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Comparison of Fracture Risk by Using FRAX Score with and without DEXA Scan in Patients Presenting to Endocrine Unit

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Abstract

Background: To compare the fracture risk using FRAX with and without Bone Mineral Density (BMD) for predicting 10-year probability of major osteoporotic fracture (MOF) and hip fracture. **Methods:**This was a cross-sectional study conducted at Diabetes and Endocrinology unit, Bir hospital. In individuals aged 50 or above, fracture risk assessment was done initially with FRAX without BMD and then BMD assessment with DEXA scan was done and FRAX score with BMD was calculated. Patients with similar treatment recommendations on both FRAX with BMD and without BMD were placed in the concordance group whereas patients with different recommendations were placed in the discordant group. **Results:** A total of 82 patients were included in the study out of which63(76.82%) patients showed concordance whereas 19(23.17%) showed discordance. The concordance was higher in patients with osteopenia with 37(90.24%) patients showing concordant recommendations whereas the concordance proportion was lower in patients with osteoporosis (63.42%). Among the various risk factors for osteoporotic fracture, only age showed statistically significant difference between the two groups with a higher age having a greater concordance.**Conclusion:** Fracture risk assessment with BMD and without BMD give similar fracture risk prediction only in patients with osteopenia. The concordance rate is higher in the osteopenia group as compared to the osteoporosis group. Further larger studies are required in Nepal to achieve a more statistically significant conclusion.

Key words: BMD; fractures; FRAX; osteoporosis.

Introduction

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.[1] In patients, who have undergone BMD assessment by Dual energy X-ray absorptiometry(DEXA) scan, a BMD T-score ≤-2.5 at any site is an indication for initiating anti-osteoporotic treatment.[2]

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However, only using BMD alone as a criteria for initiating treatment to minimize fracture risk has limitations as DEXA machines are not widely available, testing is costly and there are other factors apart from BMD that may contribute to fracture risk.3 The Fracture Risk Assessment Tool (FRAX) is used to calculate the 10-year probability of Major Osteoporotic Fracture (MOF) and hip fracture using important clinical risk factors and demographic data, with BMD being an optional input variable.4 However, in a low resource setting like ours, BMD data may not always be available due to various reasons, FRAX without BMD would be an important tool if it could predict future fracture risk almost comparable to FRAX with BMD and help to initiate definitive treatment.

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In this study, the aim was to compare the fracture risk by using FRAX score with and without DEXA scan in patients presenting to Endocrine unit.

METHODS

This was a cross-sectional study conducted in the Diabetes and Endocrine unit. Ethical clearance was obtained from the Institute Review Board (IRB No-1519/2080/81) and data was collected for 1 year from February 2024 to January 2025 from patients who had given written consent to enroll in the study.Fracture risk was first assessed using the FRAX calculator without BMD (based only on risk factors). The FRAX tool uses the following demographic and clinical risk factors: body weight (in kg), height (in centimeter), Body mass index (BMI), history of previous osteoporotic fracture, history of parental fracture, current smoking status, alcohol consumption of three or more units per day, oral glucocorticoid exposure currently or for more than three months in the past one year, history of Rheumatoid arthritis (RA) and presence of risk factors for secondary osteoporosis(Type-1 diabetes, untreated hyperthyroidism, hypogonadism and premature menopause). For assessing FRAX in patients receiving steroids, steroid specific FRAX was used.5FRAXscore was calculated using an online calculator(https://www.sheffield.ac.uk/FRAX/tool).4After calculating FRAX without BMD, the patient was sent for BMD evaluation by DEXA scan. The DEXA scan machine used during the study was HOLOGIC – Horizon Wi model (S/N304713M). Patients whose DEXA scan revealed osteopenia in hip joint or osteoporosis at any site as per WHO were included in the study.Patients with Chronic kidney disease, Chronic liver disease, malignancy orprevious use of anti-osteoporotic treatment were excluded. In patients whose BMD assessment showed osteopenia at femoral neck, fracture risk was again assessed using FRAX with BMD. Femoral neck BMD (grams/sq cm) was used as the input variable for FRAX with BMD. The FRAX tool we have used in the study is based on Caucasian population as there was no proper data for Nepalese population. The results were categorized as either recommending treatment (10-year probability of MOF≥ 20% or of hip fracture ≥ 3% or BMD showing osteoporosis at hip/spine) or not recommending treatment (10-year probability of MOF <20% or hip fracture < 3%). If FRAX results with and without BMD were similar, they were defined as concordant, whereas if the results were dissimilar, they were considered discordant. Patient characteristics and risk factors
in the concordant group and the discordant group were then compared. A separate subgroup analysis was done in patients with osteopenia comparing them with patients with osteoporosis.

