Endokrynologia Polska/Polish Journal of Endocrinology
Tom/Volume 60; Numer/Number 2/2009
ISSN 0423–104X

WHO fracture risk calculator (FRAX™) in the assessment of obese patients with osteoporosis

Zastosowanie kalkulatora ryzyka złamania Światowej Organizacji Zdrowia (FRAX™) u otyłych chorych z osteoporozą

Edward Franek[1, 2], Hanna Wichrowska[1], Dariusz Gozdowski[3], Monika Puzianowska-Kuźnicka[2]

[1]*Department of Internal Diseases, Endocrinology, and Diabetology, CSK MSWiA, Warszawa*
[2]*Department of Endocrinology, Medical Research Centre, Polish Academy of Sciences, Warszawa*
[3]*Department of Applied Statistics and Bioinformatics, Warsaw University of Life Sciences*

Abstract

Introduction: Recently, a new fracture risk-assessment calculator (FRAX™) has been introduced. The aim of this study was to assess its usefulness for the re-assessment of fracture risk in obese patients and re-assignment to treatment.
Material and methods: 350 obese female patients were included. In all of them, 10-year fracture risk was calculated using FRAX™ (with and without T score value).
Results: If major osteoporotic fracture risk was calculated with BMD, it was low in most of the patients (in 82.1% of those treated, and in 95.9% of those not treated it was below 10%). Mean risk values were significantly higher in the treated (7.7 [3;39]%) than in the non-treated group (4.6 [2.1;14]%). The reason for start of treatment in 95 out of 106 patients was a sustained low-energy fracture, low BMD, or both.
Conclusions: The WHO fracture risk calculator may be a useful tool in treated obese females with osteoporosis. The information regarding 10-year fracture risk may change the treatment strategy at least for those in whom the decision of treatment was based solely on low BMD.
(Pol J Endocrinol 2009; 60 (2): 82–87)

Key words: *Osteoporosis, fracture, 10-year fracture risk, FRAX™*

This paper was supported by a grant from the Ministry of Science and Higher Education (N 404 026 31/1581)

Streszczenie

Wstęp: Niedawno wprowadzono do diagnostyki kalkulator oceniający ryzyko złamania (FRAX™). Celem niniejszej pracy była ocena jego użyteczności w celu oceny ryzyka złamania u otyłych kobiet i ponownej kwalifikacji do leczenia.
Materiał i metody: Do badania włączono 350 otyłych kobiet. U wszystkich oceniono 10-letnie ryzyko złamania przy pomocy kalkulatora FRAX™ (bez oraz z wartością Tscore).
Wyniki: Ryzyko głównego złamania osteoporotycznego obliczone z wprowadzeniem wartości Tscore było niskie u większości chorych (u 82,1% chorych leczonych i 95,9% nieleczonych wynosiło poniżej 10%). Średnie wartości ryzyka były znamiennie wyższe u chorych leczonych (7,7 [3; 39]%) niż u nieleczonych (4,6 [2,1; 14]%). Przyczyną rozpoczęcia leczenia u 95 ze 106 pacjentów było złamanie niskoenergetyczne, niskie BMD lub oba razem.
Wnioski: Kalkulator ryzyka złamania Światowej Organizacji Zdrowia może być użyteczny u leczonych z powodu osteoporozy otyłych kobiet. Informacja dotycząca 10-letniego ryzyka złamania może zmienić strategię leczenia przynajmniej u tych chorych, u których decyzja była podjęta na podstawie niskiej BMD. **(Endokrynol Pol 2009; 60 (2): 82–87)**

Słowa kluczowe: *osteoporoza, złamanie, 10-letnie ryzyko złamania, FRAX™*

Praca powstała dzięki grantowi Ministerstwa Nauki i Szkolnictwa Wyższego (N 404 026 31/1581)

Introduction

Osteoporosis is a very common disease. About 50% of Caucasian women of more than 60 years of age suffer from an osteoporotic fracture [1]. In the US a quarter of a million hip fractures occur annually [2]. Osteoporotic fractures generate enormous costs, estimated, over 10 years ago, at almost USD 15 billion annually [3]. In 2005 the cost increased to USD 17 billion [4]. Fractures result in an increased risk of death [5] and a reduced quality of life. Therefore, the primary aim of antiosteoporotic treatment is a reduction in the number of incident fractures.

