Rheumatology International
https://doi.org/10.1007/s00296-023-05412-4

Rheumatology
INTERNATIONAL

OBSERVATIONAL RESEARCH

An observational study of the radiofrequency echographic multi-spectrometry (REMS)-based fragility score of the lumbar spine and total fracture risk at 5 years in women

Stoyanka Vladeva[1] · Elena Bischoff[2] · Nikola Kirilov[3] · Fabian Bischoff[4] · Zguro Batalov[5] · Anastas Batalov[5]

Received: 16 July 2023 / Accepted: 28 July 2023

Abstract

A novel fragility score (FS) parameter, obtained during radiofrequency echographic multi-spectrometry (REMS), was developed to estimate the ultrasound-based skeletal fragility. The aim of our study is to assess the REMS-based FS of the lumbar spine (LS) among the Bulgarian women and to compare their characteristics acquired with REMS between fracture risk classes corresponding to a total fracture risk at 5 years for major osteoporotic fractures (MOF). A total of 100 Bulgarian women, who underwent a screening for osteoporotic fracture risk using the REMS technology, were included in a prospective observational study. The mean age was 60 years (years) ± 13.9 standard deviations. We assessed the FS of the LS and for each subject. The fracture risk class (R1–R7) was identified using a table combining measured REMS *T* score and FS values. The mean FS was 36.9 ± 17.4 SD (range: 18.5–84.3). Twelve subjects (12%) were classified into the R6 group, twenty-three (23%) into the R5, sixty-one (61%) into R4, and four (4%) into R3. Statistical analysis showed significant difference in age, height, BMD, *T* score, *Z* score, age of menopause, FRAX for MOF, and FRAX for hip fractures between the risk class groups. This is the first study which showed the REMS-based FS of the lumbar spine among the Bulgarian women. *T* score alone is not a good predictor of fractures. Our study showed that its use in combination with the fragility score obtained during REMS offers a robust assessment of the fracture risk at 5 years for MOF.

Keywords Fragility score · Lumbar spine · REMS · Fracture risk · Women

Introduction

In an aging society, diseases of the elderly are becoming more and more important in everyday medical practice [1–3]. Osteoporosis is of particular importance affecting the musculoskeletal system. It is a disease of the bone metabolism with a steady decrease in bone density. With increasing age, the microarchitecture of the bone changes in such a way that there is a thinning and reduction of the bone trabeculae structure in the spongiosa. As a consequence, the bone can no longer bear the bodyweight and the risk of so-called osteoporotic (fragility) fractures increases [4, 5]. Such fragility fractures are usually caused by low-energy trauma. The dual-energy X-ray absorptiometry (DXA) measurement is still the gold standard for diagnosing osteoporosis. The bone mineral density is measured at axial sites: lumbar spine and hip [6, 7]. In the recent years, an ultrasound-based technique has been developed to measure the bone mineral density (BMD) using a radiofrequency echographic

Elena Bischoff, Nikola Kirilov, Fabian Bischoff, Zguro Batalov and Anastas Batalov have contributed equally to this work.

✉ Stoyanka Vladeva
drVladeva@abv.bg

1 Department of Health Care, Faculty of Medicine, Trakia University, Stara Zagora, Bulgaria

2 Department of Internal Diseases, Pharmacology, Paediatrics, Social Medicine, Emergency Medicine, Computer Technology, Infectious Diseases, Physiotherapy and Rehabilitation, Epidemiology and Tropical Diseases, Faculty of Medicine, University Prof. Dr. Assen Zlatarov, Burgas, Bulgaria

3 Department of Orthopedics and Traumatology, University Hospital UMBAL Dr. Georgi Stranski, Pleven, Bulgaria

4 Rheumatology Practice, Stara Zagora, Bulgaria

5 Department of Internal Diseases, Clinic of Rheumatology, Medical University of Plovdiv, University Hospital 'Kaspela', Plovdiv, Bulgaria