Sampling technique and sample size calculation

Patients were recruited by consecutive sampling until the sample size was completed. Sample size was estimated based on proportion probability of high risk major osteoporotic fracture from study by Prawiradilaga et al.[6] The probability of high-risk fracture without BMD (P1)was 23.3% and the probability of high-risk fracture without BMD (P2) was 6.9%. Considering Power (1-β) of 80% and level of significance (1-α/2) of 5%, sample size (n) was estimated as 74 participants. After adjusting for 10% non- response, the final sample size was estimated to 82 participants.

All statistical analyses were performed using SPSS version 25. Data were presented as mean and standard deviation (SD) or proportions

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for continuous and categorical variables, respectively. A Student t-test, Wilcoxon rank sum test, and Chi-square or Fisher's exact test were used to compare variables between groups and calculate P-values as appropriate. P-values < 0.05 were considered statistically significant.

RESULTS

A total of 82 individuals were included in the study. The mean age group of participants was 66.78 years(SD=8.49). The majority of participants were females (n=60,73.20%) (Table 1).

Table 1: Baseline characteristics of the participants

Baseline characteristics		Total participants (n=82)	Patients with Osteoporosis (n=41)	Patients with Osteopenia (n=41)
Sex	Male	22(26.80%)	9(21.90%)	13(31.70%)
	Female	60(73.20%)	32(78.10%)	28(68.30%)
Presence of Diabetes mellitus		42(51.21%)	15(36.58%)	27(65.85%)
Active smoker		17(20.73%)	13(31.70%)	4(9.75%)
Alcohol consumer 3 or more units per day		4(4.87%)	1(2.43%)	3(7.31%)
Steroid users		14(17.07%)	8(19.51%)	6(14.63%)
Risk factors for Secondary osteoporosis		23(28.04%)	15(36.58%)	8(19.51%)

More than half of the patients had Type 2 Diabetes Mellitus (51.20%). In our study, FRAX with BMD and FRAX without BMD produced concordant results for 63 out of 83 patients (76.81%). Among the 63 subjects, 37 patients met the treatment threshold whereas 26 did not when FRAX tool with or without BMD was used for calculation of 10-year fracture risk (Table 2).

Table 2: Proportion of patients with concordant and discordant results

Treatment recommendations		Frequency (n)	Proportion (%)
Discordance (n=19)	Missed treatment	16	19.51
	Overtreatment	3	3.65
Concordance (n=63)	Treatment	37	45.12
	No treatment	26	31.72
Total		82	100.00

The patients in the concordant and discordant groups were also compared on the basis of risk factors mentioned in the FRAX algorithm (Table 3).

Table 3: Comparison of risk factors in concordant and discordant groups

Risk factors as per FRAX algorithm	Concordance (n=63)	Discordance (n=19)	p-value
Age (in years)			
Mean (SD)	68.10 (8.40)	62.42 (7.11)	**<0.014**$^{+}$
Median (IQR)	70 (63 – 74)	64(55.3 – 66)	
Sex			
Female	48 (76.19%)	12 (63.15%)	0.26$^{\#}$
Male	15 (23.80%)	7(36.85%)	
BMI (kg/m^2)			
Mean (SD)	24.19 (4.80)	25.07 (5.00)	0.62^{+}

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Active smoker	13 (20.63%)	4 (21.05%)	0.54#
Alcohol consumer	4 (6.34%)	0 (0.00%)	0.56*
Previous fracture	7 (11.11%)	1(5.30%)	0.67*
Steroid users	10 (15.87%)	4 (21.05%)	0.72#
Risk factors for Secondary osteoporosis	18(28.57%)	5 (26.31%)	0.16*
Rheumatoid Arthritis	0(0%)	1 (5.30%)	0.23*

+ Mann-Whitney U Test; # Pearson Chi-square test; * Fisher's exact test;
Level of significance is set at p<0.05
BMI: Body Mass Index
Bold signifies statistical significance

The only risk factor that had statistically significant difference between the concordant and discordant groups was age (p<0.014), showing there is more concordance with increasing age. None of the other binary variables were found to have a statistically significant difference between the two groups. Patients with osteoporosis and osteopenia were compared separately as well (Table 4).

