
Article:
Povoroznyuk, V.V., Johansson, H., Grygorieva, N.V. et al. (6 more authors) (2021) Ukrainian FRAX version in the male osteoporosis management. Pain, Joints, Spine, 11 (2). pp. 53-61. ISSN 2224-1507

https://doi.org/10.22141/2224-1507.11.2.2021.236563

УДК 614.2:331.25 DOI: https://doi.org/10.22141/2224-1507.11.2.2021.236563

V.V. Povoroznyuk[1], **H. Johansson**[2, 3], **N.V. Grygorieva**[1], **J.A. Kanis**[3, 4], **A.S. Musiienko**[1], **M. Lorentzon**[3, 5], **N.C. Harvey**[6], **E.V. McCloskey**[4, 7], **E. Liu**[3]

[1]State Institution "D.F. Chebotarev Institute of Gerontology of the NAMS of Ukraine", Kyiv, Ukraine
[2]Sahlgrenska Osteoporosis Centre, Institute of Medicine, University of Gothenburg, Sweden
[3]Mary McKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia
[4]Centre for Metabolic Bone Diseases, University of Sheffield Medical School, Sheffield, UK
[5]Sahlgrenska Osteoporosis Centre, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine and Clinical Nutrition, Sahlgrenska Academy, University of Gothenburg, Sweden
[6]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK
[7]MRC and Versus Arthritis Centre for Integrated Research in Musculoskeletal Ageing, Mellanby Centre for Musculoskeletal Research, University of Sheffield, Sheffield, UK

Ukrainian FRAX version in the male osteoporosis management

For citation: Bol', sustavy, pozvonočnik. 2021;11(2):53-61. doi: 10.22141/2224-1507.11.2.2021.236563

Abstract. ***Background.*** At present, FRAX is a well-known and widely-used risk assessment tool for major osteoporotic fractures. The Ukrainian version of the FRAX algorithm was presented in 2016; with the "intervention threshold" for additional DXA examination and antiosteoporotic treatment of the Ukrainian women published in 2019. However, the data on its possible uses in men are limited. The ***purpose*** of the study was to evaluate the possibilities of using the previously developed criteria of the Ukrainian FRAX algorithm in Ukrainian men. ***Materials and methods***. We examined 653 outpatients aged 40–88 years (mean age (M ± SD) — 60.5 ± 11.8 years). We analyzed the results both in the general group and in the age subgroups; in particular, with an account of low-trauma fractures, included in the FRAX calculation, and compared them with the corresponding indices of the Ukrainian women. ***Results***. The most frequent (26.6 %) risk factor for osteoporotic fractures in the group of Ukrainian men was a history of low-trauma fracture (the corresponding index in women was 51.3 %), its presence being the reason for antiosteoporotic treatment initiating. Following upon the risk of major osteoporotic fractures calculated by FRAX, only 6.7 % of men without previous fractures were found to require additional DXA examination in order to re-evaluate the osteoporotic fracture risk, and none had a high fracture risk. 73 % of men without fractures did not have any risk factor included in the FRAX algorithm. ***Conclusions.*** This study showed a greater need for both antiosteoporotic treatment without DXA assessment and additional densitometric examination for the osteoporotic fracture risk assessment for the Ukrainian women rather than men, along with a special attention to the presence of previous fractures in men, and consideration of other risk factors for osteoporosis, even those not included in this FRAX algorithm.

Keywords: FRAX; risk of osteoporotic fractures; osteoporosis; men

Introduction

Osteoporosis and its complications (low-energy fractures) remain a topical medico-social issue of a global status, and results in a decrease of life expectancy, limited self-care of patients and deteriorated life quality [1-3]. According to the recent data, every 3 seconds low-energy fractures occur across the world, and over about 9 million osteoporosis-related fractures occur annually. Osteoporosis is more common in women; this fact being associated with gender-related peculiarities of bone structure and growth, along with the age-related rate of bone loss. For instance, every one in three women experience osteoporotic fractures happening over the age of 50, and every one in five men do so later in their lives [1], however, the mortality rate in

Для кореспонденції: Григор'єва Наталія Вікторівна, доктор медичних наук, професор, провідний науковий співробітник відділу клінічної фізіології та патології опорно-рухового апарату, ДУ «Інститут геронтології імені Д.Ф. Чеботарьова НАМН України», вул. Вишгородська, 67, м. Київ, 04114, Україна; e-mail: crystal_ng@ukr.net; контактний тел.: +38 (067) 445 76 08.
For correspondence: Nataliia Grygorieva, MD, PhD, Professor, Leading Research Fellow at the Department of clinical physiology and pathology of locomotor apparatus, State Institution "D.F. Chebotarev Institute of Gerontology of the NAMS of Ukraine", Vyshgorodska st., 67, Kyiv, 04114, Ukraine; e-mail: crystal_ng@ukr.net; phone: +38 (067) 445 76 08.
Full list of authors information is available at the end of the article.

males during the first year after femoral fracture is significantly higher (by 51 %), compared to the respective rate in women (37.5 %) [2]. A recent European study [3] showed that only 63 % of men receive anti-osteoporotic treatment (out of those necessitating it), although this number has increased by about 17 % since 2010, but the timely diagnosis and treatment of osteoporotic fractures remains a burning issue.

