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Original Article

An Assessment Tool for Predicting Fracture Risk in Postmenopausal Women

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Abstract. Due to the magnitude of the morbidity and mortality associated with untreated osteoporosis, it is essential that high-risk individuals be identified so that they can receive appropriate evaluation and treatment. The objective of this investigation was to develop a simple clinical assessment tool based on a small number of risk factors that could be used by women or their clinicians to assess their risk of fractures. Using data from the Study of Osteoporotic Fractures (SOF), a total of 7782 women age 65 years and older with bone mineral density (BMD) measurements and baseline risk factors were included in the analysis. A model with and without BMD *T*-scores was developed by identifying variables that could be easily assessed in either clinical practice or by self-administration. The assessment tool, called the FRACTURE Index, is comprised of a set of seven variables that include age, BMD *T*-score, fracture after age 50 years, maternal hip fracture after age 50, weight less than or equal to 125 pounds (57 kg), smoking status, and use of arms to stand up from a chair. The FRACTURE Index was shown to be predictive of hip fracture, as well as vertebral and nonvertebral fractures. In addition, this index was validated using the EPIDOS fracture study. The FRACTURE Index can be used either with or without BMD testing by older postmenopausal women or their clinicians to assess the 5-year risk of hip and other osteoporotic fractures, and could be useful in helping to determine the need for further evaluation and treatment of these women.

Keywords: Bone mineral density; Fracture risk; Hip fracture; Osteoporosis; Postmenopausal women; Risk assessment

Introduction

Osteoporosis and its consequent increase in fracture risk is a major health concern for postmenopausal women and older men, and has the potential to reach epidemic proportions. Approximately 1.5 million fractures that occur annually in the United States are attributable to osteoporosis [1]. A 50-year-old Caucasian woman has a 16% risk of a hip fracture and a 32% chance of a vertebral fracture occurring in her remaining lifetime [2]. Even more striking, women with prevalent vertebral deformities have a risk of sustaining a subsequent vertebral fracture that is five times that of women without prevalent vertebral deformities [3,4].

The risk of hip and other fractures, like the risk of heart disease, is multifactorial. Over the last 5 years, several studies have shown that bone mineral density (BMD) can predict hip fractures, and that BMD at the hip is more strongly predictive of hip fractures than BMD at other sites [5–9]. Further, several studies have examined the role of non-BMD risk factors and found that they play a significant and independent role in the

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prediction of hip fracture [6,9–11]. In the Study of Osteoporotic Fractures (SOF), Cummings and others [6] showed that a number of risk factors were predictive of hip fracture risk in Caucasian women over age 65 years, even after adjustment for age and calcaneal BMD. In a sample of more elderly women, the EPIDOS study reported that factors such as age, gait speed, and neuromuscular and visual impairments were independent predictors of hip fracture [9,11].

Unfortunately, the direct application of these results in a clinical setting is not straightforward, since both of these studies used more risk factors than would be practical to assess in a physician's office, and some of the risk factors, such as functional status, could not be easily evaluated. The SCORE risk assessment tool was developed to identify postmenopausal women likely to have low femoral neck BMD [12]. A Rotterdam study recently produced an algorithm for prediction of hip fracture risk that was based on a sample of men and women age 55 years and older [10]. However, no simple algorithms have been proposed specifically to examine risk of hip fracture among older Caucasian women, the group that accounts for approximately 75–80% of hip fractures in the USA [13–15].

The goal of this analysis was to use SOF data to develop a simple clinical algorithm based on a small number of risk factors that could be used to predict the risk of hip, nonvertebral, and vertebral fractures in older Caucasian women, and to validate the model using data from another large study of fractures, the EPIDOS study [11]. We aimed to develop an algorithm that could be used for assessment with and without BMD measurement, using risk of fracture rather than risk of low BMD as the outcome variable of interest.

Subjects and Methods

Subjects

The study population consisted of 9704 women (99.7% Caucasian) who were ambulatory and at least 65 years of age [6]. These women were recruited from population-based listings such as health plan memberships and voter registration lists in the cities of Portland, Oregon; Minneapolis, Minnesota; Baltimore, Maryland; and in the Monongahela Valley, Pennsylvania during the period from 1986 to 1988. This analysis excluded Caucasian women who either had a previous hip fracture or had undergone bilateral hip replacement. The participants in the SOF study may not be representative of older women, as they were community-based and, as volunteers, were likely to be healthier than women of the same age in the general population. All subjects provided informed consent, and the study was approved by the appropriate review committees.

Assessment of Risk Factors

Questionnaire and Interview

Demographic information and a complete health history were obtained during study visits. Participants were asked about any fracture history, and current and past therapy with specific classes of medications including hormones (estrogen and thyroid), diuretics, corticosteroids, anticonvulsants, anxiolytic drugs, antacids and sleeping aids [6]. The questionnaire also included questions about dietary calcium and caffeine intake, walking, exercise, and the number of hours spent daily sitting and lying down. The difficulty experienced in performing other common daily activities was also assessed.

