EVALUATION OF OSTEOPOROSIS RISK FACTORS WITH FRAX SCORE IN ELDERLY

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Abstract: World Health Organization (WHO) sustains the introduction in clinical practice of fracture risk assessment tool (FRAX), an algorithm for evaluation of the fracture risk. FRAX is a tool approved for evaluation of fracture risk using the measurement of bone mineral density (BMD) at hip by dualenergy x-ray absorptiometry (DXA) assessment. For each subject, this algorithm evaluates fracture risk like age, sex, weight, height, previous fracture, parental history of fracture, smocking, treatment with glucocorticoids, alcohol consumption, rheumatoid arthritis. Recent studies demonstrated the utility of introduction in FRAX for some another parameters, such as fall risk, bone markers, using of ultrasonographic assessment of bone mass density and diabetes mellitus. In Romania, FRAX is still little used by family doctors and specialist doctors. Although it has a number of limitations, FRAX should be used in medical activity to identify elderly at increased risk of osteoporotic fractures.

INTRODUCTION

In 2008, FRAX was developed by the WHO task force based on the results of the research of Sheffield University (UK), like a prediction method for identifying the risk of fracture for women and men, for a treatment decision. FRAX was build to include some personal clinical data of the subject; the fracture risk can be calculated with or without the value of the BMD.

The evaluation of BMD by DXA is still difficult because in Romania, there are still few DXA machines due to the high price of appliances. If DXA scan is available, for FRAX we introduce the BMD of the femoral neck and we can calculate the estimated risk for a fracture in the next 10 years in untreated patients between 40-90 years old. FRAX is calibrated to use BMD at the hip and is not validated for assessment in another sites (spine).(1) In National Osteoporosis Foundation (NFO) Guide, the treatment of osteoporosis is recommended when FRAX value is $\geq 3\%$ for hip fracture or $\geq 20\%$.(2)

Clinical risk factors used in FRAX

The clinical factors included in FRAX are common. Age is the first factor included, the software accepts subjects between 40-90 years old. Osteoporosis is also present in men, gender parameter being also included in FRAX. Most studies demonstrated that osteoporosis is more frequently in women after menopause by decreasing the level of estrogens.

Weight and height are included in FRAX based on the fact that a high body mass is associated with the stimulation of osteoblastic activity. If the subject had previous fracture, this is included in this tool, because it demonstrates previous osteoporosis. Some studies proved that the risk of fracture is influenced by the number of prior vertebral fractures. The number and severity of vertebral fractures give details about future fracture. Regarding another sites of previous fractures, the evidence is less clear, but the presence of a past vertebral, humeral and hip fractures are more predictive of future fractures.(3)

Regarding medical history, the presence of a fractured hip in a family member represents another risk factor for osteoporosis. FRAX uses a parental history of hip fracture because a fracture at other sites would be a risk factor.

If the subject is a smoker, FRAX includes this factor, as well. A meta-analysis coordinated by WHO demonstrated, by large cohorts, the negative influence of smoking in increasing the fracture risk. Recent data shows that the fracture risk is lower in ex-smokers compared with current smokers.(1,4)

Patients treated with glucocorticoids had a high risk for osteoporosis and they were included in FRAX, too. If a patient was exposed less than 3 months, FRAX should not be taken into account. FRAX does not take into account the duration of exposure to glucocorticoids. Higher cumulative doses impart a higher fracture risk.(3) Inhaled glucocorticoids, used usually for pulmonary diseases are not associated with a high fracture risk.(3) Other causes of osteoporosis are vitamin D deficiency, hyperparathyroidism and rheumatoid arthritis. Regarding rheumatoid polyarthritis, some studies demonstrated a certain association between functional disability and clinical fracture risk in patients with rheumatoid arthritis.(4)

The alcohol consumption (>3 drinks a day) represents a risk factor for osteoporosis included in FRAX.(1) A unit of alcohol varies in different countries from 8 to 10 g of alcohol. Alcohol consumption has a dose-dependent effect, because a higher ingestion is associated with a high risk for osteoporosis and fracture.(3)

Figure no.	1. FRAX	tool in	UK	(1)
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Country : DK	Name / ID :	Allocat the real	(80093.)
Questionnoire: 1. Age Oxforen 40-00 ver Age: Date of birt [55] v	ers) or Date of birth t: MCDT	10. Secondary of Respectors of He 11. Notobal 5 on nears units per day (2) Ne 12. Fernoral neck IMAC (gitter/) [Select2006, +	Cites
1 Der Of	fels Famale	Ciesr Ca	colate
4. Height (on)	165	BMI 23.9 The bety year probability of fracture 1	. e
5. Provinus Recture	No erves	without state	
6. Parent Rectured hip		Major esteoporatio	0.5
7. Current smoking	. No Over	· Hp fracture	1.5
E. Olucconten cu	⊛No ⊖Yes	Water Brook Collinson	1.0
9. Elheumoteid orfinitio	willio West	SHOW THE OWN COMPOSITE	

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Limitations of FRAX

A number of doctors have found that FRAX formula is missing a number of factors with an obvious impact on fracture risk, such as the falls risk, bone markers and BMD measurements at other sites (lumbar spine) and with quantitative ultrasonography QUS.(4)

Recent data shows a high mortality from diabetes mellitus but this does not influence the high fracture risk. FRAX underestimates the risk of osteoporosis and fracture seen in diabetics, but it showed good concordance with fractures in patients without diabetes. Diabetes was associated with an increased risk of fracture, independent of FRAX derived with BMD. Based on this, diabetes might be considered for inclusion in future FRAX formula.(5)