Published online: 12 August 2023

multi-spectrometry (REMS). This technique analyzes the patient-specific ultrasound data in terms of absorption and reflection on the bone and compares the results with a reference model. Previous studies have already been able to demonstrate the comparability of REMS and DXA, and thus prove REMS usable for the diagnosis of osteoporosis [8]. To be able to assess the need for therapy, an individual fracture risk profile is required for each patient. The higher the risk of future osteoporotic fractures, the more likely it is that the patient will receive a special therapy. There are BMD-dependent and BMD-independent prediction tools, such as the fracture risk assessment tool (FRAX) [9]. The novel fragility score (FS) parameter, obtained during REMS scan of lumbar spine (LS) and/or femoral regions, has been developed to estimate the ultrasound-based skeletal fragility. The final output of FS is provided through innovative fully automatic algorithm that performs a series of spectral and statistical analyses, involving the ultrasound images and the radiofrequency signals (RF). RF signals correspond to specific region of interest (ROI) of the vertebral and femoral surfaces. For each echographic line, the RF segment belonging to ROI has been determined through 200-point Hamming window signal reflected from the surface when the amplitude of RF signal envelope reaches 15% of each peak value [10]. Each FS value is acquired during an echographic bone structure analysis through a comparison between patient-specific spectral profiles with population-based models of "fractured" and "non-fractured" subjects. This value corresponds to the percentage of analyzed bone segments whose spectral features are more similar to those of a "fractured" bone model rather than to those of a ''non-fractured" one. FS assesses the quality of the bone microarchitecture and the actual bone strength independently of BMD. FS was found to closely correlate with the 10-year FRAX® fracture risk computed including the femoral neck BMD [11, 12].

The aim of our study is to assess the REMS-based FS of the lumbar spine among the Bulgarian women and to compare their characteristics, BMD, *T* score, *Z* score, FRAX for major osteoporotic fractures (MOF), and FRAX for hip fractures (HF) between fracture risk classes corresponding to a total fracture risk at 5 years for MOF.

Methods

We conducted a prospective observational study to assess the FS of the LS among the Bulgarian women. The patient population consisted of 100 female subjects, who underwent a screening for osteoporotic fracture risk using the REMS technology, fulfilling the following criteria: age above 20 years and no significant walking impairments. The study was approved by the Ethics Commission for Scientific Research of the Faculty of Medicine, Trakia University, Stara Zagora, Bulgaria. All the enrolled patients voluntarily entered the study after signing an informed consent. The acquisition and assessment were carried out by the same health professional for all subjects. A dedicated echographic device (EchoStudio), equipped with a convex transducer operating at the normal frequency of 3.5 MHz, was placed in a trans-abdominal position under the sternum to visualize the ROI of L1 lumbar vertebra, and moving it down to L4 according to the provided instructions. The device using radiofrequencies generates a patient-specific spectrum, which is compared to reference models and estimates the BMD. Consequently, a *T* score is calculated and the patient can be classified as healthy, osteopenic or osteoporotic according to the World Health Organization (WHO). The FS is a parameter that allows to estimate skeletal fragility using the ultrasound scan performed with REMS. It is a dimensionless parameter calculated by comparing the raw ultrasound spectral analysis with reference models of fragile and non-fragile bones and can vary from 0 to 100, in proportion to the degree of fragility, independently from BMD [13]. Low values of FS are associated with good bone microarchitecture and with a low osteoporotic fracture risk at the analyzed LS. On the other hand, high values of FS are associated with degraded bone microarchitecture and with an increased osteoporotic fracture risk at the analyzed lumbar spine. For ease of interpretation, the FS value for the current patient is represented by a circled cross which is plotted against age on a color-coded graph, as shown in Fig. 1.

The physician can identify the risk class corresponding to the current patient combining measured REMS *T* score and FS values using the interpretation table, Fig. 2.

In the matrix the columns are related to the *T* score classification (normal, osteopenia, and osteoporosis) obtained by an echographic scan, while the rows are related to the

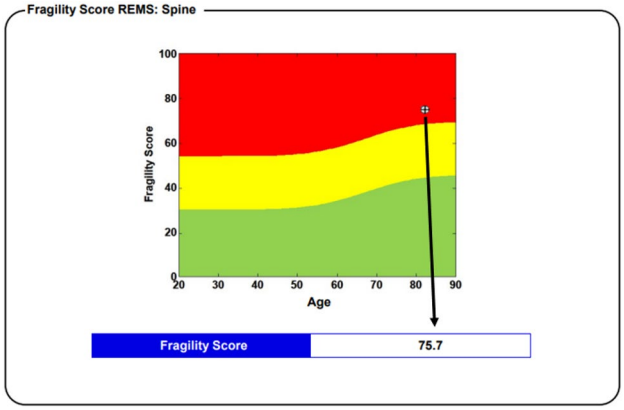

Fig. 1 FS graph obtained by lumbar spine acquisition. The circled cross shows the FS value on the graph. Color codes: the green area is representative of "normal" bone quality; the yellow area is representative of "decreased" bone quality; the red area is representative of "low" bone quality

Combining Matrix of REMS BMD and Fragility Score

REMS FRAGILITY SCORE Classification	REMS T-SCORE classification		
	NORMAL	OSTEOPENIA	OSTEOPOROSIS
NORMAL	R1	R3	R5
DECREASED	R2	R4	R6
LOW	R3	R5	R7

Fig. 2 Matrix to identify the risk class for lumbar spine

FS classification (normal, decreased, and low). Risk class can range from R1 to R7. A high risk class corresponds to a higher fracture risk. The FS calculated from REMS scan on LS refers to the total risk for MOF (spine, forearm, hip or shoulder fracture). Once the risk class (R1–R7) is identified for the patient through the matrix described above, it is possible to quantify the patient-associated fracture risk range expressed in terms of ‰ per 5 years, Fig. 3. The risk class related to the current patient is highlighted in the table using black borders on the specific risk class cell [14].

