.023	0.000	0.100	0.190

a. Under the nonparametric assumption; b. Null hypothesis: true area = 0.5.

trauma, tibia shaft tenderness, and BMI of 25 or less are the weakly effective criteria. Fracture after the age of 50 years, vertebral spine tenderness, and increase in dorsal kyphosis are the moderately effective criteria (Table 2).

Logistic regression and ROC analysis evaluation

Eighteen clinical risk indices that are obtained can be used for both men and woman. However, in the next step, which is model creation, the 2 indices that are specific to women are removed from the model.

In the research, the model consists of 16 variables (minimally, weakly and medium effective criteria) and sample size is 356 (nwomen = 326, nmen = 30). Six of these variables are found to be significant. These variables are back pain, lower back pain, use of cortisone for more than 3 months, vertebral spine fragility, BMI below 25 and increased dorsal kyphosis.

According to the logistic regression results, back pain increases the risk of OP by 3,702 times, lower back pain increases the risk by 3,105 times, use of cortisone for more than 3 months increases the risk by 4,091 times, vertebral fragility increases the risk by 6,509 times, dorsal kyphosis increases the risk by 10,124 times, and obesity decreases the risk by 7,519 times (Table 3).

The model with these 6 variables has an accuracy of 89.9% with 0.948 for the area under the curve at a confidence interval of 95% (0.925-0.971). The diagnostic test is found to have a perfect differentiation ability. The optimum value for the threshold of sensitivity is 0,386 (Fig. 1).

DISCUSSION

In this study, we constructed clinical risk factors (syndromic criteria) with the help of DXA,

Figure 1. ROC Curve of OSTEORISKAPP clinical risk indices.

which is the golden standard test, for diagnosing osteoporosis that can lead to mortality and morbidity. The study was completed with 356 participants with an age of 50 years and above.

The syndromic criteria will improve the OP management for people with an age above 50 years, providing an approach that is efficient for both patients and doctors, inexpensive and easily accessible.

We determined 18 syndromic criteria in the study. According to the likelihood ratio, 4 of these criteria are minimally effective (age above 65, age of menarche above 13, menopause younger than the age of 47 and height of 155 cm or less), 11 are weakly effective (widespread body or bone pain, back pain, low back pain, fracture at an age below 50, use of cortisone for more than 3 months, rheumatoid arthritis, family history of OP, parental history of gibbus or a history of low traumatic fracture, tibial shaft fragility or BMI of 25 or below), and 3 are moderately effective (history of low traumatic fracture above the age of 50, vertebral spinous fragility and increased dorsal kyphosis).

In the model with 16 clinical risk indices that are statistically significant for both sexes, 6 of the variables (back pain, low back pain, use of cortisone for more than 3 months, vertebral spine fragility, BMI of 25 or below and increased dorsal kyphosis) are significant. The model with these 6 variables has an accuracy of 89.9% with 0.948 as the area under the curve with a 95% confidence interval (0.925-0.971). The diagnostic test is found to have perfect differentiation ability. The optimal value for the threshold of sensitivity is 0.386.

The widest prevalence study performed in

Turkey showed that the OP rate above age of 50 is 24.8% (14). Furthermore, KASTÜRKOS research showed that the femur neck OP frequency is 19.6% for age above 50 (15). In this study, the OP prevalence is 39.3%, which is higher than that in similar studies. Because this research study is aimed at determining syndromic criteria, it is performed at third level medical institution with high prevalence to investigate as many factors as possible related to OP.

The average age of menarche is 13.4 years and the average age of menopause is 46.5 in our study, which are consistent with various studies performed in Turkey (16, 17). The majority of the participants of this study are female (91.6%), which can be because DXA scans are requested for female patients at gynecology and obstetrics clinics to monitor the problems caused by menopause. Similarly, they are mostly requested for female patients with high risk factors from clinical settings, such as physical therapy and rehabilitation and endocrinology. Research shows that the OP rate for age above 65 years is high compared to 50-64 years of age. A decrease in the bone mineral density proceeds faster for women, especially after menopause. Bone loss of 2-5% each year after menopause results in high OP rates.

Participants with back pain, lower back pain and widespread body pain have a higher OP diagnosis rate in the study, which agrees with similar studies in the literature. Strong relationships between lower back pain and low BMD levels are detected in the study by Gaber *et al.* (18). By contrast, another study performed in individuals with chronic lower back pain does not indicate a relationship between the BMD level and lower back pain (19). In another study, back pain and lower back pain are considered as complications of OP (20).