Examinations

Weight, height, waist and hip circumferences, knee height and body mass index were measured. Neuromuscular function was also assessed by observing the subjects' ability to rise from a chair, number of step-ups completed, strength of grip, right triceps force (elbow extension), knee extension, hip abduction, walking speed, and ability to walk and stand in a tandem position with eyes open or closed. Cognitive function was tested using a modified version of the Mini-Mental State Examination, and visual acuity, depth perception, and contrast sensitivity were assessed. Blood pressure and pulse were also measured.

Bone mineral density of the proximal femur was measured during a second examination using dual-energy X-ray absorptiometry (DXA; Hologic, Waltham, MA). This second measurement was completed in 7786 women (82%) of the original study population.

Ascertainment of Fractures

Every 4 months, the women were contacted about possible fractures, with 99% of these contacts being completed. Copies of radiographic reports were obtained for all reported fractures and used to confirm fractures. In addition, hip fractures were confirmed by review of radiographs. Nonvertebral fractures excluded fractures resulting from major trauma. Vertebral fractures were assessed using morphometry to measure vertebral heights from two serial radiographs obtained approximately 3.7 years apart [3]. A 20% and 4 mm decrease in vertebral heights for each vertebral level (L4–T4) was used to define a new vertebral fracture [15].

Methods Used in this Study for the Prediction of Fracture Risk

For this analysis, follow-up commenced from the second SOF visit, when DXA was first performed. Women with a hip fracture before that time or with a traumatic hip fracture were excluded. We used the period from the second visit to 5 years later (or to first fracture before

that time) for hip and nonvertebral fractures. Spinal radiographs were obtained an average of 3.7 years apart, at the first and third SOF visits.

The goal of this analysis was to develop an index based on a small number of risk factors that are easily assessed. We began with the risk factors identified for hip fractures in an earlier analysis of SOF using baseline risk factors and with 4.1 years of follow-up [6]. We selected the set of risk factors from the final multivariable model that could be easily assessed in a primary care clinical setting (i.e., those that required no additional tests or complex questions). We also considered some of the variables that were strongly associated but did not remain in the final multivariable model. A total of 20 variables were used in this stage of the analysis (Table 1).

We then performed logistic regression analysis on each of the 20 potential risk factors, followed by modeling with adjustment for age for each variable. We chose for consideration in the multivariable analysis those risk factors that were statistically significant ($p < 0.05$), had a strong enough relationship to have an impact in the final model, and were common enough to be clinically relevant. For dichotomous risk factors, these last two criteria were implemented by requiring at least a 10% prevalence for a variable with an age-adjusted odds ratio (OR) of 1.5, and an 8% prevalence for one with an OR of 1.75. Any prevalence was sufficient for a variable with an OR of 2.0 or higher. Continuous variables were dichotomized to obtain a 20–25% prevalence of those in the high-risk category and criteria for dichotomous risk factors were applied.

Table 1. Distribution of potential risk factors among 7782 Caucasian women

Characteristic	All subjects	
	n	%
Evaluated at visit 2		
Age (years)		
65–69	2132	27.4
70–74	2982	38.3
75–79	1672	21.5
80–84	722	9.3
85 +	274	3.5
Fracture after age 50	3049	39.2
Fall in last 12 months	2304	30.2
Weight $\leqslant$125 lbs (57 kg)	1660	21.8
Total hip *T*-score		
$\geqslant$–1	2335	16.5
–1 to –2	2928	15.8
–2 to –2.5	1233	37.6
<–2.5	1286	30.0
Current smoker	603	7.8
Currently taking thyroid medication	1018	13.3
Any weight loss since age 25	1166	15.3
Body Mass Index $\leqslant$–22.4	1520	20.0
Height $\geqslant$–66 inches (1.7 m) at age 25	2150	27.7
Current caffeine intake $\leqslant$0.14 g/day	3876	50.1
Evaluated at visit 1		
Takes walks for exercise	4089	52.6
Uses arms to stand from a chair	311	4.4
Long-term benzodiazepine use	678	8.8
$\leqslant$4 hours on feet per day	684	8.8
Previous hyperthyroidism	730	9.6
Maternal hip fracture after age 50	811	10.4
Lying pulse > 80 bpm	837	10.8
Self-reported health poor to fair	1187	15.3
Drank alcohol in the past 12 months	5547	71.3

All variables meeting these criteria were put into a multiple logistic regression model. Separate models were run with and without BMD included. The variables in the final model were selected based on a combination of attaining statistical significance in predicting hip fracture, clinical and public health considerations, and ease of assessment. When highly correlated, competing predictors were significant in age-adjusted models, we chose the most easily assessable predictor (e.g., weight as opposed to body mass index, BMI). We also examined the ability of risk scores to predict other types of fractures in SOF, including nonvertebral fractures and morphometric vertebral fractures.