In our study, we assessed the FS of each subject and according to the combination of the measured REMS *T* score and FS values using the interpretation table, we classified the subjects in the risk classes from R1 to R7. Comorbidities and risk factors were recorded and assessed using the FRAX tool (https://frax.shef.ac.uk/FRAX/tool.aspx). Furthermore, we compared the subjects' characteristics (age, weight, height, body mass index (BMI), and age of menopause) as well as the total BMD and total *T* score of the LS, BMD for each vertebra from L1 to L4, FRAX MOF, FRAX HF and FS between the risk classes.

Statistical analyses

Descriptive statistics, including mean, median, standard deviation (SD), standard error of the mean, minimum and maximum were used for weight, height, body mass index (BMI), age of menopause, total BMD and *T* score of LS, BMD and *T* score for each vertebra L1–L4, FRAX MOF, FRAX HF and FS. Kruskal–Wallis test was used to analyze the differences between the means of the variables in the different risk class groups.

Total Fracture Risk at 5 years (‰)

Risk class	Risk of major osteoporotic fracture per 1000 subjects per 5 years
R1	≤ 5
R2	[5-10]
R3	[10-20]
R4	[20-35]
R5	[35-60]
R6	[60-100]
R7	> 100

Fig. 3 Total fracture risk at 5 years (‰) for lumbar spine

Results

Patients' characteristics

Of the 100 patients, who were enrolled, 82 (82%) subjects were postmenopausal. The mean age was 60 years (years) ± 13.9 years SD with range 32–91 years The mean weight and height of the subjects were 75.6 kg ± 14.2 kg (minimum 53 kg and maximum 103 kg) and 163.4 cm ± 8 cm (minimum 150 cm and maximum 186 cm), respectively. BMI had a mean of 28.4 kg/m^2 ± 5.3 kg/m^2 (min. 20.8 kg/m^2 and max. 40.2 kg/m^2). The mean age of menopause was 48 years ± 13 years (36–52 years), as shown in Fig. 4.

Bone mineral density and fragility of the lumbar spine

REMS-based BMD of the total LS had a mean value of 0.904 g/cm^2 ± 0.108 SD g/cm^2 (with range between 0.692 g/cm^2 and 1.135 g/cm^2) with mean REMS-based *T* score of – 1.4 ± 0.9 SD (range between – 3.2 SD and 0.8 SD). The mean total REMS-based *Z*-score of the LS was 0.0 SD ± 0.9 SD (range –1.8 and 2.5 SD). The mean REMS-based BMD values increased from L1 to L4 (0.773 g/cm^2, 0.901 g/cm^2, 0.907 g/cm^2, and 0.970 g/cm^2, respectively), as shown in Fig. 5.

The mean REMS-based fragility score was 36.9 ± 17.4 SD with minimum of 18.5 and maximum of 84.3. The mean FRAX MOF was 6.4% ± 6.1% (1.5–26.5%) and FRAX HF was 2.3% ± 3.3% (0.1–12.1%), as shown in Fig. 6.

Risk class groups according to the total fracture risk at 5 years for MOF

Of total 100 patients, 12 subjects (12%) were classified into the R6 group, 23 (23%) into the R5 group, 61 (61%) into R4 group, and 4 (4%) into R3. There were no subjects belonging to group R1, R2 or R7. The mean

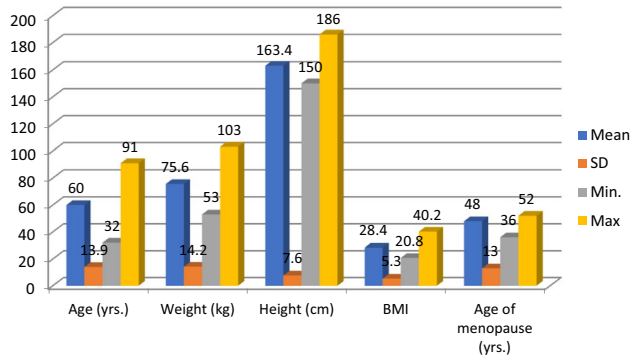

Fig. 4 Patients' characteristics; *SD* standard deviation, *Min* minimum, *Max* maximum

