EUROPEAN JOURNAL OF BIOMEDICAL AND PHARMACEUTICAL SCIENCES
http://www.ejbps.com

ISSN 2349-8870
Volume: 3
Issue: 6
173-177
Year: 2016

THE RISK OF OSTEOPOROTIC FRACTURES ACCORDING TO THE FRAX MODEL IN RHEUMATOID ARTHRITIS PATIENTS IN SLEMANI PROVINCE

Dr. Raouf R. Mirza*

FRCP (London), MR(London), M.Phil (Leeds-England)

***Corresponding Author: Dr. Raouf R. Mirza**
London.

Article Received on 15/04/2016 **Article Revised on 06/05/2016** **Article Accepted on 27/05/2016**

ABSTRACT

Background: Rheumatoid arthritis is a chronic systemic autoimmune disease, joint inflammation is induced primarily by autoreactive immune cells and the overproduction of proinflammatory cytokines which mediate long term cartilage degradation and bone erosion and may increase the risk of osteoporosis and fracture. **Objectives:** To determine if FRAX calculations without BMD (*FRAX*) and with BMD (*FRAX/ BMD*) would produce identical predictions for the 10-year probability of hip fracture and other major osteoporotic fractures; and to assess the effect of smoking on the prediction on that risk. **Patients and methods:** A prospective study carried out in a convenient sample of 153 RA patients selected from RA patients were categorized into two groups one group (53 RA patients assessed by FRAX with BMD) and another (100 RA patients assessed by FRAX without BMD). **Results:** Prediction of major osteoporotic fracture for RA patients assessed by FRAX without BMD was <10% in 65% , 10-20% in 22% and >20% in 13% . Prediction of hip fractures for RA patients assessed by FRAX without BMD was <3% in 66% , 3-10% in 27% and >10% in 7% of them. Prediction of major osteoporotic fracture for RA patients assessed by FRAX with BMD revealed that mean percentage was 17.5±14.8 %, 37.7% of them <10%, 37.7% of them 10-20% and 24.5% of them >20%. Prediction of hip fractures was <3 for 43.4% of RA patients assessed by FRAX with BMD, 3-10% for 34% and >10% for 22.6% of them. **Conclusion** The results indicated that here is significant association between predictions of major osteoporotic fractures (<10%) and RA patients assessed by FRAX without BMD, and for hip fractures >10% and RA patients assessed by FRAX with BMD,). Smoking of RA patients in present study was significantly risk factor for high prediction of osteoporotic fractures detected by both methods (with or without BMD).

KEYWORDS: Rheumatoid arthritis, FRAX, Osteoporosis.

INTRODUCTION

Rheumatoid arthritis (RA) is a chronic systemic autoimmune disease, characterized by inflammation of multiple joints, particularly the small joints of the hands and feet. Joint inflammation is induced primarily by autoreactive immune cells (T- and B-cells and mac-rophages) and the overproduction of proinflammatory cytokines, especially tumor necrosis factor-α, interleukin (IL)-1β, IL-6, and IL-17, which are centrally involved in the pathogenesis of RA. These autoreactive immune cells and proinflammatory cytokines mediate long-term cartilage degradation and bone erosion, resulting in joint dysfunction. Furthermore, these immunological factors may increase the risk of osteoporosis and fracture in RA patients by enhancing osteoclastogenesis.[1-2]

The incidence of osteoporosis is doubled in patients with RA compared to the general population, leading to an increased rheumatoid comorbidity.[3] Several case-control studies have documented a high rate of vertebral and hip fractures in patients with RA.[2,4] World Health Organization (WHO) defines osteoporosis as bone mineral density (BMD) that is ≥2.5 SDs below the young-adult mean value (T-score, −2.5 or lower) in postmenopausal women and in men over 50 years of age. BMD with a T-score of −1 to −2.5 is classified as osteopenia.[5] According to the National Health and Nutrition Examination Survey (NHANES), approximately 10% of women and 2% of men aged 50 years and above in the U.S. have osteoporosis. In the same age group, about 49% of women and 30% of men have osteopenia.[6] The World Health Organization Fracture Risk Assessment Tool (FRAX®) has been developed to estimate a 10-year absolute risk of sustaining a hip fracture and other major osteoporotic fractures (clinical spine, forearm, hip, or shoulder fracture). The FRAX calculation tool is available on the internet http://www.shef.ac.uk/FRAX.