We converted the final multivariable logistic equation into a simple additive score by the following steps. First, we noted that the logistic probability was an exponential function of an additive combination of the logistic coefficients multiplied by the risk variables. Since all variables were binary indicators, the additive portion of the logistic function was the sum of the coefficients for the risk factors that were present. The sum of the coefficients should be highly correlated with the predicted probability from the logistic model. As a second step, we approximated this additive function by multiplying the coefficients by an arbitrary constant (2, selected to yield approximately integer-valued additive factors) and rounded to the nearest digit. This yielded a simple additive score. We then tested the correlation of this simple additive score with the original logistic probability.

The results from the model with and without BMD measurement were compared, and since they were found not to be substantially different, the instrument with and without BMD measurement included the same factors. Competing models were compared based on sensitivity and specificity considerations. The total score was then used to form the FRACTURE Index, which we propose as a screening tool to assess the risk of fractures in postmenopausal women. The sensitivity, specificity, and positive predictive value were calculated, and a receiver operating characteristic (ROC) curve was graphed for comparing several potential cutpoint values of the FRACTURE Index. Our objective was to identify specific cutpoints that balance both sensitivity and specificity.

Validations of Model

The models were validated as predictors of hip fracture in the EPIDOS study. EPIDOS was a prospective study of risk factors for hip fracture conducted in France that included 7575 women aged 75 years or older recruited from voter registration lists in five French areas in 1992–

93 and who have been followed by mail or telephone every 4 months [11]. The total hip BMD was not directly derived from the output of the Lunar instrument used in EPIDOS. Hence, the scans were reanalyzed by one of the EPIDOS investigators (D. Hans) to measure the total hip BMD. The prediction equations developed in SOF were applied to the subset of patients in EPIDOS for whom reanalysis of the scans was feasible (n = 6679). The women were then grouped into five categories based on score values and the risk of fracture was reported in each category for the models with and without BMD assessment.

Results

A total of 7782 women with DXA hip measurements and complete follow-up of hip fractures were included in this analysis. For this population, the distribution of potential risk factors are presented in Table 1. Overall, the mean age of the women was 73.3 years and the mean total hip BMD was 0.76 g/cm^2, corresponding to a T-score of -1.5. A total of 231 (3%) women had hip fractures during the 5 years of follow-up. Compared to those without hip fracture, the women who fractured were, on average, 3.8 years older (77.0 vs 73.2 years), had lower total hip BMD (0.65 g/cm^2 vs 0.76 g/cm^2), and had lower body weight (61.8 kg vs 66.7 kg). All three comparisons were statistically significant at $p < 0.001$. In addition, those who fractured were more likely to have had a maternal history of hip fracture and were more likely to have had at least one fracture since menopause.

In the age-adjusted models, several factors were significantly associated with hip fracture risk (Table 2). The variables selected for the final model included: total hip BMD; weight less than 125 pounds (57 kg); history of any fracture after age 50 years; history of maternal hip fracture after age 50; use of arms to stand up from a chair; and currently smoking.

Logistic regression models were fit using the variables from the final multivariable model, with and without BMD (Table 3). The logistic coefficients were similar in the models with and without BMD, with the exception of the coefficient for weight. Weight and BMD were not independently predictive as weight was not significant when BMD was entered into the model. However, in order to make the models more consistent, the coefficient for weight from the model without BMD was used in the model with BMD. Thus, the resulting scores for all predictors were the same in the models with and without BMD. Note that although the maximum possible score (FRACTURE Index; Table 4) was 11 without BMD (5 points for age > 85, 2 for use of arms to stand, and 1 for the remaining four predictors), and 15 with BMD (an additional four points for having a BMD with T-score < -2.5), we observed a maximum of 9 and 13, without and with BMD, respectively, in the study population. The correlation between the predicted probabilities

Table 2. Risk factors predictive of hip fracture in age-adjusted logistic regression model

	Hip fracture (n = 231) n (%)		No hip fracture (n = 7551) n (%)		Age-adjusted model OR (95% CI)
Predictors included in final model					
Age (years)					
65–69	25	(10.8)	2107	(27.9)	
70–74	65	(28.1)	2917	(38.6)	
75–79	67	(29.0)	1605	(21.3)	
80–84	47	(20.3)	675	(8.9)	
85 +	27	(11.7)	247	(3.3)	
Fracture after age 50	130	(56.3)	2919	(38.7)	1.8 (1.4–2.3)
Maternal hip fracture after age 50	33	(14.3)	778	(10.3)	1.6 (1.1–2.3)
Weight ⩽125 lbs. (57 kg)	88	(38.9)	1572	(21.3)	2.0 (1.5–2.6)
Current smoker	22	(9.6)	581	(7.7)	1.7 (1.1–2.8)
Uses arms to stand from a chair	30	(14.4)	281	(4.1)	2.6 (1.7–3.9)
Total hip T-score					
⩾–1	15	(6.5)	2320	(30.7)	1.0
–1 to –2	60	(26.0)	2868	(38.0)	2.9 (1.6–5.1)
–2 to –2.5	50	(21.6)	1183	(15.7)	5.3 (2.9–9.5)
<–2.5	106	(45.9)	1180	(15.6)	9.6 (5.5–16.8)
Predictors not included in final model					
⩽4 hours on feet per day	36	(15.6)	648	(8.6)	1.6 (1.1–2.3)
Drank alcohol past 12 months	138	(59.7)	5409	(71.7)	0.7 (0.5–0.9)
Self-reported health poor to fair	46	(19.9)	1141	(15.1)	1.4 (1.0–1.9)
Previous hyperthyroidism	33	(14.7)	697	(9.5)	1.5 (1.0–2.2)
Lying pulse > 80 bpm	38	(16.5)	799	(10.6)	1.5 (1.1–2.2)
Weight loss since age 25	73	(32.3)	1093	(14.8)	2.2 (1.6–2.9)
Currently taking thyroid medication	40	(17.9)	978	(13.2)	1.5 (1.1–2.1)
Body mass index ⩽22.4	77	(34.1)	1444	(19.6)	2.0 (1.5–2.6)
Height ⩾66 inches (1.7 m) at age 25	76	(33.0)	2074	(27.5)	1.4 (1.1–1.9)
Current caffeine intake ⩽0.14 g/day	125	(54.6)	3751	(50.0)	1.1 (0.9–1.5)

