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Original article

The optimal cut-off values of FRAX without BMD for predicting osteoporosis fracture risk in the older adults at Nan, Thailand

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A R T I C L E I N F O

Keywords:
FRAX
Fragility fracture
Osteoporosis
Community
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A B S T R A C T

Objectives: The World Health Organization developed the Fracture Risk Assessment Tool (FRAX) to assess the risk of having fragility fractures in the next 10 years. The FRAX tool is different by country, race, gender, and age. This study is a community-based study aiming to identify the optimal cut-off values of FRAX for the identification of older individuals who are at high risk of osteoporosis fractures in both genders.

Methods: This cross-sectional, analytic study was conducted by using health screening data of the older adults aged 60–90 living in the 3 biggest districts of Nan province, Thailand. Validity and optimal FRAX major osteoporotic fracture (MOF) and hip fracture (HF) cut-off values in both genders were determined.

Results: Of 36,042 older adults included in the study, 1624 older people had a history of fragility fractures. Older females were 3.2 and 2.5 times more likely to have fragility fractures and hip fractures than males, respectively. The optimal cut-off values of FRAX MOF for predicting fragility fractures were 3.0% for males and 6.3% for females. The optimal cut-off values of FRAX HF for predicting hip fractures were 1.1% for males and 3.3% for females.

Conclusions: A simple screening tool like the FRAX which is available in the annual health screening activities has the potential to be used to predict the risk of developing fragility fractures in rural areas of Thailand. Different cut-off values should be used in females and males because the risk of MOF and HF of both genders is significantly different.

1. Introduction

Osteoporosis is defined as a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fracture [1]. Fragility fractures resulting from low-energy trauma, such as a fall from standing height or less, are a sign of underlying osteoporosis. The most common fragility fractures are hip fractures, vertebral compression fractures, distal forearm fractures, and proximal humeral fractures [2]. A patient who has sustained 1 fragility fracture is at high risk of experiencing secondary fractures, especially in the first 2 years following the initial fracture [3]. The global trend of an aging society has been recognized and concern among healthcare providers. All of these fractures in older adults have major consequences on patients' quality of life as they cause substantial pain and disability, which results in a loss of independence, and increased risk of morbidity and mortality [4]. The primary focus of osteoporosis care is to find people at risk of fractures in order to treat osteoporosis and take action to prevent falls.

The Fracture Risk Assessment Tool (FRAX) is a risk prediction tool that is reliable and well-recognized by many countries around the world [5]. The World Health Organization developed FRAX to assess the risk of having fractures including hip fracture (HF), and major osteoporotic fracture (MOF) in the next 10 years. Its algorithm is based on the individual analysis of each patient, correlating the risk factors: age, gender, body mass index (BMI), history of bone fragility fractures, family history of HF, smoking, prolonged use of corticosteroids, rheumatoid arthritis, other causes of secondary osteoporosis and high alcohol consumption in combination with bone mineral density (BMD) [6,7]. The National Osteoporosis Foundation (NOF) of the United States of America and Osteoporosis Canada recommended treatment when FRAX MOF ≥20% or FRAX HF ≥ 3%, for both males and females [8]. In clinical practice, FRAX without BMD has been used in several studies to screen for people at risk of osteoporosis fractures. This is done to provide education and raise awareness of the importance of self-care and prevention in the community [9–12].

The FRAX tool is different by country, race, gender, and age.

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Table 1
Population by age group and gender.

Age, yrs	Male (%) (N = 16,833)	Female (%) (N = 19,209)	Total (%) (N = 36,042)
60–64	5330 (31.7%)	5851 (30.4%)	11,181 (31.0%)
65–69	4682 (27.8%)	5145 (26.8%)	9827 (27.3%)
70–74	2983 (17.7%)	3359 (17.5%)	6342 (17.6%)
75–79	1934 (11.5%)	2164 (11.3%)	4098 (11.4%)
80–84	1190 (7.1%)	1550 (8.1%)	2740 (7.6%)
85–90	714 (4.2%)	1140 (5.9%)	1854 (5.1%)

Previous studies from Thailand were hospital-based, meaning that the study population consisted entirely of patients with clinical symptoms. Furthermore, most of the patients were postmenopausal women [13–15]. On the other hand, this study is a community-based study aiming to identify the optimal cut-off values of FRAX for the identification of older individuals who are at high risk of osteoporosis fractures in both genders.