The tool evaluates risk based on easily obtainable clinical risk factors, such as age, history of previous fractures, long-term glucocorticoid therapy, low body

mass index (BMI), family history of hip fracture, cigarette smoking, and excess alcohol intake, with or without information on BMD.[8,9] Therapeutic interventions are recommended if the 10-year risk of fractures is more than 20% for major osteoporotic fractures (MOF) and more than 3% for hip fractures.[11]

MATERIALS AND METHODS

Study design and settings: A prospective study carried out in center of Rhematological diseases in Slemani between September 2014 and May 2015.

Population of the study: All RA patients attended Department of Rheumatology, General Hospital in Slemani and Rheumatology consultation center in Slemani were population of the study**.**

Sampling: A convenient sample of 153 RA patients was selected from RA patients visiting center of Rhematological diseases in Slemani. The patients were categorized into two groups one group (53 RA patients assessed by FRAX with BMD) and another (100 RA patients assessed by FRAX without BMD).

Data collection: The data were collected by the researcher through direct interview with fulfilling a prepared questionnaire. RA patients were diagnosed according to the 2010 American College of Rheumatology (ACR)/European League Against Rheumatism (EULAR) classification criteria for RA.

Fifty three patients were referred to rheumatology unit for bone density measurement by DXA machine. All 153 RA patients whom enrolled in this study underwent medical history that assessed from their interview to include: name, age, gender, body weight, height, address as well as history of chronic disease, rheumatologic disorder, also family history of osteoporosis and personal history of fragility and smoking habit.

The BMD of both hips were tested by bone densimeter, Lunar IDXA Series X-Ray Tube Housing Assembly, Madison, WI USA (manufactured at 2011), before the examination the weight and height of patients, body mass index (BMI) was calculated by dividing weight in kilograms by the square of the height in meters. Body mass index: BMI was categorized as normal if BMI (kg/m^2) was< 25, overweight if BMI was 25–29.9, and obese if BMI was ≥30.[18]

We used FRAX Turkey because the Turkish patients of similar characteristics comparing with the Kurdish patients and the nearest country to Kurdistan having dependable FRAX tool model is Turkey according to the (http://www.shef.ac.uk/FRAX/tool.aspx?country=6), and thus offer the best FRAX tool to be used to measure fracture risk in patients at risk of osteoporosis. [15-17]

Statistical analysis: All patients' data were entered using computerized statistical software; Statistical Package for Social Sciences (SPSS) version 17 was used. Descriptive statistics presented as (mean ± standard deviation) and frequencies as percentages. **Kolmogorov Smirnov analysis verified the normality of the data set.** Multiple contingency tables conducted and appropriate statistical tests performed, Chi-square used for categorical variables and ANOVA analysis to compare between more than two means (Fishers exact test was used when more than 20% of the cells less than 5). In all statistical analysis, level of significance (p value) set at ≤ 0.05 and the result presented as tables and/or graphs. Statistical analysis of the study was done by a community medicine specialist.

RESULTS

A total 153 RA patients were included in present study (53 RA patients assessed by FRAX with BMD and 100 RA patients assessed by FRAX without BMD). Mean age of RA patients assessed by FRAX with BMD was 57±8.6 years, 45.3% of them were 50-59 years age. Females were more than males with male to female ratio as 0.06:1.

Mean age of RA patients assessed by FRAX without BMD was 55.1±10.4 years, 37% of them were 50-59 years age. Females were more than males with male to female ratio as 0.14:1.

Mean BMI of RA patients assessed by FRAX with BMD was 31.02±6.6 Kg/m^2, 47.2% of them were obese and 9.4% of them had morbid obesity. One third of RA patients assessed by FRAX with BMD were smokers.

Mean BMI of RA patients assessed by FRAX without BMD was 28.3±5.1 Kg/m^2, 38% of them were obese, 29% were normal and 2% of them had morbid obesity. Only 18 patients were smokers and all of them were non-drinking alcohol.

Mean T-score of RA patients assessed by FRAX with BMD was (-1.8±1.7), 20 patients had osteopenia and 19 patients had osteoporosis, figure 1.

Variable	FRAX with BMD	FRAX without BMD	χ^2	P
	No.(%)	No.(%)		
Major osteoporotic fractures			10.4	0.005
<10%	20(23.5)	65(76.5)		
10-20%	20(47.6)	22(52.4)		
>20%	13(50.0)	13(50.0)		
Hip fractures			10.4	0.005
<3%	23(25.8)	66(74.2)		
3-10%	18(40.0)	27(60.0)		
>10%	12(63.2)	7(36.8)		