The problem of the adult male population in Ukraine suffering from osteoporosis has its specific aspects. According to the data collected by the Ukrainian Scientific-Medical Center of Osteoporosis, 28.4 % men aged 50 years and older have low bone mineral density (BMD) indices by the dual-energy X-ray absorptiometry (DXA) measurements, while 6.7 % had osteoporosis. Our findings rely on the data by the State Statistical Service of Ukraine of 01.01.2020 [4] and show that in Ukraine over 123 thousand men aged 50 years and older have osteoporosis and about 560 thousand men had osteopenia.

Nowadays, according to the recommendations of international societies [5-9], BMD, measured by DXA, is a key criterion for the osteoporosis diagnosis, which is used to confirm it. For the postmenopausal women and men aged 50 years or over, the SD reduction by 2.5 is the basis for confirmation of the osteoporosis diagnosis. However, recent studies have shown that this indicator, though important, is not an exclusive criterion of fracture probability assessment. The latter may be associated with the numerous so-called "clinical risk factors", including age, gender, a number of comorbidities and medication history. Across the world, the most commonly validated osteoporotic fracture risk questionnaire is FRAX (Fracture Risk Assessment Tool), which is automatically calculating the 10-year probability of major osteoporotic fractures (hip, shoulder, forearm and clinical spine fractures), and separately, provides indications of imminent hip fractures in men and women aged 40 years and older, considering 11 clinical risk factors, with and without taking into account the femoral neck BMD [10]. Today, the FRAX algorithm is included in many international and country-specific guidelines of osteoporosis and its complications' treatment [11], and significantly expands the range of options for the timely and effective treatment of osteoporosis and its complications.

The FRAX has been in practice since 2008, and is currently available online (https://www.sheffield.ac.uk/FRAX/tool.aspx?lang=en) in 35 languages for 65 countries with 71 models [10]. The latest systematic analysis [11] of the diagnostic and treatment intervention thresholds for osteoporosis and its healthcare model and treatment costs [10]. The Ukrainian version of FRAX was presented in 2016 [12]. In 2019, the "intervention thresholds" for additional examination and treatment of women were published [13]. However, there are no data of similar thresholds being implemented for men. All the above-mentioned facts became the foundation for this study.

The **purpose** of this study was to assess the possible options of the earlier developed criteria use for the Ukrainian version of FRAX algorithm for the Ukrainian males.

Materials and methods

To achieve this goal, a cross sectional study was conducted at SI «Dmitry F. Chebotarev Institute of Gerontology of the National Academy of Medical Sciences of Ukraine». In this study, we have observed 653 male outpatients, aged 40-88 years (mean age (M ± SD) – 60.5 ± 11.8 years). Their received parameters were analyzed both as a total group, depending on the presence of low-energy fractures (part of the FRAX algorithm), and in separate age subgroups.

The study was approved by the Ethics Committee of SI «Dmitry F. Chebotarev Institute of Gerontology of the National Academy of Medical Sciences of Ukraine» (protocol №5 of May 17, 2017) and performed from September 2017 to December 2020. All the study participants signed their informed consents for participation.

The 10-year probability of major osteoporotic fractures (MOF) and hip fractures (HF) was assessed online, using the developer's website (https://www.sheffield.ac.uk/FRAX) and the Ukrainian version of the questionnaire (version 4.1), per developer's recommendations. The calculation was performed with and without taking into account the femoral neck BMD.

The BMD was measured by DXA, with two devices (PRODIGY, GEHC Lunar, Madison, WI, USA and DISCOVERY Wi, Hologic, Inc. USA), where T- and Z-score values were automatically calculated by the Densitometer Software. The height and body weight were measured using routine calculations.

The statistical analyses were carried out by means of Statistica 10.0 software. The obtained results were tested according to the rule of normal distribution (Shapiro-Wilk test). Depending on the distribution, the results were presented in the following manner: mean (M) and its standard deviation (SD) or median (Me) and lower and upper quartiles (25Q–75Q). The quantitative data were presented as 'n', frequency of the index in the sample (%) also was being assessed.

In order to develop the intervention threshold, the National Osteoporosis Guideline Group (NOGG) methodology was used, which was first applied in the United Kingdom [13] and later in other countries [10, 19, 20].

Methodology of the FRAX algorithm criteria development and "intervention criteria" for the Ukrainian version

The presence of low-energy fractures is accepted as an osteoporosis treatment criterion for both postmenopausal women and men aged 50 years and older in most national and international guidelines [6-9, 11]. According to the WHO, a low-energy fracture (fragility fracture) is a fracture caused by a force equivalent to falling from a standing height or even smaller. The most common localizations of fractures associated with a low BMD are hip, shoulder, forearm bones, and clinically significant vertebral fractures, which belong to the MOF group. Whereas the previous low-energy fracture was considered an initiating criterion for an anti-osteoporotic treatment, the "intervention threshold" for men without a history of fractures was an age-dependent 10-year MOF risk, calculated using the

Ukrainian FRAX model, which is equivalent to a similar indicator of men with a prior low-energy fracture. The calculation was performed for all age groups with a body mass index of 25 kg/m^2.

The criteria of diagnostic intervention or anti-osteoporotic treatment initiation were similar to those used by various national and international guidelines for women [11, 14] and developed specifically for Ukraine [13] (Table 1):

1). the 10-year MOF probability, below which neither DXA scan nor treatment should be considered ('lower assessment threshold');

2). the 10-year MOF probability, above which treatment intervention may be recommended regardless of the BMD level ('upper assessment threshold').