2. Methods

This cross-sectional analytic study was conducted by using health screening data of older adults aged 60–90, of both genders, living in the 3 biggest districts of Nan province (Muang Nan, Phu Phiang, and Wiang Sa), Thailand from the database of all public health service facilities in the district in 2019. The data consisted of age, gender, weight, height, and history of fractures in the common site of fragility fractures (hip, distal radius, proximal humerus, vertebra) from a fall from standing height or less.

BMI was calculated as a person's weight in kilograms divided by the square of height in meters. The Thai version of the FRAX score without the BMD (https://frax.shef.ac.uk/FRAX/tool.aspx?lang=th) was then used to calculate the 10-year probability of MOF and HF.

Demographic characteristics were described in numbers, percentages, mean, and standard deviation. Independent samples T-test was utilized to compare differences in age, BMI, FRAX MOF, and FRAX HF between the presence or absence of fragility fracture. Logistic regression analysis was used to predict the risk of having a fragility fracture or HF, presented as an adjusted odds ratio, based on gender. Receiver operating characteristic (ROC) curves and area under curve (AUC) were computed to determine the sensitivity and specificity of the FRAX MOF score on the risk of fragility fracture and the FRAX HF score on the risk of HF. In addition, Youden's index was used to determine the optimal cut-off values of FRAX MOF and FRAX HF scores. The statistical analyses were performed by using SPSS version 26 statistical software (IBM Corporation, Armonk, New York). The level of statistical significance used in the analysis was set at < 0.05. This study was approved by the Research Ethics Committee of the Nan Hospital (Nan Hos. REC No. 032/2023).

Table 2
Site of fragility fractures by gender (number of times = 1708).

Site of fractures	Vertebra (%)	Proximal humerus (%)	Distal forearm (%)	Hip (%)	Total (%)
Male	52 (15.5)	27 (8.1)	75 (22.4)	181 (54.0)	335 (19.6)
Female	191 (13.9)	85 (6.2)	505 (36.8)	592 (43.1)	1373 (80.4)
Total	243 (14.2)	112 (6.6)	580 (33.9)	773 (45.3)	1708 (100)

Table 3
Comparison of age, BMI, FRAX MOF and gender by history of fragility fracture.

Risk factors	Number without fragility fractures (N = 34,418)	Number of fragility fractures (N = 1624)	Adjusted odds ratios	95% confidence interval	P-value*
Age, yrs	69.24 ± 7.2	76.46 ± 8.0	1.1	1.087, 1.111	< 0.001
BMI, kg/m^2	22.43 ± 3.7	20.96 ± 3.9	1.0	0.955, 0.686	< 0.001
FRAX MOF	4.97 ± 2.7	7.74 ± 2.9	1.0	0.999, 1.076	0.056
Male	3.84 ± 2.5	5.51 ± 2.9	1.0	0.974, 1.073	0.371
Female	6.01 ± 2.5	8.30 ± 2.8	1.1	1.019, 1.152	0.010
Gender					
Male	16,507 (48.0%)	326 (20.1%)	reference		
Female	17,911 (52.0%)	1298 (79.9%)	3.2	2.700, 3.708	< 0.001

BMI, body mass index; FRAX, Fracture Risk Assessment Tool; MOF, major osteoporotic fracture.

3. Results

The total number of older adults aged 60–90 years was 36,042. Most of them were females (19,209 cases (53.3%)). The mean BMI was 22.37 ± 3.75 kg/m^2. Their mean age was 69.57 ± 7.4 years old. The majority of the participants were in the 60–64 years old group (31.0%) (Table 1, Fig. 1).