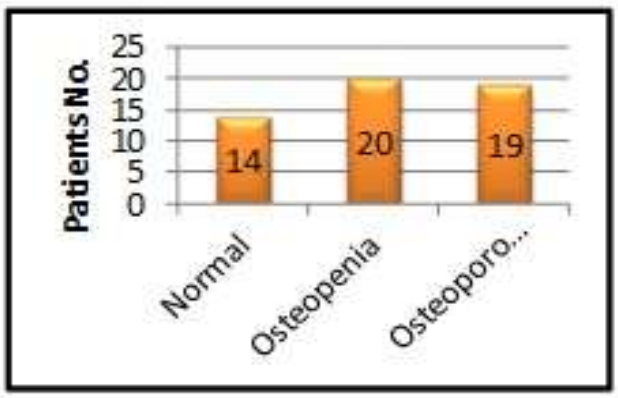

Figure 1: T-Score distribution of RA patients assessed by FRAX with BMD

No significant association was observed between each of age, gender, smoking and BMI for patients assessed by FRAX with and without BMD (p>0.05) table 1.

Table 1: Distribution of RA patients demographic, BMI and lifestyle characteristics according to use of FRAX with and without BMD.

Variable	**FRAX** with BMD	**FRAX** without BMD	χ^2	**P**
	No.(%)	**No.(%)**		
Age			3.7	0.2
40-49 years	9(22.5)	31(77.5)		
50-59 years	24(39.3)	37(60.7)		
60-69 years	15(40.5)	22(59.5)		
≥ 70 years	5(33.3)	10(66.7)		
Gender			1.9	0.1
Male	3(18.8)	13(81.3)		
Female	50(36.5)	87(63.5)		
BMI			1.6	0.08
Normal	12(29.3)	29(70.7)		
Overweight	11(26.2)	31(73.8)		
Obese	25(39.7)	38(60.3)		
Morbid obesity	5(71.4)	2(28.6)		
Smoking			2.9	0.08
Yes	16(47.0)	18(53.0)		
No	37(31.1)	82(68.9)		

There was a significant association between predictions for major osteoporotic fractures (<10%) and RA patients assessed by FRAX without BMD (p=0.005). A significant association was observed between predictions for hip fractures >10% and RA patients assessed by FRAX with BMD (p=0.005). All these findings were shown in table 2.

Table 2: Distribution of major osteoporotic and hip fractures prediction according to use of FRAX with and without BMD.

Major osteoporotic fracture	**Age**	**BMI**	**T-score**
	Mean±SD	**Mean±SD**	**Mean±SD**
<10%	53±8.2	36.2±4.9	-0.2±1.2
10-20%	56±8.03	30.06±5.3	-2.1±0.8
>20%	64.4±5.0	24.4±3.5	-3.6±0.8
ANOVA (*P value*)	<0.001	<0.001	<0.001

ANOVA analysis revealed that age was significantly increased with high prediction percentage of major osteoporotic fractures for patients assessed by FRAX with BMD (p<0.001), on other hand, BMI and T-scores were significantly decreased with high prediction percentage of major osteoporotic fracture for patients assessed by FRAX with BMD (p<0.001), table 3.

Table 3: Distribution of age, BMI and T-scores according to major osteoporotic fractures prediction for patients assessed by FRAX with BMD.

ANOVA analysis revealed that age was significantly increased with high prediction percentage of major osteoporotic fractures for patients assessed by FRAX without BMD (p<0.001). BMI was significantly decreased with high prediction percentage of major osteoporotic fractures for patients assessed by FRAX without BMD (p<0.001) table 12.

Table 4: Distribution of age and BMI according to major osteoporotic fracture prediction for patients assessed by FRAX without BMD.

Major osteoporotic fracture	**Age**	**BMI**
	Mean±SD	**Mean±SD**
<10%	52.1±8.2	29.2±5.4
10-20%	58.5±9.8	28.1±3.9
>20%	64.1±13.4	24.2±3.08
ANOVA (*P value*)	**<0.001**	**0.004**

ANOVA analysis revealed that age was significantly increased with high prediction percentage of hip fractures for patients assessed by FRAX with BMD (p<0.001), on other hand, BMI and T-scores were significantly decreased with high prediction percentage of hip fractures for patients assessed by FRAX with BMD (p<0.001), table 13.

Table 5: Distribution of age, BMI and T-scores according to hip fractures prediction for patients assessed by FRAX with BMD.

Hip fractures	Age	BMI	T-score
	Mean±SD	Mean±SD	Mean±SD
<3%	53.2±8.9	35.7±5.4	-0.2±1.2
3-10%	57.1±7.4	29.6±4.6	-2.3±0.4
>10%	64±4.9	24.02±3.2	-3.7±0.9
ANOVA (*P value*)	**0.001**	**<0.001**	**<0.001**

significantly increased with high prediction percentage of hip fractures for patients assessed by FRAX without BMD (p<0.001). BMI was significantly decreased with high prediction percentage of hip fractures for patients assessed by FRAX without BMD (p<0.001).table 14.