The findings of this study show that participants with a family history of fracture have a higher rate of OP. Similar results are obtained in various studies in the literature (21, 22). In recent years, the effects of genetics on the OP pathogenesis have been studied and numerous possible genes have been reported to affect bone mass (23).

According to the results, the rate of OP is less for those with menarche at age 13 or less. An early age of menarche results in higher exposure to estrogen, which leads to a high bone density (24). BMD and early menopause are generally believed to be related, but there is no single definition and threshold value for early menopause. In Gallagher *et al.*, patients who started menopause before the age of 45 had an increased

risk for bone fracture (25). In a study of American women, those with menopause before the age of 48 had low scores for the femur, vertebral and radial BMD (26). Our findings are in agreement with those studies as the OP rate was lower in women with menopause above the age of 47 years. In recent years, many studies have analyzed the relationship between OP and obesity. Body weight imposes a burden on the skeleton and affects bone density in a positive way. Additionally, estrogen stored in the fatty tissue has a positive impact on the bone density. There are some researches which showed BMI correlated positively with spine BMD (27). Ersoy *et al.* reported that as the BMI decreases, the incidences of OP and osteopenia increase (28). Villareal *et al.* reported that loss of weight in the elderly decreases the hip BMD (29). Another study showed that BMI is protective in that people with a BMI of 30 or more have a 33% lower risk of OP (30).

Metabolic Syndrome (MS) is characterized by abdominal obesity, impaired glucose tolerance, hypertension and dyslipidemia. There have been many studies about the relationship between MS and bone metabolism. Low-grade inflammation in MS patients is associated with bone loss and a study has shown that a significant association between MS, low BMD and vertebral fractures was found (31).

The first complaint of OP patients is usually

back pain and gibbus related to vertebral fractures. As people get older, the number of vertebral fractures increases, disk distances shrink and dorsal kyphosis occurs. The OP Foundation recommends that 4 cm of shortening should be considered a sign of silent vertebral fracture (32). In another study, shortening by 7 cm or more is linked to vertebral fracture, whereas our study shows that shortening of 5 cm or more indicates a higher risk of OP (33). When a normal person stretches out both arms alongside, the distance is called a fathom. The height of a person is very close to the fathom distance. However, OP patients' heights are usually shorter than their fathoms. In agreement with this, the rate of OP in this study is higher for those with a difference between the fathom and height of 5 cm or more.

Table 4 shows the risk factors in OP and fracture indices in different tools. Aside from these indices, additional risk factors are found, such as age of menarche above 13 years, menopause at younger than age 47, frequent body pain, back pain, waist pain, bone fracture before 50 years of age, family history of OP, parents with gibbus, tibial shaft fragility, bone fracture after 50 years of age, vertebral spine fragility and increase in dorsal kyphosis.

Strengths of the study: The study is based on detailed history and physical examination of patients.

Table 4. Clinical risk factors included in each tool

	FRAX	SCORE	ABONE	ORAI	OST	OSTEORISKAPP
Age	X	X	X	X	X	
Weight	X	X	X	X	X	X
Previous low energy fractures	X	X				
Estrogen therapy		X	X	X		
Rheumatoid arthritis	X	X				
Height	X					X
Parental hip fractures	X					X
Smoking	X					
Alcohol	X					
Glucocorticoid therapy	X					X
Secondary osteoporosis	X					
Sex	X					
Ethnicity		X				
First menstrual age						X
Menopause age						X
Frequent body pain						X
Back pain						X
Waist pain						X
Bone fracture before 50 years of age						X
OP history in family						X
Parental gibbus						X
Tibial shaft fragility						X
Bone fracture after 50 years of age						X
Vertebral spine fragility						X
Increase in dorsal kyphosis						X

As many criteria were evaluated, more risk factors are determined as useful for diagnosis than in prior studies. A more accurate diagnosis will be obtained with these criteria. According to risk assessment models, such as FRAX, ORAI, RISK and SCORE, the inclusion of several additional risk factors, anatomical measurement and examination makes the study more powerful.

All patients in the study population are examined by the same researcher, making the results more consistent. All participants are evaluated by the gold standard method of DXA. For risk scoring, research is conducted in different communities. This study is essential because it is the first risk scoring assessment study in Turkey and has results that are applicable to Turkish society.

Drawbacks of the study: Because the study is conducted at one centre, it may not represent the general population. For example, the level of education of the study participants is higher than the average level of education in Turkey. Data such as the medical and family history are collected based on participants' statements. Memory may be a confounding factor. Because the study is performed in a university hospital, the prevalence of OP is high and the specificities of the obtained syndromic criteria are low, although the sensitivities are high.