OR, odds ratio.

Table 3. Multivariable model for prediction of 5-year risk of hip fracture without and with BMD assessment

Predictor	Assessment without BMD evaluation[a]	Co-efficient	Assessment with BMD evaluation[a]	Co-efficient	Number of Points
Age (per 5 years after 65)	1.6 (1.4–1.8)	0.095	1.4 (1.3–1.6)	0.073	0–5
Fracture after age 50	1.7 (1.3–2.3)	0.529	1.5 (1.1–2.0)	0.387	1
Maternal hip fracture after age 50	1.5 (1.0–2.3)	0.407	1.4 (0.9–2.1)	0.347	1
Weight $\leqslant$125 lbs (57 kg)	1.8 (1.4–2.5)	0.608	1.2 (0.9–1.7)	0.195	1
Current smoker	1.5 (0.9–2.5)	0.429	1.3 (0.8–2.2)	0.289	1
Uses arms to stand from a chair	2.5 (1.6–3.8)	0.910	2.3 (1.5–3.5)	0.819	2
Total hip *T*-score					
$\geqslant$–1		N/A	1.0		0
–1 to –2		N/A	2.7 (1.5–5.0)	1.011	2
–2 to –2.5		N/A	4.7 (2.5–8.7)	1.545	3
<-2.5		N/A	7.0 (3.9–12.8)	1.950	4

NA, not applicable; BMD, bone mineral density.
[a]Odds ratio and 95% confidence interval.

Table 4. FRACTURE Index questions and scoring

	Point value
1. What is your current age?	
Less than 65	0
65–69	1
70–74	2
75–79	3
80–84	4
85 or older	5
2. Have you broken any bones after age 50?	
Yes	1
No/Don't know	0
3. Has your mother had a hip fracture after age 50?	
Yes	1
No/Don't know	0
4. Do you weigh 125 pounds or less?	
Yes	1
No	0
5. Are you currently a smoker?	
Yes	1
No	0
6. Do you usually need to use your arms to assist yourself in standing up from a chair?	
Yes	2
No/Don't know	0
If you have a current bone density (BMD) assessment, then answer next question.	
7. BMD results: Total Hip *T*-score	
T-score $\geqslant$–1	0
T-score between –1 and –2	2
T-score between –2 and –2.5	3
T-score <–2.5	4

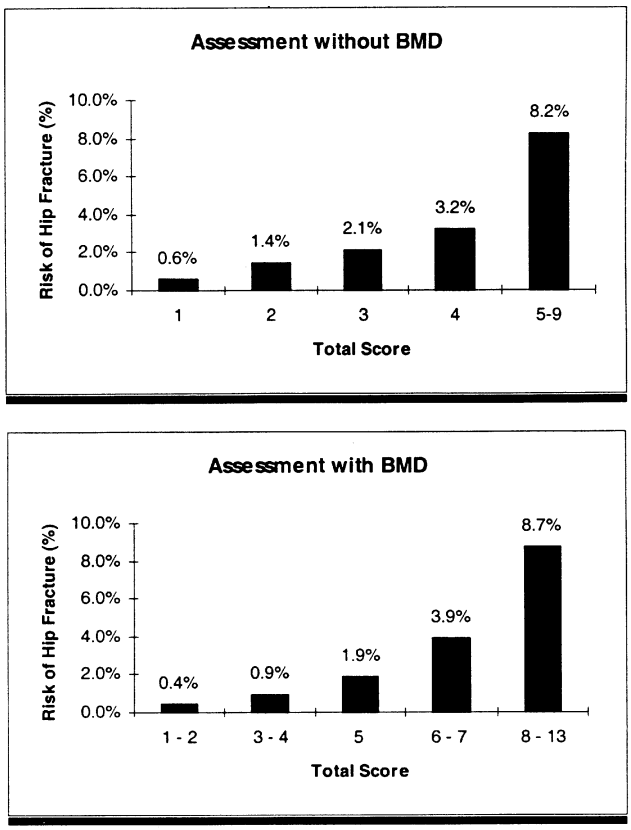

Fig. 1. Five-year risk of hip fracture by quintiles of FRACTURE Index.

calculated from the multivariable logistic model and the additive score was 0.85 in the model with and without BMD, suggesting that the score provides a very good approximation to the corresponding logistic prediction equation.