For the proper selection of patients for treatment, an estimation of the fracture risk is necessary. Bone mass is only one of numerous risk factors (skeletal and non-skeletal), and although its predictive ability is rather high [6],

Edward Franek, M.D., Ph.D. Department of Internal Medicine, Endocrinology, and Diabetology, Central Clinical Hospital MSWiA, ul. Wołoska 137, 02–507 Warszawa, tel.: +48 22 508 14 05, fax: +48 22 508 14 00; e-mail: edward.franek@cskmswia.pl

it is not sufficient for accurate risk prediction. Additionally, in many countries and sites BMD measurement is not available. Different approaches were made in order to select those risk factors which contribute substantially to fracture risk and to avoid those which are collinear to others.

Recently a new fracture risk assessment calculator was introduced [7], allowing for calculation of fracture risk from the following risk factors: age, sex, body mass index, previous fractures, parent fractured hip, current smoking and glucocorticoid use, rheumatoid arthritis, secondary osteoporosis, alcohol (3 or more units daily), and femoral neck BMD T score (it is not possible to calculate fracture risk from spine BMD). All risk factors accessible for the given person may be entered, and all of the missing ones may be omitted in this web-page calculator [8].

The aim of this study was to assess the usefulness of this new tool for the reassessment of fracture risk and re-assignment to treatment in obese patients treated in an osteoporosis ambulatory centre. We hypothesized that many obese patients receiving antiosteoporotic treatment have low fracture risk and, therefore, it is possible that in many of them treatment is not necessary.

Material and methods

All obese patients of the Osteoporosis Centre of the Central Clinical Hospital of the Ministry of Internal Affairs, who gave their consent, were included in the study.

The examined population consisted of three groups — non-treated subjects, patients treated only with calcium and vitamin D, and bisphosphonate treated patients (treated also with calcium and vitamin D). In all patients, medical history regarding previous clinical fractures, parent fractured hip, current smoking and glucocorticoid use, rheumatoid arthritis, secondary osteoporosis, and alcohol use was collected. In the treated patients, any fractures sustained up to the referral time, as well as age, smoking, and alcohol status at the referral were noted.

In all the patients, dual energy X-ray absorptiometry was performed in three sites (spine, hip, and forearm), and total body DEXA was performed. Additionally, in each patient, serum calcium, phosphate, PTH, CTX, glucose, creatinine, and cholesterol concentrations were assessed.

Ten-year fracture risk was calculated for hip fracture (HipF), as well as for major osteoporotic fracture (MOF), using a WHO fracture risk calculator (FRAX™). Two thresholds were assumed for each fracture type: 10 and 20% for major osteoporotic fracture (< 10% was regarded as low risk, 10–20 as intermediate risk and > 20% as high risk) [9]. The thresholds for hip fracture were set as 5 and 10%. For each patient, fracture risk was calculated twice, with and without entering the femoral neck BMD data.

Statistical methods

Data are presented as mean ± SD or median, minimal, and maximal value or number (percentage). Statistical significance of the differences between the groups was calculated using Mann-Whitney test (for 2 groups, e.g. bisphosphonate treated and non treated) or χ^2 test (testing independence in 2 × 2 contingency tables).

Results

In the population of nearly 2000 female patients of the Osteoporosis Centre, 350 obese patients were found. They were referred mostly because of back pain, but also because of sustained fracture. Between them, 106 were treated with bisphosphonate, 96 with calcium and vitamin D only, and 148 were not treated. The basal data of the patients are given in Table I.

As it is shown in Table I, patients in the bisphosphonate- and calcium/vitamin D-treated group were older and had lower BMI than the non-treated subjects. They also had significantly lower BMD. Serum concentration of bone resorption marker (CTX) was significantly (almost 20%) lower in bisphosphonate-treated vs. non-treated patients. Calcium, phosphate, PTH, and creatinine concentration were similar in all groups.