The number of older people with a history of fractures was 1624 (4.5%). There were 81 older people with a history of more than 1 fragility fracture. Three hundred and twenty-six (20.1%) were male and

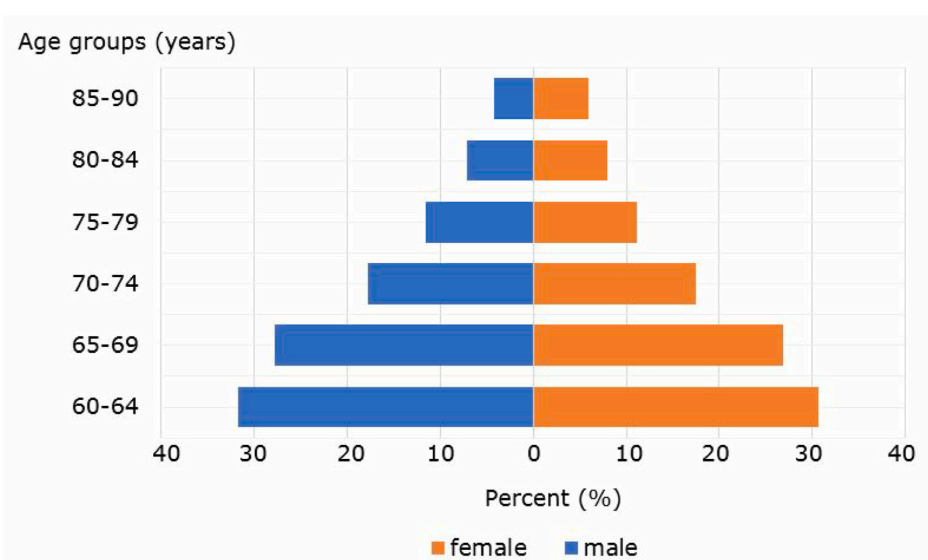

Fig. 1. Population by age groups and genders.

Table 4
Comparison of age, BMI, FRAX HF and gender by history of hip fracture.

Risk factors	Number without hip fracture (N = 35,269)	Number of hip fracture (N = 773)	Adjusted odds ratios	95% confidence interval	P-value*
Age, yrs	69.35 ± 7.3	79.59 ± 7.2	1.2	1.135, 1.174	< 0.001
BMI, kg/m^2	22.41 ± 3.7	20.31 ± 3.8	1.0	0.923, 0.980	0.001
FRAX HF	1.56 ± 1.6	4.13 ± 2.3	1.0	0.932, 1.095	0.811
Male	0.99 ± 0.9	2.40 ± 1.5	1.0	0.768, 1.185	0.671
Female	2.07 ± 1.9	4.66 ± 2.2	1.1	0.959, 1.155	0.284
Gender					
Male	16,652 (47.2%)	181 (23.4%)	reference		
Female	18,617 (52.8%)	592 (76.6%)	2.5	2.008, 3.218	< 0.001

Values are expressed as number (%) or mean ± standard deviation. BMI, body mass index; FRAX, Fracture Risk Assessment Tool; HF, hip fracture.

1298 (79.9%) were female (male to female ratio was 1:4.0). Common sites of fragility fracture were as follows: hip (773 (45.3%)), distal forearm (580 (33.9%)), vertebra (243 (14.2%)), and proximal humerus (112 (6.6%)), (Table 2).

Older females were 3.2 and 2.5 times more likely to have fragility fractures and hip fractures than males, respectively. Older people with a history of fragility fracture were older than those without fracture with an average age of 76.46 ± 8.0 years old vs 69.24 ± 7.2 years old ($P < 0.001$) and higher FRAX MOF (7.74 ± 2.9 vs 4.97 ± 2.7; $P = 0.056$) (Table 3). Older people with a history of HF were older (79.59 ± 7.2 years old vs. 69.35 ± 7.3 years old; $P < 0.001$), had higher FRAX HF (4.13 ± 2.3 vs 1.56 ± 1.6; $P = 0.811$) than the older without fracture (Table 4). However, the mean BMI in the group of fragility fracture (20.96 ± 3.9 vs 22.43 ± 3.7; $P < 0.001$) and the group of HF (20.31 ± 3.8 vs 22.41 ± 3.7; $P < 0.001$) were significantly lower than the group of without history of fracture (Tables 3, 4).