There was a strong relationship between the FRACTURE Index and hip fracture risk. For the model without BMD measurement, the risk in the lowest (approximate) quintile was 0.6% and rose to over 8.2%, a multiplicative increase of approximately 14 (Fig. 1). There was an even stronger relationship to risk of hip fracture with BMD measurement included in the model: From the lowest to highest quintile, there was an approximate 22-fold increase in risk (0.4% to 8.7%).

The ROC curve, depicting the level of sensitivity and specificity associated with the FRACTURE Index with and without BMD measurement, is presented in Fig. 2. The area under the ROC curve was 0.714 in the model

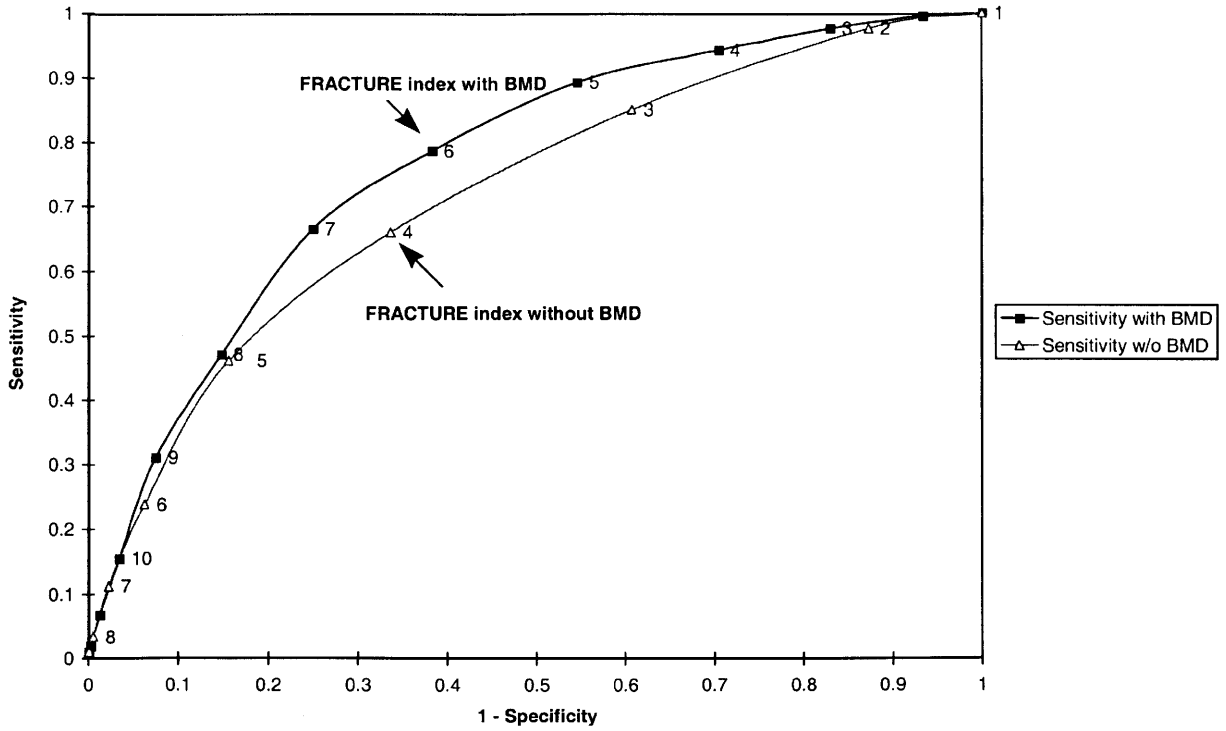

Fig. 2. Receiver operating characteristic curves for FRACTURE Index with and without bone mineral density (BMD) measurements.