In conclusion, early diagnosis of OP often occurs in postmenopausal women, and it is important to take precautions related to OP to both decrease the cost of diagnosis and treatment in the health system and morbidity.

In this study, we tried to improve the diagnostic criteria for OP, making them efficient, inexpensive, easy to use and practical. Additionally, the syndromic diagnostic criteria, including evaluation of physical exam findings in the context of risk factors, eliminate the need to refer the patients for scanning, decreasing excess radiation.

We found that the minimally effective criteria are as follows: age above 65, age of menarche above 13, menopause below the age of 47 and height of 155 cm or less. Weakly effective criteria are widespread body or bone pain, back pain, low back pain, fracture at an age below 50, use of cortisone for more than 3 months, rheumatoid arthritis, family history of OP, parent(s) with gibbus or a history of a low traumatic fracture, tibial shaft fragility or BMI of 25 or below.

This study may be extended to longer term, larger patient sampling to determine the criteria that have high specificity in the primary healthcare setting and that can better reflect the prevalence of OP.

Conflict of interest

The authors declare that they have no conflict of interest.

References

1. Klibanski A, Adams-Campbell L, Bassford TL, Blair SN, Boden SD, Dickersin K, Gifford DR, Glasse L, Goldring SR, Hruska K, Johnson SR, McCauley LK, Russell WE. Osteoporosis prevention, diagnosis, and therapy. *Journal of the American Medical Association*. 2001;285(6):785-795.
2. Kannus P. International osteoporosis foundation: The facts about osteoporosis and its impact. Lyon: International Osteoporosis Foundation; 2003.
3. Aranha L, Mirón Canelo J, Alonso Sardón M, Del Pino Montes J, González S. Health-related quality of life in Spanish women with osteoporosis. *Revista de Saúde Pública*. 2006;40(2):298-303.
4. Stafford RS, Drieling RL, Hersh AL. National trends in osteoporosis visits and osteoporosis treatment, 1988-2003. *Archives of internal medicine*. 2004;164(14):1525-1530.
5. Nguyen TV, Center JR, Eisman JA. Osteoporosis: underrated, underdiagnosed and undertreated. *Medical Journal of Australia*. 2004;180(5):S18.
6. Vestergaard P, Rejnmark L, Mosekilde L. Osteoporosis is markedly underdiagnosed: a nationwide study from Denmark. *Osteoporosis International*. 2005;16(2):134-141.
7. Leslie WD, Schousboe JT. A review of osteoporosis diagnosis and treatment options in new and recently updated guidelines on case finding around the world. *Current osteoporosis reports*. 2011;9(3):129-140.
8. Cadarette SM, Jaglal SB, Murray TM, McIsaac WJ, Joseph L, Brown JP. Evaluation of decision rules for referring women for bone densitometry by dual-energy x-ray absorptiometry. *Jama*. 2001;286(1):57-63.
9. Cadarette SM, McIsaac WJ, Hawker GA, Jaakkimainen L, Culbert A, Zarifa G, Ola E, Jaglal SB. The validity of decision rules for selecting women with primary osteoporosis for bone mineral density testing. *Osteoporosis International*. 2004;15(5):361-366.
10. Cadarette S, Jaglal S, Murray T. Validation of the simple calculated osteoporosis risk estimation (SCORE) for patient selection for bone densitometry. *Osteoporosis International*. 1999;10(1):85-90.
11. Aytaç A, Eryılmaz HY. Vajinal Akıntı Tanılama Formu (VATF) Kullanılarak Konulan Tanıların Uyum Analizi. *Maltepe Üniversitesi Hemşirelik Bilim ve Sanatı Dergisi*. 2009;2(1):22-33.
12. Organization WH. Sexually transmitted and other reproductive tract infections: a guide to essential practice. 2005.
13. Hayden SR, Brown MD. Likelihood ratio: a powerful tool for incorporating the results of a diagnostic test into clinical decisionmaking. *Annals of emergency medicine*. 1999;33(5):575-580.
14. Tuzun S, Eskiuyurt N, Akarımak U, Sarıdoğan M, Senocak M, Johansson H, Kanis JA; Turkish Osteoporosis Society. Incidence of hip fracture and prevalence of osteoporosis in Turkey: the FRACTURK study. *Osteoporosis International*. 2012;23(3):949-955.
15. Aslan A, Karakoyun Ö, Güler E, Aydın S, Gök V, Akkurt S. Kastamonu'da yaşayan Türk kadınlarında kemik mineral yoğunluğu, osteoporoz yaygınlığı ve bölgesel risk faktörlerinin değerlendirilmesi: Kastürkos çalışması. *Eklem Hastalık Cerrahisi*. 2012;23:62-67.
16. Tekgül N, Saltık D, Şen Y, Kurt ES. 15-49 yaş kadınlarda ortalama menarş yaşı. *Sted*. 2005;14:76.
17. Vicdan K, Kükner S, Dabakolu T, Ergin T, Keleş G, Gokmen O. Demographic and epidemiologic features of female adolescents in Turkey. *Journal of Adolescent Health*. 1996;18(1):54-58.