Table 6: Distribution of age and BMI according to hip fractures prediction for patients assessed by FRAX without BMD.

Hip fractures	Age	BMI
	Mean±SD	Mean±SD
<3%	52.07±8.1	29.2±5.3
3-10%	57.9±10.5	27.3±4.05
>10%	73.1±7.6	23.7±3.1
ANOVA (*P value*)	**<0.001**	**0.01**

There was significant association between smoking and major osteoporotic fracture for both patients assessed by FRAX with or without BMD (P <0.05)

Table 7: Distribution of smoking and major osteoporotic fracture for both patients assessed by FRAX with or without BMD

Variable	<10%	10-20%	>20%	χ^2	P
	No. (%)	No. (%)	No. (%)		
Smoking (For patients assessed by FRAX without BMD)				8.4*	**0.01**
Yes	8 (44.4)	4 (22.2)	Yes		
No	57 (69.5)	18 (22.0)	No		
Smoking (For patients assessed by FRAX with BMD)				18.3	**<0.001**
Yes	2 (12.5)	4 (25.0)	10 (62.5)		
No	18 (48.6)	16 (43.2)	3 (8.2)		

There was significant association between smoking and hip fracture for both patients assessed by FRAX with or without BMD (P <0.05)

Table 8: Distribution of smoking and hip fracture for both patients assessed by FRAX with or without BMD

Variable	<3%	3-10%	>10%	χ^2	P
	No.(%)	No.(%)	No.(%)		
Smoking (For patients assessed by FRAX without BMD)				15*	**0.001**
Yes	8 (44.4)	5 (27.8)	Yes		
No	58 (70.7)	22 (26.8)	No		
Smoking (For patients assessed by FRAX with BMD)				12.7	**0.001**
Yes	2 (12.5)	6 (37.5)	8 (50.0)		
No	21 (56.8)	12 (32.4)	4 (10.8)		

DISCUSSION

Rheumatoid arthritis (RA) is the most common form of inflammatory arthritis in adults and is characterized by chronic, progressive, systemic inflammation leading to substantial pain, disability, and other morbidities.[19] The recently updated National Osteoporosis Foundation (NOF) guidelines recommend treatment of individuals with an increased risk of fracture based on the FRAX®.[20] In present study, there was a significant association between predictions for major osteoporotic fractures 10-20% and RA patients assessed by FRAX without BMD (p<0.05). This finding is consistent with results of Gadam RK, et al study in USA (2013)[22] who did a cross-sectional review of patients requiring screening for osteoporosis as part of their routine medical care. It concluded that in most cases, FRAX alone provides the same prediction as FRAX with BMD.

With FRAX, treatment is recommended if the 10-year risk is ≥20% for MOF and/or ≥3% for hip fractures in patients with osteopenia [25]. Because BMD data may not always be available, it was important to determine if FRAX alone is an accurate fracture prediction tool.

Present study revealed a significant association between predictions for hip fractures >10% and RA patients assessed by FRAX with BMD (p<0.05). This finding is similar to results of Geusens P, et al study in Netherlands (2010) [26]. In present study elderly age RA patients were significantly associated with high prediction of osteoporotic fractures for both prediction techniques (FRAX with or without BMD). This finding is consistent with results of Hisppisley-Cox J, et al study in UK (2009) [28] and Berry SD, et al study in USA (2013) [29]. The current data showed significant association between BMI and major osteoporotic fracture and hip fracture . This finding is similar to results of Briot K, et al study in

UK (2013) [32] and Giangergorio LM, et al study in Canada (2011) [33].

Cigarette smoking of RA patients in present study had high significant risk factor for high prediction of osteoporotic fractures detected by both methods (FRAX with or without BMD). This finding is similar to results of Hisppisley-Cox J, et al study in UK (2009) [10] and Giangergorio LM, et al study in Canada (2011) [15].

The FRAX® tool is easy to use, but it has limitations. First, several risk factors can be indicated only as present or absent (i.e., glucocorticoid therapy and previous fracture), without taking into account the time of exposure to a given fracture risk or the number of events that are expression of risk.

CONCLUSIONS

We concluded that in most cases, FRAX alone provides the same prediction as FRAX with BMD, Smoking of RA patients in present study was significantly risk factor for high prediction of osteoporotic fractures detected by both methods (FRAX with or without BMD)and elderly age RA patients were significantly associated with high prediction of osteoporotic fractures for both prediction techniques (FRAX with or without BMD).