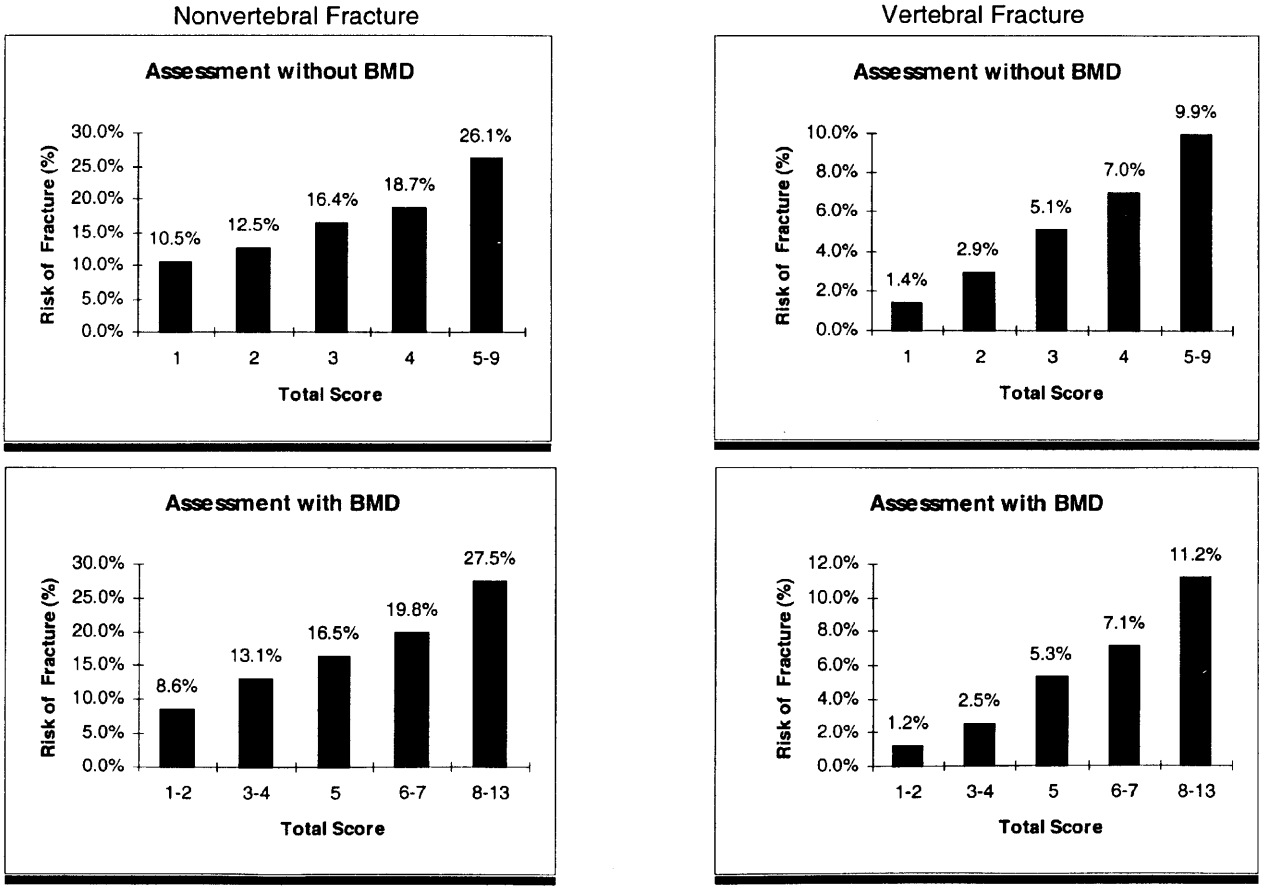

Fig. 3. Five-year risk of nonvertebral and vertebral fracture by quintiles of FRACTURE Index score.

Table 5.. Application of FRACTURE Index: hypothetical examples

FRACTURE Index Predictor Variables	Patient 1		Patient 2		Patient 3	
	Status	Point value	Status	Point value	Status	Point Value
Age (years)	70	2	70	2	70	2
Fracture after age 50	No	0	Yes	1	Yes	1
Maternal hip fracture after age 50	No	0	No	0	Yes	1
Weight $\leqslant$125 lbs (57kg)	Yes	1	No	0	Yes	1
Current smoker	No	0	Yes	1	No	0
Uses arms to stand from chair	No	0	No	0	No	0
Total hip *T*-score	Not assessed	–	–1.5	2	–2.3	3
Total Points		3		6		8
Total possible		11		15		15

without BMD measurement and 0.766 in the model with BMD measurement. In the model without BMD assessment, dichotomization of the FRACTURE Index at a cutpoint of four results in a sensitivity of 66.0%, specificity of 66.3%, and positive predictive value (PPV) of 5.6%. In the model with BMD assessment, dichotomization of the FRACTURE Index at a cutpoint of six results in a sensitivity of 78.6%, specificity of 61.7%, and PPV of 5.8%. Using a higher cutpoint in either model increases the specificity, thereby reducing the number of false positives, but this effect is accompanied by a sharp decline in the sensitivity, with an increase in false negatives. The reverse is true if a lower cutpoint is used.

The index was also predictive of any nonvertebral fracture and vertebral fracture (Fig. 3). For example, for the index without BMD assessment, the risk of a nonvertebral fracture increased from 10.5% in the lowest quintile to 26.1% in the highest. Similarly, the risk of vertebral fracture increased from 1.4% to 9.9% from the lowest to highest quintile. The gradient of risk was even steeper when BMD measurement was included in the index.