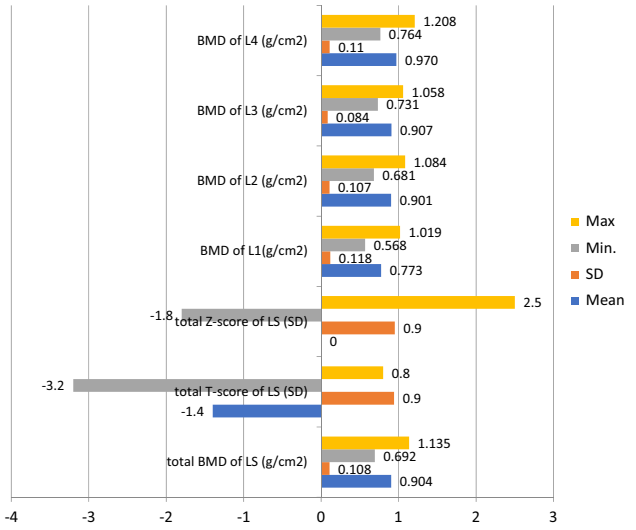

Fig. 5 REMS-based BMD, *T* score, and *Z* score values of LS; *SD* standard deviation, *Min* minimum, *Max* maximum

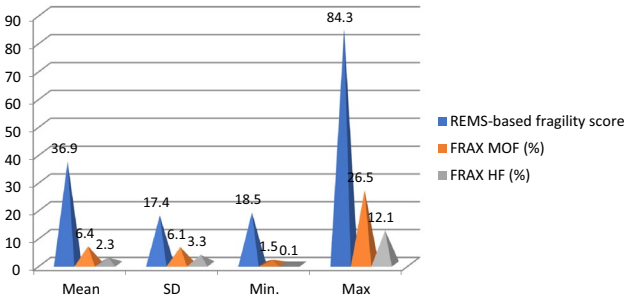

Fig. 6 REMS-based fragility score, FRAX MOF, and FRAX HF assessed with BMD of the LS; *SD* standard deviation, *Min* minimum, *Max* maximum

age increased significantly in the groups from R3 to R6 (34 years, 54 years 66 years, and 86 years, respectively), $p = 0.002$. The mean height decreased significantly as follows—179.5 cm in R3, 163.3 cm in R4, 162.2 cm in R5, and 158.3 cm in R6, $p = 0.004$. Weight and BMI did not show significance ($p > 0.05$). The higher the FS, the lower the mean menopause age was with significant differences between the risk class groups (R4, R5, and R6), $p = 0.001$. Total mean REMS-based BMD, REMS-based *T* score and *Z* score values differed significantly between the risk class groups ($p = 0.049$, $p = 0.031$, $p = 0.023$, respectively). Interestingly the total mean REMS-based BMD and REMS-based *T* score values were similar in the R3, R4, and R5 risk groups whereas its values abruptly decreased in the R6 risk group (REMS-based BMD = 0.746 g/cm^2 and REMS-based *T* score = – 2.7 SD). Contrary to these results, the lowest mean REMS-based *Z* score appeared in the risk class group R3. The mean REMS-based BMD of L1 and L4 differed significantly between the risk groups, $p = 0.041$ and $p = 0.032$, respectively. The mean REMS-based BMD of L2 was on the border with significance ($p = 0.046$) and the mean REMS-based BMD of L3 was not significant ($p = 0.098$). As expected, the mean REMS-based fragility score increased in the risk class groups: 19 in R3, 27.8 in R4, 43.9 in R5, and 77.3 in R6, $p < 0.001$. The mean FRAX MOF and FRAX HF increased significantly from R4 to R6 with *p* values of 0.025 and 0.010, respectively, (3.6% and 0.6%, respectively, in the group of R4; 10.7 and 4.4, respectively, in the group of R5; 12.2 and 6.3, respectively, in the group of R6), as given in Table 1.

Discussion

Fragility fractures represent an epidemic problem worldwide, as the population ages at a rate much greater than once predicted [15, 16]. Fragility fractures account for 0.83% of the burden of non-communicable disease worldwide and 1.75% in Europe, where they are associated with more disability-adjusted life years than many other chronic non-communicable diseases [17]. Furthermore, using the standard definition of osteoporosis in the context of the osteodensitometry (*T* score less than or equal to −2.5 SD), approximately 50% of all fractures would be missed [18, 19]. For this reason, it is important to identify patients with increased fracture risk at early stage to prevent fragility fractures. The REMS method offers the opportunity to assess FS independently from BMD and then to identify the fracture risk class corresponding to the combination of the current patient measured REMS-based *T* score and FS values using a specific interpretation table.

The mean REMS-based FS in the current study (36.9) was higher than that (31.2) in the study of Pisani et al. with dataset of 1289 female subjects on similar mean age. In their prediction model, a cutoff value of FS = 37.2 of the lumbar spine was demonstrated as REMS-based indicator for incident fragility fractures at 5 years in the female population. The female subjects in our study showed FS comparable to this cutoff value, and thereby high risk for incident fragility fractures at 5 years [12].