The curve of FRAX MOF in males (AUC: 0.727, 95% CI:0.702–0.753; $P < 0.001$) and FRAX MOF in females (AUC: 0.735, 95% CI: 0.721–0.749; $P < 0.001$) were also significantly different (Fig. 2). As a result, the optimal cut-off value of the FRAX MOF in males was 3.0%, with the maximum Youden's index of 0.384, at the sensitivity of 74.2% and the specificity of 64.1%, while the cut-off value of the FRAX MOF in females was 6.3%, with the maximum Youden's index of 0.369, at the sensitivity of 73.6% and the specificity of 63.3% (Table 5).

The curve of FRAX HF in males (AUC: 0.828, 95% CI: 0.800–0.857; $P < 0.001$) and FRAX HF in females (AUC: 0.814, 95% CI: 0.798–0.830; $P < 0.001$) were also significantly different (Fig. 3). As a result, the optimal cut-off value of the FRAX HF in males was 1.1%, with the maximum Youden's index of 0.516, at the sensitivity of 78.5% and the specificity of 73.2%, while the cut-off value of the FRAX HF in females was 3.3%, with the maximum Youden's index of 0.529, at the sensitivity of 75.0% and the specificity of 77.9% (Table 6).

4. Discussion

This study is the first community-based study in Thailand to assess the prevalence of fragility fractures and to identify the optimal cut-off values of FRAX MOF and FRAX HF for predicting fragility fractures

Table 5
FRAX MOF cut-off values in the fragility fractures.

FRAX MOF	Sensitivity (%)	Specificity (%)	Youden's index
Male			
2.650	81.0	54.6	0.355
2.750	78.8	58.1	0.370
3.000	**74.2**	**64.1**	**0.384***
3.300	71.5	65.9	0.373
3.650	69.0	66.6	0.357
Female			
5.700	76.7	60.0	0.368
5.950	76.7	60.0	0.368
6.300	**73.6**	**63.3**	**0.369***
6.550	73.2	63.5	0.367
6.800	73.0	63.8	0.368

FRAX, Fracture Risk Assessment Tool; MOF, major osteoporotic fracture.