The 'Lower assessment threshold' was established according to the age-related 10-year MOF probability, equivalent to the one characteristic of subjects with no clinical risk factors, in order to exclude the requirement for BMD measurements in men without clinical risk factors. The 'Upper assessment threshold' was established in line with the NOGG recommendations [14], as 1.2 times higher than the "intervention thresholds".

The men with a history of low-energy fractures were considered candidates for an anti-osteoporotic treatment, without the requirement for an additional BMD assessment. For subjects without a history of low-energy fracture, the recommendations were based on an estimate of the 10-year MOF probability, which corresponded to the indices of each age subgroups.

When determining a 10-year MOF probability below the "lower assessment threshold", additional testing or anti-osteoporotic treatments were not recommended. If the 10-year MOF probability exceeds the "upper assessment threshold", all the men were advised to start an anti-osteoporotic treatment without an additional DXA scan. Individuals with a 10-year MOF probability between the "upper and lower assessment threshold" were to be referred to the DXA scan for the BMD measurement, and further their probability of fractures was to be reassessed. According to the data of DXA measurement, a 10-year MOF probability was reassessed, along with BMD of femoral neck. Individuals were considered eligible for treatment whenever the 10-year MOF probability was higher than the "intervention threshold", namely in case of a reduced BMD (osteopenia) confirmed by the DXA. The FRAX data obtained from men were compared with the ones obtained from women (3179 women, aged 40-90 years) [13].

Results

It was detected that 48.5 % of the surveyed men had a history of fractures, 54.9 % of those were low-energy ones, and within the framework of all registered fractures, 49.5 % were referred to as major osteoporotic fractures. In the total group of subjects, these values were equal to 26.6 % and 24 % respectively (Table 2). The age distribution of the examined sample showed that 21.9 % of all persons were aged 40-49 years (n = 143), 25.0 % – 50-59 years (n = 163), 27.6 % – 60-69 years (n = 180), 19.8 % – 70-79 years (n = 129), and 5.8 % – 80-89 years (n = 38). The clinical characteristics of the examined men are presented in Table 2.

Analyzing the FRAX-MOF indices with no account of DXA in the total sample, we observe a non-parametric distribution of parameter with a significant shift towards the low indices. The 10-year MOF and HF probability in the total group of men with no account of BMD measurements was 2.3 and 0.5 % respectively. They got higher whenever the BMD index was included into the FRAX calculations, both for the individuals with no fractures or for the men with a history of low-energy fractures (Table 3).

In all age groups, except for subjects aged 80-89 years, the FRAX values for MOF were higher with the BMD consideration, compared to the corresponding value calculated without BMD (Fig. 2) both for the individuals with a history of fractures or for those without it.

Among the examined subjects, 174 subjects (26.6 %) had a diagnosed osteoporotic fracture, which was considered an

Table 1. The 10-year major osteoporotic fracture (MOF) probability and intervention and additional assessment criteria according to the Ukrainian version of FRAX algorithm, %

Age (years)	Intervention threshold (%)	Lower assessment threshold (%)	Upper assessment threshold (%)
40	5.5	2.4	6.6
45	6.1	2.7	7.3
50	6.7	3.1	8.1
55	7.5	3.5	9.1
60	8.3	4.0	10
65	8.8	4.4	11
70	9.6	5.0	12
75	11	6.0	13
80	11	6.7	13
85	11	6.9	13
90	10	6.0	12

indication for anti-osteoporotic therapy with no additional examination. Among the remaining 479 men with no history of fractures, 447 subjects (68.5 % of the total cohort, 93.3 % subjects with no history of fractures) had a low MOF risk and required no treatment or further reassessment. A moderate fracture risk was revealed in 32 individuals (6.7 % of the group with no fractures, 4.9 % of the total cohort), whose FRAX was reassessed after the inclusion of the femoral neck BMD values. After the calculations were made, 23 subjects were relegated to a low risk category (3.5 %) and the remaining 9 subjects – to a high risk group (1.4 % of the total cohort).

Analysis of our findings depending on the age-related DXA examination and treatment requirement reveals that in all the age groups most men did not need an additional DXA measurement in order to choose a further management tactic. The number of subjects requiring an additional DXA measurement diminished with age; it accounted for 21.2 % in the age group of 40-44 years and 2.9 and 4.2 % in the age group of 75-79 and 80-84 years, respectively (Table 4).

The MOF risk comparison performed to analyse the male and female population by the intervention criteria revealed that among the examined men only 28 % required anti-osteoporotic treatment; among the examined female subjects the similar index accounted for 57 % (out of those, 26.6 % males and 51.3 % females had a history of osteoporotic fracture).

While assessing FRAX-MOF without DXA consideration, we found that only a small share of women (0.7 % of total examined cohort) had a high risk of fractures and required anti-osteoporotic treatment and neither man had high FRAX-MOF indices.

Every one in three women (29.7 %) and most men (68.5 %) did not require any further examination due to the low fracture risk rates.

18.3 % women and only 4.9 % men required DXA examination in order to reassess the osteoporotic fracture risk. Having reassessed the fracture risk with BMD consideration, 12.9 % women had a low fracture risk and required neither treatment nor additional examination, while 5.4 % women required anti-osteoporotic treatment. For men, the counterpart values were significantly lower, accounting for 3.5 and 1.4 %.