REFERENCES

1. McInnes IB, Schett G. The pathogenesis of rheumatoid arthritis. N Engl J Med., 2011; 365: 2205-2219.
2. Sinigaglia L, Nervetti A, Mela Q, Bianchi G, Del Puente A, Di Munno O, Frediani B, Cantatore F, Pellerito R, Bartolone S, et al. A multicenter cross sectional study on bone mineral density in rheumatoid arthritis: Italian Study Group on Bone Mass in Rheumatoid Arthritis. J Rheumatol, 2000; 27: 2582-9.
3. Bollerslev J, Harris ST, Leder BZ. Medicines and bone loss. J Clin Endocrinol Metab, 2013; 98: 33A-34A.
4. NIH Consensus Development Panel on Osteoporosis Prevention, Diagnosis, and Therapy. Osteoporosis prevention, diagnosis, and therapy. JAMA, 2001; 285: 785-795.
5. . Kanis JA, Melton LJ 3rd, Christiansen C, Johnston CC, Khaltaev N. The diagnosis of osteoporosis. J Bone Miner Res., 1994; 9: 1137-1141.
6. . Looker AC, Melton LJ 3rd, Harris TB, Borrud LG, Shepherd JA. Prevalence and trends in low femur bone density among older US adults: NHANES 2005-2006 compared with NHANES III. J Bone Miner Res., 2010; 25: 64-71.
7. Silverman SL. The clinical consequences of vertebral compression fracture. Bone., 1992; 13: S27-31.
8. Riggs BL, Melton LJ 3rd. The worldwide problem of osteoporosis: insights afforded by epidemiology. Bone, 1995; 17: 505s-11s.
9. World Health Organization. Physical status: The use and interpretation of anthropometry: Report of a WHO Expert committee. Technical report series 854, Geneva, 1995.
10. Kanis, J.A. et al. FRAX and the assessment of fracture probability in men and women from the UK. OsteoporosInt, 2008; 19(4): 385-97.
11. Kanis, J.A. on behalf of the WHO Scientific Group (2008). Assessment of osteoporosis at the primary health-care level. Technical Report. Sheffield, WHO Collaborating Centre, University of Sheffield, UK.(www.shef.ac.uk/FRAX).
12. Kim SY, Schneeweiss S, Liu J, Daniel GW, Chang CL, Solomon DH, et al. Risk of osteoporotic fracture in a large population-based cohort of patients with rheumatoid arthritis. Arthritis Research & Therapy, 2010; 12: R154. Available on: http://arthritis-research.com/content/12/4/R154.
13. Rubin KH, Abrahamsen B, Friis-Holmberg T, Hjelmborg JVB, Hermann AP, Barkmann R, et al. Comparison of different screening tools (FRAX®, OST, ORAI, OSIRIS, SCORE and age alone) to identify women with increased risk of fracture. A population-based prospective study. Bone, 2013; 56: 16-22.
14. Gadam RK, Schlauch K, Izuora KE. FRAX Prediction without BMD for Assessment of Osteoporotic Fracture Risk. Endocr Pract, 2013; 19(5): 780–784.
15. Dawson-Hughes B, Tosteson AN, Melton LJ 3rd. Implications of absolute fracture risk assessment for osteoporosis practice guidelines in the USA. Osteoporos Int, 2008; 19: 449–458.
16. Tre´mollieres FA, Ribot CA, Pouille JM, Drewniak N, Laparra J, Dargent-Molina P. Fracture Risk Prediction Using BMD and Clinical Risk Factors in Early Postmenopausal Women: Sensitivity of the WHO FRAX Tool. Journal of Bone and Mineral Research, 2010; 25(5): 1002–1009.
17. Hippisley-Cox J, Coupland C. Predicting risk of osteoporotic fracture in men and women in England and Wales: prospective derivation and validation of Q Fracture Scores. BMJ, 2009; 339: b4229.
18. Berry SD, Samelson J, Pencina MJ, McLean RR, Cupples A, Broe KE, et al. Repeat Bone Mineral Density Screening and Prediction of Hip and Major Osteoporotic Fracture. JAMA, 2013; 310(12): 1256-1262.
19. Briot K, Paternotte S, Kolta S, Eastell R, Felsenberg D, Eastell R, et al. Prediction of Major Osteoporotic Fractures in Women from the General Population: The OPUS Study. PLoS ONE, 8(12): e83436.
20. Giangregorio LM, McCloskey E, Leslie WD, Kanis JA. FRAX Underestimates Fracture Risk in Patients with Diabetes. Journal of Bone and Mineral Research, 2012; 27(2): 301–308.