18. Gaber T-Z, McGlashan K, Love S, Jenner J, Crisp A. Bone density in chronic low back pain: a pilot study. *Clinical rehabilitation*. 2002;16(8):867-870.
19. Bergenud H, Nilsson B, Uden A, Willner S. Bone mineral content, gender, body posture, and build in relation to back pain in middle age. *Spine*. 1989;14(6):577-579.
20. Lewiecki EM, Laster AJ. Clinical applications of vertebral fracture assessment by dual-energy x-ray absorptiometry. *The Journal of Clinical Endocrinology & Metabolism*. 2006;91(11):4215-4222.
21. Grainge M, Coupland C, Cliffe S, Chilvers C, Hosking D. Association between a family history of fractures and bone mineral density in early postmenopausal women. *Bone*. 1999;24(5):507-12.
22. Gennari L, Becherini L, Falchetti A, Masi L, Massart F, Brandi M. Genetics of osteoporosis: role of steroid hormone receptor gene polymorphisms. *The Journal of steroid biochemistry and molecular biology*. 2002;81(1):1-24.
23. Tural Ş, Kara N, Alaylı G, Ad FTVR. Osteoporoz genetiği. *Türk Osteoporoz Dergisi*. 2011;17:100-109.
24. Ho AY, Kung AW. Determinants of peak bone mineral density and bone area in young women. *Journal of bone and mineral metabolism*. 2005;23(6):470-475.
25. Gallagher JC. Effect of early menopause on bone mineral density and fractures. *Menopause*. 2007;14(3):567-571.
26. Kritz-Silverstein D, Barrett-Connor E. Early menopause, number of reproductive years, and bone mineral density in postmenopausal women. *American Journal of Public Health*. 1993;83(7):983-988.
27. Oros S, Ianas O, Vladioiu S, Giurcaneanu M, Ionescu L, Neacsu E, Voicu G, Stoiceanu M, Rosca R, Neamtu C, Badiu C, Dumitrache C. Does Obesity Protect Postmenopausal Women Against Osteoporosis? *Acta Endocrinologica-Bucharest* 2012; 8(1):67-76.
28. Ersoy FF, Passadakis SP, Tam P, Memmos ED, Katopodis PK, Ozener C, Akçiçek F, Camsari T, Ateş K, Ataman R, Vlachojannis JG, Dombros AN, Utaş C, Akpolat T, Bozfakioğlu S, Wu G, Karayaylali I, Arinsoy T, Stathakis PC, Yavuz M, Tsakiris JD, Dimitriades CA, Yılmaz ME, Gültekin M, Karayalçın B, Yardimsever M, Oreopoulos DG. Bone mineral density and its correlation with clinical and laboratory factors in chronic peritoneal dialysis patients. *Journal of bone and mineral metabolism*. 2006;24(1):79-86.
29. Villareal DT, Shah K, Banks MR, Sinacore DR, Klein S. Effect of weight loss and exercise therapy on bone metabolism and mass in obese older adults: a one-year randomized controlled trial. *The Journal of Clinical Endocrinology & Metabolism*. 2008;93(6):2181-2187.
30. Barrera G, Bunout D, Gattás V, de la Maza MP, Leiva L, Hirsch S. A high body mass index protects against femoral neck osteoporosis in healthy elderly subjects. *Nutrition*. 2004;20(9):769-771.
31. Popa FL, Stanciu M, Banciu A, Berteanu M. Association Between Low Bone Mineral Density, Metabolic Syndrome and Sex Steroids Deficiency in Men. *Acta Endocrinologica-Bucharest* 2016; 12(4):418-422.
32. Foundation N. Clinician's guide to prevention and treatment of osteoporosis. National Osteoporosis Foundation; Washington, DC; 2013.
33. Siminoski K, Warshawski R, Jen H, Lee K. The accuracy of historical height loss for the detection of vertebral fractures in postmenopausal women. *Osteoporosis international*. 2006;17(2):290-296.