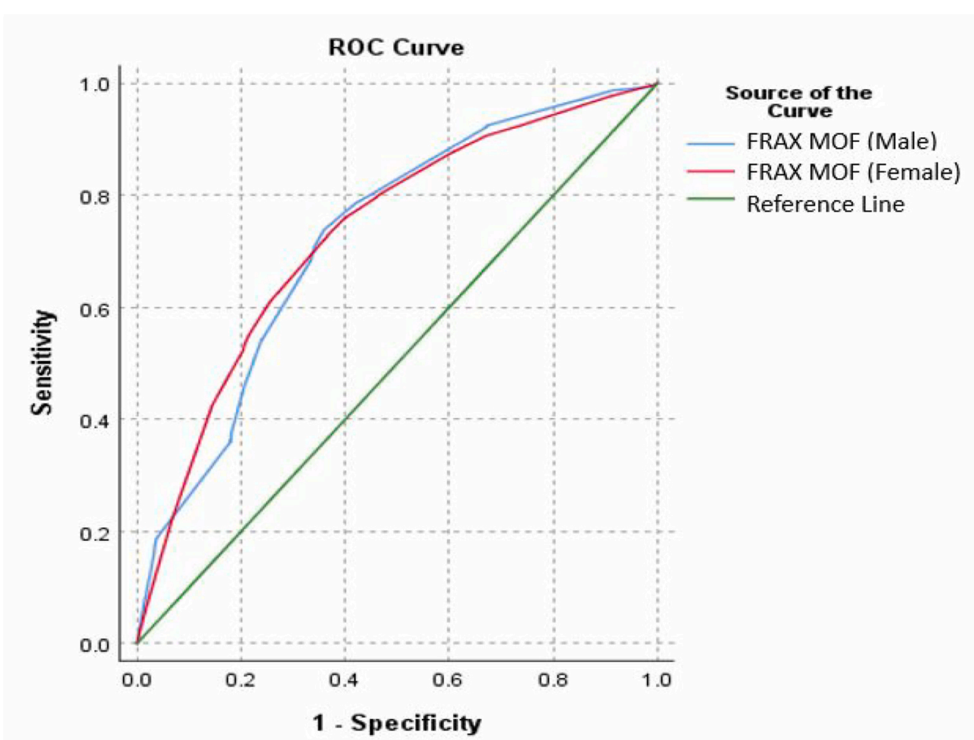

Fig. 2. Receiver operating characteristic (ROC) curves of the Fracture Risk Assessment Tool major osteoporotic fracture (FRAX MOF) in the fragility fracture of male and female.

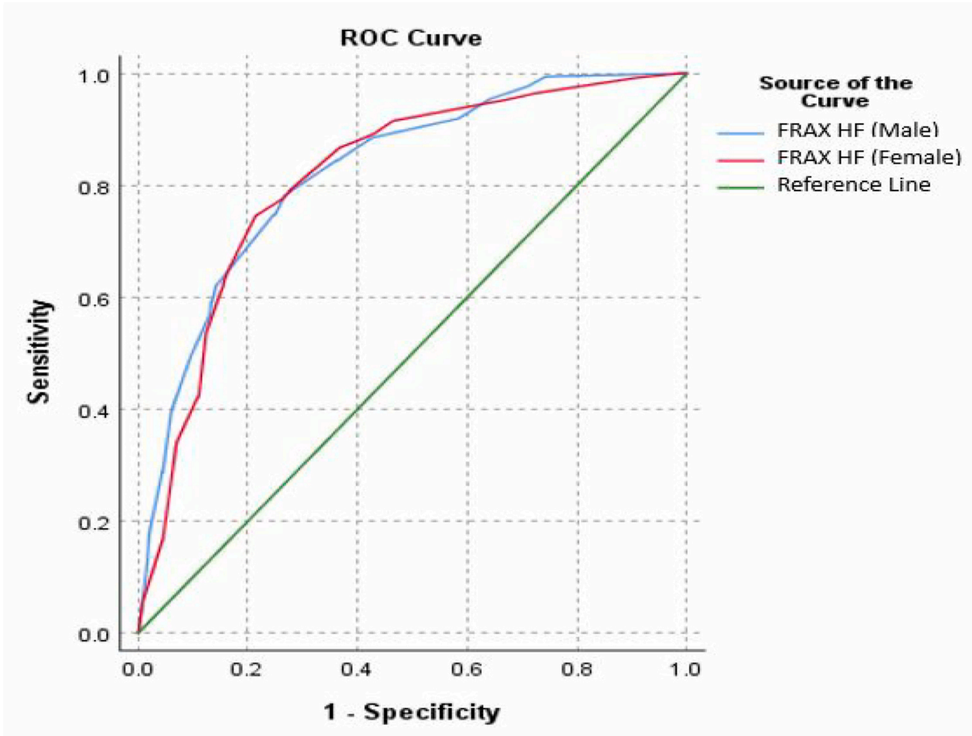

Fig. 3. Receiver operating characteristic (ROC) curves of the Fracture Risk Assessment Tool hip fracture (FRAX HF) in the hip fracture of male and female.

Table 6
FRAX HF cut-off values in the hip fractures.