In the elderly, the prevention of osteoporosis is important for a good quality of life because osteoporosis fractures produce important disability, health care costs, and mortality among postmenopausal women and older men. For this preventive activity, FRAX is a practical tool with proved utility in medical practice. Many studies using epidemiologic data demonstrated that at least half the population burden of osteoporosis-related fractures affects persons with osteopenia.(2,6)

The femoral neck BMD is entered in FRAX formula as a T-score in male and female patients derived using the NHANES III database for female Caucasians aged 20-29 years old.(7)

This data demonstrates that FRAX is a useful tool but some researchers recognised several limitations. FRAX does not take into account the dose or duration of glucocorticoid therapy or the number, type, severity, or recency of a fragility fracture, which are clinical variables known to affect fracture risk.(7,8)

Table no. 1. Limitation of FRAA (5	Table no.	1.	Limitation of FRAX	(3)
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FRAX strengths	FRAX limitations		
Derives a probability of fracture, i.e. accounts	Absence of low BMD		
for life expectancy. Can be used with or without	may influence		
BMD	therapeutic response		
Applicable to men (aged 50 years+) as well as	Not suitable for young		
postmenopausal women	men and women with		
	secondary causes of		
	osteoporosis		
Constructed from meta-analyses of CRFs in	Important risk variables		
prospective population-based cohorts worldwide	not included		
Readily administered in primary care	Does not take account of		
	exposure effect (e.g. dose		
	of glucocorticoids,		
	number of prior		
	fractures)		
Simple to administer	Simpler models do just as		
	well		
Multiple access (web, iPhone, paper charts, hand	These technologies not		
held calculators, densitometry equipment, FRAX	universally available		
pad for patients)			
31 country-specific models	Not all countries		
	available due to		
	limitations in		
	epidemiology		
Designed for primary care	Not all CRFs are		
	included, e.g. falls,		
	markers of bone		
XX7 11 1 1 1 1	turnover, prior treatment		
worldwide validation	Not validated in all		
DMD imput based on a well well-deted	Description of the second second		
Bivit input based on a well-validated site	boes not incorporate		
(Temoral neck) that can be standardised across	other bone mineral		
manufacturers	assessments, e.g. QUS,		
Ethnic specific models available for the USA	Does not take account of		
and Singapore	geographic variation		
and singapore	within countries		
Models can be undeted with new for-two-	The models har-		
death risks	outdated because of new		
utalli lisks	information		
	mormation		

Stimulates new epidemiological research	Global intervention thresholds cannot be derived
Informs practice guidelines	Must be incorporated in new drug development (in the EU)
Informs drug development and registration	Complicates health technology assessment
Can be used in cost-effectiveness analyses	Leaves room for clinical judgement
Leaves room for clinical judgement	Reversibility of risk challenged in the case of alendronate
Identifies a risk amenable to a therapeutic intervention (HT, raloxifene,bazedoxifene, risedronate, clodronate, strontium ranelate, denosumab)	

QUS quantitative ultrasonography, HT hormone therapy Some risk factors for fracture that are not included in

FRAX formula (diabetes mellitus) influenced the accuracy of the FRAX score.(5)

The initial recommendation of utility of FRAX was to use this tool only in subjects without any treatment for osteoporosis. To avoid the use of FRAX in patients on treatment in the United States, the NOF and the International Society for Clinical Densitometry (ISCD) developed the "FRAX filter", which inactivated the calculation of FRAX in DXA software if the patient was receiving osteoporosis therapy.(9)

FRAX cannot be used to follow response of an osteoporosis treatment. Recent data from a large study from Manitoba recommended that FRAX score can be used in patients who are in a period of drug holiday from bisphosphonate therapy.(10)

A large study performed in postmenopausal women over 6 years shows that FRAX with BMD and to a lesser extent also without BMD predict major osteoporotic and vertebral fractures in the general population.(11)

Of 13 tools used in the evaluation of fractures risk, a meta-analysis demonstrated that FRAX is most useful with scientific validation.(12)

Different studies observed the limitation of FRAX and proposed an improving of accuracy thereof to include information about falls, additional causes of secondary osteoporosis, biochemical markers of bone turnover, BMD measurements at the lumbar spine and concurrent osteoporosis treatment.(13,14)

In the elderly, FRAX is a good predictor of a major osteoporotic fracture but also for fractures related with low BMD.(15)

The algorithm of FRAX in the United States was recently revised, including now asymptomatic vertebral fractures but the results have not been yet evaluated completely.(16)

CONCLUSIONS

FRAX is an online risk calculator to quantify the risk

of developing a hip or other osteoporotic fractures over 10 years. FRAX was included in the clinical guidelines to identify the subjects with a high risk of fracture for a good

recommendation of osteoporotic therapy. In Romania, FRAX algorithm has been calibrated, being the first country-specific fracture prediction model. The application of FRAX in current medical activity is slow.

Romanian FRAX tool is a good tool for clinical practice, very useful for specialist doctors or for family doctors.(17)

The Romanian FRAX specific fracture prediction model is not commonly used by family doctors and specialists nowadays.

FRAX remains a useful algorithm to evaluate the 1.2016 n 47

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osteoporosis-related fracture risk and indicates the moment of starting a specific osteoporotic treatment in women and men.

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