The percentage of subjects who had sustained a non-vertebral fracture was significantly higher in both (calcium/vitamin D and bisphosphonate) treated groups in comparison with non-treated subjects. Fracture risk was significantly higher in bisphosphonate- and calcium/vitamin D-treated patients in comparison with non-treated subjects. However the calculated fracture risk of major osteoporotic fracture was higher than 20% only in a few patients in all these groups. Conversely, in the bisphosphonate group 95 patients out of 106 had sustained a previous osteoporotic fracture, had a low BMD (T score lower than –2.5 at hip or spine or forearm; the latter in only 6 patients), or both.

A comparison of fracture risk calculated with or without BMD is shown in Table II (for MOF) and Table III (for HipF). As can be seen, if fracture risk was calculated with BMD data, it was below 10% in the majority of patients. Conversely, if it was calculated without BMD, in a substantial number of patients the result was between 10 and 20%. As is shown in both Tables II and III, the percentage of patients with low risk (< 10% or < 5%) was significantly higher, whereas the percentage of patients with intermediate risk (10–20% or 5–10%) was significantly lower when calculated with BMD. A comparison of the percentage of patients with high

Table I. *Basal data of bisphosphonate treated, calcium and vitamin D treated, and non-treated patients*

Tabela I. *Wyjściowe dane chorych stosujących bisfosfoniany lub suplementację wapnia i witaminy D oraz niestosujących żadnego leczenia*

Parameter	Non-treated (n = 148)	Ca and Vitamin D treated (n = 96)	Treated (n = 106)
Age	66.5 ± 8.3	71.8 ± 7.8***	74.0 ± 6.9***
Weight [kg]	83.9 ± 11.2	81.0 ± 12.2*	75.1 ± 9.6***
Height [cm]	157.0 ± 6.7	155.3 ± 5.5*	152.0 ± 5.7***
BMI [kg/m^2]	34.3 ± 4.0	33.6 ± 4.5	32.6 ± 4.0***
Extravertebral fractures (%)	14.3	38.5***	45.3***
Current smoking (%)	9.5	2.1*	4.7
Neck T score	–0.50 (–2.5; +2.3)	–1.0 (–2.9; +3.1)***	–2.3 (-3.8; +0.8)***
Neck BMD	0.993 ± 0.118	0.873 ± 0.140***	0.761 ± 0.118***
L1-4 T score	–0.10 (–3.8; +4.5)	–1.35 (–3.9; +4.8)***	–2.5 (–4.1; +1.2)***
L 1-4 BMD	1.180 ± 0.168	1.026 ± 0.205***	0.930 ± 0.144***
Radius 33% T score	–0.70 (–4.1; +1.9)	–1.75 (–5.0; +1.10)***	–2.5 (–6.5; +1.0)***
Radius 33% BMD	0.665 ± 0.082	0.591 ± 0.096***	0.530 ± 0.103***
Calcium [mmol/l]	2.33 ± 0.100	2.33 ± 0.101	2.32 ± 0.101
P [mg/dl]	3.26 ± 0.44	3.24 ± 0.45	3.24 ± 0.49
CTX	0.326 ± 0.205	0.309 ± 0.196	0.263 ± 0.192***
PTH [pg/ml]	32.7 ± 14.2	33.2 ± 14.7	34.7 ± 14.6
Glucose [mg/dl]	100.5 ± 25.4	93.7 ± 14.6	94.2 ± 12.9
Creatinine [mg/dl]	0.75 ± 0.22	0.77 ± 0.18	0.78 ± 0.22
10-year risk of MOF calculated without BMD	6.1 (1.94; 30)	11.0 (2.52; 32)***	13 (3.04; 54)***
10-year risk of femur neck fracture calculated without BMD	1.22 (0.13; 20)	3.73 (0.18; 21)***	4.96 (0.25; 47)***
10-year risk of MOF calculated with BMD	4.6 (2.1; 14)	6.8 (2.9; 19)***	7.7 (3; 39)***
10-year risk of femur neck fracture calculated with BMD	0.3 (0; 9.2)	0.7 (0.1; 6.8)***	0.9 (0.1; 31)***