Table 4: Comparison of risk factors in Osteopenia and Osteoporosis

	Osteopenia (n=41)		p-value	Osteoporosis (n=41)		p-value
	Concordance (n=37)	Discordance (n=4)		Concordance (n=26)	Discordance (n=15)	
Age (in years)						
Mean (SD)	71.25 (7.50)	70.6 (7.90)	0.25^	70.85 (7.90)	62.76 (6.47)	**<0.001**^
Median (IQR)	74.5 (60– 76)	75 (63 – 75.5)		72.50 (58 – 84)	63 (53 – 74)	
Sex						
Male	9 (24.32%)	4 (100%)	**0.007***	6(23.07%)	3 (20%)	1.00#
Female	28 (75.68%)	0 (0%)		20(76.93%)	12 (80%)	
BMI (kg/m^2)						
Mean (SD)	26.20 (4.60)	22.50 (2.30)	**0.022**+	22.30 (4.20)	25.60 (5.21)	<0.074+
Median (IQR)	25.50 (23.50 – 28.00)	22.5 (20.90 – 23.20)		21.60 (19.20 – 25.40)	24.1 (22.52 – 28.80)	
Active smoker	4 (10.81%)	0 (0%)	1.00*	9(34.61%)	4 (26.67%)	0.76*
Alcohol consumption	3 (8.10%)	0	1.00*	1 (3.84%)	0 (0%)	0.64*
Previous fracture	2 (5.40%)	0	1.00*	5 (19.23%)	1 (6.67%)	0.38*
Steroid users	5 (13.51%)	1 (25 %)	0.48*	5 (19.23%)	3 (20%)	1.00*
Rheumatoid Arthritis	0	1 (25%)	0.09*	0	0	NA

^ Independent t-test; + Mann-Whitney U Test; # Pearson Chi—square test; * Fisher's exact test; Level of significance is set at p<0.05, BMI: Body Mass Index, NA: not applicable

In 41 patients with osteopenia, the proportion of patients with concordant recommendations was 90.20% (n=37). Comparing the different risk factors among the two groups, statistically

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significant difference was seen in the following risk factors: gender and BMI. Higher BMI and female gender were associated with concordant recommendations. Patients in the discordant group had a lower BMI compared to the concordant group (26.21 vs 22.50). However, there were only four patients in the discordant group and the data was skewed. Likewise, all of these four patients were males aged above 75 years and these patients had more than one risk factor. This may have led to statistically significant difference between the two groups in a small sample size. In patients with osteoporosis in either hip or spine, the proportion of patients with concordant recommendations was much lower (63.41%, n=26) as compared to the osteopenia group. On comparing the different risk factors, statistically significant difference between two groups was seen in age ($p<0.001$) and BMI ($p<0.001$). The mean age in the patients showing concordance was higher when compared to the discordant group (70.85 vs 62.76 years). The difference in BMI between the two groups was just opposite to the result obtained in patients with osteopenia. The mean BMI was higher in the patients showing discordance (25.61 kg/m2) when compared to the patients showing concordance (22.30 kg/m2) (Table 4).