FRAX HF	Sensitivity (%)	Specificity (%)	Youden's index
Male			
0.850	85.1	63.3	0.484
0.950	85.1	63.6	0.487
1.100	**78.5**	**73.2**	**0.516***
1.250	75.1	74.9	0.500
1.350	75.1	75.0	0.501
Female			
2.950	77.7	73.2	0.509
3.150	77.7	73.2	0.509
3.300	**75.0**	**77.9**	**0.529***
3.450	65.5	82.9	0.485
3.600	63.7	83.7	0.474

FRAX, Fracture Risk Assessment Tool; HF, hip fracture.

and hip fractures in the older population. The prevalence of fragility fracture in this study was 4.5%. Hip and distal forearm fractures were the most common fractures and accounted for up to 80% of all fragility fractures in Nan province, and most were single fractures. The risk of fragility fracture and HF in older females was 3.2 and 2.5 times higher than in males, respectively.

The optimal cut-off values of FRAX MOF for predicting fragility fractures were 3.0% for males and 6.3% for females. The optimal cut-off values of FRAX HF for predicting hip fractures were 1.1% for males and 3.3% for females. This suggests that FRAX cut-off values should be gender specific.

A comparison of FRAX without BMD values from community-based studies similar to this study in Asia by Liu et al. [16] in Chinese postmenopausal women found that the cut-off for FRAX MOF were $\geq$4.95% and FRAX HF $\geq$ 0.95%, which were similar to the values in this study. The study by Kanis et al. [17] in Singaporeans found that the FRAX MOF was $\geq$7.5% and FRAX HF $\geq$ 2.8%, which are higher than the values in this Thai study.

The study by Yingyuenyong [13] in Thailand studied the FRAX without BMD in Thai postmenopausal women. The results showed that the FRAX MOF was 9.8% and the FRAX HF was 4.9%. Amphansap T. studied the FRAX HF in patients treated at the osteoporosis and metabolic bone clinic. The results showed that the FRAX HF was 4.3% [15]. Teeratakupisarn et al. [18] studied patients who had undergone osteoporosis screening. The FRAX HF value was 2.4%, with males and females having values of 1.7% and 2.6%, respectively. However, these previous studies from Thailand were conducted in a hospital-based setting, which consisted entirely of female patients with clinical symptoms, without the consideration of their male counterparts. By conducting a community-based study, which encompassed both healthy people and patients who presented with clinical symptoms in both genders, the findings of this study can have important implications for clinical practice and public health. For clinical practice, FRAX MOF and FRAX HF can be used for the early identification of older people who are at high risk of fragility fractures and hip fractures. These patients can then be targeted with preventive measures, such as calcium and vitamin D supplementation, exercise, and fall prevention strategies. From the public health perspective, the findings of this study can be used to raise awareness of osteoporosis and fragility fractures among the older population. Public health campaigns can be developed to educate the older population about the risk factors for fragility fractures and the importance of preventive measures. Shepstone et al. [10] and Martin-Sanchez et al. [11] describe the usefulness of FRAX as a screening tool to determine the risk of osteoporosis fractures and to provide primary prevention management. The method was able to effectively reduce the incidence of fractures. However, it is important to note that FRAX is a risk assessment tool, and it should not be used in isolation to make decisions about treatment. Other factors, such as clinical history, physical examination, and laboratory findings, should also be considered.

Several limitations of this study should be outlined. First, the FRAX score is a measure of the risk of hip and major osteoporotic fracture in the next 10 years. However, this study is cross-sectional, which may lead to inaccurate estimates. Further longitudinal studies are needed. Another limitation is that the study was conducted in a single community in Thailand. Therefore, the results may not be generalizable to the entire older population in Thailand.

5. Conclusions

A simple screening tool like the FRAX which is available in the annual health screening activities has the potential to be used to predict the risk of developing fragility fractures in rural areas of Thailand. Different cut-off FRAX values should be used in females and males because the risk of MOF and HF of both genders is significantly different.

CRediT author statement

Worapong Sucharitpongpan: Single author for this paper.

Conflicts of interest

The author declares no competing interests.

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