We were also able to show that there are significant differences between the fracture risk classes according to the current age, the age of menopause, height, and fragility score. Furthermore, REMS-based BMD, *T* score, *Z* score values, and FRAX-based risk assessments for MOF and for HF differed significantly between the fracture risk classes.

Increasing age is a well-known risk factor for osteoporosis proven in several studies [20–22]. Based on our results, we could show that age and the age of menopause are significant risk factors for increased fragility. The length of time a woman is in the menopause seems to be particularly

Table 1 Descriptive statistics of the subjects and *p* values: age, weight, height, BMI, age of menopause, REMS-based BMD (total LS), REMS-based *T* score (total LS), REMS-based *Z* score (total LS), REMS-based BMD of each lumbar vertebra, FRAX MOF, FRAX HF, and REMS-based FS

	N	Mean	Median	Std. deviation	Std. error	Minimum	Maximum	*p* value
Age (years)								
R3	4	34.00	34.00	7.4	2.3	32	36	0.002
R4	61	54.00	56.00	7.8	2.0	37	65	
R5	23	66.00	70.00	8.1	3.3	52	74	
R6	12	86.00	84.00	4.7	2.7	82	91	
Total	100	60.00	59.00	13.9	2.7	32	91	
Weight (kg)								
R3	4	72.75	72.00	16.2	4.1	69	76	0.606
R4	61	74.50	73.00	13.1	3.3	53	94	
R5	23	83.17	86.00	18.3	7.5	60	103	
R6	12	67.33	72.00	10.8	6.2	55	75	
Total	100	75.58	73.00	14.2	2.8	53	103	
Height (cm)								
R3	4	179.5	180.5	6.2	1.2	172	186	0.004
R4	61	163.3	164.0	7.2	1.8	150	179	
R5	23	162.2	162.0	3.3	1.3	158	166	
R6	12	158.3	158.0	1.5	0.9	157	160	
Total	100	163.4	163.00	7.6	1.5	150	186	
BMI (kg/m^2)								
R3	4	22.55	22.9	3.5	1.6	20.8	24.6	0.217
R4	61	27.9	26.86	4.2	1.1	21.7	35.8	
R5	23	31.7	32.87	7.4	3.0	23.4	40.2	
R6	12	26.8	28.13	4.0	2.3	22.3	30.0	
Total	100	28.4	27.33	5.3	1.02	20.8	40.2	
Age of menopause (yrs.)								
R3	–	–	–	–	–	–	–	0.001
R4	47	50	49	4.3	1.3	41	52	
R5	23	49	47	5.6	2.5	38	51	
R6	12	45	48	2.3	1.3	36	50	
Total	82	48	46	13.1	3.0	36	52	
BMD (g/cm^2)								
R3	4	0.965	0.971	0.054	0.010	0.920	0.998	0.049
R4	61	0.909	0.898	0.079	0.020	0.739	1.052	
R5	23	0.955	0.951	0.138	0.056	0.798	1.135	
R6	12	0.746	0.761	0.049	0.028	0.692	0.786	
Total	100	0.904	0.898	0.108	0.021	0.692	1.135	
T score (SD)								
R3	4	– 1.1	– 1.1	0.6	0.1	– 1.4	– 0.8	0.031
R4	61	– 1.3	– 1.4	0.7	0.2	– 2.8	– 0.3	
R5	23	– 0.9	– 0.9	1.3	0.5	– 2.3	0.8	
R6	12	– 2.7	– 2.6	0.4	0.2	– 3.2	– 2.4	
Total	100	– 1.4	– 1.4	0.9	0.2	– 3.2	0.8	
Z score (SD)								
R3	4	– 0.6	– 0.55	0.6	0.2	– 1.0	– 0.3	0.023
R4	61	– 0.3	– 0.4	0.7	0.2	– 1.8	1.0	
R5	23	1.0	–0.9	0.9	0.4	– 0.1	2.5	
R6	12	– 0.1	0.0	0.6	0.5	– 0.5	0.4	
Total	100	– 0.0	– 0.1	0.9	0.2	– 1.8	2.5	

Table 1 (continued)