Table contains mean values and standard deviations (mean ± SD) or values of median, minimal, and maximal values (Me [min; max])

*, **, ***significant difference with non-treated patients according Mann-Whitney or χ^2 test, respectively, at 0.05, 0.01, and 0.001 probability level

(> 20% or > 10%) fracture risk showed that the risk of MOF calculated without BMD was significantly higher in calcium /vitamin D — and bisphosphonate treated patients (whereas it was similar for non-treated patients) as compared with the risk calculated by BMD. The percentage of patients with high risk of hip fracture calculated with both methods was similar in the treated and non-treated subjects.

Discussion

From the results of this study, it follows that the calculated fracture risk of major osteoporotic fracture in most obese patients in the examined population was lower than 10%, and the risk of hip fracture was lower than 5%. If fracture risk is calculated using BMD, the percentage of patients with intermediate or high risk is lower, whereas the number of patients with low risk is higher than if it is calculated without BMD (Table II and III). One should remember that if the BMD value is not introduced in the calculator, FRAX™ automatically uses the BMI value for this purpose. As this was high in the examined patients, the fracture risk should be lower. In spite of this, hip fracture as well as MOF risk calculated without BMD was significantly higher than calculated with BMD (Table I and III).

It should be explained why the given fracture risk thresholds are assumed in this study. It is not clear how high the risk of fracture should be regarded as an intervention threshold. In general, it can and shall be different in various populations, depending on the financial ability of those paying [10]. For example, in the United Kingdom a threshold of 7% (assessed with BMD) was proposed for major osteoporotic fracture risk. The assessment thresholds (risk threshold which requires testing BMD and calculating the risk with its value) may

Table II. *Comparison of risk of major osteoporotic fracture calculated with or without BMD*

Tabela II. *Porównanie ryzyka poważnego złamania osteoporotycznego oszacowanego z uwzględnieniem lub bez uwzględnienia BMD*

		Fracture risk (%) calculated with BMD			
		< 10%	10–20%	> 20%	Together
Not treated					
Fracture risk (%) calculated without BMD	<10%	75.7	0.0	0.0	75.7***
	10–20%	19.6	2.7	0.0	22.3***
	> 20%	0.7	1.4	0.0	2.0
	Together	95.9	4.1	0.0	
Calcium/vitamin D treated					
Fracture risk (%) calculated without BMD	< 10%	43.8	0.0	0.0	43.8***
	10–20%	43.8	5.2	0.0	49.0***
	> 20%	0.0	7.3	0.0	7.3**
	Together	87.5	12.5	0.0	
Bisphosphonate treated					
Fracture risk (%) calculated without BMD	< 10%	25.5	0.0	0.0	25.5***
	10–20%	53.8	5.7	2.8	62.3***
	> 20%	2.8	8.5	0.9	12.3*
	Together	82.1	14.2	3.8	

*, **, ***significant difference between percentage of patients with the same class of fracture risk calculated with or without BMD according to χ^2 test, respectively, at 0.05, 0.01, and 0.001 probability level

Table III. *Comparison of risk of hip fracture calculated with or without BMD*

Tabela III. *Porównanie ryzyka złamania bliższego odcinka kości udowej oszacowanego z uwzględnieniem lub bez uwzględnienia BMD*

		Fracture risk (%) calculated with BMD			
		< 5%	5–10%	>10%	Together
Not treated					
Fracture risk (%) calculated without BMD	<5%	85.8	0.7	0.0	86.5***
	5-10%	11.5	0.0	0.0	11.5***
	>10%	2.0	0.0	0.0	2.0
	Together	99.3	0.7	0.0	
Calcium/vitamin D treated					
Fracture risk (%) calculated without BMD	< 5%	60.4	1.0	0.0	61.5***
	5–10%	35.4	1.0	0.0	36.5***
	> 10%	1.0	1.0	0.0	2.1
	Together	96.9	3.1	0.0	
Bisphosphonate treated					
Fracture risk (%) calculated without BMD	< 5%	50.0	0.0	0.0	50.0***
	5–10%	38.7	0.0	2.8	38.7***
	> 10%	4.7	2.8	0.9	7.5
	Together	93.4	2.8	3.8	