Thus, our analysis demonstrates that women rather than men have a certain requirement for the anti-osteoporotic

Table 2. Characteristics of the examined men

Parameters	M±SD (Min-Max) or n (%)
Age, years	60.5±11.8 (40.0-88.0)
Height, cm	175.2±7.5 (135.0-198.0)
Weight, kg	83.9±15.2 (39.0-125.0)
Body mass index, kg/m^2	27.3±4.5 (15.0-51.9)
History of fractures, any age, n (%)	317 (48.5)
History of low-energy fractures, n (%)	174 (26.6)
History of parental hip fractures, n (%)	42 (6.4)
Smoking, n (%)	106 (16.2)
Alcohol consumption (3 or more units per day), n (%)	8 (1.2)
Secondary osteoporosis, n (%)	24 (3.7)
Rheumatoid arthritis, n (%)	20 (3.1)
Intake of glucocorticoids, n (%)	32 (4.9)
BMD of femoral neck	0.80±0.17 (0.34-1.42)

Note: BMD – bone mineral density.

Table 3. The 10-year major osteoporotic fracture (FRAX-MOF) probability depending on the presence of fractures

Groups / Indicators	Total group	Subjects without fractures	Men with previous fractures
MOF without BMD (%)	2.3 [2.0-4.1]	2.1 [1.9-2.5]	4.7 [4.3-5.0]
HF without BMD (%)	0.5 [0.2-1.1]	0.3 [0.2-0.6]	1.3 [0.8-2.0]
MOF with BMD (%)	2.7 [2.0-4.4]	2.3 [1.9-3.1]	5.4 [4.0-7.9]
HF with BMD (%)	0.6 [0.2-1.3]	0.4 [0.1-0.8]	1.6 [0.8-2.9]

Notes: the results are presented in the following manner: Me [Q25-Q75]; MOF – calculation of FRAX for major osteoporotic fractures; HF – calculation of FRAX for hip fractures.

treatment without DXA consideration and additional densitometric examination in order to assess the osteoporotic fracture risks.

The risk reassessment due to the "intervention criterion" for 431 men whose 10-year major osteoporotic fracture (MOF) probability values remained within the frameworks of "lower-to-higher probability threshold" (required the additional DXA examination). The BMD measurements demonstrated that 85.4 % subjects (n=368) did not require anti-osteoporotic treatment, while 63 subjects (14.6 % of the total category) required osteoporotic treatment. The age-related evaluation of the need for anti-osteoporotic treatment following the BMD measurements demonstrated that in the age group of 45-49 years this index was 6.7 %, while in the age group of 70-74 years this index was 22.4 %. Furthermore, we received evidence of index diminishment in the age group of 80 years and over (23.8 % in the age group of 80-84 years and no men in the age group of 85-89 years).

Discussion

Osteoporosis and its complications are an important medical and social issue both in Ukraine and all over the world [1-3]. The recent studies held in 5 countries of the European Union and Sweden show that the number of fractures will increase from 2.7 million in 2017 to 3.3 million in 2030 (by 23 %), and the annual costs associated with fractures (i.e. 37.5 billion euros in 2017) will increase by 27 % [3].

Nowadays, the most widely-used tools for confirmation of osteoporotic diagnosis and assessment of the low-energy fracture probability are DXA and FRAX. In the postmenopausal women and men aged 50 years and older, the same BMD values (T ≤ -2.5 SD) are used to confirm the disease [5-7]. Among men aged 50-69 years, the indications for BMD measurement are the age of 70 years and over, presence of the bone loss contributing factors (such as the low BMI levels, a history of previous

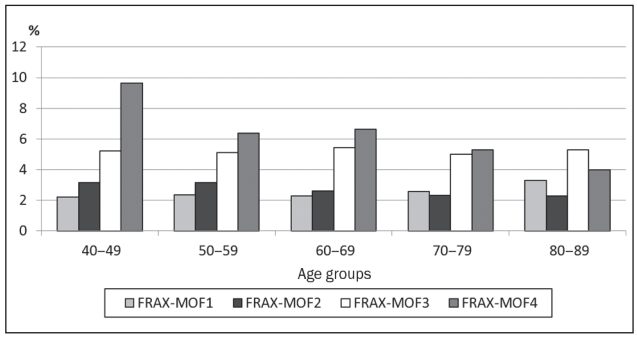

Fig. 2. The 10-year major osteoporotic fracture (FRAX-MOF) probability depending on the presence of previous fractures and the method of calculation

Notes: FRAX-MOF1 – calculation without taking into account BMD for subjects without previous fractures; FRAX-MOF2 – calculation with BMD for subjects without previous fractures; FRAX-MOF3 – calculation without taking into account BMD for subjects with previous fractures; FRAX-MOF4 – calculation with BMD for subjects with previous fractures.