	N	Mean	Median	Std. deviation	Std. error	Minimum	Maximum	*p* value
BMD (g/cm^2) L1								
R3	4	0.929	0.922	0.076	0.018	0.898	0.974	0.041
R4	61	0.770	0.782	0.085	0.026	0.583	0.886	
R5	23	0.829	0.825	0.133	0.054	0.677	1.019	
R6	12	0.620	0.635	0.047	0.027	0.568	0.659	
Total	100	0.773	0.782	0.118	0.025	0.568	1.019	
BMD (g/cm^2) L2								
R3	4	0.975	0.974	0.124	0.023	0.902	1.050	0.046
R4	61	0.898	0.888	0.083	0.022	0.744	1.062	
R5	23	0.976	1.016	0.130	0.065	0.788	1.084	
R6	12	0.734	0.734	0.075	0.053	0.681	0.787	
Total	100	0.901	– 0.888	0.107	0.023	0.681	1.084	
BMD (g/cm^2) L3								
R3	4	0.948	0.948	0.065	0.023	0.902	0.996	0.098
R4	61	0.926	0.924	0.077	0.021	0.784	1.058	
R5	23	0.889	0.880	0.066	0.033	0.828	0.970	
R6	12	0.775	0.776	0.062	0.045	0.731	0.820	
Total	100	0.907	– 0.916	0.084	0.018	0.731	1.058	
BMD (g/cm^2) L4								
R3	4	1.052	1.046	0.085	0.032	1.002	1.114	0.032
R4	61	0.986	0.977	0.072	0.023	0.864	1.102	
R5	23	1.029	1.011	0.147	0.073	0.890	1.208	
R6	12	0.811	0.829	0.042	0.024	0.764	0.842	
Total	100	0.970	0.963	0.109	0.025	0.764	1.208	
Major osteoporotic fracture %								
R3	–	–	–	–	–	–	–	0.025
R4	61	3.6	3.3	1.3	0.4	1.5	5.8	
R5	23	10.7	9.7	8.7	3.6	1.9	26.5	
R6	12	12.2	12.2	7.7	5.5	6.7	17.6	
Total	96	6.4	4.4	6.1	1.3	1.5	26.5	
Hip fracture %								
R3	–	–	–	–	–	–	–	0.010
R4	61	0.6	0.5	0.4	0.1	0.1	1.2	
R5	23	4.4	3.2	4.5	1.8	0.2	12.1	
R6	12	6.3	6.3	4.8	3.4	2.9	9.7	
Total	96	2.3	1.1	3.3	0.7	0.1	12.1	
Fragility score								
R3	4	19.0	18.9	2.1	3.2	18.50	19.7	< 0.001
R4	61	27.8	28.5	4.8	1.2	21.7	34.7	
R5	23	43.9	43.0	7.6	3.1	35.5	55.1	
R6	12	77.3	75.7	6.3	3.6	72.0	84.3	
Total	100	36.9	31.7	17.4	3.4	18.5	84.3	

relevant. The longer a woman has been in the menopause or the earlier a woman enters the menopause, the greater the fragility of the bones appears. Minaković et al. could demonstrate that women who entered into menopause before the age of 45 had a high risk of hip fracture (OR: 1,652; 95% CI 1138–2399; $p < 0.01$) and a higher mean FRAX score for HF compared to women in whom menopause started after the age of 45 (Me = 1.60 vs. 1.30, $p < 0.004$) [23]. The number of years with estrogen deficiency lead to risk of BMD reduction and results in loss of bone strength [24]. Our study showed that it is important to detect females with early menopause for increased risk of fragility fractures at an early stage and to include subjects in a REMS follow-up program to monitor the changes of FS in brief intervals.

Furthermore, our results showed that current height has a significant impact on fragility risk. The taller a patient is currently, the lower the risk of fragility. This could be mainly due to the fact that the patients in a higher fracture risk group already have vertebral compression fractures, and therefore appear smaller on average. Our results are consistent with those of Compston et al. [25]. They were also able to determine a significant difference in body size for patients with incidence fractures. According to their results, people with an osteoporotic fracture were, on average, significantly shorter than people with a non-osteoporotic fracture. The group around Adami et al. came to similar conclusions [26]. They were also able to demonstrate a significantly smaller height in patients with osteoporotic fractures. Gunnes et al. dealt with the question of whether body size generally has an influence on fractures [27]. They were able to find an increase in the risk of hip fractures with increasing height. They make the greater impact of the fall responsible for the increased risk in taller people.

The analysis of the REMS-based BMD showed a steady decrease in the BMD in relation to the risk class groups. This means, the higher the fracture risk, the lower the BMD. The REMS-based *T* score depending on BMD together with FS are parameters in the matrix to identify the fracture risk class and this could be the reason why subjects with lower BMD are in a higher fracture risk group. In spite of this fact, we observed some exceptions. For example, the total REMS-based BMD and the BMD of L1, L2, and L4 measured in the risk class group R5 were higher than those measured in the risk class group R4. The differences in BMD were statistically significant between the risk class groups at L1, L2, and L4 as well as at the total spine. At L3, there was a steady decrease in BMD values between the risk class groups, but there was not any statistical significance. There is no study that is using REMS which compared BMD values between the fracture risk classes corresponding to a total fracture risk at 5 years for MOF.