*, **, *** significant difference between percentage of patients with the same class of fracture risk calculated with or without BMD according χ^2 test, respectively, at 0.05, 0.01, and 0.001 probability level

vary substantially depending on age and the presence of a previous fracture [11]. In Poland, facing a lack of good cost-effectiveness data and the shortage of the health service budget, the intervention threshold for MOF was set arbitrarily at 20%, and the assessment threshold at 10% [9]: these values were used in this study. It is not clear, again, how high (or low) the assessment and intervention thresholds for hip fracture should be. In this study, the rather high thresholds of 5 and 10% were also set arbitrarily.

Looking at Tables II and III, one can see that the number of patients with high and intermediate risk is higher in both treated groups. However, even in the bisphosphonate-treated group the number of high-risk patients is rather low (for MOF 3.2%, if the risk was calculated with BMD — Table II) and that of low risk patients is rather high (31.1% for MOF — Table II). Remembering that 95 out of 106 treated patients had sustained an osteoporotic fracture or had a low BMD, or both, it seems that these two factors (low BMD or sustained fracture) lead, in most of the examined patients, to the decision of treatment implementation.

On the other hand, only a small number of non-treated patients had a FRAX™-calculated high fracture risk. Therefore, it seems that these patients were properly assessed and assigned to the non-treatment strategy even without 10-year fracture risk calculation.

The question arises whether treatment should be stopped, at least in patients whose risk fracture is low and who had not sustained an osteoporotic fracture. Another question is whether treatment should be introduced in patients with high fracture risk. To answer such a question, a prospective study would be necessary. However, it seems that calculation of fracture risk could not only serve as a case-finding strategy, allowing the identification of patients who need treatment, but FRAX™ may also be useful in re-assessing treated obese patients and changing the strategy, at least in some of them.

The calcium and vitamin D treated patients' results are located between those of the bisphosphonate-treated and not-treated groups (Table I). Interpretation of these data is not easy. Looking at Tables II and III, one can see that a high risk of fracture was not found in any patient from this group (when calculated with BMD). Therefore, it seems that no anti-fracture treatment is necessary in these patients. On the other hand, 38.5% of patients from this group had sustained a fracture, which could be an indication for treatment. Again, a prospective study would be necessary to answer the question of whether they should be treated or not. A stratum of obese patients was not separated in any of the large osteoporosis studies [12–23].

This study has many limitations. First, the FRAX™ calculator was designed for case finding, that is for risk assessment and assignment for treatment in not-treated individuals. Therefore, applying it for different, treated and non-treated, populations may be inappropriate. However, as we collected data regarding smoking, alcohol, fracture, and age at the referral time, the 10-year fracture risk estimated in the treated subjects is in fact the risk they had before treatment. Anyway, we do not feel that introducing the actual data would change the risk substantially. We did not note in the treated patients any fracture after referral, and none of them had ceased smoking in this time.

This study was conducted on a selected population of obese subjects, who were referred to the Osteoporosis Centre. Therefore, the percentage of high risk patients may be higher than in the general population (there are no data of the FRAX™-calculated fracture risk of the general population of obese patients in the literature). No prospective data assessing the outcomes depending on the calculated fracture risk are available in obese subjects.

However, looking at the numbers, it seems that in the population of obese patients referred for different reasons to the Osteoporosis Centre, the percentage of patients who sustained a fracture or have low BMD (and, in consequence, start bisphosphonate therapy) is rather high (Table I).

Using FRAX™, it is not possible to calculate the fracture risk for the Polish population. This possibility may be available soon, as the data regarding incidence and risk of hip fracture in Poland have recently been published [24]. However, until now it has not been possible; therefore, the calculated risk figures must be regarded as estimates.

In summary, the WHO fracture risk calculator may be a useful tool in treated obese females with osteoporosis. The information regarding 10-year fracture risk may change the treatment strategy, at least in some of them.

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