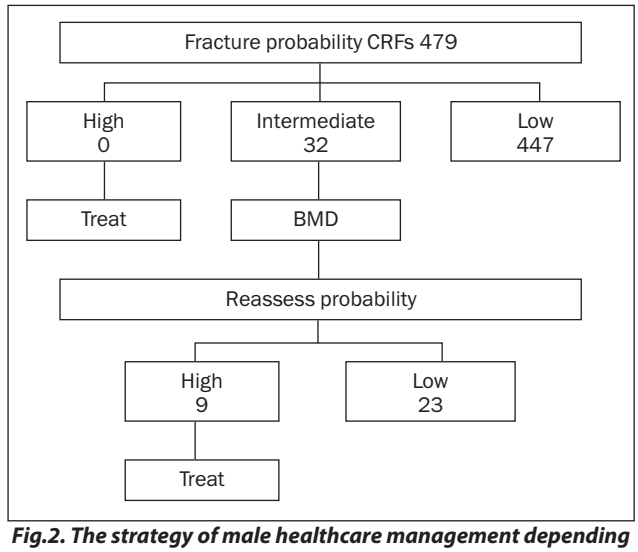

Fig.2. The strategy of male healthcare management depending on the major osteoporotic fracture risk

Table 4. The distribution of 10-year major osteoporotic fracture (FRAX-MOF) probability depending on the age and management tactics, %

Management tactic / Age subgroups	I	II
40-44	78.8	21.2
45-49	86.5	13.5
50-54	85.7	14.3
55-59	90.9	9.1
60-64	93.9	6.1
65-59	96.7	3.3
70-74	100.0	0.0
75-79	97.1	2.9
80-84	95.8	4.2
85-89	100.0	0.0

Notes: I – do not require either examination or treatment (FRAX-MOF values are below than the "lower probability threshold"); II – require additional DXA measurement and fracture risk reassessment.

Table 5. Male/female distribution (as to 10-year MOF probability) for subjects requiring diagnostic/therapeutic interventions

Groups / Indices	n (%)		FRAX-MOF		FRAX-HF	
	Males	Females	Males	Females	Males	Females
Total group	653 (100)	3719 (100)	3.1	8.8	1.3	3.3
Subjects with a fracture* history	174 (26.6)	1906 (51.3)	6.5	11.6	2.6	4.7
Subjects with a low fracture risk	470 (72.0)	1585 (42.6)	2.6	4.7	0.6	1.2
Subjects recommended treatment	183 (28.0)	2134 (57.4)	6.8	11.8	2.9	4.9
Subjects with no fractures requiring treatment (by FRAX)	9 (1.4)	228 (6.1)	11.6	13.1	7.5	6.5
Subjects who do not require DXA examination	32 (4.9)	681 (18.3)	6.4	6.9	2.7	2.5

Notes. FRAX-MOF – 10-year major osteoporotic fracture probability, FRAX-HF- 10-year hip fracture probability; DXA – Dual X-ray absorptiometry.

fractures, medication with adverse effects on bone tissue or the presence of comorbidities with adverse effects on bone tissue). By contrast to the DXA indices used to confirm the osteoporosis diagnosis (T ≤ -2.5 SD) being consistent for the men aged 50 years and older, the male MOF risk grew with age, though not as significantly as among females.

Analysis of the FRAX informative value while assessing the probability of osteoporotic fractures in men proves [15-17] its good prognostic value, although the informative value may depend, in particular, on the used interventions thresholds [17-19]. Nowadays, there are three models of interventions thresholds: the first one uses stable indicators for people of different ages and genders, the second is an age-dependent approach, and the third – a hybrid model (using a combination of the above-mentioned models with various sequences). The first approach is typical for the US and Latin American countries, while in Europe the healthcare providers use all three models. The informative value of separate risk detection tools for osteoporotic fractures and their combinations continues to be studied, although the existing data indicate their different discriminant properties in certain age groups, certain populations, and with certain comorbidities [16].

The 10-year prospective multicenter study conducted by Marques A. et al. [17] evaluated the FRAX informative value with and without BMD, predicting the probability of MOF in 2626 people aged 40 years (minimum follow-up of 8.5 years). The prognostic significance of FRAX without BMD, assessed by the ROC analysis, exceeded the corresponding value only as far as BMD was concerned (both for MOF (AUC = 0.76; 95 % confidence interval (CI): 0.72-0.79) and for HF (AUC = 0.78; 95 % CI: 0.69-0.86); however, a significant improvement in the informative value of FRAX in combination with DXA was not achieved (for MOF, AUC = 0.78; 95 % CI: 0.74-0.82, p = 0.25), respectively; for HF: AUC = 0.79; 95 % CI: 0.69-0.89, p = 0.72). The area under the ROC curve (AUC) was larger in men than in women, and, if in the latter case, the FRAX both with and without BMD downplayed the MOF number and overestimated the HF number, in case of men, the number of fractures was within 95 % CI (both with and without BMD).

Another multicenter prospective cohort study [18] assessed the informative value of various approaches to the fracture probability in men, using the Osteoporosis Self-Assessment Tool (OST) and FRAX (excluding BMD) before DXA screening, and involved 4,043 people aged 70 years and older. At the beginning of treatment, the authors were guided by the 2014 National Osteoporosis Foundation (NOF)'s recommendations; the "cut-off" values for treatment initiation being based on FRAX and stable (9.3 %), in compliance with the 2011 USPSTF (US Preventive Services Task Force)'s recommendations. Among 5.3 % of the surveyed men, the T-value was ≤ -2.5 SD at the hip level (namely femoral neck) or lumbar spine, and 29.2 % required anti-osteoporotic treatment in compliance with NOF recommendations. Comparative ROC analysis of different questionnaires revealed that OST had better discriminating properties (AUC = 0.68) than FRAX (AUC = 0.62; p = 0.004) in terms of osteoporosis diagnostification, later confirmed by DXA. The sensitivity and specificity indicators confirming the diagnosis of osteoporosis for OST, as far as the "<2" criterion was concerned, amounted to, respectively, 0.83 and 0.36; in case of FRAX MOF – to 0.59 and 0.59, as far as "9.3 %" criterion was concerned, in line with the USPSTF's recommendations. However, the FRAX and DXA correlation may not always provide some extra informative value to the osteoporosis screening [15], and the use of stable indicators, such as the interventions thresholds, has proved that they are less informative, so this approach is not recommended by the European and numerous country-specific guidelines [6, 11, 13, 20, 21].