In our study, we also demonstrated that low REMS-based *T* score was a significant marker of increased fracture risk. The group R5 showed a slightly higher value than R4. This could be due to the allocation of the individual patient values to the respective risk groups using the algorithm. Risk group R5 can have both a *T* score corresponding to osteoporosis paired with normal REMS-based FS and a *T* score corresponding to osteopenia paired with a low REMS-based FS. In our case, it can be assumed that more patients in risk group R5 have a *T* score corresponding to osteopenia and a low REMS-based fragility score. Our results agree with the statements by Adami et al. who were able to demonstrate in their work a lower REMS-based *T* score in the population with incidence fractures compared to patients with non-incidence factures [26]. Analogous, Pisani et al. were able to demonstrate in their work that patients with an osteoporotic fracture have a lower REMS-based *T* score than those without fractures [12].

In the analysis of the REMS-based *Z* score, which is defined as bone density compared to the average values for a person of the same age and gender, we were able to demonstrate that *Z* score in the risk class R3 was significantly lower than those in the risk class R6. According to the study of Williams et al., a low DXA-based *Z* score in healthy men or women indicates a generally low risk for fracture and is adequately treated with good nutrition, exercise, and healthy lifestyle [28]. Analogous, in our study, we could not demonstrate correlation between low *Z* score and high fracture risk class. This aspect has not been investigated in a previous study using REMS.

FRAX is a well-established prediction model for estimating osteoporotic fracture risk for MOF and HF [29, 30]. With regard to FRAX, we were able to show significant differences in FRAX MOF and FRAX HF between the fracture risk classes. Similarly, Pisani et al. showed a close correlation between FRAX and the risk class groups of the fragility score. They also found that FS was more accurate in predicting fractures than FRAX [12]. The REMS-based FS was considered an excellent predictor for fracture risk by Pisani et al. and Ciardo et al. [12, 13]. Both groups prospectively examined patients and divided them into two groups: fractured and non-fractured. Both working groups were able to demonstrate a better degree of sensitivity of the REMS FS for fractures compared to the REMS *T* score and DXA *T* score with the same specificity.

The current study has some limitations. First, the population consists of many young subjects, due to generalized enrollment criteria and some risk classes remain unrepresented. The second limitation is the availability of risk factors and comorbidities only in the context of the FRAX questionnaire. Lastly, no alternative technique such as DXA to measure the BMD values was used to compare the REMS-derived values.

Conclusion

Fracture risk is country and population specific and, so far, no such study has been conducted. This is the first one which showed the REMS-based FS of the lumbar spine among the Bulgarian women. *T* score alone is not a good predictor of fractures. Our study showed that its use in combination with the fragility score obtained during REMS offers a robust assessment of the fracture risk at 5 years for MOF.

Funding None.

Declarations

Conflict of interest The authors declare no conflict of interest.

Ethical approval The study was approved by the Ethics Commission for Scientific Research of the Faculty of Medicine, Trakia University, Stara Zagora, Bulgaria. (Protocol number: 26, Date 01.06.2023).