DISCUSSION

Historically, patients with osteoporosis (BMD T score <-2.5) were considered as high risk for osteoporotic fracture. However just relying upon BMD alone, large number of patients with osteopenia who had high fracture risk were missed.7 Though low BMD is an important risk factor for osteoporotic fracture, there are other independent risk factors which all have a significant risk for osteoporotic fracture. So, to incorporate these risk factors, FRAX calculator was developed by the WHO.4 The WHO introduced the FRAX for use in estimating the 10-year probability of hip fracture as well as other major osteoporotic fractures (spine, forearm, or humerus) in untreated patients with osteopenia. Our findings suggested that FRAX without BMD provided identical treatment recommendations as FRAX with BMD in 76.82% patients which included males and postmenopausal females aged 50-80 years of age. The percentage of concordance in our study was somewhat less when compared to study by Gadam et al[7] and Simpkins et al.8 The percentage of concordance was also lower in our study when compared to a study done in North Indian population which bears a similar character to our population, by Pankaj et al.9 In all these studies the concordance proportion was around 85%. However, the basic difference with our study was that these studies only involved patients with osteopenia whereas our study included patients with osteopenia as well as osteoporosis in equal numbers. Comparing only patients with osteopenia, the concordance rate in our study was 90.2% which is slightly higher than in these studies, but the sample size in our study was smaller compared to these studies. A study by Bari et al included patients with confirmed osteoporosis (Hip/Spine).[10] FRAX without BMD was calculated and compared to DEXA scan. In this study 29% total patients with confirmed osteoporosis were missed. This finding is similar to our study where 35% of patients with osteoporosis were missed. This underestimation of fracture risk in our study may be because of various reasons. One reason for this discordance is that FRAX takes account of only femoral neck BMD so patients with osteoporosis in spine may have been missed.[11] In our study, 36.5%(n=15) patients with osteoporosis showed discordant results. Out of these 15 patients, 9 patients had osteoporosis only in the spine and these patients

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were missed when FRAX without BMD was used. The other reason may be the different cutoffs for threshold of initiation of anti-osteoporotic therapy. A large-scale study by Napassorn et al[12] compared Fracture risk with or without BMD in Thai population and like our study, included both patients with osteopenia as well as osteoporosis. The concordance was 83.8%, higher than ours. However, the criteria for treatment initiation used in the study was different from ours. In our study, treatment initiation was recommended if Hip/Spine BMD T score ≤-2.5- or 10-year probability of a MOF≥20% or hip fracture ≥3%. But in that Thai study, treatment initiation was based on the national guidelines of Thailand, which includes 10-year Hip fracture risk ≥3% as the criteria for treatment initiation and doesn't take account BMD only. This difference in cutoffs for treatment initiation may also have shown more discordance in our study. On comparing the various risk factors, besides low BMD, younger age was found to be more likely to obtain discordant recommendations. The mean age in the concordant group was 68.10 years and in the discordant group was 62.42 years. This observation is in contrast to other studies by Gadam et al[7], Chen et al[13] and Napassorn et al[12]. In these studies, older age was more likely to show discordant results. This contrast observation in our study may be attributed to involvement of equal number of patients with osteoporosis and the treatment threshold used in our study (Hip/Spine BMD T score ≤-2.5- or 10-year probability of a MOF ≥20% or hip fracture ≥3%). Elderly patients are more likely to have osteoporotic BMD values in the spine and these patients were mostly not missed leading to higher mean age in the concordant group. Other clinical factors like gender, BMI, smoking, alcohol, risk factors for secondary osteoporosis, steroids, RA were also evaluated however no effect on concordance was seen. This finding is also similar to other studies Napassorn et al.[12] Interesting observation was seen in patients with previous fracture, out of eight patients with a previous osteoporotic fracture, seven patients showed concordance while only one patient showed discordant (young age, high BMI). In spite of this, a statistical significance could not be established, may be due to a smaller sample size. Our study must be interpreted within the context of its strength and limitations. This study was a prospective one and we included patients with both osteopenia and osteoporosis. We also had several limitations. We had to depend on the FRAX for Caucasian population as FRAX for Nepal wasn't available at the time of research. In our study, a significant portion of patients were diabetic, which also may had influenced results.[14] Newer fracture risk assessment tools like FRAX plus have included DM also as a risk factor. [15]

This is a first study of this type in Nepal. In view of limited accessibility of DEXA scan in Nepal, if a higher concordance could have been established by using FRAX without BMD, this could have been implemented on a bigger scale. But about 35% patients who would have required definitive treatment would have been missed by using FRAX without BMD. Further large-scale prospective studies are required to establish a country specific data and intervention threshold or a certain cutoff in FRAX without so that definitive treatment can be initiated. This study may provide valuable insights for future large studies.

CONCLUSION

Fracture risk assessment using FRAX with BMD and without BMD have similar fracture risk predictions in patients with osteopenia but the concordance for the fracture risk is lower in

patients with osteoporosis. Future larger studies with FRAX tool based on Nepalese population are required for a more definitive comparison.

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