The MOF risk factor assessment in the Ukrainian men has shown that a history of osteoporotic fractures was the most frequent risk factor (26.6 %), other risk factor being significantly more rare (parental hip fracture – 6.4 %; smoking – 16.2 %; alcohol addiction – 1.2 %; secondary osteoporosis – 3.7 % ; rheumatoid arthritis – 3.1 %; glucocorticoid use – 4.9 %).

In Ukraine, the comparison of male and female populations as to the principal osteoporotic fracture risks in association with the interventions criteria revealed that in the total group of examined subjects under one third (26.6 %) of males and a half (51.3 %) of females had a history of osteoporotic fractures and required anti-osteoporotic treatment with no additional examination. The assessment of FRAX-MOF indices among other subjects (without a history of fractures) demonstrated that only a small group of women (1.5 % subjects with no fractures, 0.7 % total examined cohort) had a high fracture risk and required anti-osteoporotic treatment, while no man had any high FRAX-MOF indices.

Over half (60.9 %) of the female group and most males (93.3 %) without a history of fractures did not require any additional examination associated with a low risk of fractures. Over a third (37.6 %) of female group and only 6.7 % males without fractures required DXA examination in order to reassess the osteoporotic fracture risk.

Our findings suggest that in the group of males without fractures only in under a third (27 %) of the examined group there are osteoporotic risk factors included in the FRAX algorithm, outlining their low level of risk. The above-mentioned facts testify to the fact that one should recommend fracture risk evaluation targeting, first and foremost, for men with at least one clinical risk factor. The reassessment of "interventions thresholds" for the Ukrainian males becomes an alternative option, which is possible only after exploring the economic foundations of this approach.

Our study confirms a higher demand for the anti-osteoporotic treatment without DXA and for an additional densitometric examination in order to reassess the osteoporotic fracture risks, for women rather than men in Ukraine. This finding is in line with the ones by other authors. There is a further need for the risk assessment of osteoporosis and its complications in men with a history of low-energy fractures. The development of national guidelines on osteoporosis diagnostics and treatment in men along with the FRAX validation based on the economic efficacy should implement some effective measures of osteoporosis prophylaxis and treatment in Ukraine.

The *limitations* of this study include: only one research center of Ukraine being the study site, which may not be fully representative of all the Ukrainian men. In addition, some important risk factors for fractures, common for men, are not included in the FRAX algorithm (e. g. chronic obstructive pulmonary disease, hepatic disease, androgen deprivation, seronegative spondyloarthritis, a history of smoking, high risk of falls, etc.), although they may have a significant effect on the rate of bone loss and the risk of fractures. Their mandatory consideration in the calculation of FRAX should increase its informative value and be recommended for the clinical practice.

Conclusions

The major osteoporotic fracture risk factor assessment in the Ukrainian males demonstrated that a history of low-energy fractures was the most frequent (26.6 %) osteoporotic risk factor (the corresponding index for women is 51.3 %); its presence being the reason for the anti-osteopotic treatment initiation. After the calculation of the MOF risk by FRAX, only 6.7 % males without a history of fractures required DXA examination in order to reassess the osteoporotic fracture risk; none of them had high MOF risk values. 73 % males without fractures had ant risk factors included into the FRAX algorithm. It implies that fracture risk evaluation is recommended, first and foremost, for males with at least one clinical risk factor, and other risk factors not included in the algorithms should also be considered.

The present study demonstrated a higher demand for either an anti-osteoporotic treatment without DXA measurement or an additional densitometric examination aimed at the reassessment of osteoporotic fracture risk for the Ukrainian women rather than the Ukrainian men. Further attention should be paid to the risk assessment of osteoporosis and its complications among the males with a history of low-energy fractures.

Conflicts of interests. Authors declare the absence of any conflicts of interests and their own financial interest that might be construed to influence the results or interpretation of their manuscript.

References

1. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int. 2006 Dec;17(12):1726-33. https://doi.org/10.1007/s00198-006-0172-4.

2. Bentler SE, Liu L, Obrizan M, et al. The aftermath of hip fracture: discharge placement, functional status change, and mortality. Am J Epidemiol. 2009 Nov 15;170(10):1290-9. https://doi.org/10.1093/aje/kwp266.

3. Borgström F, Karlsson L, Ortsäter G, et al; International Osteoporosis Foundation. Fragility fractures in Europe: burden, management and opportunities. Arch Osteoporos. 2020 Apr 19;15(1):59. https://doi.org/10.1007/s11657-020-0706-y.