For practical application of the FRACTURE Index, Table 5 depicts three hypothetical examples of individual women with varying levels of risk of an osteoporotic fracture. In Patient 1, BMD was not assessed. The FRACTURE Index totaled 3 out of a possible 11 points for assessing an increased fracture risk. Patient 2 had a BMD assessment, and the FRACTURE Index totaled 6 out of a possible 15 points. Patient 3 also had a BMD assessment, and the FRACTURE Index totaled 8 out of a possible 15 points. It would appear that Patient 3 is at higher risk of fracture compared with the other two patients described above.

In order to validate these prediction equations, we applied them to the 6679 women (mean age, 80.5 years) in the EPIDOS study. Data were available for 4 years of follow-up, and 261 women had a first hip fracture during this period. Women were grouped into five categories based on their risk score value. For each category, the risk of hip fracture for the assessment with and without BMD measurement is given in Fig. 4. For the assessment

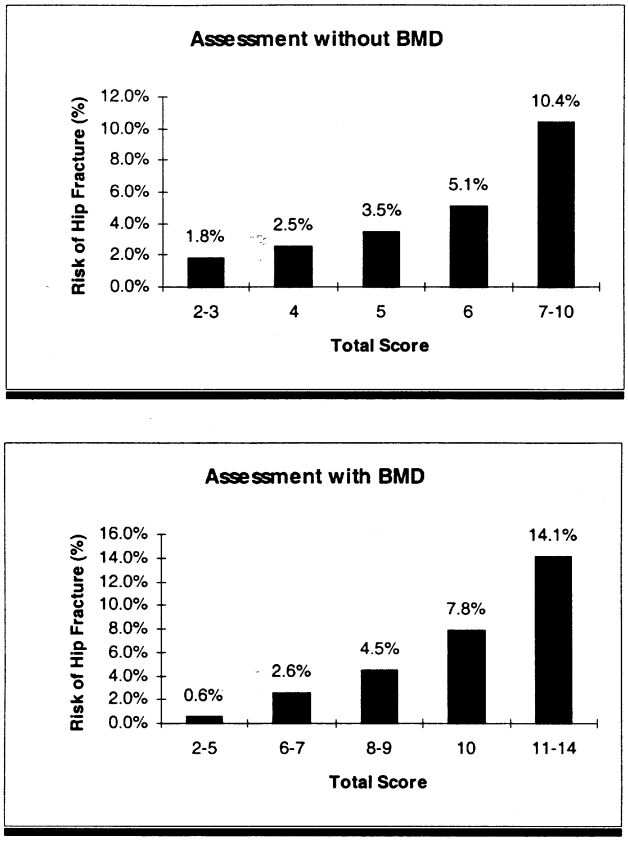

Fig. 4. Validation of FRACTURE Index using the EPIDOS database. Risk of hip fracture in EPIDOS subjects (mean follow-up of 4 years) by categories of FRACTURE Index.

without BMD measurement, the risk increases from 1.8% in the lowest risk group to 10.4% in the highest, while for the assessment including BMD measurement the risk increases from 0.6% to 14.1%. While the score values for the risk categories differ in the SOF and EPIDOS populations, the pattern of hip fracture risk is similar in both populations, with increasing score values predicting increased risk of fracture. A stronger relationship exists between score values and risk of hip fracture when BMD measurement is included in the model.

Discussion

Using data from a large prospective cohort of older Caucasian women, we have shown that a simple index derived from easily assessed risk factors strongly predicted the risk of hip fracture over 5 years, with an increase in risk of almost 14-fold for subjects from the lowest to highest quintile of index scores. Inclusion of total hip BMD measurement in the model improved risk prediction further, so that there was almost a 22-fold increase in risk from lowest to highest score quintiles. Furthermore, the index was also predictive of other types of osteoporotic fractures, including vertebral fractures and nonvertebral fractures. This suggests that the indices might be quite useful as general tools for assessment of fracture risk, to indicate which women require more complete clinical assessment and intervention to reduce fracture risk.

It is useful to consider the ability of BMD and risk factors to predict hip fracture risk in a more general context of risk factors and chronic disease. A recent analysis showed that the gradient of risk for hip BMD predicting hip fracture was much stronger than the gradient of risk of cholesterol levels for predicting heart disease [16]. The risk gradient with our FRACTURE index, which included risk factors in addition to hip BMD, further increased our ability to predict hip fractures.

Several recent studies have examined non-BMD predictors of hip fracture. The EPIDOS study reported that neuromuscular factors, including slow gait speed, reduced visual acuity, and difficulty on the tandem stand test predicted hip fracture risk [11]. A recent analysis of data from the Rotterdam study examined prediction of hip fracture risk in a population of men as well as women, in a much younger cohort (average age 68.1 years) than the SOF study population [10]. This analysis generally found similar predictors to those found in the SOF study, including age, history of fracture, use of a walking aid, current smoking, and lower limb disability. They also found that hip BMD was similarly predictive of hip fracture risk (OR of 1.5 per 0.05 g/cm^2 decrease of the femoral neck). The only predictor in our model that was not among the significant predictors found in that study was family history of fracture, which was not specifically mentioned and may not have been examined in their study. Since their risk score is multiplicative, rather than additive, and based on different categories than ours, the two indices cannot be directly compared.