References

1. Maresova P, Javanmardi E, Barakovic S et al (2019) Consequences of chronic diseases and other limitations associated with old age—a scoping review. BMC Public Health 19:1431
2. Jordan KM, Cooper C (2002) Epidemiology of osteoporosis. Best Pract Res Clin Rheumatol 5(16):795–806
3. Salari Sharif P, Abdollahi M, Larijani B (2011) Current, new and future treatments of osteoporosis. Rheumatol Int 31:289–300
4. Föger-Samwald U, Dovjak P, Azizi-Semrad U, Kerschan-Schindl K, Pietschmann P (2020) Osteoporosis: pathophysiology and therapeutic options. EXCLI J 19:1017–1037
5. Bouee S, Lafuma A, Fagnani F, Meunier PJ, Reginster JY (2006) Estimation of direct unit costs associated with non-vertebral osteoporotic fractures in five european countries. Rheumatol Int 26:1063–1072
6. Krugh M, Langaker MD (2022) Dual-energy X-ray absorptiometry. In: StatPearls. StatPearls Publishing, Treasure Island. https://www.ncbi.nlm.nih.gov/books/NBK519042/
7. Carey JJ, Buehring B (2018) Current imaging techniques in osteoporosis. Clin Exp Rheumatol 36(Suppl 114):115–126
8. Di Paola M, Gatti D, Viapiana O et al (2019) Radiofrequency echographic multispectrometry compared with dual X-ray absorptiometry for osteoporosis diagnosis on lumbar spine and femoral neck. Osteoporos Int 30:391–402
9. Diez-Perez A et al (2019) Radiofrequency echographic multispectrometry for the in-vivo assessment of bone strength: state of the art—outcomes of an expert consensus meeting organized by the european society for clinical and economic aspects of osteoporosis, osteoarthritis and mus. Aging Clin Exp Res 31:1375–1389
10. Pisani P et al (2017) A quantitative ultrasound approach to estimate bone fragility: a first comparison with dual X-ray absorptiometry. Measurement 101:243–249
11. Greco A et al (2017) Ultrasound fragility score: an innovative approach for the assessment of bone fragility. Measurement 101:236–242
12. Pisani P, Conversano F, Muratore M, Adami G, Brandi ML, Caffarelli C, Casciaro E, Di Paola M, Franchini R, Gatti D, Gonnelli S, Guglielmi G, Lombardi FA, Natale A, Testini V, Casciaro S (2023) Fragility Score: a REMS-based indicator for the prediction of incident fragility fractures at 5 years. Aging Clin Exp Res 35(4):763–773
13. Ciardo D, Pisani P, Lombardi FA et al (2021) POS0163 Incident fracture risk prediction using the fragility score calculated by lumbar spine radiofrequency echographic multi spectrometry (REMS) scans annals of the rheumatic diseases. Ann Rheum Dis 80:294
14. Fragility score module-User Manual, rev.02 02/04/2020, 6–8/13
15. Mears SC, Kates SL (2015) A Guide to improving the care of patients with fragility fractures, edition 2. Geriatr Orthop Surg Rehabil 6(2):58–120
16. Barcelos A, Lopes DG, Canhao H, da Cunha Branco J, Rodrigues AM (2021) Multimorbidity is associated with fragility fractures in women 50 years and older: a nationwide cross-sectional study. Bone Rep 15:101139
17. Harvey N, Dennison E, Cooper C (2010) Osteoporosis: impact on health and economics. Nat Rev Rheumatol 6:99–105
18. Wainwright SA, Marshal LM, Ensrud KE (2005) Hip fracture in women without osteoporosis. J Clin Endocrinol Metabol 90:2787–2793
19. Stone KL, Seeley DG, Lui LY, Cauley JA, Ensrud K, Browner WS et al (2003) BMD at multiple sites and risk of fracture of multiple types: longterm results from the study of osteoporotic fractures. J Bone Miner Res 18:1947–1953
20. Kanis JA (2002) Diagnosis of osteoporosis and assessment of fracture risk. Lancet 359(9321):1929–1936
21. Khosla S, Riggs BL (2005) Pathophysiology of age-related bone loss and osteoporosis. Endocrinol Metab Clin 34(4):1015–1030
22. Gheita TA, Hammam N (2018) Epidemiology and awareness of osteoporosis: a viewpoint from the middle east and north africa. Int J Clin Rheumatol 13(3):134–147
23. Minaković I, Zvekić-Svorcan J, Janković T, Vuksanović M, Mikić D, Bošković K (2023) Early menopause and risk of fractures-a preventable gap. Iran J Public Health 52(3):534–541
24. Nguyen HH, Wong P, Strauss BJ et al (2017) Delay in estrogen commencement is associated with lower bone mineral density in turner syndrome. Climacteric 20(5):436–441
25. Compston JE, Flahive J, Hosmer DW, Watts NB, Siris ES, Silverman S, GLOW Investigators (2014) Relationship of weight, height, and body mass index with fracture risk at different sites in postmenopausal women: the global longitudinal study of osteoporosis in women (GLOW). J Bone Miner Res 29(2):487–493
26. Adami G, Arioli G, Bianchi G, Brandi ML, Caffarelli C, Cianferotti L, Quarta L (2020) Radiofrequency echographic multi spectrometry for the prediction of incident fragility fractures: a 5-year follow-up study. Bone 134:115297
27. Gunnes M, Lehmann EH, Mellstrom D, Johnell O (1996) The relationship between anthropometric measurements and fractures in women. Bone 19(4):407–413
28. Williams S, Khan L, Licata AA (2021) DXA and clinical challenges of fracture risk assessment in primary care. Cleve Clin J Med 88(11):615–622. https://doi.org/10.3949/ccjm.88a.20199
29. Kanis JA, Johansson H, Harvey NC, McCloskey EV (2018) A brief history of FRAX. Arch Osteoporos 13(1):118. https://doi.org/10.1007/s11657-018-0510-0
30. Senosi MR, Fathi HM, Baki NMA, Zaki O, Magdy AM, Gheita TA (2022) Bone mineral density, vitamin D receptor (VDR) gene polymorphisms, fracture risk assessment (FRAX), and trabecular bone score (TBS) in rheumatoid arthritis patients: connecting pieces of the puzzle. Clin Rheumatol 41(5):1333–1342