4. State Statistics Service of Ukraine. Distribution of the permanent population by sex, separate age groups and type of locality. Available from: http://database.ukrcensus.gov.ua/MULT/Dialog/statfile_c.asp.

5. ISCD Official Positions – Adult. 2019. Available from: https://iscd.org/learn/official-positions/adult-positions/.

6. Kanis JA, Bianchi G, Bilezikian JP, Kaufman JM, Khosla S, Orwoll E, Seeman E. Towards a diagnostic and therapeutic consensus in male osteoporosis. Osteoporos Int. 2011 Nov;22(11):2789-98. https://doi.org/10.1007/s00198-011-1632-z.

7. Watts NB, Adler RA, Bilezikian JP, et al; Endocrine Society. Osteoporosis in men: an Endocrine Society clinical practice guideline. J Clin Endocrinol Metab. 2012 Jun;97(6):1802-22. https://doi.org/10.1210/jc.2011-3045.

8. Cosman F, de Beur SJ, LeBoff MS, et al; National Osteoporosis Foundation. Clinician's Guide to Prevention and Treatment of Osteoporosis. Osteoporos Int. 2014

Oct;25(10):2359-81. https://doi.org/10.1007/s00198-014-2794-2.

9. Almohaya M, Alobedollah A, Kendler DL. Management of Male Osteoporosis: an Update. Current Treatment Options in Rheumatology. 2018;4:355-366. https://doi.org/10.1007/s40674-018-0107-1.

10. Kanis JA, Johansson H, Harvey NC, McCloskey EV. A brief history of FRAX. Arch Osteoporos. 2018 Oct 31;13(1):118. https://doi.org/10.1007/s11657-018-0510-0.

11. Kanis JA, Harvey NC, Cooper C, Johansson H, Odén A, McCloskey EV; Advisory Board of the National Osteoporosis Guideline Group. A systematic review of intervention thresholds based on FRAX : A report prepared for the National Osteoporosis Guideline Group and the International Osteoporosis Foundation. Arch Osteoporos. 2016 Dec;11(1):25. https://doi.org/10.1007/s11657-016-0278-z.

12. Povoroznyuk VV, Grygorieva NV, Kanis JA, et al. Epidemiology of hip fracture and the development of FRAX in Ukraine. Arch Osteoporos. 2017 Dec;12(1):53. https://doi.org/10.1007/s11657-017-0343-2.

13. Povoroznyuk V, Grygorieva N, Johansson H, et al. FRAX-Based Intervention Thresholds for Osteoporosis Treatment in Ukraine. Journal of Osteoporosis. 2021;2021:ID 2043479. https://doi.org/10.1155/2021/2043479.

14. Compston J, Cooper A, Cooper C, et al; National Osteoporosis Guideline Group (NOGG). UK clinical guideline for the prevention and treatment of osteoporosis. Arch Osteoporos. 2017 Dec;12(1):43. https://doi.org/10.1007/s11657-017-0324-5.

15. Harvey NC, McCloskey E, Kanis JA. Use of FRAX(®) in men. Joint Bone Spine. 2016 Oct;83(5):477-8. https://doi.org/10.1016/j.jbspin.2016.03.007.

16. Adler RA, Hastings FW, Petkov VI. Treatment thresholds for osteoporosis in men on androgen deprivation therapy: T-score versus FRAX. Osteoporos Int. 2010 Apr;21(4):647-53. https://doi.org/10.1007/s00198-009-0984-0.

17. Marques A, Lucas R, Simões E, Verstappen SMM, Jacobs JWG, da Silva JAP. Do we need bone mineral density to estimate osteoporotic fracture risk? A 10-year prospective multicentre validation study. RMD Open. 2017 Sep 26;3(2):e000509. https://doi.org/10.1136/rmdopen-2017-000509.

18. Diem SJ, Peters KW, Gourlay ML, et al; Osteoporotic Fractures in Men Research Group. Screening for Osteoporosis in Older Men: Operating Characteristics of Proposed Strategies for Selecting Men for BMD Testing. J Gen Intern Med. 2017 Nov;32(11):1235-1241. doi: 10.1007/s11606-017-4153-4. https://doi.org/10.1007/s11606-017-4153-4.

19. Jain S, Bilori B, Gupta A, Spanos P, Singh M. Are Men at High Risk for Osteoporosis Underscreened? A Quality Improvement Project. Perm J. 2016 Winter;20(1):60-4. https://doi.org/10.7812/tpp/14-190.

20. Tuzun S, Eskiyurt N, Akarirmak U, et al; Turkish Osteoporosis Society. The impact of a FRAX-based intervention threshold in Turkey: the FRAX-TURK study. Arch Osteoporos. 2012;7:229-35. https://doi.org/10.1007/s11657-012-0101-4.

21. Clark P, Denova-Gutiérrez E, Zerbini C, et al. FRAX-based intervention and assessment thresholds in seven Latin American countries. Osteoporos Int. 2018 Mar;29(3):707-715. https://doi.org/10.1007/s00198-017-4341-4.