An analysis examining the predictors of hip fracture was performed earlier in this same cohort. In that final multivariable model, a total of about 17 predictors were identified for 192 hip fractures over a mean follow-up time of 4.1 years. Our analysis differs from the earlier SOF analysis in a number of ways. Most importantly, that analysis included only calcaneal BMD. Ours is the first analysis from SOF to confirm that clinical predictors are useful even after adjustment for BMD at the hip. The analysis from the EPIDOS study described above generated similar predictors [8] among an older French cohort.

The SOF was conducted in the USA among a population of healthy women over the age of 65 who were primarily Caucasian. Therefore, the applicability of the FRACTURE Index to groups outside the USA or to non-white women is not clear. While the FRACTURE Index was strongly predictive of fracture in the EPIDOS population, the EPIDOS population is on average about 10 years older than the SOF population, and therefore has generally higher values for the FRACTURE Index. In addition, there are probably systemic differences in fracture risk between women in France and the USA. For these reasons, we believe our results are most generalizable to USA Caucasian women.

After a systematic review of the available evidence about assessment of osteoporotic fracture risk, the National Osteoporosis Foundation (NOF) concluded that pharmacologic treatment should be offered to women who have had vertebral fractures [17,18]. In addition, the NOF also recommended that it is worthwhile to assess bone density in all white women over the age of 65 years regardless of risk factors present, and in women 50 or older who have a strong risk factor for fracture. The FRACTURE Index risk assessment tool is consistent with the NOF guidelines in that it identified a similar set of risk factors for fracture.

The FRACTURE Index will be useful in identifying postmenopausal women who are at high risk of hip, nonvertebral, and vertebral fractures over the subsequent 5 years, and for whom further clinical assessment and intervention are most warranted. Interventions may include both risk factor modification and pharmaceutical interventions. Among the risk factors in our model, only two, smoking and weight, are potentially modifiable. The risk of falling, while not included in our final model, has been associated with an increased risk of hip fracture, and therefore prevention strategies should be implemented in older women [11,19]. Pharmaceutical intervention is important to consider in those women at highest risk of hip fracture, particularly those known to have low BMD or prevalent fractures. Several therapies have been shown effective in reducing risk of vertebral fractures in women with moderately low BMD [20–22]. While bisphosphonates also are effective in reducing risk of nonvertebral and hip fractures, these reductions may be limited to women with BMD *T*-scores below –2.5 or to those with existing vertebral fractures [20,22,23].

Our results show that risk factors independent of BMD assessment are predictive of hip and other osteoporotic fractures, supporting the assessment of fracture risk when BMD testing is not available. However, our results do suggest that BMD has some additional predictive ability, over and above that for risk factors alone. The fact that reductions in nonvertebral and hip fractures with bisphosphonates are most apparent in those with lowest hip BMD suggests that hip BMD should be performed, when possible, before initiating therapy.

There were some limitations of this study. The FRACTURE Index was developed from a cohort of healthy older Caucasian women in the USA, from which housebound and institutionalized women were excluded, and validated against a similar group of older French women. Furthermore, men and persons with secondary causes of osteoporosis (especially those taking glucocorticoids) were not included in the analysis, so the FRACTURE Index should not be used in these groups. Secondly, we limited the risk factors to those measured in SOF and to those easily assessable. Some risk factors, such as a history of radiologic vertebral fracture, are predictive of future fracture risk but were not included in our model since we considered them difficult to assess in a primary care setting.

The relationship between age and risk of hip fracture is very strong, and age was the most important single component of this index. Other risk factors also made important contributions to the value of the risk score for individuals. While 5 points are possible from age, an additional 10 points are possible in the model with BMD included for the other risk factors. However, since in practice most of the other risk factors are correlated with age, the higher values of the FRACTURE Index tend to occur more often in older women. Based on the results of our analyses, we would recommend that postmenopausal women with a total score of 4 or above without BMD assessment, or a total score of 6 or above with BMD assessment, should certainly undergo further evaluation by a physician. Other patients may also require assessment, irrespective of the risk score on the FRACTURE Index. For example, the NOF has recommended that all white women over 65 have a bone density measurement [18].

In conclusion, we have developed a simple scoring system to assess risk of hip fracture in older, postmenopausal Caucasian women. This index can be used either with or without BMD testing by women or their clinicians to assess 5-year risk of hip and other osteoporotic fractures, and will be helpful in guiding further assessment and treatment decisions in these women.

Appendix. Investigators in the Study of Osteoporotic Fractures Research Group

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The Kaiser Permanente Center for Health Research, Portland, Oregon: T. Hillier (principal investigator, E. Harris (co-principal investigator), E. Orwoll (co-investigator), H. Nelson (co-investigator), Mikel Aiken (biostatistician). Marge Erwin (project administrator), Mary Rix (clinic coordinator), Jane Wallace, Kathy Snider, Kathy Canova, Kathy Pedula, JoAnne Rizzo.

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Investigators in the Study of Osteoporotic Fractures Research Group are listed in the Appendix.

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