Отримано/Received 10.05.2021
Рецензовано/Revised 21.05.2021
Прийнято до друку/Accepted 31.05.2021

Information about authors

Vladyslav Povoroznyuk, Professor, Head of Department of clinical physiology and pathology of musculo-skeletal system, State Institution "D.F. Chebotarev Institute of Gerontology of the NAMS of Ukraine", Kyiv, Ukraine; https://orcid.org/0000-0002-1256-8002

H. Johansson, University of Sheffield Medical School, Beech Hill Road, Sheffield S10 2RX, UK; https://orcid.org/0000-0002-7720-9297

Nataliia Grygorieva, MD, PhD, Professor, Leading Research Fellow at the Department of clinical physiology and pathology of locomotor apparatus, State Institution "D.F. Chebotarev Institute of Gerontology of the NAMS of Ukraine", Vyshgorodska st., 67, Kyiv, 04114, Ukraine; e-mail: crystal_ng@ukr.net; phone: +38 (067) 445 76 08; https://orcid.org/0000-0002-4266-461X

John A. Kanis, Professor Emeritus, University of Sheffield Medical School, Beech Hill Road, Sheffield S10 2RX, UK; https://orcid.org/0000-0002-3129-4326

Anna Musiienko, PhD, Junior Research Fellow at the Department of clinical physiology and pathology of musculo-skeletal system, State Institution "D.F. Chebotarev Institute of Gerontology of the NAMS of Ukraine", Kyiv, Ukraine; https://orcid.org/0000-0002-1672-1991

Lorentzon M., Mary McKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia; https://orcid.org/0000-0003-0749-1431

Nicholas C. Harvey, MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK; https://orcid.org/0000-0002-8194-2512

Eugene V. McCloskey, University of Sheffield Medical School, Beech Hill Road, Sheffield S10 2RX, UK; https://orcid.org/0000-0003-0177-8140

Enwu Liu, Mary McKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia; https://orcid.org/0000-0003-2580-3523

Conflicts of interests. Authors declare the absence of any conflicts of interests and their own financial interest that might be construed to influence the results or interpretation of their manuscript.

Поворознюк В.В. [1], Johansson H.[2, 3], Григор'єва Н.В.[1], Kanis J.A.[3, 4], Мусієнко А.С.[1], Lorentzon M.[3, 5], Harvey N.C.[6], McCloskey E.V.[4, 7], Liu E.[3]

[1]ДУ «Інститут геронтології імені Д.Ф. Чеботарьова НАМН України», м. Київ, Україна

[2]Sahlgrenska Osteoporosis Centre, Institute of Medicine, University of Gothenburg, Sweden

[3]Mary McKillop Institute for Health Research, Australian Catholic University, Melbourne, Australia

[4]Centre for Metabolic Bone Diseases, University of Sheffield Medical School, Sheffield, UK

[5]Sahlgrenska Osteoporosis Centre, Department of Internal Medicine and Clinical Nutrition, Institute of Medicine and Clinical Nutrition, Sahlgrenska Academy, University of Gothenburg, Sweden

[6]MRC Lifecourse Epidemiology Unit, University of Southampton, Southampton, UK

[7]MRC and Versus Arthritis Centre for Integrated Research in Musculoskeletal Ageing, Mellanby Centre for Musculoskeletal Research, University of Sheffield, Sheffield, UK

Українська версія FRAX у менеджменті остеопорозу в чоловіків

Резюме. ***Актуальність***. На сьогодні FRAX — загальновідомий і широко вживаний інструмент оцінки ризику основних остеопоротичних переломів. Українська версія алгоритму FRAX була презентована у 2016 році, а у 2019 році були опубліковані «межі втручання» щодо додаткового обстеження й лікування для жінок України, проте дані щодо можливостей її використання в чоловіків обмежені. Вищезазначене стало підґрунтям для проведення даного дослідження. ***Мета дослідження —*** оцінка можливостей використання раніше розроблених критеріїв української версії алгоритму FRAX в українських чоловіків. ***Матеріали та методи.*** Обстежено 653 амбулаторних чоловіків віком 40–88 років (середній вік (M ± SD) — 60,5 ± 11,8 року). Показники аналізували як у загальній групі, так і в окремих вікових підгрупах, зокрема, залежно від наявності низькоенергетичних переломів, які входять у розрахунок FRAX, і порівнювали з відповідними показниками українських жінок. ***Результати.*** Найбільш частим (26,6 %) фактором ризику остеопоротичних переломів в українських чоловіків був низькотравматичний перелом в анамнезі (відповідний показник у жінок становив 51,3 %), і саме його наявність була підставою для ініціації антиостеопоротичного лікування. Лише 6,7 % чоловіків без переломів в анамнезі після розрахунку ризику основних остеопоротичних переломів за FRAX потребували обстеження за допомогою двохенергетичної рентгенівської абсорбціометрії (ДРА) для переоцінки ризику остеопоротичних переломів, і жоден не мав високих показників ризику переломів. 73 % обстежених чоловіків без переломів не мали жодного фактора ризику, включеного в алгоритм FRAX. ***Висновки.*** Дане дослідження продемонструвало більш високу потребу як в антиостеопоротичному лікуванні без виконання ДРА, так і в додатковому денситометричному обстеженні для додаткової оцінки ризику остеопоротичних переломів у жінок України порівняно з чоловіками, необхідність приділяти особливу увагу наявності малотравматичних переломів в анамнезі в оцінці ризику остеопопорозу і його ускладнень у чоловіків і необхідність урахування інших факторів ризику остеопорозу, не включених у даний алгоритм FRAX.

Ключові слова: FRAX; ризик остеопоротичних переломів; остеопороз; чоловіки